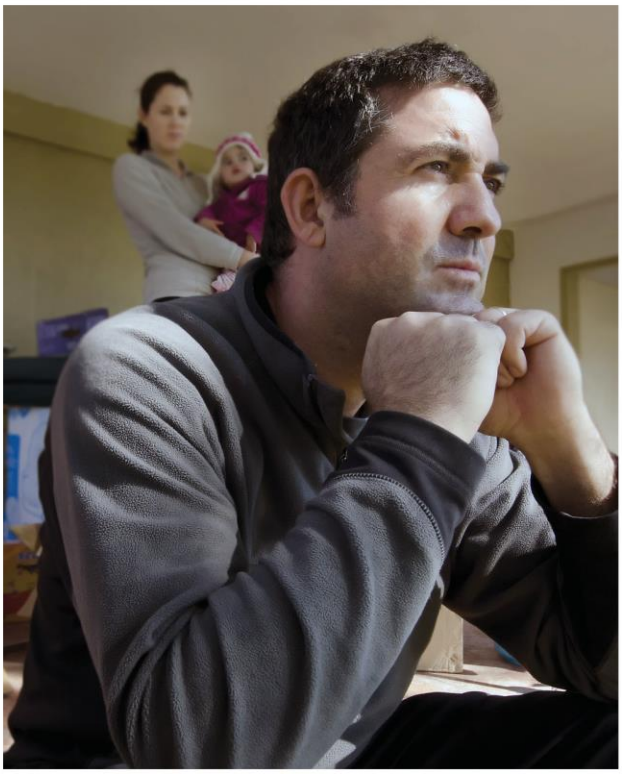

National Research Action Plan

Responding to the Executive Order *Improving Access to Mental Health Services for Veterans, Service Members, and Military Families (August 31, 2012)*

Department of Defense
Department of Veterans Affairs
Department of Health and Human Services
Department of Education

August 2013

Executive Summary

On August 31, 2012, President Obama issued an Executive Order (the Order) directing the Departments of Defense (DoD), Veterans Affairs (VA), Health and Human Services (HHS), and Education (henceforth referred to as "the agencies"), to develop a National Research Action Plan (NRAP) on posttraumatic stress disorder (PTSD), other mental health conditions, and Traumatic Brain Injury (TBI) "to improve the coordination of agency research into these conditions and reduce the number of affected men and women through better prevention, diagnosis, and treatment."

Section 5 of the Order highlights how a limited understanding of underlying mechanisms of PTSD, the long-term consequences of TBI, and warning signs for tragic outcomes such as suicide is hampering progress in prevention, diagnosis, and treatment. Therefore, the NRAP includes research strategies to accelerate discovery of underlying mechanisms and rapidly translate this understanding into actionable tools for prevention, early diagnosis, and better treatment. The Order also calls for the establishment of a comprehensive longitudinal study of 100,000 service members focused on PTSD, TBI, and related injuries. To attain these goals, the Order urged research agencies to improve data sharing as appropriate and with appropriate privacy and confidentiality protections, and harness new tools and technologies (e.g., electronic health records). Importantly, the Order directs the NRAP to improve coordination between agencies and ultimately reduce the number of affected individuals.

In this NRAP, the agencies outline coordinated research efforts to accelerate discovery of the causes and mechanisms underlying PTSD, TBI, and other co-occurring outcomes like suicide, depression, and substance abuse disorders. It describes research to rapidly translate what is learned into new effective prevention strategies and clinical innovations: biomarkers to detect disorders early and accurately; and efficacious and safe treatments to improve function and quality of life and to promote community participation and reintegration. The NRAP also describes research to accelerate the implementation of proven means of preventing and treating these devastating conditions. Many collaborative efforts are already under way.

To achieve these goals, the NRAP agencies have identified key cross-cutting research priorities spanning conditions that will be pursued over the next 12 months. Examples of these priorities include the need to:

- Perform ongoing portfolio analyses of existing and emerging diagnostics, therapeutics and outcome measures for PTSD, TBI, and related injuries using the agencies' "Interagency Research Continuum Approach" model.
- Continue to develop processes to standardize, integrate, and share data as appropriate. The recent directive from the White House Office of Science and Technology Policy on *Increasing Access to the Results of Federally Funded Scientific Research* and the recent Executive Order on *Making Open and Machine Readable the New Default for Government Information* posit that open sharing of machine-readable data fuels scientific discovery and innovation, and specify that public agencies will be held accountable for ensuring their data are standardized, integrated, and shared where appropriate.
- Initiate a process to define a minimum set of general and topic-specific common data elements (CDEs) that can be adopted for PTSD and suicide prevention research to

potentially integrate with the Federal Interagency TBI Research CDEs. The agencies commit to reporting on progress in reducing delays and barriers currently impeding the timely sharing of data resources created and owned by federal agencies.

- Increase the inventory of scarce research resources (e.g., tissue samples, blood, and cerebrospinal fluid), facilitating access for scientific purposes (with appropriate human subjects' protections related to privacy and confidentiality). To accomplish this, the agencies will leverage existing pathology archives to initiate development of a virtual tissue (brain) repository for PTSD, TBI, and suicide research. Activities will also include (1) incorporating appropriate agreements either between the investigator and resourcing agency (material transfer agreement) or between agencies (interagency agreement) and (2) processes for securing consent to obtain brain tissue from donor (premortem) or representative (postmortem).
- Build new tools and technologies to understand the underlying mechanisms of PTSD, TBI, suicide, and other conditions. Appropriate NRAP-participating agencies will continue to fund innovative research for the Brain Research through Advancing Innovative Neurotechnologies Initiative. The DoD will leverage the Brain Research through Advancing Innovative Neurotechnologies initiative efforts and continue to fund complementary work.
- Adapt existing research initiatives to maximize their impact. The comprehensive 100,000 service member study called for by the Order (Army STARRS) has been established. The agencies will explore the feasibility of a longitudinal follow-up of Army STARRS to find actionable factors that can be used to improve early detection, and effective prevention and treatment of suicide, PTSD, TBI, and comorbidities. The follow-up study will include the ability to consent for the donation of postmortem brains and begin to establish necessary procedures for timely collection and preservation of tissue.
- Continue to leverage existing and emerging information technology to improve existing care for individuals with PTSD, TBI, suicidality, and other conditions. Agencies already harnessing information to answer research questions will continue to evolve the learning health care system model and provide lessons learned to agencies interested in developing this model.
- Utilize tools for agencies to coordinate and share the research they support. The agencies will identify a common database and explore the feasibility of utilizing it to share the research they support with other federal agencies and with researchers outside of the federal government, where appropriate.

The ability to leverage existing and emerging information technology will be a key factor in successfully coordinating and accelerating research under the NRAP. Transparent and accessible information about the agencies' ongoing and planned efforts will guide the agencies and researchers alike to reduce overlap, eliminate redundancies, identify gaps, and focus new research questions. Publicly accessible databases that contain information about funded grants (e.g., National Institutes of Health [NIH] Research Portfolio Online Reporting Tools, which is used by VA and NIH) act as repositories for government-sponsored research. A new commitment will be to analyze the costs, benefits, and utility of moving the DoD's medical research onto the NIH Research Portfolio Online Reporting Tools system as well as related systems such as Electronic Research Administration Commons, thus promoting a higher level of transparency and analysis across agencies and for the public. Beyond the transparent sharing of data about funded studies, a commitment will be made to promote the standardization and sharing of de-identified study level (raw) data, with the appropriate consent, confidentiality and privacy protections within legal authority. Many smaller studies are able to involve only a modest number of participants; therefore, the ability to share study data when appropriate will increase the power for analyses and potentially accelerate research progress. In addition, large-scale studies supported by each agency provide a platform for rich secondary data analyses when study-level data are shared. Central repositories such as the Federal Interagency Traumatic Brain Injury Research Informatics System may be leveraged in these data-sharing efforts. The agencies have begun discussions to determine how to more efficiently share data; details can be found in the report.

Funding and Prioritization

The agencies intend to focus and collaborate on the topics identified in this document. These efforts will be supported within existing agency budgets. The agencies will follow their established planning, programming, and budgeting processes and priorities will be supported as feasible within available resources. In a time of constrained resources, the agencies will continue to direct resources to high-priority activities.

This NRAP will complement the 2013 Interim Report of the Interagency Task Force on Military and Veterans Mental Health (May 2013) to ensure that Veterans, service members, and their families receive necessary mental health services and support. Close collaborations between the agencies will expedite fulfillment of the strategies outlined in the NRAP. The DoD, VA, HHS, and the Department of Education understand the gravity and urgency of the problems and are committed to advancing the health of our military and nation through their collective research. To ensure progress and success, the agencies will schedule formal joint review and analysis of efforts. Further, continued analysis of needs using the Interagency Research Continuum Approach is planned. The Agency research working group co-chairs will be responsible for overseeing the formation of any necessary new workgroups or initiatives to deliver on the plans of this NRAP. Collectively, these activities will support the Order's research goals to prevent suicide, to reduce the number of individuals affected by PTSD, TBI, and comorbidities, and to improve the quality of life of

NRAP Vision for the Future

The agencies anticipate that basic insights, garnered through NRAP efforts, will help lead to translational advances in the prevention, diagnosis, and treatment of PTSD, TBI, suicidal behaviors, and co-occurring conditions, including substance abuse, in service members, Veterans, and their families. Subsequently, better preventive and therapeutic interventions would be expected to help lead to improved health, function, and quality of life for people experiencing these conditions, and their families.

those who do experience these conditions through better-coordinated and synchronized efforts to accelerate progress in prevention, diagnosis, and treatment.

Key Themes Specific to PTSD, TBI, and Suicide Prevention Research

Beyond the research priorities spanning conditions (presented previously) and looking deeper into specific research needs for PTSD, TBI, and or suicide prevention, the themes highlighted here are examples of topics described in greater detail in the full report. Please note that the bullets under each research area are organized along the Interagency Research Continuum Approach, described earlier, and are not placed in order of importance or priority. Also note that all of these research areas are expected to include consideration of co-occurring disorders, including substance use disorders.

PTSD: Biomarkers, Mechanisms, and Treatment Research

- Replicate and confirm emerging data on promising biomarker candidates and other diagnostic tools for PTSD, including genome-wide associations, plasma molecules, and methylation patterns.
- Optimize risk and resilience screening tools and test new PTSD prevention and treatment interventions that target underlying mechanisms and causal pathways.
- Enhance current PTSD evidence-based treatment delivery to be briefer, more durable, and more efficacious in treating service members, Veterans, and their family members, including individuals with multiple mental and physical health issues, including substance abuse.

TBI: Biomarkers, Diagnosis, Mechanisms, and Treatment Research

- Determine whether blast-induced TBI is a unique pathobiological entity and, if so, define the neuropathology of blast injury and in a subsequent step evaluate appropriate imaging technologies for their ability to identify the blast pathology in histologically characterized brain tissue. Utilize these imaging tools in service members and Veterans to determine whether blast, or repetitive blast injury, is a risk factor for chronic neurodegeneration or other chronic neurologic disorders.
- Develop a more precise system for classifying and staging TBI to enhance diagnosis and prognosis and enable targeted therapies and personalized medicine.
- Support validation studies of proteomic, imaging, neurophysiologic and other potential biomarkers and diagnostic tools to improve accurate diagnosis, monitor course of illness and enable evaluation of promising pharmacologic and nonpharmacologic treatments, including rehabilitation treatments, for their ability to increase functional outcomes such as community participation and reintegration.

Suicide Prevention Research

- Add a longitudinal component to the Army STARRS project to identify modifiable psychosocial and environmental risk and protective factors, clinically actionable biomarkers, and neurobiological mechanisms for preventing suicide and continue to support the Military Suicide Research Consortium to rapidly translate findings and develop effective interventions.
- Optimize clinical suicide risk assessment tools to guide decisions on intervention, referral, and follow-up.
- Develop and test rapid, brief, and effective prevention and treatment interventions for suicide (including suicide ideation and attempts) applicable to a variety of settings, with rigorously designed randomized controlled trials that address comorbid problems.

Table of Contents

List of Acronyms

Army STARRS	Army Study to Assess Risk and Resilience in Servicemembers
BRAIN	Brain Research through Advancing Innovative Neurotechnologies
CAP	Consortium to Alleviate PTSD
CDC	Centers for Disease Control and Prevention
CDE	Common Data Element
CENC	Chronic Effects of Neurotrauma Consortium
CNS	Central Nervous System
DHP	Defense Health Program
DoD	Department of Defense
ED	Department of Education
EHR	Electronic Health Record
FITBIR	Federal Interagency Traumatic Brain Injury Research
FOA	Funding Opportunity Announcement
GWAS	Genome-Wide Association Studies
HHS	Department of Health and Human Services
HIV	Human Immunodeficiency Virus
IOM	Institute of Medicine
MHRN	Mental Health Research Network
MSRC	Military Suicide Research Consortium
mTBI	mild Traumatic Brain Injury
MVP	Million Veteran Program
NAASP	National Action Alliance for Suicide Prevention
NADHAP	National Addiction and HIV Data Archive Program
NIDA	Brain Research through Advancing Innovative Neurotechnologies
NIDRR	National Institute on Disability and Rehabilitation Research
NIH	National Institutes of Health
NIMH	National Institute of Mental Health
NINDS	National Institute of Neurological Disorders and Stroke
NRAP	National Research Action Plan
Order	Executive Order
PTSD	Posttraumatic Stress Disorder

RDoC	Research Domain Criteria
RePORTER	Research Portfolio Online Reporting Tools
TBI	Traumatic Brain Injury
TBIMS	Traumatic Brain Injury Model Systems Centers Program
TBIMS-NDB	TBIMS National Database
TRACK-TBI	Transforming Research and Clinical Knowledge in TBI
VA	Department of Veterans Affairs

Background

Since September 11, 2001, more than 2.5 million service members have deployed to Iraq and Afghanistan in Operation Enduring Freedom, Operation Iraqi Freedom, and Operation New Dawn. Military forces sent to fight those wars have exhibited a number of unique features, including: (1) an all-volunteer military that has experienced multiple deployments to the war zone, (2) substantial use of the reserve components of the military and National Guard, (3) deployment of high numbers of women and parents of young children, and (4) a high number of military personnel surviving severe injuries that in previous wars would have resulted in death. The Armed Forces Health Surveillance Center data list 266,810 cases of TBI occurring in the military between 2000–2012. Over 80% of these were the result of non-combat injuries. Among combat injuries, blast is a common cause. Military service exposes service members to a variety of stressors, including exposures to death, risk to life, sustained threat of injury or actual injury, and the day-to-day family stress inherent in all phases of the military life cycle and its transitions. Stress is a major contributor to both the onset and exacerbation of substance abuse and mental health problems and is related to a variety of negative physical health outcomes. A comprehensive assessment of the physical, psychological, social, and economic effects of deployment on service members, their families, and communities is provided in the 2013 Institute of Medicine (IOM) report "Returning Home from Iraq and Afghanistan: Assessment of Readjustment Needs of Veterans, Service Members, and Their Families."

Though significant and continuing improvements in outer tactical vests (body armor) and helmets have limited fatal injuries, many service members return with a traumatic brain injury (TBI), symptoms or diagnosis of posttraumatic stress disorder (PTSD), suicidal thoughts or behaviors, and/or related comorbidities. These comorbidities or co-occurring conditions are defined herein as mental health disorders, including depression; substance abuse related to alcohol, tobacco, and other drugs, including the misuse and abuse of prescription drugs; and chronic pain, each of which can complicate the prevention and treatment of PTSD, TBI, and suicidal behaviors. One study of returning Veterans who were seen in Department of Veterans Affairs (VA) health care facilities revealed that nearly one-third of them received at least one mental health or psychosocial diagnosis. Another study estimated that only 23% to 40% of returning service members who screen positive for a mental disorder seek mental health care. Family members are also impacted by the multiple stressors associated with deployment and reintegration. Overall, the need for mental health, and substance abuse, and chronic pain services for service members, Veterans, and their family members is anticipated to increase in coming years as the Nation endures the effects of more than a decade of military conflict. Additional sections of the President's August 31, 2012 Executive Order (the Order) address steps the agencies are taking to improve education and awareness, and access to services and treatment. An interagency Task Force (described in the following paragraphs) published their first report on these efforts in May 2013. These ongoing efforts are outside the scope of this National Research Action Plan (NRAP).

Researchers are attempting to answer questions across the research continuum from basic science aimed at understanding the disorders that are the focus of this Order through prevention, treatment, follow-up care, and services research directed at improving the delivery and modality of care. However, fundamental gaps in scientific knowledge remain that highlight the critical need for advancing the research described here. For example, the lack of an objective measure of

mild (mTBI) makes it difficult to adequately diagnose individuals or to determine risk of injury. Improved techniques are needed to determine when and what symptoms are attributable to the traumatic (physical) event, to understand the brain events that give rise to the post-concussive syndrome concurrent with PTSD symptoms, and to elucidate the neural basis of the interaction between mTBI, PTSD, depression, and suicidality. To this point in time, there has not been a definitive study of the neuropathologic effects of blast injury in those who have died.

A significant concentration of the country's best scientists and resources have led to major advances in other threatening health conditions, such as the conversion of human immunodeficiency virus infection from a fatal illness to a manageable chronic illness and a 60% drop in stroke rates over the past 60 years. A similar concerted scientific attack is warranted to determine the neural basis of PTSD and the functional deficits associated with TBI. Without such an effort, the burden of illness due to PTSD and TBI in service members, Veterans, and their families will continue. Current PTSD pharmacotherapy and medications are inadequate, with somewhat limited success in treating individuals with PTSD. Evidence-based approaches for reducing suicide risk are also limited, and the relationships between PTSD, TBI, suicide, and co-occurring conditions are not well understood. Researchers must also evaluate the impact of context, including the population (e.g., active duty, Reserve/Guard, Veterans, and families) and setting (e.g., deployed austere environments versus medical centers) in their studies.

The federal research funding agencies specified in the August 31, 2012 Order including the Departments of Defense (DoD), VA, Health and Human Services (HHS), and Education (ED) (henceforth referred to as "the agencies"), have distinct but complementary missions; hence, their existing funded research programs collectively address a broad range of mental health issues and can be successfully leveraged to establish and advance the NRAP to benefit service members, Veterans, and their families. The Order (see Appendix) sets the stage for the agencies to join forces in identifying related research priorities to better understand and reduce symptoms and to maximize function and community reintegration through optimal prevention, screening, diagnosis, and treatment advances. This report summarizes the interagency response to Section 5 in the Order.

Critical to the development of this NRAP was an understanding of the agency-specific activities related to the requirements specified in the Order. This background was provided in a Joint Review and Analysis meeting (January 2013) on research related to PTSD, TBI, suicide prevention, and substance abuse. Agency representation at the meeting included DoD, VA, ED (represented by the National Institute on Disability and Rehabilitation Research [NIDRR]), and HHS (represented by the National Institute of Health's [NIH's] National Institute of Neurological Disorders and Stroke [NINDS], National Institute of Mental Health, and National Institute on Drug Abuse).

A variety of activities are under way in support of the NRAP, including funded research projects within the agencies' complementary portfolios in PTSD, TBI, and suicide prevention research that also address comorbidities such as substance abuse. The DoD's Systems Biology Initiative and the Millennium Cohort and Family Cohort Studies, the VA's Million Veteran Program, and NIH's biomarker and mechanistic research programs all hold promise to inform advancement of prevention and treatment interventions. Notably, the DoD alone has invested more than $100 million in TBI biomarker discovery and development since 2007; other agencies have also supported this increased focus. The DoD and the Centers for Disease Control and Prevention

(CDC) are partnering with the Brain Trauma Foundation to develop a clinically meaningful classification system of mTBI/concussion that will enable improved clinical assessment of current status and prognosis. Suicide prevention research includes the DoD's Military Suicide Research Consortium (MSRC) and the National Institute of Mental Health and Department of the Army's Study to Assess Risk and Resilience in Servicemembers (Army STARRS) program. The agencies also support research that contributes to a better understanding of the mental health needs of military/Veteran families and the best ways to prevent, treat, and provide services for them (see text box).

On April 2, 2013, President Obama announced the NIH Brain Research through Advancing Innovative Neurotechnologies (BRAIN) initiative. The BRAIN initiative will involve the NIH, the Defense Advanced Research Projects Agency, the National Science Foundation, and several private laboratories and foundations working toward the next generation of tools for decoding the intricate language of the brain. This unique project aims to give scientists a more complete set of tools and information for understanding how the brain functions, and how we think, learn, and remember both in health and in the context of neurological and psychiatric conditions that are the focus of the Order and of great concern to service members, Veterans, and their families.

Studying the Health of Military Families

The agencies are funding a wide variety of studies relevant to military/Veteran family members, including research focused on:

- Basic epidemiology to understand risk and resilience factors of military families and communities
- Suicide bereavement in service members and their families
- Developing interventions to enhance resilience, address and prevent relationship problems, and support families during deployment
- Helping families aid Veterans with PTSD and alcohol abuse
- Determining the effectiveness of web-enhanced support tools for military families
- Determining the effects of military deployment of parents on adolescent mental health

Research shows that behavioral health disorders, especially substance use disorders (SUDs), frequently co-occur in people experiencing the target problems discussed in the Order (TBI, PTSD, and suicide). Despite strict prohibitions on illicit drug use in the military, as well as a broad, random drug testing program, there are indications of rising rates of drug use (to include prescription drug misuse and abuse, as well as heavy alcohol use, and tobacco use), among the active duty population. These concerns are not limited to active duty—research shows SUDs are rarely treated in young Veterans. Comorbidities can complicate efforts to effectively intervene with other, targeted health conditions. However, the results of long-term randomized controlled trials have shown that substance abuse prevention can have a positive effect on a wide array of behaviors. In addition, SUD treatment can mitigate negative mood and in some cases, treatment for PTSD has been shown to improve SUD outcomes, while integrated treatments addressing both SUDs and PTSD can improve both conditions. Suicide risk may also be lowered by treatment of SUDs.

A few factors complicate the matter of addressing SUDs and conducting research in military or Veteran populations: (1) concerns about confidentiality of military medical records; (2) impact of zero tolerance policies for illicit drugs and SUDs on the careers of service members; (3) lack of appropriate screening and assessment protocols specifically for SUD issues, and (4) uncertainty

about how SUDs may impact a Veterans' disability claims. Although current illegal drug use is less prevalent in Veterans than in the general population, there are still subpopulations for which there is concern. For example, research shows that Veterans with PTSD are more likely to receive opioid prescriptions and thus may have higher risk of addiction and other negative consequences. In addition, the presence of co-occurring disorders, common among Veterans, often complicates treatment.

It is expected that all initiatives supported by this action plan will address comorbidities when they exist including SUDs through coordination, goal setting, and common efforts. The agencies are independently and jointly funding studies focused on substance abuse research in military personnel, Veterans, and their family members. There have also been collaborations established that include joint reviews and analyses of portfolios and joint funding opportunities (e.g., 2010 NIH-VA Request for Applications [RFA] and 2013 NIH-DoD RFA). Substance abuse research funded by the agencies spans the research continuum from basic science through implementation research.

Data-sharing efforts include the DoD/NIH Federal TBI Research Informatics System for TBI clinical research (a central repository for TBI-related clinical research data that will also link to existing databases to facilitate sharing of information), the VA computing infrastructure, and NIDRR's TBI Model Systems National Database (TBIMS-NDB), which contains prospective data on the clinical progress and outcomes of individuals with moderate to severe TBI. The VA Polytrauma Rehabilitation Centers have partnered with NIDRR to establish a VA TBI Database that includes many of the same data elements found in the TBIMS-NDB. The U.S. Army Research Institute of Environmental Medicine has developed the Total Army Injury and Health Outcomes Database, which is a versatile system that joins multiple personnel and health data sets from various DoD agencies and links data on demographics, health outcomes, health habits, and chemical exposures. Finally, research may benefit in multiple ways from the use of aggregate, de-identified electronic health record data by providing information to better understand the scope of a problem being investigated and whether implementation of evidence-based practices is effective.

Recently initiated activities include two joint DoD/VA consortium efforts to support PTSD and TBI biomarker studies (the Consortium to Alleviate PTSD, and the Chronic Effects of Neurotrauma Consortium), new treatment studies to be generated from the basic research biomarker studies, and new treatment response studies to be incorporated into clinical trials. New and planned initiatives also include joint agency RFAs for research that are aimed at improving the health of service members, Veterans, and their families.

The agencies have collaboratively developed an interagency approach for strategic research planning that builds upon the framework initially developed by the DoD. This "Interagency Research Continuum Approach" is a research framework within which studies can be organized along a progression that includes seven topic areas: foundational science, epidemiology, etiology, prevention and screening, treatment, follow-up care, and implementation (services) research (**Figure 1**). This also facilitates analysis of gaps and identification of future areas of focus. Please note that "comparative effectiveness" research (listed under Treatment in Figure 1) refers to research that evaluates the effectiveness of different treatment options, procedures, or tests for specific diseases, conditions, or disorders; for example, the effectiveness of psychotherapies for PTSD.

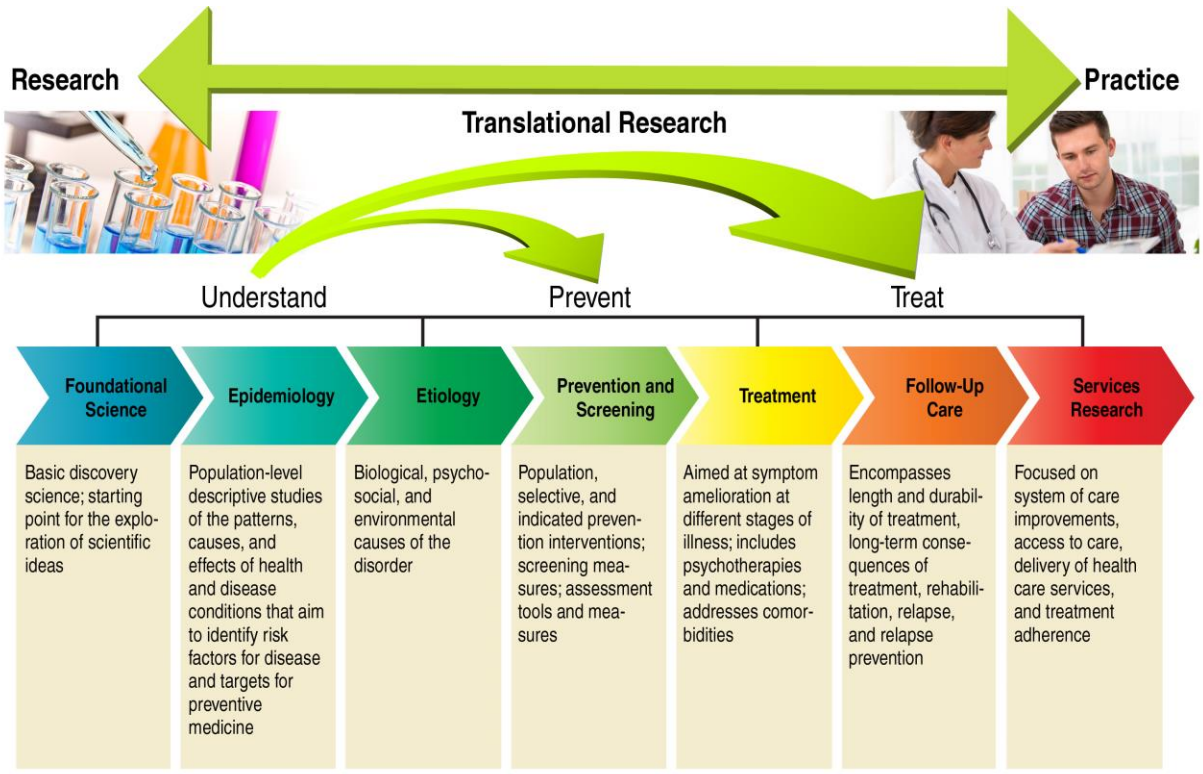

Figure 1. The Agencies' Interagency Research Continuum Approach

The integration of research findings into health care systems through evidence-based practices is needed to address the Order's goal of improving access to mental health and substance abuse services. The Order established the Military and Veterans Mental Health Interagency Task Force to oversee efforts aimed at improving capacity and enhancing quality of care for service members, Veterans, and their families. It is anticipated that the efforts of the Task Force will enable the service systems to become the platform to integrate and embed emerging evidence-based practices and develop "learning health care systems" in which the health care providers, systems, and patients participate in the generation of knowledge on trends in health and illness, the testing and identification of best practices, and the assessment of the impact of practice changes.

The Task Force may also identify existing or new interagency working groups to address the planning, performance, and completion of the tasks outlined in the NRAP. Such entities have already been utilized with success. However, the closer engagement required by the proposed plan would benefit from agency-specific/unique capabilities in personnel, programs, and funding to enhance the translation of research findings to clinical use. Coordination of strategic research and development plans would enable agencies to synchronize program announcements based upon the outcomes of research that may be funded by

Funding and Prioritization

The agencies intend to focus and collaborate on the topics identified in this document. These efforts will be supported within existing agency budgets. The agencies will follow their established planning, programming, and budgeting processes and priorities will be supported as feasible within available resources. In a time of constrained resources, the agencies will continue to direct resources to high-priority activities.

other agencies in earlier stages (e.g., NINDS funds a discovery project on biomarkers that the other agencies could leverage into epidemiological and clinical validation studies across a wide patient population).

The sections that follow elucidate the results of the agencies' Interagency Research Continuum Approach to address the research areas specified in the Order. The NRAP describes some of the highest priorities for accelerating discovery of the causes and mechanisms underlying PTSD, TBI, and other outcomes like suicide, depression, and substance abuse. It describes research to rapidly translate what is learned into new clinical innovations including the development of biomarkers to detect brain disorders early and accurately; highly effective prevention strategies; and highly efficacious and safe treatments. The NRAP also describes research to widely implement proven means of preventing and treating these devastating conditions. Across these efforts, the NRAP strives to achieve the same level of urgency, specificity of deliverables and timelines, as well as accountability, as expressed in the Order.

In addition to the detailed research priorities specific to each section of the Order, the agencies have identified the following **cross-cutting actions** that will be pursued within the next 12 months:

- Perform ongoing portfolio analyses of existing and emerging diagnostics, therapeutics and outcome measures for PTSD, TBI, and related injuries using the agencies' "Interagency Research Continuum Approach" model.
- Continue to develop processes to standardize, integrate, and share data as appropriate. The recent directive from the White House Office of Science and Technology Policy on *Increasing Access to the Results of Federally Funded Scientific Research* and the recent Executive Order on *Making Open and Machine Readable the New Default for Government Information* posit that open sharing of machine-readable data fuels scientific discovery and innovation, and specify that public agencies will be held accountable for ensuring their data are standardized, integrated, and shared.
- Initiate a process to define a minimum set of general and topic-specific common data elements that can be adopted for PTSD and suicide prevention research to potentially integrate with the Federal Traumatic Brain Injury Research common data elements. The agencies commit to reporting on progress in reducing delays and barriers currently impeding the timely sharing of data resources created and owned by federal agencies.
- Increase the inventory of scarce research resources (e.g., tissue samples, blood, and cerebrospinal fluid), facilitating access for scientific purposes (with appropriate human subjects' protections related to privacy and confidentiality). To accomplish this, the agencies will leverage existing pathology archives to initiate development of a virtual tissue (brain) repository for PTSD, TBI, and suicide research. Activities will also include (1) incorporating appropriate agreements either between the investigator and resourcing agency (material transfer agreement) or between agencies (interagency agreement) and (2) processes for securing consent to obtain brain tissue from donor (premortem) or representative (postmortem).
- Build new tools and technologies to understand the underlying mechanisms of PTSD, TBI, suicide and other conditions. Appropriate NRAP-participating agencies will continue to fund innovative research for the BRAIN Initiative. The DoD will leverage the BRAIN initiative efforts and continue to fund complementary work.

- Adapt existing research initiatives to maximize their impact. The comprehensive 100,000 service member study called for by the Order (Army STARRS) has been established. The agencies will explore the feasibility of a longitudinal follow-up of Army STARRS to find actionable factors that can be used to improve early detection, and effective prevention and treatment of suicide, PTSD, TBI, and comorbidities. The follow-up study will include the ability to consent for the donation of post mortem brains and begin to establish necessary procedures for timely collection and preservation of tissue.
- Continue to leverage existing and emerging information technology to improve existing care for individuals with PTSD, TBI, suicidality and other conditions. Agencies already harnessing information to answer research questions will continue to evolve the learning healthcare system model, and provide lessons learned to agencies interested in developing this model.
- Utilize tools for agencies to coordinate and share the research they support where appropriate. The agencies will identify a common database to explore the feasibility of utilizing it to share the research they support with other federal agencies and with researchers outside of the Federal government, where appropriate.

The co-chairs (DoD, VA, HHS, and ED) of the Interagency Research Committee (responsible for writing this NRAP) or their designees will be responsible for overseeing the formation of any necessary workgroups or initiatives to deliver on the plans of this NRAP and provide the Task Force with yearly progress reports related to achieving the NRAP goals.

PTSD: Biomarkers, Mechanisms, and Treatment Research

In response to a traumatic event, people commonly experience PTSD-like symptoms, e.g., hyperarousal or reliving the event. Afterwards, many individuals progressively improve and symptoms recede. Those who continue to experience distress may develop PTSD. They may also report symptoms that reflect a variety of comorbid conditions including TBI, depression, and substance abuse. Symptoms typically vary from person to person. The overall goals of PTSD research studies are to (1) reduce the number of individuals who develop PTSD following trauma (through early diagnosis and preventive interventions) and (2) reduce the number of individuals with chronic PTSD (through treatments that also address substance-related and other comorbidities).

Areas of research focus include:

Mechanisms. The mechanisms underlying the development of PTSD and comorbid conditions following traumatic exposure need to be better elucidated to enable the identification of individuals at risk. These mechanisms may be revealed through a variety of research activities including neuroimaging, animal studies, post-mortem analyses, and laboratory-based investigations focused on identifying physiological and neurochemical contributions, and other psychological, contextual, and environmental factors, including pre-existing conditions (e.g., substance abuse). As cognitive science evolves to reveal how dysfunction in memory, learning, and attention processes contribute to the development, prevention, and treatment of mental illness, researchers need to translate these findings into prediction models and novel prevention and treatment interventions. The National Institute of Mental Health (NIMH) has launched the Research Domain Criteria (RDoC) project, which will be enhanced to define basic dimensions of functioning (e.g., fear circuitry) to be examined across units of analysis from the level of genes to neural circuits to behaviors that are predictive of symptoms and/or reflect the etiology or persistence of a disorder. Information gathered from the RDoC project will pave the way for understanding the mechanisms responsible for phenotypes involved in disorders like PTSD and developing and testing new interventions.

Biomarkers for early diagnosis. Research is needed to identify and characterize biomarkers that can predict increased vulnerability to the development of PTSD, indicate changes in the spectrum of symptoms associated with worsening function, and demonstrate at the biologic level a positive response to intervention. A biomarker (biological marker) is an objectively measured indicator that ideally is capable of reflecting normal, at risk, and disease states. Cognitive markers, e.g., cognitive tests of attention, memory, and executive functioning, may be among the most promising predictors for PTSD. Biosignatures are an extension of the biomarker concept that combine different measures across biological, environmental, and social influences that will be valuable in identifying the complex origins of disorders such as PTSD. Similar to the way physicians assess heart disease risk in patients by coupling blood test panels for cholesterol and triglyceride levels with measures of hypertension and high blood pressure, scientists can develop a biosignature for PTSD by combining cognitive measures and imaging data, serum and cerebrospinal fluid markers, and highly relevant physiological markers for related symptoms.

Researchers funded through the large-scale DoD Systems Biology Initiative have identified candidate biomarkers that may signal the presence of PTSD in humans. Building upon this effort is the joint DoD and VA CAP award (see text box), which will enable investigators to jointly pursue the Order requirements related to establishing surrogate and clinically actionable biomarkers for early PTSD diagnosis and treatment effectiveness. NIMH is also supporting a substantial number of research projects focused on identifying biomarkers to predict increased vulnerability to PTSD. In addition, with the consent of participating Veterans, the VA's Million Veteran Program is building one of the world's largest databases of genetic, military exposure, lifestyle, and health information, providing a platform for biomarker research. Another ongoing program that features a substantial amount of biomarker research is Army STARRS, which is described in more detail later in this report.

Consortium to Alleviate PTSD (CAP)

The CAP is a new research effort focused on biomarker discovery and development with the aim of identifying biomarkers for subacute and chronic PTSD that can be used for therapeutic and outcome assessment. With funding from DoD and VA, this represents a major investment to advance knowledge related to biomarkers and clinical utility. A CAP award is expected to be finalized by September 2013.

Biomarkers for targeted treatment. The identification and validation of biomarkers for PTSD will ultimately enable practitioners to assess the effectiveness of prevention and treatment interventions. Clinicians would be able to match individuals with the most effective prevention and treatment protocols based on the individual's clinical profile, which may include medications, psychotherapy, and integrative and complementary medicine treatments alone or in combination. Research may also reveal populations at risk for specific comorbidities, subsequently enabling the development and testing of interventions to prevent these problems as well as effectively treat these conditions if they occur. Thus, another important goal of the NRAP is to facilitate the development of more personalized treatments; that is, individually tailored interventions with measurable responses (see text box "Vision for Moving PTSD Treatment Research into Practice").

Treatments. Psychotherapies and pharmacological medications are widely used to treat PTSD. When evidence-based psychotherapy treatment for PTSD is provided, up to 60% of patients respond successfully. However, individual preferences play an important role in the selection of intervention. Individuals who do not respond to one treatment may be reluctant to try other treatments, and preferences relative to the types of therapies available (e.g., pharmacotherapy, psychosocial therapy, and complementary and alternative medicine) may have a significant impact on overall outcome. The use of combined therapies holds promise to address urgent mental health needs. In addition, individuals with PTSD commonly present with substance use disorders. Therefore, treatment research described in this NRAP will examine ways to optimally treat comorbid conditions (e.g., integrative versus sequential treatments). TBI will also be examined as a comorbid condition for the military and Veteran population with PTSD.

There are no medications developed specifically for the treatment of PTSD. The two medications approved by the U.S. Food and Drug Administration for PTSD (the antidepressants sertraline and paroxetine) show modest efficacy. Many medications are used "off-label" to treat PTSD symptoms but lack scientific evidence that they are beneficial. Few treatment interventions target underlying biological causes or mechanisms of the disease. Investment by the pharmaceutical industry in new medications for PTSD has declined in recent years. Federal stakeholders will

pursue the development of therapeutics targeting biomarkers and mechanisms uncovered in the course of research as well as assess the utility of repurposed or off-label treatments. A well-studied example of this would be prazosin's ability to treat sleep disturbances in individuals with PTSD (prazosin is approved for treating hypertension). Further, new partnerships (e.g., public–private collaborations) will be pursued to aid in the identification of potential pharmacological targets for the prevention and treatment of PTSD. All of these research efforts would be enhanced by the development of a virtual tissue (brain) repository for PTSD. The value of tissue-based study presents opportunities to understand underlying biology impossible to discover in vivo.

The agencies' Interagency Research Continuum Approach for PTSD research and the major focus areas in each of the seven topic areas are shown in **Figure 2**. For the VA, NIMH, and NIDA, the numbers of studies represent the numbers of projects active in FY12, and Follow-Up Care research for NIMH and NIDA was included in Treatment and/or Services Research. For the DoD, the grant numbers represent the cumulative number of active studies funded from FY07–FY12.

Vision for Moving PTSD Treatment Research into Practice

The aspirational vision is to provide practitioners with the most effective ways to prevent or treat PTSD in the civilian and military populations, including service members, Veterans, and their families. Individuals exposed to traumatic events would routinely participate in systematic evaluation on broad dimensions of risk with progressively intensive diagnostic evaluations. Individualized and staged interventions would be planned to minimize severity of acute stress and prevent the development of PTSD. Results would then be weighted/combined in an automated algorithm to determine risk for PTSD and associated comorbidities (especially substance related) to inform care and follow-up. Evaluations would inform interventions targeted at mitigating negative psychological symptoms and consequences. Individuals seeking care for PTSD would undergo a thorough medical, psychiatric, and substance abuse history and assessment to yield a health risk profile indicative of the underlying cause/type of impairment. The individual would then be matched to receive treatment known to target/address the specific underlying cause/type of his/her disorder. Throughout a course of treatment, effectiveness of any administered treatment(s) would be measured. Researchers would have knowledge of both fixed and modifiable systems, circuits, and molecules to focus treatment development and refinement studies. New interventions thus will move faster from discovery/development to use in clinical care, thereby expanding treatment options.

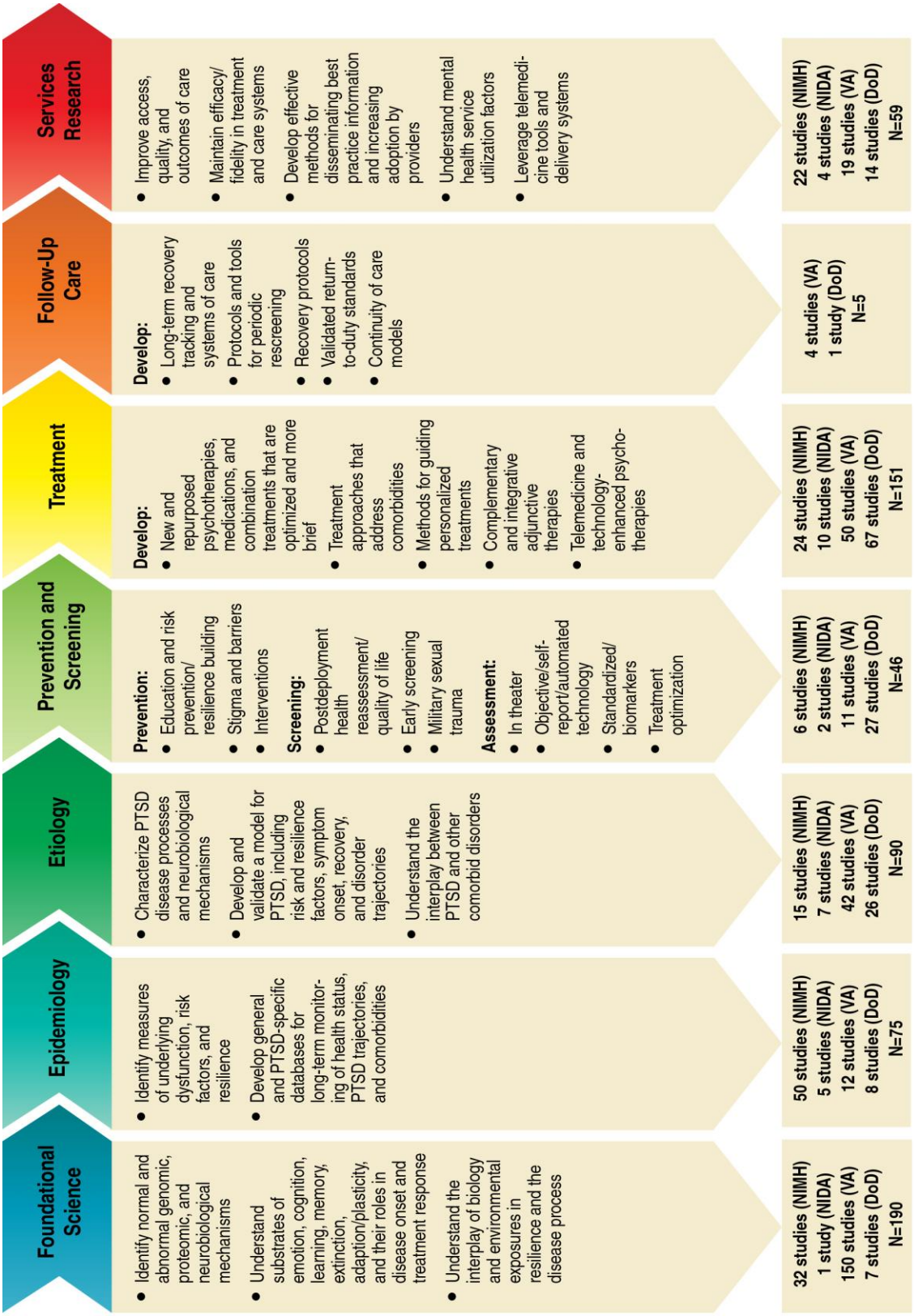

Figure 2. The Agencies' Interagency Research Continuum Approach for PTSD Research

Follow-Up Plan to Achieve the Vision for PTSD Research:

It is anticipated that findings from ongoing and newly initiated studies will directly inform future research specifically in areas of underlying mechanisms and biomarkers that in turn will inform prevention and treatment intervention advances. Notably, the agencies are dedicated to discussing/sharing new findings, reassessing goals, and informing new collaborative activities with each other (e.g., a meeting on biomarkers in high-risk cohorts and joint portfolio reviews). As studies conclude, the agencies will review research findings that pertain to prevention and health promotion and treatment interventions for PTSD and co-occurring conditions to identify those that warrant further investigation or those that are appropriate to implement within health care systems. The actions presented in the following time frames form the vision for PTSD research. Please note that the bullets within each time frame are organized by the order in the Interagency Research Continuum and are not placed in order of importance or priority.

Immediate Actions (within 1 year)

- Fund new exploratory research on structural and/or functional changes in the brain immediately following trauma exposure to identify early changes indicative of the future development of PTSD and comorbidities.
- Review emerging genomic and molecular findings on causal pathways and changes that contribute to PTSD and perform critical replication of preliminary findings.
- Continue to expand NIMH RDoC efforts by funding new applications to develop and test neural system measures that may be applicable to the spectrum of posttraumatic stress symptoms and comorbid psychiatric conditions.
- Increase the inventory of scarce research resources (e.g., tissue samples, blood, and cerebrospinal fluid), facilitating access for scientific purposes (with appropriate human subjects' protections related to privacy and confidentiality). To accomplish this, the agencies will leverage existing pathology archives to initiate development of a virtual tissue (brain) repository for PTSD research. Activities will also include (1) incorporating appropriate agreements either between the investigator and resourcing agency (material transfer agreement) or between agencies (interagency agreement) and (2) processes for securing consent to obtain brain tissue from donor (premortem) or representative (postmortem).
- Establish preliminary sex-specific risk allele biomarkers for PTSD to enrich and enhance risk prediction measures. This will aid in the identification of new targets for the development of prevention and treatment interventions.
- Publish program announcements, complete review of applications, and fund studies from interagency funding opportunities addressing PTSD biomarkers, substance abuse prevention, and wellness interventions for service members, Veterans, and their families.
- Convene an interagency biomarker working group to explore early findings from ongoing biomarker efforts and plan data-sharing opportunities to facilitate additional analyses of both published results and raw data.
- Continue research to improve and optimize the effectiveness and delivery of:
  - Current evidence-based prevention and treatment interventions (including psychotherapies, combination therapies, and adjunctive treatments) and available medications for PTSD and comorbidities; and

  - Service modalities for PTSD and comorbidities (e.g., telemedicine and web-based).
- Continue research on the safety and efficacy of medications, psychotherapeutics, and combination treatments targeting underlying mechanisms of PTSD and comorbidities.

Short-Term Actions (2–4 years)

- Disseminate findings (e.g., peer-reviewed publications, conferences, and briefings) from at least three genome-wide association studies with military, Veteran, or other high-risk cohorts to determine genetic patterns associated with PTSD and comorbidities.
- Identify and confirm whether potential biomarkers have clinical value for PTSD by utilizing studies that contain phenotypic and genetic data (e.g., Million Veteran Program, Marine Resiliency Study, and South Texas Research Organizational Network Guiding Studies on Trauma and Resilience).
- Establish a validated PTSD assay from the DoD's systems biology effort for objective diagnosis and monitoring of treatment response.
- Identify brain circuitry changes related to treatment response and disseminate findings (e.g., peer-reviewed publications, conferences, and briefings) from at least two translational trials.
- Leverage results from biomarker research (e.g., data emanating from CAP-funded projects) and embed follow-on biomarker studies in select clinical trials to explore biological changes or markers that are associated with treatment response to better match individuals to treatments.
- Disseminate findings (e.g., peer-reviewed publications, conferences, and briefings) from translational trials that are targeting either (1) a putative mechanism in PTSD with the novel use of medications (e.g., CRF [corticotropin releasing factor] antagonist and mifepristone) or (2) comorbidities with PTSD.
- Conduct research to optimize psychotherapeutic intervention approaches (e.g., repackaging, shortening, or integrating them) to achieve more rapid and long-lasting benefit.
- Disseminate findings (e.g., peer-reviewed publications, conferences, and briefings) from randomized controlled trials aimed at improving and optimizing PTSD treatment (e.g., psychotherapeutic and combination psychotherapeutic and pharmacological treatment protocols, including those for comorbid conditions).

Long-Term Actions (5–10 years)

Looking to the future, the agencies are striving to deliver research results that will move the field closer to realizing the PTSD vision (summarized earlier) of optimal prevention, diagnosis, and treatment for each individual. Realizing this vision requires continued investments in relevant research and a commitment by the agencies to important high-priority collaborative endeavors in the coming years. A forward leaning, aggressive vision is essential to achieve the "long-term actions" described here; however, steps toward these items are already under way or as noted in the following paragraphs will begin in shorter time frames, and the pace toward full implementation will be accelerated under the NRAP.

Focus areas for consideration in this longer term horizon include:

- Develop the systematic ability to combine data from valuable DoD, NIH, and VA cohort studies for a deep longitudinal view of putative biomarkers, to enhance clinical measures and improve the classification and prediction of PTSD. While some analyses can occur in shorter time frames, early phase work toward more systematic combined analyses will be dedicated to understanding the existing barriers to achieving this objective and developing plans for implementation. Over the longer term, efforts will focus on working to overcome the barriers and conducting analyses.
- Identify the requirements that would be needed to potentially establish a coordinated clinical treatment registry across VA, DoD, and civilian health care systems and clinical trials to collect common clinical and other measures that may lead to improved treatment outcomes. Ultimately, this effort could enhance clinical measures and improve the classification and prediction of PTSD by integrating and analyzing individual-level data from prior PTSD risk studies with a large number of acute trauma patients to develop models for combining clinical and biomarker data to predict risk of PTSD onset and lessen the severity of the disorder in those with PTSD. To achieve this objective from the present state of disparate service and research funding systems, early phase work in a shorter time frame will be focused on assessing the landscape of such systems, including their capabilities and limitations. Later phase efforts will concentrate on the institution of commonalities so that analyses can occur. Any such effort would include a clear policy process to ensure informed consent of patients.
- Enhance new and emerging infrastructure (e.g., NIMH experimental medicine project for Fast Fail Trials in Mood and Anxiety Spectrum Disorders, VA and DoD clinical trials infrastructure) to accelerate the testing of novel and repurposed pharmacological interventions. This may include partnering with pharmaceutical companies that identify compounds that may have the potential to treat underlying PTSD mechanisms. Initial work on this objective will include the identification of potential targets. This will be followed by further work on partnership development. Partnership development will take time to establish the working relationships in a structured way (Cooperative Research and Development Agreements for data use, sharing, intellectual property, etc.), as well as move compounds to trials.

As new efficacious interventions are developed, the next steps will focus on determining how to enhance treatment-seeking behavior and reduce barriers to care, as well as utilizing standardized training procedures for professionals to implement evidence-based interventions with fidelity in health care systems and evaluate on an ongoing basis.

TBI: Biomarkers, Diagnosis, Mechanisms, and Treatment Research

TBI is a complex and heterogeneous injury that includes a spectrum of severities ranging from mild (also known as a concussion) to moderate, severe, and penetrating. It can result in temporary symptoms or enduring disabilities, depending on factors such as the severity and location of the injury, the age at injury, and the number of injuries over time. Common issues resulting from TBI include: (1) the post-concussion syndrome of attention/concentration deficit, headache, dizziness, sleep disorder, depressed mood, irritability; (2) longer-term difficulties with cognition, behavioral and mental health, communication, and sensory processing (common after moderate or severe TBI); and (3) chronic traumatic encephalopathy as a result of repeated mTBI, which has also been linked with other delayed, neurodegenerative diseases such as Alzheimer's-type dementia, amyotrophic lateral sclerosis (Lou Gehrig's disease), and Parkinson's-like symptoms.

Currently 266,810 cases of TBI have occurred in the military 2000–2012. Most of these are mild TBI and approximately 15%–20% are deployment related. Most of the combat wounds observed in the conflicts in Operation Enduring Freedom/Operation Iraqi Freedom were caused by explosive weapons, such as improvised explosive devices. The effects of these blast exposures on the brain are not well understood. It is unclear whether blast injury is similar to the pathologically characterized impact injuries or acceleration/deceleration injuries. Therefore, any existing unique neuropathological features of blast injury are critical to define in order to guide research efforts aimed toward helping those exposed to blast TBI in the military. Animal models of blast injury could be exceedingly valuable to study relevant injury mechanisms if there is a clinically significant human pathology to model. A neuropathology laboratory has been established at Uniformed Services University of the Health Sciences (USUHS) for the purpose of defining the pathology of blast injury funded by the USUHS-NIH Center for Neuroscience and Regenerative Medicine and the U.S. Army Medical Research and Materiel Command. Clear consent is required for the comprehensive examination of brain tissue in deceased military personnel. Due to the sensitive nature of requesting consent for brain examination at the time of death, access to tissue has remained a barrier for understanding blast-related injuries.

Challenges for TBI research and clinical care include imprecise diagnostic tools and criteria used to classify the severity and type of TBI; a limited understanding of the impact of co-occurring conditions; gaps in understanding of mechanisms underlying injury and recovery, including the effects of gender, ethnicity, and socioeconomic background; paucity of research data on the social, psychological, and economic impacts of TBI on families and communities; uncertainty about the ability of preclinical models to reproduce the spectrum of injuries and co-occurring conditions; and a nascent understanding of ways to harness neuroplasticity to increase repair and recovery. Notably, a military context that poses a unique challenge is the role of multiple mechanisms ("blast-plus") as compared to single mechanism injuries (e.g., motor vehicle accident or sports concussion). To facilitate treatment advances for service members and Veterans with TBI, it will be necessary to better understand both the mechanism of underlying injury and its long-term health needs.

Areas of research focus include:

Diagnostic tools and definitions. Current definitions of TBI as well as the tools currently used to diagnose it are imprecise. The DoD and CDC, in partnership with the Brain Trauma Foundation, have funded an effort to develop a clinically meaningful classification system of mTBI/concussion that will enable improved clinical assessment of current status and prognosis. The International TBI Common Data Elements (CDEs) Project has recommended a battery of instruments to be used in TBI epidemiological and interventions research, but evidence demonstrating the utility or superiority of the recommended instruments over other measures is limited. NINDS has funded "Transforming Research and Clinical Knowledge in TBI" (TRACK – TBI), a pilot project to evaluate the utility and feasibility of the CDEs. DoD has funded the data analysis component of TRACK – TBI. These three successful interagency collaborations underscore the value and need for additional research to create more precise classifications of injury type and severity and more sensitive diagnostic tools to ultimately enable personalized medicine for TBI. There is also the opportunity for leveraging emerging imaging modalities and body fluid-derived biomarkers for improved diagnostics, but validation will be required before they are ready for clinical use.

Biomarkers for identification, management, and treatment effectiveness. Preliminary evidence supports the potential for use of bodily fluid (e.g., blood, serum, and cerebrospinal fluid) biomarkers to detect mTBI/concussion. Animal studies have indicated that changes in gene expression in white blood cells may identify inflammation related to TBI. However, identification of sensitive and specific biomarkers requires a more precise classification system for TBI, similar to the systems used for spinal cord injury and cancer. Biomarkers may inform research and clinical investigation as well as the management of both acute and chronic stages of TBI. Of particular interest are biomarkers indicative of the potential neurodegenerative effects of TBI, such as chronic traumatic encephalopathy and dementia. In short, biomarkers to detect injury, predict short- and long-term outcomes, and monitor response to treatment are all needed. Studies are under way to identify and test biomarkers, but none are currently ready for clinical use. There is an urgent need to systematically evaluate existing and emerging biomarker technologies for their ability to improve accurate diagnosis, detect acute and chronic illness, identify patterns of recovery, predict outcomes, and monitor the response to treatment.

Chronic Effects of Neurotrauma Consortia (CENC)

The DoD and VA are jointly sponsoring the CENC award, which will fund a large consortia to:

- Establish the association of the chronic effects of mTBI and common comorbidities;
- Determine whether there is a causative effect of chronic mTBI/concussion on neurodegenerative disease and other comorbidities;
- Identify diagnostic and prognostic indicators of neurodegenerative disease and other comorbidities associated with mTBI/concussion; and
- Develop and advance methods to treat and rehabilitate chronic neurodegenerative disease and comorbid effects of mTBI/concussion.

A CENC award is expected to be finalized by September 2013.

Mechanisms. Following TBI, most patients show some degree of functional improvement over time. However, relatively little is known about the mechanisms that underlie recovery or about ways to harness neuroplasticity to optimize improvements. Research is needed to identify

patterns of brain structure and function that are associated with either recovery or poor response to treatment. Given emerging evidence regarding the chronic effects of TBI, a better understanding of the relationship between neurotrauma and neurodegeneration is needed for the development of effective medical and rehabilitation interventions (see text box on the CENC). The nature of brain injuries incurred in the current military conflicts has highlighted the need to better understand the effects of repetitive brain trauma on neuropathology, neurological function, and mental health. The fielding of blast and impact sensors is anticipated to enable more precise identification of those exposed to possible concussive events. Once these devices have been validated as accurate in identifying possible events, they can then be correlated with clinical findings to determine whether injury severity can be accurately predicted.

Preclinical modeling. While basic science is essential to improving diagnostics and treatments for TBI, the ability to model TBI in animals has been less successful. None of the treatments found to be effective in preclinical animal models have successfully progressed through a Phase III clinical trial for clinical use in humans. The limited human postmortem brain tissue samples available for study have not allowed for sufficient comparison with animals. The differences in mass, shape, and white/gray matter ratios between rodent and human brains make it difficult to reproduce the effects of TBI in a manner that physically and structurally scales from rodents to humans. Animal models rarely address the short- and long-term comorbidities and/or chronic effects associated with TBI nor do they clearly address the recovery/rehabilitation phase.

Systems biology approaches that integrate animal and human findings with computational modeling of injury mechanisms and high performance computing have the potential to enable previously impossible levels of cross-correlation and analysis of research data. However, challenges in collecting human postmortem brain tissue have impeded progress in this area. A coordinated military, Veteran, and civilian tissue repository effort to make postmortem tissue available for research purposes is critical. Notably, the DoD has established the first DoD brain tissue repository to study TBI in service members. To guide the development and validation of animal models, especially for blast and mTBI, further postmortem human tissue research will be needed, and efforts to encourage donation of postmortem tissue with appropriate consent will help to advance this research.

Treatments. Over 30 clinical trials of TBI pharmacological therapies have failed to produce a U.S. Food and Drug Administration-approved treatment for acute TBI. There is limited evidence of the effectiveness of both pharmacological and nonpharmacological interventions, including rehabilitation treatments, due in part, to underpowered studies and the limited validated assessment tools that are sensitive enough to detect treatment effects. Research on treatment efficacy and effectiveness has also been hampered by difficulties in defining the active ingredient of many experience-based treatments that are commonly used in rehabilitation. The concurrent application of multiple treatments, including pharmacological and nonpharmacological interventions, poses another challenge. Rigorous definitions of rehabilitation treatments are needed as well as research regarding the customization of therapies to an individual's injury, predisposing factors, and co-occurring conditions.

Assessment. The International CDE Project for TBI has recommended a battery of "gold standard" outcome measures and assessments for TBI research; however, collectively these take several hours to implement. A shorter assessment tool that is both comprehensive and sensitive across the range of injury severities is clearly needed. Possibilities include several computer-

assisted outcome assessment tools that have recently been developed. The NIH Toolbox for Assessment of Neurological and Behavioral Function is a multidimensional set of brief measures that assess cognitive, emotional, motor, and sensory function in individuals from 3 to 85 years of age. The NINDS-funded Neuro-QOL is a set of self-report measures that assesses the health-related quality of life of adults and children with neurological disorders, and the NIDRR-funded TBI-QOL measures health-related quality of life specifically for people with TBI. These tools have the potential to fill an important gap by providing a comprehensive assessment of functional outcomes and quality of life following treatment while also being brief, freely accessible, and reliable. However, these tools need further validation before they are ready for clinical use in persons with TBI.

Co-occurring and pre-existing conditions. Major challenges to mechanistic and treatment-related research on TBI include difficulties in distinguishing the effects of PTSD and other comorbidities, such as sensory, endocrine, cognitive, behavioral, and sleep dysfunctions, from the central nervous system injury itself. In other words, the symptoms and sequelae of TBI can overlap with many other disorders. Of concern are reports of suicide in persons, including Veterans who have sustained TBI, who were found to have tau deposits in the brain diagnostic of chronic traumatic encephalopathy. Additionally, evidence is emerging that pre-existing factors, be they physical, social, cultural, or health-related, have an effect upon the course and outcome of TBI. The common approach to intervention—independently treating symptoms associated with each diagnosis—is known to be less than optimal and is, in many cases, ineffective. Research is needed to identify effective integrated, team-based models of treatment for persons with TBI that address both pre-morbid and co-occurring conditions.

Substance abuse is a known co-occurring condition with TBI with detrimental outcomes for persons with TBI and their families. For the general population of persons receiving health care services, Screening, Brief Intervention, Referral to Treatment (SBIRT) is standard of care for alcohol and tobacco, according to U.S. Prevention Services Task Force reports. However, despite being standard of care, SBIRT is not always implemented. NIDRR and other agencies within Department of Education have funded the development of an adapted SBIRT protocol for persons with TBI. Initial studies of this adapted protocol have concluded that the addition of multimedia educational components to the standard SBIRT protocol is having an impact on knowledge and beliefs, which in turn reduce substance abuse. Additional research investigating substance abuse in persons with TBI is needed including, but not limited to, further validation of best practices for screening, brief intervention, and referral to treatment.

The agencies' Interagency Research Continuum Approach for TBI research and the major focus areas in each of the topic areas are shown in **Figure 3**. For the NIH, VA, and NIDRR, the numbers of studies represent the numbers of projects active in FY12. For the DoD, the grant numbers represent the cumulative number of studies active between FY07 and FY12.

Since numerous TBI-related projects spanned the areas of epidemiology and etiology, or foundational science and epidemiology, these three topic areas were combined when totaling the numbers of studies funded by each agency.

Figure 3. The Agencies' Interagency Research Continuum Approach for TBI Research

Vision for Accelerating TBI Research to Improve Health Care and Outcomes

The aspirational vision for TBI research is to identify evidenced-based therapies that are effective in maximizing short- and long-term health and function, community participation and reintegration for persons with TBI in civilian and military populations, including service members, Veterans, and their families. Effective treatments, including rehabilitation treatments, would be personalized to address the specific type of injury and co-occurring conditions (especially substance related), considering patient preferences for care. A clinically relevant classification system for TBI across the spectrum of injury severities, age, gender, and chronic conditions, including mild single and repetitive injuries would be available to advise patients about their diagnosis, prognosis, and treatment options. More sensitive, reliable, and efficient tools ("gold standards") would be available for evaluating the effectiveness of treatments on an individual's physical, cognitive, and psychosocial functioning and quality of life.

Follow-Up Plan to Achieve the Vision for TBI Research:

Data generated from ongoing and newly initiated studies are anticipated to directly inform future research specifically in the areas of diagnosis, mechanisms, and biomarkers that in turn will inform prevention and treatment intervention advances for TBI. The agencies are holding regularly scheduled meetings dedicated to discussing/sharing new findings, reassessing goals, and updating collaborative activities among the partners. Specific follow-up actions are presented in the following time frames. Please note that the bullets within each time frame are organized by the order in the Interagency Research Continuum and are not placed in order of importance or priority.

Immediate Actions (within 1 year)

- Complete the current DoD-CDC-Brain Trauma Foundation mTBI/concussion classification project to clarify what is known and unknown about mTBI and the critical gaps that need to be addressed. Identify a process for developing a clinically relevant system to replace the current mild/moderate/severe nomenclature.
- Increase the inventory of scarce research resources (e.g., tissue samples, blood, and cerebrospinal fluid), facilitating access for scientific purposes (with appropriate human subjects' protections related to privacy and confidentiality). To accomplish this, the agencies will leverage existing pathology archives to initiate development of a virtual tissue (brain) repository for TBI research. Activities will also include (1) incorporating appropriate agreements either between the investigator and resourcing agency (material transfer agreement) or between agencies (interagency agreement) and (2) processes for securing consent to obtain brain tissue from donor (premortem) or representative (postmortem).
- Facilitate coordination of portfolio analysis and collaboration on research projects of shared interest by exploring the possibility of participation of the DoD and NIDDR in the NIH Electronic Research Administration system, which provides support for the full life cycle of grants administration functions for the NIH, VA, and several other agencies.
- Determine whether point of injury blast and impact sensors can be correlated to mechanism and severity of brain injury.

- Establish an interagency working group to review and report on existing and novel diagnostic tools and treatments for TBI to improve the evidence base for TBI management.
- Coordinate within and between agencies involved in the Brain Research through Advancing Innovative Neurotechnologies initiative to ensure a balance of basic and translational science so that more maturely developed technologies can be utilized clinically as soon as possible.
- Continue to support clinical trials that are evaluating the effectiveness of therapies to improve outcomes and quality of life following TBI.

Short-Term Actions (2–4 years)

- Support research focused on systematically characterizing blast neuropathology related to military service and comparing and contrasting it to the neuropathology of impact TBI. Test neuroimaging technologies to establish a means of identifying pathobiological markers of TBI regardless of mechanism in service members and Veterans. If there are verifiable and clinically significant differences between blast- and impact-induced TBI, develop scalable animal and in vitro models, if feasible, to identify and leverage biological pathways for study of therapies and the process of recovery.
- Develop a better understanding of the quantitative relationship between the level or number of repetitions of blast exposure and severity of TBI in animal models and humans.
- Determine whether co-occurring and pre-existing conditions exacerbate impact- and blast-related neuropathology.
- Develop initiatives for basic and clinical research focused on increasing the understanding of mechanisms of recovery after TBI and discovering ways to harness neuroplasticity to improve outcomes.
- Support validation studies of proteomic, imaging, neurophysiologic, and other potential biomarkers and diagnostic tools using the TBI CDEs, the FITBIR Informatics System and existing TBI clinical networks (e.g., TRACK-TBI, TBIMS, CENC, and VA Centers of Excellence). These studies may focus on early diagnosis, neuro-anatomic correlation of symptoms, classification of degrees of injury, markers of neural patterns of good recovery vs. poor recovery, or biomarkers in studies of therapeutic target engagement.
- Continue to support the FITBIR Informatics System as a national resource for TBI research and enhance the system to include with appropriate consent advanced analytical tools, pipelines for importing and exporting data (especially neuroimaging data); electronic data capture for emergency rooms, intensive care units, sports, and battlefields; and legacy data.
- Promote collaboration, meta-analysis and sharing of de-identified individual TBI study data in CDE format across agencies through the population of existing federal databases with FITBIR data, where possible, appropriate, and permissible. Activities to support this collaboration include implementing the use of global unique identifiers, the TBI CDEs, and consent forms that allow for data sharing across agencies for new studies, when possible, appropriate, and permissible.

- Develop efficient, affordable, comprehensive, valid, and sensitive tools for assessing functional outcomes and quality of life over time. Evaluate the utility of the NIH Toolbox for Assessment of Neurological and Behavioral Function, the Neuro-QOL, and the TBI-QOL and other tools that meet scientific standards to improve clinical assessment and enable measurement of treatment effectiveness specific to the TBI population.

Long-Term Actions (5–10 years)

- Develop a more precise system for classifying and staging TBI to enhance diagnosis and prognosis and enable targeted therapies and personalized medicine. The approach will be to (1) support natural history and other prospective, observational studies and (2) share data from these studies, with appropriate privacy protections, to enable computational analysis of large, high-quality data sets that include impact and blast injuries, military and civilian populations, acute and chronic phases, and the entire spectrum of age, severity, and the continuum of care.
- Determine the acute and chronic effects of TBI as well as the genetic, gender, ethnic, and environmental (epigenetic, socioeconomic, and cultural) protective and risk factors that influence susceptibility to injury and subsequent outcomes including the development of chronic traumatic encephalopathy, Alzheimer's and other neurodegenerative diseases. The approach will be to utilize new and existing longitudinal research initiatives (e.g., CENC, TBIMS-NDB, and Million Veteran Program) to study the chronic effects of TBI, including medical, neurological, psychiatric, and psychosocial complications, and to study genetic and epigenetic protective and risk factors.
- Identify causal relationships between posttraumatic alterations in brain function and symptoms, functional outcomes, and quality of life through greater integration of basic and clinical research. Integrate preclinical and clinical research to investigate causal relationships for all ages, injury types, and severities and for acute, subacute, and chronic stages. This will provide a foundation for developing targeted treatments and pharmacodynamic biomarkers.
- Evaluate promising pharmacological and nonpharmacological treatments, including rehabilitation treatments for their ability to increase functional outcomes such as community participation and reintegration.
- Develop and test models for optimal team-based, integrated treatment of TBI and co-occurring conditions to improve upon the existing practice of independently treating biological targets and/or symptoms of each condition.
- Conduct research on the social, psychological, and economic effects of deployment-related TBI on military families and on communities. Diverse indicators of family and community well-being should be examined.
- Conduct research on the long-term health needs of service members and Veterans with TBI and the resources needed for long-term care and planning.

Suicide Prevention Research

Suicide prevention is a major research priority that benefits from and is dependent on cross-agency, collaborative efforts to maximize the ability to effectively address the problem. Suicide is the 10th leading cause of death in the United States, claiming twice as many lives per year as homicide. Suicide attempts are up to 30 times more common than suicide deaths and are more frequent among younger persons. Having made a suicide attempt is one of the most highly predictive factors for later suicide death. Individual characteristics, such as a history of childhood abuse and mental and/or substance use disorders, can interact with current or ongoing stressors (e.g., relationship disruptions, financial or social losses, and shameful experiences) to increase suicide risk. Civilian and military suicide rates have been rising in recent years. Because individuals become suicidal for many different reasons, and not all individuals in suicidal crises will be seen in health care settings, multiple intervention approaches in multiple contexts are needed. Interventions are also needed to address how to identify and promote effective help-seeking behavior and reduce/treat underlying co-occurring mental health disorders.

Research indicates that no single factor has emerged as predictive of suicide in the military population. Some factors (such as repeated deployment) that have been hypothesized to be contributing to the increase in suicides in recent years have not been demonstrated to drive this increase (e.g., many suicides precede deployment). Almost half of the accidental and undetermined deaths investigated in the Army during 2006–2009 involved drugs or alcohol, and three-quarters of these deaths involved prescription drugs; however, the exact role of substance use in these deaths is not understood. Some studies have shown an association between suicide and TBI. However, the low base rate of suicide makes disentangling this challenging. Overall, factors leading to suicide are extremely complex, and research is under way to better understand the role of concussions and other comorbid factors.

Many individuals who die by suicide are seen in health care systems close to the time of death. Evidence demonstrates that providing continuity of care through transitions (within a health care system and from military to civilian settings) is important. Other health care system improvements that reduce suicide risk for individuals include providing 24-hour crisis services; increasing treatment adherence and managing patients with comorbid substance use disorders; and for practitioners, providing regular training to frontline clinical staff on the management of suicide risk. Other factors that may help reduce suicide have been identified; e.g., limiting access to lethal means significantly lowers suicide risk. Furthermore, treatments such as psychotherapies focused on mitigating suicidal thoughts among suicide attempters have been shown to reduce attempts by half in the 12 months following treatment. Small proof-of-concept studies show promise for fast-acting medications (e.g., ketamine) in reducing suicide ideation, but more research is needed. Longer-term research is needed to better understand the factors that build resilience and offer protection from suicidal behaviors and promote wellness and recovery.

The agencies have an ongoing partnership focused on suicide prevention research efforts[1] in many areas directly relevant to the Order. The U.S. Army and NIMH jointly initiated Army

[1] When not specified otherwise, the efforts described for suicide prevention research include preventing completed suicides as well as suicide behaviors to include suicide attempts and suicide ideation.

Study to Assess Risk and Resilience in Servicemembers (Army STARRS)[2] to examine how psychosocial, biological, and genetic factors convey risk/resilience for suicide, as well as related conditions (e.g., mental health disorders and substance-related disorders). The Military Suicide Research Consortium (MSRC) was created by the DoD to develop and validate effective interventions to prevent suicide among active-duty service members and Veterans (see text box). The National Action Alliance for Suicide Prevention's Research Prioritization Task Force is co-chaired by the NIH and the National Council for Suicide Prevention. The Research Prioritization Task Force is developing a proposed agenda by September 2013 to inform both the public and private sectors efforts to reduce suicide attempts and deaths in the next 10 years. The Defense Suicide Prevention Office's Translation and Implementation of Evaluation and Research Studies, which involves the DoD, military services, VA, and NIMH, translates knowledge accrued from evaluation and research studies into practical guidelines for military leaders, chaplains, and clinical and nonclinical support personnel, which will benefit service members, Veterans, and their families. The NIMH is also developing a research study portfolio analysis tool that will have the capacity to conduct systematic searches and analyses of funded studies among the agencies and private sector foundations, which will contribute to the Interagency Research Continuum Approach for suicide prevention.

Military Suicide Research Consortium

The DoD MSRC represents a unique collaboration among the world's experts in suicide research, including military, VA, and academic partners to produce evidence-based effective suicide prevention interventions. The MSRC complements the Army STARRS epidemiological study. The goal of MSRC research is to develop effective risk assessment methods, and prevention and treatment interventions to decrease suicide among active duty service members and Veterans. Funded projects are examining strategies to reduce suicide risk, to prevent re-attempts, and to understand bereavement among military families after a Veteran or active duty member of the military has died by suicide. In addition, the MSRC has developed an extensive data warehouse containing thousands of peer reviewed journal articles on military and Veteran mental health disorders, risk assessment and prevention, focused in particular on suicide and suicide-related research.

Findings emanating from the VA's nationwide suicide prevention program, Mental Illness Research Education and Clinical Centers, and Centers of Excellence will contribute to an understanding of what is working within the VA health care systems and identify factors for targeted research. A joint VA-DoD database of suicide history and health care information is being developed to serve programmatic evaluation needs. The National Action Alliance for Suicide Prevention's Research Prioritization Task Force will continue to solicit findings on research advances from the agencies, including the VA National Centers of Excellence in Suicide Prevention.

The agencies' Interagency Research Continuum Approach for suicide prevention research, including the major focus areas within each topic area, is shown in **Figure 4**. For the VA, NIMH, and NIDA, the numbers of studies represent the numbers of projects active in FY12, and Follow-Up Care research for NIMH was included in Treatment and/or Services Research. For the DoD, the numbers represent the cumulative number of active studies funded from FY07–FY12.

[2] Additional details on Army STARRS are presented in the Comprehensive Longitudinal Mental Health Study section of this report.

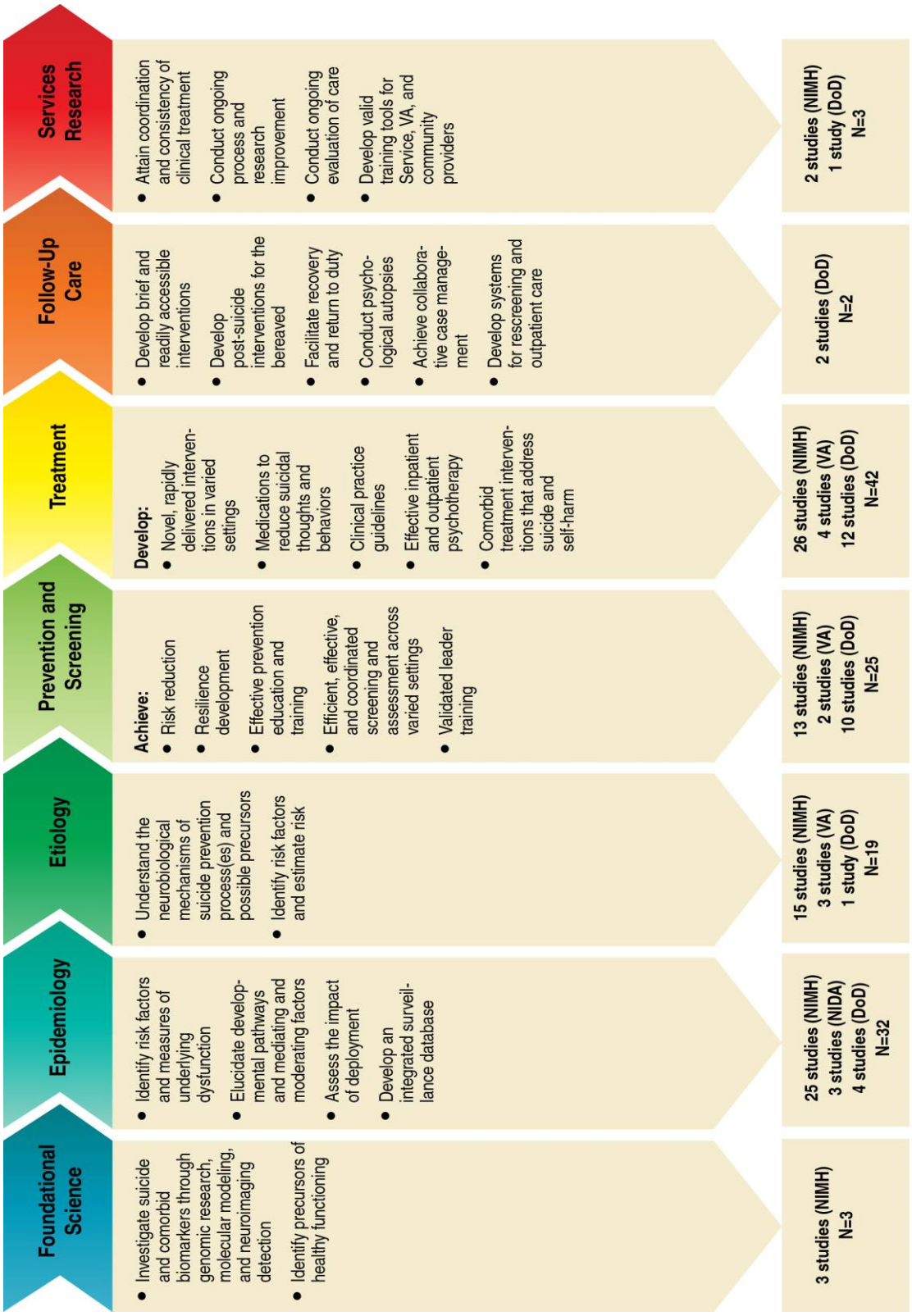

Figure 4. The Agencies' Interagency Research Continuum Approach for Suicide Prevention Research

Follow-Up Plan to Achieve the Vision for Suicide Prevention Research:

Critical research to meet the priorities of the Order includes enhanced use of surveillance data and longitudinal studies; testing screening approaches; timely and comprehensive sharing of data with appropriate safeguards; and the development and testing of new prevention and treatment interventions when targets are identified. Research focused on alcohol and substance use in the military, including Veterans and their families, is also important. Beyond the actions identified in the following paragraphs, additional information relevant to suicide prevention activities is found in the Comprehensive Longitudinal Mental Health Study section of this report. The following plan describes how the vision for suicide prevention research can be met over time. Please note that the bullets within each time frame are organized by the order of the Interagency Research Continuum and are not placed in order of importance or priority.

Vision to Advance Suicide Prevention Research

The aspirational vision for suicide prevention research is to achieve a significant reduction in attempted and completed suicides in the civilian, military, and Veteran populations through evidence-based prevention and treatment advances. There is hope that with new knowledge gained from research applied to practice, an individual who has made a suicide attempt or has suicidal thoughts would receive lifesaving care. Such an individual would seek help early through available resources such as a 24-hour hotline (Veterans Crisis Line) or online resources (Veterans Crisis Line website or VA Community Provider Toolkit). Modifiable risk and protective factors (e.g., reduced substance use and improved problem solving) could be targeted to avert reattempts. Evidence-based prevention programs that build resilience, reduce risk, and prevent the emergence of suicidal behaviors would be implemented in diverse systems of care and populations, with positive impact on suicide prevention.

Immediate Actions (within 1 year)

- Develop and test theoretical models to advance the science of understanding precursors and causes of suicide and its prevention.
- Increase the inventory of scarce research resources (e.g., tissue samples, blood, and cerebrospinal fluid), facilitating access for scientific purposes (with appropriate human subjects' protections related to privacy and confidentiality). To accomplish this, the agencies will leverage existing pathology archives to initiate development of a virtual tissue (brain) repository for suicide prevention research. Activities will also include (1) incorporating appropriate agreements either between the investigator and resourcing agency (material transfer agreement) or between agencies (interagency agreement) and (2) processes for securing consent to obtain brain tissue from donor (premortem) or representative (postmortem).
- Continue the development of integrated surveillance and survey database management systems across the DoD and VA.
- Disseminate findings (e.g., peer-reviewed publications, conferences, and briefings) from completed evidence synthesis reviews related to suicide prevention addressing key questions such as risk factors and assessment, and prevalence of co-occurrence of suicide with mTBI.

- The MSRC will identify the next set of research studies aimed at developing and testing suicide prevention interventions in clinical trials.
- Disseminate emerging findings and translate findings into next steps for intervention research utilizing programs such as the Defense Suicide Prevention Office's Translation and Implementation of Evaluation and Research Studies.
- Initiate novel efforts to create clinical tools with high specificity and sensitivity to identify at-risk individuals using minimally intrusive techniques.
- Evaluate research findings as they become available to determine what type of follow-up most effectively enhances treatment adherence and decreases suicidal behavior in high-risk individuals.
- Continue ongoing investigations aimed at encouraging implementation of evidence-based suicide assessment and management techniques in current care delivery settings (e.g., counseling and addictions treatment). Future research efforts will focus on improving provider training, developing and testing quality improvement measures, and assessing patient satisfaction.

Short-Term Actions (2–4 years)

- Empirically establish whether screens for suicide prevention can be used with adult patients and high-risk young adult/pediatric populations in health care settings (emergency medicine, primary care).
- Develop and test rapid, brief, and effective prevention and treatment interventions for suicide applicable to a variety of settings, with rigorously designed randomized controlled trials that address comorbid problems.
- Initiate an interagency collaboration between Army STARRS and the MSRC that will build upon the strengths of each program and facilitate rapid translation of Army STARRS findings into intervention research efforts.
- Develop and test evidence-based "chain-of-care" practices for individuals transitioning from inpatient to outpatient treatment and to specialty follow-up care.
- Investigate the utility of psychological autopsies to discover previously unknown risk factors or comorbidities for further clinical investigation.
- Develop and test return-to-duty and return-to-work protocols with evidence-based criteria.

Long-Term Actions (5–10 years)

Looking to the future, the agencies are working together to support research to reduce suicide in the civilian, military, and Veteran populations. Reaching this goal will only be possible by sustaining investments in relevant research and determining the best ways for agencies to focus on new high-priority, collaborative endeavors in the coming years. Priorities for consideration in this longer-term horizon include the following:

- Examine long-term outcomes of prevention interventions delivered early in life to determine whether these interventions impact behaviors related to suicide through existing and future longitudinal studies.
- Conduct multisite, rigorously designed, randomized controlled trials that test rapid-acting, brief interventions that address suicide risk factors, prevent suicide ideation and attempts, and can be utilized in emergency care settings through existing partnerships with consortiums and joint interagency partnerships.

Comprehensive Longitudinal Mental Health Study

In addition to the broad research goals of the NRAP, the Order also directs DoD and HHS to engage in a "comprehensive longitudinal mental health study with an emphasis on PTSD, TBI, and related injuries to develop better prevention, diagnosis, and treatment options. The agencies shall continue ongoing collaborative research efforts, with an aim to enroll at least 100,000 service members by December 31, 2012, and include a plan for long-term follow-up with enrollees through a coordinated effort with the Department of Veterans Affairs." Ongoing collaborative efforts that can be leveraged to address these requirements are highlighted in the following paragraphs.

The Army Study to Assess Risk and Resilience in Servicemembers (Army STARRS)

The Army and NIMH jointly initiated Army STARRS to examine how psychosocial, biological, and genetic factors convey risk/resilience for suicide, as well as related conditions. Army STARRS' component studies (Historical Administrative Data Study, New Soldier Study, All Army Study, Soldier Health Outcomes Study, and the Pre/Post Deployment Study) examine historical and administrative data collected by the Army in conjunction with original data collected from soldiers in all phases of Army service. As of late 2012, more than 100,000 soldiers volunteered to participate in Army STARRS.

Discussion of emerging findings as well as strategic planning is ongoing involving both scientists and federal agencies involved in relevant activities. Meetings held have included the DoD and VA and their funded scientists, as well as those funded by NIH. Plans to share Army STARRS data with the broader scientific community have also been established to maximize the utility of these data to improve the lives of service members, Veterans, and their families.

Army STARRS' Historical Administrative Data Study provides an example of the types of analyses possible utilizing existing aggregate data on soldiers to address questions regarding readjustment. The Historical Administrative Data Study includes de-identified data maintained in multiple Army and DoD data systems that have been integrated to find factors that protect soldiers' well-being and factors that suggest mental health risk. To ensure confidentiality, personally identifiable information is removed, and analyses are performed only on aggregate de-identified data.

Follow-Up Plan:

Army STARRS will continue through June 2014. Interim Progress Reports are provided to the Secretary of the Army, Chief of Staff of the Army, and Vice Chief of Staff of the Army to accelerate dissemination of actionable results to commanders who have the capacity to enact needed changes. These Interim Progress Reports include the most recent civilian and VA findings to give the appropriate context of actionable results to senior Army leaders. Findings will also be published and disseminated through peer-reviewed publications. One goal is for Army STARRS' data to inform new and better targeted diagnostic and intervention tools.

The action plan for Army STARRS includes several activities to maximize short-term results from this unique study and to ensure that the data platform is established as a critical national resource now and for the future, with all appropriate governance, intellectual property, and custody rights vested in the appropriate federal agency.

Immediate Actions (within 1 year)

- Develop tools to better identify elevated risk for suicide or other adverse mental health outcomes. The Army might then be able to use this information to develop targeted approaches to mitigate risk and ensure the health of soldiers. This research will also inform our understanding of suicide in the overall population, leading to more effective prevention and treatment interventions for service members and civilians.
- Continue ongoing data collection and analyses, including initial biomarker assays; analyses focused on psychiatric and substance abuse disorders to inform better prevention, diagnosis, and treatment options; exploring patterns of suicide risk in the New Soldier Study, All Army Study, and Pre/Post Deployment Study; comparing data from the Soldier Heath Outcomes Studies to matched controls to better understand the acute and chronic factors that contribute to suicide attempts and deaths; and disseminating findings.
- Explore the feasibility of a longitudinal follow-up of the comprehensive Army STARRS to find actionable factors that will lead to early detection and effective prevention and treatment of suicide, PTSD, TBI, and comorbidities. The study will include clear consent for the donation of postmortem brains and begin to establish necessary procedures for timely collection and preservation of tissue.

Short-Term Actions (2–4 years)

- Continue strategic planning for the next phase of Army STARRS.
- Establish data-sharing agreements to enable the project to continue in a manner that fosters collaboration across agencies, service branches, and scientists.

Long-Term Actions (5–10 years)

- Conduct a longitudinal follow-up with Army STARRS participants through Army, DoD, VA, and civilian records and recontact individuals (regardless of participant status and source of health care) to conduct studies focused on identifying surrogate and clinically actionable biomarkers, neurobiological mechanisms that may lead to suicidal behavior in blast-exposed individuals, and psychosocial and environmental risk factors for risk and resilience to suicide, PTSD, TBI, and comorbidities as these conditions may emerge with the passage of time and transitions that occur as part of military service. The overall goal is to rapidly translate findings and develop effective interventions.

Summary: The ability to monitor some cohort of the more than 100,000 enrolled participants over the long term capitalizes on the initial Army STARRS investment. To make this monitoring study feasible, data on emerging mental disorders and suicidal behaviors, and service member and Veteran health care use need to be integrated. Establishing Army STARRS as a national resource offers great hope for better understanding the long-term impact of traumatic events, particularly service members' experiences with combat, related military stressors, and transition to civilian life. Finally, the ongoing and planned scientific objectives of Army STARRS are directly relevant toward addressing the complex issues of PTSD, TBI, suicide prevention, and related comorbidities called for throughout the Order.

Additional Collaborative Efforts

Other ongoing collaborative efforts can be leveraged to address the requirements of Section 5c in the Order, including The Millennium Cohort Study (which includes service member and family

cohorts), and the Million Veteran Program (MVP). Funded by the DoD and supported by military, VA, and civilian researchers, the Millennium Cohort Study is the largest prospective health project in military history. It was designed to examine the effects of military service on physical and mental health outcomes and includes longitudinal cohorts of more than 200,000 service members and 10,000 spouses. The MVP is a landmark national research program that is building one of the world's largest medical databases by collecting blood samples and health information from one million Veteran volunteers. Data collected from the MVP will be stored anonymously for research to study how genes affect health. More than 175,000 Veterans have already enrolled in the MVP (May 2013), and 50 VA medical centers nationwide are currently participating.

Sharing PTSD, TBI, and Suicide Prevention Research

The data-sharing requirements described in the Order impact both sharing of information related to funding activities across agencies and, where appropriate, research study-level data. The development and adoption of Common Data Elements (CDEs) for research present the potential for streamlining information sharing. Within NRAP activities, a task will be to define a minimum set of general and topic-specific CDEs that may be adopted in PTSD, TBI, and suicide prevention research. The general CDEs may also be applied to research on co-occurring conditions (where demographic data are collected, etc.). The effort should result in a minimum set of defined demographic CDEs for research purposes to best accomplish study objectives while simultaneously facilitating the comparability of data. Of note, these efforts are not focused on sharing personally identifiable clinical data across providers of care. Instead, the agencies are focused on data-sharing activities for research purposes that contain de-identified clinical data (e.g., Mental Health Research Network and Federal Interagency Traumatic Brain Injury Research [FITBIR] Informatics System) as well as de-identified data generated through primary research. Plans must address issues surrounding de-identification and protection from re-identification of data. Data sharing plans that are developed must also consider understandable language for informed consent, individual privacy, confidentiality, agencies' authority, and other policies related to data use and sharing within a research context.

As data are shared between entities expanding beyond the initial research database, and particularly relevant to genetic data, maintaining privacy, confidentiality, and data protection will be paramount, especially for the population covered by the NRAP. It is important to consider how best to protect the identity and therefore the information of research participants.

In February 2013, Dr. John Holdren, Director of the White House Office of Science and Technology Policy (OSTP), issued a memorandum to the heads of executive departments and agencies entitled, *Increasing Access to the Results of Federally Funded Scientific Research.* That memorandum requires agencies to develop plans to increase access to the results of federally funded scientific research including publications and data. Specifically, it requires agencies to develop policies that "maximize access, by the general public and without charge, to digitally formatted scientific data created with Federal funds," with exceptions for protecting confidentiality, privacy, and proprietary interests.[3] Both the White House memorandum and an Executive Order issued in May 2013 on *Making Open and Machine Readable the New Default for Government Information* posit that open sharing of machine-readable data fuels scientific discovery and innovation. Consistent with the spirit of this memorandum and Executive Order, the DoD, VA, HHS, and Department of Education will pursue improved data sharing for research in TBI, PTSD, and related injuries and neurological conditions, and suicide prevention in concert with emerging government-wide efforts to increase access to the results of federally funded scientific research, aligned with protecting human subjects' privacy and confidentiality. Furthermore, responsibility for ensuring data sharing is not limited to data resources created as the result of taxpayer-funded extramural research but may extend to data resources created and owned by federal agencies themselves. The agencies intend to promote transparency with regard

[3] The memorandum also specifies that each agency shall submit its draft plan to OSTP within 6 months of its publication. Since the memo was released on February 22, 2013, the estimated response date of the agencies is August 22, 2013. All wording regarding data sharing in the NRAP is subject to and could be superseded by the final plans of the agencies in response to this OSTP memorandum.

to their federal data repositories where doing so does not supersede the protection of privacy, confidentiality, or other legal authority.

Sharing Funding Information Across Agencies

Accessible electronic information about ongoing and planned efforts supported by the federal government is a key component to coordinating and accelerating research. Transparent and accessible information can guide funding agencies and researchers alike to reduce overlap, eliminate redundancies, identify gaps, and focus new research questions. Electronic access to funded databases that yields information about grants funded in different areas of research allows the entire scientific community to increase understanding of ongoing efforts and hone development of the next generation of scientific questions. Publicly accessible databases that contain information about funded grants (e.g., NIH Research Portfolio Online Reporting Tools, which is used by the VA and NIH) act as repositories for government-sponsored research. Some of the DoD research portfolio information is available on publicly accessed websites; however, a new commitment will be to move the DoD's medical research onto the NIH Research Portfolio Online Reporting Tools via Electronic Research Administration Commons, thus promoting an even higher level of transparency and analysis. The agencies will continue the annual review and analysis process; the most recent meeting was held in January 2013. These efforts serve to foster interagency collaborations and cross-pollination among researchers, with the ultimate goal of accelerating research progress and reducing/preventing redundancy of efforts.

Sharing De-identified Research Study-Level Data as Appropriate

Access to study-level data for the purpose of secondary data analysis is important for research in general. Data sharing with appropriate consent, confidentiality, and privacy protections within legal authority allows for an increase in the amount of data that can be combined or compared by the community of scientists. Many small-sized studies are able to involve only a modest number of participants; therefore, the ability to share data when appropriate will increase the power for analyses and potentially accelerate research progress. In addition, large-scale studies supported by each agency provide a platform for rich secondary data analyses when data are shared. The agencies are committed toward ensuring that data produced with federal funding are shared, where appropriate and within legal authority, with consent and proper de-identification to prevent risk for identification (protecting individual privacy).

Examples of study-level, data-sharing efforts include:

- The FITBIR Informatics System has been established to provide a central repository for TBI-related clinical research data. FITBIR was funded by the DoD and subsequently developed and managed by the NIH. De-identified clinical data are entered into FITBIR utilizing the TBI CDEs, which were developed to allow more precise comparisons of TBI research data. Research data from newly funded NINDS and Defense Health Program TBI clinical research projects are required to be entered into FITBIR. Although not required, clinical research data from previously funded projects can also be entered into FITBIR. Additionally, the TBI CDE project is developing data standards to allow expansion of FITBIR to preclinical work, enabling advancement of preclinical knowledge and improved modeling of TBI. This data repository standardizes the collection of research data and allows access to researchers outside of the original research studies to re-analyze and compare data across studies.

- The standardization and sharing of de-identified study-level (raw) data by the NIH. Many types of research grants supported by the NIH are required to have plans for sharing de-identified data acquired as part of a study. For example, an investigator-initiated application with direct costs greater than $500,000 in any single year is required to address data sharing. Furthermore, any NIH study conducting genome-wide association studies, used to identify common genetic factors that influence health and disease, is required by NIH policy to (1) share de-identified data (genotypic and phenotypic) through a centralized repository and (2) submit documentation that describes how the institutions have considered the interests of the research participants (e.g., privacy and confidentiality). The purpose of this NIH policy is to maximize investments and foster science for the benefit of the public. This requirement is supported by resources such as the NIH genome-wide association studies website (http://gwas.nih.gov).
- The National Institute on Disability and Rehabilitation Research established the longitudinal TBI Model Systems National Database (TBIMS-NDB) to provide a data repository for clinical data on persons with moderate or severe TBI who receive treatment in the Model Systems network of centers. This database has been shown to be nationally representative of persons with moderate to severe TBI who receive inpatient rehabilitation. It offers decades of information on clinical progress and outcomes following TBI. The National Institute on Disability and Rehabilitation Research and the VA have also partnered to create a VA Polytrauma Rehabilitation Centers TBI Database that includes many of the same data elements found in the TBIMS-NDB.
- The VA computing infrastructure allows for de-identified study data to be accessible to VA researchers. While not limited to PTSD or TBI, this environment allows appropriate sharing of research data within the VA. Notably, VA study-level data sharing is defined in data use agreements and carefully considers safeguarding Veteran stakeholders information related to de-identification.
- The NIH Toolbox for the Assessment of Neurological and Behavioral Function (http://www.nihtoolbox.org). This brief set of measures, assessing cognitive, emotional, motor, and sensory function from 3–85 years of age, meets the need for a standard set of measures that can be used as a "common currency" across diverse study designs and settings. The NIH Toolbox can be used in many types of research, including research seeking to measure changes in neurological and behavioral function over time and evaluating intervention and treatment effectiveness.

Follow-Up Plan:

The overall goal for the NRAP related to de-identified data sharing is centered on accelerating research progress. The major emphasis is on sharing data, as appropriate, describing funded research studies to facilitate an understanding of what is being supported across agencies, increase transparency in the public domain, and reduce redundancy. Planned compilation of funded research studies and common coding of categories of

Vision for Research Data Sharing

De-identified research data sharing, ideally, would be collaborative and promote team science to more rapidly and effectively fill gaps in knowledge that will ultimately improve health care and outcomes. The scientific community would be able to submit and access research data in a participatory manner to test new hypotheses, combine data sets for meta-analyses, and compare and contrast findings across disorders, the lifespan, and the continuum of care. Research data elements would be standardized to the greatest extent possible and also aligned with clinical data elements to enable greater integration of research and clinical practice.

research across the spectrum from basic to implementation research will allow researchers to search for various topics across agencies to identify ongoing work (e.g., all studies that examine PTSD and suicide attempts) and facilitate the next generation of research questions. Joining with the NIH and VA, the DoD will pursue utilization of Electronic Research Administration Commons, IMPAC II, and related systems for research study portfolio management.

The agencies have begun discussions related to determining how to enhance research data-sharing efforts as appropriate. Data-sharing efforts will require close and continued collaboration between federal agencies dedicated to addressing challenges specific to research to meet the overall goal to increase access to study-level data.

Some exemplars of the type of activities that will meet the requirements of the Order are as follows:

- Continue to convene the joint DoD/VA/HHS/ED strategic portfolio reviews in the areas of TBI, PTSD, suicide prevention, and substance abuse research.
- Explore expansion of the Psychiatric Genomics Consortium (https://pgc.unc.edu/index.php) to include PTSD cohorts. Research funded by federal agencies may deposit de-identified genotypic and phenotypic data to facilitate meta-analyses, replication, and extension of early findings.
- Improve the delivery of health care services in the private sector by sharing research findings and data through agencies (e.g., Agency for Healthcare Research and Quality), consensus development conferences (e.g., NIH Consensus Development Program), and practice-based research.
- Develop a minimum set of defined CDEs for adoption and use in PTSD, TBI, and suicide prevention research.
- Plan to expand FITBIR to include preclinical research data. CDEs for preclinical models will be developed. Methods will be developed to enable researchers with existing or even completed research to more easily align their data with the CDEs, which may be expanded to relevant mental health elements. Entry of data into FITBIR is a requirement for all DoD-funded TBI research projects and will be a requirement for NIH TBI clinical research projects.
- Facilitate the collaboration of FITBIR with TBIMS-NDB, the International TBI Research Initiative, and other related/relevant data repositories that can be leveraged for research, as permissible.
- Encourage use of the National Addiction and HIV Data Archive Program (NADHAP) (http://www.icpsr.umich.edu/icpsrweb/NAHDAP/) for the purpose of archiving data. Researchers can use the NADHAP to upload data sets relevant to substance abuse and military and Veteran populations and use data from the NADHAP for the purpose of secondary data analysis.
- Encourage use of NIH Funding Opportunity Announcement PAR-13-080, "Accelerating the Pace of Drug Abuse Research Using Existing Data." The purpose of this Funding Opportunity Announcement is to invite applications proposing the innovative analysis of existing social science, behavioral, administrative, and neuroimaging data to study the etiology and epidemiology of drug-using behaviors (defined as alcohol, tobacco, prescription, and other drugs) and related disorders, associated HIV risk behaviors, prevention of drug use and HIV, and health service utilization.

Electronic Health Records and Research and Clinical Care

An electronic health record (EHR) is an evolving concept defined as a systematic collection of electronic health information about individuals or populations. It is a record in digital format that is theoretically capable of being shared across different health care settings. In some cases this sharing can occur by way of network-connected, enterprise-wide information systems and other information networks or exchanges. Current and future sharing capabilities will be limited to the extent that the systems can be integrated. EHRs may include a range of data, including demographics, medical history, medication and allergies, immunization status, laboratory test results, radiology images, vital signs, personal stats such as age and weight, and billing information.

EHRs primarily support clinical workflows but may also serve as a data resource that supplements research. In addressing the Order's requirement related to EHRs, the agencies have focused on research applications, specifically those related to existing VA and DoD EHRs, such as enhancing the ability to query records to understand targeted populations prior to study, improving the ability to scope proposed problems and develop hypotheses, and identifying sites that can serve as recruiting centers within large systems such as the VA. A fundamental requirement of the use of EHR data in research is the protection of an individual's confidentiality and privacy. For example, including information on participation in a particular research study in the medical record may have far-ranging privacy implications as medical record information is shared. Therefore, implementations of EHR use for research purposes must ensure confidentiality within the health care setting as well as the research setting while satisfying the need for an accurate continuous care record.

EHRs can provide valuable data for tracking and improving patient care. Various population health management systems have been implemented to reduce re-hospitalization and comorbidities in civilian populations at risk for diseases such as diabetes, chronic obstructive pulmonary disease, and cardiovascular disease. Algorithms implemented via such systems provide feedback to clinicians to improve patient engagement and are delivered through the clinical EHR. It is conceivable that in the future similar strategies could be used to identify individuals requiring a particular "prevention" intervention or treatment related to TBI or PTSD, as well as those eligible for clinical trials. One example of this is the Mental Health Research Network (MHRN) established by NIMH. Currently, the MHRN consists of 11 research sites at member institutions affiliated with nonprofit, integrated health care delivery systems. MHRN member institutions belong to a consortium of 16 health care delivery organizations with integrated research divisions known as the HMO Research Network. In addition to MHRN, HMO Research Network has attracted other NIH-funded research programs including the Cancer Research Network and the Cardiovascular Research Network, as well as several programs funded by the Agency for Health Care Research and Quality.

The parent HMOs for MHRN members provide care for approximately 11 million individuals and offer substantial resources that are useful for the conduct of mental health research. These resources include data for large, well-defined, and diverse patient populations; long-established administrative and medical records; long-standing patient privacy and confidentiality protections; physician and patient web portals; biospecimen resources; linkages to other data systems such as population-based patient registries; and capacity for rapid identification and

accrual of subjects to longitudinal retrospective and prospective cohorts for observational studies or clinical trials. To date, MHRN investigators have enhanced a Virtual Data Warehouse to harmonize mental health diagnosis and treatment data across all sites of the MHRN, establishing standard definitions for key exposures and mental health outcomes. They also developed procedures for distributing standard programs and aggregating data across sites. Other accomplishments include conducting observational studies using the Virtual Data Warehouse to analyze practice variation across multiple sites; organizing patient-reported outcomes data across sites; implementing a centralized online platform for administration of standardized clinical measures across multiple sites; and developing procedures for online electronic informed consent and protection of personally identifiable information and transfer of sensitive data. Procedures have also been established for the multisite collection of biological specimens, including consent, and specimen collection and use.

Since current International Classification of Diseases diagnostic codes (versions 9/10) do not define TBI using the VA/DoD definition, it is difficult for the agencies to use retrospective data for epidemiological and systematic analyses. Hurdles(e.g., "big data" approaches to identifying new patterns and disease processes and time courses) must be addressed while preserving individual privacy and confidentiality. It is anticipated that EHRs might have the capability to address these needs and will also contribute to the creation of a continuous "learning" health care system. The VA is currently exploring the strategy of point-of-care research based on clinical care outcomes obtained directly from EHRs and using these outcomes data to generate knowledge about treatment choices. For example, clinicians could utilize the PTSD Checklist in clinical practice and log outcomes from treatment over time in the EHR. With appropriate confidentiality and consent procedures, the PTSD Checklist results could then be extracted from the medical record to determine the impact of treatment and inform treatment choices.

Vision for Using Health Data to Improve Outcomes

Ideally, an individual's EHR would be continuous or accessible across care providers, systems of care, and individuals' lifetimes. Individuals would be able to access records in a participatory manner to improve accuracy and continuity of care. A population dashboard utilizing EHR would be used to monitor trends in health and illness in relation to practice changes. EHRs would also be used by health care providers to identify patients meeting certain risk profiles based on trends emerging from other patients with similar histories. Research studies aimed at improving patient outcomes will build on EHR information with appropriate protections and informed consent in research studies aimed at improving patient outcomes. Overall, it is hoped that data-driven systems would effectively and efficiently improve the mental health and substance abuse care of service members, Veterans, and civilians.

EHRs and Research

The Order directs making better use of EHRs to gain insight into the risk and mitigation of PTSD, TBI, and related injuries. This is relevant across research activities, and the agencies are dedicated to determining potential EHR applicability among ongoing/new efforts and assessing where EHR use is feasible and appropriate. However, the work related to meeting the Order requirement is not in concert with a predetermined time line, as specific barriers may have to be addressed (outside the scope of this NRAP) and authority for data use may have to be modified.

While the action plan for addressing the topics of PTSD, TBI, and suicide prevention will be coordinated through the agencies respective research offices, agency stakeholders (e.g., Military Health System, Tricare Management Activity) and other experts will be required to address the objectives for EHR use in research, including medical informatics, privacy, confidentiality of records, and information technology. Together, the agencies will work with the Office of the National Coordinator for Health Information Technology to advance information and cooperation for emerging developments in EHRs related to the support of research, including to:

- Develop a model for a population dashboard(s) that could be voluntarily used in health systems utilizing EHRs to monitor trends, patterns, as well as impact of events on TBI/PTSD and mental health.
- Consider expanding the MHRN to include additional health systems and investigators to focus on improvements in the prevention and treatment of TBI, PTSD, and mental health and substance abuse.

Conclusion

Funding and Prioritization

The agencies intend to focus and collaborate on the topics identified in this document. These efforts will be supported within existing agency budgets. The agencies will follow their established planning, programming, and budgeting processes, and priorities will be supported as feasible within available resources. In a time of constrained resources, the agencies will continue to direct resources to high-priority activities.

The vision for PTSD, TBI, and suicide prevention research described here will be achieved through close, continued collaborations across agencies and throughout the scientific community. Agency collaborations will occur formally through joint portfolio review and analyses of efforts aligned with the NRAP. All of these activities will support the research goals outlined in Sections 5a and 5b of the Order, which include preventing suicide; reducing the number of individuals affected by PTSD, TBI, and substance-related and other comorbidities; and improving the quality of life of those who do experience these conditions through better coordinated and synchronized efforts to accelerate progress in prevention, diagnosis, and treatment. Additionally, Army STARRS and other large collaborative efforts (e.g., Millennium Cohort Study and Million Veteran Program) are responsive to Section 5c of the Order, which directs that the DoD and HHS engage in a comprehensive longitudinal mental health study with an emphasis on PTSD, TBI, and related injuries to develop better prevention, diagnosis, and treatment options. New large collaborations (e.g., Consortium to Alleviate PTSD and Chronic Effects of Neurotrauma Consortium) will also directly respond to the Order and contribute to our goal to advance effective diagnosis and prevention and treatment interventions. The agencies look forward to fulfilling this NRAP with the anticipation that it will directly benefit Veterans, military service members, and their families.

Documents Consulted

The following documents were referenced in preparation of this report:

- 2013 Interim Report of the Interagency Task Force on Military and Veterans Mental Health, Issued in May 2013.
- Army Health Promotion Risk Reduction Suicide Prevention Report. Issued in July 2010.
- Gulf War and Health, Volume 7: Long-Term Consequences of Traumatic Brain Injury. IOM. 2009. Washington, DC: The National Academies Press.
- Increasing Access to the Results of Federally Funded Scientific Research. Memo issued in February 2013 by Dr. John Holdren, Director of the Office of Science and Technology Policy.
- Making Open and Machine Readable the New Default for Government Information. Executive Order issued on May 9, 2013, by President Barack Obama.
- National Institute of Mental Health Strategic Plan. Issued in August 2008.
- Psychological Health and Traumatic Brain Injury Portfolio Review and Analysis Report. (Summary of the meeting sponsored by the DHP and held on July 28, 2010, at Fort Detrick, Maryland.)
- Psychological Health and Traumatic Brain Injury Portfolio Review and Analysis Report. (Summary of the meeting sponsored by the DHP and VA, and held on November 30–December 1, 2011, at Fort Detrick, Maryland.)
- Psychological Health and Traumatic Brain Injury Portfolio Review and Analysis Report. (Draft summary of the meeting sponsored by the DHP, VA, NIH, and ED, and held on January 6–7, 2013, at Fort Detrick, Maryland.)
- Returning Home from Iraq and Afghanistan: Assessment of Readjustment Needs of Veterans, Service Members, and Their Families. IOM. 2013. Washington, DC: The National Academies Press.
- Returning Home from Iraq and Afghanistan: Preliminary Assessment of Readjustment Needs of Veterans, Service Members, and Their Families. IOM. 2010. Washington, DC: The National Academies Press.
- Substance Use Disorders in the U.S. Armed Forces. IOM. 2012. Washington, DC: The National Academies Press.
- Toward Precision Medicine: Building a Knowledge Network for Biomedical Research and a New Taxonomy of Disease. IOM. 2011. Washington, DC: The National Academies Press.

Appendix: The Executive Order

The White House

Office of the Press Secretary

For Immediate Release August 31, 2012

Executive Order – Improving Access to Mental Health Services for Veterans, Service Members, and Military Families

EXECUTIVE ORDER

IMPROVING ACCESS TO MENTAL HEALTH SERVICES FOR VETERANS, SERVICE MEMBERS, AND MILITARY FAMILIES

By the authority vested in me as President by the Constitution and the laws of the United States of America, I hereby order as follows:

Section 1. Policy. Since September 11, 2001, more than two million service members have deployed to Iraq or Afghanistan. Long deployments and intense combat conditions require optimal support for the emotional and mental health needs of our service members and their families. The need for mental health services will only increase in the coming years as the Nation deals with the effects of more than a decade of conflict. Reiterating and expanding upon the commitment outlined in my Administration's 2011 report, entitled "Strengthening Our Military Families," we have an obligation to evaluate our progress and continue to build an integrated network of support capable of providing effective mental health services for veterans, service members, and their families. Our public health approach must encompass the practices of disease prevention and the promotion of good health for all military populations throughout their lifespans, both within the health care systems of the Departments of Defense and Veterans Affairs and in local communities. Our efforts also must focus on both outreach to veterans and their families and the provision of high quality mental health treatment to those in need. Coordination between the Departments of Veterans Affairs and Defense during service members' transition to civilian life is essential to achieving these goals.

Ensuring that all veterans, service members (Active, Guard, and Reserve alike), and their families receive the support they deserve is a top priority for my Administration. As part of our ongoing efforts to improve all facets of military mental health, this order directs the Secretaries of Defense, Health and Human Services, Education, Veterans Affairs, and Homeland Security to expand suicide prevention strategies and take steps to meet the current and future demand for mental health and substance abuse treatment services for veterans, service members, and their families.

Sec. 2. Suicide Prevention. (a) By December 31, 2012, the Department of Veterans Affairs, in continued collaboration with the Department of Health and Human Services, shall expand the capacity of the Veterans Crisis Line by 50 percent to ensure that veterans have timely access, including by

telephone, text, or online chat, to qualified, caring responders who can help address immediate crises and direct veterans to appropriate care. Further, the Department of Veterans Affairs shall ensure that any veteran identifying him or herself as being in crisis connects with a mental health professional or trained mental health worker within 24 hours. The Department of Veterans Affairs also shall expand the number of mental health professionals who are available to see veterans beyond traditional business hours.

(b) The Departments of Veterans Affairs and Defense shall jointly develop and implement a national suicide prevention campaign focused on connecting veterans and service members to mental health services. This 12 month campaign, which shall begin on September 1, 2012, will focus on the positive benefits of seeking care and encourage veterans and service members to proactively reach out to support services.

(c) To provide the best mental health and substance abuse prevention, education, and outreach support to our military and their family members, the Department of Defense shall review all of its existing mental health and substance abuse prevention, education, and outreach programs across the military services and the Defense Health Program to identify the key program areas that produce the greatest impact on quality and outcomes, and rank programs within each of these program areas using metrics that assess their effectiveness. By the end of Fiscal Year 2014, existing program resources shall be realigned to ensure that highly ranked programs are implemented across all of the military services and less effective programs are replaced.

Sec. 3. Enhanced Partnerships Between the Department of Veterans Affairs and Community Providers. (a) Within 180 days of the date of this order, in those service areas where the Department of Veterans Affairs has faced challenges in hiring and placing mental health service providers and continues to have unfilled vacancies or long wait times, the Departments of Veterans Affairs and Health and Human Services shall establish pilot projects whereby the Department of Veterans Affairs contracts or develops formal arrangements with community based providers, such as community mental health clinics, community health centers, substance abuse treatment facilities, and rural health clinics, to test the effectiveness of community partnerships in helping to meet the mental health needs of veterans in a timely way. Pilot sites shall ensure that consumers of community-based services continue to be integrated into the health care systems of the Department of Veterans Affairs. No fewer than 15 pilot projects shall be established.

(b) The Department of Veterans Affairs shall develop guidance for its medical centers and service networks that supports the use of community mental health services, including telehealth services and substance abuse services, where appropriate, to meet demand and facilitate access to care. This guidance shall include recommendations that medical centers and service networks use community-based providers to help meet veterans' mental health needs where objective criteria, which the Department of Veterans Affairs shall define in the form of specific metrics, demonstrate such needs. Such objective criteria should include estimates of wait-times for needed care that exceed established targets.

(c) The Departments of Health and Human Services and Veterans Affairs shall develop a plan for a rural mental health recruitment initiative to promote opportunities for the Department of Veterans Affairs and rural communities to share mental health providers when demand is insufficient for either the Department of Veterans Affairs or the communities to independently support a full time provider.

Sec. 4. Expanded Department of Veterans Affairs Mental Health Services Staffing. The Secretary of Veterans Affairs shall, by December 31, 2013, hire and train 800 peer to peer counselors to empower veterans to support other veterans and help meet mental health care needs. In addition, the Secretary shall continue to use all appropriate tools, including collaborative arrangements with community based providers, pay setting authorities, loan repayment and scholarships, and partnerships with health care workforce training programs to accomplish the Department of Veterans Affairs' goal of recruiting, hiring, and placing 1,600 mental health professionals by June 30, 2013. The Department of Veterans Affairs also shall evaluate the reporting requirements associated with providing mental health services and reduce paperwork requirements where appropriate. In addition, the Department of Veterans Affairs shall

update its management performance evaluation system to link performance to meeting mental health service demand.

Sec. 5. Improved Research and Development. (a) The lack of full understanding of the underlying mechanisms of Post Traumatic Stress Disorder (PTSD), other mental health conditions, and Traumatic Brain Injury (TBI) has hampered progress in prevention, diagnosis, and treatment. In order to improve the coordination of agency research into these conditions and reduce the number of affected men and women through better prevention, diagnosis, and treatment, the Departments of Defense, Veterans Affairs, Health and Human Services, and Education, in coordination with the Office of Science and Technology Policy, shall establish a National Research Action Plan within 8 months of the date of this order.

(b) The National Research Action Plan shall include strategies to establish surrogate and clinically actionable biomarkers for early diagnosis and treatment effectiveness; develop improved diagnostic criteria for TBI; enhance our understanding of the mechanisms responsible for PTSD, related injuries, and neurological disorders following TBI; foster development of new treatments for these conditions based on a better understanding of the underlying mechanisms; improve data sharing between agencies and academic and industry researchers to accelerate progress and reduce redundant efforts without compromising privacy; and make better use of electronic health records to gain insight into the risk and mitigation of PTSD, TBI, and related injuries. In addition, the National Research Action Plan shall include strategies to support collaborative research to address suicide prevention.

(c) The Departments of Defense and Health and Human Services shall engage in a comprehensive longitudinal mental health study with an emphasis on PTSD, TBI, and related injuries to develop better prevention, diagnosis, and treatment options. Agencies shall continue ongoing collaborative research efforts, with an aim to enroll at least 100,000 service members by December 31, 2012, and include a plan for long term follow up with enrollees through a coordinated effort with the Department of Veterans Affairs.

Sec. 6. Military and Veterans Mental Health Interagency Task Force. There is established an Interagency Task Force on Military and Veterans Mental Health (Task Force), to be co chaired by the Secretaries of Defense, Veterans Affairs, and Health and Human Services, or their designated representatives.

(a) Membership. In addition to the Co-Chairs, the Task Force shall consist of representatives from:

(i) the Department of Education;

(ii) the Office of Management and Budget;

(iii) the Domestic Policy Council;

(iv) the National Security Staff;

(v) the Office of Science and Technology Policy;

(vi) the Office of National Drug Control Policy; and
(vii) such other executive departments, agencies, or offices as the Co-Chairs may designate.

A member agency of the Task Force shall designate a full time officer or employee of the Federal Government to perform the Task Force functions.

(b) Mission. Member agencies shall review relevant statutes, policies, and agency training and guidance to identify reforms and take actions that facilitate implementation of the strategies outlined in this order. Member agencies shall work collaboratively on these strategies and also create an inventory of mental health and substance abuse programs and activities to inform this work.

(c) Functions.

(i) Not later than 180 days after the date of this order, the Task Force shall submit recommendations to the President on strategies to improve mental health and substance abuse treatment services for veterans, service members, and their families. Every year thereafter, the Task Force shall provide to the President a review of agency actions to enhance mental health and substance abuse treatment services for veterans, service members, and their families consistent with this order, as well as provide additional recommendations for action as appropriate. The Task Force shall define specific goals and metrics that will aid in measuring progress in improving mental health strategies. The Task Force will include cost analysis in the development of all recommendations, and will ensure any new requirements are supported within existing resources.

(ii) In addition to coordinating and reviewing agency efforts to enhance veteran and military mental health services pursuant to this order, the Task Force shall evaluate:

(1) agency efforts to improve care quality and ensure that the Departments of Defense and Veterans Affairs and community based mental health providers are trained in the most current evidence based methodologies for treating PTSD, TBI, depression, related mental health conditions, and substance abuse;

(2) agency efforts to improve awareness and reduce stigma for those needing to seek care; and

(3) agency research efforts to improve the prevention, diagnosis, and treatment of TBI, PTSD, and related injuries, and explore the need for an external research portfolio review.

(iii) In performing its functions, the Task Force shall consult with relevant nongovernmental experts and organizations as necessary.

Sec. 7. General Provisions. (a) This order shall be implemented consistent with applicable law and subject to the availability of appropriations.

(b) Nothing in this order shall be construed to impair or otherwise affect:

(i) the authority granted by law to an executive department or agency, or the head thereof; or

(ii) the functions of the Director of the Office of Management and Budget relating to budgetary, administrative, or legislative proposals.

(c) This order is not intended to, and does not, create any right or benefit, substantive or procedural, enforceable at law or in equity by any party against the United States, its departments, agencies, or entities, its officers, employees, or agents, or any other person.

BARACK OBAMA

THE WHITE HOUSE,
August 31, 2012