U.S. ARMY MEDICAL RESEARCH AND DEVELOPMENT COMMAND (USAMRDC)
CONGRESSIONALLY DIRECTED MEDICAL RESEARCH PROGRAMS (CDMRP)
TRAUMATIC BRAIN INJURY AND PSYCHOLOGICAL HEALTH RESEARCH PROGRAM (TBIPHRP)
VIRTUAL STAKEHOLDERS MEETING
27–28 APRIL 2021

Summary of Stakeholder-Defined Research Gaps and Areas of Focus

A stakeholders meeting for the Fiscal Year 2021 (FY21) TBIPHRP was held virtually on 27–28 April 2021. The stakeholders meeting provided a forum for an open dialogue among experts, including researchers, clinicians, program managers, and lived-experience subject matter experts, to identify gaps in research and topic areas that aligned with the congressional language used to establish the TBIPHRP, including the following.

- Treatments for posttraumatic stress disorder (PTSD) from sexual trauma
- Traumatic Brain Injury (TBI) prevention
- Long-term studies of TBI
- TBI diagnostics
- TBI treatments

During the meeting, stakeholders participated in a breakout session exercise and plenary group discussions to focus on specific areas of interest and allow for free exchange of ideas. A summary of stakeholder responses and rationale is provided below. These are not the official gaps of the program for the FY21 cycle. *The stakeholder-defined gaps will be used by the TBIPHRP Programmatic Panel Members in the determination of the program strategy for funding opportunities. Please refer to future funding opportunities for any final gaps and focus areas associated with a specific application receipt cycle.*

A. Overview Presentations

To provide a common understanding of TBI and psychological health (PH) research efforts, leaders and partners from various organizations presented overviews of their organizations' efforts. Dr. Dwayne Taliaferro, the TBIPHRP Program Manager, presented an overview of previous CDMRP-led and -managed research efforts (Enclosure 1) as well as responses to a Request for Information released prior to this meeting (Enclosure 2). Ms. Kathy Lee introduced the Warfighter Brain Health Initiative and its comprehensive strategy and action plan (Enclosure 3). CDR Travis Polk described the Combat Casualty Care Research Program and their efforts to address military TBI challenges (Enclosure 4). CDR Christopher Steele provided an overview of the Military Operational Medicine Research Program, describing both its Blast, Blunt, Accelerative, and Neurosensory Portfolio and its Psychological Health and Resilience Portfolio (Enclosure 5). Dr. Stuart Hoffman and Dr. Cendrine Robinson introduced the U.S. Department of Veterans Affairs' research efforts, focusing on investments and initiatives addressing TBI and psychological health portfolios, respectively (TBI, Enclosure 6; PH, Enclosure 7). Dr. Timothy Hoyt reported on the Psychological Health Center of Excellence (PHCoE) and its efforts to support the Military Health System through surveillance, gaps analysis, and policy development (Enclosure 8). CAPT Carlos Williams provided an overview

of the National Intrepid Center of Excellence (NICoE) and its role in the Defense Intrepid Network to provide comprehensive clinical care and research for TBI and brain health (Enclosure 9). Finally, Dr. Ramona Hicks introduced One Mind as a non-profit organization supporting mental health and brain injury research through a variety of partnerships and research opportunities (Enclosure 10).

B. TBI Breakout Sessions

i. Etiology, Pathology, and Prevention

Overall, stakeholders felt that research into TBI required a hierarchy of prioritization for specific needs. Stakeholders identified a need to differentiate TBI in civilian versus military settings, as well as blast versus impact TBIs. They noted that classification of injury was also needed to understand injury complexity, severity, dose effects, pathology, dealing with under-diagnosis, and lack of clinical care. Stakeholders also identified heterogeneity of TBI and patients as an area of poor understanding. They proposed that phenotypes and endophenotypes for differentiating injuries and patient populations required model validation. Stakeholders also suggested that current care pathways could be defined as eye, verbal, and motor areas to enhance and clarify research focus. Stakeholders proposed that the use of basic and state-of-the-art tools and technology in the quantification and qualification of injuries, including Department of Defense (DOD)-specific injury and across the TBI spectrum, would be highly beneficial. Stakeholders also appreciated the use of U.S. Food and Drug Administration (FDA)-approved tools and the Glasgow Coma Scale (GCS) to aid in diagnosis and prognosis of mild, moderate, and severe conditions. Stakeholders then discussed neurodegenerative exposure and chronic traumatic encephalopathy (CTE), identifying gaps in understanding the population that exhibits resilience and those who succumb to neurodegenerative decline.

Next, stakeholders discussed TBI comorbidities and secondary insults, noting challenges in treatment adherence and behavioral issues that arise, or coexist, with TBI. They emphasized the importance of documenting outcomes observations as directly or indirectly related to TBI. Stakeholders also identified risk communication as a gap. They noted that other modifying factors impede risk categorization for some patients and clustering of risk factors overall. Stakeholders suggested that multimodal biomarkers as well as risk communication tools were required to assess the contributions of various factors, such as pre-injury, injury, comorbidities and complications, to the ultimate characterization of a TBI.

Finally, stakeholders discussed long-term outcomes as an additional gap for TBI research and care. They identified the prevention of cumulative injuries to the Warfighter as a major component of these efforts, suggesting that historical efforts of prevention were inadequate and should be challenged. As with earlier discussions, stakeholders proposed that multimodal biomarkers for early detection of comorbidities, neurodegeneration, and other factors leading to chronic complications from TBI should also be considered.

ii. Screening/Prognosis/Diagnosis – Differences Between Civilian and Military TBI (and Within Different Types of Military TBI)

Stakeholders first identified insufficient neurocognitive assessments as a gap. They proposed that modern technologies for dynamic testing could be leveraged in this area, and that solutions

for improved neurocognitive testing need not be developed solely by the brain research community. Stakeholders also discussed the role that federal and state regulations play in certain institutions as a barrier to research and care. They identified institutional cultures as another barrier negatively impacting neurocognitive assessments due to unequal accessibility across groups. Stakeholders next identified multimodal characterization tools as a gap. They noted that providers did not utilize the same characterization tools for TBI, leading to poor standardization, sensitivity, specificity, and stratification of TBIs and patients. Stakeholders further proposed integrating the plethora of diagnostic devices and standardizing the use of an appropriate tool per the level of care needed per TBI and patient. They noted that such standardization efforts should incorporate regulatory considerations, such as FDA requirements.

As in the previous session, stakeholders identified the lack of objective diagnostic and prognostic biomarkers as a gap to predicting long-term impact of TBI and guiding clinical pathways. They further noted that there was not a clinical trial pipeline for continuous discovery and validation of leading biomarker candidates. Thus, stakeholders proposed that a translational pathway was needed to move the field toward a point-of-care solution. They also suggested the creation and maintenance of a highly collaborative, open-science ecosystem as a mechanism for advancing TBI research and care.

Stakeholders then discussed caregiver involvement in the TBI screening and diagnosis process. They noted that often, caregivers were not being effectively employed and educated in the care and support of TBI patients. Stakeholders proposed that informing and engaging caregivers in the screening and diagnosis process would improve care compliance and alleviate other TBI-related stress and symptoms for both the TBI patient and their caregivers. They suggested that a systems-wide approach incorporating the family environment and psychosocial support be adopted for TBI management and recovery.

Stakeholders additionally discussed issues associated with TBI screening in severe polytrauma. They noted a paucity of trauma care-based early diagnostics for these patients. They also suggested that clinical, demographic, community, and societal factors influenced response to care and should be taken into account.

iii. Interventions (Development) Addressing Both Acute and Chronic Care

Stakeholders began their discussion by focusing on drug interventions. They noted that more often than not, drug development efforts focused on alleviating symptoms rather than addressing the underlying TBI. Stakeholders also suggested that there were not enough studies comparing outcomes across single time points and multiple recovery trajectories. They suggested that platform trials offered a mechanism for evaluating many different drugs with continuous, consistent outcomes measures. Additionally, stakeholders noted that application of biomarkers in clinical drug design as secondary endpoints or for trial enrichment/stratification could address gaps in conducting clinical trials for TBI interventions. They also suggested that standardized, evidence-based criteria should be enhanced to better inform the intended population of a particular trial or intervention. Regarding device-based interventions, stakeholders recommended coordinating with the FDA's Digital Health Center of Excellence to address problems with availability, cost, and standardization of tools and interventions to be evaluated in randomized controlled trials. Additionally, they suggested that new clinical trial designs are needed to

validate, repurpose, and deploy TBI-focused devices and technologies at scale. Stakeholders advocated for comparing and contrasting device and pharmaceuticals designed as TBI interventions.

Next, the stakeholders examined rehabilitation and supportive services. They noted that standardization of the documentation of services, not necessarily the services themselves, was a gap in this area. Stakeholders also suggested that collaborative work with psychological health professionals, including studies that evaluate TBI and associated polytrauma, would address additional gaps in TBI care. They noted that heterogeneity of TBI inclusive of behavioral health was not fully incorporated into systems of care. Further, they proposed that research funding and investments in capable information technology systems would be essential to advancing services research. As in the other TBI sessions, they noted that identifying objective markers could address the heterogeneity of TBI phenotypes and be used for predicting outcomes or personalizing care. As with research efforts, stakeholders suggested that interdisciplinary efforts be adopted within systems of TBI care. They proposed that such models could tailor the resources required for care of each individual. Stakeholders also highlighted the importance of implementation science in these efforts. They identified nutrition, diet modification, and prevention treatment as potential intervention fields that could be evaluated and implemented to manage TBI care.

Stakeholders then discussed developing common data elements (CDEs) to bridge gaps between preclinical and clinical research through to delivery of care. They noted that such CDEs could address bi-directional challenges with translational goals and promote adoption of treatments to benefit the Warfighter. Stakeholders specifically lamented a poor understanding of how systems of care affect the efficacy of clinical trials. To address this gap, stakeholders suggested that adaptive trials could be used to the common benefit of clinical studies addressing civilian and military populations. Stakeholders also noted that that large animal models should employ the same statistical rigor applied to human studies to ensure translation of findings.

iv. Rehabilitation and Return to Duty (RTD)

Stakeholders noted that a small amount of success had been achieved in determining trajectories of long-term TBI outcomes. Specifically, model TBI systems revealed multiple pathways of acute and chronic recovery and that subsets of patients suffered worse or significantly worse outcomes than others. Stakeholders asserted that dose-response curves for various rehabilitation strategies and correlations with specific military functions were unknown. They proposed the use of biomarkers to identify the trajectories of long-term outcomes, including more deleterious outcomes, and the long-term effects of brain injury during recovery. Additionally, they suggested that predictors for acute and post-acute phases of recovery would be different and should be distinguished. Stakeholders also identified gaps in understanding phenotypes as they related to acute and long-term recovery for TBIs of all severities.

Stakeholders identified a gap in devices and tools for post-acute treatment interventions and translation of research to practice. They noted that algorithms and overarching strategies applicable to the topic areas and gaps previously discussed could also inform RTD decisions. Stakeholders acknowledged that some tools had been developed for rehabilitation and thus would be more advanced than those developed for acute or post-acute care. They also identified

an opportunity for advances in post-rehabilitation military medicine to translate to civilian care. Stakeholders called attention to the importance of being able to establish when chronic disease models for recovery should be applied. They also commented on the importance of endophenotype development and the use of existing datasets for refinement.

Finally, stakeholders discussed decision support tools and relevant technologies to support return to activity decisions, including RTD for the Warfighter and return to work/school/play for civilians. They proposed that future capabilities should be use functional thresholds to determine an individual's fitness for return to activity. Stakeholders also hypothesized a hierarchical model to conceptualize a patient's specific disease state, which would then inform therapy for optimal efficacy. Considerations for this model included patient and family/caregiver input regarding intervention implementation. For Service Members, stakeholders identified inadequate feedback loops with military commanders at the nascent stage and poor usage of existing datasets to make informed RTD decisions. As discussed in other sessions, stakeholders noted that platform designs could adapt to many environments and offer a cost- and time-effective strategy to achieve solutions in decision support.

C. Psychological Health Breakout Sessions

i. Suicide Prevention

The discussion of lethal means safety focused on both the messages and the messengers that can most effectively discuss safe firearm storage for preventing suicide. Additionally, messages regarding firearms safety would be differentially received from different messengers. Stakeholders agreed that, while clinician and public health messaging was important, the incorporation of specific messengers, such as peers, other gun owners, other military leaders, and gun rights organizations like the National Rifle Association (NRA), were essential to reaching as many people as possible. They also noted a significant gap in understanding how to personalize firearm safety messaging and how to leverage motivational decision-making models to improve message effectiveness. Furthermore, firearms safety was identified as related to other safety concerns within the military and wider communities, including but not limited to domestic violence and interpersonal violence. Stakeholders discussed this gap as an opportunity to tailor messaging to reduce suicide attempts as well as other instances of violence. Additional considerations included alternative suicide prevention means and safety messaging for those stationed outside of the continental U.S. (OCONUS), where firearms access may be limited.

Next, stakeholders noted a gap in the ability to reach Service Members at risk of suicide prior to an attempt and discussed difficulties identifying those at the highest risk. Stakeholders acknowledged that suicide attempts using firearms more often result in death than by other means, thus these target populations require identification before acting on suicidal thoughts or ideation. Specifically regarding Service Members, stakeholders identified possible delays in seeking help for suicidal thoughts or ideation due to concerns about impacts on their careers as a barrier to reaching this population. Vertical relationships and institutional stressors related to military Service were also discussed as important considerations for reducing overall suicide risk for Service Members. Stakeholders next identified the three-month period following a suicide attempt as the highest risk period for a successful secondary attempt. They proposed that new ideas were needed to optimize clinician interactions with patients during subsequent, required

follow-ups, noting that these appointments often served simply to assess a need for re-hospitalization. Instead, follow-up visits could be used as an opportunity to reduce overall suicide risk if properly leveraged, although specific activities or modalities to be completed during these appointments was noted as a gap.

Additionally, stakeholders acknowledged that Service Members returning to a unit after a suicide attempt reported feeling socially isolated. They noted that reduced social connectedness upon return to the workforce, along with a lack of understanding how peers and unit leadership can best assist those returning to work, contributed to increased suicide risk in the months following an attempt. Thus, helping Service Members re-integrate socially, both at work and in their personal lives, emerged as an essential part of the framework for suicide prevention. Stakeholders also considered that increasing social connectedness for all Service Members could prevent suicide attempts due to loneliness or social isolation. Finally, stakeholders agreed that all of these strategies and gaps need to be adapted to, or alternatives developed for, a multi-domain operations (MDO) environment. This included strategies for suicide prevention while in theatre or in remote locations where access to mental health care may be limited.

ii. Prevention, Diagnosis, and Treatment of PTSD, Adjustment Disorders, Depression, and other Mental Health Disorders

Stakeholders largely agreed that there was a lack of validated rapid assessment tools for diagnosis of mental health disorders. They noted that tools and assessments were needed for accurate diagnoses and for evaluation of fitness for RTD or return to combat. Improvements in rapid diagnosis were deemed particularly important in an MDO environment, where it was expected that Service Members would be unable to be rapidly evacuated and therefore, care must be accessed in theatre. Stakeholders suggested that wearable technology, artificial intelligence, and software programs could improve the effectiveness of assessment tools and should be considered when developing new evaluation tools. They further emphasized that clinicians needed tools to rapidly and accurately differentiate between differing, complex mental health disorders to provide the quickest and most effective pharmacological or psychosocial treatment(s).

Next, embedded behavioral health (EBH) services emerged as an important piece of the mental health framework; however, stakeholders noted significant gaps in evaluating the effectiveness of these services and the mechanisms behind successful EBH services. Specifically, they lamented the poor understanding of adjustment disorders, the most commonly diagnosed mental health disorders in the military, and suggested that new insights would be required to develop treatments for these disorders. When discussing PTSD, stakeholders emphasized the importance of delivering interventions before deployment, as many Service Members seek treatment about trauma experienced in a previous deployment when they begin a new deployment, which triggers the onset of PTSD symptoms. They proposed that making effective interventions available after large-scale traumatic events, including combat deployments, was essential to some Service Members, but noted that many would recover with no intervention. This dichotomy could lead to inaccurate effectiveness data when evaluating a new approach; thus, stakeholders recommended that studies be designed so that interventions are not started until approximately 30 days after the trauma and only include the population still indicating risk for a mental health disorder.

Overall, stakeholders agreed that performing research on Service Members was fraught with regulatory, temporal, and location challenges, sometimes rendering essential studies completely infeasible. The need to identify accurate civilian analog models was proposed as a mechanism for accelerating research to be ultimately implemented in military environments. Additionally, stakeholders noted that Service Members often enter the military with significant risk factors for mental illness, including but not limited to sexual abuse, domestic violence, and other forms of interpersonal violence. They suggested that these risk factors showed the interconnectedness of themes across the psychological health landscape and the need to identify at-risk Service Members for preventative interventions before they develop a mental health disorder.

iii. Sexual Assault and Harassment Prevention and Recovery

Stakeholders noted that Service Members could enter the military with multiple risk factors for sexual assault, including previous sexual violence as well as demographic risk factors (i.e., people of color, indigenous populations, LGBTQ persons, and those aged 18-24 years). They identified that these risk factors could also intersect and overlap with other mental health disorders, including PTSD. Overall, stakeholders suggested that identifying at-risk populations could offer the opportunity to provide them with precise prevention education and support, emphasizing that these efforts must be achieved without increasing stigma. For all sexual assault reduction strategies, they identified a need for accurate assessments of short- and long-term effectiveness.

Next, cultural alcohol norms emerged as an important consideration, as alcohol dependence and episodic binge drinking was highly related to sexual harassment and assault. Stakeholders reported that current literature highlighted a gap in effective interventions for poor drinking habits, which impacts sexual assault risk in the military population. Stakeholders identified military norms and hypermasculinity as additional cultural elements intertwined with sexual assault prevention. For example, they noted that Service Members can be encouraged to embrace a "warrior ethos" that may contribute to an environment where sexual harassment and assault are tolerated.

Additionally, stakeholders identified a lack of studies on sexual assault perpetrators, partly because those studies face regulatory concerns over study participant privacy. Previous studies showed that sexual assault perpetrators almost always had a history of sexual harassment, but that many perpetrators of only harassment never escalated to assault. Thus, stakeholders suggested that studies of perpetrators could identify additional risk factors for the progression to perpetration. They proposed that determining the factor or elements that lead to escalation could inform prevention practices. On the other hand, stakeholders identified a need for re-integration strategies targeting victimized Service Members returning to a unit after an incident. They suggested that re-integration strategies could include other unit members who might also need support following a traumatic event. Finally, stakeholders reported a gap in bystander education and how to reduce barriers and stigma for reporting sexual harassment and assault. They suggested that identifying effective messages for bystanders could encourage a safer overall environment for Service Members.

iv. Resilience Building and Family Well-Being

Stakeholders focused on two overarching gaps: evaluating the definition of resilience as well as the questions being asked within family well-being research to determine if the questions and definition served the mission effectively. They noted that Service Members were not building resilience in a vacuum, but toward specific issues and stressors, and that distinction may require translation to improve treatment and prevention strategies. They further determined that resilience and family well-being were matrix issues and should be addressed alongside other concerns, such as child neglect, substance abuse, other forms of abuse, and interpersonal violence.

Throughout the discussion, stakeholders identified the threat of career and financial consequences as a substantial barrier to help-seeking for family or mental health challenges by either the Service Member or someone in their family. Stakeholders also identified a need for a framework whereby people are shielded from some potential consequences to encourage help-seeking earlier in the progression of a mental health disorder or family challenge. Additionally, seeking help earlier could contribute to resilience and overall well-being. Stakeholders identified a lack of integration of mental health and other resilience resources available outside the DOD. Further, they noted that building community ties in garrison could improve accessibility of non-DOD resources for Service Members and increase their awareness of available options. In this vein, new market strategies were identified as needed to increase participation in resiliency and well-being programming. Stakeholders appreciated that families who have experienced multiple traumatic combat deployments could find traditional marketing aimed at making them "more resilient" insulting. Thus, they suggested conducting more research into effective messaging for resiliency programming within the military culture and at different points throughout an individual's career, as well as for messaging targeted toward families.

Next, stakeholders identified substance abuse as an overarching concern, noting that detrimental alcohol habits were still widely accepted and even encouraged in both military and American culture. They proposed that research is needed for changing cultural alcohol norms with the goal of teaching Service Members and their family healthier coping mechanisms. As with help-seeking, stakeholders noted that career and financial consequences could deter reporting of alcohol abuse or related substance abuse offenses, which could allow the issues to persist. Finally, stakeholders agreed that resilience and family well-being were inextricably linked to other psychological health concerns including but not limited to suicide, PTSD, sexual assault, and interpersonal violence.

D. Concurrent Management of PH and TBI Research

Stakeholders noted that keeping PH and TBI research separated could have detrimental impacts on research quality, as new ideas from diverse perspectives might spark innovation in either field. They specifically emphasized "cross-pollination" opportunities for diverse experts to discuss topics outside of their expertise. Further, the stakeholders agreed that TBI and PH connect in numerous ways for Service Members and their families outside of these superficial categorizations. They suggested that complex statistical models were needed to identify mechanisms for treatment modalities, given the intersectionality of TBI and PH symptoms. Further, the overlap of symptoms within different disorders also presented an opportunity to

develop treatment approaches for a broad range of disorders by focusing on common symptomatology and comorbidities. However, the stakeholders also noted that the high degree of overlap in symptoms and diagnosis of PH and TBI presented a gap in the ability to distinguish which symptoms come from which particular injury or issue. Thus, they proposed a potential need for precision medicine approaches to determine the source of a specific symptom and to develop targeted interventions.

Stakeholders acknowledged that primary care physicians were often the first and only point of contact for the majority of Service Members who experience TBI and PH. Thus, they proposed strengthening the primary care system for TBI and PH assessments. Family and caregiver involvement, and thus research, also emerged as an essential part of the treatment and prevention framework for both TBI and PH. Stakeholders identified other common risk factors for severe TBI and PH issues, including financial concerns, legal concerns, family unrest, and social disconnection. Stakeholders emphasized that the TBIPHRP should allow for and encourage research proposals that address both PH and TBI concerns simultaneously to maximize the impact of the research and outcomes.

E. Final Topics and Gaps

After each of the breakout sessions, stakeholders agreed upon the following topics and gaps.

i. TBI

a) Etiology, Pathology, and Prevention

- Classification of Injury (Etiology, Severity, Dose Effects, Secondary Injury, Pathology)
    - Vet standard system of classification for acute injury and chronic effects that includes the use of basic and state-of-the-art tools/technology to quantify and qualify injury, across the spectrum of TBI, including DOD-specific injury
    - Identify clinical endophenotypes and biomarker profiles that will allow testing of clinical management interventions
    - Leverage extant technology and knowledge to build a more clinically relevant understanding of cerebral edema, axonopathy, and other key secondary mechanisms that can promote primary/secondary prevention and amelioration and enhanced management approaches
- Role of Pre-Injury Factors, Complications, Comorbidities, and Secondary Insults
    - Risk communication tools are needed to focus on what injury and secondary difficulties mean and how they impact outcomes
    - Understanding interactions across pre-injury factors, injury factors, comorbidities, and complications and how treatments can be optimized in the face of these issues both acutely and chronically

- Multi-modal biomarker application and new discovery to expand the ability to classify objectively, monitor recovery, assess novel interventions, support outcome measurement, and anticipate early decline or comorbidities
- Risk communication tools are needed to focus on meaning and significance of factors (pre-injury, injury, complication, comorbidities) in the acute and chronic phases as they relate to outcomes

- Long-Term Outcomes
  - How do we prevent and mitigate long-term TBI effects based on an understanding of thresholds of exposure?
  - Understanding the trajectories and pathobiology of acute and chronic recovery in terms of chronic conditions (e.g., post-traumatic epilepsy, post-traumatic headache) and neurodegeneration (e.g., dementia, Parkinson's disease) vs. neuroplasticity
  - Multi-modal use of existing and new biomarkers to enhance classification, monitor recovery, assess novel interventions, support outcome measurement, and provide early detection of decline/comorbidities and neurodegeneration
  - Risk communication tools are needed to focus on what factors impact the development and effects of chronic complications, neuroplasticity, and degeneration

b) Screening/Prognosis/Diagnosis – Differences Between Civilian and Military TBI (and Within Different Types of Military TBI)

- Neurocognitive Assessments (or other screening capabilities)/Screening Tools Evaluation
  - Consensus on neurocognitive assessments and evaluation of new technologies/techniques
  - Qualifications of those doing the assessment
  - Connection between initial diagnosis of TBI and later diagnosis (residuals)
  - Screening capability for clinical or rehab provider that supports specific cultural and access needs and incorporates latest state of the science
  - There is no way to optimally combine/integrate different assessments
- Objective Biomarkers of TBI for Mild/Moderate and Severe
  - Lack of diagnostic and prognostic markers that predict long-term impact (neuroimaging, fluid, etc.) for mild TBI
  - Leading candidate markers require refinement/validation
  - Lack of clinical trials pipeline for leading TBI biomarker candidates

- Caregiver Involvement
    - Caregivers are not being effectively engaged and educated to support those impacted by TBI (including culturally appropriate approaches)
- TBI Screening in Severe Polytrauma
    - Lack of early diagnostics for TBI based on trauma care higher priorities
    - Pre-existing determinants that may influence response to clinical care

c) Interventions (Development) Addressing Both Acute and Chronic Care

- Drug Interventions
    - There are not enough disease-modifying TBI drugs in the pipeline (Discovery)
    - There are not enough treatment trials that are focusing on symptoms (Repurposed)
    - There are not enough studies incorporating trajectories of outcome (versus single time point)
    - Missing large animal models for disease modifying drugs
- Rehabilitation and Supportive Services
    - There is little standardization in services that are applied (standardized documentation and delivery); e.g., not all cognitive rehab is the same
    - There is little research into the effectiveness and validation of services applied
    - It is unclear how [settings, provider] should deliver these services and what their qualifications should be
- System of Care (comparative efficacy)
    - There is no evidence that one system of care works better than another
    - Implementation science on interventions in TBI systems of care
- Devices and Technologies
    - Validation approaches for treatment devices are insufficient (e.g., prescription digital therapeutics)
    - The use of devices and technologies to measure response to treatment
    - Not enough validated devices are deployed at scale (implementation science)

d) Rehabilitation and Return to Duty

- Post-Acute Treatment Interventions and Translation of Research to Practice
    - Rehab-based treatments, technologies, and education; their dosage and delivery; and their uptake to service delivery (with stakeholder input and involvement)
    - Understanding secondary effects of treatments (with stakeholder input and involvement)

- Development and implementation of Chronic Disease Management Model (with stakeholder input and involvement)

- Trajectories of Long-Term Outcomes
  - Understanding the long-term effects of brain injuries as they relate to recovery (for all severities of injury), including the role of chronic comorbidities
  - Biomarkers of treatment efficacy (e.g., blood, saliva, neurophysiology, imaging) (for all severities of injury)
  - Phenotypes as they relate to acute and long-term recovery (for all severities of injury)
  - Dose response curve is unknown
- Decision Support Tools and Relevant Technologies to Support RTD
  - Standards of performance for objective assessment of RTD/transition
  - Understanding of the impact of occupational specialty and individual factors on performance and readiness for return to activity (e.g., RTD, work, driving)
  - With input from relevant stakeholders, need to define what constitutes successful return to activity (e.g., RTD, work, play, school) and what treatments, tools, and technologies are needed to support return to activity

ii. Psychological Health

a) Suicide Prevention

- Lethal Means Safety with an Emphasis on Firearms
  - Are lethal means safety interventions effective in increasing safety behaviors and/or reducing suicide-related outcomes associated with firearms?
  - Can lethal means safety interventions be effectively implemented in ways that are culturally acceptable to commanders and Service Members?
- Promoting Connectedness Among Individuals and Within Communities Through Modeling Peer Norms and Enhancing Community Engagement May Protect Against Suicide
  - Need to develop effective Peer Norm Programs to normalize protective factors for suicide such as help-seeking and promoting peer connectedness. Such programs may leverage leadership qualities and social influence of peers to shift group-level beliefs and promote positive social and behavioral change.
  - Need to develop effective Community Engagement Approaches for the military that foster connectedness through participation in community, religious, and physical activities. These activities provide community-wide connectedness, resulting in a number of improved psychosocial outcomes.

- Implementation of Cognitive Behavioral Strategies for Suicide Risk Reduction
    - Which components of safety and crisis response planning interventions contribute most directly to reduction in risk for suicidal thoughts and behaviors and can be readily implemented in DOD?
    - How are cognitive behavioral therapies for suicide behaviors being effectively trained, implemented, and disseminated in DOD?

b) Prevention, Diagnosis, and Treatment of PTSD, Adjustment Disorders, Depression, and Other Mental Health Disorders

- Screening and Prevention: Effective Screening Tools and Prevention Interventions for PH Issues
    - Lack of validated objective screening tools for PTSD, and military-relevant screening tools for Adjustment Disorders (AdjDs) and Acute Stress Reactions (ASRs)
    - Lack knowledge of trajectories of AdjDs as an outcome of stressors, and effective prevention interventions for addressing AdjDs and ASRs
    - Pharmacologic interventions to prevent ASRs and PTSD
- Treatment: Interventions That Can Support Prolonged Field Care of Psychiatric Casualties, Especially in Service-Specific Environments
    - Lack of validated PH assessments and interventions for use in a prolonged care setting
    - Lack of training on how to enable PH intervention at the unit/team/peer level
- Implementation: Need for Improved Implementation and Understanding of the Outcomes of EBH Models Across the Services That are Aimed at Early Detection and Intervention to Prevent PH Casualties
    - Lack of rapid assessments and treatments for PTSD, severe AdjDs, and ASRs to restore Service Members to duty where no medic or BH officer is available
    - Long-term outcomes of Service Members who have received EBH interventions are not well understood

c) Sexual Assault and Harassment Prevention and Recovery

- Assessment of Factors Influencing Sexual Assault Prevention and Response
    - Development of an empirically validated construct inclusive of culture, climate, and continuum of harm, and identifying how organizational-level constructs influence interpersonal and individual conditions, choices, and behaviors
    - Data from influencers, bystanders, and perpetrators
    - Valid indicators of short and intermediate sexual assault prevention and response outcomes for use in prevention and response planning, programs, and policy evaluation

- Development and Evaluation of Sexual Assault Prevention Activities
    - Development and evaluation of prevention policies, programs, and practices. Specifically, novel methodologies, cross-cutting approaches, leadership tools, and tailored/selected prevention
    - Adaptation of existing evidence-based and evidence-informed prevention activities for the military context
- Institutional Response to Sexual Assault
    - Understanding of processes of shame, stigma, and institutional betrayal in the victim experience as well as for the unit and evaluating approaches to mitigate these experiences
    - Understanding of barriers to reporting and factors that contribute to retaliation within the unit, support network, and command levels. Evaluation of approaches to mitigate barriers and prevent retaliation
    - Policies, procedures, and practices that contribute to attrition or successful reintegration of victims

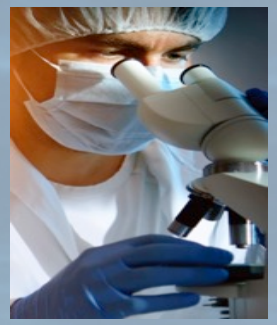
d) Resilience Building and Family Well-Being

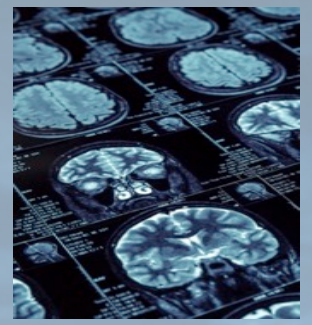
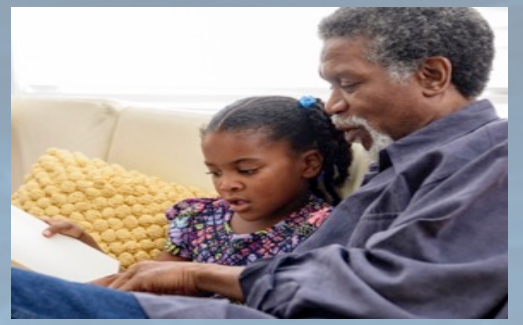
- Service Member and Small Team Resilience, Readiness
    - Capacity to optimize and enhance resilience to military and life stressors (incorporating/integrating family)
    - Effective ways to prepare Service Members and units for missions and to help reset between deployments within the Sustainable Readiness Model
    - Effective ways to remove barriers to help-seeking and to change culture and policy around support, proactively addressing accumulation of risk
- Family Readiness/Resilience (Families as they exist, not how we define them)
    - Effective solutions to support relationships, parenting, preparedness, readiness, and resilience to military and life stressors and adjustment
    - There is inadequate preparation and skill development for families to manage military demands and potential secondary exposure
    - Efficient and effective ways (including policies) to empower families and connect them with tailored support and resources
- Alcohol and Substance Use
    - Effective solutions for addressing specific elements of military culture identified as being associated with increases in alcohol use, especially impacts of leadership attitudes, group characteristics, and group identification factors
    - Solutions to provide and incentivize positive options and substitutes for alcohol and substance use
    - Effective ways to remove barriers to help-seeking

Enclosure 1
Overview of CDMRP

Overview of the Congressionally Directed Medical Research Programs

Dwayne Taliaferro, Ph.D.
TBIPHRP Program Manager

The views expressed in this presentation are those of the author and may not reflect the official policy or position of the Department of the Army, Department of Defense, or the U.S. Government

CDMRP
Department of Defense

WHO is the CDMRP?

- Department of Defense
  - Department of the Army
    - Army Futures Command
      - U.S. Army Medical Research and Development Command (USAMRDC)
        - Congressionally Directed Medical Research Programs

CDMRP Department of Defense

History

- **In 1992, grassroots efforts heightened political awareness of breast cancer**
- **Congress appropriated $210M to the FY93 DOD budget for a new Breast Cancer Research Program (BCRP)**
- **The USAMRDC was directed to manage the BCRP**
- **The Army sought the advice of the National Academy of Medicine (previously the Institute of Medicine), which resulted in:**
  - A two-tier review process – peer and programmatic reviews
  - A new research model – incorporating consumers into program policy, investment strategy, and research focus
- **Since 1996, additional research programs and topics have been added by Congress and administratively managed by the CDMRP**

CDMRP Department of Defense

CDMRP FY21 Appropriations

Program	FY21 $M
Alcohol and Substance Abuse Disorders	$4.0
Amyotrophic Lateral Sclerosis	$40.0
Autism	$15.0
Bone Marrow Failure	$7.5
Breast Cancer	$150.0
Chronic Pain	$15.0
Combat Readiness	$10.0
Duchenne Muscular Dystrophy	$10.0
Epilepsy	$12.0
Gulf War Illness	$22.0
Hearing Restoration	$10.0
Joint Warfighter Medical	$40.0
Kidney Cancer	$50.0
Lung Cancer	$20.0
Lupus	$10.0
Melanoma	$30.0
Military Burn	$10.0
Multiple Sclerosis	$20.0

Program	FY21 $M
Neurofibromatosis	$20.0
Neurotoxin Exposure Treatment Parkinson's	$16.0
Orthotics and Prosthetics Outcomes	$15.0
Ovarian Cancer	$35.0
Pancreatic Cancer	$15.0
Peer Reviewed Alzheimer's	$15.0
Peer Reviewed Cancer (20 Topics)	$115.0
Peer Reviewed Medical (42 Topics)	$370.0
Peer Reviewed Orthopaedic	$30.0
Prostate Cancer	$110.0
Rare Cancers	$17.5
Reconstructive Transplant	$12.0
Scleroderma	$5.0
Spinal Cord Injury	$40.0
Tick-Borne Disease	$7.0
Traumatic Brain Injury and Psychological Health Research	$175.0
Tuberous Sclerosis Complex	$8.0
Vision	$20.0

TOTAL = $1.5B

Vision and Mission

Vision

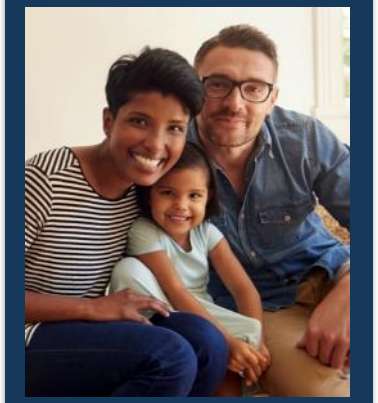
Transform healthcare for Service Members and the American public through innovative and impactful research

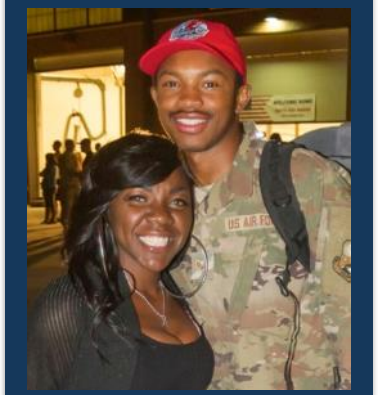
Mission

Responsibly manage collaborative research that discovers, develops, and delivers health care solutions for Service Members, Veterans, and the American public

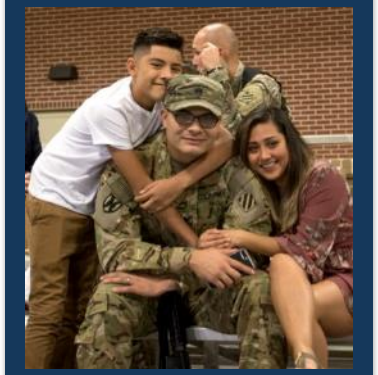
CDMRP Department of Defense

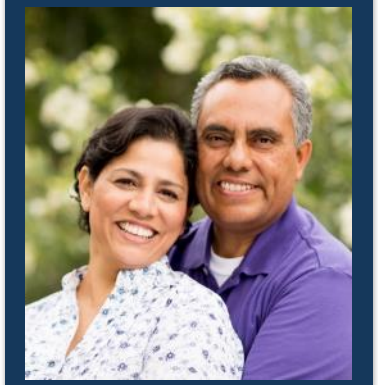
Hallmarks

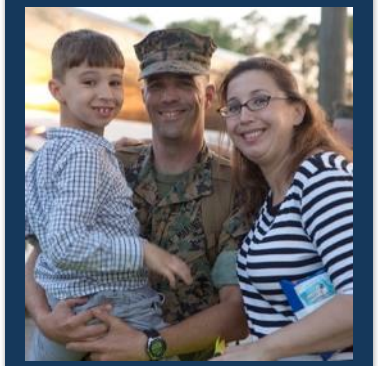




- **Targeted research funds are added to the DOD budget by Congress**
- **Funds high-impact innovative research**
- **Avoids duplication with other funding agencies and targets unfunded/unmet gaps**
- **Follows the National Academy of Medicine-recommended model for application review**
- **Consumers participate throughout the process**
- **Annually adapts each program's vision and investment strategy allowing rapid response to changing needs**
- **Funding flexibility**
  - Funds obligated up front; limited out-year budget commitments
  - No continuation funding
  - No "pay line"; funding recommendations are based on portfolio composition, adherence to intent of mechanism, and relative impact, in addition to technical merit





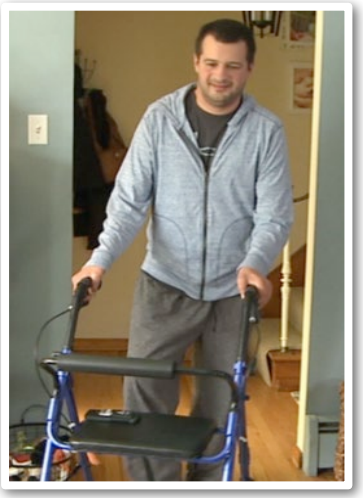


CDMRP Department of Defense

Consumers

Grassroots consumer efforts led to targeted research funding and the creation of the CDMRP. The voices and experiences of consumers play a pivotal role in the growth of CDMRP research programs.

Over 7,200 consumers representing over 1,200 organizations have served on CDMRP Peer Review and Programmatic Review panels



Unique Partnerships

CDMRP and the USAMRDC Strategic Process

Core Outcomes

Fielded Medical Knowledge

Fielded Medical Materiel

Research to produce medical knowledge

Core Programs

RESEARCH & DEVELOPMENT
Medical Research & Technology Program

DEVELOPMENT & ACQUISITION
Medical Advanced Development Program

ACQUISITION & LOGISTICS
Medical Logistics Program

CSI Programs

Congressional Special Interest (CSI) Programs

Programs directed by Congress

Outcomes

Targeted Outcomes

Additional Supported DOD Programs/Projects: Program Area Directorates/Joint Program Committees

Medical Simulation and Information Sciences

- Health Informatics Technology Research
- Medical Capabilities to Support Dispersed Operations
- Medical Simulation and Training

Combat Casualty Care

- Battlefield Resuscitation for Immediate Stabilization of Combat Causalities
- En Route Care
- Prolonged Care
- Neurotrauma

Military Infectious Diseases

- Bacterial Diseases

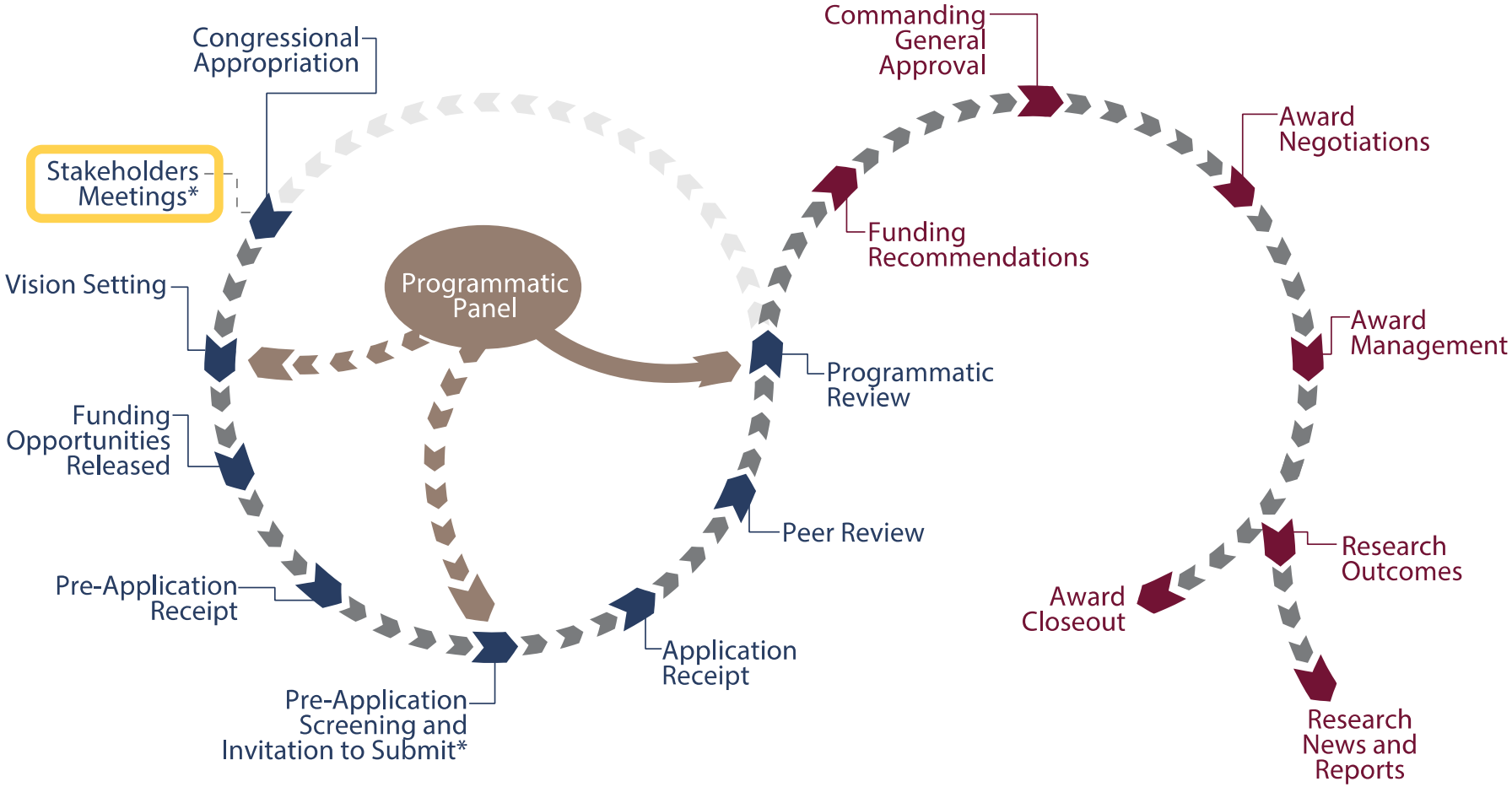
Radiation Health Effects

- Biomedical Technology for Radiation Medical Countermeasures

Military Operational Medicine

- Environmental Health and Protection
- Injury Prevention and Treatment
- Physiological Health and Performance
- Psychological Health and Resilience

Program Cycle

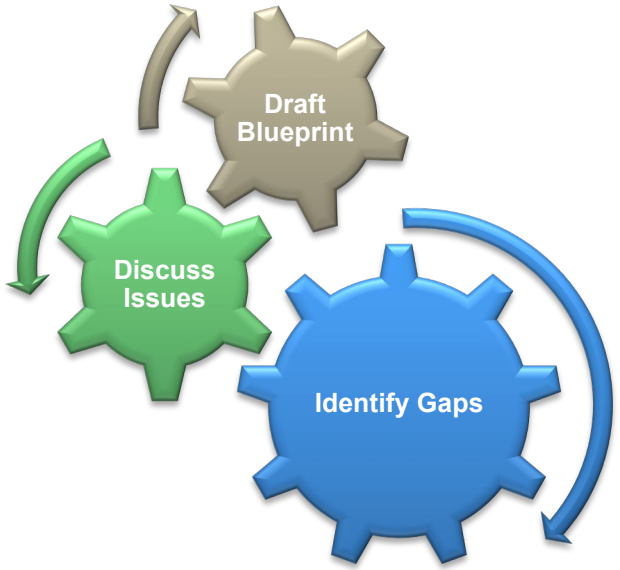


*As needed

Stakeholders Meeting

◆ Purpose and Intent

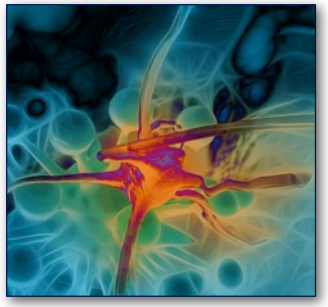
- A stakeholder is a person or group who has an interest – vested or otherwise – in an enterprise and whose support is required in order for an enterprise to be successful
  - ❖ http://searchcio.techtarget.com/definition/stakeholder
- Subject Matter Experts are brought together to discuss the knowledge gaps, research landscape, identify the outcome and product needs for patient care, and recommend a way forward toward a successful research funding program
- Build a better program → account for all voices and opinions while focusing on the outcome of improving traumatic brain injury and psychological health outcomes



Vision Setting

At Vision Setting each year, the Programmatic Panel recommends an investment strategy, considering factors such as:

- Congressional language
- Current research landscape
- Emerging technologies
- Research gaps
- Impact
- Portfolio composition



CDMRP Department of Defense

Award Mechanisms Pipeline

Research Awards

Closing gaps through innovative and impactful research

Initial Concepts	Early Ideas	Clinical/ Translational	Team Science	Clinical Trials
• Concept • Exploration-Hypothesis Development	• Idea • Synergistic Idea • Idea Development	• Translational Research • Therapeutic Development	• Clinical Trial • Pilot Clinical Trial	• Consortium • Multi-Team • Synergistic Idea • Translational Partnership

Predoctoral	Postdoctoral	Physician Scientist	New Investigator	Established Investigator

Funding for all career stages

Funding Opportunities

- **Numerous types of award mechanisms**
  - Tailored to the goals of each program
  - May vary from year to year
- **Each funding opportunity is made available through a Program Announcement (PA) or program-specific Broad Agency Announcement (BAA)**
- **Pre-announcement release**
  - CDMRP website and email blast
- **Funding opportunity postings**
  - Grants.gov (CFDA 12.420)
  - electronic Biomedical Research Application Portal (eBRAP) system
  - CDMRP website
  - FedBizOps.gov (BAAs)

CDMRP Department of Defense

Two-Tier Review Process

To develop funding recommendations that balance the most meritorious science across many disciplines and offer the highest promise to fulfill the programmatic goals set forth in the relevant Program Announcement

Peer Review

- **Criterion-based evaluation of full proposal**
- **Determination of "absolute" scientific merit**
- **Outcome: Summary Statements**
  - No standing panels; reviewers are recruited based on expertise needed
  - No contact between applicants, reviewers, and program staff

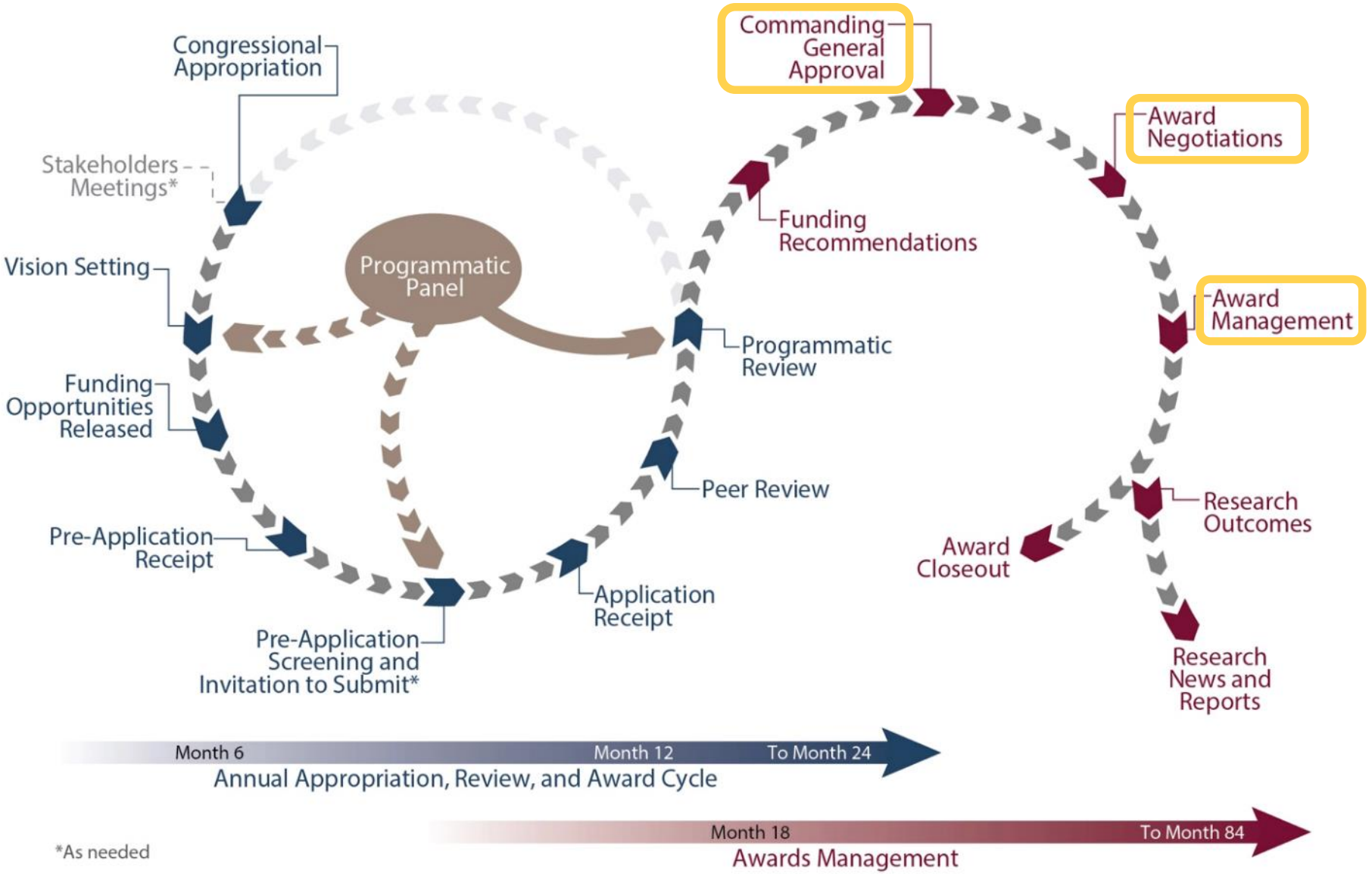
Partnership

Programmatic Review

- **Comparison among proposals of high scientific merit**
- **Determination of adherence to intent, program relevance, and potential for impact**
- **Outcome: Funding Recommendations**
  - No "pay line" (portfolio balance)
  - Funds obligated up-front; limited out-year budget commitments (but milestones imposed)
  - No continuation of funding

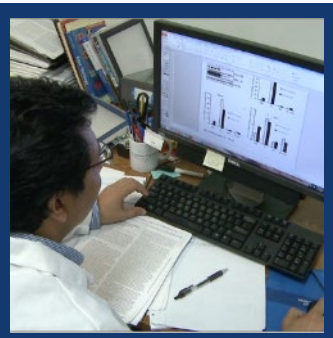
https://cdmrp.army.mil/about/2tierRevProcess

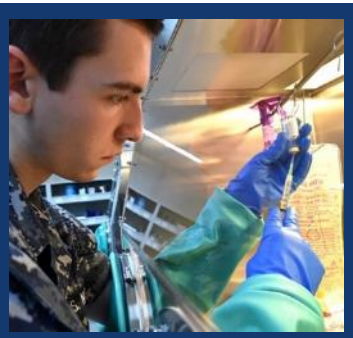
Program Cycle



For more information, please visit:

cdmrp.army.mil

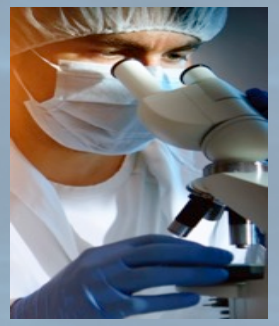


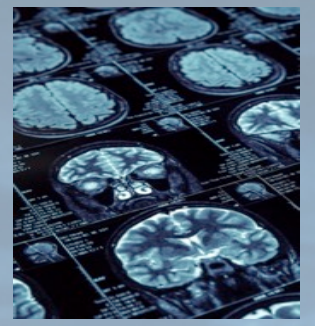
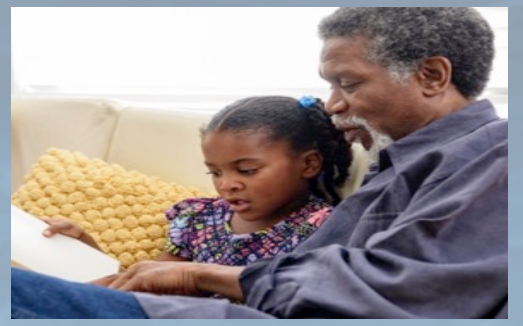



Enclosure 2
Overview the TBIPHRP Congressional Language and Request for Information

Overview of TBIPHRP Congressional Language, Research Portfolios and RFI

Dwayne Taliaferro, Ph.D.
TBIPHRP Program Manager

The views expressed in this presentation are those of the author and may not reflect the official policy or position of the Department of the Army, Department of Defense, or the U.S. Government

CDMRP
Department of Defense

Key Messages

- Congressional language provides inspiration and guidance to the Traumatic Brain Injury and Psychological Health Research Program (TBIPHRP)

- The Congressionally Directed Medical Research Programs (CDMRP) now manages the TBIPHRP appropriation

- There is a large existing investment in traumatic brain injury (TBI) and psychological health (PH) research

- Stakeholder Request for Information responses provide a snapshot of the needs from the community

- Taken together, there is opportunity for the TBIPHRP to make an impact

A Recognized Need

- Since the beginning of post-9/11 combat operations in Afghanistan and Iraq, the number of TBIs sustained and PH issues experienced by members of the U.S. Armed Forces has significantly increased

> *"Traumatic brain injury (TBI) and psychological health issues have emerged as a significant cause of death to the war fighters in Iraq and Afghanistan.*
>
> *Whether mild, moderate or severe brain injury, the level of assessment and standard of care provided to the war fighter is in need of enhancement.*
>
> *Diagnosis, treatment, and rehabilitation must be at a level to ensure the best possible outcome.*
>
> *To this end, the bill … to address all levels of brain injury and psychological health issues that servicemembers and their families have experienced during the Global War on Terror."*

--FY09 House of Representative Explanatory Statement for the Consolidated Security, Disaster Assistance, and Continuing Appropriations Act

- **FY 2007 -** Congress recognized the need and appropriated $301 million (M) for TBI and PH medical research

FY21 Congressional Language

"The Committee recognizes that traumatic brain injury (TBI), including mild-TBI and concussion, continues to be a significant health issue affecting servicemembers both in training and during combat operations....

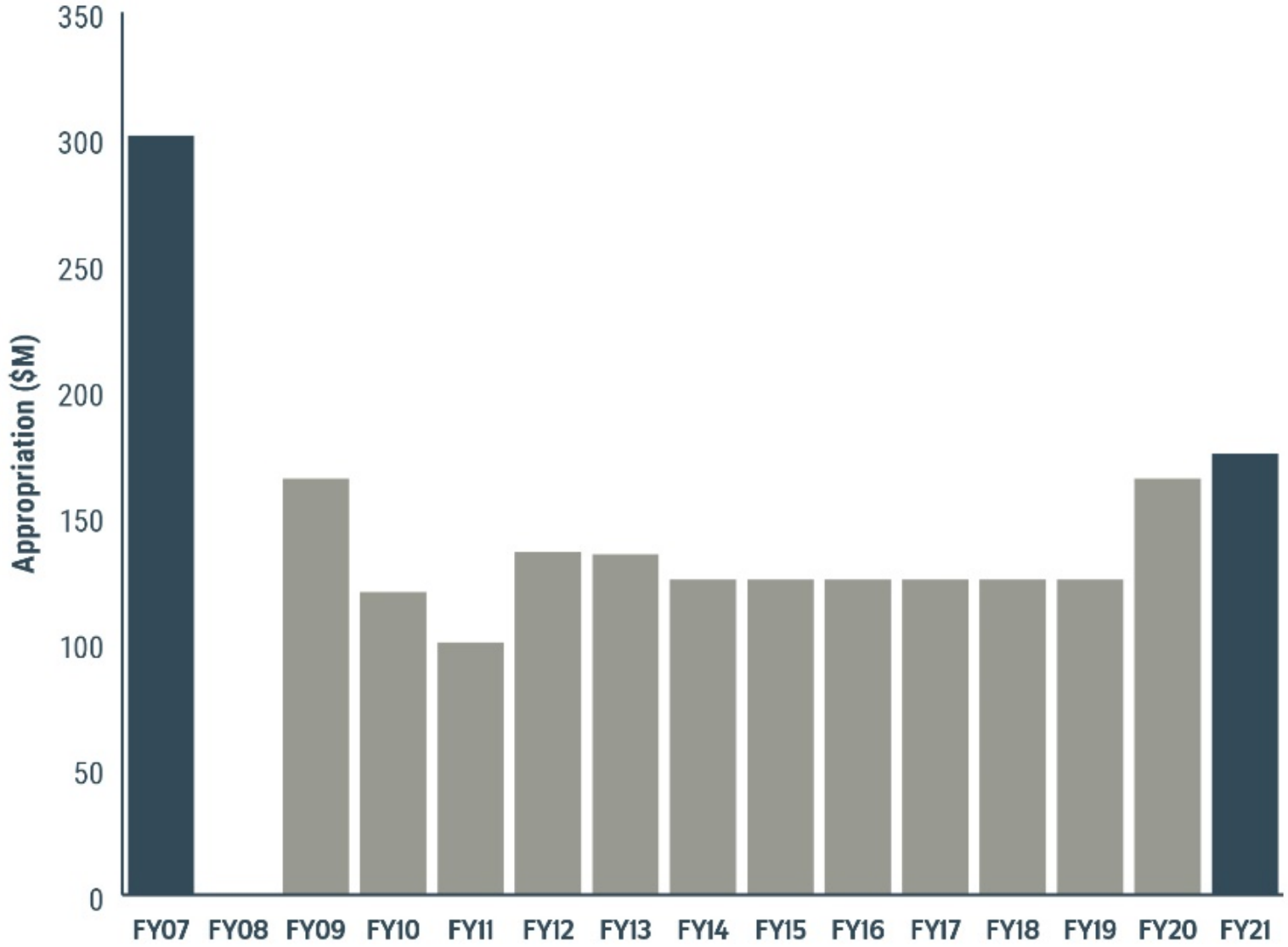
...While the Committee recommendation includes $175,000,000 to continue research on traumatic brain injury and psychological health, the Committee believes additional efforts would help advance the understanding of TBI injuries sustained by servicemembers."

--From the House Report 116-453

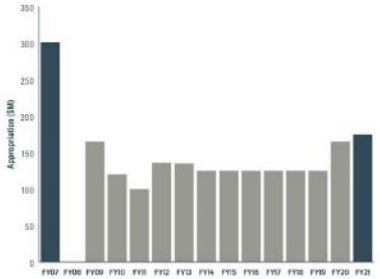
Research Areas for Consideration

- Treatments for posttraumatic stress disorder (PTSD) from sexual trauma
- TBI injury prevention
- Long-term studies of TBI
- TBI diagnostics
- TBI treatments, to include post-traumatic headache and migraine

Appropriation History



PH/TBIRP to TBIPHRP



FY07

CDMRP managed as the PH/TBIRP

FY08

No PH/TBIRP funds appropriated

FY09-20

Joint Program Committees managed as PH/TBIRP with program and award support from CDMRP as requested

FY21

CDMRP managed as the TBIPHRP

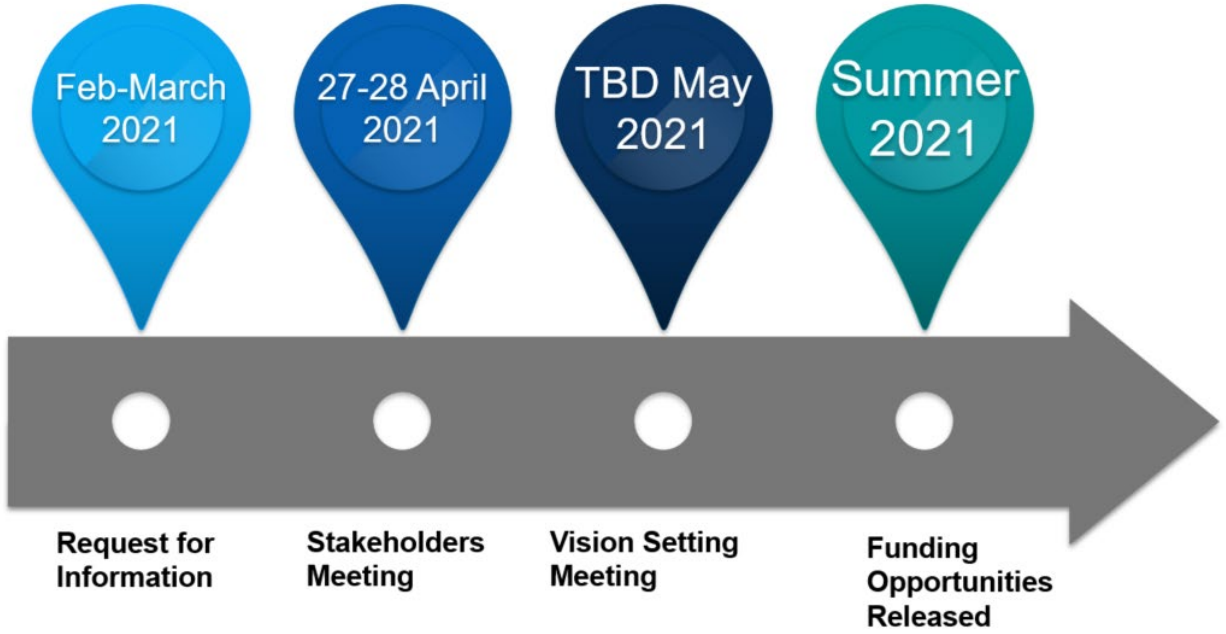
TBIPHRP Initiation

What is changing

- Program name will change from PH/TBIRP to TBIPHRP
- Follow CDMRP management processes
- Strategic guidance will be provided by a **Programmatic Panel** with representation from government, academia, consumers, industry, and other specialty areas as applicable

What is not changing

- Focus on the yearly congressional guidance and research for Service Members and public benefit
- Inclusion of the Joint Program Committees, tri-Service, interagency partners, consumers, and scientific community



Stakeholders Meeting

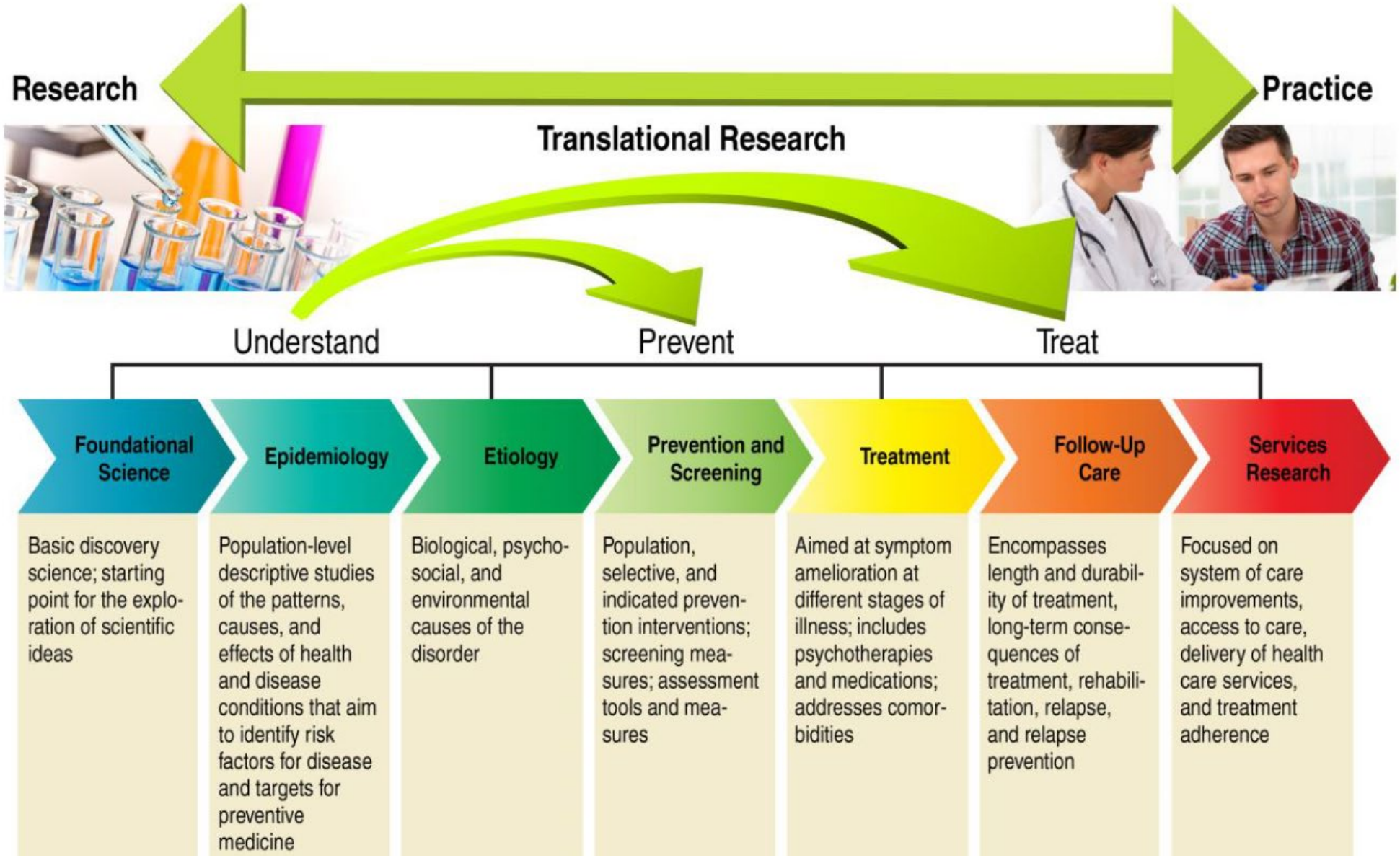
Meeting Activities

- Overview presentations from various organizations conducting or participating in TBI and PH research and care
- Participate in focused breakout sessions to discuss current states, desired future states, and gaps in specific areas of TBI and PH research and care
- Identify research gaps in specific areas of TBI and PH research
- Discuss concurrent management strategies for TBI and PH research endeavors

Outcomes

- Prioritized gaps for TBI and PH research and care to inform programmatic directions and future funding opportunities
  - *All identified gaps and priorities are pre-decisional and may not necessarily reflect the final focus of FY21 TBIPHRP funding opportunities.*

National Research Action Plan Provides a Framework



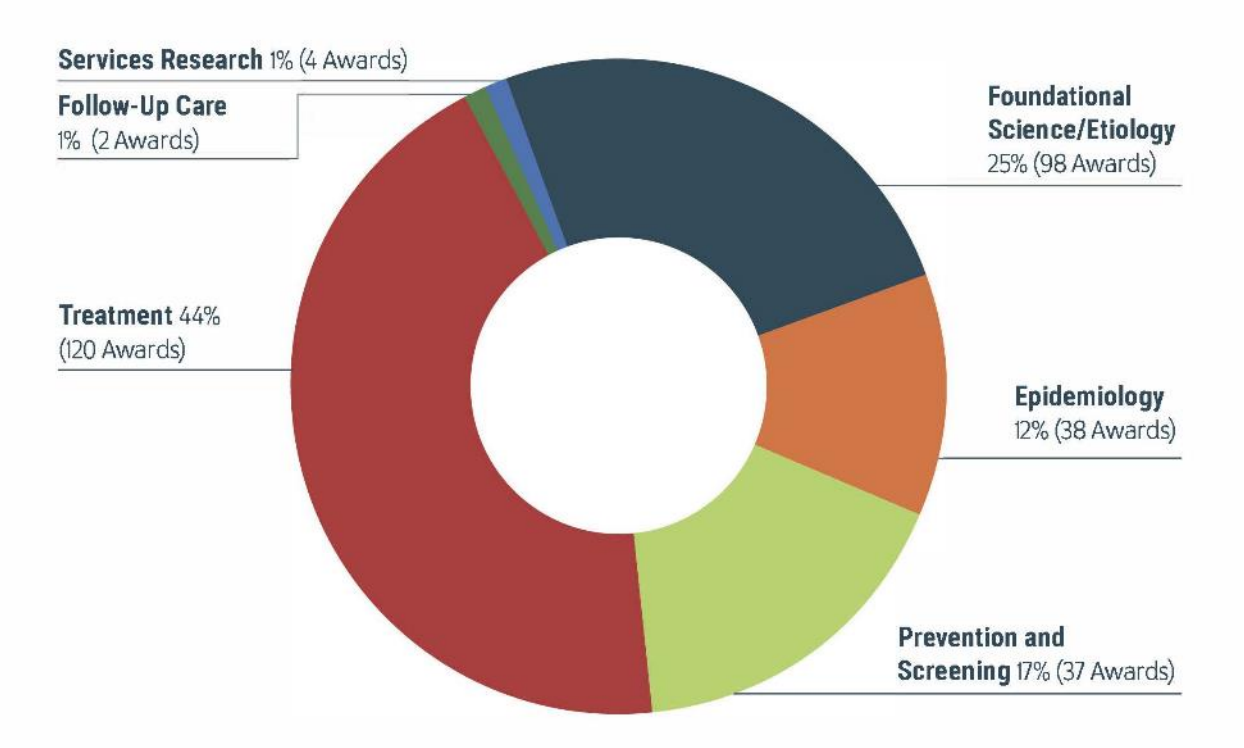
Relevant CDMRP-Managed Research

- **Pages 18-20, 28-29 in Stakeholders Book**
- **Snapshot of CDMRP-managed awards with relevance to TBIPHRP**
  - FY14-FY19
  - Includes relevant CDMRP-managed independent programs and CDMRP-managed awards on the behalf of the Joint Program Committees (e.g., Combat Casualty Care or Military Operational Medicine): $765M
- **Key stats**
  - $295M, 153 awards PH
  - $470M, 299 awards TBI

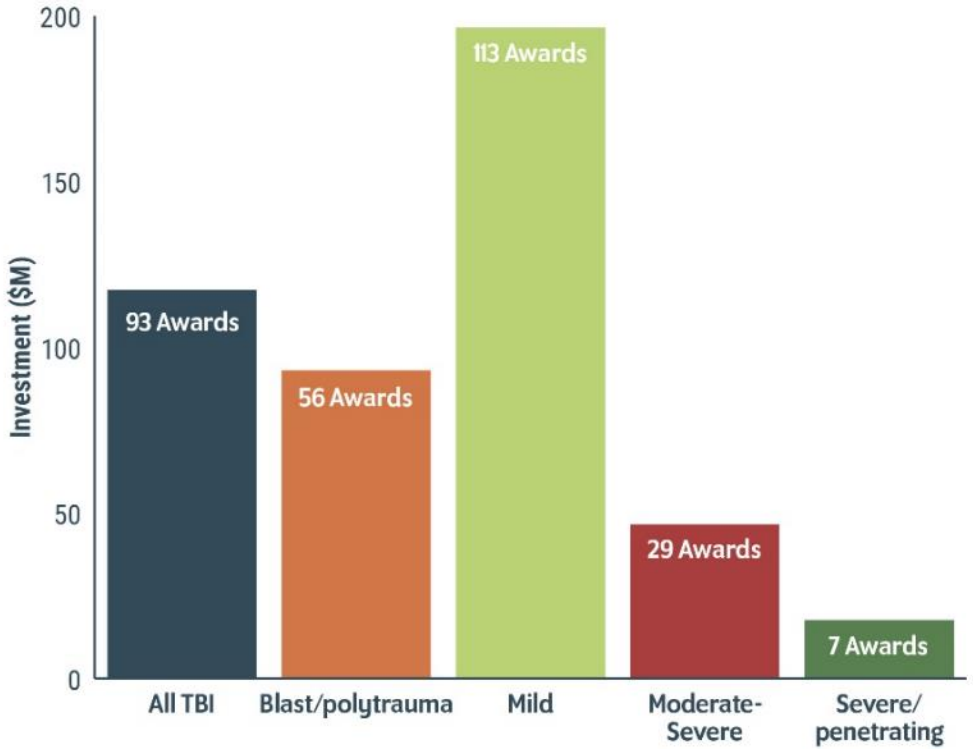
CDMRP-Managed Investment by Focus ($M)

Data may not be a complete representation of the CDMRP portfolio and are not suitable for audit purposes

Relevant CDMRP-Managed TBI Research



CDMRP-Managed TBI Awards: Funding per NRAP Research Continuum Category (by Percent Investment, Number of Awards

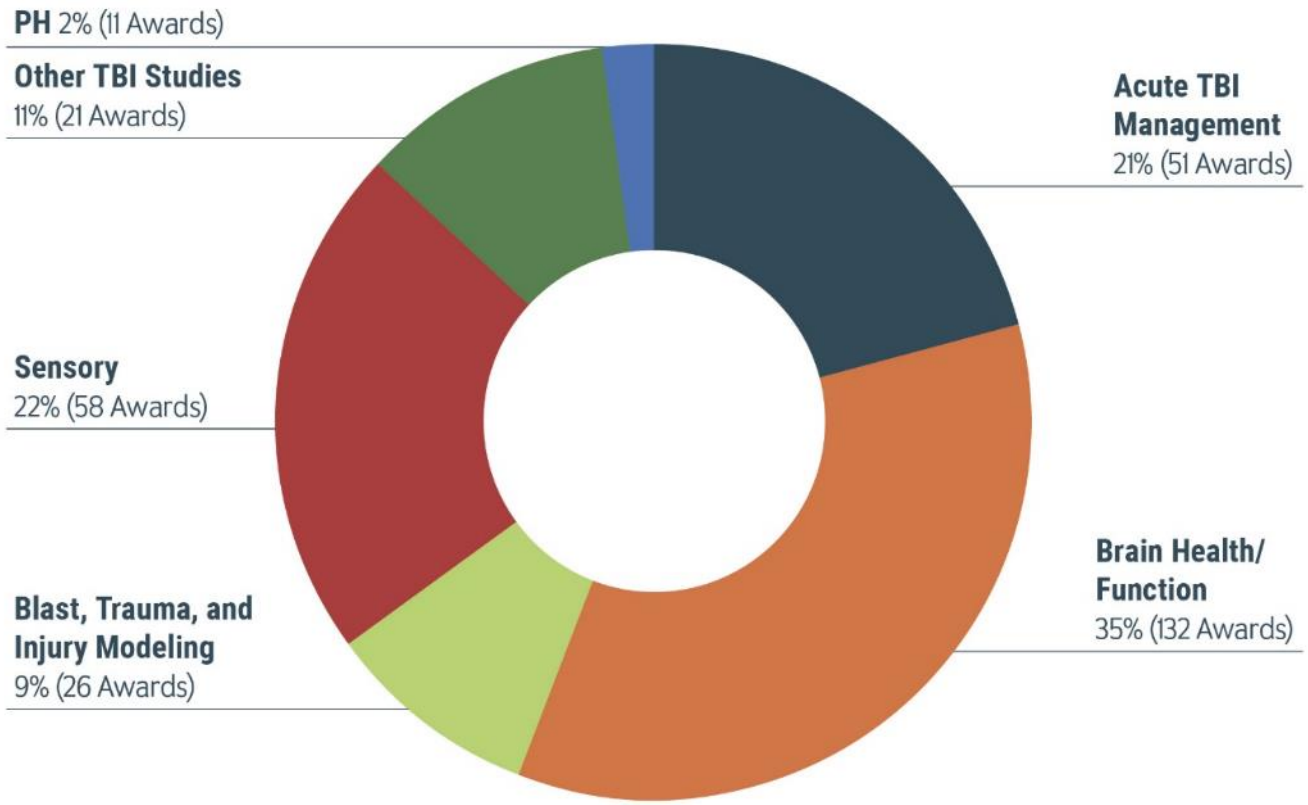


CDMRP-Managed TBI Awards: Funding per TBI Type.

Data may not be a complete representation of the CDMRP portfolio and are not suitable for audit purposes

Relevant CDMRP-Managed TBI Research

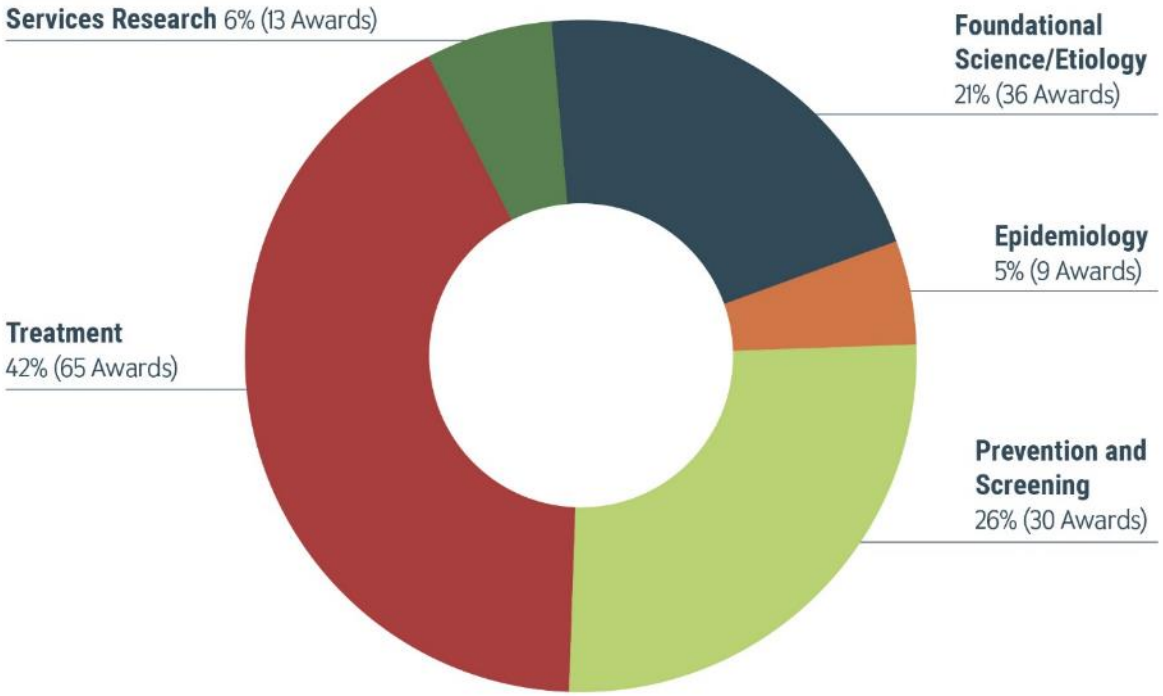
- **Acute TBI Management**
  - Emergency/point-of-injury care
  - Hemodynamics
- **Blast, Trauma and Injury Modeling**
  - Modeling, blast modeling, or other TBI-related modeling studies as the primary foci; includes polytrauma
- **Brain Health/Function**
  - Functionality, structure, mechanism, systems, and physiological consequences of brain tissue after TBI
  - Measure/evaluate, facilitate, and/or rehabilitate cognitive function after TBI
- **Other**
  - Quality of life
  - Locomotion/movement
  - Pain
  - Other studies (clinical resources, unable to classify)
- **PH**
  - PTSD, depression, anxiety, adjustment order, etc., either occurring with a TBI or impacting military Service
- **Sensory**
  - Auditory, visual, vestibular, or combination



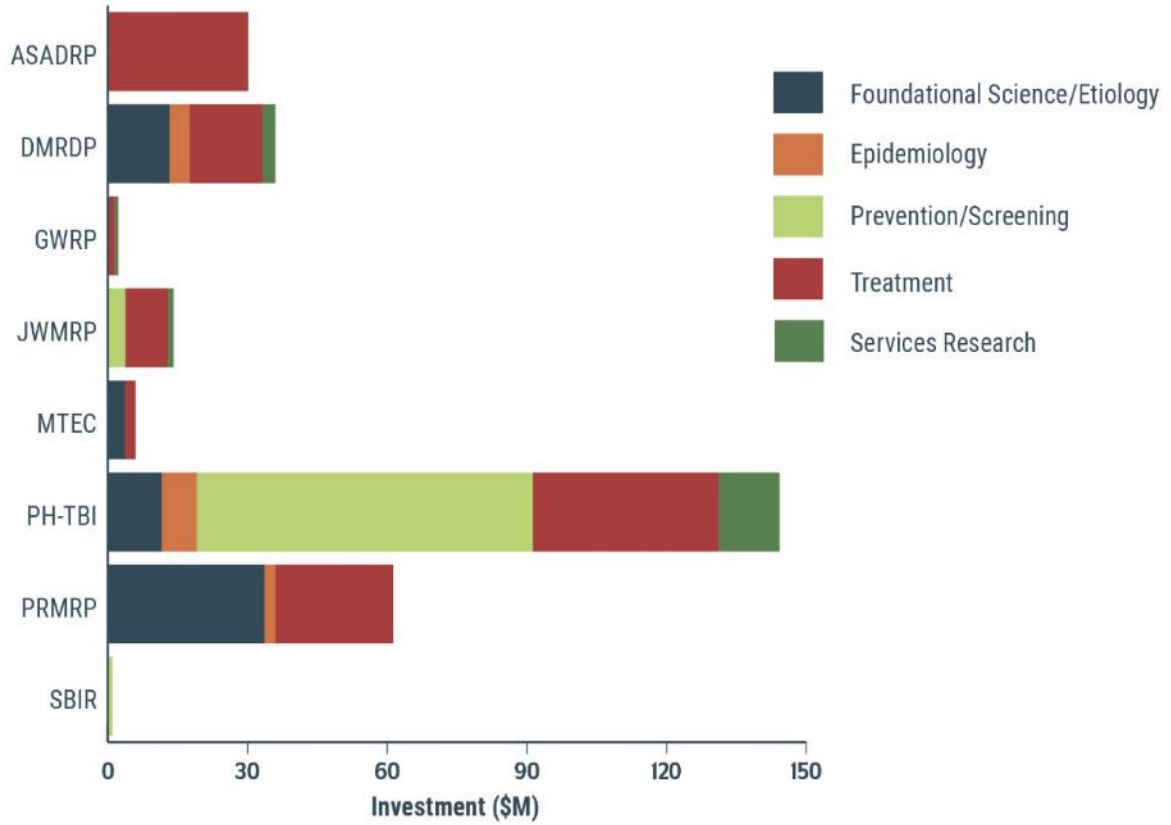
CDMRP-Managed TBI Awards: Funding per TBI Type.

Data may not be a complete representation of the CDMRP portfolio and are not suitable for audit purposes

Relevant CDMRP-Managed PH Research



CDMRP-Managed PH Awards: Funding per NRAP Research Continuum Category (by Percent Investment, Number of Awards).

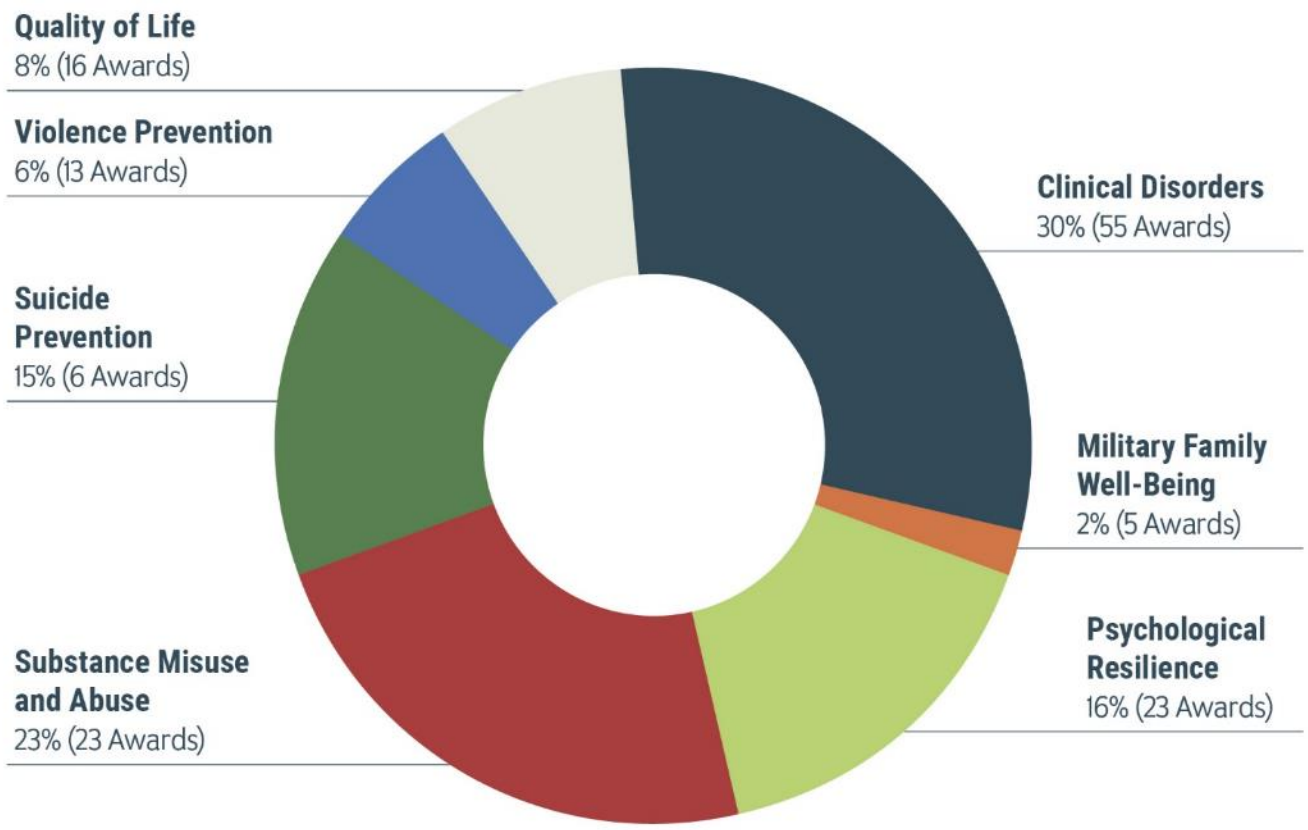


CDMRP-Managed PH Awards: Funding per NRAP Research Continuum Category by Research Program.

Data may not be a complete representation of the CDMRP portfolio and are not suitable for audit purposes

Relevant CDMRP-Managed PH Research

- **Mental Disorders**
  - Mental health disorders including PTSD, depression, anxiety, adjustment disorder, etc. either occurring as a result of military service or impacting mission readiness/return to duty
- **Military Family Well-being**
  - Impact of military service on families, addressing sequelae of military service, and promoting family resilience
- **Psychological Resilience**
  - Risk/protective factors for negative mental health outcomes (to include those impacting minority populations such as LGBT individuals) and enhancing individuals' abilities to cope and bounce back in the face of adversity
- **Substance Misuse and Abuse**
  - Understanding and preventing the misuse of alcohol and other substances and those aimed at treating alcohol and substance use disorders
- **Suicide Prevention**
  - Suicidality as well as those addressing postvention (e.g., promoting healing or mitigating negative outcomes following a suicide death)
- **Violence Prevention**
  - Sexual assault, sexual harassment, workplace violence, intimate partner violence, hazing/bullying, etc.



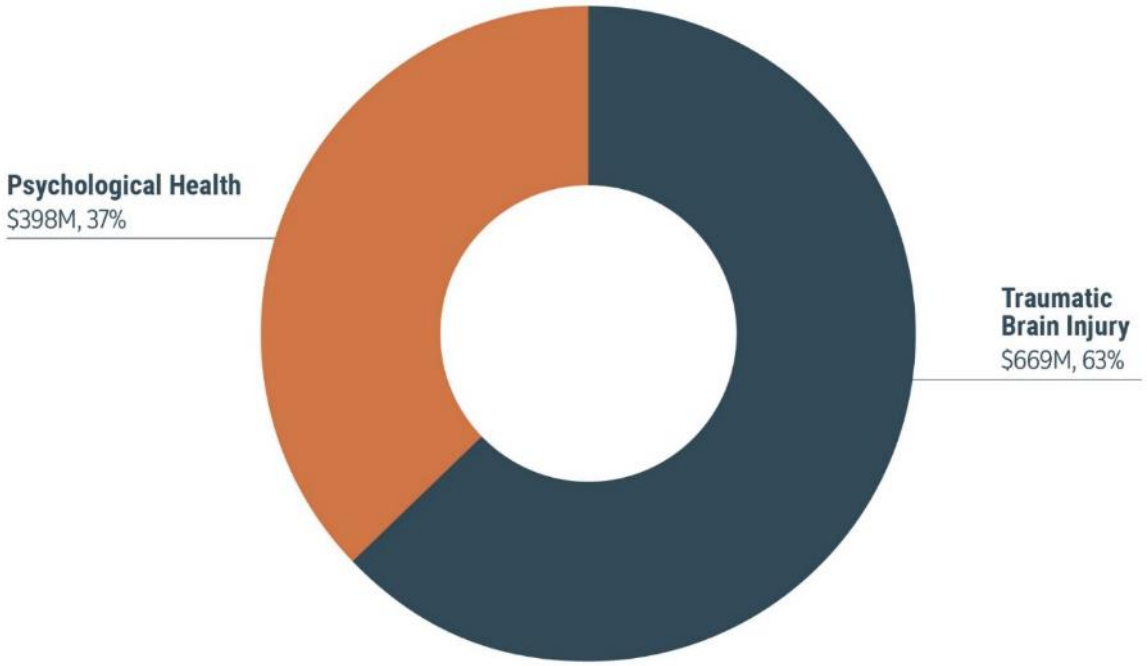
CDMRP-Managed PH Awards: Funding per PH Research Area (by Percent Investment, Number of Awards).

Data may not be a complete representation of the CDMRP portfolio and are not suitable for audit purposes

Relevant NIH-Managed Research

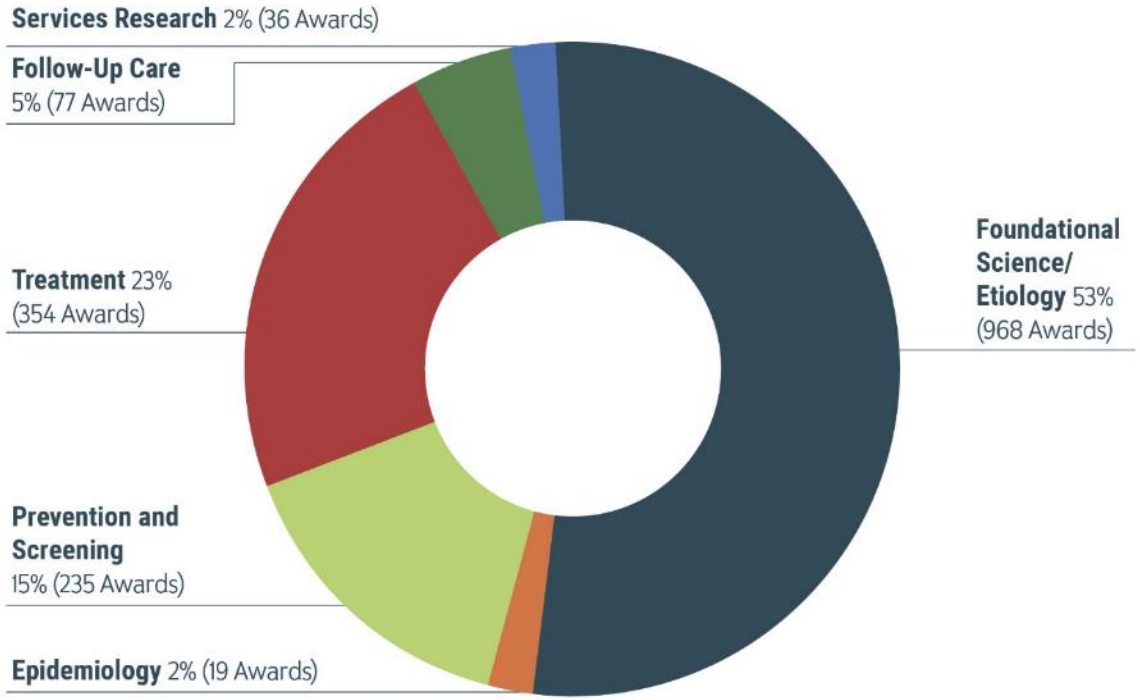
- **Pages 20-22, 30-31 in Stakeholders Book**
- **Snapshot of National Institutes of Health (NIH) investment with relevance to TBIPHRP**
  - FY14-FY19
  - TBI data provided by National Institute of Neurological Disorders and Stroke
  - PH data pulled for Federal Reporter
    - Filtered for military-relevant keywords
- **Key Stats**
  - $398M, 947 awards PH
  - $669M, 1,689 awards TBI

NIH-Managed Investment by Focus ($M)

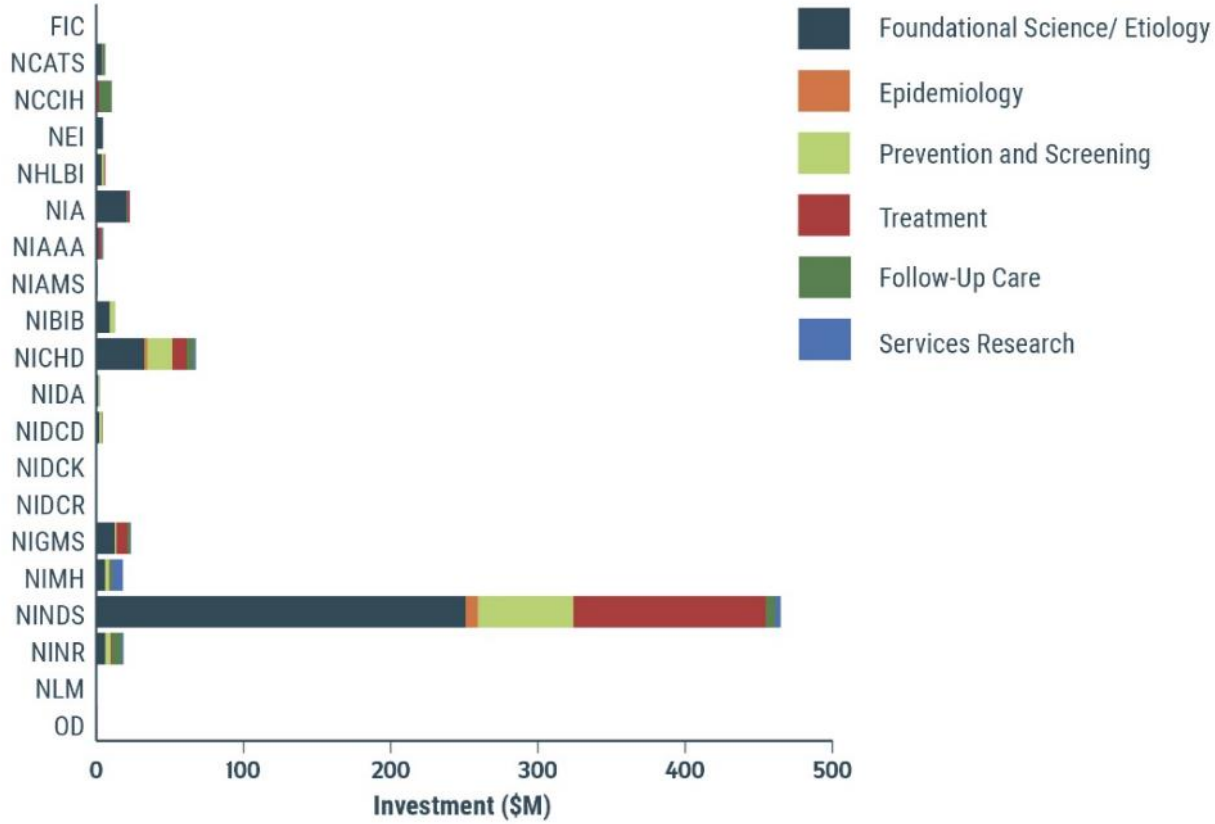


Data may not be a complete representation of the NIH portfolio and are not suitable for audit purposes

Relevant NIH-Managed TBI Research



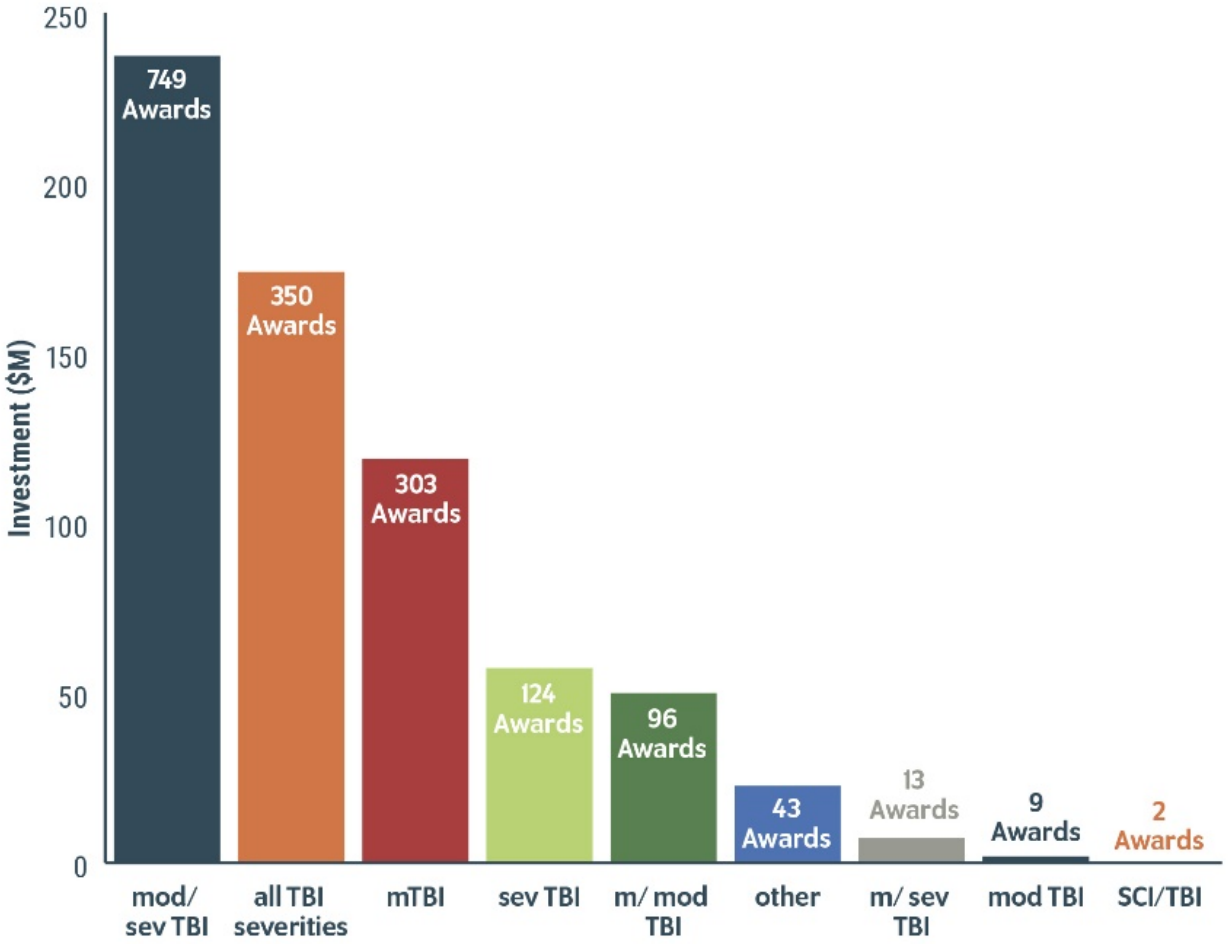
NIH-Managed TBI Awards: Funding per NRAP Research Continuum Category (by Percent Investment, Number of Awards).



NIH-Managed TBI Awards: Funding per NRAP Research Continuum Category by NIH Institute.

Data may not be a complete representation of the NIH portfolio and are hot suitable for audit purposes

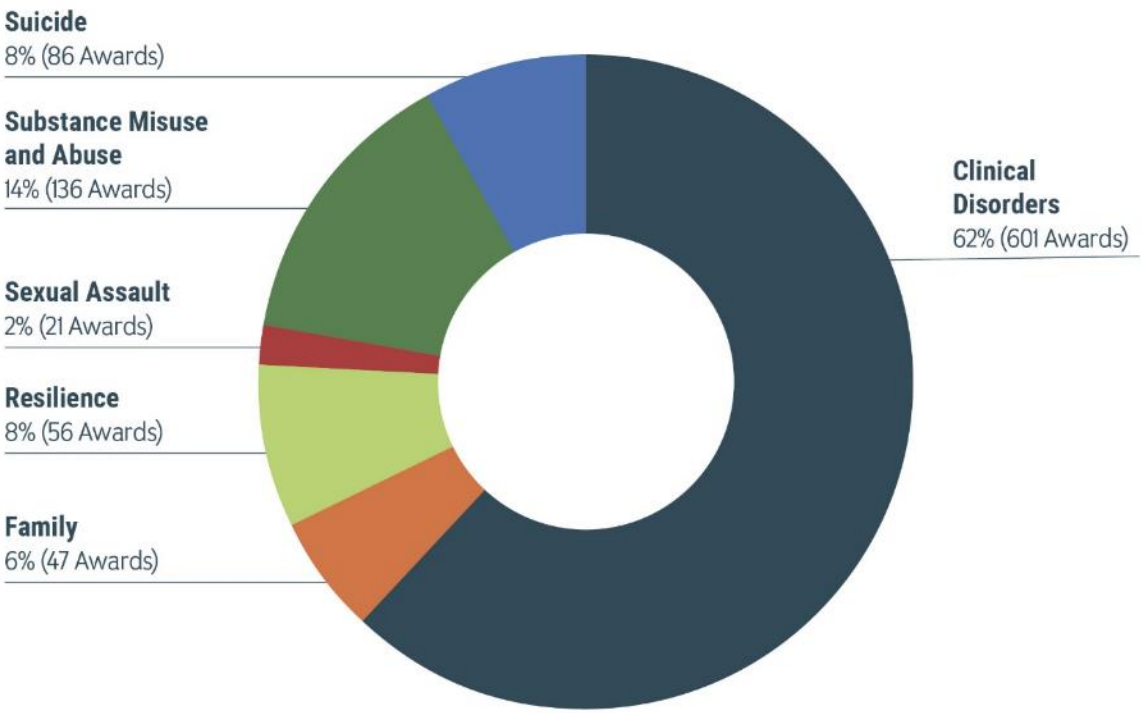
Relevant NIH-Managed TBI Research



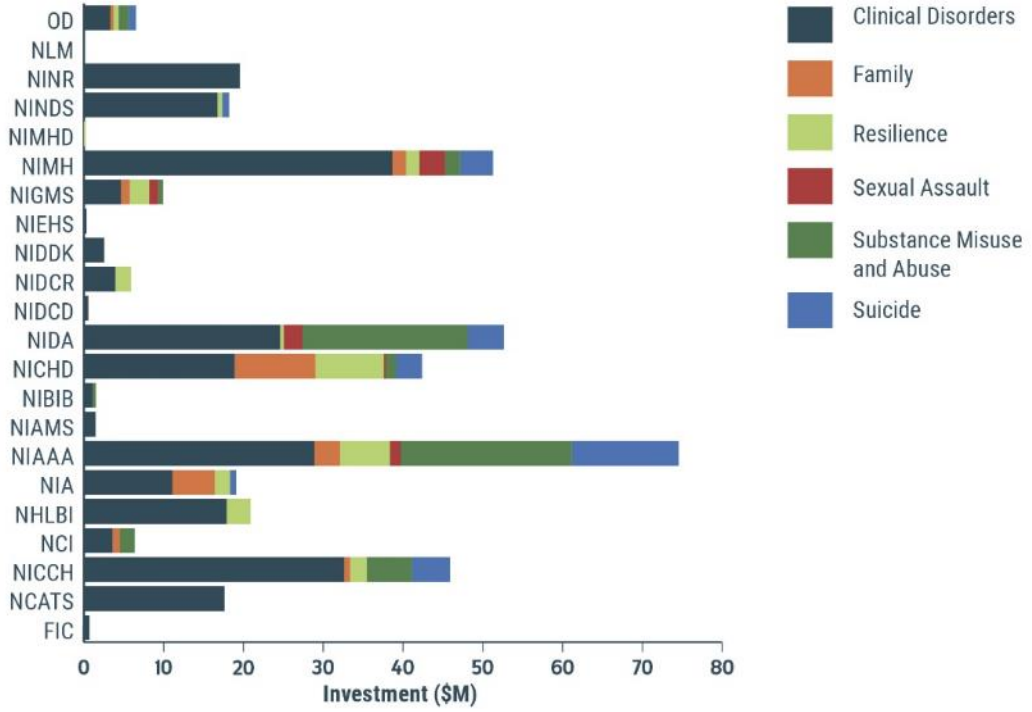
NIH-Managed TBI Awards: Funding per TBI Type.

Data may not be a complete representation of the NIH portfolio and are hot suitable for audit purposes

Relevant NIH-Managed PH Research



NIH-Managed PH Awards: Military-Relevant PH Funding by Research Area.



NIH-Managed PH Awards: Military-Relevant PH Funding by NIH Institute

Data may not be a complete representation of the NIH portfolio and are hot suitable for audit purposes

Request for Information (RFI) Responses

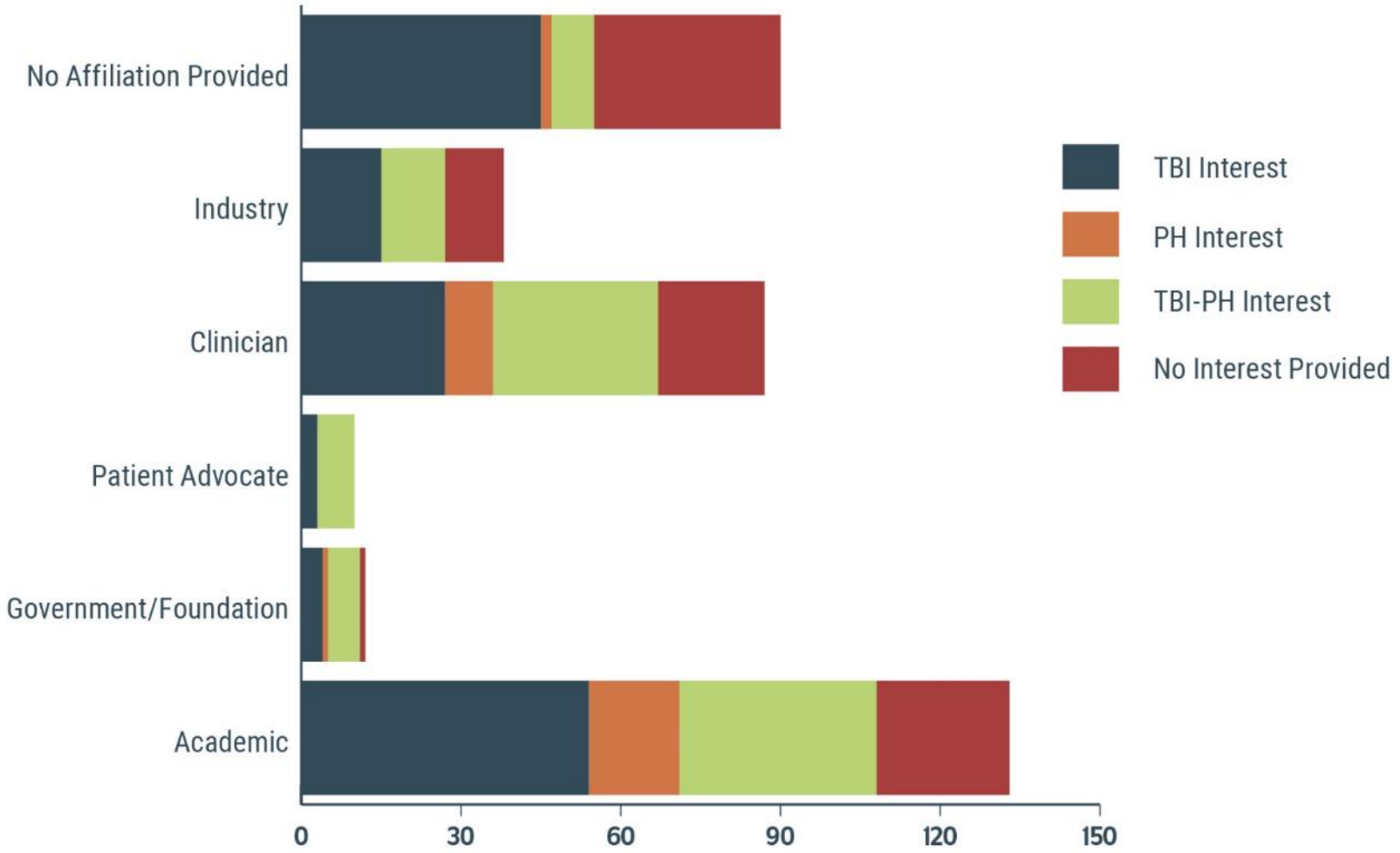
TBI and PH Research-Specific

- In your opinion, which of the following **National Research Action Plan research categories** will have the most impact on TBI research?
- What are **the top three specific research areas, knowledge, or clinical capabilities** that are currently missing or not well-funded and, if funded, could make a significant impact on the state of the science and clinical outcomes?
- What **elements from the patient or care provider perspective** (e.g., quality of life) require additional research or emphasis?

TBIPHRP Opportunities

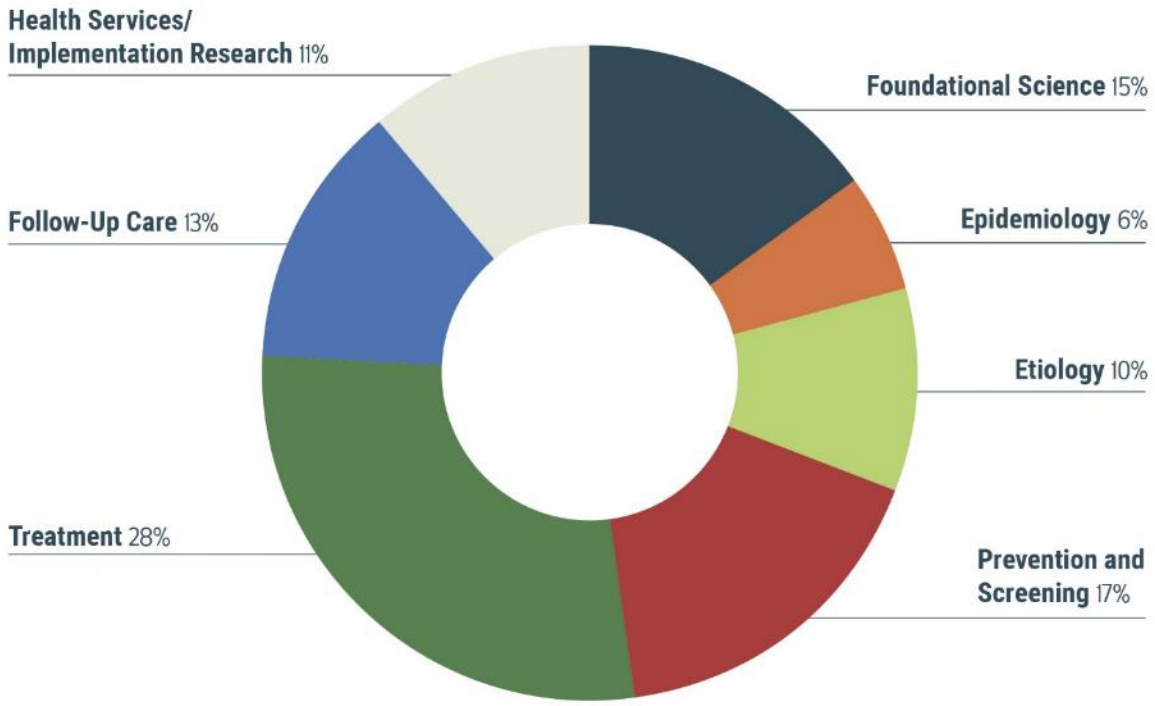
- What are the **barriers** (e.g., scientific, administrative, financial, collaborative, or other) to translating findings to clinical practice and how can they be addressed by the TBIPHRP?
- **What types of funding opportunities** could the TBIPHRP release that uniquely respond to the current research gaps and obstacles to clinical impact?

RFI Response Demographics



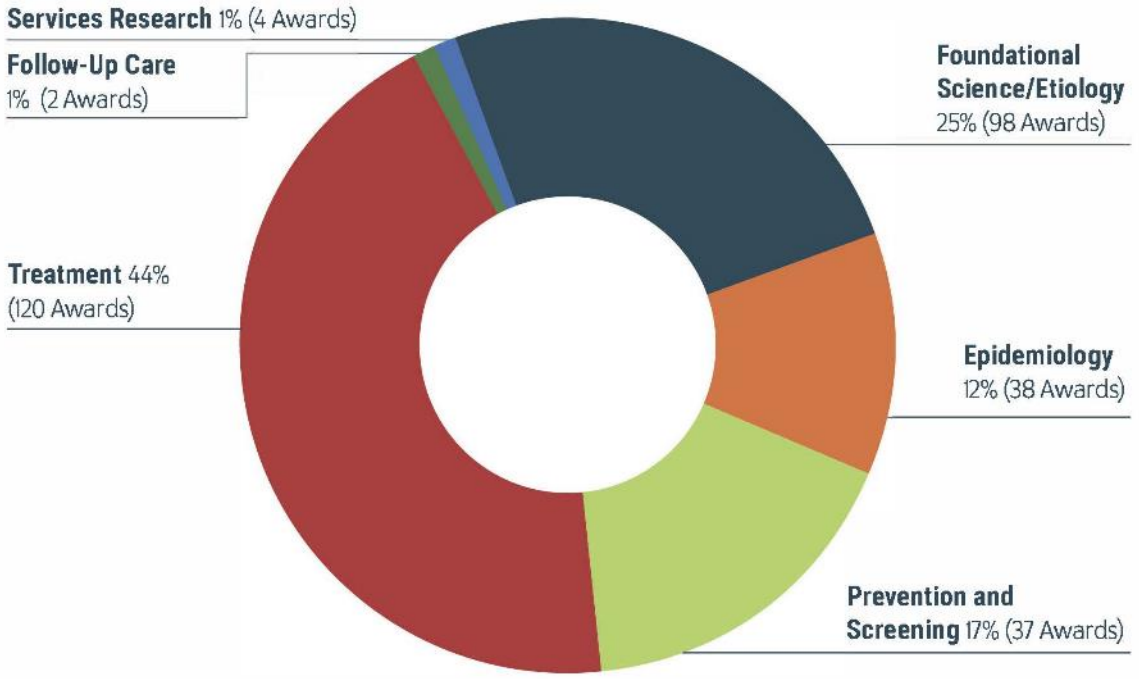
TBI Q1: Top Three Research Categories

◆ Q1 Responses



NRAP Research Continuum Categories Deemed Most Impactful for TBI Research.

◆ CDMRP-Managed Data

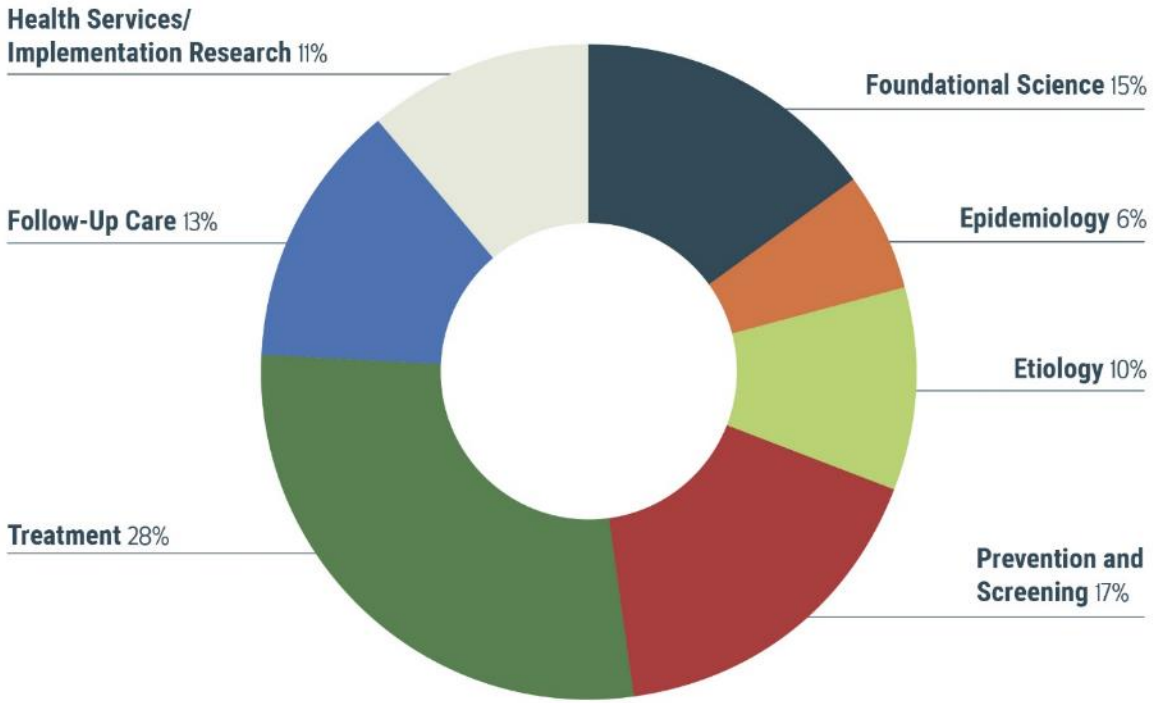


CDMRP-Managed TBI Awards: Funding per NRAP Research Continuum Category (by Percent Investment, Number of Awards).

Data may not be a complete representation of the CDMRP portfolio and are not suitable for audit purposes

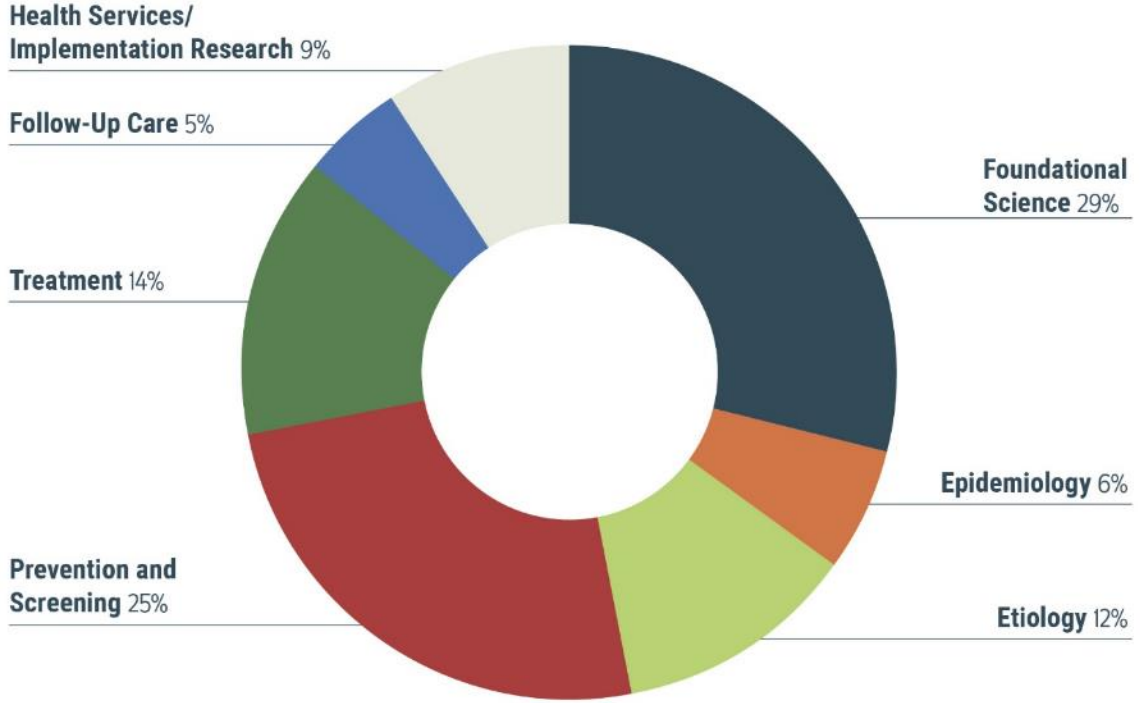
TBI Q2: Top Three Missing Gaps, Knowledge, or Capabilities

◆ Q1 Responses



NRAP Research Continuum Categories of Specific Research Areas, Knowledge, or Clinical Capabilities Needed in TBI Research and Care

◆ Q2 Responses



NRAP Research Continuum Categories of Specific Research Areas, Knowledge, or Clinical Capabilities Needed in TBI Research and Care

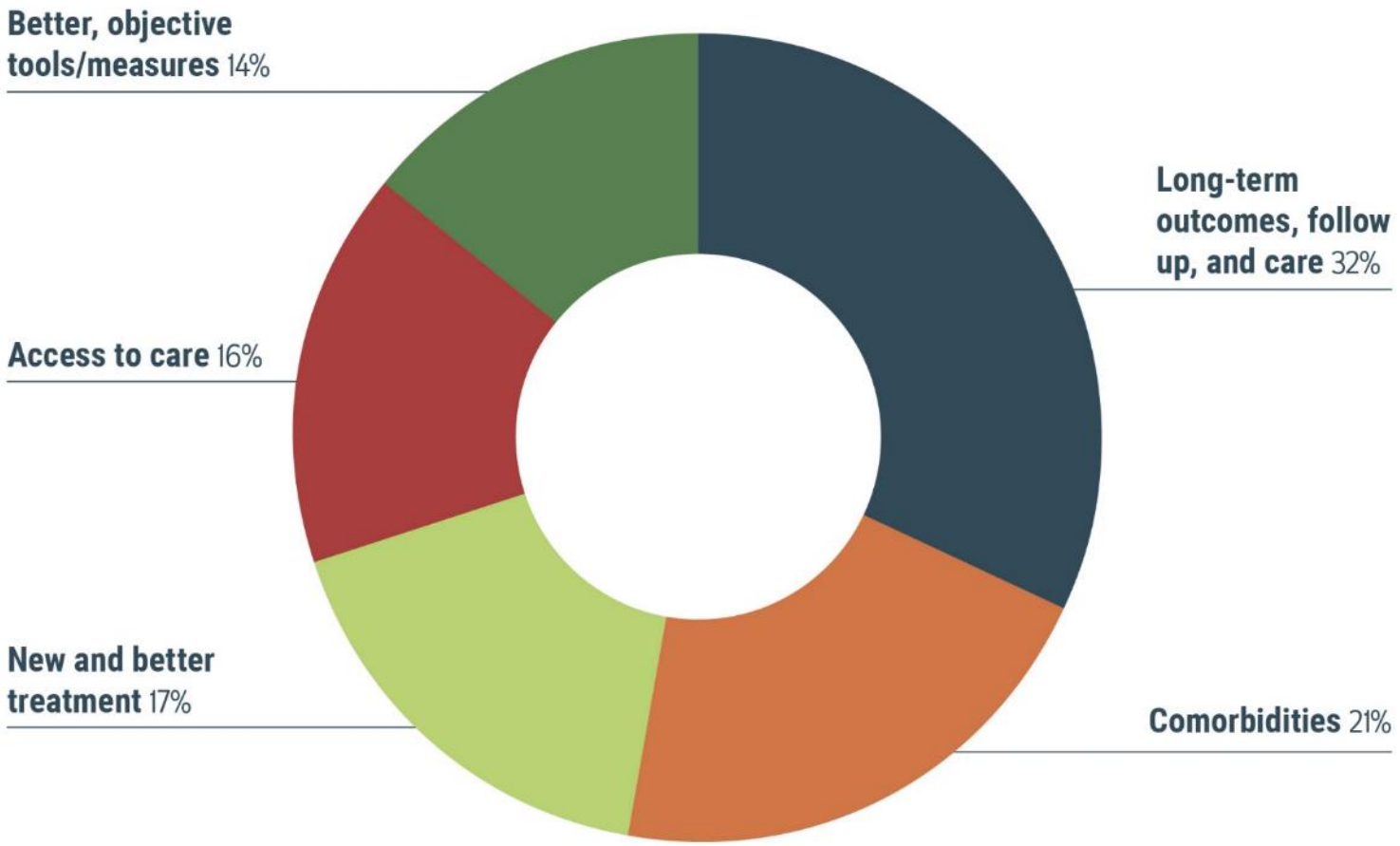
TBI Q2: Top Five Gaps Within Top Three Categories

Treatment
- Comorbidities
- New, better treatments
- Treatment optimization
- Rehabilitation including cognitive
- Point of injury/acute treatment

Foundational Science
- Mechanisms of TBI
- Better animal/preclinical models
- Blast outcomes and exposure
- Multimodal neuroimaging

Prevention and Screening
- Better objective measures
- Biomarkers
- Point of injury assessments
- Early, comprehensive diagnosis
- Preventative measures

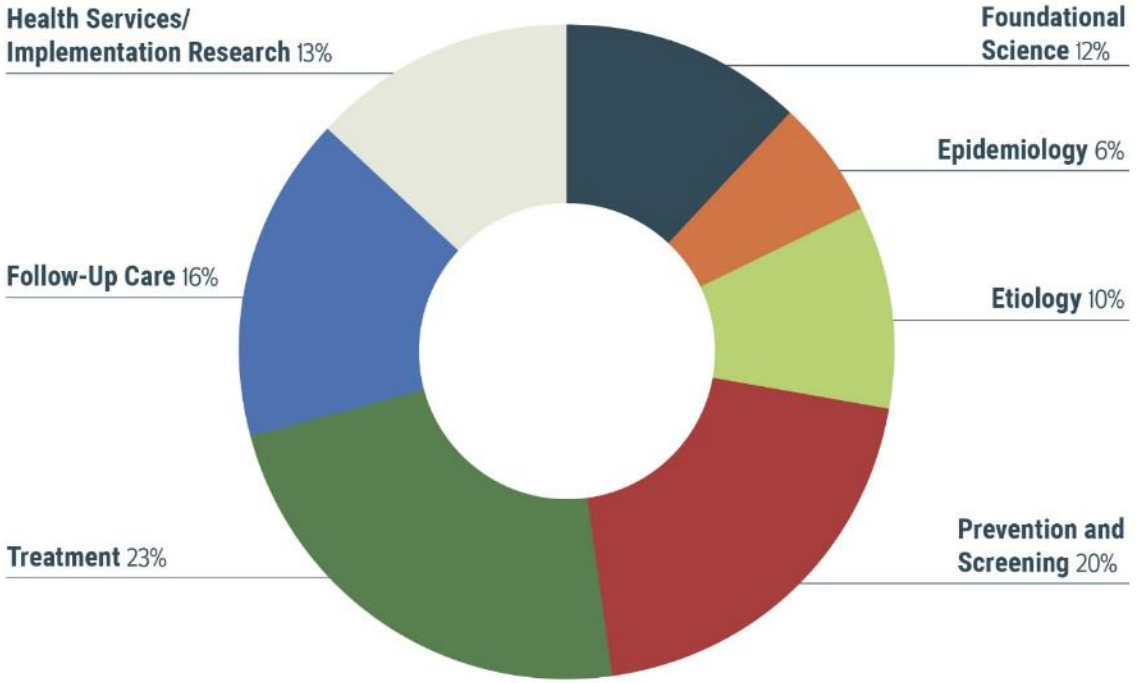
TBI Q3: Missing Elements from Patient/Provider Perspective



Specific Patient Care or Provider Perspective Areas Needed in TBI Research and Care

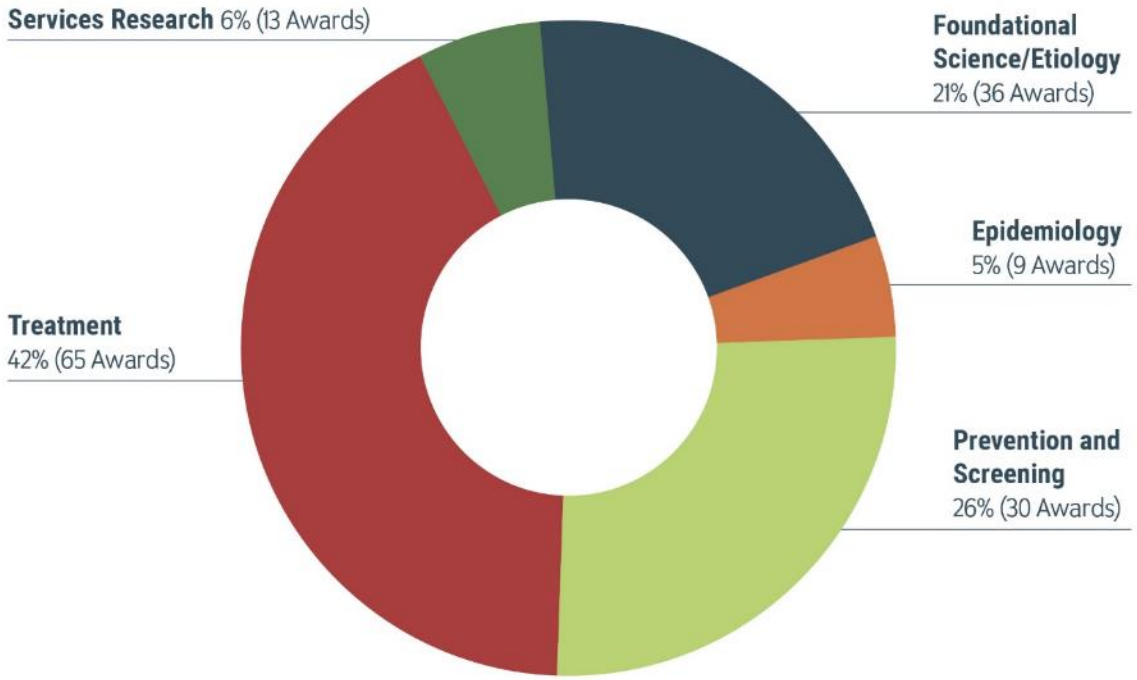
PH Q4: Top Three Research Categories

◆ Q4 Responses



NRAP Research Continuum Categories Deemed Most Impactful for PH Research.

◆ CDMRP-Managed Data

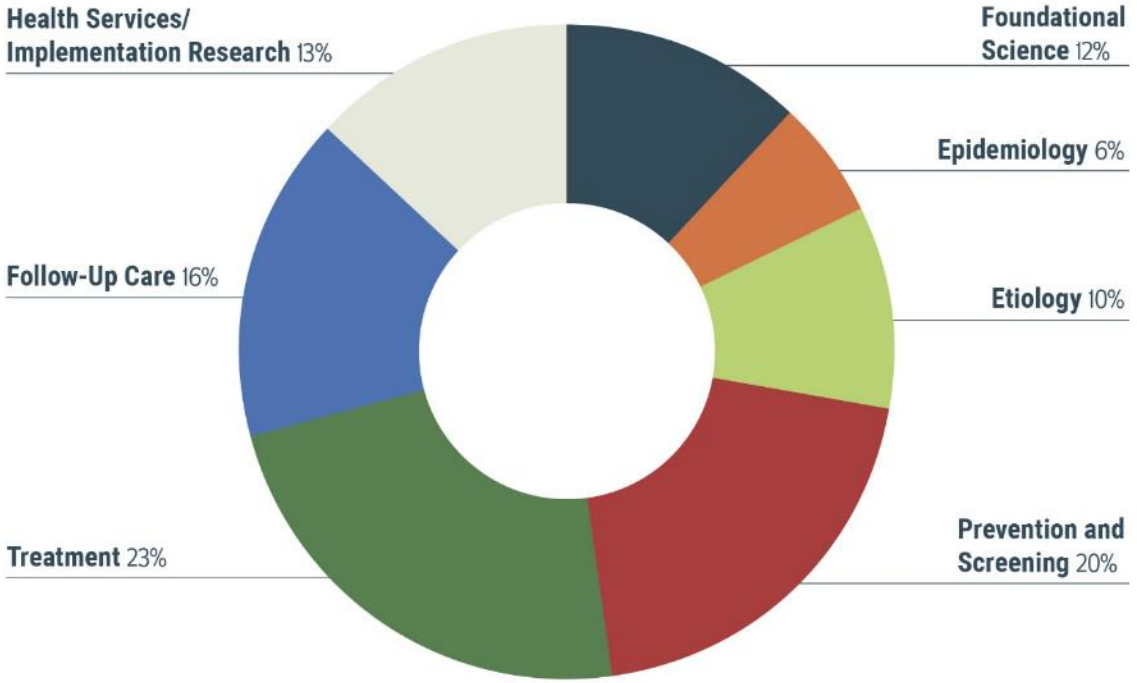


CDMRP-Managed PH Awards: Funding per PH Research Area (by Percent Investment, Number of Awards).

Data may not be a complete representation of the CDMRP portfolio and are not suitable for audit purposes

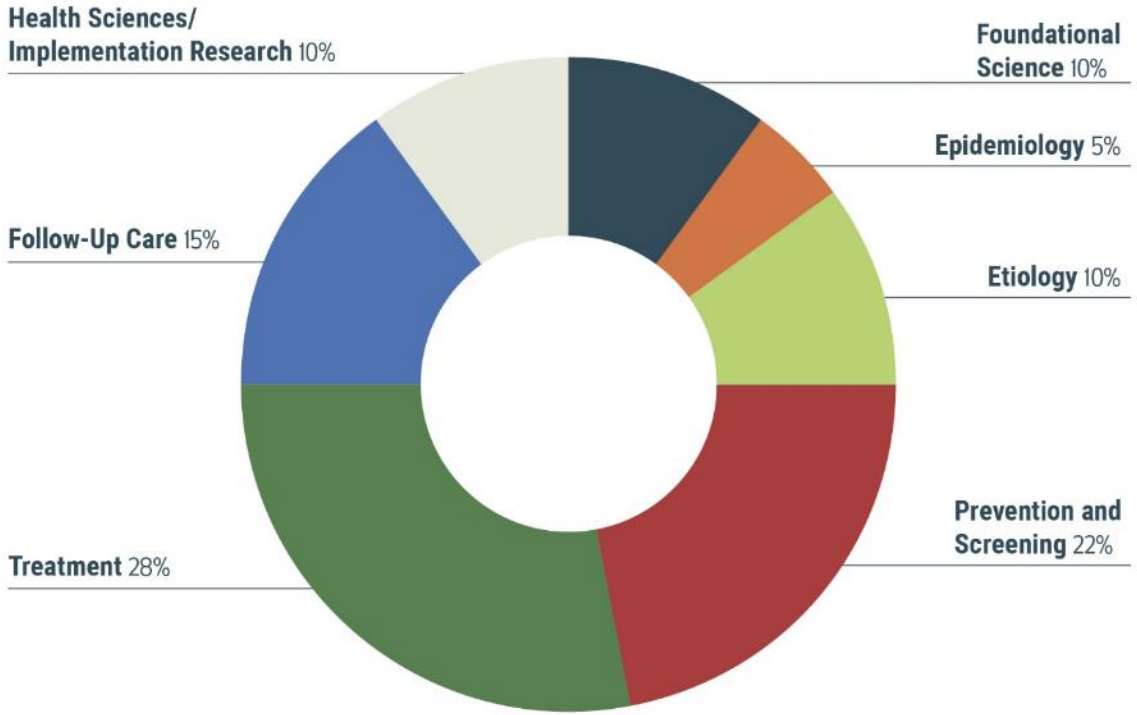
PH Q5: Top Three Missing Gaps, Knowledge, or Capabilities

◆ Q4 Responses



NRAP Research Continuum Categories Deemed Most Impactful for PH Research.

◆ Q5 Responses



NRAP Research Continuum Categories of Specific Research Areas, Knowledge, or Clinical Capabilities Needed in PH Research and Care.

PH Q5: Top Five Gaps Within Top Three Categories

Follow-Up Care

- Long-term care, outcomes, and interventions
- Better follow-up contact/communication
- Access to care
- Wearables to support follow-up

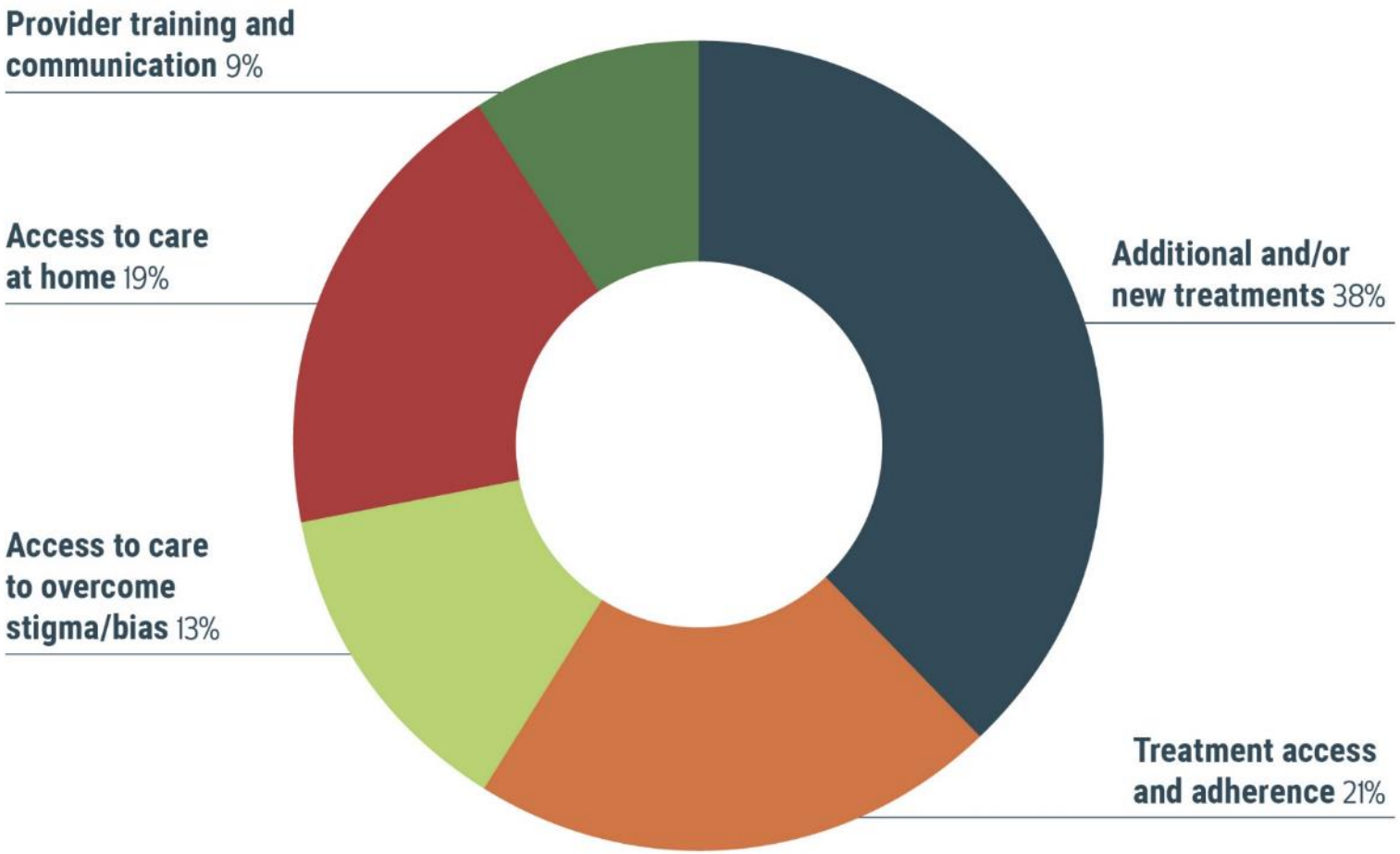
Prevention and Screening

- Better objective tools and measures
- Biomarkers
- Risk factors
- Psychological health screening
- Resiliency

Treatment

- Comorbidities
- New, better treatments
- Combination treatments
- Access to treatment at home

PH Q6: Missing Elements from Patient/Provider Perspective



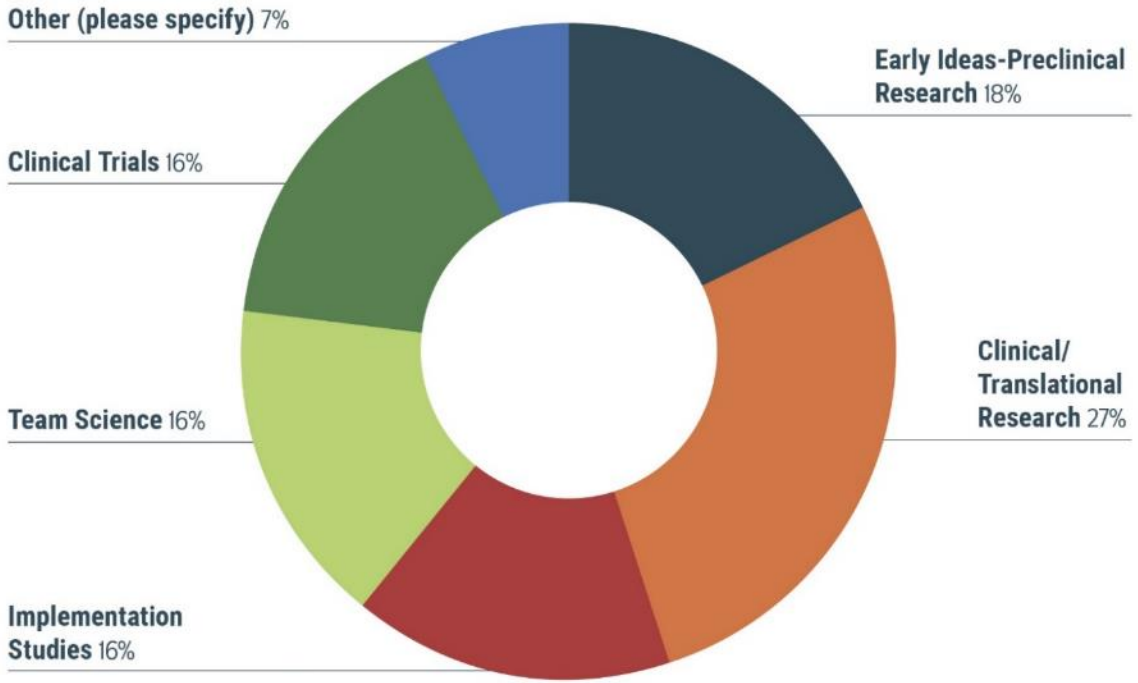
Specific Patient Care or Provider Perspective Areas Needed in PH Research and Care

Q7: Barriers to Translation

Word Cloud of Barriers to Translating Findings to Clinical Practice for Consideration by the TBIPHRP.

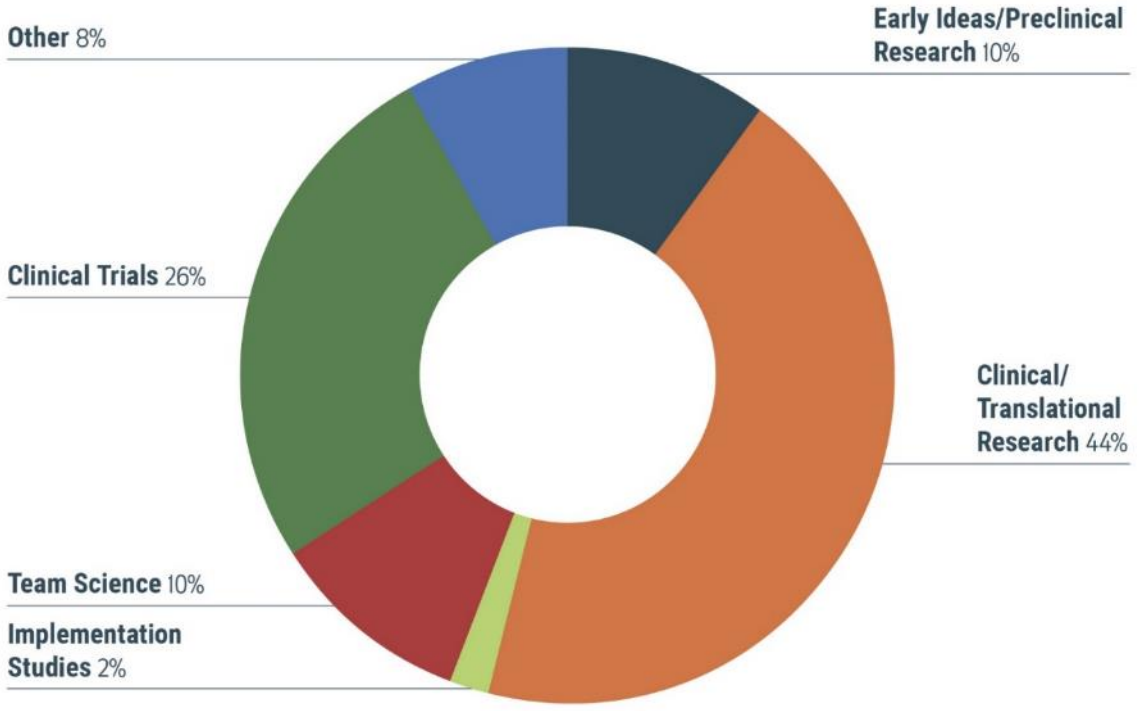
Q8: TBIPHRP Funding Opportunities Suggestions

◆ RFI



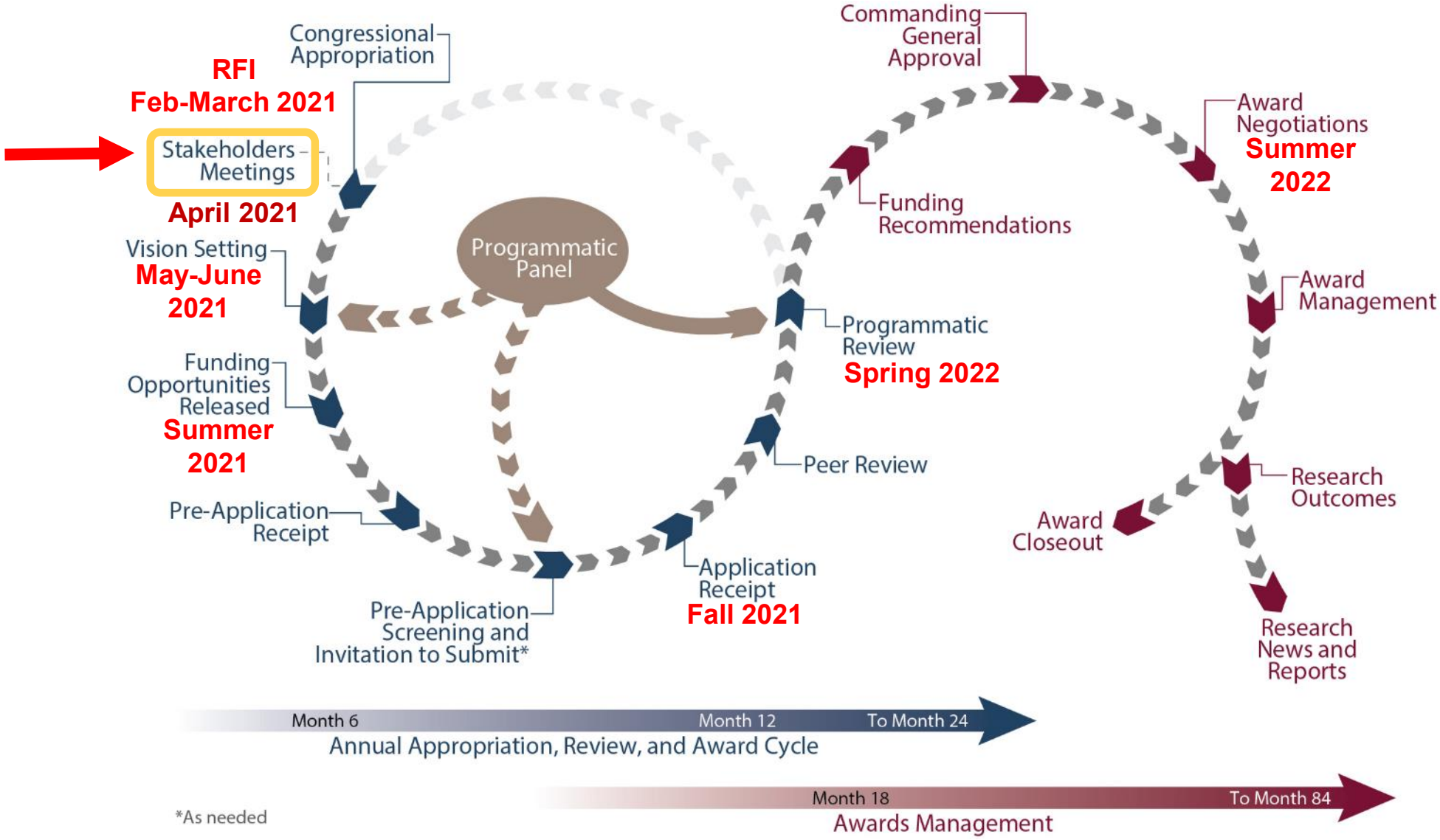
Types of Funding Opportunities to Respond to Current Research Gaps and Obstacles to Clinical Impact for Consideration by the TBIPHRP.

◆ FY14-FY19 PHTBIRP Award Mechanisms



FY14-FY19 PHTBIRP Funding Opportunities.

FY21 TBIPHRP Program Cycle



Stakeholders Meeting

Meeting Activities

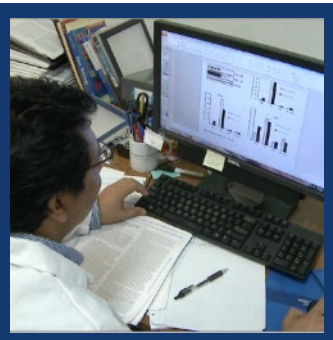
- Overview presentations from various organizations conducting or participating in TBI and PH research and care
- Participate in focused breakout sessions to discuss current states, desired future states, and gaps in specific areas of TBI and PH research and care
- Identify research gaps in specific areas of TBI and PH research
- Discuss concurrent management strategies for TBI and PH research endeavors

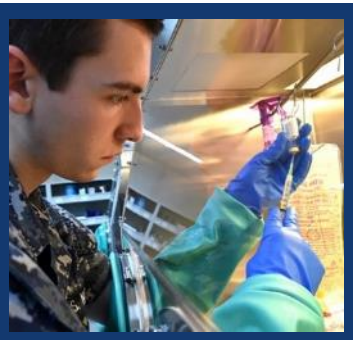
Outcomes

- Prioritized gaps for TBI and PH research and care to inform programmatic directions and future funding opportunities
  - *All identified gaps and priorities are pre-decisional and may not necessarily reflect the final focus of FY21 TBIPHRP funding opportunities.*

For more information, please visit:

cdmrp.army.mil






Breakout Session Topic Areas

◆ Traumatic Brain Injury

- Etiology, Pathology, and Prevention
- Screening/Prognosis/Diagnosis – Differences between Civilian and Military TBI (and Within Different Types of Military TBI)
- Interventions (Development) Addressing Both Acute and Chronic Care
- Rehabilitation and Return to Duty

◆ Psychological Health

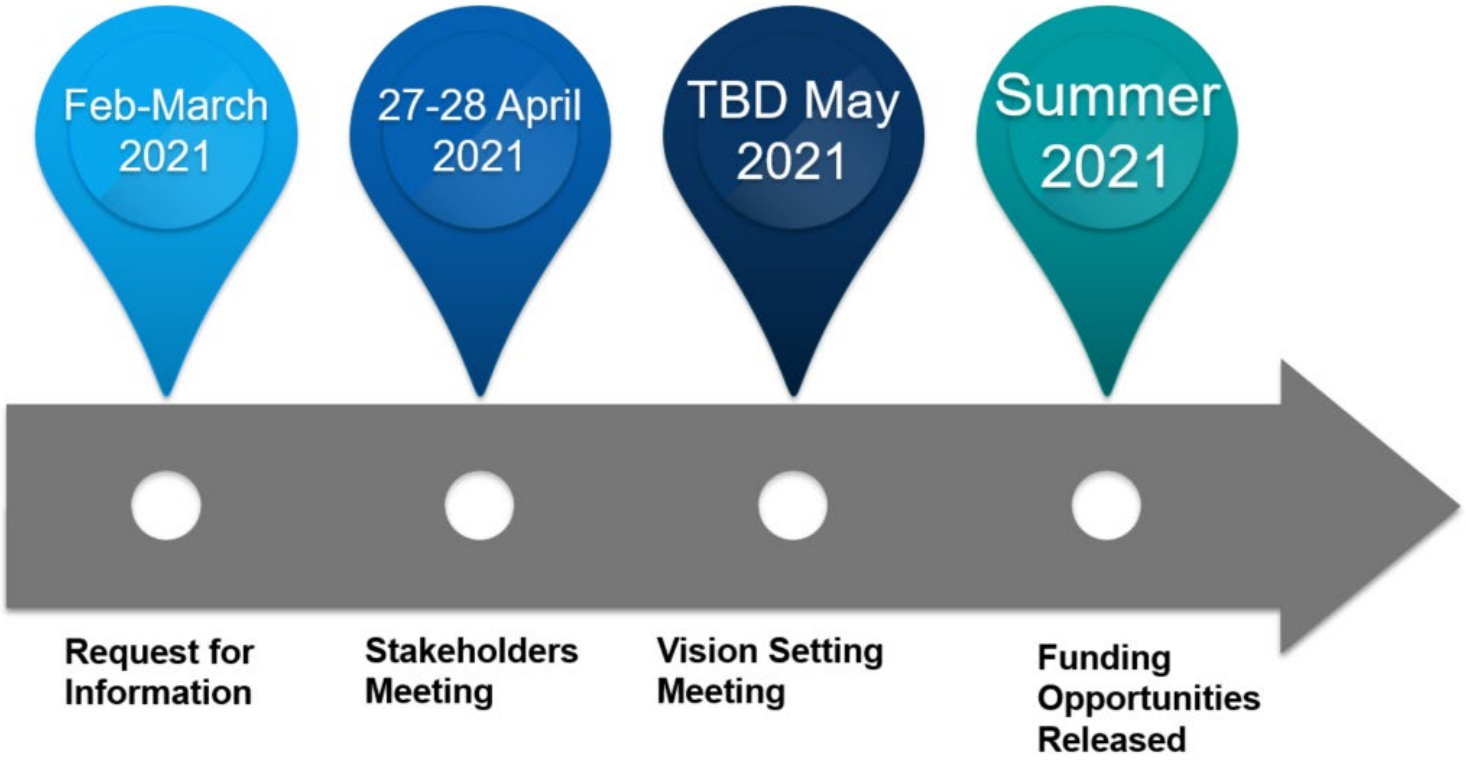
- Suicide Prevention
- Prevention, Diagnosis, and Treatment of PTSD, Adjustment Disorders, Depression, and other Mental Health Disorders
- Sexual Assault and Harassment Prevention and Recovery
- Resilience Building and Family Well-Being

Breakout Session Expectations

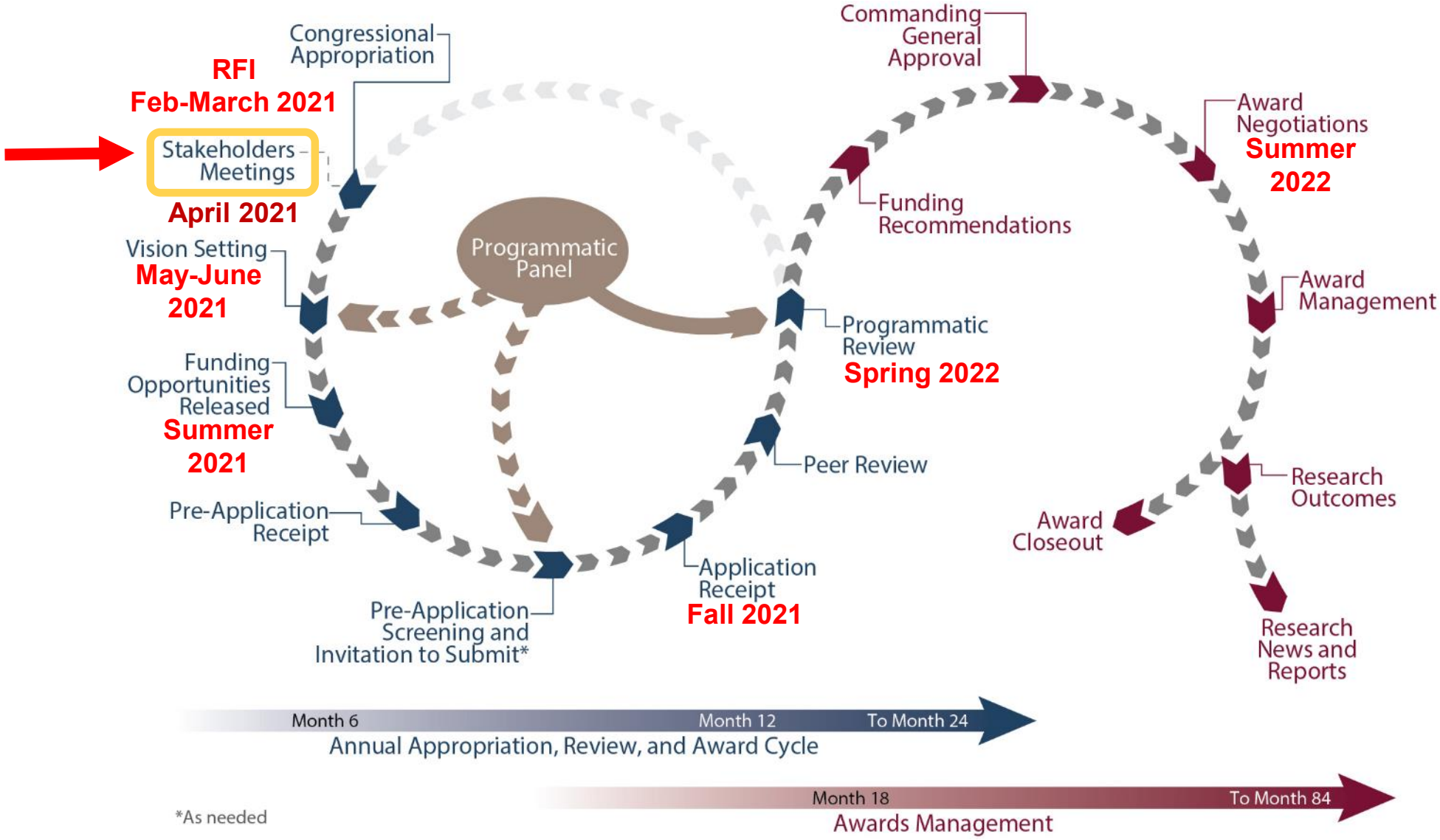
- This is an opportunity to hear unique ideas and perspectives
- We want to hear from you, but one at a time!
- State your "headline" first, then the supporting information as necessary
- We will be monitoring the chat and will capture your comments even if not discussed
- We want to discuss research needs and gaps, not solutions
- There will be a post-meeting survey to prioritize identified gaps and needs

Next Steps

- **Survey to prioritize breakout gaps**
  - *All identified gaps and priorities are pre-decisional and may not necessarily reflect the final focus of FY21 TBIPHRP funding opportunities*
- **Meeting summary will be posted to CDMRP website**



FY21 TBIPHRP Program Cycle



Enclosure 3
Overview of Department of Defense Warfighter Brain Health Initiative

DoD Warfighter Brain Health Initiative
TBIPHRP Stakeholders Meeting
27 APR 2021

Kathy Lee, MS, CRNP, ANP-BC

DoD Warfighter Brain Health Lead

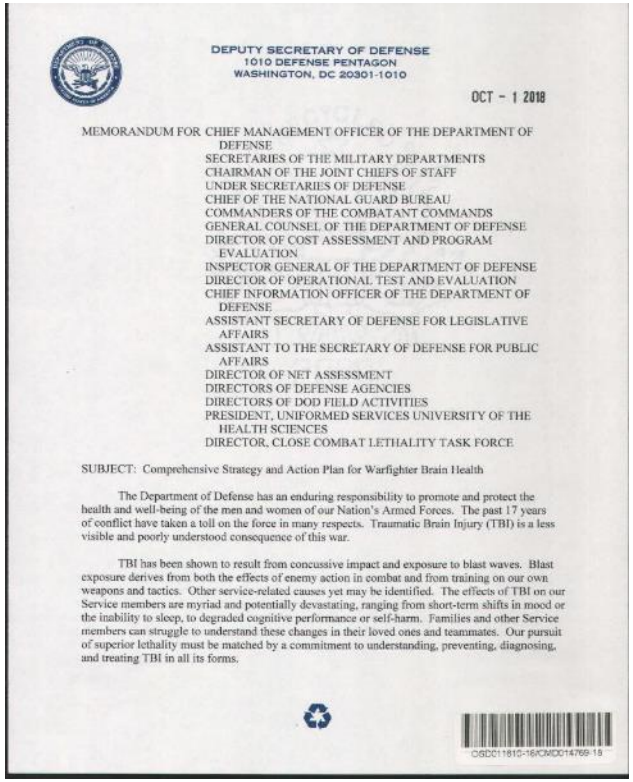
Warfighter Brain Health Initiative

* To identify requirements, assess capabilities, and recommend Doctrine, Organization, Training, Materiel, Leadership & Education, Personnel, Facilities, and Policy (DOTMLPF-P) solution approaches to improve the ability to monitor, optimize, restore, and support brain health across warfighters' lifecycle.

WBH Strategy and Action Plan: Authority and Guidance

On 1 October 2018, the Deputy Secretary of Defense provided his direction for a Comprehensive Strategy and Action Plan for Warfighter Brain Health

- Develop Department-wide Comprehensive Strategy and Action Plan to address:
  1. Brain Health: Cognitive and Physical Performance
  2. Brain Exposures
  3. Traumatic Brain Injury
  4. Late and Long-Term Effects



DEPUTY SECRETARY OF DEFENSE
1010 DEFENSE PENTAGON
WASHINGTON, DC 20301-1010

OCT - 1 2018

MEMORANDUM FOR CHIEF MANAGEMENT OFFICER OF THE DEPARTMENT OF DEFENSE
SECRETARIES OF THE MILITARY DEPARTMENTS
CHAIRMAN OF THE JOINT CHIEFS OF STAFF
UNDER SECRETARIES OF DEFENSE
CHIEF OF THE NATIONAL GUARD BUREAU
COMMANDERS OF THE COMBATANT COMMANDS
GENERAL COUNSEL OF THE DEPARTMENT OF DEFENSE
DIRECTOR OF COST ASSESSMENT AND PROGRAM EVALUATION
INSPECTOR GENERAL OF THE DEPARTMENT OF DEFENSE
DIRECTOR OF OPERATIONAL TEST AND EVALUATION
CHIEF INFORMATION OFFICER OF THE DEPARTMENT OF DEFENSE
ASSISTANT SECRETARY OF DEFENSE FOR LEGISLATIVE AFFAIRS
ASSISTANT TO THE SECRETARY OF DEFENSE FOR PUBLIC AFFAIRS
DIRECTOR OF NET ASSESSMENT
DIRECTORS OF DEFENSE AGENCIES
DIRECTORS OF DOD FIELD ACTIVITIES
PRESIDENT, UNIFORMED SERVICES UNIVERSITY OF THE HEALTH SCIENCES
DIRECTOR, CLOSE COMBAT LETHALITY TASK FORCE

SUBJECT: Comprehensive Strategy and Action Plan for Warfighter Brain Health

The Department of Defense has an enduring responsibility to promote and protect the health and well-being of the men and women of our Nation's Armed Forces. The past 17 years of conflict have taken a toll on the force in many respects. Traumatic Brain Injury (TBI) is a less visible and poorly understood consequence of this war.

TBI has been shown to result from concussive impact and exposure to blast waves. Blast exposure derives from both the effects of enemy action in combat and from training on our own weapons and tactics. Other service-related causes yet may be identified. The effects of TBI on our Service members are myriad and potentially devastating, ranging from short-term shifts in mood or the inability to sleep, to degraded cognitive performance or self-harm. Families and other Service members can struggle to understand these changes in their loved ones and teammates. Our pursuit of superior lethality must be matched by a commitment to understanding, preventing, diagnosing, and treating TBI in all its forms.

OSDC11810-16/CMD014769-18

WBH Scope

- Warfighter brain health is defined as the physical, psychological, and cognitive status that affects a warfighter's capacity to function adaptively in any environment and impacts readiness, operational capability, mission effectiveness, and the goal to achieve overmatch or superior lethality. [Source: Deputy Secretary of Defense Memorandum, “Comprehensive Strategy and Action Plan for Warfighter Brain Health,” dated October 1, 2018 and National Defense Strategy, January 2018]
- The capability for early identification and mitigation of potential hazardous exposures to brain health, especially for the risk of TBI, should lead to the reduction of injury and long term and late effects in a warfighter’s life
- Strategy needs to address three Cohorts of Warfighters (Apprentice, Journeyman, and Master); hence not a “one size fits all” approach

Brain Health Priorities and Concerns: Crucial for a WBH Strategy & Plan

Disconnect Between Operational and Medical Communities	• There is perceived disconnect between the efforts of the operational (those preparing for combat) and medical communities on translating brain health information to the SM in time to help them.
The "Warrior Mindset"	• SMs have a desire to complete the mission despite brain exposures, injury or illness. SMs often compare themselves to other SMs who may be in a worse condition, therefore discrediting their own struggles or concerns.
Concerns for Diminished Training	• There were multiple concerns over the new emphasis on blast overpressure exposures and brain health and how safety and training changes may dilute their training opportunities. This may make it difficult to maintain deployment readiness and combat effectiveness.
Limited Information on Health Hazards, Adverse Effects, Protection Measures and Mitigation Strategies	• SMs want to know what brain exposures are most damaging to them and informed outright if they are at increased risk of exposure or injury while performing a specific training activity. They want brain exposures tracked, monitored and documented into a record that transfers and is visible to the veteran's hospital, should they require medical care after leaving active service.
Lack of Resources for Those Already Affected	• SMs want more resources (clinical tools, protocols, research solutions) for those who have been in the military for longer periods of time and may be noticing changes in their functional abilities.
Infrequent Periodic Health Scans/ Evaluations	• SMs would like to have general physical and brain health assessments, scans or tests occur on a more frequent and periodic basis across the career lifecycle along with aggressive follow-up if deficits are identified.

WBH Strategy and Action Plan: Overview

- The WBH framework supports maximizing the strength, resilience, and readiness of our Forces to meet and exceed the objectives of protecting the homeland and maximizing combat effectiveness (National Defense Strategy)
- Consists of five Lines of Effort, 18 objectives, and 53 associated activities for the deliberate, prioritized and rapid development (and/or refinement/sustainment) of end to end solutions
- Final draft is pending endorsement by Executive Committee

WBH Comprehensive Strategy and Action Plan: Overview

Vision:
Optimize Warfighter brain health and performance to maximize Joint Force superiority and lethality in all operating environments

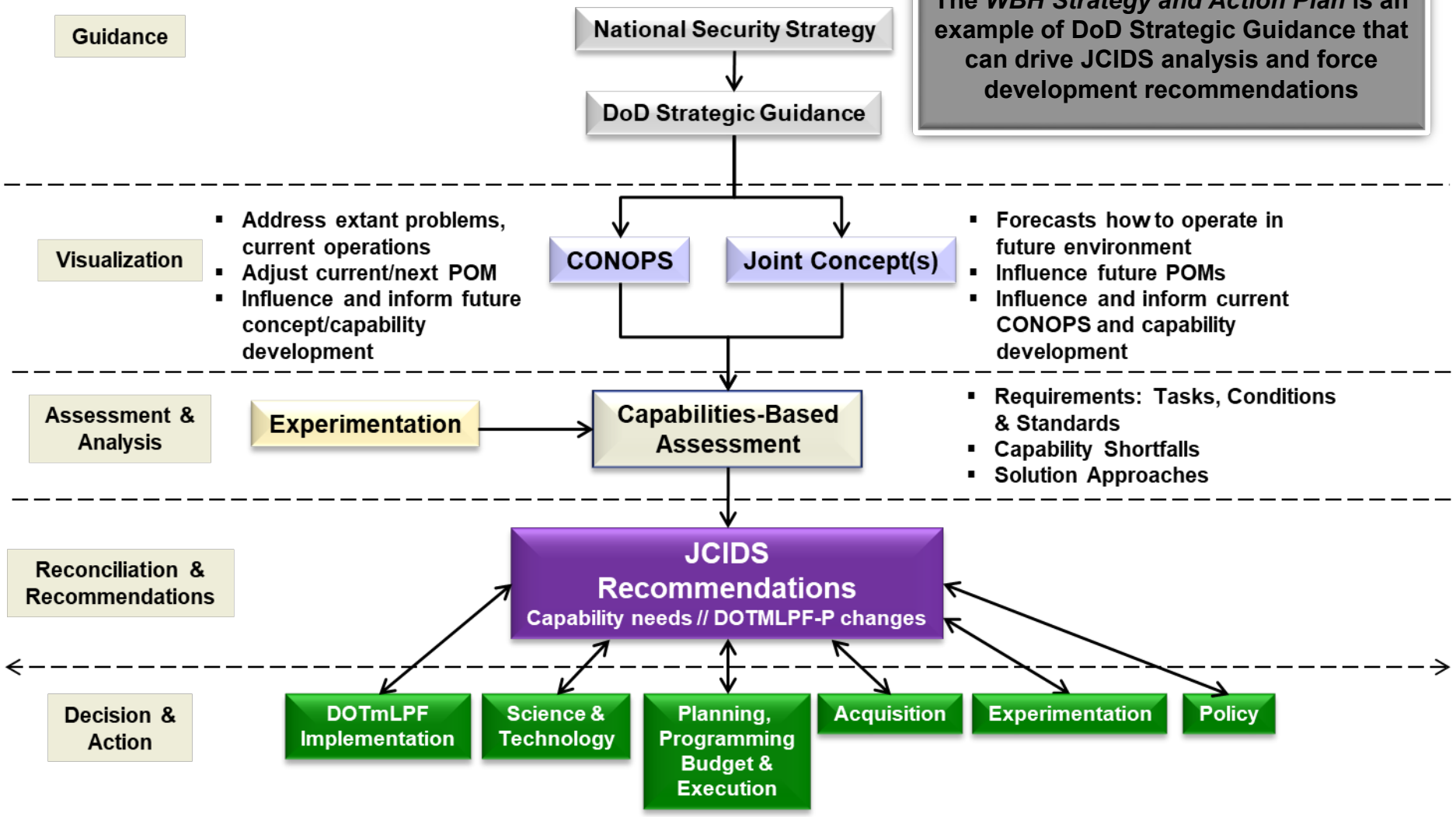
Mission:
Act rapidly to provide products, practices, and policies to directly impact Warfighter brain health and performance

LOE	LOE #1: Optimize Cognitive and Physical Performance	LOE #2: Identify, Monitor, and Mitigate Brain Exposures	LOE #3: Prevent, Recognize, and Minimize the Effects of Traumatic Brain Injury	LOE #4: Reduce or Eliminate Long-Term/ Late Effects	LOE #5: Advance Warfighter Brain Health Science
Objectives	**1a.** Establish cognitive and physical performance baselines to identify performance changes **1b.** Enhance current cognitive and physical performance to achieve superior lethality and readiness **1c.** Restore cognitive and physical performance after brain exposure or injury **1d.** Raise awareness and convey best practices that maximize cognitive and physical performance	**2a.** Understand the known and emerging threats and hazards to brain health **2b.** Monitor warfighters for brain exposures **2c.** Reduce the risks of brain exposures that may negatively impact brain health	**3a.** Reduce risks of TBIs that may negatively impact brain health **3b.** Educate stakeholders regarding the signs and symptoms of TBI and a means to report it **3c.** Reduce the effects of TBIs on brain health and performance **3d.** Optimize medical care to return warfighters to full duty following TBI	**4a.** Understand the characteristics and causes of the long-term consequences of known and emerging brain exposures and/ or TBI **4b.** Mitigate long-term and late effects of TBI through effective treatment and rehabilitation **4c.** Collaborate with the VA and other government agencies to provide a seamless transition for care for those with long-term and/or late effects	**5a.** Align brain health research and acquisition to current and emerging threats and operational requirements **5b.** Maximize warfighter brain health research opportunities for partnerships with other government agencies, industry, and academia **5c.** Enable researchers to have access to valid data regarding brain exposures and brain injuries and related brain health effects **5d.** Translate research findings into knowledge and materiel products, practices, and policies to maintain and optimize warfighter brain health

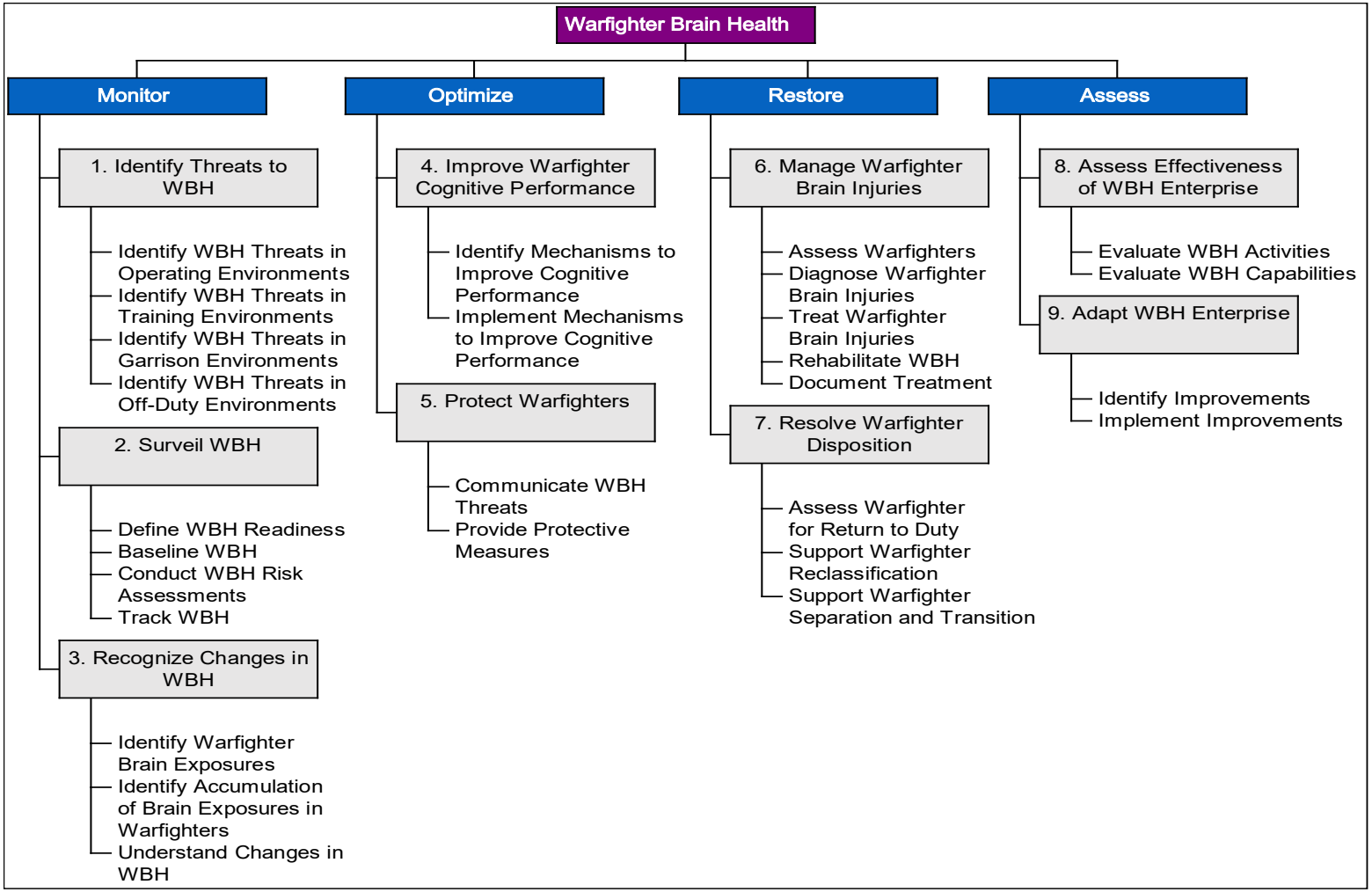
COGNITIVE SURVEILLANCE MONITORING

What is Joint Capabilities Integration and Development Systems (JCIDS)? How is this related to Warfighter Brain Health?

The *WBH Strategy and Action Plan* is an example of DoD Strategic Guidance that can drive JCIDS analysis and force development recommendations



WBH Capabilities Based Assessment: Operational Activity Model (OV-5a)*



*shows the capabilities and tasks required to mitigate threats to WBH.

WBH Initial Capabilities Document (ICD) Examples

- Develop ways to distinguish between a diagnosis of TBI and other physical and psychological health conditions.
- Develop ways to reliably predict symptom trajectory for patients who might have TBI, post-traumatic stress disorder (PTSD), or both insults simultaneously.
- Conduct research to improve the ability to treat co-occurring TBI and psychological health conditions, including PTSD.
- Conduct research to understand the demographic, sex, gender, genetic, medical history, injury, and exposure history factors that affect how warfighters respond to brain exposures and injuries.
- Conduct research to understand the effect of co-occurring conditions to brain exposures and injuries that influence functional outcomes for warfighters, including performance.
- Conduct research to improve understanding of onset and progression of brain injury symptoms, including how to distinguish them from symptoms caused by other stressors or exposures, to improve brain injury detection and screening.

WBH Priorities

- Cognitive Surveillance Monitoring
  - The warfighter's ability to make expedient, effective decisions on the battlefield
  - Identifying a decrease in cognitive performance over time supports SM-level intervention to improve operational readiness

WBH Priorities

- Known and Emerging Brain Threats Monitoring
  - Blast overpressure* (include underwater and subterranean exposures)
  - Blunt force impact
  - High G acceleration/vibration/recoil
  - Incoming/Near missed impact (ex. Ballistic Missiles)
  - Ballistic Projectiles
  - Directed energy
  - Chemical-Biological-Gas toxins
  - Other environmental hazards

WBH Priorities

- Address Effects of Traumatic Brain Injury
  - Develop protective and preventative measures
  - Promote early diagnosis
  - Evidence-based treatment strategies
- Mitigate long-term and late effects
  - Understand characterizes and causes
  - Models to forecast
  - Collaboration with VA and other Government Agencies

Enclosure 4
Overview of Combat Casualty Care Research Program TBI Portfolio

TBIPHRP
Stakeholder Meeting

27-28 April 2021

Travis M. Polk, MD, FACS
Commander, Medical Corps, U. S. Navy
Director
Combat Casualty Care Research Program
Chair, Joint Program Cmte-6

Combat Casualty Care Research Program

Vision: Optimize survival & recovery from combat related injury in current & future operational scenarios

Mission: Drive medical innovation through ***requirements-driven*** development of knowledge & materiel solutions for the acute & early management of combat related trauma including point of injury, en-route & facility based care

TBI Scope: Close military-relevant gaps in combat-related traumatic brain injury (TBI) from point of injury through evacuation from theater

Lines of Effort:

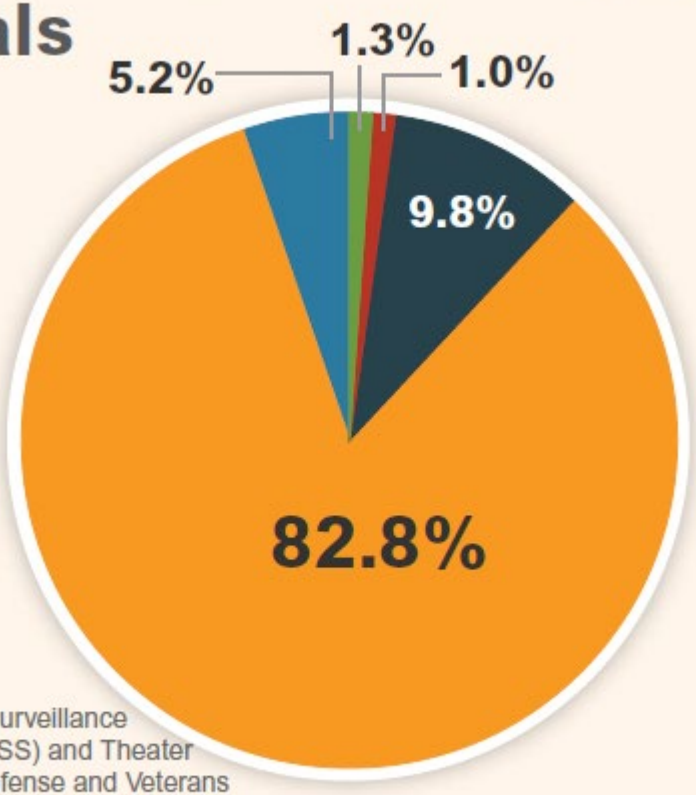
- Rapid detection and diagnosis of TBI at point-of-injury, including prognostic indicators for prolonged field care
- Forward deployable capabilities to monitor critical physiological parameters in TBI patients
- Innovative therapeutic strategies to improve outcomes across the spectrum of acute TBI severity including polytrauma

Traumatic Brain Injury in the DoD

DoD Numbers for Traumatic Brain Injury
Worldwide — Totals

2000-2019 Q3

Penetrating	5,279
Severe	4,110
Moderate	40,378
Mild	342,747
Not Classifiable	21,344
Total - All Severities	**413,858**



Source: 2000 to 2018 Q1 data provided by the Armed Forces Health Surveillance Branch (AFHSB) using the Defense Medical Surveillance System (DMSS) and Theater Medical Data Store (TMDS); data starting 2018 Q2 provided by the Defense and Veterans Brain Injury Center (DVBIC) using the MHS Data Repository (MDR).

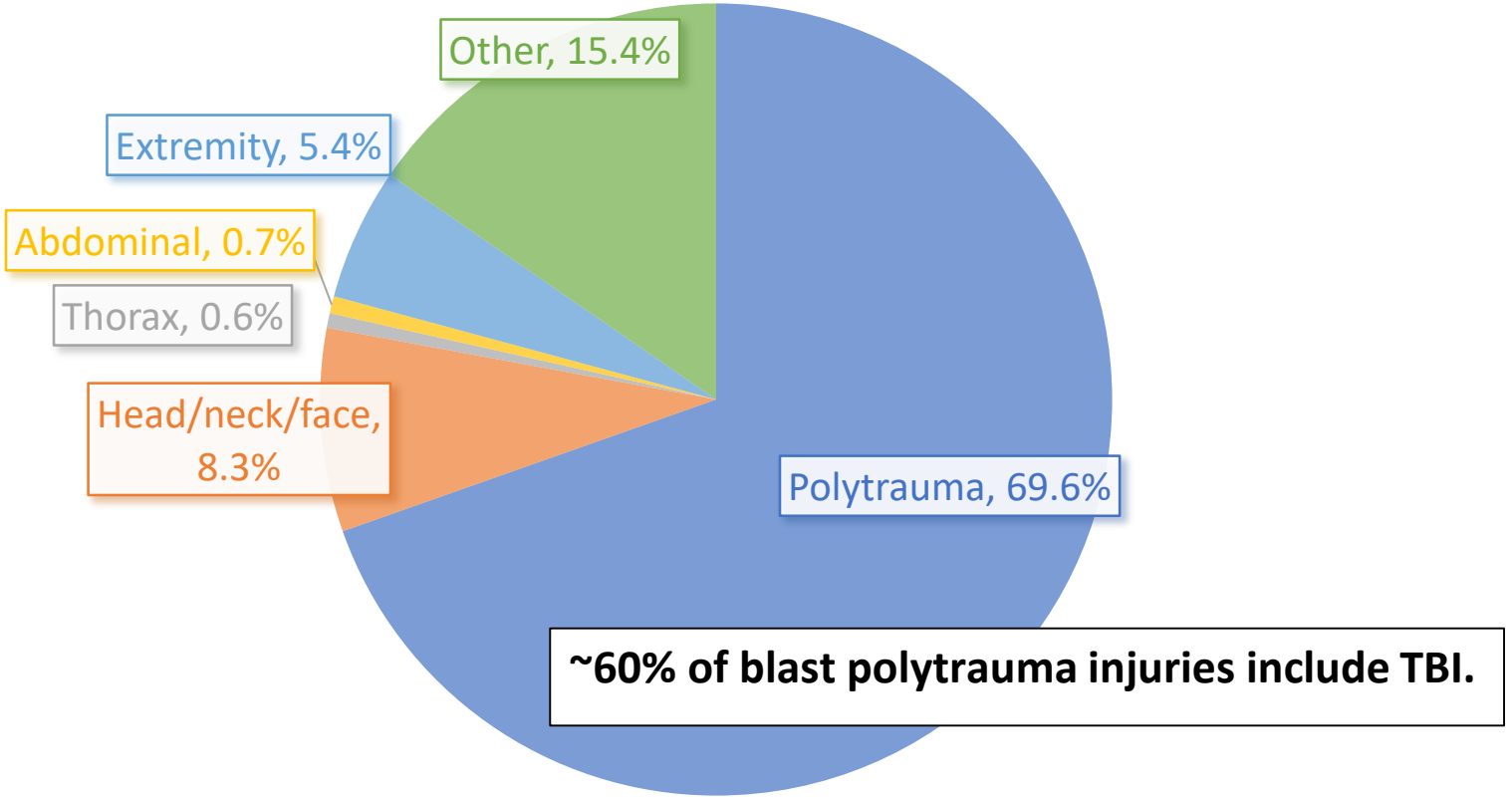
Prepared by the Defense and Veterans Brain Injury Center (DVBIC)

2000-2019 Q3, as of November 08, 2019

*Percentage may not add to 100% due to rounding.

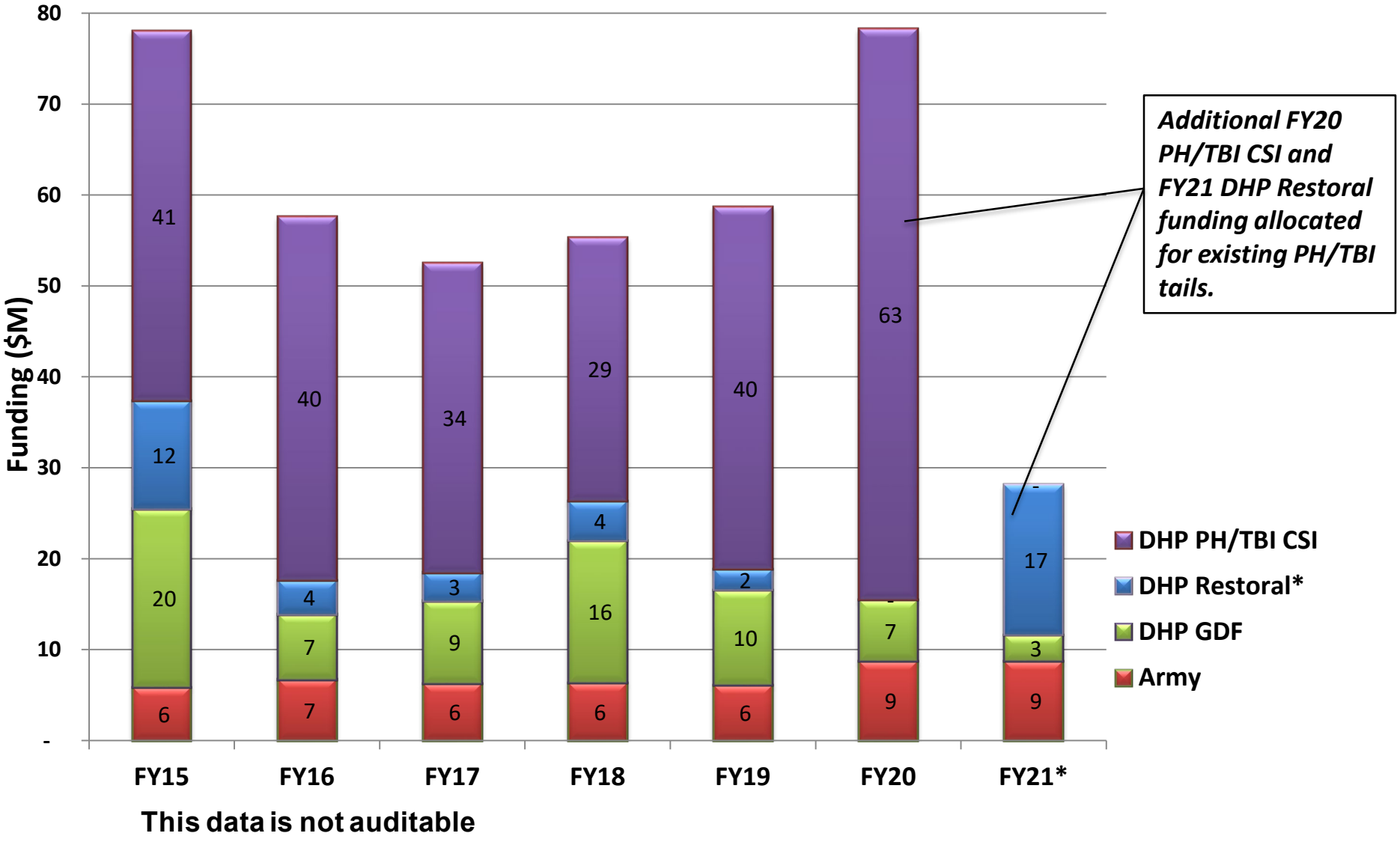
TBI and Polytrauma

Mechanism of injury, military operations 2007-2017



DoD Trauma Registry, Emergency War Surgery , 5th Ed, 2018 (piechart)
Okie S. Traumatic brain injury in the war zone. New England Journal of Medicine. 2005;352(20):2043–7

FY15-21 CCCRP Neurotrauma Funding



This data is not auditable

Military TBI Challenges

- High rate of concomitant injuries (polytrauma)
- High numbers of concussions, but also significant burden of injury from moderate/severe/penetrating TBI
- Unique challenges of austere environment and prolonged evacuation
- Limited capability to objectively diagnose and triage TBI at point-of-injury and early echelons of care (Highly dependent upon evacuation and head CT)
- Limited TBI specific interventions at point-of-injury and early echelons of care
- Need for objective measures for “return to duty” following mTBI

Collaborations with DoD, Federal, and Private Entities

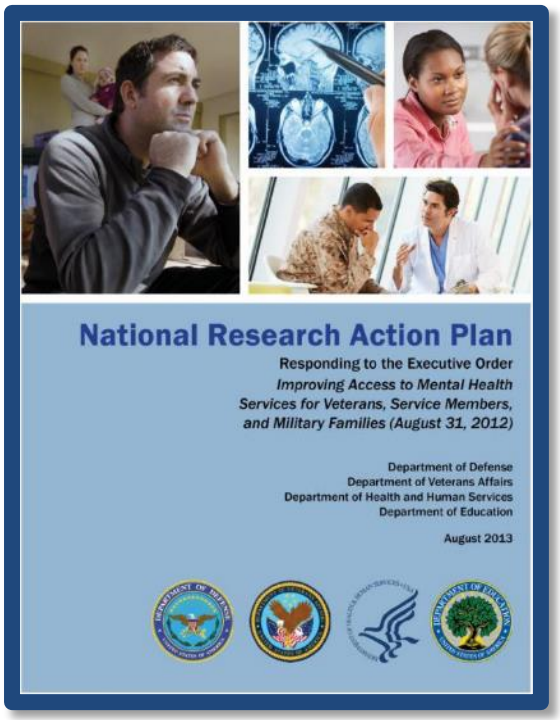
Effort	Partners
National Research Action Plan (NRAP)	DoD, VA, DHHS (NIDILRR, NIH/NINDS), CDC
DoD TBI Advisory Council (TAC)	MRDC, DVBIC, USU, DoD Departments, USSOCOM
Federal Interagency Traumatic Brain Injury Research (FITBIR)	DoD, NIH, VA, Academia
International Initiative for TBI Research (InTBIR)	NIH, Ontario Brain Institute , One Mind, DoD, European Commission
TBI End Points Development (TED)/Targeted Evaluation, Action, and Monitoring of TBI (TEAM-TBI)	DoD, NIH, FDA, Academia, Industry, Wings for Vets
Transforming Research And Clinical Knowledge in TBI (TRACK-TBI)	DoD, NIH
Concussion Assessment Research and Education (CARE)	DoD, NCAA
Chronic Effects of Neurotrauma Consortium (CENC) & Long-Term Impact of Military-Relevant Brain Injury Consortium (LIMBIC)	DoD, VA, Academia, Industry

National Research Action Plan

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

Executive Order 13625 – August 31, 2012

- Interagency Task Force established for implementing the Executive Order
- Section 5 of the Executive Order directs DoD, VA, HHS and Education to develop a National Research Action Plan (NRAP)



NRAP Development and Implementation

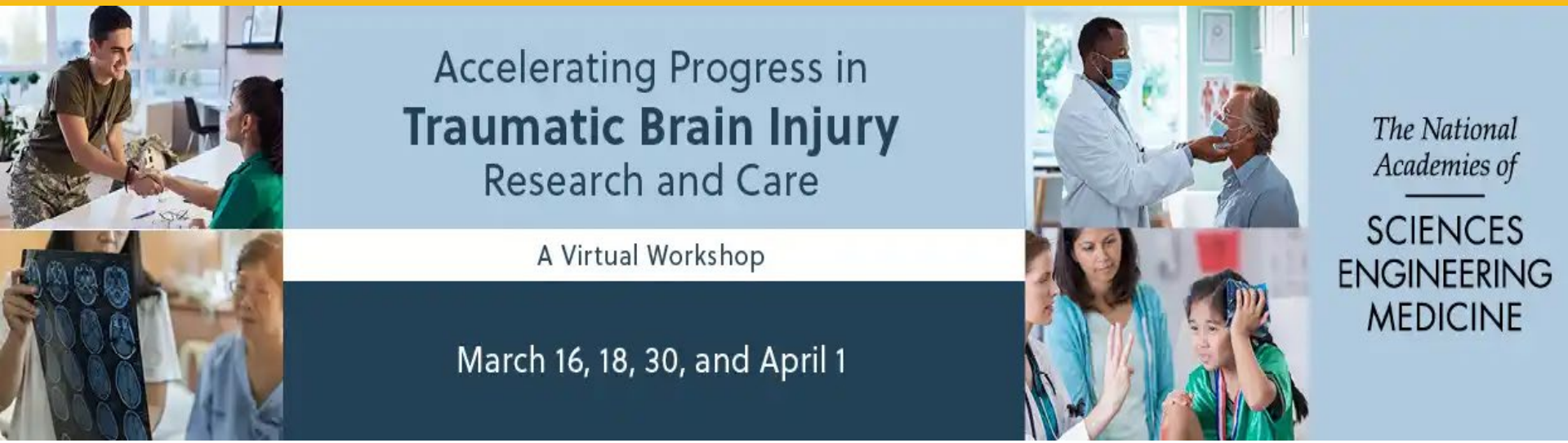
- The NRAP is a 10-year blueprint for interagency research to enhance the diagnosis, prevention, and treatment of PTSD and TBI, and to improve suicide prevention
- President Obama released Plan on 10 August 2013
- Includes immediate, short-term, and long-term initiatives
- Includes total of 86 initiatives; one initiative can include
  - more than 100 projects
- Represents both a strengthening of ongoing coordination/collaboration activities as well as directing new activities
- Interagency committee that directs an unprecedented research collaboration

DoD	• OSD Health Affairs • Defense Health Agency • US Army Medical Research and Development Command
VA	• VA Office of Research and Development
HHS	• National Institute of Mental Health • National Institute of Neurological Disorders and Stroke • National Institute on Drug Abuse • National Institute on Alcohol Abuse and Alcoholism • National Institute on Disability, Independent Living, and Rehabilitation Research

National Research Action Plan (NRAP): Focus Areas (2014-2019)

	Foundational Science	Epidemiology	Etiology	Diagnosis, Prevention and Screening	Treatment	Follow-up Care	Services Research
Major Focus Areas	➢Characterize the pathobiology of TBI and comorbidities from the molecular to systems scales ➢Understand the biomechanics of blast and impact TBI and their relationship to acute and chronic pathology	➢Develop a clinically useful definition and staging criteria of TBI ➢Leverage the FITBR, TBIMS national database and related data repositories to improve the understanding of the natural history, injury trajectories, and relationships of comorbidities in the spectrum of TBI patients ➢Develop long-term studies to identify the nature of risk factors and frequency of chronic effects	➢Develop appropriately scaled and standardized animal models of blast and impact TBI ➢Understand genetic, epigenetic, environmental, socioeconomic, gender, and ethnic differences in predisposition and recovery ➢Understand the interplay between TBI and other comorbid disorders	➢Prevention: ➢Education and risk prevention ➢Stigma & barriers to seeking treatment ➢Personal protective equipment ➢Screening: ➢Serum biomarkers ➢Physiologic biomarkers ➢Assessment: ➢Automated neurocognitive assessments ➢Advanced imaging	➢Develop: ➢Biomarkers that detect the effectiveness of specific treatment interventions ➢New/repurposed medications and combination treatments ➢Neuromodulation /neural plasticity approaches ➢Approaches that address comorbidities ➢Methods for guiding personalized treatments ➢Adjunctive therapies (complementary and integrative)	➢Develop: ➢Improved, validated short- and long-term rehabilitation strategies ➢Biomarkers for assessment of recovery ➢Long-term recovery tracking and systems of care ➢Protocols and tools for periodic rescreening ➢Recovery protocols ➢Validated return-to-duty standards ➢Continuity of care models	➢Improve access, quality, and outcomes of care ➢Maintain efficacy/fidelity in treatment and care systems ➢Develop effective methods for disseminating best practice information and increasing adoption by providers ➢Identify improved uniform mechanisms for health care provider and caregiver education, training, and respite. Ensure transfer of training through the use of advanced technologies such as simulations
# of DoD Projects (2014-2019)	232	63		177	200	39	33

NASEM TBI Consensus Study (2021)



Goals:

- Explore and assess the public and military health burden of TBI
- Examine the current landscape of TBI research and identify opportunities for acceleration
- Improving TBI systems of clinical care from acute care through rehabilitation.

Deliverable: The report will provide a roadmap for advancing both research and clinical care over the next decade; identify major barriers and knowledge gaps that are impeding progress in the field; and highlights opportunities for collaborative action (both intergovernmental and public-private) that could accelerate progress in TBI research and care.

Exemplar Initiatives/Programs/Research

- **OTA strategy-Competitive Staged Awards with Options**
  - **Stage One – Complete TRL 5**
    - Option for Preclinical studies, including GLP animal safety & toxicityto support IND applications
    - IDE review by CDRH
    - Option to proceed to Stage Two
  - **Stage Two – Complete TRL 6**
    - IND application prepared and submitted Phase 1 clinical trials completed, data support proceeding to Phase 2 clinical trial.
    - Class III device safety demonstrated, support proceeding to clinical safety & effectiveness trials. For 510(k), info & data support production of final prototype and final testing in a military operational environment
- **Federal Interagency TBI Research (FITBIR) Data Repository**
  - Mandatory submission for appropriate studies funded by NIH and DoD.
  - ~80,000 subjects account for ~4.3M data sets
  - ~1.5M data sets have been shared with the FITBIR community
  - FY19 CCCRP funded 7 projects for analysis of FITBIR data
- **Partnerships and Consortium**
  - TBI Endpoint Development (TED)
    - First biomarker accepted by FDA Medical Device Development Tools (MDDT)
    - Unique neuroimaging signature predictive of patients who have sustained mild TBI, but are more likely to develop chronic symptoms and be refractory to care.

Top 3 Research Priorities

TBI therapeutics (particularly pharmaceuticals)

- » Concrete milestones, clear deliverables and transition plans, regulatory expertise

TBI management solutions for combat environment (diagnostics and therapeutics)

- » Material products: Size, weight, power, cube, expertise/provider, low logistical footprint, adoptability, operational constraints
- » Knowledge products of military relevance:

  mTBI vs moderate /severe/penetrating TBI

TBI definitions/lexicon/endpoints

Other considerations: Flexible award strategies and leverage partnerships/consortium

- » Other Transaction Authority
- » Targeted consortia to achieve/obtain deliverables

CCCRP
Combat Casualty Care Research Program

Questions?

CDR Travis M Polk, MC, USN, travis.m.polk2.mil@mail.mil

Enclosure 5
Overview of Military Operational Medicine Research Program
Psychological Health Portfolio

Military Operational Medical Research Program (MOMRP), JPC5 Overview

CDR Christopher Steele, Director

US Army Medical Research and Development Command (MRDC)

MOMRP Overview

MOMRP portfolio serves to ensure Service members are

responsive to the challenges of training
resilient to the rigors of combat
resistant to longitudinal stressors

Develops capabilities and delivers solutions to:

- Prepare for the fight and stay in the fight
- Enable Service members to overcome external and internal stressors
    - *External factors* include heat, cold, blast and repeated impacts (operating weapons systems, physical injury)
    - *Internal factors* are both physiological and psychological

MOMRP Mission and Portfolios

Develop effective biomedical countermeasures against operational stressors and to prevent physical and psychological injuries during training and operations in order to maximize the health, readiness and performance of Service members and their Families, in support of Multi-Domain Operations, Army CFT and SECDEF Lethality Priorities, and Human Performance Optimization & Enhancement and DoD Total Force Fitness concepts.

JROC approved Joint Military Operational Medicine Initial Capabilities Document, NOV 2018

Science

ENVIRO

Environmental Health and Protection

THREATS

- Heat/Humidity Stress
- Dehydration
- Cold Stress
- Dust/Air Pollution
- Toxic Industrial Chemicals/Materials
- Water Contaminants
- Altitude & Undersea Hypoxia

INJURY

Injury Prevention and Reduction

THREATS

- **Musculoskeletal Injury**
- Blast Overpressure
- Blunt Head/Body Trauma
- Face/Eye/Spinal Injury
- **Acoustic Trauma**
- Directed Energy Injury
- Degraded Visual Environment

PHYSIO

Physiological Health and Performance

THREATS

- Disaggregated/Continuous Operations
- Sleep Deficit and Circadian Desynchrony
- Sustained Fatiguing Work (Physical/Mental)
- Malnutrition
- Dietary Supplements Misuse

PSYCH

Psychological Health (PH) and Resilience

THREATS

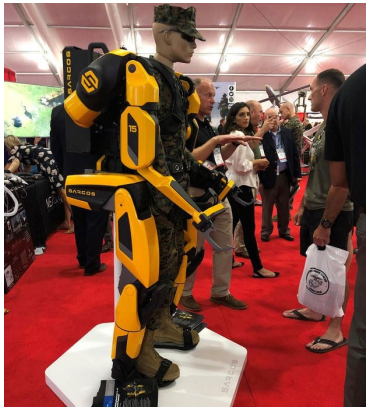
- PTSD/Other PH Disorders
- Suicide Behavior
- Alcohol/Other Drug Use
- Co-occurring Mental Disorders
- Access/Retention in Behavioral Health Care
- Family Transitions and Well-being

- MILCOHORT Epidemiology Efforts
- Biomedical Performance Enhancement
- Wearables for Health, Readiness and Performance

Service Member

MOMRP Blast, Blunt, Accelerative & Neurosensory Portfolio

- **Optimize Warfighter brain health, function and readiness through prevention, protection and advanced neurosensory treatments**
- **Develop medical criteria to support development and fielding of personal protective equipment, weapon systems, and vehicular platforms**
- **Address the challenges of subclinical, repetitive exposures to brain health**



MOMRP Blast, Blunt, Accelerative, and Neurosensory Strategic R&D Directions

- **ARMY** Functional Objectives:
  - **FO1: Improved PPE for advanced survivability and protection**
  - **FO2: Preserved medical readiness for the Force after operational exposures to subclinical impacts**
  - **FO3: Preserve neurosensory function in MDO**

- **JPC** (Joint) Directions: Development of exposures standards for repeated blast exposures:
  - **Goal 1: Address FY18 NDAA Section 734: Determination of the contributions of cumulative blast exposures in order to develop joint DoD blast safety exposure standards.**
  - **Goal 2: Algorithm(s) that predict the risk of neurological impairment from repeated blast exposure.**

- **JPC** Directions: Sensory Protection and Treatment:
  - Goal 1: Joint DoD medical protection and performance criteria for hearing protection devices (HPDs) to reduce injury risk and improve use of HPDs by Service members in multi-domain operations.
  - **Goal 2: Treatment mitigation solutions for acute and chronic sensory dysfunction (auditory, visual, and balance dysfunction).**
  - Goal 3: Tools to monitor and provide intervention capabilities that will prevent/mitigate hearing loss and tinnitus from hazardous noise exposure.

MOMRP Blast, Blunt, Accelerative, and Neurosensory Recommendations

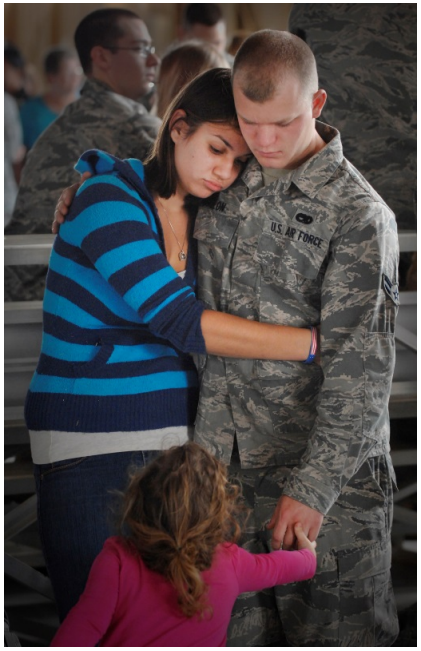
- **Near term research programs:**
  - TBI Prevention initiatives
  - Development of exposure limits for repeated low level blast exposure standards.
  - Computational models of brain injury and translation of animal models to humans.
  - Brain injury ***mechanistic research*** to determine injury thresholds for blunt, blast and ballistic threats.

- **Long term strategic research program to protect against emerging threats in extreme environments and multi-domain battlefield:**
  - Validate injury criteria and medically valid standards for helmets against acute and repetitive blunt impact, ballistic induced blunt impact, and blast induced injury criteria (e.g., hemorrhage) with and without PPE up to 150 psi.
  - Validate human biomechanical and physiologic response to head support mass effects on ground Soldier populations.
  - Establish brain health and performance dose response curves relating neurophysiological performance and environmental sensor measures in extreme environments.

Psychological Health and Resilience Portfolio

- **Deliver evidence-based solutions and inform policies to optimize, enhance, and sustain Service Member, unit and Family psychological health, well-being, and readiness**
- **Reduce negative impacts of training, garrison and operational stressors**





Sub-Portfolios:

- » Suicide Prevention
- » Family Related Issues
- » Resilience
- » Sexual Harassment and Assault Prevention
- » Alcohol and Substance Use

MOMRP Psychological Health and Resilience Strategic R&D Directions

ARMY Functional Objectives:

- **FO1: Neurocognitive tools to minimize stress-related decrements in cognitive performance and behavioral health**
- **FO2: Multi-dimensional leadership strategies to improve targeted behavioral health outcomes that contribute to readiness and risk reduction**
- FO3: Tools to improve recognition of morally/ethically ambiguous situations and to guide disciplined decision making for navigating moral challenges in the MDO
- FO4: Rapid assessment tools and tailored recommendations for leaders to address emerging risks to behavioral health
- FO5: Integrated training and tools to enhance small-team adaptability and cohesion that contribute to behavioral health and performance
- FO6: Pharmacologics, nutraceuticals and/or supplements to limit stress-related performance decrements

JPC Directions: Early Assessment & Interventions to Support Service Member & Family Psychological Health

- **Goal 1: Evidence-based multi-modal assessments that build upon empirical evidence to identify the behavioral health (BH) needs of Service members.**
- Goal 2: Preventive strategies early in the military lifecycle that target the issues identified by the assessment to promote healthy behavior and mitigate Service member BH difficulties in high-stress occupations.
- Goal 3: Evidence-based interventions and joint DoD guidance that promotes psychologically resilient military families and community networks over the military life cycle.
- Goal 4: Promote and develop evidence-based prevention programs to reduce the rates of sexual assault and sexual harassment

MOMRP Psychological Health – Sexual Assault Strategic R&D Directions

Goal

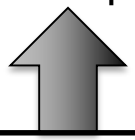
» Promote and develop evidence-based prevention programs to reduce the rates of sexual assault and sexual harassment

Objectives

» Develop/tailor interventions that are effective or have efficacy for relevant military stakeholders (e.g. DoD SAPRO)

» Develop and disseminate the implementation of existing or developed interventions

» Identify and target modifiable risk and protective factors for victimization and perpetration



- ❖ Skills-based, prevention programs (e.g., healthy relationships, skills to aid others, empowerment)
- ❖ Public health prevention
- ❖ Viable options for policy change
- ❖ Service members' ecological framework impacting readiness (i.e. individual, relationship, unit, installation, community, and society)

MOMRP Psychological Health and Resilience Recommendations

- Emphasis on gap and requirements-driven research aimed at delivering actionable information and evidence-based solutions
- Leverage requirements and strategic documents (e.g., DOD Suicide Prevention Research Strategy, Joint MOM ICD)
- Research on breakout session topics that are threatening Service member and military family health, readiness, and retention (there have been some DHA divestments here)
- Programmatic and strategic coordination to avoid unnecessary duplication and redundancy of effort
- Leverage recent cross-cutting initiative…

MOMRP Psychological Health- Sexual Assault Recommendations

Assessment of Factors Influencing Sexual Assault Prevention and Response

» Ensure prevention and response activities are comprehensive and address individual, interpersonal, and organizational factors – particularly as assessed at the organizational level where less research has been conducted – by developing an empirically validated construct inclusive of culture, climate, and continuum of harm, and identifying how organizational-level constructs influence interpersonal and individual conditions, choices, and behaviors.

» Focus data collection efforts on data from influencers, bystanders, and alleged perpetrators.

» Identify and validate indicators of sexual assault prevention and response outcomes for use in prevention and response planning, program and policy evaluation.

Institutional Response to Sexual Assault

» Identify the processes of shame, stigma, and institutional betrayal as reported in the victim experience as well as for the unit, and evaluate approaches and processes to mitigate these experience or perceptions.

» Identify barriers to reporting and factors that are associated with retaliation within the unit, support network, and command levels. Evaluate approaches to mitigate barriers and prevent retaliation.

» Identify the policies, procedures, and practices that contribute to the attrition or successful reintegration of victims.

Development and Evaluation of Sexual Assault Prevention Activities

» Develop and evaluate prevention policies, programs, and practices.

» Adapt existing evidence-based and evidence-informed prevention activities for the military.

Dissemination and Implementation Methods

» Identify the optimal delivery mechanisms for sexual assault prevention and response knowledge, skills, and norms across the military career cycle.

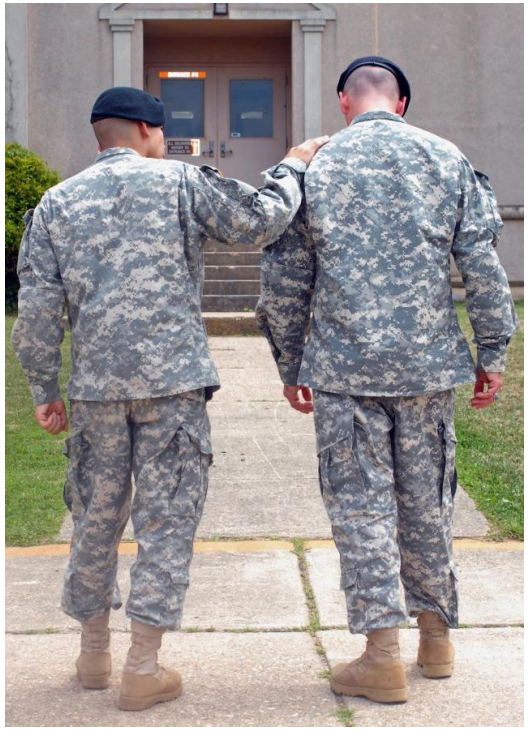
» Develop and implement a process to consistently disseminate and archive DoD-funded sexual assault prevention and response research so that such research and related findings are accessible and available DoD-wide.

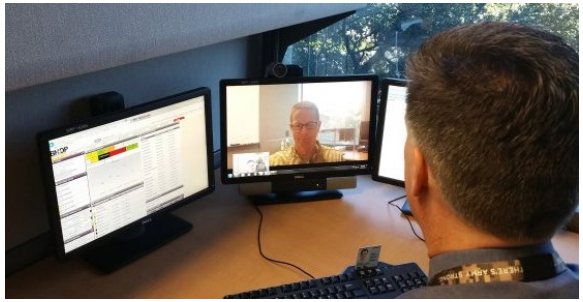
Comprehensive Cross-Cutting Prevention to Decrease Harmful Behaviors in Service Members

- Proposals focused on optimizing health promotion via prevention initiatives for the military that provide education and skills, protective environments, and healthy climates and relationships in efforts to prevent various forms of violent, abusive, or harmful behaviors.
- Topic Areas of Interest:
  - Suicide ideation and behaviors and non-suicidal self-injury
  - Sexual violence (sexual harassment and assault)
  - Harassment (e.g., gender and racial discrimination, retaliation)
  - Domestic abuse (intimate partner violence)
  - Alcohol and substance use, misuse, and disorders
  - Psychological health issues
- **FOCUS AREA #1:** Community Based Participatory Research (CBPR) - Use CBPR/participatory action research to enhance the military community relevance of research and to develop, assess, and sustain cross-cutting prevention that is culturally grounded in the military community(-ies).
- **FOCUS AREA #2:** Measurement and Assessment - Novel methodologies to efficiently identify and/or collect short-, medium-, and long-term indicators of effectiveness of cross-cutting prevention programming.
- **FOCUS AREA #3:** Effective Primary Prevention Programming - Develop and/or adapt and test primary prevention (addressing individual, relationship, team, leader, community, and/or systems-level aspects) programming for the military context.

Psychiatry & Clinical Psychology Disorders Portfolio

- **Understand the brain-based biological underpinnings of psychological health disorders (PTSD and others)**
- **Develop evidence-based prevention and intervention strategies to mitigate the impact of psychological trauma and restore psychological health to Service Members**





MOMRP Psychological Health Clinical Disorders Strategic R&D Directions

ARMY Functional Objectives:

- FO1: Clinical practice guidelines for medics at point of need
- FO2: Rapid recovery from acute stress with non-pharmacologic interventions
- FO3: Rapid recovery from acute stress with pharmacologic interventions
- FO4: Passive sensing and other biomarkers for acute stress response prediction and assessment

JPC Directions: Screening and prevention: Develop solutions for rapid objective screening & prevention of PTSD and/or other PH issues that threaten readiness and RTD

- Goal 1: Solutions to understand, prevent, and mitigate Adjustment Disorders
- Goal 2: Pharmacological interventions to prevent PTSD
- Goal 3: Validate successful biomarkers for objective PTSD screening

JPC Directions: Treatment & Implementation: Develop solutions to maximize PTSD recovery through treatment-matching approaches and evidence-based strategies to navigate context-specific barriers and facilitators to EBT implementation in the MHS.

- Goal 1: Characterize new PH delivery challenges & potential solutions
- Goal 2: Further document efficacy of novel & adjunct PTSD treatments – must be cost-effective to implement
- Goal 3: Precision treatment solutions that leverage large PTSD consortia data and repositories

MOMRP Psychological Health Clinical Disorders Recommendations

- Leverage requirements and strategic documents (e.g., Joint MOM ICD)
- Focus on programmatic and strategic coordination for planned integration of PH materiel solutions *(e.g., algorithms, apps)* into larger DoD solutions and systems at their inception *(e.g., BHDP, HRAPS, medical support systems and evacuation, Connected Health)*
- Avoid more reiterations, combinations & repackaged psychotherapy treatment trials *(first understand what we have learned about implementation barriers and supports!)*
- *Focus on early identification and early intervention for all PH challenges – Biomarkers to support earlier identification and improved treatment*

Enclosure 6
Overview of U.S. Department of Veterans Affairs TBI Portfolio

VA Office of Research & Development
Traumatic Brain Injury Portfolio

Stuart Hoffman, Ph.D.
Senior Health Science Officer for TBI
Office of Research and Development

VA | U.S. Department of Veterans Affairs

Introduce Organization

VA Office of Research and Development Mission

Vision: The Office of Research and Development (ORD) aspires to discover knowledge, develop VA researchers and health care leaders, and create innovations that advance health care for our Veterans and the Nation.

The mission of VA Research is fourfold:

- To improve Veterans' health and well-being via basic, translational, clinical, health services, and rehabilitative research;
- To apply scientific knowledge to develop effective individualized care solutions for Veterans;
- To attract, train, and retain the highest-caliber investigators, and nurture their development as leaders in their fields; and
- To assure a culture of professionalism, collaboration, accountability, and the highest regard for research volunteers' safety and privacy.

Organization Nuts and Bolts

What is your environment?

Where do you operate within your organization or larger community?

- VA has three main administrations: Health, Benefits, and Cemeteries.
- Office of Research and Development (ORD) is part of the Veterans Health Administration, an integrated health care system and has come to be viewed as a model for superior bench-to-bedside research.
- ORD is an intramural funding program consisting of 4 Research Services: Biomedical Laboratory, Clinical Science, Health Services, and Rehabilitation

FY 2020

Active research sites nationwide	**103**
Active funded principal investigators	**3,616**
Active funded research projects (including VA funding and other sources)	**7,288**
Total congressional appropriation for VA medical and prosthetic research	**$750M**

What makes your organization unique?

- VA Research fully focuses on health issues that affect Veterans.

Organization Nuts and Bolts

- How does your organization identify priorities?
  - Through surveys, field-based meetings, town halls, regular meetings with Veteran Service Organizations, and Congressional interest
- What are your priorities?
  - Increase Veterans' access to high-quality clinical trials
  - Increase the substantial real-world impact of VA research
  - Put VA data to work for Veterans
  - Actively promote diversity, equity, and inclusion within our sphere of influence
  - Build community through VA research
- How do you measure success or progress towards priorities?
  - Growth in the nationwide network of clinician-investigators and study sites
  - Increase the number of discoveries translated into routine clinical practice.
  - Improve the use of large-scale datasets, e.g., Million Veterans Program, to reduce the time from discovery to clinical implementation
  - Have a research community that mirrors the diversity of this Nation and its Veterans
  - Data, resource, and knowledge sharing, e.g., , ORD is developing a phenomic library to enhance research and clinical care

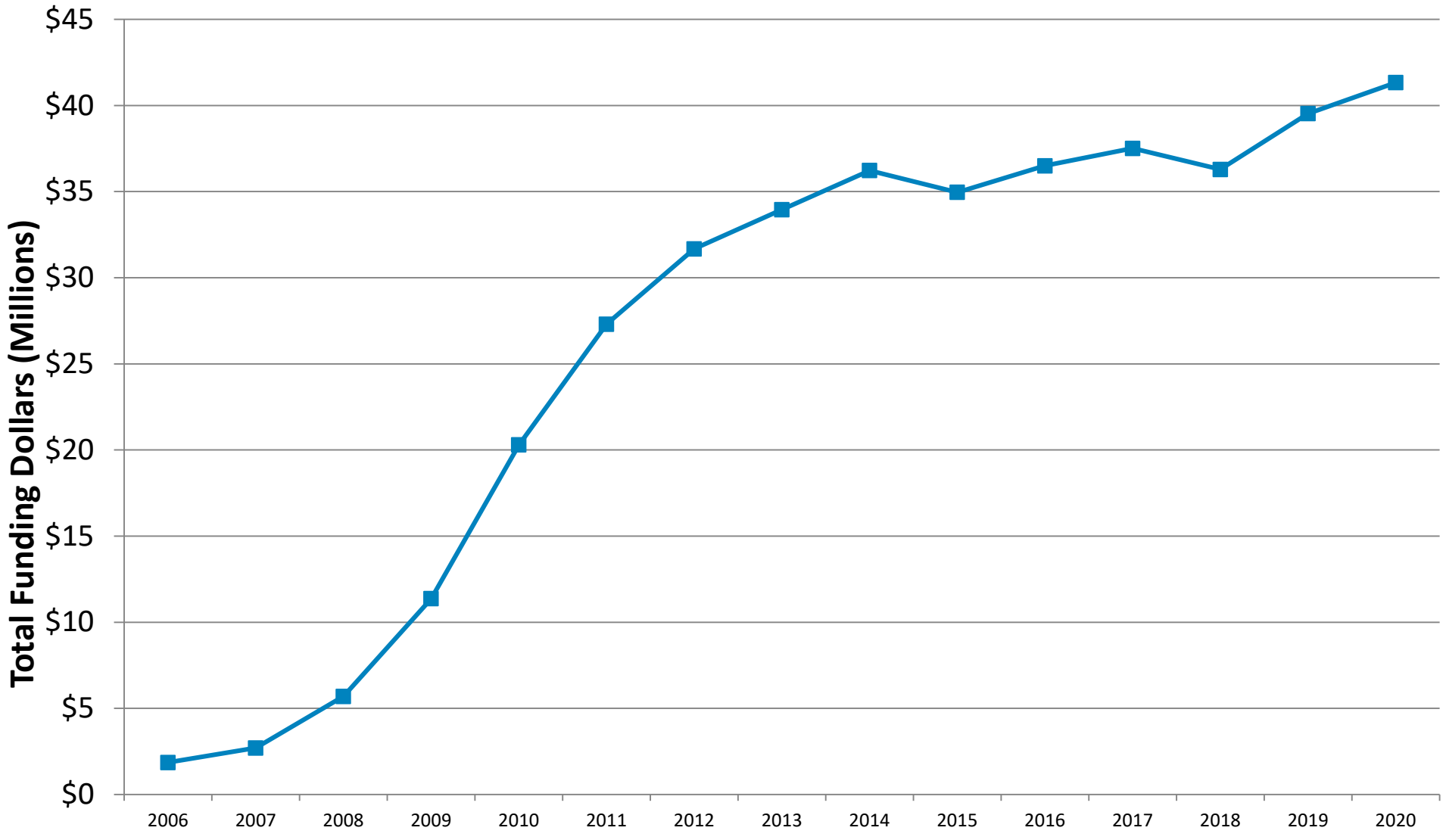
Organization Nuts and Bolts

- How do you transition your successes and progress to your key stakeholders and end users?
  - Utilizing ORD Communications
  - Annual National Radio Tours for key research areas
  - Organizing a VA research day on the Hill
  - Communication with Veteran Service Organizations
  - VA-wide Webinars, online learning modules through VA Talent Management System, online availability of clinical practice guidelines and Evidence Synthesis Reviews

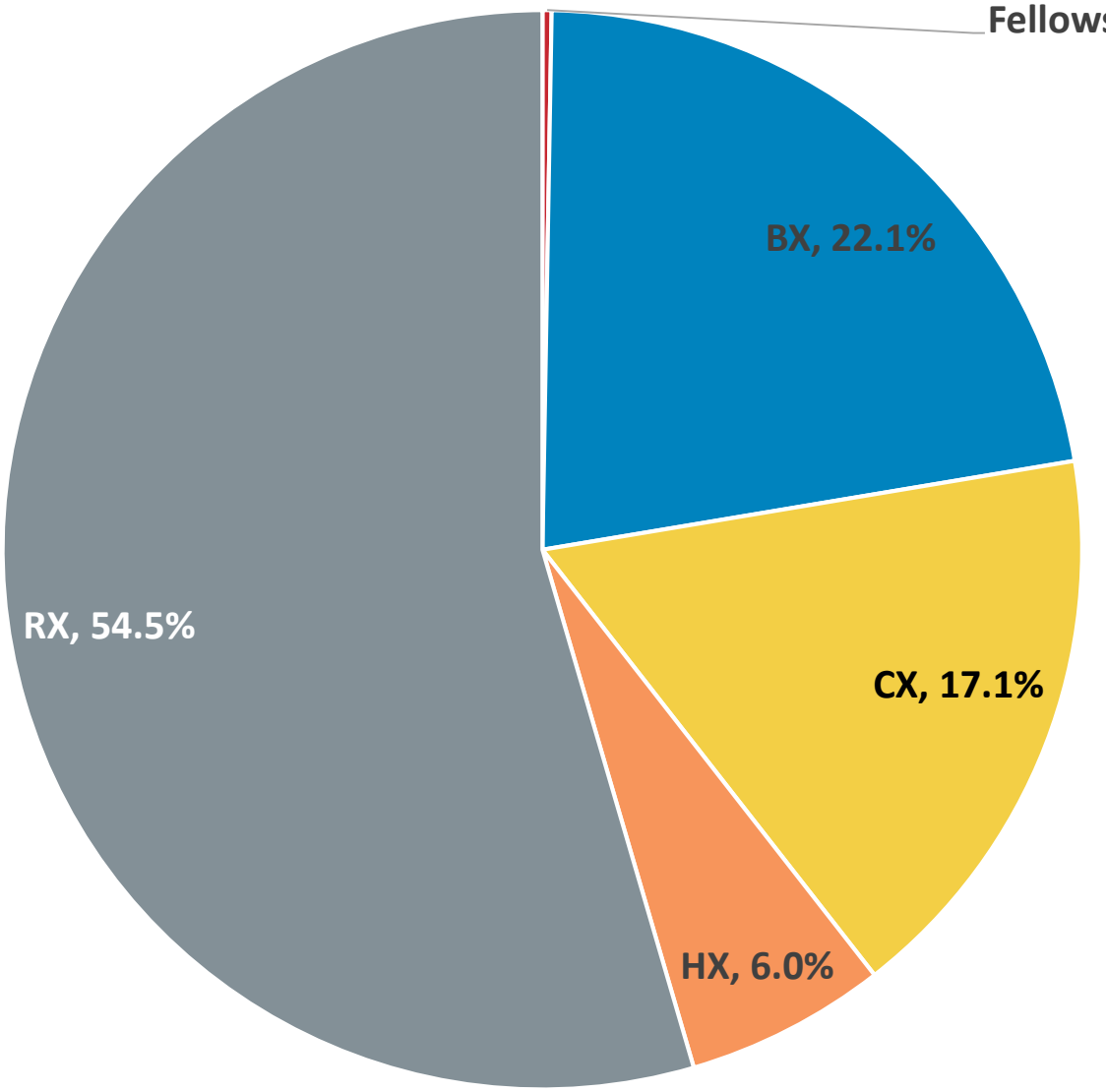
TBI Research Portfolio

- FY20: 186 active studies; $41.3 Million for the year
- Includes: clinical trials, epidemiological studies, pilot studies, career development awards, infrastructure
- The studies covered the NRAP Research Continuum Approach: foundational science epidemiology, etiology, screening, treatment follow-up care, and Services Research
- Active integration within VA, particularly with
  - Patient Care Services and its Rehabilitation Services
  - Polytrauma System of Care
  - outside VA with other Federal agencies, Foundations, and private partners

VA ORD FY06 – FY20 Investment: TBI Research

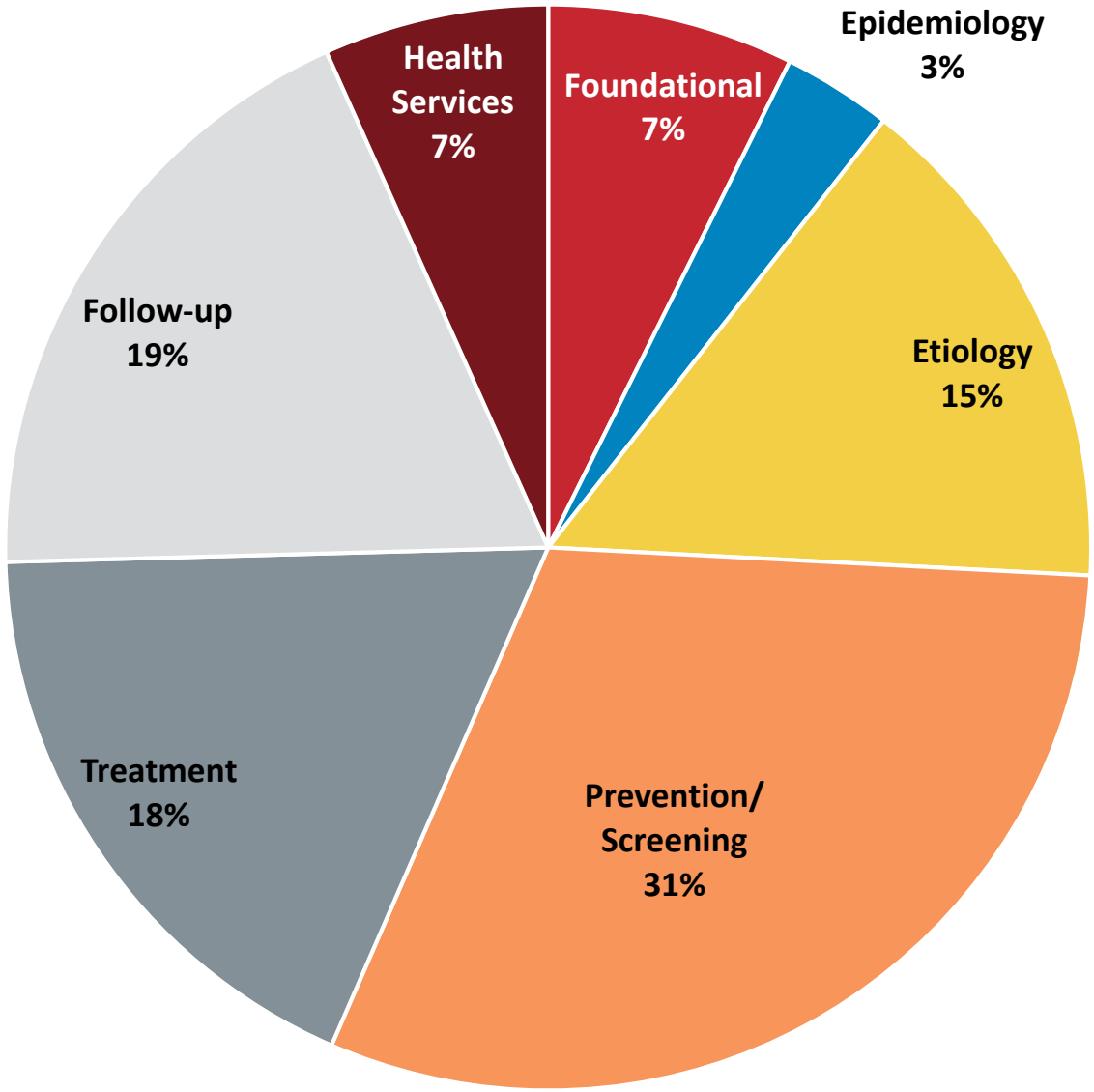


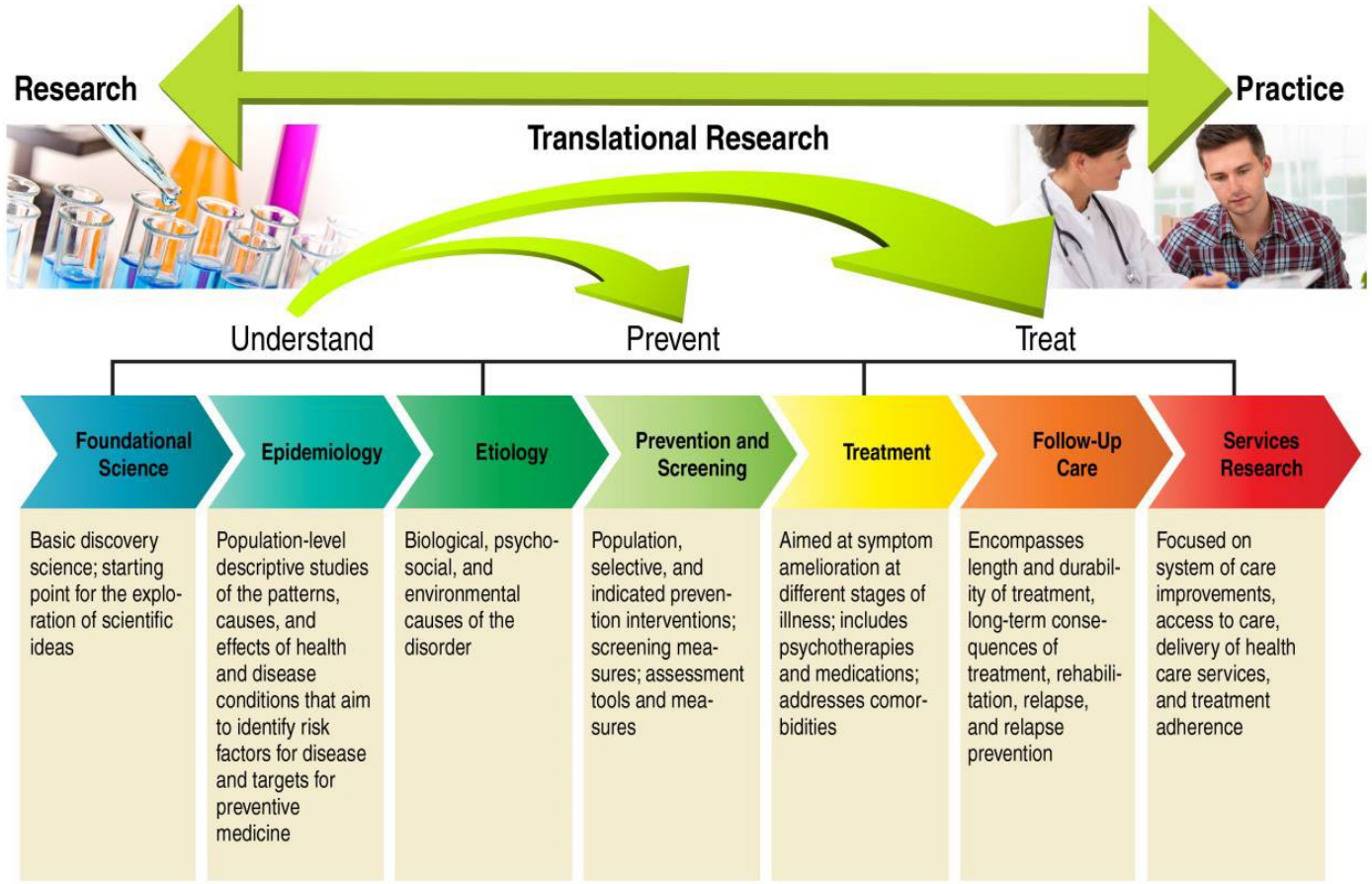
VA ORD FY20 Investment: Breakdown of Funding by Service FY20



BX = Biomedical Laboratory
RX = Rehabilitation
CX = Clinical Science
HX = Health Services
FY20 total = $41.3M

Breakdown of Funding Based Upon NRAP Priorities





TBI Initiatives

- **The VA Open Field Blast Core facility in Columbia, Missouri**
  - Enable the conduct of preclinical studies to provide key insights into the disease processes associated with primary blast exposure and may provide links to neuronal degeneration, cognitive, and neurobehavioral decline. Achievements
- **Interagency Resource Center for preclinical models of TBI**
  - Establishing preclinical common data elements and an online catalog of preclinical models of TBI with standardized procedures.
  - Purpose is to increase the translational potential of preclinical TBI research
- **Launching an ORD Health Services Research and Development (HSR&D) innovation initiative**
  - "Does Protecting Service-Connected Disability Income Motivate Return to Work in Veterans with TBI and PTSD?"
  - The initiative's long-term goal is to determine whether protection of disability benefits is associated with return to work or increase in work hours among Veterans with TBI/PTSD.

TBI Research Programs

- **RR&D Translational Research Center for TBI and Stress Disorders (TRACTS)**
  - Promotes multidisciplinary research aimed at improving our understanding of the complex cognitive and emotional problems faced by Iraq and Afghanistan Veterans.
- **The VA/DOD Long-term Impact of Military-relevant Brain Injury Consortium (LIMBIC)**
  - Continues the activities of CENC. LIMBIC's overarching goal is to improve understanding of the impact of TBI on service members and Veterans. This program will fund a longitudinal study and associated TBI research to include the collection of relevant imaging and tissue samples. Ultimately, this knowledge will inform acute and chronic TBI care.
- **RR&D Brain Rehabilitation Research Center (BRRC)**
  - Develops and tests treatments that harness neuroplasticity to substantially improve or restore motor, cognitive, and emotional functions impaired by neurologic disease or injury.

TBI Research

- **Chronic elevation of plasma vascular endothelial growth factor-A (VEGF-A) is associated with a history of blast exposure**
  - Biomarker for cognitive disability diagnosis and monitoring. Elaine Peskind Puget Sound VAMC
- **Cerebral perfusion is associated with blast exposure in military personnel without moderate or severe TBI**
  - Potential future diagnostic and therapeutic target David Salat Boston VA Healthcare System
- **Mild traumatic brain injury impacts associations between limbic system microstructure and post-traumatic stress disorder symptomatology**
  - Potential neuroimaging biomarker for risk of PTSD when there is a TBI and provide insight into treatment mechanisms, and to improve long-term monitoring of patient health. Regina McGlinchey Boston VA Healthcare System

Top 3 Research Gaps/Priorities

- **Detection, diagnosis, monitoring of remote TBI**
  - TBIs are still going undiagnosed, no current assessment for monitoring progressive changes over time.
- **Understand the contribution of repetitive TBI to mental health conditions**
  - There are higher rates of depression, PTSD, and suicide those with a TBI history.
- **Personalize neurorehabilitation**
  - Specifying therapy based on genomic, phenomic, and lifetime history.
  - Develop strategies to enhance the effectiveness of rehabilitation to improve outcomes and quality of life.

Enclosure 7
Overview of U.S. Department of Veterans Affairs Psychological Health Portfolio

VA Office of Research & Development
Psychological Health Portfolio

Cendrine Robinson, PhD
Scientific Program Manager
Rehabilitation Research & Development
Office of Research and Development

VA | U.S. Department of Veterans Affairs

VA Office of Research and Development

VA Office of Research and Development Mission

Vision: The Office of Research and Development (ORD) aspires to discover knowledge, develop VA researchers and health care leaders, and create innovations that advance health care for our Veterans and the Nation.

The mission of VA Research is fourfold:

- To improve Veterans' health and well-being via basic, translational, clinical, health services, and rehabilitative research;
- To apply scientific knowledge to develop effective individualized care solutions for Veterans;
- To attract, train, and retain the highest-caliber investigators, and nurture their development as leaders in their fields; and
- To assure a culture of professionalism, collaboration, accountability, and the highest regard for research volunteers' safety and privacy.

VA Office of Research and Development: Environment

- **What is your environment?**
  - Where do you operate within your organization or larger community?
    - VA has three main administrations: Health, Benefits, and Cemeteries.
    - Office of Research and Development (ORD) is part of the Veterans Health Administration, an integrated health care system and has come to be viewed as a model for superior bench-to-bedside research.
    - ORD is an intramural funding program consisting of 4 Research Services: Biomedical Laboratory, Clinical Science, Health Services, and Rehabilitation

    FY 2020

Active research sites nationwide	**103**
Active funded principal investigators	**3,616**
Active funded research projects (including VA funding and other sources)	**7,288**
Total congressional appropriation for VA medical and prosthetic research	**$750M**

  - What makes your organization unique?
    - VA Research fully focuses on health issues that affect Veterans.

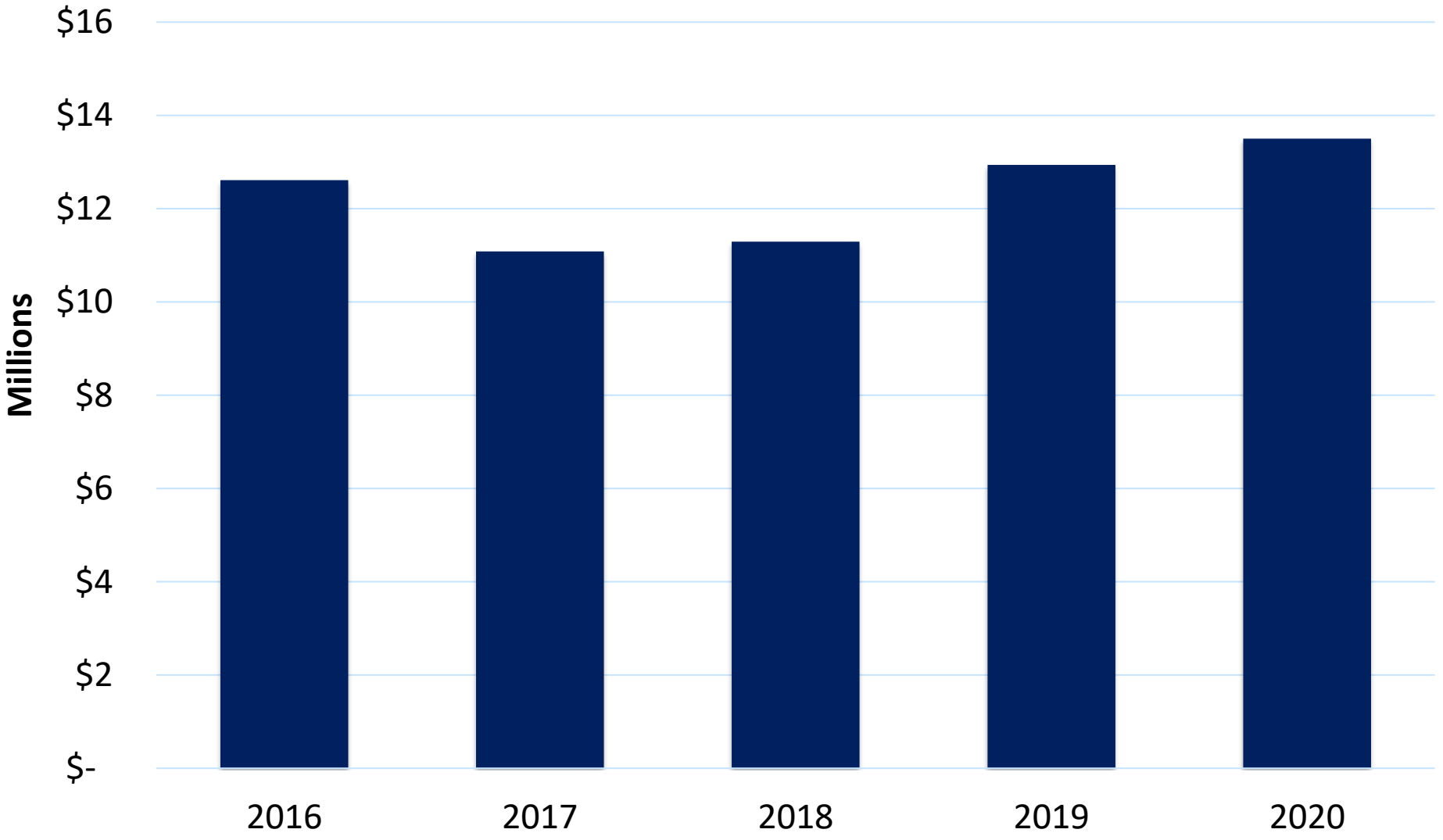
VA Office of Research and Development: Priorities

- **How does your organization identify priorities?**
  - Through surveys, field-based meetings, town halls, regular meetings with Veteran Service Organizations, and Congressional interest
- **What are your priorities?**
  - Increase Veterans' access to high-quality clinical trials
  - Increase the substantial real-world impact of VA research
  - Put VA data to work for Veterans
  - Actively promote diversity, equity, and inclusion within our sphere of influence
  - Build community through VA research
- **How do you measure success or progress towards priorities?**
  - Grow the nationwide network of clinician-investigators and study sites
  - Increase the number of discoveries translated into routine clinical practice.
  - Improve the use of large-scale datasets, e.g., Million Veterans Program, to reduce the time from discovery to clinical implementation
  - Have a research community that mirrors the diversity of this Nation and its Veterans
  - Data, resource, and knowledge sharing, e.g., , ORD is developing a phenomics library to enhance research and clinical care
- **How do you transition your successes and progress to your key stakeholders and end users?**
  - Utilizing ORD Communications
  - Annual National Radio Tours for key research areas
  - Organizing a VA research day on the Hill
  - Communication with Veteran Service Organizations
  - VA-wide Webinars, online learning modules through VA Talent Management System, online availability of clinical practice guidelines and Evidence Synthesis Reviews

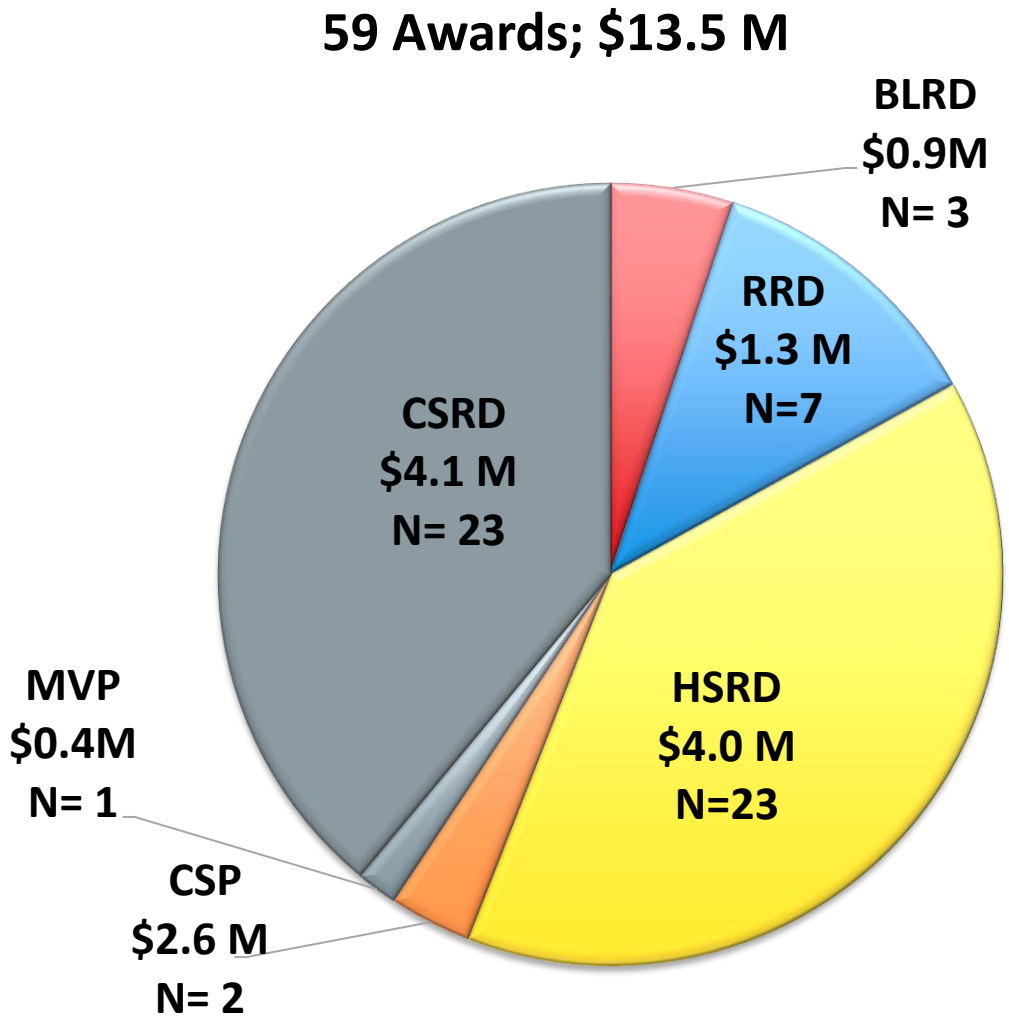
Suicide Prevention Research Portfolio

- FY20: 59 active studies; $13.5 Million for the year
- Includes: clinical trials, epidemiological studies, pilot studies, career development awards, infrastructure
- Examining biology and risk factors, assessment, prevention and treatment interventions, outreach and service delivery
- Active integration within VA, particularly with
  - Office of Mental Health and Suicide Prevention (OMHSPP)
  - Mental Illness Research, Education, and Clinical Centers (MIRECC)
  - outside VA with public and private partners

VA ORD FY16 – FY20 Investment: Suicide Prevention Research



VA ORD FY20 Suicide Prevention Awards by Service



BLRD = Basic Science
RRD = Rehabilitation
CSRD = Clinical Science
HSRD = Health Services
MVP = Genomics
CSP = Large Multi-site Trials

Suicide Prevention Initiatives

SPRINT CORE

Suicide Prevention Research Integrated Network – Consortium of Research

- Serve as a collaborative network of VHA and non-VHA researchers dedicated to conducting high-quality, high-priority, and high impact health services research
- Synthesize and maintain a "state of the science" data repository containing information about VHA and non-VHA suicide prevention research activities and VA clinical operations-funded projects
- Work with stakeholders to identify gaps in research to create a focused research agenda
- Provide a hub-based infrastructure with rapid funding to support innovation and high-impact team science projects that address priorities
- Disseminate suicide prevention research findings and products and facilitate implementation

VA STORM and REACH VET implementation and facilitation

- Through programs like BDSI, VA continues to improve and validate predictive analytics while implementing REACH Vet
- REACH Vet facilitation strategies study is still in data collection

Suicide Prevention Exemplar Studies

- **Project Life Force**: **Involving family members in Suicide Safety Planning -** in this randomized controlled trial, Veterans in the suicide safety planning group reported significantly less suicidal ideation and greater suicide-related coping relative to the control group (PI: Marianne Goodman, RRD)
- **Development and Evaluation of a Veteran-Informed Means Restriction Intervention for Suicide Prevention** – this project has established feasibility of engaging firearm owners (Veterans and non-Veterans), including gun store owners and concealed carry instructors, into a community coalition. As a result, the team is using coalition input to develop safe firearm storage messaging and materials to be tested in a follow-up study. (PI: Joseph Constans and Gala True, HSRD)
- **The "AIM Study": Investigating whether Actigraphy and Ideation Measures can Promote Patient Safety—**The goal of this study is to determine if suicide risk prediction can be improved by using a novel actigraphy measure, alone or in conjunction with other tests or database elements. Study results suggest the possibility that implicit association testing may have distinct clinical relevance or application in an inpatient setting in helping predict what patients may need more frequent safety checks or restrictions in privileges, etc. (PI: Eric Smith, CSRD)

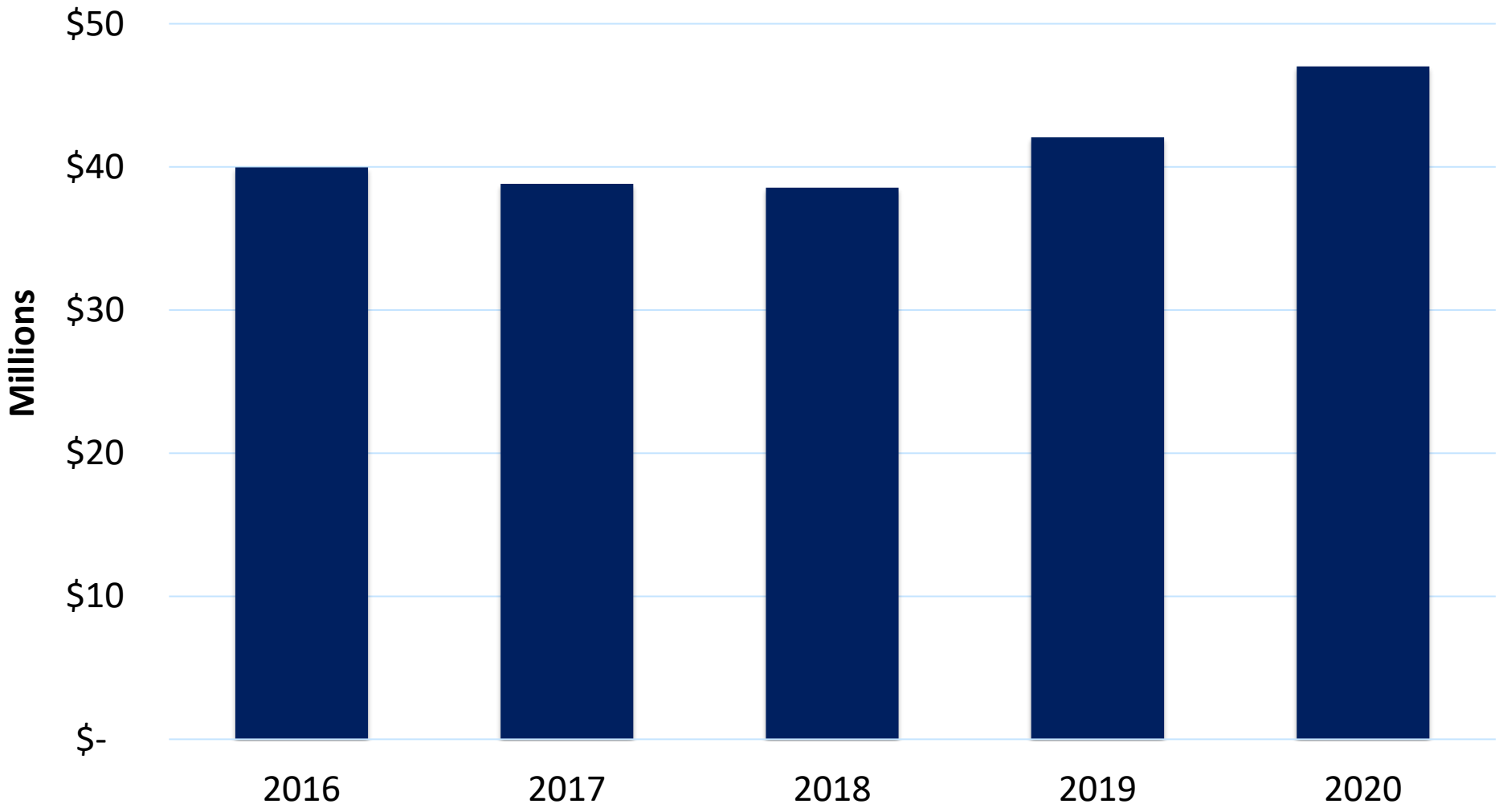
PTSD Portfolio

- FY20– 195 unique projects across all the four ORD Services and Cooperative Studies Program (CSP)

- FY20- $47 Million invested, which is a slight increase over previous years and the most invested in 5 years

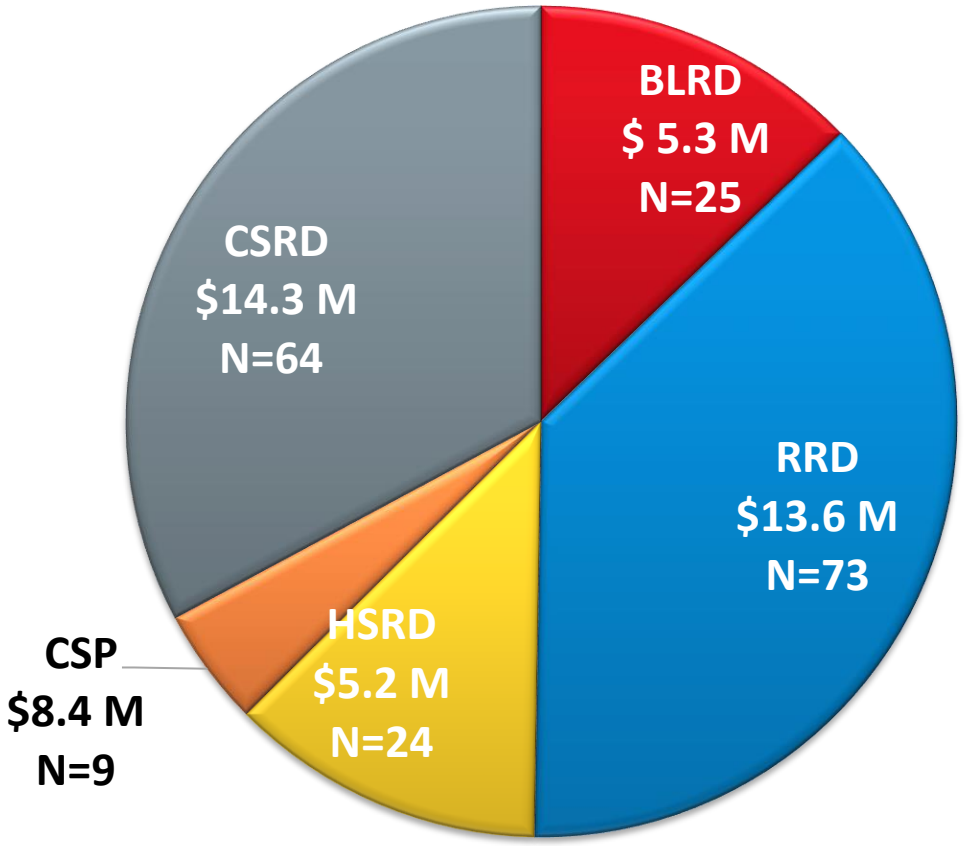
- Continued investments in collaborative initiatives, including PTSD Psychopharmacology Initiative

VA ORD FY16 – FY20 Investment: PTSD



VA ORD FY20 PTSD Awards by Service

195 Awards; $47.0 M



BLRD = Basic Science
RRD = Rehabilitation
CSRD = Clinical Science
HSRD = Health Services
MVP = Genomics
CSP = Large Multi-site Trials

PTSD Initiatives

Psychopharmacology Initiative (PPI)

- Established in 2016 to support research into new medications for PTSD
- 13 clinical trials have been funded
- Efforts on the way to further expand the work and develop a master protocol

VA Biorepository Brain Bank

- human tissue bank that collects, processes, stores and makes research specimens available for scientific studies
- 267 Brains received with 110 potential donors who have given informed consent
- PTSD researchers are invited to apply for tissue and data collected from Veterans and Non-Veterans with PTSD

Evidence Synthesis Program Reports

- Compendium - Evidence on Ketamine or Esketamine Use for Depressive Disorders, PTSD, or Suicide (2020)
- Relationship of Deployment-related Mild Traumatic Brain Injury to Posttraumatic Stress Disorder, Depressive Disorders, Substance Use Disorders, Suicidal Ideation, and Anxiety Disorders: A Systematic Review (2019)

PTSD Exemplar Studies

Genomics of Posttraumatic Stress Disorder among Veterans [CSP #575B] (Stein & Gelernter)

- GWAS and bioinformatic analyses, including 146,660 European-Americans (EAs) and 19,983 African-Americans (AAs) in the US Million Veteran Program, to identify genetic risk factors relevant to Intrusive reexperiencing of trauma -- the most characteristic symptom cluster of PTSD.
  - Among EAs, 8 distinct significant regions were identified.
  - No significant associations were observed in the AA part of the sample.
  - Published September 2019 in Nature Neuroscience
- Polygenic risk for PTSD is significantly predictive of re-experiencing symptoms in the MVP dataset, although specific loci did not replicate.
  - These results demonstrate the role of genetic variation in the biology of risk for PTSD and highlight the necessity of conducting sex-stratified analyses and expanding GWAS beyond European ancestry populations.

Validation of the PTSD Primary Care Screen [HSR&D IIR 15-103] (Bovin)

- In this diagnostic study of 396 primary care–seeking veterans, the 5-item PC-PTSD-5 was both diagnostically accurate and acceptable to participants. A cut point score of 4 best balanced the false negatives and false positives, although women may require a lower cut point (i.e., a score of 3). Like its predecessor, the PC-PTSD-5 is an effective and efficient tool for PTSD screening in Veterans Affairs primary care clinics.

Top 3 Research Gaps/Priorities

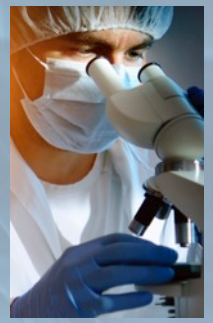
- Suicide Prevention: Research focused on Veterans at imminent risk for suicide
- Suicide Prevention: Expand research to further include community and relationship factors
- PTSD: Improving the adherence of Veterans to treatment regimens and completion of treatment

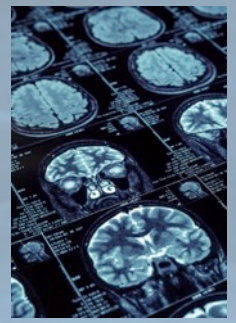
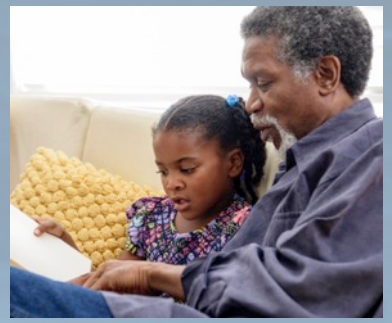
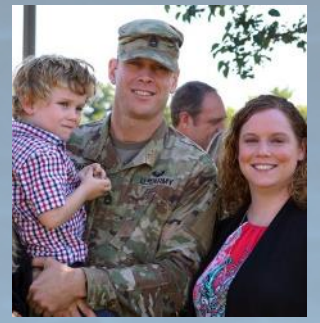
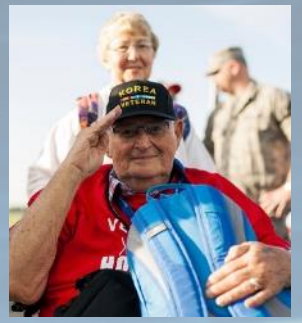
Enclosure 8
Overview of Psychological Health Center of Excellence

Introduction to the Psychological Health Center of Excellence (PHCoE)

CUTTING EDGE RESEARCH

Dr. Tim Hoyt
Psychological Health Center of Excellence

The views expressed in this presentation are those of the author and may not reflect the official policy or position of the Department of the Army, Department of Defense, or the U.S. Government

CDMRP Department of Defense

Psychological Health Center of Excellence

- **Vision**
  - Be the trusted source and partner to facilitate evidence-based research and clinical practices across the continuum of care to enhance the psychological health of the military community.
- **Mission**
  - Improve the lives of our nation's Service members, veterans, and their families by advancing excellence in psychological health care, readiness, and prevention of psychological health disorders.
- **Defense Health Agency**
  - The Psychological Health Center of Excellence (PHCoE) is located within the Defense Health Agency's Research and Development Directorate (J-9).

Priorities

Prevention & Outreach	**Prevention & Outreach:** Promote mental health, link beneficiaries with services, and support efforts including public mental health campaigns, stigma reduction, and transitions
Implementation Science	**Implementation Science:** Systematically apply methods of science to study and promote the adoption of evidence-based practice change in pilot and/or enterprise settings
Evidence Synthesis & Gap Analysis	**Evidence Synthesis & Gap Analysis:** Evaluate and translate the latest research evidence on pertinent psychological health treatments and topics to support the Military Health System (MHS) to inform future research activities and funding, clinical practice, and policy
Health Services & Population Research	**Health Services & Population Research:** Generate new findings and knowledge by conducting psychological health research and analyses, leveraging existing and novel data sets, and health-related behavior surveys
Surveillance & Medical Intelligence	**Surveillance & Medical Intelligence:** Utilize administrative data to answer epidemiological questions and to characterize current trends within the MHS care delivery system
Policy Analysis & Development	**Policy Analysis & Development:** Review, create and analyze pertinent psychological health policies
Evidence-Based Practice Support	**Evidence-Based Practice Support:** Develop and disseminate empirically-based information and products

CDMRP Department of Defense

PHCoE: Performance & Analytics Branch

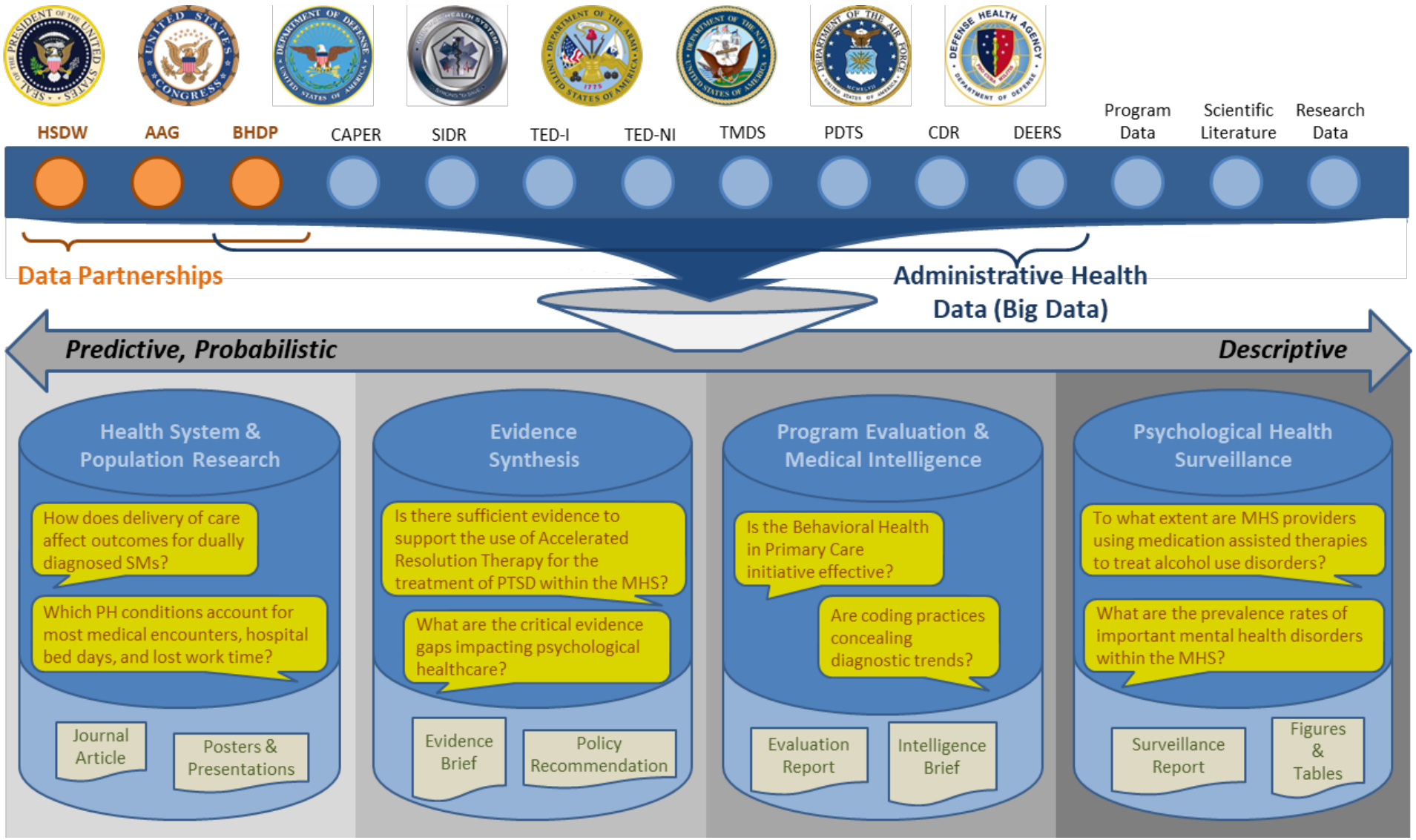
Gather Requirements

Examine Data

Analyze Needs and Gaps

Develop Operational Questions *(Selected Examples)*

Deliver PHCoE Products to the MHS



PHCoE: Research Branch – Lines of Effort

Evidence Synthesis & Gaps

- ***Evidence Briefs***
  Brief reviews of existing and potential psychological health treatments
- ***Rapid Reviews***
  Timely reports tailored to Military Health System (MHS) stakeholder requests to inform health care decisions
- ***Systematic Reviews***
  Comprehensive, rigorous syntheses to address important clinical questions, identify research gaps, and inform policy
- ***Research Gaps Analyses***
  Inform PH research direction and funding by identifying gaps in current research of priority topics

Health Services & Population Research

- ***Health Services and Population Research***
  Analyses of large military datasets combined from multiple sources to provide uniquely comprehensive, population level health services and psychological health data
- ***Outcomes and Policy***
  Delivery of research reports and policy memos to leadership and MHS stakeholders to inform PH healthcare delivery

Dissemination & Implementation

- ***Practice-Based Implementation Network***
  Application of dissemination and implementation science for adoption of evidence-based psychological health practices and improved clinical care

Evidence Briefs

- **Brief (1-2 pages) summaries of evidence for treatment of a specific disorder.**
- **Great for providers looking at evidenced-based care or whose military patients want to compare the benefits of one treatment to another.**
- **Over 80 published on pdhealth.mil. Examples:**
  - Present-Centered Therapy for Posttraumatic Stress Disorder
  - Ketamine for Suicidality
  - Cognitive Behavioral Therapy for Generalized Anxiety Disorder
  - Buprenorphine/Naloxone for Opioid Use
  - Topiramate for Alcohol Use Disorder
  - Repetitive Transcranial Magnetic Stimulation for MDD

Cognitive Behavioral Therapy for Adjustment Disorder

Psychological Health Center of Excellence Psych Health Evidence Briefs October 2018

Q. What is cognitive behavioral therapy?

A. Cognitive behavioral therapy (CBT) is one of the most researched treatments in psychotherapy (Butler, Chapman, Forman, & Beck, 2006). Components of CBT include behavioral activation; challenging negative automatic thoughts, cognitive errors, and misattributions; problem solving; and interpersonal interventions. In clinical practice, the specific CBT components used are determined by the individual patient's symptoms (Persons, Davidson, & Tompkins, 2000). Adjustment disorder (AD) is diagnostically brief, with symptoms typically developing within three months of stressor onset, and lasting no more than six months post-stressor. Because of that brevity, behavioral activation-focused CBT as well as solution-focused CBT may be indicated in the treatment of AD (Carta, Balestrieri, Murru, & Hardoy, 2009).

Q. What is the theoretical model underlying CBT for AD?

A. CBT is based on Beck's theory of depression (Beck, 1967; Beck, 2008) and has been adapted for the treatment of other mental health conditions to include anxiety disorder, trauma disorders, and adjustment disorders (Cully & Teten, 2008). Like other forms of CBT, the treatment for AD includes a focus on the maladaptive thoughts and beliefs associated with the stressor, the practice of relaxation strategies to reduce distress, and the development and use of problem solving skills. Notably, adjustment disorders in the military are highly prevalent given the many substantial adjustments that service members make due to entering service, adjusting to the culture of the military, leaving friends and family behind, deploying, and frequently moving, to name a few.

Q. Is CBT recommended as a front-line treatment for AD in the Military Health System (MHS)?

A. There is no VA/DoD clinical practice guideline (CPG) on the treatment of AD.

The MHS relies on the VA/DoD clinical practice guidelines (CPGs) to inform best clinical practices. However, in the absence of an official VA/DoD recommendation, clinicians should look to CPGs published by other recognized organizations, and may rely on knowledge of the literature and clinical judgement.

Q. Do other organizations with CPGs for the treatment of AD recommend CBT?

A. No. No CPGs on the treatment of AD were identified.

Q. Do other authoritative reviews recommend CBT as a front-line treatment for AD?

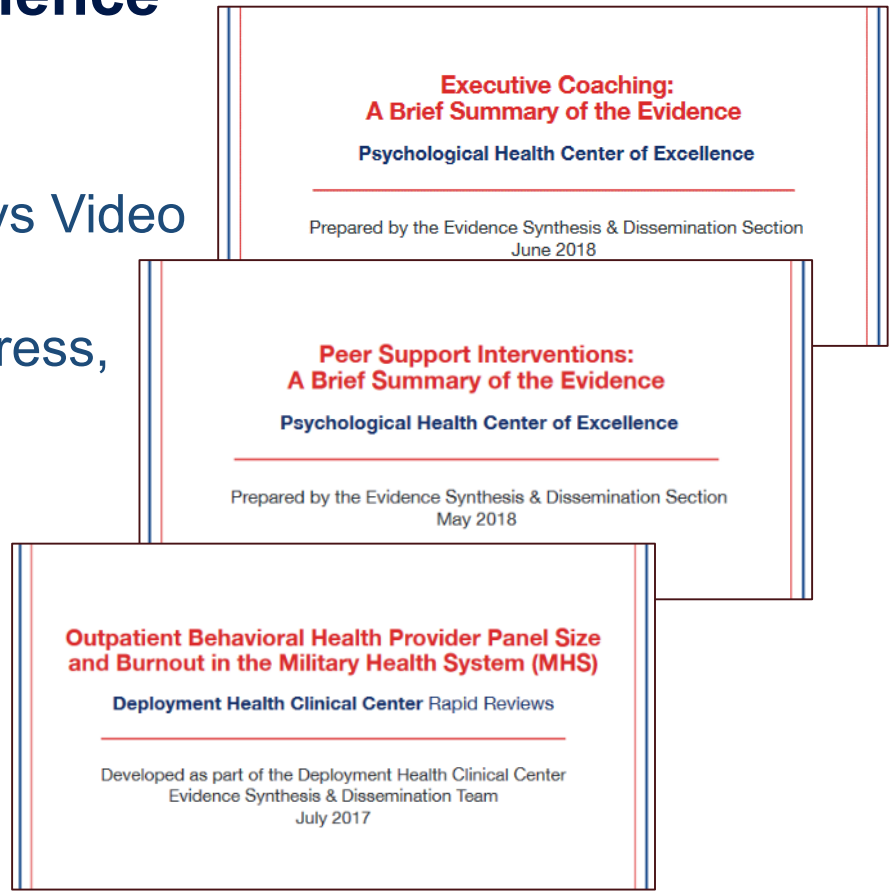
A. No. Other authoritative reviews have not substantiated the use of CBT for AD.

Several other recognized organizations conduct systematic reviews and evidence syntheses on psychological health topics using similar grading systems as the VA/DoD CPGs. These include the Agency for Healthcare Research and Quality (AHRQ) and Cochrane.

- AHRQ: No reports on AD were identified.
- Cochrane: A 2012 systematic review of interventions to facilitate return to work in adults with AD found that CBT did not significantly reduce the time to return to work compared to no treatment, but did not report on the effect of CBT on reducing AD symptoms (Arends et al., 2012).

Rapid Reviews and Reports

- **PHCoE produces rapid reviews to provide key MHS stakeholders with timely information about the state of the science for specified topics.**
  - Effect of the COVID-19 Pandemic on Suicidal Behavior
  - Telehealth Treatments for Mental Health Disorders- Phone vs Video Teleconferencing vs Face-to-Face
  - Effects of mindfulness meditation on workplace wellness, stress, and occupational outcomes
  - Benefits of bereavement leave
  - Alcohol-Related Sexual Assault/Harassment in the Military



Systematic Reviews vs Rapid Reviews

	Systematic Reviews	Rapid Reviews
Time to Complete	• 12 months or more	• 1 – 6 months
Review Topic	• Comprehensive key questions addressing effectiveness, safety, cost, etc.	• Limited number and complexity of key questions
Search Strategy	• Sensitive, systematic search for published and grey literature	• Abbreviated search using a limited number of databases and resources • May apply restrictions such as publication date, study types, language, etc.
Screen and Select	• Inclusive, pre-defined criteria for inclusion • Dual review and selection of studies • Rigorous full-text review and comprehensive data elements for extraction	• Narrow criteria for inclusion, which may be iteratively redefined based on search results • Single reviewer screening and selection of studies • Limited data elements for extraction
Synthesis and Conclusions	• Qualitative and quantitative synthesis of findings • May include meta-analysis • Comprehensive critical appraisal of individual studies and quality of evidence assessment	• Descriptive summary of findings • Characteristics of included studies • May include critical appraisal of individual study designs

Clinical Support Tools

- **Clinical support tools, or resources, are educational materials and decision aids for primary care and specialty care providers, patients, and families.**
- **The tools provide evidence-based prevention and treatment practices that are consistent with Department of Veterans Affairs (VA) and Department of Defense (DoD) Clinical Practice Guidelines for Psychological Health.**
- **Topics:**
  - Major Depressive Disorder (MDD)
  - Substance Use Disorder
  - Suicide Risk
  - PTSD & Acute Stress Disorder
  - Opioid Therapy for Chronic Pain
- **PHCoE Website: www.pdhealth.mil**

PHCoE: Research Gap Analyses

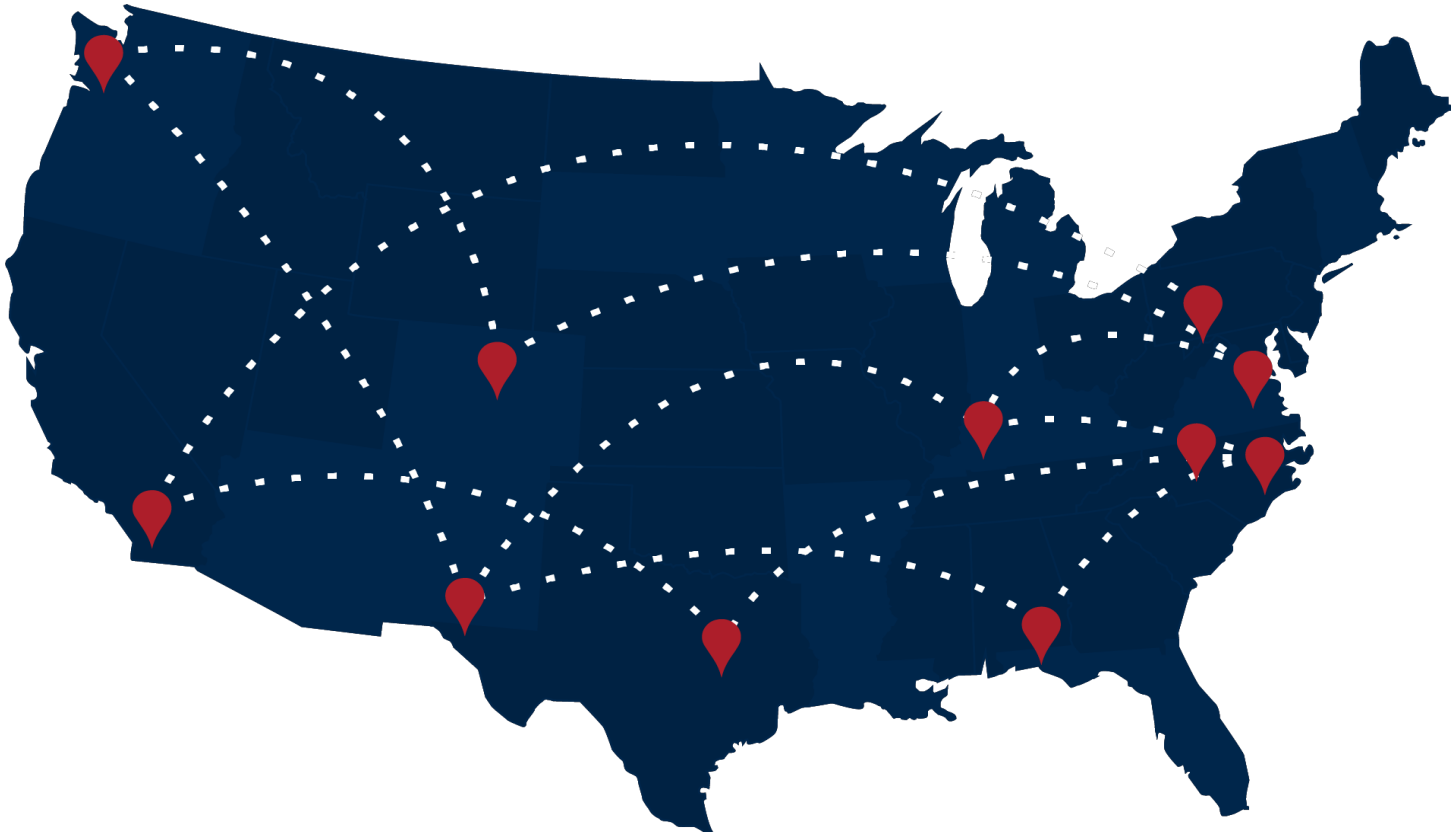
- **Inform and prioritize research funding and increase the likelihood that comprehensive research portfolios will target areas of greatest need and potential for impact on military readiness**
- **The Gaps Report is used to inform calls for research from CDMRP and MOMRP**
- **Researchers who address an identified gap may be more competitive in obtaining research funding**
- **https://www.pdhealth.mil/research-analytics/evidence-synthesis-research-gaps-analysis/psychological-health-research-gaps**

Year	2016	2017	2018	2019
Topic (final number of gaps identified)	PTSD (11) Depression (6)	SUD • Alcohol Use Disorder (9) • Prescription Opioids (4) • Novel Synthetic Drugs (5)	Adjustment Disorder (11)	Suicide Prevention (35)
Example of high priority gap	Conduct head-to-head comparative effectiveness trials of efficacious PTSD treatments that include better controls.	Examine the effects of leadership attitudes, group characteristics, and group identification factors on drinking in the military.	Develop and test the effectiveness of interventions that address reaction to the stressor in preventing adjustment disorders	More research on the effectiveness of lethal means safety interventions to increase safety behaviors and/or reduce suicide-related outcomes

Enclosure 9
Overview of National Intrepid Center of Excellence

National Intrepid Center of Excellence (NICoE)

a member of the
Defense Intrepid Network for TBI and Brain Health



28 April 2021

Carlos Williams, MD, MPH, MBA
Captain, MC, US Navy
Director, NICoE

Agenda

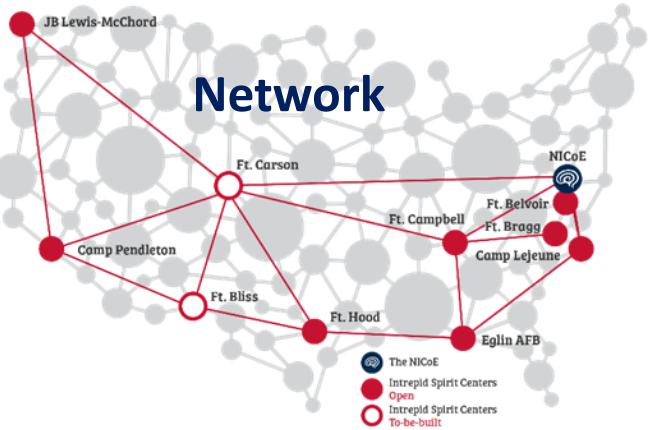
- History of the Network
- Overview of the NICoE
- Overview of the Network
- Network Focus Areas
  - Clinical Care
  - Research
  - Education
  - Network Support
- Network Value
- Summary

History of the Defense Intrepid Network

Since September 11, 2001, the succession of military conflicts in the global war on terrorism represents the longest sustained military operation in US history, resulting in thousands of service members suffering from combat-related traumatic brain injury (TBI) and behavioral health comorbidities which came to be known as the “invisible wounds of war”.

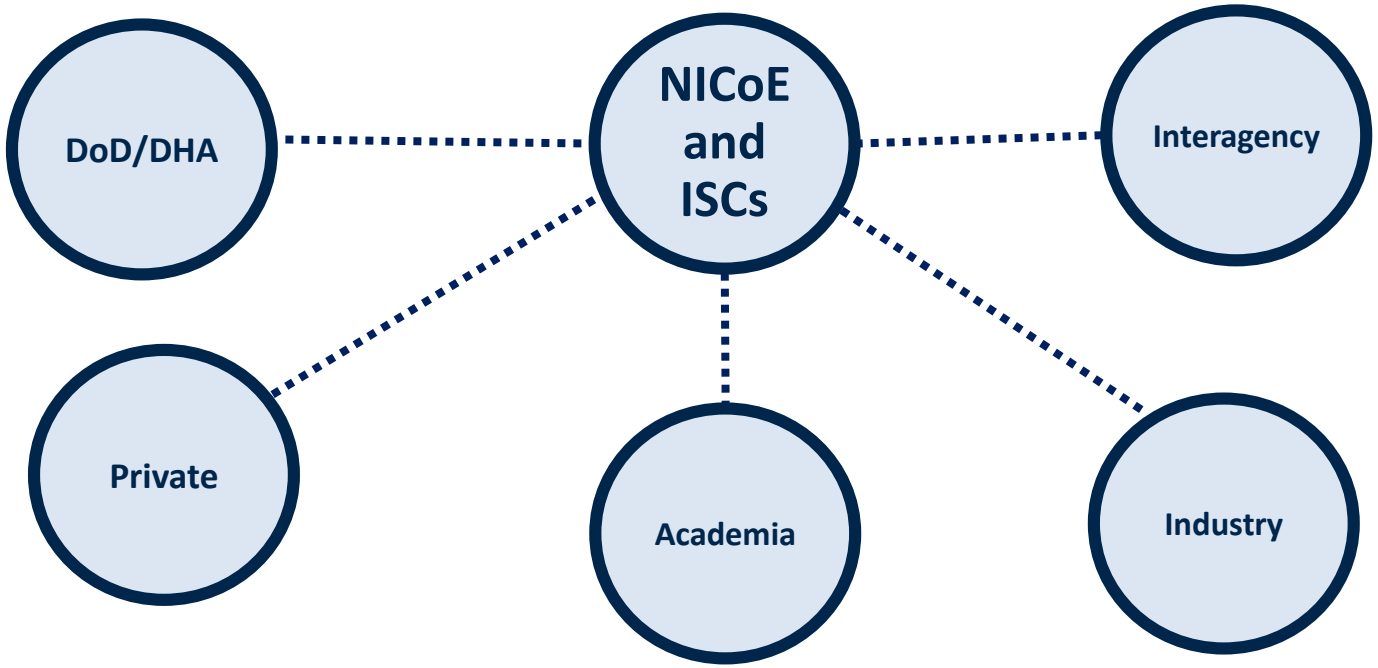
Guided by recommendations from blue ribbon panels established in 2007, the 2008 National Defense Authorization Act (NDAA) directed the Department of Defense to establish a comprehensive plan for programs to prevent, diagnosis, treat and rehabilitate service members with TBI, PTSD and other mental health conditions to the fullest extent possible. Congress further instructed translational research to better understand the etiology of TBI and developed preventative interventions and new therapies and mandated dissemination of this practices.

Secretary of Defense Gordon England accepted the gift from the American People through the Intrepid Fallen Heroes Fund to build the NICoE, the “premier diagnosis, treatment and research center for TBI and psychological health.” The Center opened on **June 24, 2010** as a proof-of-concept for the use of an interdisciplinary holistic care and research platform with state-of-the-art technological advances. In keeping with the goal for dissemination of an effective model of care, the first Intrepid Spirit Center (ISC) at **Ft Belvoir opened on September 11, 2013**. Since then the network has grown to 11 sites – the NICoE and ten ISCs.



Partnerships Are At the Core of What We Do

- Uniformed Services
- Traumatic Brain Injury Center of Excellence (TBICoE)
- U.S. Army Aeromedical Research Laboratory (USAARL)
- Walter Reed Army Institute of Research (WRAIR)
- Uniformed Services University of the Health Sciences (USUHS)
- Center for Neuroscience & Regenerative Medicine (CNRM)
- Naval Medical Research Center



- National Institutes of Health (NIH): NIMH, NINR, NIA
- Department of Veterans Affairs (VA)
- National Center for Post-Traumatic Stress Disorder (NCPTSD)
- National Endowment for the Arts (NEA)

- University of Maryland
- George Washington University
- University of Cincinnati
- University of Pennsylvania
- University of Michigan
- Drexel University
- University of North Carolina
- University of Utah
- University of Pittsburgh
- QIMR Berghofer Medical Research Institute

Note: Organizations listed on this slide are only sample of Network partners

National Intrepid Center of Excellence (NICoE) Overview

Clinical Programs and Offerings

- TBI Outpatient Services
- TBI Intensive Outpatient Program (IOP)
- TBI Inpatient Consult Service
- Brain Fitness Center
- Advanced Diagnostics and Imaging

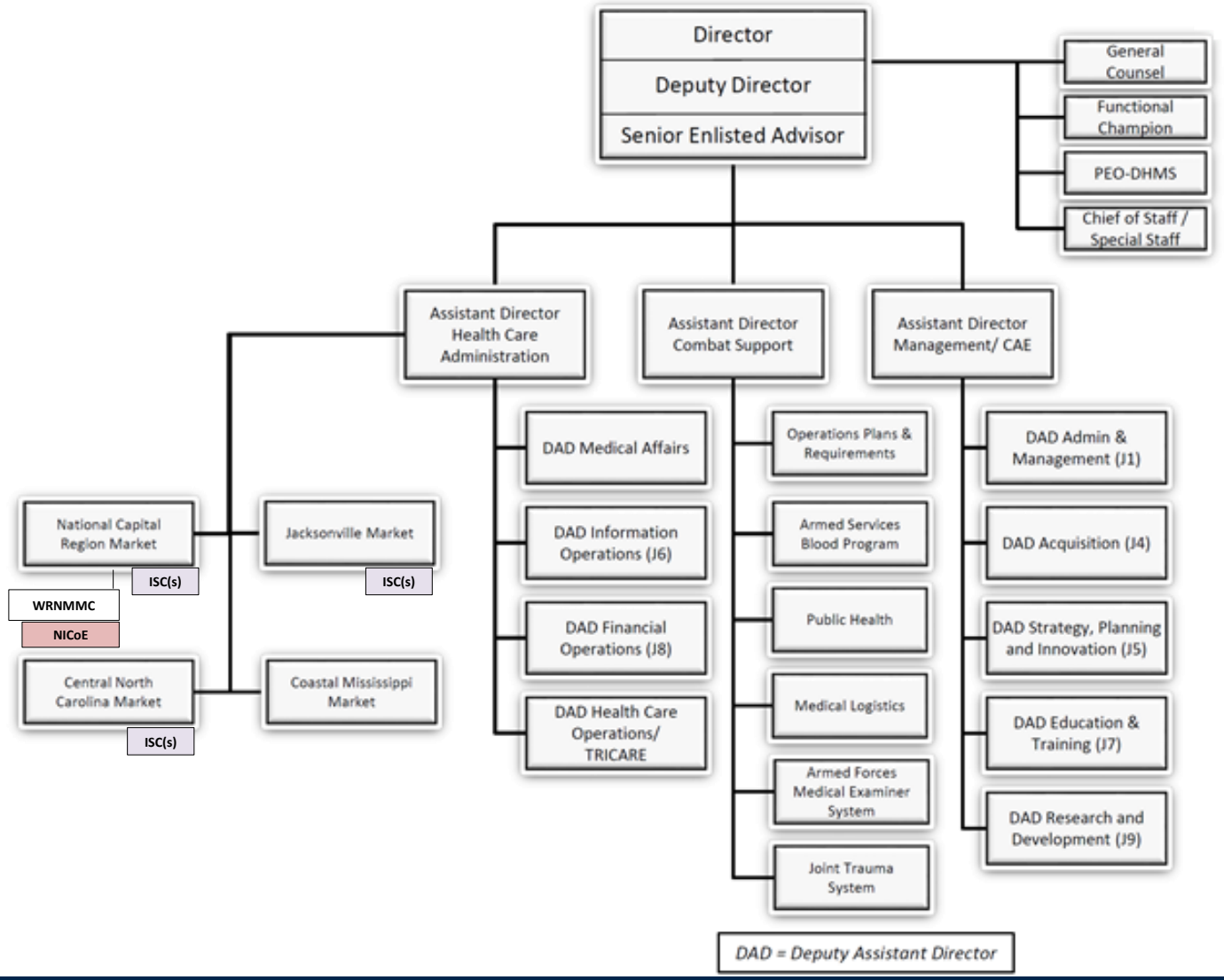
Research Activities

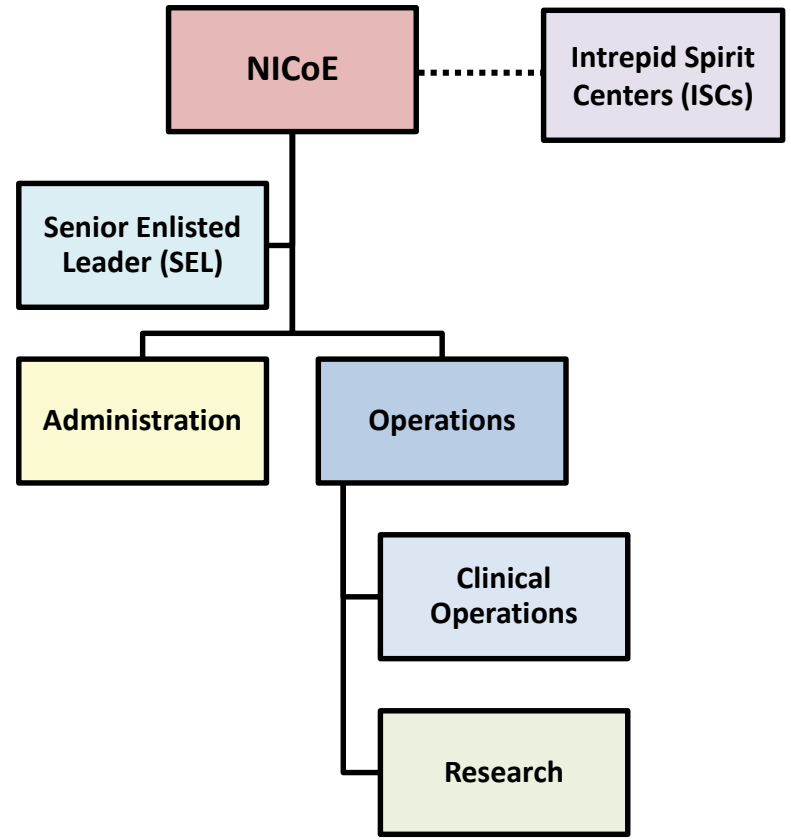
- Diverse Research Portfolio and Partnerships
- Translating Research into Practice (TRIP) Initiative

Education

- Graduate Medical Education (GME) and Clinical Research Training
- Continuing Medical Education (CME) – Grand Rounds and Webinars
- Support for the TBICoE educational initiatives

NICoE Chain of Command and Organizational Structure





Overview of the Network

The Defense Intrepid Network for TBI and Brain Health

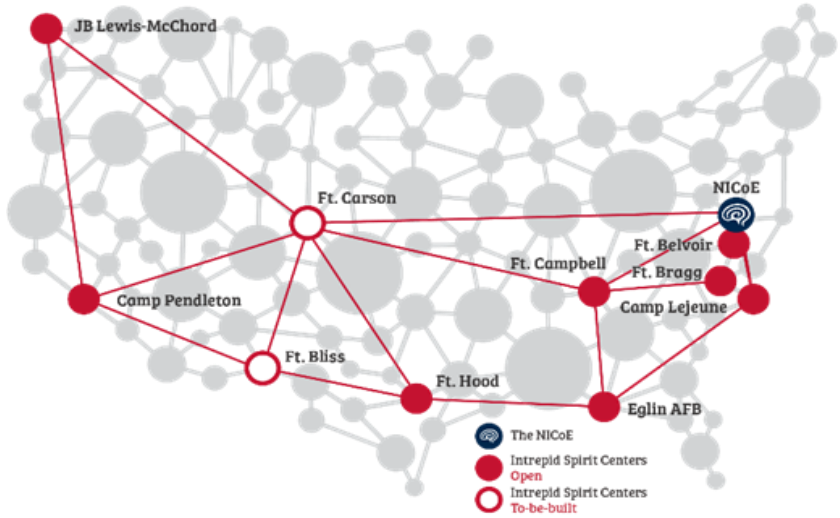
Mission: To improve the lives of patients and families impacted by TBI through integrated clinical practice, research, and education

Vision: To be the global-leading network for TBI and brain health clinical care, research, and education for military members and beneficiaries

2021 Goals:

- Refine the Network's foundational interdisciplinary patient-centric holistic care model to achieve maximal Warfighter Readiness and optimize efficacy and efficiency
- Support synchronization of TBI assessment, treatment, and outcomes across the Military Health System (MHS) and greater brain health community
- Be a "partner of choice" within the Department of Defense and other US Government (USG) agencies, academia, and industry for research implementation as it relates to improved patient care and outcomes for TBI and associated health conditions

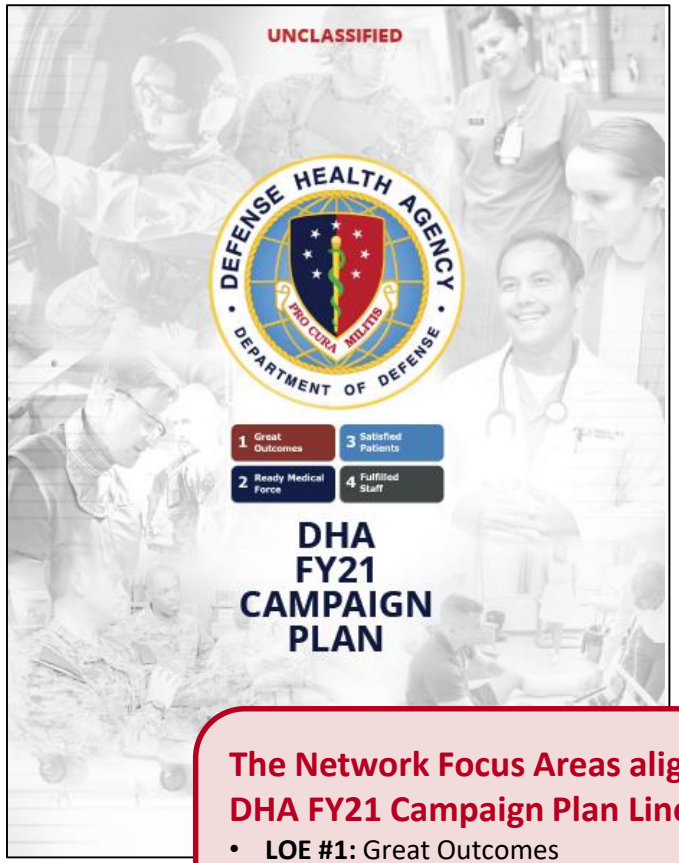
Operating Principles: Partnership, Alignment, Stewardship, and Efficiency



Network Composition:

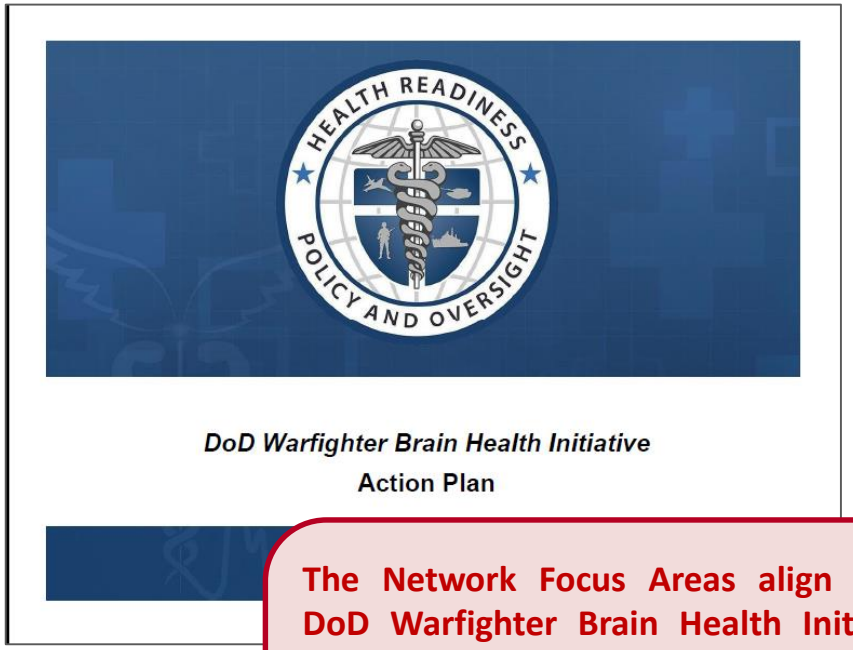
1. National Intrepid Center of Excellence, WRNMMC
2. Joint Base Lewis-McChord
3. Eglin Air Force Base
4. Camp Lejeune
5. Camp Pendleton
6. Fort Belvoir
7. Fort Bliss (*To Be Built)*
8. Fort Bragg
9. Fort Campbell
10. Fort Carson *(To Be Built)*
11. Fort Hood

The Network Aligns With/Supports DoD & DHA Priorities



The Network Focus Areas align with/support the DHA FY21 Campaign Plan Lines of Effort (LOEs)

- **LOE #1:** Great Outcomes
- **LOE #2:** Ready Medical Force
- **LOE #3:** Satisfied Patients
- **LOE #4:** Fulfilled Staff



The Network Focus Areas align with/support DoD Warfighter Brain Health Initiative Action Plan LOEs

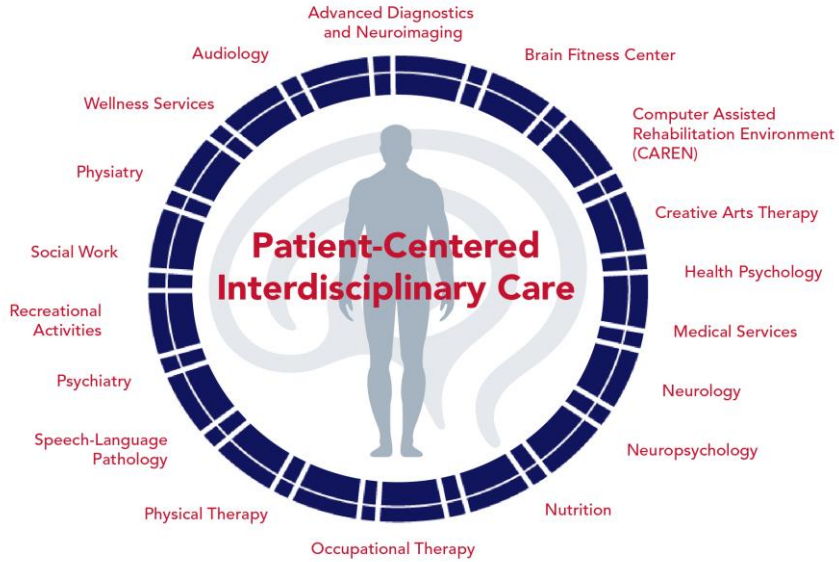
- **LOE #1:** Optimize Cognitive and Physical Performance
- **LOE #3:** Prevent, Recognize, and Minimize the Effects of Traumatic Brain Injury
- **LOE #4:** Reduce or Eliminate Long-Term/Late Effects
- **LOE #5:** Advance Warfighter Brain Health Science

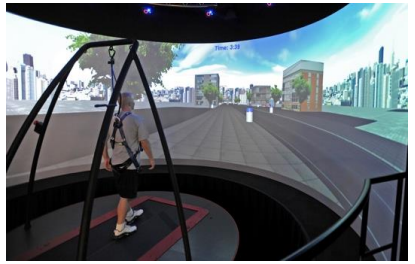
9

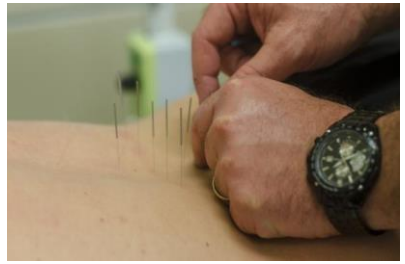
The Interdisciplinary Care Model is the Foundation of the Network

The Network's patient-centered, interdisciplinary approach to clinical care includes traditional rehabilitation, neurological, and behavioral health (BH) treatments combined with integrative medicine interventions and skills-based training. It uses a co-located, interdisciplinary team to expedite diagnostic evaluation that leverages each specialty team member to build on each other's expertise to achieve common goals and to develop a collaborative individualized treatment plan.

The patient is at the center of the care team, enhancing patient-provider rapport, and enabling a more efficient identification of goals for recovery, and providing immediate feedback of response to treatment. The rehabilitative culture of the care team emphasizes patients learning self-efficacy and self-advocacy techniques to enhance sustainable recovery beyond discharge.

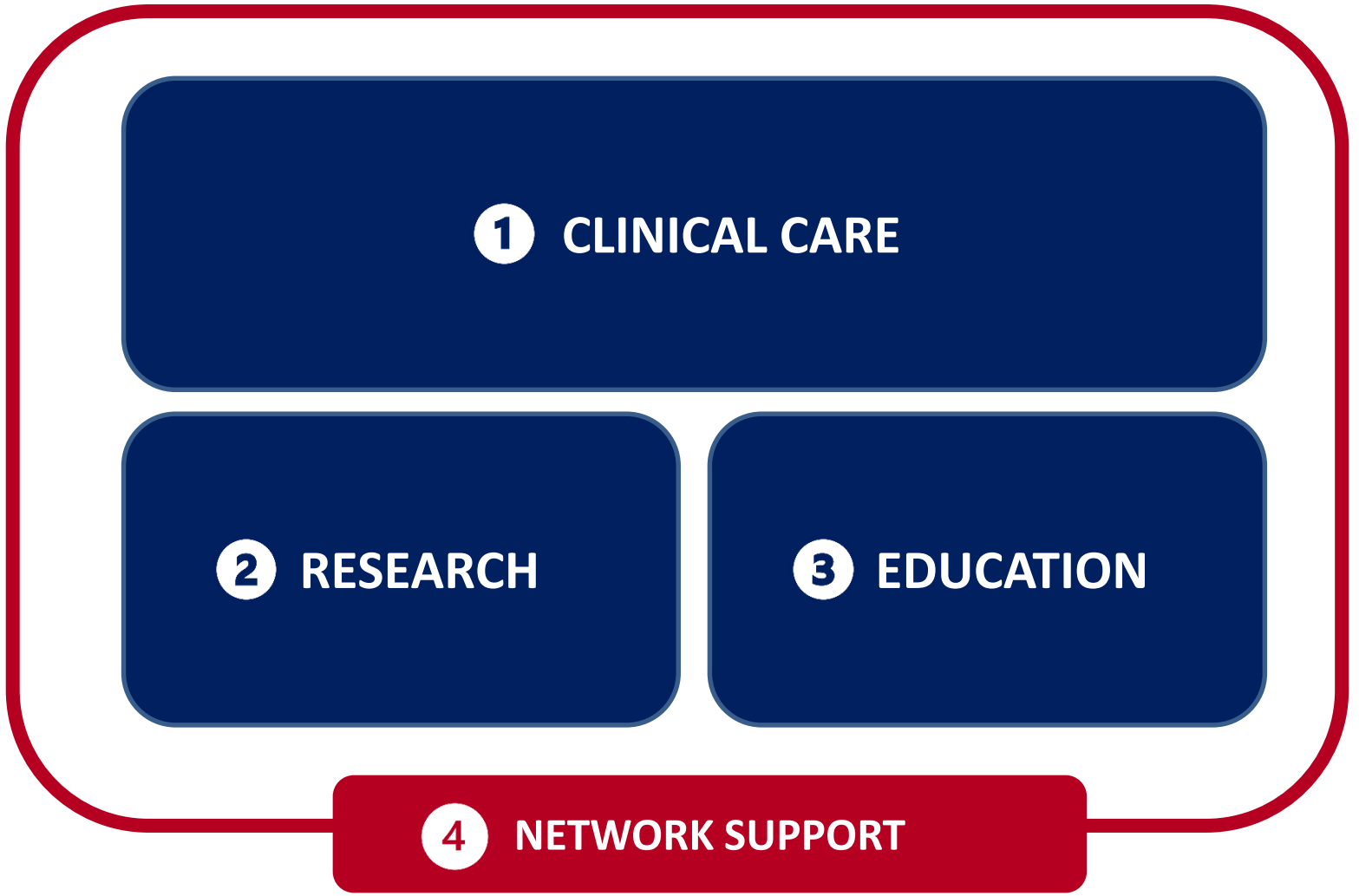




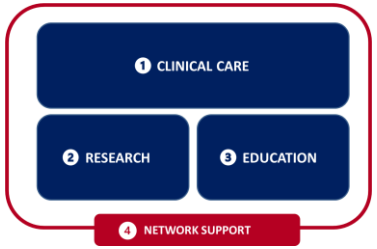


Network Focus Areas

Network Focus Areas



Network Focus Area #1 – Clinical Care



Focus: ***Synchronization of assessments, treatments, and outcomes across the network***

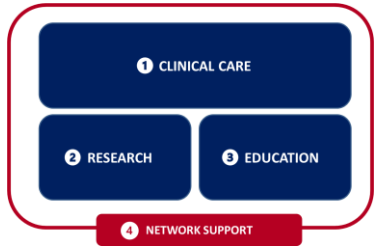
Objectives

- Synchronize clinical care based on outcomes data throughout the Network
- Serve as subject matter experts and support the continuum of TBI management (e.g. emergency department, Primary Care Providers, acute concussion clinics, as well as mild moderate and severe disease)
- Diversify, expand and sustain the Network referral pathway and base
- Identify opportunities for the Network to support the readiness needs of the Services

Specialty Community Working Groups

- Communities of like-type Network professionals serve as the foundational SMEs for synchronizing clinical assessment, treatment, and outcomes across the network
- Robust engagement and communication with Directors across the Network to enable synchronization of clinical care and sharing of lessons learned
- Partner with overall TBI Community (e.g. TBICoE, Services) to ensure synchronization within the TBI Pathway of Care

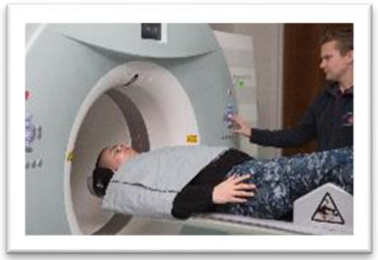
Network Focus Area #2 – Research (Translating Research Into Practice)



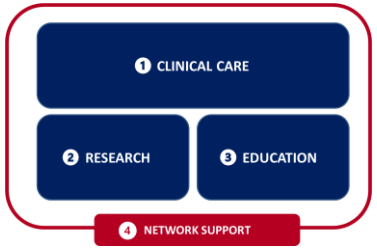
Focus: *To translate effective research outcomes into the clinical standard of care for the improvement of brain health and the management of patients with TBI*

Objectives

- Leverage the Network clinical platform to increase partnerships with academia and other stakeholders
- Evaluate and synthesize DoD/non-DoD TBI research for rapid implementation of best practices into warrior care across the Network
- Increase research partnerships across the global TBI community for the purpose of greater access to effective care modalities for TBI and Brain Health
- Increase and improve accessibility to research-funding opportunities through strategic partnerships
- Build and strengthen a Network that attracts partner engagement in relevant high-value research initiatives
- Leverage the Network's extensive collection of brain images and advanced technologies to enable research within and across the Network



Network Focus Area #3 – Education

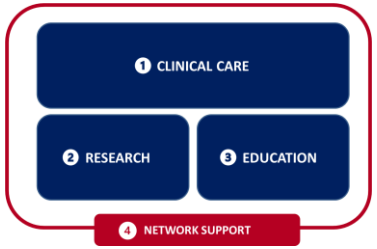


Focus: *Develop and maintain network-wide education for stakeholders*

Objectives

- Provide network-wide professional development and graduate medical education (GME) opportunities:
  - TBI Didactics
  - Grand Rounds
  - Webinars
  - Other Continuing Medical Education (CME)/Continuing Education (CE) Opportunities
  - Network Fellowships (Services-Sanctioned GME)
- Partner with key communities to help improve their readiness posture

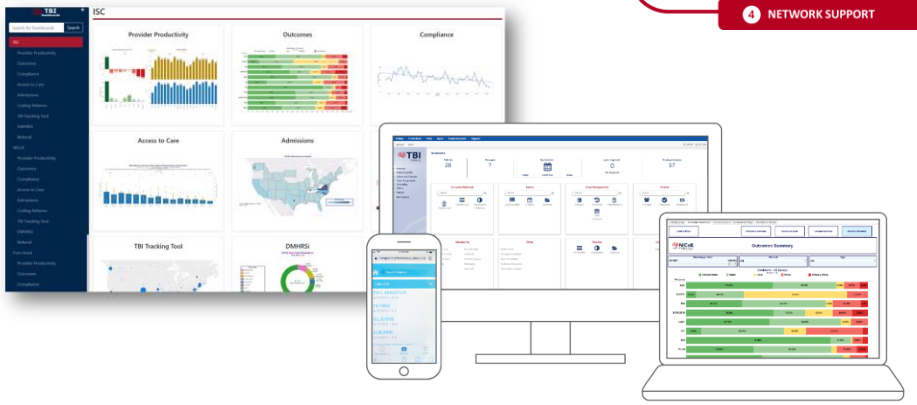
Network Focus Area #4 – Network Support



Focus: *Develop, maintain, and sustain Network activities and operations*

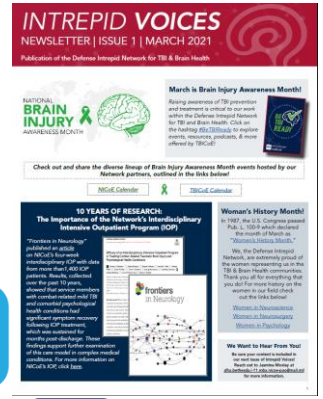
Objectives

- **Network Informatics**
  - DoD TBI Portal
  - TBI Metrics, Dashboards, and Analytical Support
  - Network Resource Center



- **Network Resource Management**
  - Develop and support Network productivity (cFTE) and targets
  - Provide expert advice from world-leading interdisciplinary TBI care organizations

- **Network Communications**
  - Website
  - Social Media
  - Publications (Intrepid Voices e-Newsletter, Network Annual Report)



Network Value

Network Clinical Value: Providing TBI Care Across the MHS

Medically Ready Force & Ready Medical Force

Number of Encounters

203,785

Number of Unique Patients

27,489

Number of Telehealth Appointments

19,251

12,695

NEUROMUSCULAR REEDUCATION

8,258

GROUP THERAPEUTIC PROCEDURES

9,324

THER PX,1+,EA 15 MN;THER EXERC

6,173

CASE MANGEMENT, EACH 15 MIN

8,850

PSYCHOTHERAPY (30-60 MINUTES)

4,826

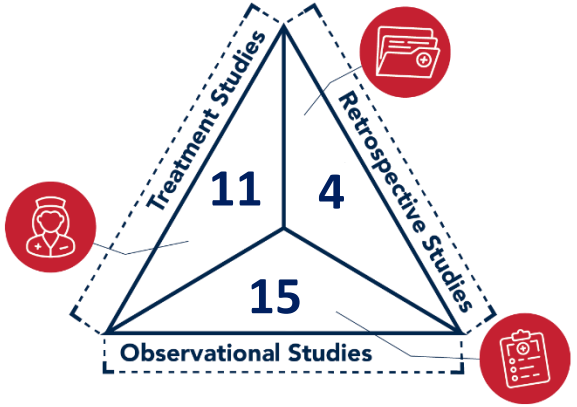
BFIEF EMOTIONAL/BEHAVIOR ASSES

Data Source: MHS Information Platform (MIP)

Network Research Value

Sample of Network Member FY20 Research

30 total studies



4 New Studies Approved

8 Grants Submitted

141 Publications & Presentations*

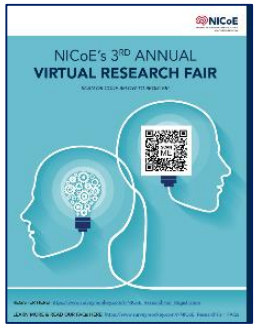
- ❑ 32 journal articles
- ❑ 5 book chapters
- ❑ 1 doctoral dissertation
- ❑ 1 government report
- ❑ 41 invited presentations
- ❑ 61 abstracts & posters

* Includes conference presentations that were canceled due to the pandemic

Highlights of Recent Network Research Products, Events, and Publications

2020 Research Booklet & QuickGuide

Link: https://go.usa.gov/xsncA



3rd Annual Research Fair

Sample of Recent Publications

Network Clinical Value: Providing TBI Care Across the MHS (cont.)

In 2020 across the MHS, **47.1%** of TBI care took place within the Network (NICoE and the Intrepid Spirit Centers)

- Including primary care, ER visits, and all outpatient clinics

Military Health System (MHS)

Medical Centers

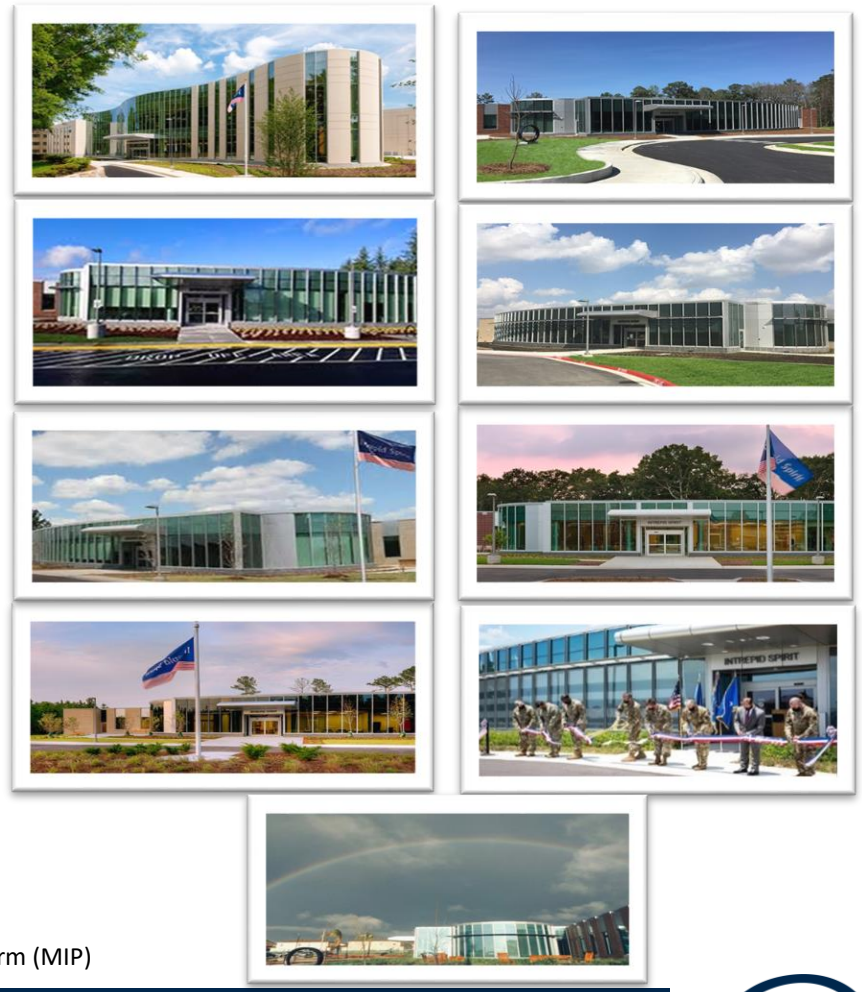
51

Ambulatory Care Clinics

381

47.1% of TBI care

The Network



In 2020, the Network provided:

- 72.4% of TBI-related GROUP appointments
- 65.1% of TBI-related PROC appointments
- 55.1% of TBI-related FTR appointments
- 52.8% of TBI-related SPEC appointments

Data Source: MHS Information Platform (MIP)

Summary – Looking Forward to 2021

We look forward to your continued partnership and support as the Defense Intrepid Network for TBI and Brain Health moves forward in 2021

Be on the look out for:

Spring 2021 – Launch of the Translating Research Into Practice (TRIP) Initiative

Late Summer/Fall 2021 – TBI and Brain Health Summit

Defense Intrepid Network for TBI and Brain Health

Camp Lejeune
180 Hospital Corps Blvd.
Camp Lejeune, NC 28547
(910) 449-1100

Camp Pendleton
2016 Jacinto Road, Bldg 2169
Oceanside, CA 92055
(760) 763-9384

Eglin AFB
1 Ash Drive
Eglin Air Force Base, FL 32542
(850) 883-9484

Ft. Belvoir
5980 9th Street, Bldg 1259
Fort Belvoir, VA 22060

Ft. Bliss (To-be-built)
5005 N. Piedras St.
El Paso, Texas 79930

Ft. Bragg
3908 Longstreet Rd
Fort Bragg, NC 28310
(910) 907-7777

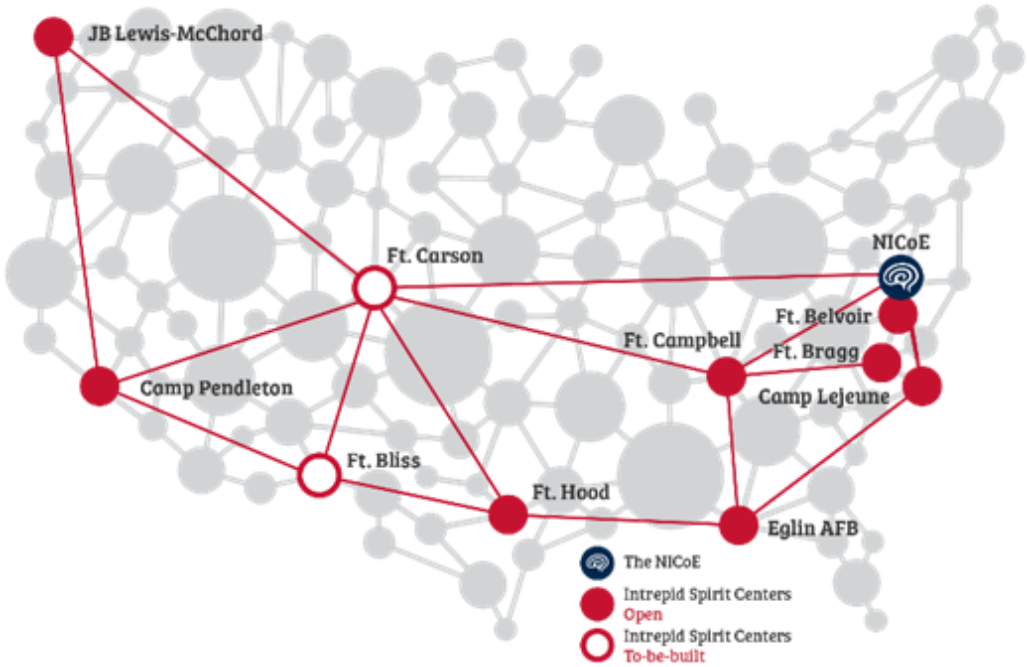
Ft. Campbell
2403 20th and Indiana Ave
Fort Campbell, KY 42223
(270) 412-5114 / (270) 412-5485

Ft. Carson (To-be-built)
Sutherland Circle, Bldg 7488/7489
Fort Carson, CO 80913
(719) 526-3286 / (719) 526-4911

Ft. Hood
36029 58th St.
Fort Hood, TX 76544
(254) 287-8179

JB Lewis-McChord
90390 Gardner Loop
Tacoma, WA 98431-1100
(253) 968-9002

The National Intrepid Center of Excellence
4860 South Palmer Road | Bethesda, MD 20889
dha.bethesda.wrnmmc.mbx.nicoe@mail.mil
(301) 319-3600



Enclosure 10
Overview of One Mind

Accelerating Brain Health for All

April 2021

One Mind

Launched in 1995 by the Staglin Family, One Mind is a non-profit organization that supports mental health science; patients and society.

One Mind's Unique Approach

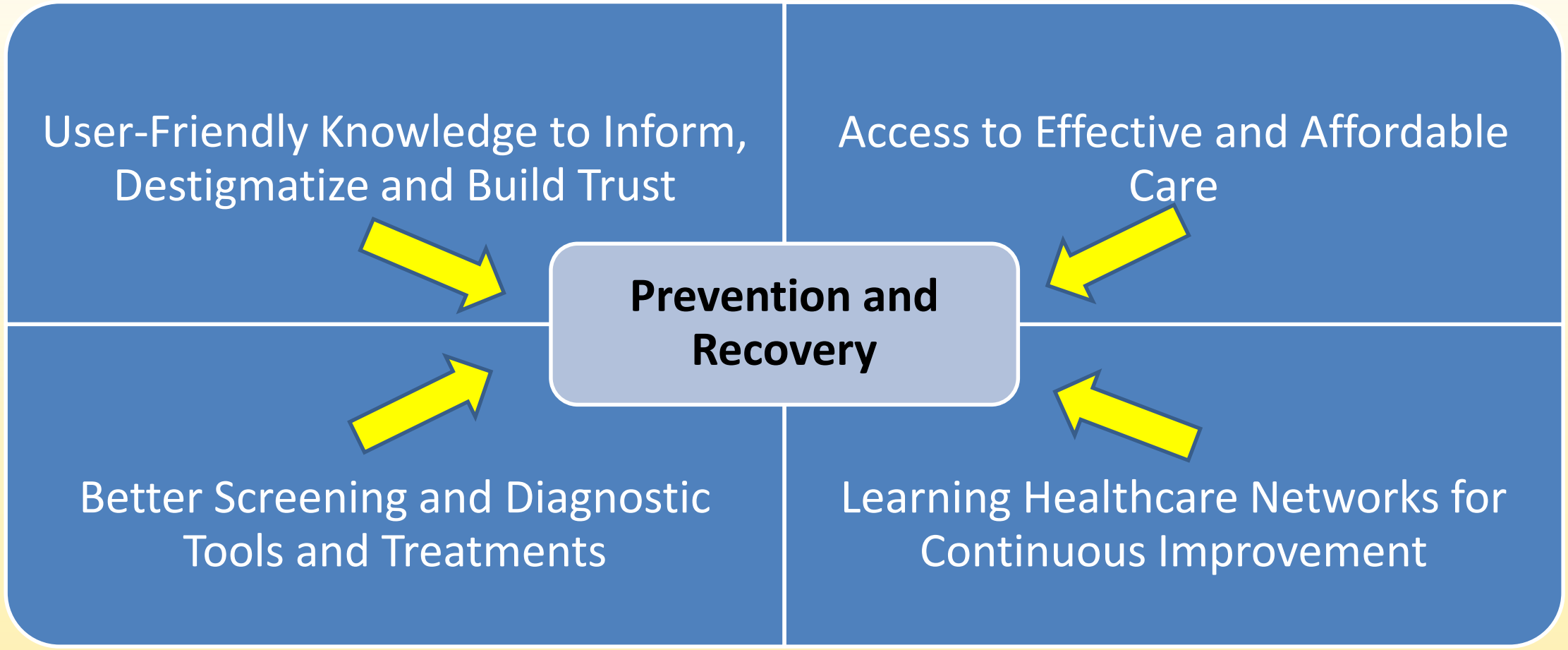
One Mind seeks public/private partnerships to support and accelerate brain research that leads to better mental health care practice and policies.

One Mind's Scientific Advisory Board is made up of ten neuroscientists with outstanding experience, knowledge and diverse perspectives. Current Co-Chairs include:

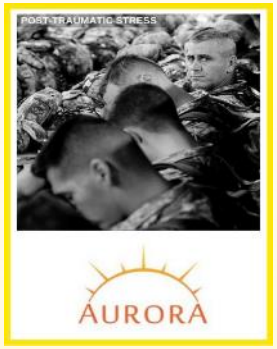
Steven Hyman, M.D. - Director of the Stanley Center for Psychiatric Research at the Broad Institute of MIT & Harvard.

Eric Nestler, M.D. Director of the Friedman Brain Institute and Dean for Academic & Scientific Affairs at the Icahn School of Medicine at Mount Sinai.

One Mind aims to change the trajectory of brain injury with multiple, integrated programs

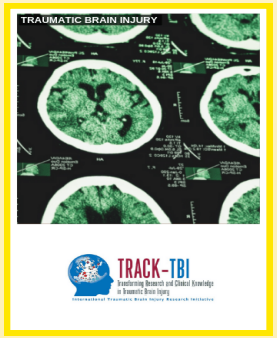


Tackling the Brain Health Crises Through Partnerships



$5.5 M

$2.0 M



$3.5 M

$1.5 M

$2.9 M

$2.7 M

$2.4 M

$9.5 M

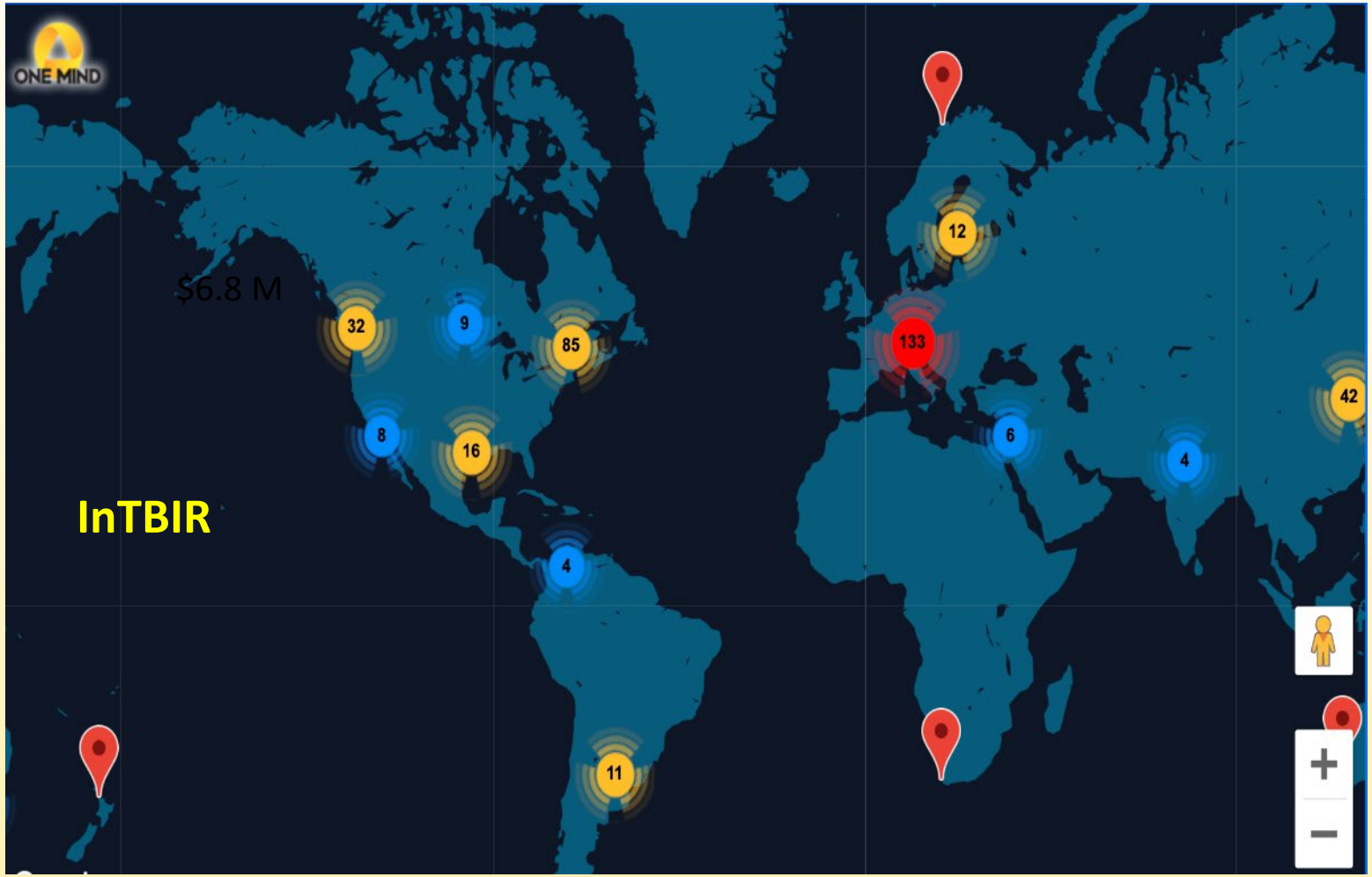
Examplar 1: TBI and PTSD Research Integration

TRACK TBI & AURORA: Overlapping Content												
	Baseline		2 weeks		8 weeks		3 months		6 months		12 months	
	TT	AU	TT	AU	TT	AU	TT	AU	TT	AU	TT	AU
Depression		X	X	X		X	X	X	X	X	X	X
Pain		X	X	X		X	X	X	X	X	X	X
PTSD		X	X	X		X	X	X	X	X	X	X
Sleep		X	X	X		X	X	X	X	X	X	X
Cognition		X	X	X		X	X	X	X	X	X	X
Substance Use		X	X	X		X	X	X	X	X	X	X
Anxiety		X	X	X		X	X	X	X	X	X	X
Demographic Information		X	X	X			X		X		X	
Disability		X	X	X		X	X	X	X	X	X	X
Alcohol		X	X	X		X	X	X	X	X	X	X
Nicotine Use		X	X	X			X	X	X	X	X	X
Current Medications		X	X	X		X	X	X	X	X	X	X
TBI	X	X										
MRI: Structural			X	X					X	X		
MRI: DTI			X	X					X	X		
MRI: Resting State			X	X					X	X		
Blood: Plasma	X	X			X	X					X	X
Blood: DNA*	X	X			X	X					X	X
Blood: RNA (PAXgene)	X	X			X	X					X	X

TBI and PTSD Research Integration: Opportunities

- Analyze MRIs of AURORA subjects using TRACK-TBI protocol to identify those with structural brain injury.
- Compare GFAP levels at 2 weeks. Does GFAP differentiate between PTSD and TBI subjects? Does non-mechanical trauma alone also produce increased GFAP levels or is it a specific biomarker for mechanical injury?
- Link AURORA and TRACK subjects to their eHRs for health utilization comparisons.
- Sex differences on recovery trajectories from PTSD and TBI is another question. What are the biological drivers? Higher estrogen levels may be protective. Analyze hormones of interest with same protocols.
- GWAS protocols align, so this provides another natural opportunity to run the data against known polygenic risk factors.
- rsfMRI and inflammation could be a highly informative pooled analysis.
- Insights about digital data gleaned from the PTSD study may be useful for future TBI studies, too.

Examplar 2: International TBI Research Initiative (InTBIR)



Phase 1

- Common Data Elements and Protocols
- TBI Subtypes
- Comparative Effectiveness Research
- Living Reviews
- GWAS studies (GAIN)
- Anti-Platelet and Anti-Coagulant (APAC) Cohort
- Data Quality and Curation for Observational Research (DAQCORD)

Phase 2

- Clinical Trials
- Living Guidelines

Examplar 3: PsyberGuide

OneMindPsyberGuide.org

- One Mind PsyberGuide is a non-profit project that aims to help people to use technology to live a mentally healthier life
- Publicly, freely available app reviews completed by expert review team
- Free of bias or endorsement

Top 3 Research Opportunities/Priorities

- Clinical Networks, Big Data and Open Science
- Cross-Diagnostic Research (especially TBI and Mental Health)
- Bi-Directional Translational Research