

Implementation of a National Trauma Research Action Plan (NTRAP)

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The 2016 report by the National Academies of Sciences, Engineering, and Medicine (NAEM) entitled *Integrating Military and Civilian Trauma Systems to Achieve Zero Preventable Deaths After Injury* is a call to action for the clinical and academic trauma communities and the country at large, which is negatively affected by lost lives and productivity stemming from the secondary effects of severe injury.¹ This report highlights the importance of establishing a “learning trauma care system” built on the foundation of continuous innovation and generation of best practices, which can only be accomplished in conjunction with a sustained and coordinated federal research investment in all aspects of injury care. This report also highlights the significant lack of federal support for trauma research funding relative to the public health burden of this condition. Over the past 50 years, beginning with the seminal report by the National Research Council, *Accidental Death and Disability: The Neglected Disease of Modern Society*, there have been seven high-profile national reports that have highlighted this discrepancy, yet there has been little progress made to establish a national trauma research investment and strategy. The 1966 report stated, “Research in trauma has suffered from the lack of recognition of trauma as a major public health problem. The most significant obstacle at present [to trauma research efforts] is the lack of long-term funding. Unpredictability of financial support hinders recruitment of competent scientists and technicians, retention of key personnel, and procurement of necessary equipment.”² A report by Moses et al.³ in 2015 quantified the discrepancy in National Institutes of Health (NIH) funding for injury at -11.8% relative to the burden of disease. Traumatic injury was the most underfunded medical condition studied (Fig. 1).

Need for a Federal Home for and Commitment to Trauma Research

In addition to the lack of federal funding, the existing national trauma research effort suffers from a lack of coordination

of research priorities. There remains no definitive federal home for trauma research. The Department of Defense (DoD) Combat Casualty Care Research program has focused on a modest investment administered through the military’s awards and acquisitions processes on critical gaps in the care of injured service members and has organized these investments into the following categories: neurotrauma and traumatic brain injury, hemorrhage control and resuscitation, en route care, and forward surgical care and intensive critical care.⁴ While the DoD trauma research program has been effective, its funding has decreased in recent years and is at risk of continued decrement as the number of injured service personnel in Iraq and Afghanistan decreases. Furthermore, the military’s top priorities in trauma and injury research do not necessarily overlap with civilian-based issues and do not include populations such as pediatric and geriatric patients. The NIH has established an Office for Emergency Care Research; however, this office directs no federal research appropriation. The modest size of and support for this office limit its influence and ability to direct the research and development priorities of other NIH institutes or civilian academia and industry. Coordination of priorities, research efforts, and research advocacy among the many different specialties that care for injured patients is also lacking. In addition, trauma care activities range from injury prevention through a continuum of care from the scene of the event through rehabilitation. Coordinating a coherent research agenda and list of priority topic areas in this diverse array of care settings and injury-related conditions is needed.

Need to Improve Innovation, Technology Transfer, and Diffusion to Clinical Practice

To improve the delivery of new and effective material products (i.e., drugs, devices, and technologies) to reduce morbidity and mortality of severely injured patients, there is a need to expand innovation and technology transfer relationships among military research centers, university-based technology innovation centers, and private industry. This requirement underscores the need for more substantial and consistent federal funding for trauma research, as this investment serves as a vital catalyst in these public-private partnerships. Specifically, federal dollars incentivize innovation and serve as a bridge to advance new ideas and concepts to regulatory approval and commercialization. In addition to expanded military, civilian university, and private partnerships, innovation, miniaturization, and automation of new devices for bleeding control, resuscitation, operative intervention, and critical care will require greater degrees

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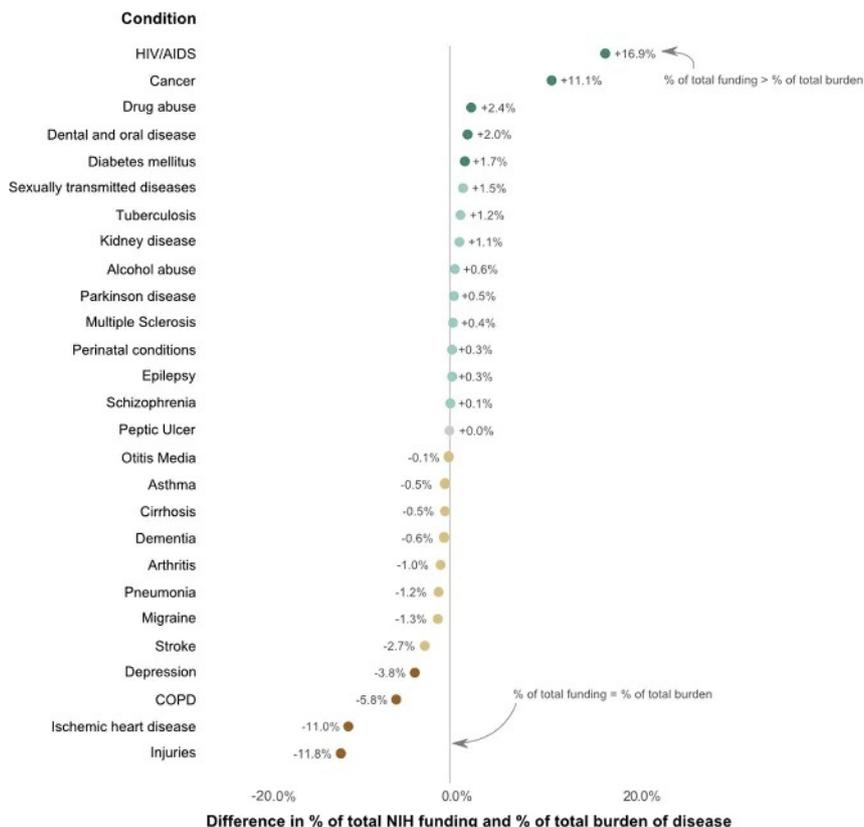


Figure 1. Proportion of NIH funding relative to the total burden of disease. Reprinted with permission from Catherine Richards, PhD.

of cross-disciplinary collaboration between the fields of emergency medical services, emergency medicine, surgery, radiology, engineering, and information technology.

Inherent Barriers to Trauma and Injury Research

There are regulatory barriers that negatively affect the ability to conduct research and deliver, in a timely manner, drugs, devices, and technologies that may positively affect patients' survival and recovery. As outlined in the NASEM report, these barriers are partially due to ambiguity in the interpretation of federal regulations, regulatory silence on specific issues, and lack of flexibility in the interpretation of data leading to approval for new therapies. Additionally, the complexity of the clinical setting, the emergency nature of care, and the severity of patient injury add to the challenge of conducting clinical research in this area. Potential investigators often struggle understanding the subtle difference between hypothesis-based research and performance improvement projects, which can lead to misinterpretation of needed regulatory and human protections approvals. The logistics of data collection across the continuum of injury care is challenging, and many studies are hindered by an inability to obtain immediate patient's consent and thus are subject to more stringent regulations guiding the exception from informed consent (EFIC) process. Further complicating the issue is a unique requirement for a high-level waiver signed by the Secretary of the Army before use of any DoD research funds to support an EFIC study. Finally, coordinating clinical studies across multiple sites and institutional

review boards can also be challenging and inefficient and is an area in need of review and improvement.

To address these issues related to trauma research, the NASEM report included two specific recommendations:

“To strengthen trauma research and ensure that the resources available for this research are commensurate with the importance of injury and the potential for improvement in patient outcomes, the White House should issue an executive order mandating the establishment of a National Trauma Research Action Plan requiring a resourced, coordinated, joint approach to trauma care research across the US Department of Defense, The US Department of Health and Human Services (National Institutes of Health, Agency for Healthcare Research and Quality, Centers for Disease Control and Prevention, US Food and Drug Administration, Patient-centered Outcomes Research Institute), the US Department of Transportation, the US Department of Veterans Affairs, and others (academic institutions, professional societies, foundations).”

“To accelerate progress toward an aim of zero preventable deaths after injury and minimizing disability, regulatory agencies should revise research regulations and reduce misinterpretation of the regulation through policy statements (i.e., guidance documents).”

To address the practical next steps in the implementation of these recommendations, the American College of

Surgeons Committee on Trauma (ACS COT) partnered with the National Highway Transportation and Safety Administration and the Department of Defense to conduct a two-day meeting on the NIH campus, Bethesda, MD, in April 2017. This meeting was attended by stakeholders from multiple federal agencies, a wide range of trauma and emergency care providers, and representatives from professional societies. The following paragraphs summarize the discussions related to the future of trauma research from that meeting along with recommendations for next steps in the development of a National Trauma Research Action plan.

Determining the Optimal Federal Home for Trauma Research

To address one of the major barriers to securing a consistent, sustainable federal appropriation for trauma research, the stakeholders believe that a federal home for trauma research needs to be identified, created, and supported. Beyond the annual appropriation dedicated to this topic that is directed through the DoD, there currently exists no other federal source of research funding that is at a level required to address this national health urgency. Establishing a federal departmental home for a substantial and consistent trauma research appropriation would also greatly enhance planning and coordination efforts and demonstrate a national commitment to the civilian academic and private innovation sectors. To address this issue during the April meeting, two pro versus con debates were held to consider options. During these deliberations, the advantages and disadvantages of the current DoD-led model were discussed, as was the potential of having a national trauma research investment be led by a new NIH institute.

As outlined in Table 1, there were several advantages identified to the NIH serving in this role, with few disadvantages other than a recognition of significant fiscal and political challenges associated with identifying new, or reappropriating existing, dollars to support such a major initiative. The DoD currently plays an important role in funding relevant research for the wounded service member, and the military's Combat Casualty Care Research Program has produced valuable knowledge and products that have translated to the care of civilian casualties. However, there remain legitimate concerns pertaining to overly strict and cumbersome processes and priorities tied to DoD-funded medical research. As an example of challenges associated with DoD-funded medical research, investigators from the National Trauma Institute recently published their experience with the management of 16 DoD-funded projects over a 4-year period and reported an average delay of 8 months from the time of local civilian institutional review board(s) approval to ratification by a necessary second level DoD Human Research Protection Office.⁵ The Resuscitation Outcomes Consortium, which conducted several DoD-funded trials under the EFIC regulations, reported an average time for regulatory approval of 10.5 months.⁶ Other limitations associated with a DoD-led model include varying commitments of funding relative to changes in the level of international military engagement (i.e., decreased interest and research funding during times of peace). Additionally, the military's requirements-driven focus often excludes priorities for civilian populations such as

those relating to pediatric and geriatric injury and civilian trauma systems. There were also concerns discussed about the degree to which the peer review process used by the DoD in the adjudication of its research awards involves true subject matter experts. It was also discussed during this panel that the military's requirements-driven mechanisms for trauma research may diminish the value of investigator-initiated strategies and that a lack of balance between the two approaches is a limitation.

The consensus of the panel and attendees at the April meeting was that a dedicated NIH Institute for Trauma Research was the preferred long-term solution. It was recognized that in the near and mid-term, efforts should maximize the mission and impact of the NIH Office of Emergency Care Research and the recently announced NIH emergency care research network (Strategies to Innovate Emergency Care Clinical Trials Network). Efforts should be made to raise the priority of medical research that is relevant to all phases of trauma and injury care in the investments made among existing NIH institutes. Additionally, as a near and mid-term goal, the panel and attendees recommended improving the civilian clinical and research communities' understanding of DoD-led funding opportunities. To the degree possible, within existing federal regulations and DoD policies, the military trauma research program should work to become more efficient and open to civilian involvement and civilian priorities. The value of these near and mid-term measures notwithstanding, the consensus of experts at the April meeting was that a new NIH institute dedicated to the broad number of medical and practice topics relevant to the injured patient remains the long-term goal.

Developing the National Trauma Research Action Plan

While the larger political challenges remain, the conference attendees overwhelmingly believe that there are practical steps that can be initiated to support the development of the National Trauma Research Action Plan (NTRAP). We propose that these efforts be managed and coordinated by the Coalition for National Trauma Research (CNTR). The CNTR was founded in 2014 as a coalition of the major professional organizations engaged in the support of trauma research. These include the American Association for the Surgery of Trauma, the Eastern Association for the Surgery of Trauma, the Western Trauma Association, the National Trauma Institute, and the ACS COT.⁷ The CNTR has also led significant and successful advocacy efforts to secure federal funding for trauma research and in just its first 2 years secured \$20 million appropriated to the DoD to support trauma research. The National Trauma Institute, which is a core member of CNTR, has experience in peer review and coordination of multicenter clinical trials as well as management of research funds allocated by the DoD. In 2017, the CNTR published a consensus-based research agenda defining research priorities for the trauma community in the areas of resuscitation, hemorrhage control, coagulation and coagulopathy, biomarkers and genetic profiling, venous thromboembolism, traumatic brain injury, organ failure and sepsis, geriatric trauma, trauma system development, prehospital care, and wound healing, and pain control.⁸ This research agenda aligns closely with the priorities of the DoD program and provides an excellent starting point for the development of the NTRAP. As the

TABLE 1. Federal Home for Funding of Trauma and Injury Research

	National Institutes of Health	Department of Defense
Advantages	<ul style="list-style-type: none"> • Steady, reliable source of funding • Prioritize research initiatives and questions • Motivate and train future investigators • Remove/Lessen political influence on research agenda • Informed and attuned study sections for peer review • Nationally centralized institutional review board and coordinated community consent • Adequately funded core for appropriately sized clinical trials • Transparent priorities and allocation process 	<ul style="list-style-type: none"> • Established executive function avoids redundancy and directs the research agenda • Established priorities based on knowledge gaps in combat casualty care and in doing so defined the broad categories of topics into which federal research appropriations can be placed and awarded • Mission focus with a requirements-driven approach to identify practical solutions • Expediency: DOD trauma research program is established and recognized by political leaders
Disadvantages	<ul style="list-style-type: none"> • Not practical in current environment based on concerns for decreasing NIH financial support • Belief within the NIH that all of the topics relating to care of the severely injured patient can be addressed within the current NIH appropriation and institutes 	<ul style="list-style-type: none"> • Focus on needs of combat soldiers may exclude civilian priority populations (pediatrics/geriatrics) • Variable funding for injury topics among many priorities for military medicine (i.e., risk of decreased level of funding based on level of combat operations) • Significantly less overall funding than NIH • Lack of investigator-initiated research limits innovation • Complex approval process • Scientific review can be overruled by mission relevance • Military-unique regulatory requirements lead to delays in some scenarios

recipient of a competitive DoD award process, the CNTR is also currently developing a national trauma research repository, which will be a critical resource to make data from current and previous DoD-funded studies available for secondary analysis.

The key components of the NTRAP include defining a stable and sustainable federal home for trauma and injury research; securing a significant and enduring federal appropriation for medical research in this topic area—an appropriation that is commensurate with the condition’s overall societal burden; engaging all stakeholders and specialties in a coordinated approach to trauma research; establishing a comprehensive and prioritized research agenda to address gaps in knowledge and promote new innovation in all areas pertaining to care of the injured patient (i.e., point of injury, en-route care, facility-based operative and intensive care and rehabilitation); expanding the infrastructure to conduct multicenter clinical research (pragmatic observational trials as well as interventional and controlled clinical trials); and addressing the regulatory barriers to trauma research. To achieve these aims, in conjunction with the DoD and other federal partners, the CNTR has proposed practical implementation strategies and is seeking funding to advance this cause. The CNTR is also seeking to broaden the coalition to include other specialty organizations that are engaged in the support of injury research.

Implementation Strategies

The following are immediate actions that can be taken to support the development of the NTRAP under the coordination of the CNTR:

1. Establish a comprehensive research agenda

Using the initial DoD-aligned CNTR research agenda as a starting point, we propose to develop a more comprehensive

agenda to support the NTRAP, which will be inclusive of the continuum of care and injury prevention as well as inclusive of all surgical subspecialties related to trauma. Eleven work groups are proposed, which include (1) prehospital and mass casualty triage and management, (2) hemorrhage control, resuscitation and critical care, (3) initial evaluation/imaging, (4) neurotrauma management, (5) orthopedic trauma, (6) burn management, (7) long-term functional outcomes/rehabilitation, (8) geriatrics, (9) pediatrics, (10) injury prevention, (11) trauma systems and informatics. The research agenda can be developed by an on-line Delphi approach, which will allow for identification of research gaps and prioritization of projects within each area.

2. Develop a “one voice” or unified advocacy strategy to attain enhanced, sustainable research funding and a federal home for trauma and injury research.

This effort will require development of a broad coalition of partner societies and existing research networks to provide a unified voice in national advocacy. It will also require engagement of the public and their congressional representatives through outreach campaigns that raise awareness of trauma as a public health urgency and the importance of trauma research as a means to achieving the goal of zero preventable deaths and disability following injury. In partnership with the American Trauma Society, we also seek to engage trauma survivors in these advocacy efforts.

3. Promote enhanced coordination of multicenter clinical trials

This strategy seeks to provide a coordinated approach among existing and future multi-institutional research networks and to develop infrastructure to support comparative effectiveness studies and pragmatic observational studies. To this end, we are seeking the development of a research collaborative using the data from the Trauma Quality Improvement

Program (TQIP) of the ACS. This program collects high-quality clinical care data from more than 600 adult US trauma centers and 99 pediatric centers. This program conducts risk-adjusted analysis of centers' outcomes and provides feedback to participating centers for quality improvement. The ACS COT has committed to providing the CNTR with direct access to TQIP data for clinical trials. The CNTR can provide the infrastructure and coordination for these projects, and we are currently exploring funding options to support this collaborative. We also seek to foster a platform for the coordination of existing and future multicenter clinical trials across the spectrum of trauma care and to establish optimal strategies to assess long-term functional outcome in this patient population.

4. Identify regulatory barriers to trauma research and support investigators

This goal can be met by establishing a working group to review research regulations and use an on-line Delphi approach to identify current barriers to trauma research and areas of misinterpretation of federal guidelines. These data can then be used to develop a best practices document for the conduct of trauma research and a toolkit for investigators, particularly for studies that require exception from informed consent procedures. In addition, we seek to partner with regulatory agencies such as the Food and Drug Administration to proactively discuss and identify optimal end points for future clinical research and work with the DoD to improve the efficiency of the regulatory review process. We seek to engage the leadership of the regulatory agencies in regulatory reform efforts and clarification of existing regulations to facilitate ethical and efficient trauma research.

Summary

While the recommendations of the NASEM report related to trauma and injury research seem challenging to achieve in the current political and fiscal environment, we believe that the practical implementation strategies—near, mid-, and long-term—outlined in this report are achievable and will lay the ground work for the development of a comprehensive National Trauma Research Action Plan. The CNTR is seeking sustainable funding to advance this cause and stands ready to implement all the

strategies previously outlined. Given the lack of progress over the past 50 years, the time to act is now.

AUTHORSHIP

EB was the primary author responsible for drafting the manuscript. All authors contributed to critical review and revisions of the manuscript.

DISCLOSURE

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