December 2023

CDMRP
DEPARTMENT OF DEFENSE
CONGRESSIONALLY DIRECTED MEDICAL RESEARCH PROGRAMS

Peer Reviewed Orthopaedic Research Program

Strategic Plan

INTRODUCTION

The Congressionally Directed Medical Research Programs, CDMRP, represents a unique partnership among the U.S. Congress, the military, and the public to fund innovative and impactful medical research in targeted program areas. Programs managed by the CDMRP have formalized strategic plans that identify: program-specific research priorities, how to best address these urgencies; short- and long-term goals, investment strategies, and ways to identify and evaluate program successes with respect to the priorities.

The Peer Reviewed Orthopaedic Research Program, PRORP, Strategic Plan identifies the high-impact research goals most important to the program and its stakeholders while providing a framework that is adaptable to changes in the medical research and clinical care environments to address those goals. This plan has been formulated to provide greater clarity of the program's goals over time. Congress appropriates funding for the PRORP on an annual basis; therefore, there is no guarantee of future funding. The PRORP Strategic Plan will be reviewed during the program's annual vision setting meeting and updated as necessary.

PRORP BACKGROUND AND OVERVIEW

In FY09, the PRORP received an initial appropriation of $112 million to provide support for research focused on optimizing recovery and restoration of function for military personnel with orthopaedic injuries sustained during combat or service-related duties. The initial appropriation originated from two appropriations acts: $61M from the Consolidated Security, Disaster Assistance and Continuing Appropriation Act, 2009, and $51M from the Supplemental Appropriations Act, 2009.

The congressional language directed the PRORP to fund "orthopedic and other trauma research, treatment and rehabilitation including regenerative medicine. This funding will continue and expand the existing orthopedic trauma research program, amputee rehabilitation and reset research, and restoration of function." Since FY09, Congress appropriated $518.5M to the PRORP. The PRORP used these funds to support 355 high-impact and clinically relevant research awards contributing to advancing treatment and rehabilitation from musculoskeletal injuries.

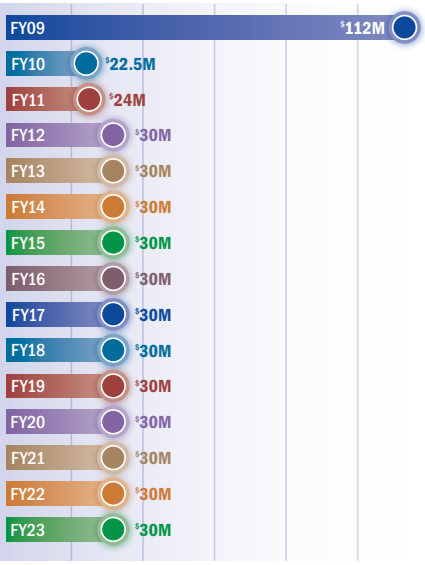


Figure 1: PRORP Appropriation, by Fiscal Year

VISION: Provide all Military Service members with orthopaedic injuries the opportunity for optimal recovery and restoration of function

MISSION: Address the most significant gaps in care for the leading burden of injury and for facilitating return-to-duty by funding innovative, high-impact, clinically relevant research to advance optimal treatment and rehabilitation from musculoskeletal injuries sustained during combat and service-related activities.

FUNDING HISTORY AND RESEARCH PORTFOLIO

Orthopaedic injuries profoundly impact military readiness and return-to- work/activity/duty. In the military, 52% of combat wounds include an extremity injury, and battlefield orthopaedic injuries are a major cause of long-term disabilities.[1] Additionally, non-combat injuries and conditions encountered during training, leisure activities, or resultant from old injuries present a major threat to service member readiness, resulting in 2 million outpatient medical encounters annually.[2] Early stabilization, treatment, and rehabilitation of orthopaedic injuries in both civilian and military populations contribute to better outcomes, particularly in the prevention of secondary complications and in minimizing morbidity. Availability of orthopaedic care and treatment as early as possible, or as close to the point of injury as possible, also minimizes limb loss and impacts to military readiness. The PRORP supports research impacting the lives of all individuals that sustain a major musculoskeletal injury.

PRORP-funded research projects support the vision and mission of the program, leading to tangible products, improvements in care techniques, updates in Clinical Practice Guidelines, and other knowledge products to help support the care and rehabilitation of persons who have sustained orthopaedic injuries. This PRORP strategic plan identifies unmet research needs for patients and prioritizes the program's research goals to effectively address the changing needs of the military and clinical care environments. This plan also describes how the PRORP intends to allocate any future appropriated funds to meet those research goals for the benefit of service members, veterans, and the public.

At program inception, the CDMRP held a stakeholders meeting in May 2009 to identify knowledge and capability gaps in the orthopaedic research and clinical care space. This meeting helped focus investment discussions for the initial and future PRORP appropriations. The program grouped the identified gaps into Focus Areas related to acute battle injuries, definitive care of battle injuries, rehabilitation, and prosthetics/orthotics and included these Focus Areas in the program's initial solicitation of research projects. The PRORP modified the Focus Areas over time during yearly vision setting meetings and categorized them into surgical care and rehabilitation topics, resulting in an evolution of the type of research funded from early-stage technologies to manage bone and cartilage damage to more integrated therapies for clinical management of disease.

The PRORP hosted a recent stakeholders meeting in September 2021 to identify current critical knowledge and capability gaps in orthopaedic research and care. Representatives from non-profit organizations, academia, industry, government institutions, and the public shared broad perspectives on barriers in research and patient outcomes, key knowledge and scientific gaps, and potential approaches for addressing orthopaedic needs. Resources shared during the meeting and outcomes of the effort are available on the CDMRP website (https://cdmrp.health.mil/prorp/default).

From these gap-finding engagements and coordination with partners from the NIH, VA, National Science Foundation (NSF), and non-government funding organizations, it became clear the PRORP could impact orthopaedic care by funding high-risk/high-reward research, multidisciplinary research, and research projects that move promising findings closer to clinical implementation and/or availability. The PRORP funded three large consortia awards, the Bridging Advanced Development for Excellent Rehabilitation Consortium, the Major Extremity Trauma and Research Consortium, and the Major Extremity Trauma and Rehabilitation Consortium. These consortia bring together military patients, leading researchers, and military treatment facility clinicians with the infrastructure, patients, and expertise of highly qualified civilian organizations to form partnerships to provided new solutions along the continuum of care for orthopaedic injuries. The PRORP also invested in applied research and large collaborative orthopaedic clinical care studies impacting clinical outcomes today. Additional information of the programs' past and current efforts can be found in the PRORP Program Book, which can be accessed on the PRORP website.

STRATEGIC DIRECTION

The orthopaedic field is vast; it includes topics in training, prevention, tissue engineering, pain control, surgical techniques and care, comorbid injuries/conditions, rehabilitation, orthotics, prosthetics, and many more. A reflection of the state of the science in any given topic area changes rapidly. In addition to recommendations from the PRORP Programmatic Panel, program staff solicit input from the service branches and experts in several related disciplines during Stakeholder meetings and engagements at professional society meetings. These engagement opportunities allow the program to keep abreast of the ever-changing research landscape and clinical environment for the military and general population. The PRORP also routinely monitors research supported by other federal and non-federal funding agencies, including but not limited to, the NIH, VA, Extremity Trauma and Amputation Center of Excellence, Small Business Innovation Research Program, NSF, Department of Defense, Society of Military Orthopaedic Surgeons, Orthopaedic Research and Education Foundation, Orthopaedic Research Society, American Academy of Orthopaedic Surgeons, and American Academy of Orthotists and Prosthetists to coordinate research funding and priorities across organizations, eliminate research duplication, and ensure that efforts are complimentary in order to best address knowledge and capability gaps.

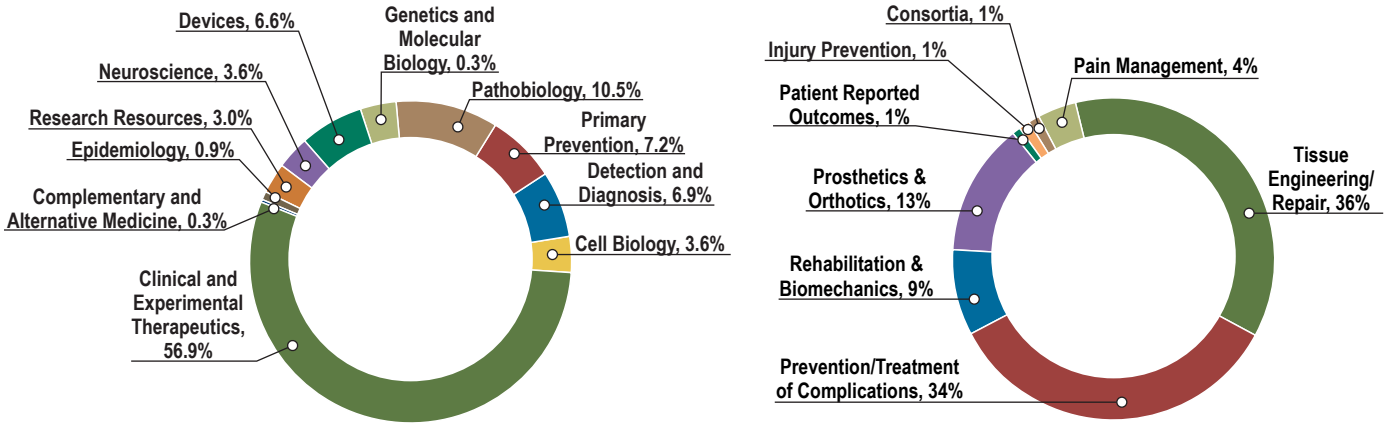


Figure 2: PRORP Investment (number of projects funded) by Scientific Area (left) and Portfolio Alignment (right), FY09-FY21

The PRORP maintains the congressional intent of the program and continues to support militarily relevant orthopaedic trauma research to treat and facilitate rapid recovery from orthopaedic injuries, and benefit service members, veterans, and the public. Congress instructed the program's appropriations focus on battle-related injuries, as these injuries are often heterogeneous and complex in nature and frequently involve multiple limb trauma, open fractures, major tissue loss, and a high degree of wound contamination. Additionally, these battle-related injuries are sustained in harsh environments where access to optimal care can be limited. Importantly, findings obtained from PRORP-supported research are also applicable to and can benefit the general population.

The PRORP supports research to addresses the needs of the nation's injured service members and veterans, the needs of the military medical personnel charged with their care and well-being, and the changing military needs of potential conflicts. The PRORP Programmatic Panel, composed of representatives from the military services, VA, and other government organizations, academia, and clinical practice, as well as the patient community, annually assesses the current research environment related to the short- and long-term care of injured patients and reviews emerging technological developments in the field.

Orthopaedic patients benefit from many successes; however, many challenges still prevent some injured patients from returning to their pre-injury level of fitness. Key challenges in military medicine, as it relates to the orthopaedic field, include identification of best practices for trauma care in a prolonged care setting; optimization of point-of-injury care to minimize or eliminate long-term complications; evaluation of rehabilitation strategies to increase return-to-duty and return-to-work rates; development of interventions that predict and treat complications; and many others. The research field's ability to address these challenges directly impacts on the readiness of the U.S. military, the rehabilitation and reintegration of veterans, and the clinical care of patients in the general public.

The 2023 PRORP Strategic Plan provides the framework for which current and near-future research investments will be made. The Programmatic Panel will continue to meet annually to review the current state of the science, priorities of the military, and immediate clinical needs in order to confirm that these priorities are still relevant and to refine the strategic plan as needed.

INVESTMENT STRATEGY

The PRORP Strategic Plan includes award mechanisms planned for the FY23-FY27 PRORP, if appropriated, to capitalize on gaps identified by stakeholders in the field and prioritized by the PRORP. It will also reflect the types of research, such as applied or solutions-driven, translational, or clinical research, that the program plans to fund, based on the needs of the field and the funding appropriated to the program by Congress. These topics and others realized during the program's annual vision setting meeting will be incorporated into Focus Areas over the next several years provided they remain consistent with congressional direction. Some areas of interest to the PRORP include:

1. Prehospital wound management, e.g., tissue preservation, infection management, temporizing strategies, and care strategies that prevent secondary injuries and complications.
2. Development of novel surgical techniques, including pre- and perioperative technologies, for enhancing limb restoration.
3. Prevention and treatment of complications following surgical treatment of musculoskeletal non-battle injuries.
4. Development of novel musculoskeletal imaging capabilities for diagnosis of underlying pathology and efficacy of interventions measurements.
5. Development of new or leveraging of existing technologies and/or personalized care approaches to augment or aid surgical care, monitor/follow recovery, assess return to activity/duty, or identify early predictors of failure.
6. Development of tissue engineering and scaffolds to augment, accelerate, or improve musculoskeletal injury treatments.
7. Development of biologics, implants/devices, combination products, pharmacologic, or non-pharmacologic interventions to improve regeneration of composite tissue.
8. Solutions for traumatic tissue loss, with a focus on nerve gaps and nerve healing with successful innervation, volumetric muscle loss, and protection or restoration of limb and wound vascularity.
9. Development of interventions to prevent, detect, modulate, or treat infection, acute inflammation, and/or pathological immune response in the context of orthopaedic repair across the continuum of care.
10. Development of strategies for longitudinal monitoring of musculoskeletal healing and functional recovery.
11. Therapies and techniques that decrease and treat complications and improve outcomes following high-energy extremity trauma.
12. Development of innovative prosthetics, orthotics, and/or robotics to assist with mobility after traumatic injury.

Since FY18, and anticipated for future years, the PRORP released three award mechanisms to help address the identified PRORP research priorities: the Applied Research Award, Clinical Translational Research Award , and Clinical Trial Award. The three mechanisms are consistent with the program's goal in funding impactful, high risk/high reward, and clinically meaningful research.

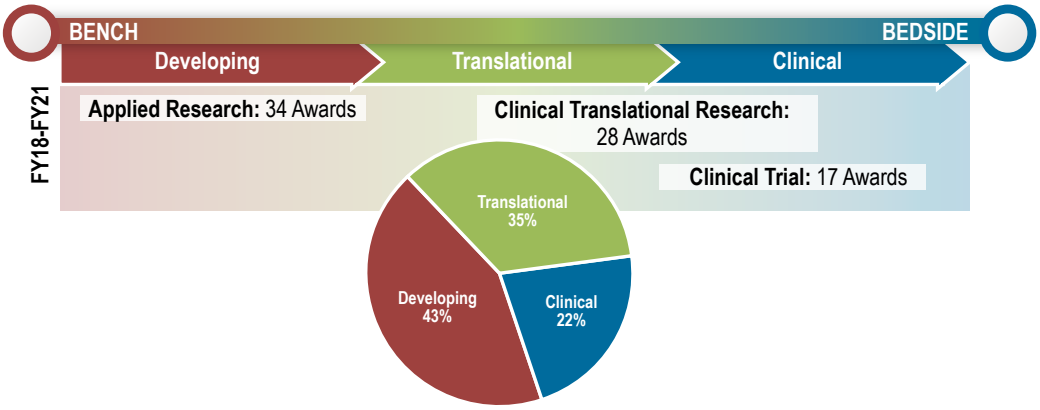


Figure 3. Recent PRORP Investment Strategy, FY18-FY21

The ARA supports applied research projects focused on advancing optimal treatment and restoration of function for individuals with musculoskeletal injuries sustained during combat- and service-related activities. Although the ARA allows basic and animal research, it is not intended to support fundamental basic research without specific application toward knowledge or tangible products. Future use of and solicitations for the ARA will depend on the needs of the research and clinical communities and goals of the PRORP.

The CTRA supports translational clinical research that may not yet be ready for a full-scale randomized clinical trial. Funded projects are expected to impact the standard of care for military, Veteran, and all patients who have sustained orthopaedic injuries. Future solicitations for the CTRA will depend on the outcomes of current research projects in areas of interests to the orthopaedic field or PRORP.

The CTA differs from the CTRA in that the CTRA allows clinical research projects, whereas the CTA is restricted to clinical trials only. The CTA mechanism is intended to support rapid implementation of clinical trials that can significantly impact treatment or management of military combat or service-related orthopaedic injuries to improve unit readiness and return to duty/work rates. Future solicitations for the CTA will be based on then-current research environment assessments to ensure the PRORP continues to move promising interventions into clinical practice without duplicating efforts underway with other federal funding agencies.

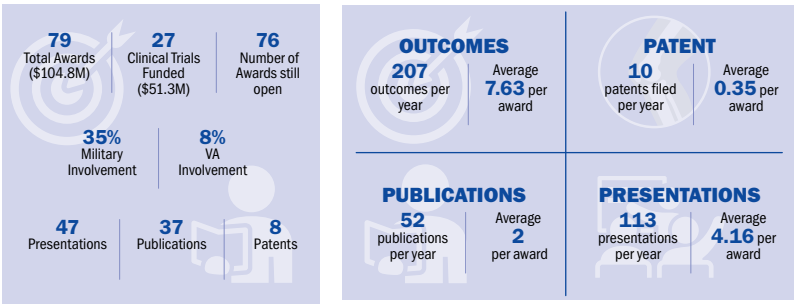
This strategy will be re-evaluated and updated as necessary during the program's annual vision setting meeting.

MEASURING PROGRESS

The PRORP identified the below priorities in the 2018 PRORP Strategic Plan and incorporated them into Focus Areas in FY18-FY22 PRORP funding opportunities. The number of awards made from FY18-FY22 for each priority is indicated below.

- Develop basic science animal models to replicate injuries or conditions that are challenging in a prolonged care scenario; *8 awards for $5.8M*
- Evaluate clinical interventions for durability in a far-forward environment or as close as possible to the point of need including:
  - Methods to prevent and/or control combat extremity wound infections (e.g., for long bone open fractures); *5 awards for $8.2M*
  - Development of novel wound protectants; *4 awards for $2.9M*
  - Improved methods for acute pain control; *no awards*
  - Advancing surgical interventions to earlier roles of care; *7 awards for $13.7M*
- Discover interventions and/or rehabilitation strategies to facilitate early return to duty for common musculoskeletal injuries, including:
  - Development of offloading and stability devices, e.g., braces and casting, for ligamentous injuries/small extremity fractures; *3 awards for $2.2M*
  - Development of optimal nonsurgical and/or surgical strategies, tools, and delivery parameters to improve functional outcomes for both immediate and eventual return to duty; *no awards* *
  - Development of protective equipment for treatment of non-severe, common battlefield musculoskeletal injuries; *no awards*
- Translate early research findings in surgical care topic areas to large animals and/or humans to move the research toward clinical trials and clinical practice; *6 awards for $14.2M*
- Identify best practices to address rejection and failure of percutaneous osseointegrated prosthetic limbs; *14 awards for $11.6M*
- Develop innovative treatment pathways and technologies to optimize complex orthopaedic injury/extremity trauma management, and minimize long-term disability; *32 awards for $45.8M*
- Develop advanced tissue regeneration therapeutics for the restoration of traumatically injured extremity tissues; *12 awards for $13.9M*

96% of these awards are still open with ongoing research activities. Although the PRORP realized some research outcomes from funded awards, the program anticipates most of the outcomes from these funding efforts will become available in the next two to four years.



FY18-FY21 **FY09-FY21**

Figure 4. Program Metrics

* Applications that addressed this priority were submitted to Focus Areas corresponding to the "Develop innovative treatment pathways and technologies to optimize complex orthopaedic injury/extremity trauma management, and minimize long-term disability" priority area. Awards were counted once to eliminate duplicative reporting.

The PRORP continues to monitor the outcomes of PRORP-funded research and their impact on the field. The following metrics, categorized into short-term and mid-term outcomes, allow the PRORP to assess progress made toward addressing the identified unanswered research questions and research priorities:

Short-term outcomes within the next three to five years: Measurable by evaluating the amount of funding invested in each strategic goal and tracking contributions to the scientific and clinical community, including publications, patents, products, and clinical trials, which will vary based on the stage of the research project.

Mid- and long-term outcomes at six or more years: Measurable by evaluating the proportion of funded investigators receiving additional awards to continue successful research, production of commercialized products, and changes in standard of care through Clinical Practice Guidelines or evidence supporting specific treatment recommendations, point-of-injury care, return-to-duty rates, and quality of life.

REFERENCES

1. Mitchell SL, Hayda R, Chen AT, Carlini AR, Ficke JR, MacKenzie EJ; METALS Study Group. The Military Extremity Trauma Amputation/Limb Salvage (METALS) Study: Outcomes of Amputation Compared with Limb Salvage Following Major Upper-Extremity Trauma. *J Bone Joint Surg Am*. 2019 Aug 21;101(16):1470-1478. doi: 10.2106/JBJS.18.00970. PMID: 31436655; PMCID: PMC7406140.
2. Molloy JM, Pendergrass TL, Lee IE, Chervak MC, Hauret KG, Rhon DI. Musculoskeletal Injuries and United States Army Readiness Part I: Overview of Injuries and their Strategic Impact. *Mil Med*. 2020 Sep 18;185(9-10):e1461-e1471. doi: 10.1093/milmed/usaa027. PMID: 32175566.