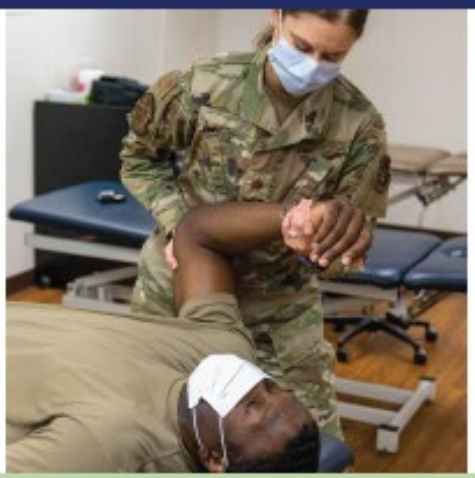
CDMRP
DEPARTMENT OF DEFENSE
CONGRESSIONALLY DIRECTED MEDICAL RESEARCH PROGRAMS


Department of Defense

Congressionally Directed Medical Research Programs

Fiscal Year 2024

Arthritis Research Program

Stakeholders Meeting – Summary and Gaps

June 2024

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Overview: CDMRP History

The Congressionally Directed Medical Research Programs, CDMRP, located within the U.S. Army Medical Research and Development Command, is a global funding organization that fosters novel approaches to congressionally targeted biomedical research areas in response to the expressed needs of its stakeholders – Congress, Service Members, their Families, Veterans, and the American public. CDMRP-managed programs are diverse but share the common goals of accelerating progress, advancing paradigm-shifting research, developing cutting edge technologies, and identifying breakthroughs and solutions that will lead to cures, improved patient care and enhanced quality of life.

CDMRP receives annual appropriations that are disease- or condition-specific, which allows flexibility to implement targeted investment strategies each year that are focused on areas of highest potential impact and highest priority needs of the patient and research communities. CDMRP accomplishes this through close coordination and continual development of strategic and research partnerships with the scientific and clinical communities, industry, other federal and nonfederal funding organizations and consumers including patients, survivors, family members and/or caregivers– all of which are critical to enabling successful outcomes.

CDMRP maintains a passionate dedication to its mission and readily adapts to emerging priorities or congressional establishment of new programs or topics. Across all programs, CDMRP funds research to benefit people in the military health care system, to include Service Members, their Family members, Veterans, and others in the civilian population.

The DOD does not request funding for CDMRP as part of the president's annual budget submission. Instead, in response to input from consumer advocates, survivors, people living with a disease or injury experience and others, Congress adds funding for the CDMRP into the annual defense appropriations bill. In FY24, Congress appropriated funds for 35 distinct programs for management by the CDMRP.

Programmatic Cycle

CDMRP executes its program cycle process for each appropriated program as shown in Figure 1. New programs begin their cycle with a public stakeholder meeting to identify key knowledge gaps and collect feedback for consideration at the program's vision setting meeting. The vision setting meeting includes the CDMRP program team and a Programmatic Panel – comprised of researchers, clinicians, consumers and other subject matter experts. The panel members consider congressional language and assess the state of the science, stakeholder-identified gaps, clinical care gaps and patient needs to help develop the program's vision and mission statements, focus areas, strategic plan, yearly investment strategy and funding opportunities. After vision setting, the program releases funding opportunities, or program announcements, to solicit research aligned with the goals established by the program. Once applications are received, the CDMRP initiates its two-tier review process.

The CDMRP developed a two-tier review model, based on recommendations from a 1993 Institute of Medicine report,[1] to ensure that each program's research portfolio reflects both the most meritorious science and the most programmatically relevant research. The IOM, now the

[1] Institute of Medicine Committee to Review the Department of Defense's Breast Cancer Research Program. A Review of the Department of Defense's Program for Breast Cancer Research. Washington, DC: National Academies Press; 1997. 1, Introduction. Available from: https://www.ncbi.nlm.nih.gov/books/NBK233671/

National Academy of Medicine, recommended a two-step review procedure for research applications composed of a scientific peer review and a separate programmatic review, as shown in Figure 1. The scientific peer review, conducted by an external panel recruited specifically for each peer review session, involves the expertise of scientists, clinicians and consumers/patient advocates and may also include specialist reviewers and military or Veteran members. The peer reviewers evaluate applications individually based on scientific and technical merit with respect to the described criteria in the funding opportunity solicitation. The CDMRP does not utilize standing peer review panels. The Programmatic Panel conducts the second tier of review to assess the applications based on the scientific peer review ratings and summaries, a balanced program portfolio, programmatic intent and potential impact. The Programmatic Panel recommends for funding scientifically sound applications that best meet the program's interests and goals. Upon approval of funding recommendations and completed negotiations, the CDMRP funds research awards. The CDMRP program team provides full life-cycle support of funded research awards and their outcomes.

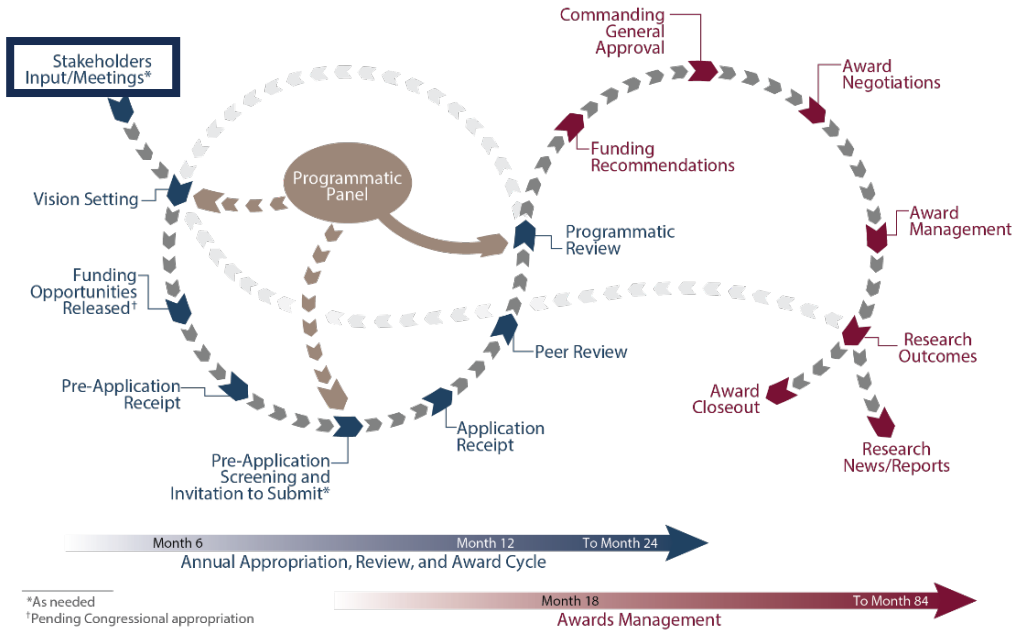


Figure 1. CDMRP Annual Program Cycle

Introduction to the Arthritis Research Program

There are more than 100 types of arthritis and related diseases that can cause inflammation, swelling or pain around one or many joints leading to disability. Arthritis causes significant individual and societal impacts. Arthritis-related health care costs and loss of earnings due to disability from arthritis resulted in an estimated cost of $303.5 billion in 2013.[2] According to the Centers for Disease Control and Prevention, arthritis is the leading cause of disability in the United States and impacts over one-third of Veterans. Osteoarthritis and spondylosis diagnoses in 39,949 and 60,475[3] Service Members, respectively, represented a notable impact to military readiness from 2016-2020. The National Health Interview Survey conducted during 2019-2021

[2] Murphy LB, Cisternas, MG, Pasta, DJ, et al. 2018. Medical Expenditures and Earnings Losses Among US Adults with Arthritis in 2013. *Arthritis Care & Research* 70(6):869-876.
[3] Update: Osteoarthritis and Spondylosis, Active Component, U.S. Armed Forces, 2016-2020. December 1, 2021.

estimated that approximately 53.2 million adults received some type of arthritis diagnosis. This number does not include juvenile forms of arthritis or individuals without a formal diagnosis from their doctor. An additional 220,000 children less than 18 years old received an arthritis diagnosis as reported by parents in a National Survey of Children's Health between 2017-2021. Furthermore, multiple comorbidities such as chronic obstructive lung disease, dementia, stroke, heart disease, cancer and diabetes are highly prevalent with arthritis.[4] The model for managing arthritis associated chronic pain accounted for over half of individuals receiving at least one opioid prescription in 2015.

The CDMRP has historically funded arthritis research under five programs, as listed below. No single CDMRP program received appropriations to specifically and solely support arthritis research until recently. Previously funded projects specifically addressing arthritis from FY18-FY23 represent a $50.5M investment:

- Tick-Borne Disease Research Program, 1 award – $0.4M
- Chronic Pain Management Research Program, 3 awards – $2.8M
- Joint Warfighter Medical Research Program, 1 award – $2.6M
- Lupus Research Program, 1 award – $0.8M
- Peer Reviewed Medical Research Program, 41 awards – $44.0M

The Further Consolidated Appropriations Act, 2024, initiated a Peer Reviewed Arthritis Research Program, ATRP, with a $10.0M appropriation. The CDMRP will manage the FY24 ATRP according to congressional intent using a competitive selection and peer review process. The program acknowledges Congress' concern about the detrimental impact of arthritis on Service Members and their retention in the military and will support research "on all forms of arthritis including osteoarthritis, post-traumatic arthritis and rheumatoid arthritis." All CDMRP-funded research must be relevant to Service Members, their Families, Veterans and/or the American public.[5]

Moment of Silence

Each CDMRP meeting begins with a Moment of Silence to remind participants of their purpose and to set the intention for the day's discussion. Mr. Steve O'Keeffe provided a Moment of Silence at the FY24 ATRP stakeholders meeting to reflect on the impact that arthritis has had on patients, their families and their caregivers. He detailed his personal arthritis journey from diagnosis through the various treatment avenues he has pursued and the founding of the organization, Angry@Arthritis. O'Keeffe also reviewed the current clinical trials being conducted and emphasized the need for better therapeutics in the field. At the conclusion of his presentation, O'Keeffe requested everyone reflect on those who are living with or are affected by arthritis.

[4] Fallon EA. 2023. Prevalence of Diagnosed Arthritis - United States, 2019-2021. *Morbidity and Mortality Weekly Report* 72(41):1101-1107. https://www.cdc.gov/mmwr/volumes/72/wr/mm7241a1.htm?s_cid=mm7241a1_w#T1_down
[5] Retrieved from: https://www.congress.gov/118/crpt/hrpt121/CRPT-118hrpt121.pdf

FY24 ATRP Stakeholders Meeting

Pre-Meeting Request for Information: Results

In response to the FY24 congressional appropriation, the ATRP released an RFI in the system for award management website, SAM.gov, from April 15-28, 2024, and broadly disseminated the availability of the request via email to subscribers of program communications from several relevant CDMRP programs and other interested parties. The ATRP released the survey in advance of the stakeholders meeting to help gather a wide breadth of stakeholder inputs. The ATRP received, tabulated, and categorized a total of 341 responses. The final results are contained within the following pages.

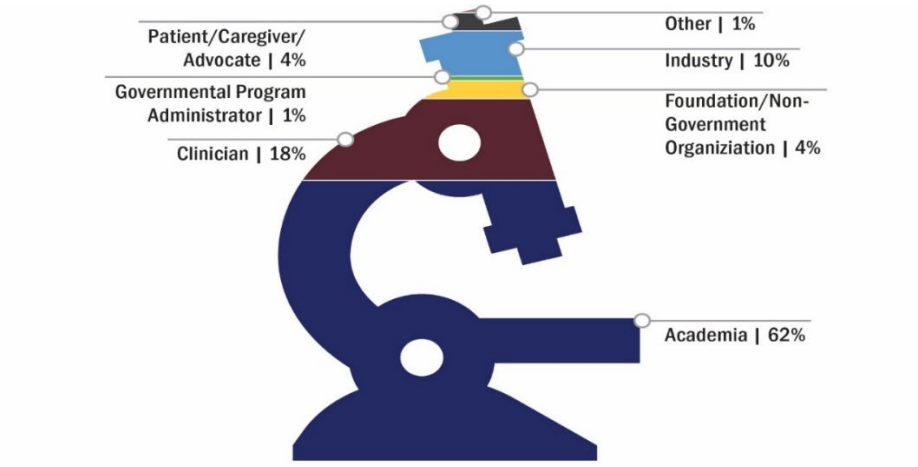


Figure 2. Analysis of the RFI Respondents' Roles Within the Arthritis Community

A total of 341 participants completed the survey. Individuals could identify with more than one role within the arthritis community; 276 respondents identified as having a role specifically in academia and 82 respondents identified as a clinician.

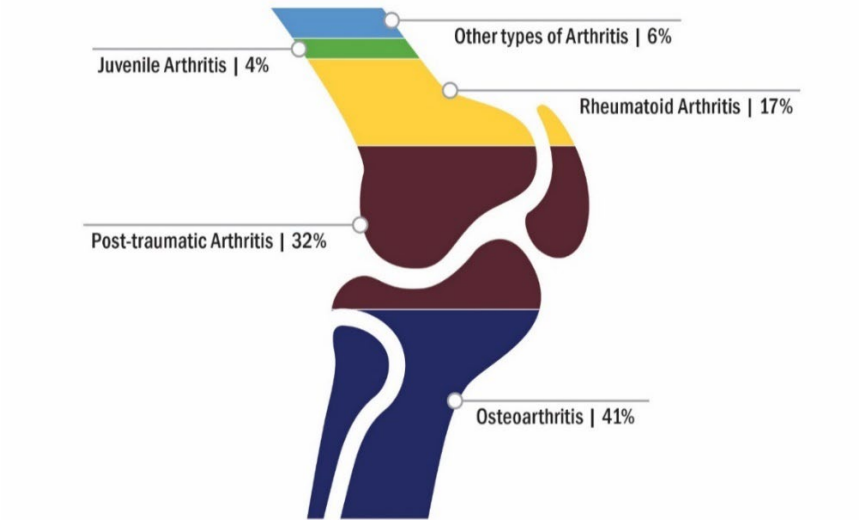


Figure 3. Analysis of the Primary Area of Expertise for the RFI Respondents

A total of 341 participants completed the survey. Individuals could select more than one area of expertise; 212 respondents identified as having expertise in osteoarthritis, and 169 respondents identified as having expertise in post-traumatic arthritis.

Research Areas Requiring Additional Investment

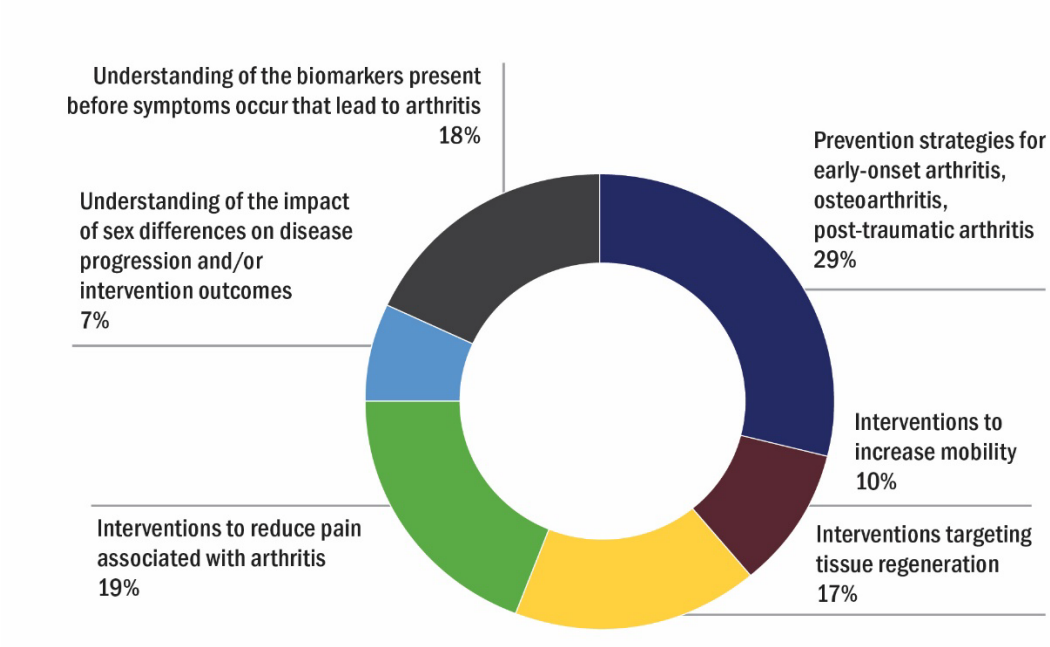


Figure 4. Research Areas Requiring Additional Investment

A total of 341 respondents provided answers for this question, represented in the pie chart above.

Suggested Areas for "Improving Understanding and Prevention for Arthritis"

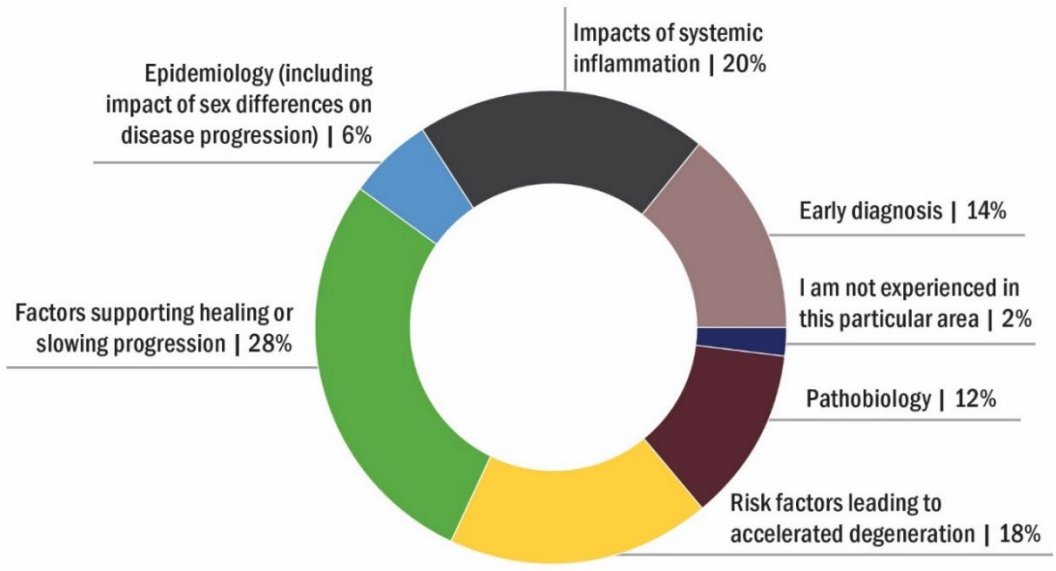


Figure 5. Research Topics That Focused on "Improving Understanding and Prevention for Arthritis" That Require Additional Investment

A total of 341 respondents provided answers for this question, represented in the pie chart above; 14 respondents noted not being experienced in this field.

Suggested Areas for "Treatment Options for Arthritis"

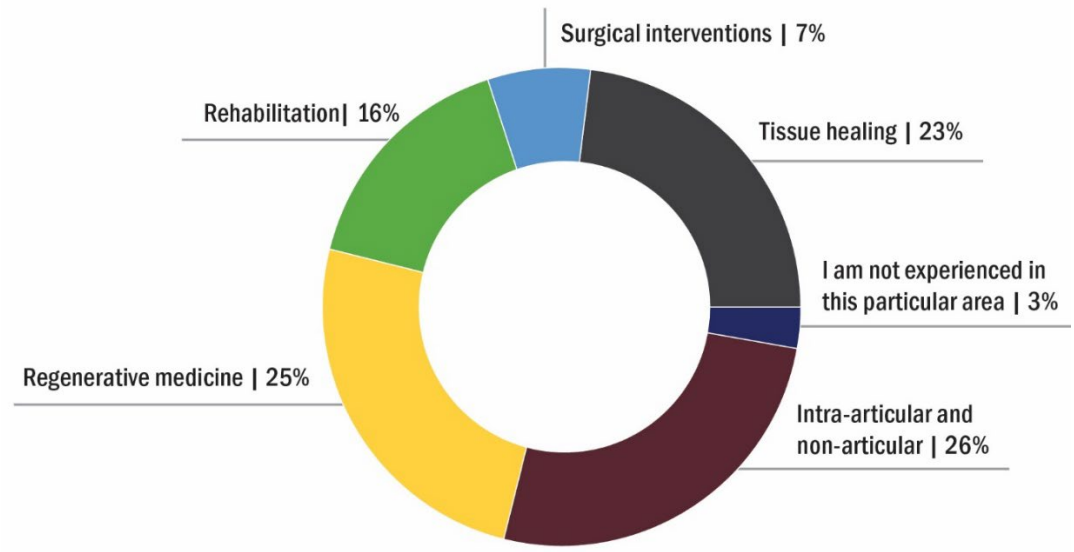


Figure 6. Research Topics That Focused on "Treatment Options for Arthritis" That Require Additional Investment

A total of 341 respondents provided answers for this question, represented in the pie chart above; 18 respondents noted not being experienced in this field.

Suggested Areas for "Improving Outcomes for Arthritis"

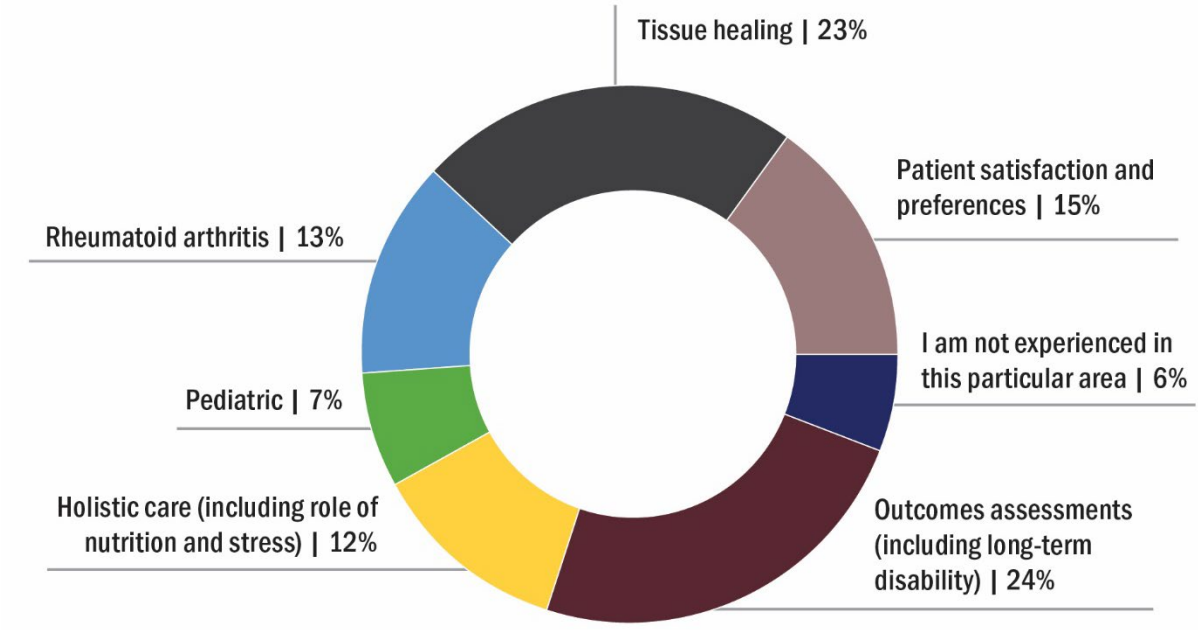
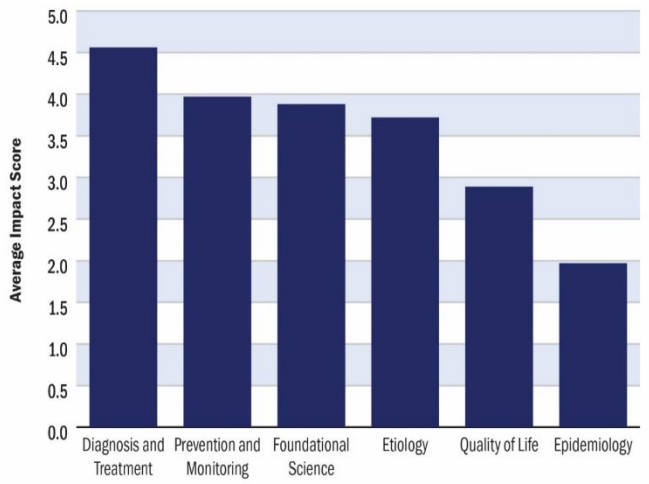


Figure 7. Research Topics That Focused on "Improving Outcomes for Arthritis" That Require Additional Investment

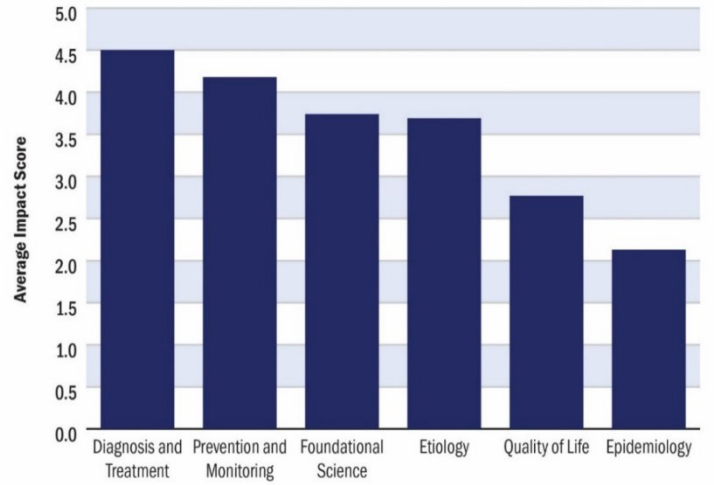
A total of 341 respondents provided answers for this question, represented in the pie chart above; 35 respondents noted not being experienced in this field.

Areas of Impact Along the Research Continuum for Arthritis Subtype

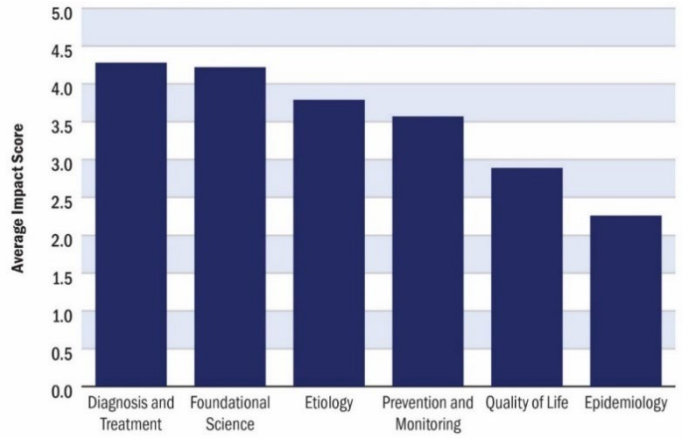
A. Osteoarthritis



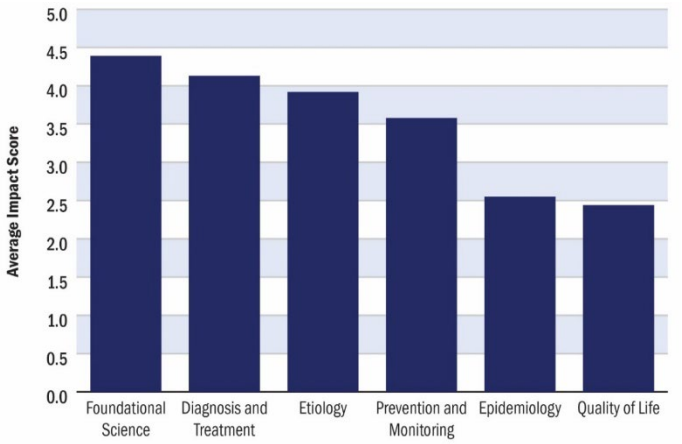
B. Post-Traumatic Arthritis



C. Rheumatoid Arthritis



D. Juvenile Arthritis



E. Other Types of Arthritis

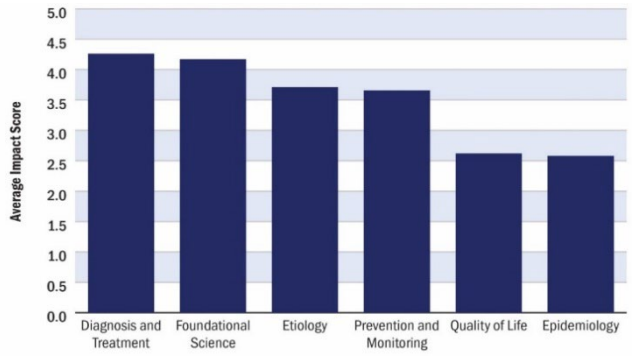


Figure 8. A-E Areas for Impact Along the Research Continuum

For each type of arthritis represented, respondents ranked the areas of the research continuum from most impactful to least impactful. **(A)** For osteoarthritis, diagnosis and treatment was the research category that RFI respondents noted have the most potential impact. A total of 189 respondents answered this question as intended. 102 either left the question blank or did not rank order their preferences as requested. **(B)** For post-traumatic arthritis, diagnosis and treatment, and prevention and monitoring were the two research categories that RFI respondents noted have the most potential impact. A total of 156 respondents answered this question as intended. 97 either left the question blank or did not rank order their preferences as requested. **(C)** For rheumatoid arthritis, diagnosis and treatment, and foundational science were the two research categories that RFI respondents noted have the most potential impact. A total of 111 respondents answered this question as intended. 83 either left the question blank or did not rank order their preferences as requested. **(D)** For juvenile arthritis, foundational science and diagnosis and treatment were the two research categories that were felt to have the most potential impact. A total of 73 respondents answered this question as intended. 172 either left the question blank or did not rank order their preferences as requested. **(E)** For other types of arthritis, diagnosis and treatment and foundational science were the two research categories that RFI respondents noted have the most potential impact. A total of 77 respondents answered this question as intended. 162 either left the question blank or did not rank order their preferences as requested.

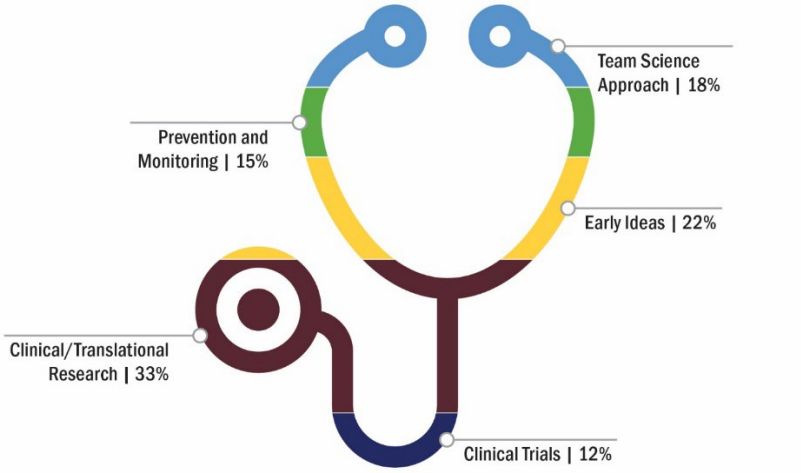


Figure 9. Analysis of the Types of Studies That Should Be Considered for Additional Investments, Across All Arthritis Types

Respondents identified clinical/translational types of research as the main priority for all types of arthritis: osteoarthritis, juvenile arthritis, rheumatoid arthritis, post-traumatic and other types of arthritis research. Respondents identified clinical trials as the lowest priority across all types of arthritis. RFI respondents answered a series of four questions asking which type of research was most important according to type of arthritis; their responses are shown in the figure above.

Objectives

Purpose

The stakeholders meeting provides an opportunity to engage arthritis researchers, clinicians and military experts, as well as those living with arthritis, in an open-dialogue forum to (1) identify knowledge and capability gaps to help inform future arthritis research funding discussions, (2) identify the most impactful areas within the research continuum for additional arthritis research funding support and (3) discuss barriers to the implementation of interventions to reduce the burden of arthritis, particularly as they relate to the detrimental impact of arthritis on readiness and retention of Service Members.

Participants

The program invited 39 representatives from arthritis consumer organizations, academia, clinical care, government institutions, industry and the public who responded to the pre-meeting RFI to the stakeholders meeting to share broad perspectives on which research initiatives could have the greatest potential to support a meaningful impact to clinical care and patient outcomes.

Outcomes

- A prioritized list of research gaps for each type of arthritis – osteoarthritis, post-traumatic arthritis, rheumatoid arthritis, juvenile arthritis and other types of arthritis – to help inform programmatic direction and future funding opportunities offered by the Arthritis Research Program

Summary of Breakout Sessions

After reviewing the pre-meeting survey results and the current arthritis funding landscape, participants discussed specific topic areas in five concurrent breakout sessions. The topic areas for discussion included osteoarthritis, juvenile arthritis, rheumatoid arthritis, post-traumatic arthritis and other types of arthritis. The program sorted participants into breakout groups based on their reported areas of expertise and informed them that the recommendations provided to the program are non-decisional. Each breakout group identified and ranked five primary research gaps for future consideration by the ATRP. The stakeholders then assigned the stage of science (e.g., preclinical, clinical, or translational) for each of the top five gaps. Breakout groups also had the option to provide additional gaps and/or general comments for consideration by the program. The Programmatic Panel will also receive the additional comments provided by the stakeholders when they meet to develop the program's vision and mission, focus areas and award mechanisms, and investment strategy.

The following outlines the top research gaps as identified and prioritized by each breakout group.

a. Osteoarthritis (Breakout lead: Jennifer Elisseeff, Ph.D.)

   Primary Gaps:

   1. New treatment modalities including combination therapies that target multiple processes (systemic and local: immune, cartilage, synovium). *[Stage of Science: preclinical, clinical and translational]*
   2. Gaps in understanding related to fundamental/clinical mechanisms to define early OA including developing new models, defining early OA diagnostics and disease classification related to therapeutic impact, and the impact of genetics, environment (diet, stress), function, aging, and sex and race differences on disease phenotype and therapeutics. *[Stage of Science: preclinical, clinical and translational]*
   3. Computational and systems approaches to discovery, therapeutic identification and clinical trials as they relate to systemic and complex joint interactions and combination therapies. *[Stage of Science: preclinical, clinical and translational]*
   4. Translating veterinary and large animal model work into clinical trials that may involve commercialization, public and private partnerships, and addressing gaps in clinical trial design related to biomarkers (including surrogate markers for joint

homeostasis and regeneration) for pain and function. *[Stage of Science: preclinical, clinical and translational]*

5. Implementation gaps including addressing barriers related to dissemination and uptake of interventions by providers and patients and engagement of the mainstream population. *[Stage of Science: clinical and translational]*

b. Post-Traumatic Arthritis, PTOA, (Breakout lead: Cale Jacobs, Ph.D.)

Primary Gaps:

1. Materiel or knowledge products for PTOA preventative management. *[Stage of Science: translational]*
2. Develop biochemical, nonbiochemical and/or computational biomarkers of PTOA development or progression. *[Stage of Science: translational]*
3. Identifying phenotypes more/less likely to develop PTOA or PTOA progression including but not limited to anatomical, biological, sex, morphology, injury characteristics, biomechanics, omics and/or psychosocial factors, lifestyle factors. *[Stage of Science: translational]*
4. Development and validation of models that are representative of the complex, multifactorial nature of PTOA, including but not limited to, injury pattern, severity of disease, medical comorbidities, psychosocial stresses, lifestyle factors. *[Stage of Science: preclinical]*
5. Materiel or knowledge products for PTOA treatment. *[Stage of Science: translational]*

c. Rheumatoid Arthritis (Breakout lead: Jennifer Barton, M.D., M.C.R.)

Primary Gaps:

1. Develop and/or evaluate comprehensive and integrative approaches for care for people with rheumatoid arthritis, with a focus on whole-person outcomes (vocational, functional, comorbidities and reproductive health). *[Stage of Science: clinical]*
2. Advance novel, high-impact concepts to preclinical status for targeted, personalized treatment of rheumatoid arthritis. *[Stage of Science: preclinical and clinical]*
3. Develop novel health care delivery strategies and novel diagnostic tools to facilitate early diagnosis and treatment. *[Stage of Science: preclinical and clinical]*
4. Describe and understand long-term outcomes, access to care and variation in treatment among older adults and other special populations with rheumatoid arthritis (by residence [urban vs. rural], sex variation, and racial and ethnic minorities). *[Stage of Science: clinical]*
5. Leverage large and complementary data sources and high-dimensional/artificial intelligence analytic approaches to evaluate novel risk factors and redefine known risk factors for rheumatoid arthritis. *[Stage of Science: preclinical and clinical]*

d. Juvenile Arthritis (Breakout lead: Catherine Poholek, M.D., Ph.D.)

Primary Gaps:

1. New treatment modalities informed by mechanistic understanding of arthritis. *[Stage of Science: preclinical and clinical]*
2. Endotyping JA including biomarkers and imaging modalities. *[Stage of Science: clinical and translational]*
3. Targeted preclinical studies that are specific for JA including model development. *[Stage of Science: preclinical]*
4. Understanding pain and its management in JA. *[Stage of Science: preclinical and clinical]*
5. Objective clinical endpoints including biomarkers, imaging and surrogate endpoints. *[Stage of Science: clinical]*

e. Other Types of Arthritis (Breakout lead: Judy Smith, M.D., Ph.D.)

Primary Gaps:

1. Identifying mechanisms associated with therapeutic ceiling in people with lack of therapeutic response including understanding noninflammatory mechanisms of pain. *[Stage of Science: preclinical and translational]*
2. Identifying predictors of developing inflammatory arthritis and inflammatory arthritis subtypes (including spondyloarthritis, psoriatic arthritis, crystal arthropathies, checkpoint inhibitor arthritis, autoinflammatory arthritis, undifferentiated arthritis). *[Stage of Science: preclinical and translational]*
3. Predictive biomarkers for better identification of rational/appropriate treatments and precision medicine. *[Stage of Science: clinical and translational]*
4. Research into novel strategies to identify treatment targets, optimize drug delivery and reduce off-target effects. *[Stage of Science: preclinical and translational]*
5. Understanding potential contributing factors to inflammatory arthritis such as microbiome, nutrition and diet. *[Stage of Science: preclinical, clinical and translational]*

Appendix 1: Meeting Attendees

Stakeholders

Breakout Group 1: Osteoarthritis

Dr. Jennifer Elisseeff (Breakout Lead)	Johns Hopkins University
Ms. Jacqueline Alikhaani	Patient Centered Outcomes Research Institute
Dr. Tamara Bush	Michigan State University
Dr. Jessica Gilbertie	Virginia Polytechnic Institute and State University
Dr. Michelle McLeod	Arthritis Foundation
Mr. Steve O'Keeffe	Angry@Arthritis
Dr. Robert Redmond	Massachusetts General Hospital
Dr. Ross Uhrich	Advanced Research Projects Agency for Health
Dr. Anna Woodbury	Emory University and Atlanta Veterans Affairs (VA) Medical Center
Dr. Chunfeng Zhao	Mayo Clinic Rochester
Dr. Xincheng Zheng	National Institutes of Arthritis and Musculoskeletal Skin Diseases

Breakout Group 2: Post-Traumatic Arthritis

Dr. Cale Jacobs (Breakout Lead)	Brigham and Women's Hospital
Dr. Kevin Baker	Henry Ford Health System
Dr. Alex Bennett	Defence Medical Services, United Kingdom
Dr. Jon Dickens	Duke University and Sparta Biomedical Incorporated
Dr. Prakash Jayabalan	Shirley Ryan AbilityLab
Dr. Karen Lyons	University of California, Los Angeles
Dr. Tim Mauntel	Defense Health Agency
Dr. Michael Valerio	Uniformed Services University of the Health Sciences

Breakout Group 3: Rheumatoid Arthritis

Dr. Jennifer Barton (Breakout Lead)	VA Portland Health Care System
Dr. Bryant England	University of Nebraska Medical Center
Ms. Shannon Garrett	Arthritis Foundation
Ms. Sydnie McConnell	Arthritis Foundation
Dr. Kamal Moudgil	University of Maryland School of Medicine, Baltimore
Dr. Sadiq Umar	University of Illinois, Chicago
Dr. Charles Washabaugh	National Institute of Arthritis and Musculoskeletal Skin Diseases
Dr. Katherine Wysham	VA Puget Sound Health Care System

Breakout Group 4: Juvenile Arthritis

Dr. Catherine Poholek (Breakout Lead)	University of Pittsburgh
Dr. Gregorio Cortes-Maisonet	GCM Medical Group, Puerto Rico
Dr. Matthew Fisher	North Carolina State University and University of North Carolina, Chapel Hill
Dr. Gautam Ghatnekar	Regranion, LLC
Dr. Jeffrey Hubbell	University of Chicago
Dr. Kristen Mueller	Arthritis Foundation

Breakout Group 5: Other Types of Arthritis

Dr. Judy Smith (Breakout Lead)	University of Wisconsin, Madison
Dr. Anne Bass	Hospital for Special Surgery/Weill Cornell Medicine
Dr. Edward Botchwey	Georgia Institute of Technology
Dr. Khaled Elsaid	Chapman University
Dr. Samuel Pope	University of Illinois, Chicago
Ms. Tiffany Westrich-Robertson	AiArthritis (International Foundation for Autoimmune and Autoinflammatory Arthritis)

The meeting was also attended by government observers from the CDMRP and U.S. Army Medical Research Acquisition Activity, as well as the Leidos contractors supporting the meeting and its proceedings.