The Journal of Rheumatology 2024;51:1226–8
doi:10.3899/jrheum.2024-0933
First Release October 24 2024

The Journal of Rheumatology

Prologue: Spondyloarthritis Unmet Research Needs Conference IV

Robert A. Colbert[1], Ellen Carroll[2], Maureen Dubreuil[3], Lianne S. Gensler[4], Nigil Haroon[5], Richard Howard[2], Alexis R. Ogdie[6], Cassie Shafer[2], Pamela F. Weiss[7], and Kristine A. Kuhn[8]

ABSTRACT. The Spondylitis Association of America (SAA) and the National Institute of Arthritis, Musculoskeletal and Skin Diseases (NIAMS) convened a conference on the campus of the National Institutes of Health (NIH) on September 28 and 29, 2023, to identify unmet needs in spondyloarthritis (SpA) research. The conference featured presentations by experts in areas of disease endotypes, pain, innovative imaging in SpA, health disparities in rheumatic diseases, and therapeutics. Members of the conference planning committee moderated the sessions and led the development of manuscripts summarizing recommendations to address unmet research needs. Early career investigators were invited to submit abstracts, which were presented at a networking session during the conference. Here, we highlight each of the sessions comprising the conference in the form of manuscripts published together as a conference summary.

Key Indexing Terms: endotypes, health disparities, medical imaging, pain, spondyloarthritis, therapeutics

The Spondylitis Association of America (SAA; Box 1) and the National Institute of Arthritis, Musculoskeletal and Skin Diseases (NIAMS) cosponsored a conference to identify unmet needs in several key areas of spondyloarthritis (SpA) research. The conference was held on September 28 and 29, 2023, on the National Institutes of Health (NIH) campus in Bethesda, Maryland. Prior to the meeting, a planning committee consisting of several leaders in adult and pediatric SpA research, along with SAA leadership (Box 2), met regularly to identify important areas in which there are significant knowledge gaps (Box 3). Internationally recognized speakers with expertise in each of these areas, from within and outside the SpA research community, were invited to give presentations at the conference. Leading up to the conference, members of the planning committee worked closely with speakers in each area to coordinate and focus presentations, and then served as session moderators. Each moderator delivered a

Box 1. SAA overview.

> The SAA is a nonprofit organization whose mission is to be a leader in the quest to cure ankylosing spondylitis and related diseases, and to empower those affected with SpA to live their lives to the fullest. The 4 pillars of the SAA's mission are research, education, advocacy, and support.
>
> The SAA was founded in 1983 and has become the face, voice, and leading nationwide nonprofit organization educating, empowering, and advocating for people living with SpA.
>
> The SAA works extensively with patients, the medical community, and partners, to provide information and resources to help people affected by SpA, and to promote and support research toward better understanding the disease and to find a cure (https://spondylitis.org).

SAA: Spondylitis Association of America; SpA: spondyloarthritis.

As part of the supplement series Spondyloarthritis Unmet Research Needs Conference IV, this report was reviewed internally and approved by the Guest Editors for integrity, accuracy, and consistency with scientific and ethical standards.

Financial support was provided by the Spondylitis Association of America and the National Institute of Arthritis, Musculoskeletal and Skin Diseases, Intramural Research Program.

[1]R.A. Colbert, MD, PhD, National Institute of Arthritis, Musculoskeletal and Skin Diseases, Bethesda, Maryland, USA; [2]E. Carroll, JD, R. Howard, BA, C. Shafer, BS, Spondylitis Association of America, Encino, California, USA; [3]M. Dubreuil, MD, MSc, Boston University School of Medicine, Boston, Massachusetts, USA; [4]L.S. Gensler, MD, Department of Medicine, Division of Rheumatology, University of California, San Francisco, California, USA; [5]N. Haroon, MD, PhD, MBA, University of Toronto, Toronto, Ontario, Canada; [6]A.R. Ogdie, MD, MSCE, Perelman School of Medicine at the University of Pennsylvania, Philadelphia, Pennsylvania, USA; [7]P.F. Weiss, MD, MSCE, Children's Hospital of Philadelphia, Philadelphia, Pennsylvania, USA; [8]K.A. Kuhn, MD, PhD, University of Colorado Anschutz Medical Campus, Aurora, Colorado, USA.

LSG has received research grant support from UCB; honoraria or consultation fees from Eli Lilly, Janssen, Novartis, Pfizer, and UCB; and is a member of the ASAS executive committee. ARO has consulted/been on the advisory boards for AbbVie, Amgen, BMS, Celgene, Corrona, Gilead, Janssen, Lilly, Novartis, Pfizer, UCB, and Takeda; and received grants from AbbVie, Pfizer, and Novartis to University of Pennsylvania, and Amgen to Forward/NDB. PFW has received grants from the NIH, PCORI, and the Spondylitis Association of America; has worked as a paid consultant for Pfizer and Novartis; and is a site investigator for an AbbVie clinical trial.

The remaining authors declare no conflicts of interest relevant to this article.

This paper does not require institutional review board approval.

Address correspondence to Dr. R.A. Colbert, National Institute of Arthritis, Musculoskeletal and Skin Diseases, 10 Center Drive, Bethesda, MD 20892, USA. Email: colbertr@mail.nih.gov.

Accepted for publication September 11, 2024.

Box 2. Spondyloarthritis Unmet Research Needs Conference IV planning committee and participating SAA staff.

Robert A. Colbert, MD, PhD (Co-Chair)
Kristine A. Kuhn, MD, PhD (Co-Chair)
Hon. Ellen Carroll, JD (ret.) (Member)
Maureen Dubreuil, MD, MSc (Member)
Lianne Gensler, MD (Member)
Nigil Haroon, MD, PhD, MBA (Member)
Alexis Ogdie, MD, MSCE (Member)
Pamela F. Weiss, MD, MSCE (Member)
Richard Howard (Chief Mission Delivery Officer, SAA)
Cassie Shafer (Chief Executive Officer, SAA)
Lisa Spiegel (Conference Planner, SAA)

Ret: retired; SAA: Spondylitis Association of America.

short presentation at the beginning of the session to introduce the topic and provide background information. Early-stage investigators engaged in SpA research were invited to submit abstracts and were sponsored to attend the conference, where they had the opportunity to present their work in a networking poster session.

In the first session, which was moderated by conference co-chair Dr. Kristine Kuhn, Drs. Kevin Deane, Laura Donlin, and Christopher Ritchlin discussed endotypes.[1] Endotypes are subtypes of health conditions that have distinct pathophysiologic mechanisms and/or outcomes, and thus can be useful to refine treatment strategies if distinct pathways amenable to targeting are identified. They summarized lessons learned from rheumatoid arthritis (RA) and psoriatic arthritis (PsA). In RA, research has been aided significantly by the Accelerating Medicines Partnership (AMP) consortium and the focus on better understanding the biology of synovial tissue and the infiltrating cells. Similar approaches are now being applied to PsA by the Elucidating the Landscape of Immunophenotypes in Psoriasis and Psoriatic Arthritis (ELLIPSS) team in the AMP–Autoimmune and Immune-Mediated Diseases (AMP-AIM) program. Speakers emphasized that a similar effort in axial SpA (axSpA), which is an even greater challenge owing to the relative inaccessibility of vertebral and sacroiliac tissue, is a key unmet need in axSpA research.

Dr. Alexis Ogdie moderated the session on understanding and managing chronic pain. Drs. Yvonne Lee and Anne-Marie Malfait discussed the pathophysiology of pain and pain sensitization, and provided examples of mechanistic studies that have been performed in RA and osteoarthritis (OA).[2] Chronic pain is a major contributor to disease burden in both axSpA and peripheral SpA. The speakers emphasized the need for a better understanding of how to recognize and manage persistent pain

Box 3. Key questions reflecting significant knowledge gaps for each conference session.

Endotypes
- Are there disease endotypes in SpA? How would we define them?
- How are endotypes currently defined in RA? How helpful are those definitions?
- Are molecular endotypes, currently based on RA synovial characteristics, informative?

Pain
- How do we better address pain in our patients with axSpA?
- How should we treat noninflammatory pain?
- How do we leverage novel insights into pain?

Imaging
- How can we image better? Where are we going next?
- What is tomorrow's path for advancing structural progression research in axSpA?
- Are there innovative imaging techniques that should be applied to SpA for diagnosis? How do we get radiologists trained?
- What role will AI play in the future of SpA imaging?

Biological variables, social constructs, and health disparities
- How do we address a range of disparities in SpA diagnosis, treatment, and research?
- What are the racial disparities in care?
- How can we engage the community in clinical research?
- How can we mitigate disparities in research participation? What lessons can we learn from SLE?
- How can institutional approaches support equity in research?

Therapeutics
- For what aspects of disease are therapeutic advancements most needed? How can we enhance evaluation of both emerging and existing therapies?
- What are emerging therapies, targets, and strategies?
- Should we reconsider trial design?
- Do we have the right outcomes for trials?
- What is the role of complementary medicine and how do we study it?

AI: artificial intelligence; axSpA; axial SpA; RA: rheumatoid arthritis; SpA: spondyloarthritis.

in the absence of systemic or local inflammation (noninflammatory pain). The speakers identified several unanswered questions regarding pain in axSpA and emphasized the need for accurate assessment and management of chronic pain across many forms of systemic inflammatory arthritis. Understanding more about the interactions between the immune system and nervous system is paramount, and identifying patients whose pain is likely to respond to targeted pharmacologic interventions is critical.

The session on imaging was moderated by Dr. Lianne Gensler, with Drs. Denis Poddubnyy, Lennart Jans, and Sharmila Majumdar contributing presentations.[3] Imaging continues to be the most specific biomarker for making a diagnosis of axSpA. Whereas plain radiographs detect damage, computed tomography (CT) is considered the reference standard. However, both involve exposure to potentially damaging ionizing radiation. Magnetic resonance imaging (MRI) is useful for monitoring disease activity and is being used increasingly to monitor structural changes. Several new MRI sequences have been developed, and deep learning techniques are being used to create synthetic CT-like images without ionizing radiation. In addition, low-dose CT imaging is being explored. Artificial intelligence is being used extensively in imaging for protocolization as well as for improving image quality and interpretation.

The session on health disparities was moderated by Dr. Maureen Dubreuil, with speakers including Drs. Elizabeth Ferucci, Hani El-Gabalawy, Sarfaraz Hasni, and Edith Williams.[4] The lack of data on health disparities in SpA was acknowledged. However, there is significant literature on disparities in the recognition and management of back pain, an important component of evaluating and diagnosing SpA. Black Americans are diagnosed less frequently with axSpA, but when diagnosed, the disease is often more active and carries more comorbidities. Although some of this may be due to the overall lower frequency of HLA-B27 in Black individuals, there is a considerable need for more research in this area addressing access to care and biases against diagnosing axSpA in the absence of HLA-B27 and in this population. Dr. El-Gabalawy discussed best practices in engaging underrepresented communities based on his expertise, experience, and research with First Nations people. There is a need to focus on understanding traditional knowledge systems, ensuring community engagement and consent, and fostering reciprocal relationships that include sharing research results and knowledge. Dr. Hasni talked about efforts to mitigate disparities in systemic lupus erythematosus research, starting with efforts to engage underrepresented minorities, individuals with disability, and older patients in clinical trials. These efforts are critical to increase the generalizability and applicability of research results. Dr. Williams discussed institutional approaches to enhancing equity in research, which includes prioritizing efforts to establish and maintain relationships. She emphasized the importance of diversity in research team members as well as in institutional review boards. The session provided a number of proposed strategies to enhance equity in clinical research in SpA.

The final session covered therapeutics and was moderated by Dr. Pamela Weiss. Drs. Laura Coates, Georg Schett, and Chenchen Wang discussed advances in our understanding of pathogenesis, the development and validation of therapeutics, and research into several nonpharmacologic interventions.[5] Reasons for the paradoxical lack of efficacy of interleukin (IL)-23 blockade in axSpA was covered. This lack of efficacy has been particularly surprising given its positive results with psoriasis and PsA, diseases that exhibit overlapping genetic predisposition with axSpA and that are responsive to IL-17 as well as tumor necrosis factor inhibition. Dr. Coates discussed issues related to the inclusion criteria and the design of trials, and comparative effectiveness approaches that would enhance generalizability and provide more practical evidence supporting guideline development. Considerations about the ethics of using placebos were also covered, and whether the outcomes we currently use are the most meaningful. Dr. Wang discussed considerable evidence that has accumulated regarding the use of mind-body therapies, such as tai chi, yoga, and acupuncture.

The articles that follow in this series provide more detail on each conference session and help chart a path to address unmet SpA research needs over the next several years.

PLAIN LANGUAGE SUMMARY

A plain language summary of this article (text or graphical) is included as online supplementary material.

REFERENCES

1. Deane KD, Donlin LT, Ritchlin CT, Kuhn KA. Are there disease endotypes in axial spondyloarthritis and how would we define them? J Rheumatol 2024;51:1229-34.
2. Lee YC, Malfait AM, Ogdie AR. Unmet needs in spondyloarthritis: understanding and managing chronic pain. J Rheumatol 2024;51:1235-40.
3. Gensler LS, Jans L, Majumdar S, Poddubnyy D. Unmet needs in spondyloarthritis: imaging in axial spondyloarthritis. J Rheumatol 2024;51:1241-6.
4. Dubreuil M, Ferucci ED, El-Gabalawy HS, Hasni S, Williams EM. Enhancing equity in clinical research: a multifaceted proposal for spondyloarthritis. J Rheumatol 2024;51:1247-53.
5. Coates L, Schett G, Wang C, Weiss PF. Unmet needs in spondyloarthritis: pathogenesis, clinical trial design, and nonpharmacologic therapy. J Rheumatol 2024;51:1254-8.