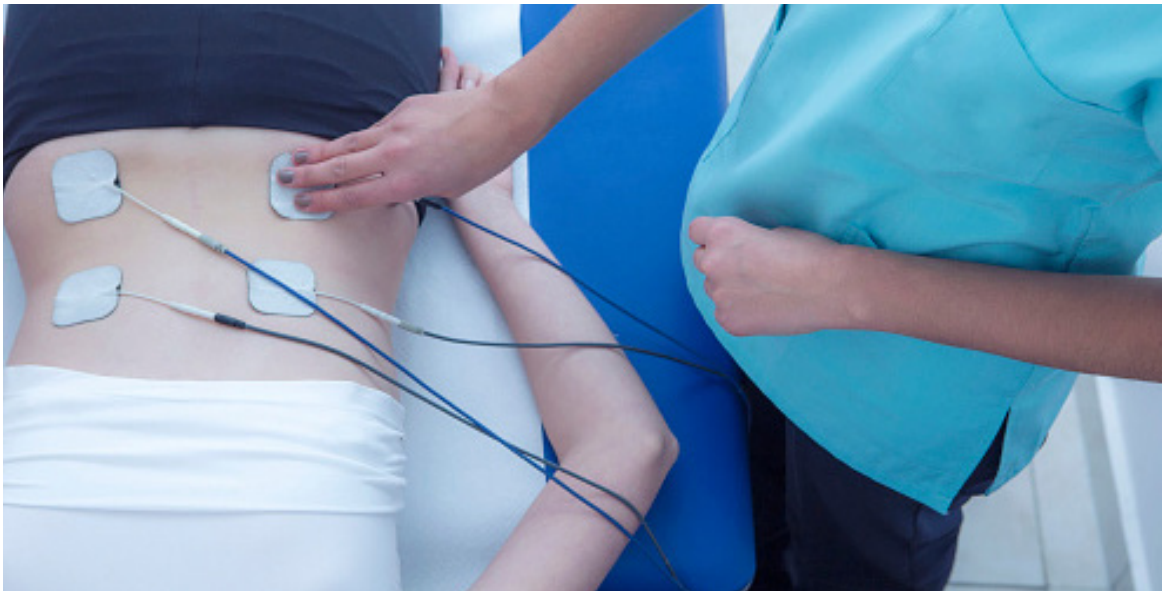
Arthritis Foundation®

JOINT Matters



Rewiring RA Treatment: The Promise of Vagus Nerve Stimulation

There's a growing buzz in the medical community about a new therapeutic option for treating rheumatoid arthritis (RA): vagus nerve stimulation (VNS). The idea of using an electrical impulse to modulate inflammation, once perceived as science fiction, is now a frontier of **bioelectronic medicine**. This field is the culmination of decades of research that have unveiled the intricate connection between the nervous system and the immune system. With the FDA approval of the **SetPoint System vagus nerve stimulator**, we are at a pivotal moment, moving from fundamental mechanisms to the deployment of a device that leverages the inflammatory reflex.

In 2002, Dr. Kevin Tracey first described the inflammatory reflex, a connection by which the brain, via the vagus nerve, can instruct the body on when to stop releasing inflammatory molecules. This discovery revealed that the vagus nerve, a critical conductor of autonomic functions, also acts as a key regulator of our innate immune response. When inflammatory cytokines are detected in the bloodstream, tissues and organs, vagal afferents signal the brain. Efferent vagal fibers are then activated, impacting visceral organs and, indirectly, the spleen. This intricate pathway, known as the cholinergic anti-inflammatory pathway (CAP), ultimately leads to acetylcholine release, which binds to receptors on macrophages, thereby inhibiting potent pro-inflammatory cytokines, such as TNF-α, IL-1β and IL-6. Thus, **the nervous system has an inherent ability to quell inflammation**.

Scientific understanding progressed from this theoretical framework to early clinical investigations. Initial proof-of-concept studies, including one using an implanted Cyberonics VNS device in seven epilepsy patients, demonstrated anti-inflammatory potential. Post-stimulation, a significant decrease in endotoxin-stimulated TNF, IL-6 and IL-1β production was observed in whole-blood samples, validating the inflammatory reflex in vivo. Building on these findings, an **84-day open-label trial**

FEATURED IN THIS STORY:

Diane Horowitz, MD, Northwell Health

in 17 RA patients, also using the Cyberonics VNS device, reported reductions in pro-inflammatory cytokines and improvements in disease activity (DAS28) across cohorts with methotrexate-intolerant, refractory or biologic-refractory RA.

Innovation in VNS methodology has progressed rapidly. Approaches include invasive VNS, involving surgical implantation of a device that delivers electrical pulses directly to the cervical vagus nerve. Non-invasive VNS options include transcutaneous VNS (tVNS), stimulating auricular or cervical branches externally. Emerging methods include focused ultrasound stimulation, targeting organs such as the spleen, and magnetic stimulation, which uses magnetic fields to induce electrical currents. These diverse strategies reflect efforts to optimize VNS delivery for therapeutic efficacy.

This extensive research culminated in the pivotal **RESET-RA study**, a multicenter, randomized, controlled trial evaluating the **SetPoint System** in patients with moderate-to-severe RA refractory to conventional and biologic/targeted synthetic disease-modifying antirheumatic drugs (DMARDs). The trial demonstrated significant efficacy and an acceptable safety profile. The active VNS arm achieved a statistically significant ACR20 response in three months, outperforming the control arm. Improvements were also observed in DAS28-CRP, HAQ-DI and reduced radiographic progression in a subgroup with erosive phenotypes. The control arm, upon crossing over to active stimulation, subsequently exhibited a similar response profile. This clinical success led to the device's FDA approval in July 2025.

At Northwell Health, we recognized this therapy's potential early on. After decades of bioelectronic medicine research, Northwell opened its Center for Bioelectronic Medicine (CBEM) in 2025. Our center is a clinical home for treating patients with bioelectronic medicine therapies, including VNS. We have established a comprehensive program for coordinating the implantation and long-term management of these devices. Our team includes a dedicated patient navigator, specialized rheumatology and neurosurgery consultation services and prior authorization support. This multidisciplinary group supports patients at every step — from initial consultation through long-term device management.

As VNS integrates into clinical practice, its applications will evolve. The FDA approval for VNS in RA, indicated for patients with active disease refractory to one or more b/tsDMARDs, provides guidance. However, the decision to pursue VNS is individualized and requires a detailed discussion between the patient and the physician. VNS can be effectively combined with existing biologic therapies, offering a synergistic approach. Yet VNS is a device, which implies a surgical procedure. Patients must understand the implications of an implantable device and potential device-related adverse events, which were rare and resolved without incident in clinical trials. While its safety profile compares favorably with that of broad immunosuppressants, these considerations remain paramount. Further research will refine its application, including the optimal timing for VNS in the disease course. Expanded use after FDA approval will shed light on adverse effects and benefits as the device is used in a larger patient population.

VNS represents a significant evolution in therapeutic approaches. It leverages the body's intrinsic anti-inflammatory mechanisms to offer a promising option for patients seeking alternatives or adjuncts to traditional pharmacologic therapy. With continued research, patient experience and dedicated bioelectronic medicine programs, we are poised to elucidate the optimal utility of bioelectronic medicine, contributing to improved outcomes for patients living with RA.

The Arthritis Foundation thanks Dr. Diane Horowitz for this editorial.

ADVOCACY UPDATE

Medicaid Work Requirements

The Centers for Medicare & Medicaid Services (CMS) has released guidance to states on Medicaid community engagement (work requirement) exemptions. The guidance requires patients to meet specific diagnostic criteria and demonstrate that they are unable to work because of their condition. It also allows self-attestation only during the first year (2027). Beginning in 2028, additional documentation may create new administrative burdens for both patients and providers. The Arthritis Foundation is working closely with the American College of Rheumatology, the Coalition of State Rheumatology Organizations and other partners to develop arthritis-specific recommendations for CMS and state Medicaid agencies. The goal is to help ensure that people with arthritis who rely on Medicaid can continue to access the care they need.

Arthritis Research Funding

In positive news, the FY27 House Defense Appropriations bill includes continued funding for the Department of Defense (DoD) Arthritis Research Program. This is an important step forward after DoD-funded research programs were cut by more than 50% in the FY26 continuing resolution last spring. Preserving funding for the Arthritis Research Program is a key advocacy priority.

Biosimilars Sustainability Survey

The Arthritis Foundation is partnering with a Biosimilars Consortium on a study examining healthcare provider experiences with biosimilars. The findings will help inform future biosimilar policy. Your perspective is valuable, and we encourage you to complete the **survey** and share your experiences.

Are you ready to make a difference? **Take the first step by visiting the Arthritis Foundation's Action Center**. There, you can find a topic that resonates with you and start advocating for change.

Arthritis Foundation Invests in Trial Readiness Through 2026 TrialLaunch Awards

The Arthritis Foundation is pleased to announce the awardees of the 2026 TrialLaunch program — an initiative to fund smaller studies that help investigators gather patient input and recruitment data to prepare detailed plans for the execution of larger clinical trials.

"TrialLaunch is an investment in the future of osteoarthritis research. By supporting trial readiness and patient engagement, we are helping accelerate the development of studies that have the potential to improve lives," says Steven Taylor, MBA, Arthritis Foundation president and CEO.

Through the TrialLaunch program, the Foundation supports early-stage trials and the development of tools that improve osteoarthritis clinical research, including new technologies, outcome measures and methods. These studies lay the groundwork for well-designed clinical trials ready for future funding from the Arthritis Foundation or other major funders. A marker of success of this pipeline is the Post-Injury Knee Arthritis Severity Outcomes (PIKASO), The Osteoarthritis Prevention Study (TOPS) and Knee Arthroplasty Activity Trial (KArAT) projects. The TrialLaunch program paved the way for these large, definitive studies designed to test whether an intervention can significantly improve outcomes for people with osteoarthritis.

Further, through the TrialLaunch program, the Osteoarthritis Clinical Trials Network (OACTN), a multicenter clinical infrastructure, also prepares for future trials. As an example, PIKASO involves several top arthritis investigators and research institutions, including Mass General Brigham, the Cleveland Clinic, Emory University, the University of Iowa and the University of North Carolina, which are all part of the OACTN. These sites could be recruited for future clinical studies that require similar services or expertise that were provided for PIKASO.

Stage A of TrialLaunch will be to develop the ideas and concepts of the investigating teams through the early steps of project planning and preparation. Upon successful completion of stage A, projects that appear feasible and highly likely to be impactful may be selected for additional Arthritis Foundation funding to complete planning activities in stage B. Then, successful completion of stage B will render the projects eligible for Foundation funding for a larger clinical trial.

The projects funded by the 2026 TrialLaunch program are described below:

Transcutaneous Auricular Vagus Nerve Stimulation for Knee Osteoarthritis Pain (VAGUS-KOA)

Kosaku Aoyagi, PT, PhD, Ohio State University

For many diagnosed with knee OA, pain becomes a constant unwanted companion. Kosaku Aoyagi, PT, PhD, assistant professor at Ohio State University, will investigate transcutaneous auricular vagus nerve stimulation (taVNS) as a novel method to reduce pain in knee OA. In this minimally invasive procedure, a segment of the vagus nerve, which carries impulses from the ear to the part of the brain that influences pain sensitivity and systemic inflammation, is stimulated using a low-intensity electrical current. If effective, taVNS may improve knee OA pain while being potentially low-cost and available for home use.

Recovery Through Transcranial Electrical Stimulation With Home-based Lower-body Strengthening Exercise After Total Knee Arthroplasty (RESHAPE-TKA)

C. Kent Kwoh, MD, University of Arizona

For individuals with severe, end-stage knee arthritis or joint trauma who have not responded to non-surgical treatments, total knee replacement is the final option. Pain after total knee arthroplasty (TKA) can impede lower-body strengthening during physical therapy and compromise the ability to perform daily tasks and activities. C. Kent Kwoh, MD, professor emeritus at the University of Arizona, aims to investigate primary motor cortex-targeted transcranial direct current stimulation (M1-tDCS) as a tool to reduce pain and improve functional outcomes after TKA. This non-invasive brain stimulation technique modulates

central nervous system pain pathways and can potentially prime the motor system to enhance responses to lower-body strengthening exercises.

INulin Supplementation for Pain In peRsons with knEe OsteoArthritis (INSPIRE-OA)

Evelyn Hsieh, MD, PhD, Yale University

Chronic pain and inflammation are hallmark symptoms of OA. Evelyn Hsieh, MD, PhD, associate professor of medicine at Yale University, will test whether inulin, a fermentable, non-digestible prebiotic fiber derived from chicory root, can attenuate metabolic dysfunction and systemic inflammation. Their study will provide a detailed characterization of the effects of inulin on knee pain and the microbiome in cases of chronic knee OA.

The OPTIGAIT Trial: Remotely Delivered Gait Retraining for Medial Knee Osteoarthritis

Scott Uhlrich, PhD, University of Utah

Individuals who inadvertently carry more physical weight and mechanical forces concentrated on the inside compartment of the knee may have faster OA progression. Thus, mitigating medial knee loading by reducing knee adduction is the key target for biomechanical interventions, like unloader braces or surgery. However, most patients and physicians prefer non-surgical treatments, making gait retraining attractive because it is non-surgical and non-pharmacologic, requiring limited clinic visits. Based on biomechanics data, Scott Uhlrich, PhD, assistant professor at the University of Utah, will investigate whether delivering gait training remotely can provide pain relief and slowed cartilage degeneration in people with medial knee OA.

Minimizing early Osteoarthritis symptoms after kNEe cartilage injury Treatment (MONET)

Cale Jacobs, PhD, Mass General Brigham

Patients undergoing surgical or non-surgical cartilage repair are at high risk of developing early OA symptoms. As part of the TrialLaunch program, a multidisciplinary team led by Cale Jacobs, PhD, director of research, Mass General Brigham Center for Sports Performance and Research, will test whether specialized pro-resolving mediator (SPM) supplementation offers a low-cost, minimal side-effect resolution to inflammation and progression to OA in this high-risk group. Specifically, the MONET clinical trial will determine whether a six-month course of SPM supplementation (*LIPINOVA®, Azur Global Nutrition*) reduces the incidence of early OA symptoms two years after cartilage repair, compared with placebo.

Vitamin K Supplementation to Improve Pain and Function in Knee Osteoarthritis: The VIKTOR-Knee Trial

Tuhina Neogi, MD, PhD, Boston University

Almost half of adults in the U.S. use vitamins as the preferred supplement to maintain health or prevent disease. Vitamin K is essential for activating the Gla protein (MGP) and other Gla-containing proteins that are involved in cartilage and bone health. Furthermore, low vitamin K levels have been associated with more severe symptoms in OA. Tuhina Neogi, MD, PhD, professor of medicine at Boston University, will test whether Vitamin K can improve cartilage health and reduce inflammation associated with knee OA.

Predicting Rheumatoid Arthritis Before Symptoms Begin

Patients at risk for **rheumatoid arthritis (RA)** often find themselves in a grey zone, where their bloodwork indicates they are at risk for RA but cannot predict for certain whether they will get a clinical diagnosis. The presence of certain antibodies puts these patients at a 20% to 70% chance of developing clinical RA within two to five years, which is far from a definitive prognosis.

Recognizing this gap, the Arthritis Foundation has awarded a 2025 **RA Research Program** grant to Marla Glass, PhD, a scientist at the Allen Institute in Seattle. With this grant, she will investigate how B cells evolve to become pathogenic, so some patients transition from preclinical (at-risk) RA to clinical RA.

"When it comes to individuals who are at risk, there have not been very many longitudinal studies performed where we have tracked features of their immune system over time. And, particularly amongst those individuals that convert to clinical RA, we have very limited information," says Glass. "A major goal I have for my research is to essentially help us better understand a person's risk for developing clinical RA and how we could think about therapeutic intervention for prevention of disease before it starts."

The Role of B Cells in RA Development

Before people start showing symptoms of RA, the immune system begins to display signs of dysfunction by producing autoantibodies, particularly those for **cyclic citrullinated peptides (ACPA) and rheumatoid factors (RF)**.

Normally, antibody-producing B cells undergo genetic changes to create highly specific receptors that can adapt to encounter new, unknown pathogens. At times, this adaptation can lead to either greater binding of B-cell receptors to self-proteins or increased inflammation. One or both mutations may be why some people develop RA.

Further, different types of B cells may contribute to the conversion from at-risk to clinical RA. Memory B cells, for example, are present in large numbers before (preclinical) and during (clinical) the onset of RA. At-risk individuals also have large populations of naive B cells that have not yet encountered their specific antigen. In addition, B cells prime T cells that are known to be the central drivers of inflammation and joint destruction in RA. In RA, it is possible that B and T cells can set up a feedback loop in which T cells encourage activation of B cells — and B cells, in turn, encourage activation of T cells, Glass notes.

What This Research Could Mean for Patients

For her Arthritis Foundation-funded research, Glass will analyze blood samples from people at risk for RA, some of whom eventually developed the disease. Using advanced molecular tools, like single-cell multi-omic profiling that can measure RNA and protein within individual cells, she will study how individual B cells behave and evolve in ACPA-positive individuals. In the future, she says, this work may improve risk assessment, identify new therapeutic targets and inform strategies to prevent disease before joint damage occurs.

"I'm thrilled to have gotten support for my research study from the Arthritis Foundation," says Glass. "I think it's going to enable us to take our research to the next level and really provide some deep insight into the preclinical phase of RA. I'm very appreciative of the funding and to also be a part of this Arthritis Foundation network now."

FEATURED IN THIS STORY:

Marla Glass, PhD, Allen Institute

Announcements

2026 Clinical Rheumatology Fellowship Awards

The rheumatology workforce shortage continues to adversely affect care for patients with arthritis, and this deficit is expected to grow in the coming years. To augment the rheumatology workforce, the Arthritis Foundation, through our Clinical Rheumatology Fellowships program, has awarded grants to support rheumatology fellowship programs at the Children's Hospital of Philadelphia, Ann & Robert H. Lurie Children's Hospital of Chicago and the University of California, San Francisco. **Read full news article**.

New Cohort of Foot and Ankle Arthritis Development Program

The **American Orthopaedic Foot & Ankle Society (AOFAS)** and the **Arthritis Foundation** are proud to announce the second cohort of participants for the **Foot and Ankle Arthritis Development Program**. This initiative offers medical students and residents a unique opportunity to gain advanced training, mentoring and exposure to foot and ankle arthritis care. **Read full news article**.

2026 Rheumatology Workforce Enrichment Grants

The workforce shortage in rheumatology remains a critical challenge. By 2030, the number of adult rheumatologists is expected to decline by 31%, leaving them unable to meet the demand, which is predicted to exceed supply by 138%. With nearly 60 million adults and children in the U.S. diagnosed with arthritis, more specialists must be trained so they can strengthen the workforce. This year's funding is the second part of a two-phase award and has been awarded to Candace Feldman, MD, MPH, ScD, of Brigham and Women's Hospital and assistant professor of medicine at Harvard Medical School, and James Jarvis, MD, professor of pediatrics at the University of Washington. **Read full news article**.

2026 CARRA-Arthritis Foundation Grant Program Awards

The Childhood Arthritis and Rheumatology Research Alliance (CARRA) and the Arthritis Foundation have announced grants — totaling nearly $2 million — to support physician-led research in pediatric rheumatology. CARRA-Arthritis Foundation Grant Program awards for 2026 will fund research in juvenile idiopathic arthritis (JIA), pediatric lupus, juvenile dermatomyositis, childhood vasculitis, autoimmune brain disease and more. There were two types of grants awarded this year — the Advancing Biosample Collection Award and the Mentored Career Development Award. **Read full news article**.

Leading the Way in Ease of Use Design

The Arthritis Foundation's Ease of Use℠ certification program certifies products and packaging that have been independently tested and proven to be easier to use for people with arthritis and others with chronic pain. As the Foundation champions life-changing resources for people living with arthritis and chronic pain, we collaborate with both consumer and healthcare companies to design and bring products and packaging to market that are easier to use. In the consumer arena, we have certified items as small as a tube of mascara or lipstick to larger items like walk-in tubs designed to make bathing easier. In the healthcare arena, certifications range from medical devices, bottles and caps and even pills with indentations, making them easier to pick up and hold. Companies that are bringing accessible design into their design process are innovatively thinking about many areas — weight, linear force, rotational force, action fatigue, joint placement, grip span and strength, sharp edges and whether tools, such as scissors, are required to open packaging. These considerations are important when thinking about how they impact someone's day-to-day activities. Ease of Use Certified products are available in retail stores and online. Certified medical devices, bottles and caps associated with various treatments are available through prescription. See products and packaging with **Ease of Use certification**.

Partners for Patients

As a healthcare provider, you're invited to join Partners for Patients, a program that connects you with patient education resources and a supportive community through the Arthritis Foundation to help improve patient care and outcomes. By becoming a partner, you'll gain access to tools that connect your patients with vital Arthritis Foundation services and support, fostering stronger collaboration and better results. Once you join, we'll highlight our partnership with you in both patient and medical communities and keep you informed with the latest updates and advancements in arthritis research and care. **Learn more about the Partners for Patients program**.

Meetings and Symposia

2026 Arthritis Foundation Osteoarthritis Clinical Trials Breakfast, Orlando, Florida, Nov. 8, 2026, 8:00 – 9:30 a.m. ET

Join the Arthritis Foundation Science Team during ACR Convergence for a complimentary breakfast and discussion at The Capital Grille focused on the future of osteoarthritis clinical research and the Foundation's TrialLaunch program. This gathering will highlight emerging innovations in OA trials, provide insight into upcoming funding opportunities and foster collaboration across the scientific community working to accelerate progress for patients. **Register now**.

COMMUNITY IN ACTION

Make an impact! Join the Arthritis Foundation's signature events happening at a location near you.

California Coast Classic Bike Tour, presented by Amgen, is a scenic bike ride that takes place over eight days and covers 525 miles along the Pacific coast on U.S. Highway 1. The tour starts in the heart of San Francisco and ends on the iconic strand of Los Angeles.

Ride Your Way With Arthritis Cycling Experience allows you to attend our signature cycling events virtually if you are unable to attend in person.

Jingle Bell Run is the most festive holiday run for a reason. Join us as we support the nearly 60 million people in the U.S. living with arthritis at the most fun holiday fundraising run. You and your hospital or practice can get involved in so many ways! Register your hospital, practice or department as a team (and encourage your patients to join). You don't want to miss out!

Gatherings and Galas include local fundraising galas, golf outings, car shows and themed parties. These fun-filled events offer festive ways to help the Arthritis Foundation and benefit our entire community.

To learn more about our events and to participate, visit arthritis.org/events.

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Educational Resources for Your Patients

Arthritis Foundation Webinars

Arthritis Foundation webinars are educational events featuring arthritis experts. These online seminars are designed to help patients better manage their pain and other symptoms. Learn about our upcoming webinars.

Live Yes! Connect Groups

Connect Groups provide supportive social connections and are open to parents/guardians of children with rheumatic diseases and adults with arthritis or rheumatic diseases. These virtual and in-person groups bring people together for fun social and informative educational events and activities focused on mutual support and positive coping strategies for living well. Learn about our Connect Groups and upcoming events.

Living Well Events

Arthritis creates a unique set of challenges that require an equally unique set of solutions. Whether it's managing symptoms like pain and inflammation or discovering new ways to achieve everyday tasks, our in-person Living Well events empower you to take control of your condition. Learn about our upcoming Living Well events.

Arthritis Foundation®