

Research Priorities for the Unified Orthopaedic Research Agenda

The mission of the Unified Orthopaedic Research Agenda is to advance science and research in musculoskeletal care through a unified research strategy. Continued and additional funding of these research priorities is necessary to improve function and mobility and reduce the socioeconomic burden of orthopaedic disorders.

Cross-Cutting Topics for Orthopaedic Research

- Patient safety
- Creating value through orthopaedic care
 - Comparative effectiveness of orthopaedic care
 - Patient-reported outcomes (PROs) as quality measures and outcomes indicators
 - Dissemination of the results of musculoskeletal research in a way that rapidly impacts clinical care
- The use of biologics (cells, growth factors) to improve musculoskeletal outcomes
- The interrelationship between musculoskeletal health and obesity and diabetes
- Promoting equal access to musculoskeletal care for all people regardless of age, race, socioeconomic status, sex (biological), or gender (societal) and eliminate disparities in outcomes

Orthopaedic Conditions with the Greatest Burden of Disease

- Arthritis and cartilage injuries
- Spinal disorders, neck and back pain
- Muscle, tendon, ligament, and nerve injuries
- Osteoporosis and bone fragility, especially fractures in the elderly and those caused by cancer
- Major limb trauma/high-energy extremity injuries
- Childhood musculoskeletal conditions

Priorities for Strengthening Orthopaedic Research

- Train and increase diversity of the next generation of orthopaedic clinician investigators and basic scientists
- Support for interdisciplinary teams of orthopaedic scientists
- Support for scientific infrastructure

Health Services Research Priorities

- Improve patient safety in the care of orthopaedic disorders
- Improve tools to measure orthopaedic outcomes; increase emphasis on patient-reported outcomes (PROs) measures
- Study comparative effectiveness in orthopaedic disorders
- Quantify of the burden of disease for orthopaedic disorders
- Research new models of dissemination and implementation of results, to more rapidly impact patient care

Clinical Research Priorities

- Use precision medicine to improve musculoskeletal outcomes
- Promote patient-centric orthopaedic care delivery
- Conduct clinical trials of biologic treatments (cells and growth factors) to enhance recovery after injury
- Expand and explore opportunities in musculoskeletal transplantation
- Investigate the role of sex and gender as a variable in orthopaedic research linking basic and clinical science

Basic and Translational Research Priorities

- Identify cellular processes that facilitate repair and regeneration of musculoskeletal tissue
- Investigate molecular mechanisms controlling growth and differentiation of cells of the musculoskeletal system
- Study the effect of metabolism on basic cellular processes involved in cells of musculoskeletal origin
- Identify cellular markers of musculoskeletal stem cells
- Explore regulation, expression, and role of musculoskeletal cytokines
- Improve animal models for tissue engineering research
- Translate the basic science of bone healing into surgical techniques to improve patient care
- Investigate the role of mechanical forces and other physical cues in musculoskeletal health and disease
- Understand the genetic basis of orthopaedic disorders

Patient Safety and Healthcare Quality

- Develop definitions for healthcare quality within orthopaedic surgery and establish methodology to obtain measurable outcomes
 - Establish framework for measuring healthcare quality: process measures, delivery infrastructure, and clinical outcomes
 - Study the feasibility of collecting reliable, valid and measurable outcomes
 - Address operational issues, including electronic medical record compliance and implementation of SCIP guidelines
 - Define outcomes of interest and appropriate timeframe of collection of clinical/functional scores and complications
 - Enhance instruments and methods for data collection
- Study the short- and long-term implications of current quality initiatives, including Centers for Medicare and Medicaid Services (CMS) hospital quality rank, CMS Meaningful Use criteria, American Joint Replacement Registry, and insurance reports on healthcare quality, cost, patient access, and hospital and provider behavior
- Develop alternative tools for national quality improvement within orthopaedic surgery (ACOs, pay-for-performance insurance pilots, bundled care plans, NSQIP, etc.)
 - Perform a critical review of existing programs and methods
- Perform high-quality studies regarding treatment indications for common orthopaedic conditions
 - Investigate the natural history of musculoskeletal disease, and the impact of increasingly common comorbidities on patient outcomes and complications Develop robust databases, encouraging collaboration among existing professional organizations
 - Perform multi-center RCTs and comparative effectiveness studies to evaluate treatment alternatives
 - Develop guidelines for appropriate use of surgical and nonsurgical treatment methods
 - Study the effect of surgical timing on clinical and economic outcomes
- Develop strategies to maximize patient safety, minimize complications, and avoid preventable adverse events
 - Define the incidence of the above problems through large, multi-institutional registries and cohort studies
 - Implement and analyze strategies to improve patient safety, including fall prevention, inpatient infection (UTI, pneumonia), and drug errors
 - Develop strategies to minimize all complications, especially post-operative infections within joint arthroplasty and spine surgery, hematologic complications (blood transfusions, DVT, PE), and readmissions and reoperations
- Study the impact of patient demographics (age, sex, race, socioeconomic status) and comorbidities (obesity, diabetes, smoking, inflammatory disorders, cancer history, mental health disorders) on the natural history of musculoskeletal disease, treatment options, and surgical outcomes while developing strategies of optimization
- Quantify the impact of orthopaedic care on the individual and society
 - Promote society level, comparative effectiveness research (long-term economic benefits to workforce of restoring productivity)
 - Develop and validate patient-reported outcomes (PROs) for comparative effectiveness studies
 - Refine measurement tools: Health-Related Quality of life / Quality-adjusted life years (QALYs)
 - Perform comparison studies with non-orthopaedic areas of care, such as government-funded renal dialysis
- Develop evidenced-based programs to help musculoskeletal patients and providers navigate the changing face of health care as mandated by the Affordable Care Act
 - Perform epidemiological studies assessing the implications on Insurance networks/coverage, referrals, non-operative, and operative care (ACOs) on delivery of musculoskeletal care
 - Educate the public on the CMS public hospital quality reporting and implications for musculoskeletal care
- Perform preclinical and clinical trials to establish safety and efficacy of biomedical implants
- Reduce the incidence and impact of musculoskeletal infection
 - Investigate non-antibiotic methods of infection treatment
 - Investigate implant materials designed to retard or prevent infection
 - Investigate previously-underestimated infectious agents (e.g. *Propionibacterium acnes*)
 - Investigate genetic and host factors, and comorbidities such as obesity and diabetes, that may predispose patients to infection after orthopaedic procedures
 - Further work on preventing musculoskeletal infection in the immunocompromised patient

Creating Value Through Orthopaedic Care

VALUE = Outcomes / Cost

Value in health care has been defined as outcomes achieved per dollar. Thus, effective research in orthopaedics will increase the value of orthopaedic care by improving outcomes and reducing cost. Improving outcomes first relies on improving how we measure outcomes. Outcome measurements should be clinically relevant, appropriate to the context of the orthopaedic condition, with attention to the patient health status, demographics, and other patient-identified factors. Outcomes in the delivery of orthopaedic care should serve as reliable and quantifiable indicators of a positive change in the overall health of our population. Both outcomes and cost should sufficiently and entirely capture the defined cycle of clinical care and its attendant components which impact the defined outcome. Unique to the value of orthopaedic surgery, outcomes and cost should also consider an enhanced quality of life, improved work force capacity, and increased productivity.

Value through research in orthopaedic surgery integrates pervasive themes within the context of the Research Priorities for the Unified Orthopaedic Research Agenda.

Arthritis and Cartilage Injuries

- Improve the ability to prevent or delay the development of arthritis and minimize -surgical intervention
 - Develop and evaluate preventive strategies to reduce the risk of injury
 - Evaluate the comparative effectiveness of treatments that maintain mobility and independence
 - Develop and evaluate acute intervention strategies following joint injuries focused on delaying or preventing the onset of posttraumatic osteoarthritis
 - Pursue high quality clinical studies to evaluate the comparative effectiveness of arthroplasty vs. non-arthroplasty management of arthritis for both the upper and lower limbs
 - Apply novel minimally-invasive imaging and surgical technologies to diagnose and treat arthritis, including radiostereometric analysis (RSA), surgical navigation, and minimally invasive and robotic surgery
 - Identify recurrence rates for arthroplasty-related complications such as surgical site infection, thromboembolic disease, or re-operations for early implant loosening to improve their prevention, detection, and treatment
 - Develop rehabilitation strategies that can optimize joint healing following joint injury or surgery
- Advance the development of validated diagnostic tools for arthritis
 - Continue development of quantitative non-invasive imaging and biochemical measures to assess the structure and composition of cartilage and other relevant joint tissues
 - Independently validate the ability of quantitative non-invasive measures to differentiate disease severity and to predict the future development of osteoarthritis
 - Enhance the ability of quantitative non-invasive measures to detect improved cartilage outcomes to better monitor the safety and efficacy of articular cartilage resurfacing and other emerging cartilage repair strategies
- Incorporate patient-reported outcomes (PROs) tools into standard diagnostic, treatment, and follow-up care
 - Develop therapies to improve the repair and regeneration of injured or arthritic joint tissues
 - Enhance the innate healing response within the damaged joint using small molecules, biological agents, and cell-based strategies
 - Develop cell-based strategies for the regeneration of cartilage and other joint tissues using stem cells and other minimally manipulated adult progenitor cell types
 - Implement a tissue engineered joint regeneration strategy by integrating expanding expertise in bio and nanomaterials, stem and progenitor cells, and biological and physical cues
 - Continue to develop and validate naturally-occurring and disease-induced animal models to evaluate the safety and efficacy of new drug and surgical interventions for osteoarthritis

- Elucidate cellular and molecular mechanisms that maintain the healthy joint and the processes by which these are disrupted in arthritis
 - Identify genetic and biological factors that influence the progression of arthritis
 - Elucidate the biological and mechanical interactions among cartilage and other joint tissues including subchondral bone, meniscus, and synovium
 - Define the interaction between physical and biological factors in the development of osteoarthritis, including after joint injury, , to identify pathways and molecular targets for medical intervention

Spinal Disorders, Neck and Back Pain

- Improve the ability to diagnose spinal disorders, including the ability to localize the source of pain, evaluate motion segment instability, and evaluate the role of muscles and connective tissues in back pain
 - Develop new clinical, electrophysiological, imaging, and psychometric tools for the diagnosis of various causes of back pain and instability
 - Develop objective clinical algorithms to distinguish various etiologies of back pain that lead to specific treatment methods for each identified disorder
 - Define the appropriate use of single or combined objective electrophysiological and imaging tools (x-rays, stereo-radiographs, EOS 2D/3D, ultrasound, CT, MRI, etc.) to identify bone, disk, and soft tissue pathologies responsible for back pain and instability
 - Define the use of diagnostic interventional modalities, such as epidural injections, selective nerve root injections, and discography
 - Improve classification systems for spinal disease, especially within deformity surgery
 - Refine spine functional scores assessment (SF-36, Oswestry Disability Index, SRS-22) and evaluate the role of computer-adaptive testing protocols
- Develop objective and scientific methods of assessing structural and functional status of paravertebral muscles and ligaments of the vertebral columns
 - Develop and validate imaging studies to assess pathologies of paravertebral muscles, ligaments, and joint capsules at the motion segments of the vertebral column
- Study the etiology and pathophysiology of spinal pain while defining the role of medical and complementary treatments
 - Explore multidisciplinary scientific approach to increase understanding of back pain
 - Encourage new collaborations among orthopaedic surgeons, physiatrists, electrophysiologists, neuroscientists, neurosurgeons, neurologists, radiologists, pain specialists, pain researchers, clinical psychologists, and psychiatrists
 - Identify specific mediators of back pain
 - Identify effective pain control methods in patients with neck or back pain
 - Develop mechanism-based treatments
 - Pilot clinical trials to compare various non-operative methods of relieving back pain (exercise, drugs, acupuncture, injections, therapy, TENs, ultrasound, other complementary methods)
 - Identify differences and similarities of pain perception related to sex, ethnicity, and genetics
 - Develop multidisciplinary programs and investigations to identify perception of pain differences
 - Identify research questions that delineate perception of pain and response to treatment
- Study the etiology and pathophysiology spinal cord injury
 - Continue the development of biological treatment options for acute spinal cord injury
 - Define the role of steroids
- Develop and compare surgical and nonsurgical treatment methods for spinal disorders
 - Determine appropriate use/indications for operative spine treatments, especially for cervical spine degenerative disorders and adult spinal deformity
 - Examine the relationship of timing of surgery and the effect on outcomes
 - Compare the intermediate to long-term results of motion sacrificing vs motion preserving spinal surgery
 - Define the appropriate use of biologics within spinal surgery

- Identify scientific rationale and evidence for new treatment methods to increase the validity of new treatment methods and clinical indications
 - Analyze clinical efficacy and patient-reported outcomes of various treatment methods through collaborative, multi-center clinical trials to promote evidence-based practice and decrease surgeons' bias and geographic variations
- Develop methods to optimize perioperative safety and minimize complications after spinal surgery
 - Standardize medical optimization protocols for patients undergoing major spine surgery (deformity)
 - Define what preoperative consults, laboratory and functional testing has been shown to reduce patient risk
 - Optimize intraoperative techniques, including anesthetic choice, high blood loss protocols, sterile techniques, and the utility of neurologic monitoring
 - Reduce complications of various treatment methods including postoperative infection, junctional deformity, spinal cord and nerve root dysfunction
- Identify risk factors for wound dehiscence, infection, postoperative junctional deformity, spinal cord root dysfunction, and failed back surgery
 - Develop effective preventive measures through a systematic approach
 - Revise and improve wound care protocols
 - Promote effective skin preparation, soft tissue handling, and closure to prevent infection
 - Promote optimal prophylactic, intra-operative, and post-operative antibiotic regimens
 - Establish guidelines for salvage spinal operations following infection
- Establish optimal fusion levels to prevent junctional kyphosis and coronal deformity
 - Develop effective treatment methods to prevent and manage junctional deformities
- Develop guidelines to minimize spinal cord and nerve root dysfunction
 - Develop more specific and sensitive clinical and electrophysiological spinal cord monitoring guidelines
- Define causes of failed back surgeries (diagnostic failures, technical failures)
- Develop a collaborative evidence-based clinical practice guideline for the treatment of spinal disorders and injuries
 - Pilot clinical trial programs
 - Establish new programs to develop small-scale pilot clinical trials on patient safety, quality care and value with respect to infection, effective spinal cord monitoring, and optimal fusion levels to prevent postoperative junctional deformity

Muscle, Tendon, Ligament, and Nerve Injuries

- Fundamental Biology
 - Understand the role of physical activity in the development of tendon, ligament, and muscle
 - Increase understanding of nerve development and regeneration
 - Characterize the relative influences of osseous anatomy, ligamentous laxity, and sex hormones on musculoskeletal disorders
- Tissue Engineering, Regeneration and Related Biology
 - Identify the signaling pathways involved with muscle, tendon, and ligament injury, repair, and hypertrophy
 - Expand knowledge of the interaction of the immune system and its role in transplantation of bone and ligaments
 - Develop biological replacements and augmentation for muscle, nerve, ligament, tendon, meniscus, and cartilage
- Exercise and Sports Biology and Mechanics
 - Develop more effective protective and preventive strategies for sports and occupations where risks of physical impairment exist
 - Develop a better understanding of the effect of activity, sex, age and other factors on fitness as well as musculoskeletal and neurological disorders
 - Analyze the forces in normal tissues and the healing of soft tissues during in vivo activities.
 - Develop new repair and reconstruction procedures and scientifically based rehabilitation protocols

- Repetitive Trauma
 - Characterize the pathomechanics of repetitive injury to muscle, tendon, ligament and nerve pathophysiology of muscle atrophy and diseases
 - Characterize the role of comorbidities, such as smoking, obesity and diabetes, on cumulative trauma disorders, and in recovery post injury
- Pain
 - Identify the links, if any, between factors that regulate microcirculation and those that mediate pain perception
- Tendon and Ligament
 - Elucidate the biology and molecular mechanisms of tendon and ligament healing and degeneration
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 - Investigate the biology of rotator cuff injury and healing with or without surgical intervention
 - Perform high quality research studies regarding the surgical and nonsurgical management of tendon and ligament pathology
- Nerve
 - Increase the understanding of the causes and basic pathophysiology of peripheral nerve disorders and their treatment
 - Develop new animal models to study peripheral nerve disorders and nerve regeneration
 - Develop new diagnostic methods to facilitate individualized treatment of peripheral nerve disorders
 - Perform research studies regarding the surgical and nonsurgical management of peripheral nerve disorders

Osteoporosis and Bone Fragility, especially fractures in the elderly and those caused by cancer

- Optimize the surgical and nonsurgical management of fragility fractures, especially of the spine and hip
- Expand the options for the treatment of low bone mass
 - Define the variables that negatively impact bone mass and strength e.g. nutritional, hormonal, chemotherapy, obesity, diabetes, aging
 - Develop rehabilitation and other therapeutic strategies to prevent primary and secondary fragility fractures
 - Develop agents and novel systems to increase bone mass, strength and other bone quality parameters
 - Study pathophysiology and develop new therapeutic strategies for primary bone tumors, especially sarcoma, and metastatic bone cancers, specifically the impact on bone strength, patient survival, and quality of life
 - Elucidate the contribution of resident bone and bone marrow cells to the initiation, progression and maintenance of cancer and bone metastasis
- Elucidate the etiologies and further understand the mechanism(s) responsible for the attainment and maintenance of peak bone mass in both sexes and all races
 - Define genetic basis for bone mass and strength differences
 - Develop patient-oriented outcomes for the assessment of bone mass and strength
 - Investigate new imaging modalities/techniques to assess bone quality
 - Develop biologic mediators and other cellular and molecular approaches to increase bone mass and strength
 - Evaluate the utility of alternate models for bone cancers and metastasis as a prelude to therapy
 - Better understand the expanding pool of systemic biomarkers (e.g. sclerostin) and how they impact patient care and diagnosis
 - Investigate sex differences related to fragility fracture location, presentation, and outcomes
- Coordinate partnerships with other medical specialties to provide multidisciplinary patient care
 - Define impact of known comorbidities (diabetes, chemotherapy, etc.) on osteoporosis progression and patient outcome
 - Identify and implement appropriate fall prevention and patient safety criteria
 - Determine appropriate assessment methodology and treatment options for cancer patients with poor bone quality and increased fracture risk
 - Improve evaluation, treatment, and osteoporosis assessment for obese patients

Major Limb Trauma / High-Energy Extremity Injuries

- Optimize surgical and nonsurgical management of major limb trauma
- Develop evidence-based clinical practice guidelines for multidisciplinary care of amputees including surgical and post-surgical limb preparation as well as prosthetic development and management
 - Promote randomized trial comparing bone bridging transtibial amputation with standard transtibial amputation
 - Investigate techniques for post-amputation limb management including the role of vacuum assisted closure
 - Evaluate multimodal strategies to mitigate phantom pain and post-amputation neurogenic pain
 - Refine post-amputation rehabilitation protocols to facilitate reintegration into society and the workplace
 - Develop patient selection and matching criteria to optimize prosthetic style and fitting for amputees
- Expand emphasis on the biologic treatment and manipulation of the fracture healing cascade
 - Develop molecular and pharmacological agents and delivery systems to accelerate normal fracture and soft tissue healing
 - Define the ideal chronological and dose response curves for fracture and wound healing growth factors and cell-mediated therapies after injury
- Refine the diagnostic modalities, elucidate the etiologies, and further develop mechanical and biological treatment strategies for fracture nonunions
 - Define biological markers of fracture nonunion
 - Investigate new imaging modalities/techniques to assess fracture healing capacity and vascularity
 - Develop biologic mediators and cell-based stimuli to initiate or enhance bone healing in nonunion scenarios
 - Further investigate the use of minimally manipulated adult progenitor cells derived from bone marrow (MSCs), adipose tissue (ADSCs), muscle (MDSCs), and dermal tissue (DDSCs) to aid fracture healing
 - Evaluate progenitor cell strategies which minimize or eliminate in-vitro culture expansion to facilitate bone defect management
 - Investigate the development of novel, synthetic, and biomimetic scaffolds which are both inductive and conducive to cell migration, proliferation, and matrix synthesis and allow for normal tissue regeneration and remodeling of bone defects
- Improve rehabilitation modalities and therapies in order to enhance recovery from injury as measured by workplace re-entry and return to daily activities
 - Develop rehabilitation protocols that are injury-specific, similar to those utilized in sports medicine and arthroplasty
 - Perform comparative effectiveness research on physical and occupational therapy treatments
 - Investigate range of motion therapy modalities including dynamic splinting after intra-articular injuries
 - Perform cost-effectiveness analyses of rehabilitation methodologies
- Enhance partnerships with other specialties in order to improve multidisciplinary care for injury patients with significant comorbidities including diabetes, obesity, substance abuse, smoking, and various mental health issues
 - Develop risk stratification algorithms in order to reduce post-injury complications
 - Evaluate co-management strategies with infectious disease specialists for post-injury infection patients
 - Define appropriate antibiotic prophylaxis regimens for specific patient populations and injury profiles
 - Investigate effects of glycemic control strategies on healing and complications in diabetic fracture patients
 - Refine treatment and surgical techniques for obese patients
 - Develop evidence based patient / injury specific thromboembolic disease prophylaxis protocols
 - Refine parameters to optimize timing of fracture fixation with concurrent head, chest, or spinal cord injury
 - Improve diagnostic and treatment modalities for elderly trauma patients
- Reduce rates of musculoskeletal infection in trauma patients
 - Investigate non-antibiotic methods of infection treatment
 - Investigate implant materials designed to retard or prevent infection
 - Investigate previously-underestimated infectious agents (e.g. *Propionibacterium acnes*)
 - Investigate genetic factors that may predispose patients to infection after orthopaedic procedures
 - Develop measures to prevent musculoskeletal infection in the immunocompromised patient

Childhood Musculoskeletal Conditions

- Perform research studies regarding the comparative effectiveness of surgical and nonsurgical management of pediatric trauma
 - Analyze cost-effectiveness of surgical versus nonsurgical management of pediatric fractures
 - Develop injury prevention programs for trauma and overuse injuries
- Perform research studies regarding the effects of poor nutrition and lack of exercise on childhood bone health to optimize peak bone mass
 - Develop bone health, nutrition, and exercise programs that promote musculoskeletal health
 - Analyze the rates of childhood and young adult osteopenia/osteoporosis in current fracture clinics
- Identify the effects of childhood obesity on the musculoskeletal system such as fracture risk, slipped capital femoral epiphysis, Blount's disease, osteoarthritis, and bone density
 - Determine the future of burden of disease of pediatric musculoskeletal disease associated with childhood obesity
 - Determine if treating obesity results in improvement in musculoskeletal disease in children
- Investigate the developmental biology of the musculoskeletal system in the child with an emphasis on bone and joint development
 - Identify genetic and physiologic pathways for disorders of musculoskeletal development including skeletal dysplasias, deformities, and disorders
 - Develop novel biologic approaches to address disorders of growth and development of the musculoskeletal system
- Design and develop orthopaedic devices that are appropriate for children and adolescents
 - Perform comparative effectiveness of pediatric devices versus adult devices for the management of musculoskeletal disorders in children
 - Expedite the FDA approval process for pediatric devices
- Investigate the genetic cause of scoliosis in order to stratify the risk and severity of scoliosis and to develop biological treatment methods
 - Elucidate the pathophysiologic processes that contribute to skeletal deformity of the spine and thorax and the mechanobiology principles that govern growth modulation of the spine and thorax
 - Perform comparative effectiveness clinical research studies on surgical versus nonsurgical treatment of scoliosis
 - Perform comparative effectiveness clinical research studies on different surgical approaches and instrumentation for the treatment of scoliosis
 - Determine the cardiopulmonary effects of treatment of scoliosis in children
- Characterize the pathophysiology and develop new therapeutic strategies for soft tissue sarcomas



**For additional information, please contact the
American Academy of Orthopaedic Surgeons**

www.aaos.org/research
researchinfo@aaos.org

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Contributing Societies: American Association for Hand Surgery (AAHS); American Association of Hip and Knee Surgeons (AAHKS); American Orthopaedic Foot and Ankle Society (AOFAS); American Orthopaedic Society for Sports Medicine (AOSSM); American Shoulder and Elbow Surgeons (ASES); Cervical Spine Research Society (CSRS); The Hip Society; J. Robert Gladden Orthopaedic Society (JRGOS); Limb Lengthening and Reconstruction Society (LLRS); Musculoskeletal Tumor Society (MSTS); North American Spine Society (NASS); Orthopaedic Rehabilitation Association (ORA); Orthopaedic Research Society (ORS); Orthopaedic Trauma Association (OTA); Pediatric Orthopaedic Society of North America (POSNA); Ruth Jackson Orthopaedic Society (RJOS); and Scoliosis Research Society (SRS).