## COMPLEMENTARY AND ALTERNATIVE MEDICINE (SL KOLASINSKI, SECTION EDITOR)

# Yoga in Rheumatic Diseases

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**Abstract** Yoga is a popular activity which may be well suited to some individuals with specific rheumatic disorders. Regular yoga practice can increase muscle strength and endurance, proprioception, and balance, with emphasis on movement through a full range of motion to increase flexibility and mobility. Additional beneficial elements of yoga include breathing, relaxation, body awareness, and meditation, which can reduce stress and anxiety and promote a sense of calmness, general well-being, and improved quality of life. Yoga also encourages a meditative focus, increased body awareness and mindfulness; some evidence suggests yoga may help reduce inflammatory mediators including C-reactive protein and interleukin-6. Yoga is best learned under the supervision of qualified teachers who are well informed about the potential musculoskeletal needs of each individual. Here, we briefly review the literature on yoga for healthy, musculoskeletal, and

rheumatic disease populations and offer recommendations for discussing ways to begin yoga with patients.

Keywords Yoga · Rheumatic diseases · Arthritis · Osteoarthritis · Rheumatoid arthritis · Systemic lupus erythematosus · Health benefits · Immune function · Musculoskeletal system

#### Introduction

Regular physical activity is essential for overall health and wellbeing, centers prominently in public health recommendations [1], and is included in treatment guidelines for arthritis [2, 3], fibromyalgia (FM) [4, 5], and other rheumatic diseases. Emerging evidence suggests that yoga,

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which offers a mind-body approach to physical activity and emphasizes healthy living, may be particularly well suited to some individuals with specific types of rheumatic disease.

## What is Yoga?

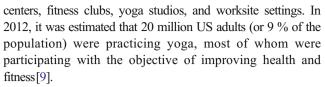
Yoga is an ancient Indian practice, dating back several thousand years, with the objective of uniting mind, body, and spirit[6]. There are several branches of yoga, which share a common underlying philosophy and include a variety of lifestyle practices. In western cultures, Hatha yoga is most commonly practiced, and the physical movements of yoga are often emphasized as a form of exercise with both physical benefits and improvements in well-being. Hatha yoga generally includes a set of physical poses (asanas) that may be fluid or static, coordinated with breathing techniques (pranayama), and deep relaxation (sivasana) and/or meditation. Hatha yoga may also include chanting, mudras (hand positions), and/or discussion of yogic philosophy.

There are many styles of Hatha yoga, each with its own style and approach, which may be optimum for different populations (Table 1). Performing the physical poses can improve fitness by increasing strength, flexibility, and balance[7, 8]. Yoga practice typically begins with a slow sequence of continuous movements to increase blood flow and warm muscles. This is followed by a series of diverse poses which can engage muscles in all areas of the body in flexion, extension, adduction, abduction, and rotation. Many yoga poses can increase muscle strength and endurance, and standing poses can also increase proprioception and balance[6]. Many poses also emphasize movement through a full range of motion to increase flexibility and mobility.

Yoga also includes additional elements that distinguish it from traditional forms of exercise. The breathing, relaxation, and meditative elements of yoga can potentially reduce stress and anxiety, distract from negative thoughts, and promote a sense of calmness, general well-being, and improved quality of life. Yoga encourages the use of a meditative focus, body awareness, and respect of individual limits while engaging in poses. Mindfulness, or orientation to the present moment with a sense of curiosity, openness, and acceptance, is also a core feature of yoga. Yoga practice also often includes discussion of core yogic principles including non-harming of self and others, appropriate energy expenditure, contentment with "what is", and ongoing self-study which may benefit persons living with rheumatic diseases.

#### Who Practices Yoga and why?

Interest in yoga has increased substantially in the past two decades, and it is now widely available in many community



According to the 2002 National Health Interview Survey (NHIS) Alternative Medicine Supplement, regular practitioners of yoga were mostly female (76 %), white (85 %), and well educated (50 % had college education)[10]. People practicing yoga were more likely than non-practitioners to rate their health as excellent, very good, or good (95 % vs. 87 %, respectively). Interestingly, having a musculoskeletal condition was independently associated with greater odds of practicing yoga regularly (OR 1.61, 95 % confidence interval 1.42–1.83).

The top five reasons reported for starting yoga were to improve flexibility (78 %), general conditioning (62 %), stress (60 %), overall health (59 %), and physical fitness (55 %)[9]. Indeed, there is substantial evidence that people who practice yoga rate their health more positively. A 2013 national survey of 1087 individuals who regularly practiced yoga reported improvements in energy (85 %), happiness (86 %), social relationships (67 %), sleep (69 %), and weight (57 %)[11]. Among German patients seen in an integrative internal medicine clinic, 12 % reported using yoga to address their chronic pain; the three most common diagnoses were spinal pain (19 %), headache (12 %), and fibromyalgia (FM) (12 %)[12].

The potential for yoga to enhance health and wellbeing seems to have been embraced by the medical community also. A 2008 market study commissioned by Yoga Journal using a nationally representative sample of US adults suggested that 6.1 %, or nearly 14 million Americans, reported that a doctor or therapist recommended yoga to them, and nearly half (45 %) stated they believed yoga would be beneficial [13].

## **Health Benefits of Yoga**

There seems to be general agreement on the potential health benefits associated with yoga. On their website, the National Center for Complementary and Alternative Medicine (NCCAM) of the National Institutes of Health (NIH) states that yoga is a safe and effective for healthy people when practiced appropriately under the guidance of a well-trained instructor, and lists several health conditions including low-back pain, for which yoga may be beneficial [14]. In the UK, the National Health Service (NHS) promotes yoga as a safe and effective method of increasing physical activity for both healthy persons and those with a range of health conditions [15].

#### Physical Fitness and Health

Overall, the reported health and fitness benefits of yoga are similar to those associated with other forms of exercise,



Table 1 Common yoga styles, characteristics and appropriateness for individuals with rheumatic diseases<sup>a</sup>

Style	Characteristics	Recommendations	
Ananda	Very gentle preparation for meditation. Affirmations combined with poses	Longer meditation in static positions may be difficult for some	
Anusara	Anatomically based. Extensive teacher training	Recommended for most people with rheumatic conditions	
Ashtanga	Specific sequence. Continuous movement. Very strenuous (sometimes called power yoga)	Not recommended because of physical rigor	
Bikram/hot	Taught in 100–110 degree room to expel toxins and increase mobility	Not recommended because of extreme heat. Cardiovascular clearance should be obtained before undertaking	
Chair	All poses practiced while sitting in a chair	Recommended for deconditioned seniors and anyone with balance or mobility limitations	
Gentle	Optimum for people with lower fitness levels. Emphasizes slower and more careful practice	Recommended for most people with rheumatic conditions	
Integral	Gentle practice including poses, breathing, chants, and meditation	Recommended for most people with rheumatic conditions	
Iyengar	Strong anatomical basis. Uses props to individualize poses	Recommended for most people with rheumatic conditions	
Kripalu	Taught in three stages with evolving emphasis. Stage one focuses on learning poses and understanding the body	First stage recommended for most people with rheumatic conditions	
Kundalini	Intended to awaken latent spiritual energy through poses, breathing, and meditation	Intensity of breathing techniques, long sitting, and expansive arm movements may be challenging for some individuals	
Pre-natal	Classes intended for expectant mothers, with a focus on mindfulness, breath, and safety	While not intended for people with rheumatic diseases, classes progress slowly with emphasis on individual attention; can be used as an alternative to more rigorous classes	
Restorative	"Resting" poses which are fully supported with props to enable muscle release and relaxation	Recommended for most people with rheumatic conditions but does not build strength, balance or flexibility. May be especially appropriate during flares or periods of fatigue	
Sivananda	Gentle practice including poses, breathing, chants, and meditation	Recommended for people with rheumatic conditions	
Vinyasa (flow)	Individualized practice. Extensive coordination between breath and movement. Extensive teacher training	Continuous movement during vinyasa yoga is often challenging and may move too quickly to enable modification and use of props. Beginner and/or gentle vinyasa is recommended with reservations for some individuals	
Yin	Often used to prepare for extended meditation in static poses. Poses are held in the full position to encourage release. Promotes flexibility but not strength or balance	May be suitable for some; however, there is a potential for overstretching and tendon inflammation	

<sup>&</sup>lt;sup>a</sup> Within styles there may be significant variability in terms of emphasis and difficulty. Before participation, discussion with the class instructor may aid understanding of the specifics for the class

especially among older populations [7, 16-20]. A 2011 systematic review of yoga studies among elderly adults concluded that yoga was associated with moderate improvements in gait, balance, flexibility, lower body strength, and weight loss[21]. However, the effect of yoga on cardiovascular conditioning is less clear. Some forms of yoga practice may not be of sufficient intensity to improve or maintain cardiovascular fitness. For example, in one study, metabolic expenditure was measured during a 30-min session of beginner level yoga using a room calorimeter. The investigators concluded that when averaged over the entire session, total metabolic expenditure reflected an overall low level of physical activity that was equivalent to walking 1.5 mph on a treadmill[22]. The large variability in yoga styles and doses, and the range of outcomes assessed, make comparisons of yoga with other forms of exercise and across studies challenging to interpret. Clearly, more research is needed to establish the conditioning effects of yoga on health.

#### Musculoskeletal System

Unfortunately, there is limited scientific evidence available on how yoga specifically affects the musculoskeletal system. Wang et al. recently studied the biomechanical impact of yoga on the lower extremity associated with the static phase of seven common standing yoga poses among seniors[23]. Not surprisingly, physical demands on the ankle, knee, and hip in the frontal and sagittal planes varied substantially across the different poses. However, because this was one of the first studies to develop biomechanical profiles of yoga poses, the investigators noted that additional work was needed to better characterize other commonly used poses, and the effects of modifications and between-pose transitions. Understanding the biomechanical profiles of yoga poses is a first step to designing evidence-based programs that can target specific joints and muscle groups to prevent or address impairments in function and mobility.



### Psychological and Immune Function

Nearly four decades of research has shown that people who practice yoga generally report improvements in mood (i.e., anxiety, depression) and ability to deal with stress, and greater feelings of emotional and social wellbeing [17, 24–26]. There is growing evidence that yoga is associated with down-regulation of the hypothalamic–pituitary adrenal (HPA) axis and the sympathetic nervous system [17]. There is some suggestion that yoga may help reduce levels of inflammatory markers including C-reactive protein and interleukin-6[27, 28].

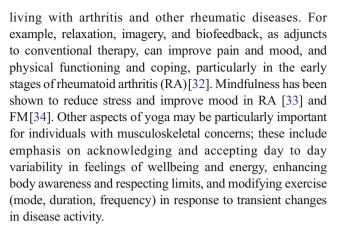
## **Health Benefits Among Clinical Populations**

In response to the growing number of studies reported in the medical literature, several systematic reviews and meta-analyses have recently been published evaluating the health benefits of yoga in clinical populations. McCall et al. recently completed a Cochrane overview of systematic reviews of yoga among adults with 13 chronic health conditions [29]. The strongest evidence of the potential benefit of yoga is for improving pain (standardized mean difference (SMD) -0.74; 95 % confidence interval (CI) -0.97 to -0.52), with similar effects evident for reductions in pain-related disability (SMD -0.79 (95 % CI -1.02 to -0.56) and improvements in mood (SMD -0.65; 95 % CI -0.89 to -0.42)[8]. There is also evidence that when added to standard treatments, yoga can improve outcomes associated with several mental health conditions including depression, anxiety (including post-traumatic stress disorder), and schizophrenia (SMD -3.25; 95 % CI –5.36 to –1.14)[30]. However, not all health conditions may benefit from yoga. For example, meta-analyses have not supported evidence of improvement of asthma [24] or menopausal symptoms [31].

There are significant challenges in conducting systematic reviews of yoga studies. For example, in the 2012 meta-analysis of yoga and pain, although higher-quality studies reported better pain outcomes, important limitations were also noted [8]. The best effects were seen in the shortest studies. Longer trials were associated with challenges associated with most exercise interventions, including suboptimum adherence. Studies were conducted in different countries and settings, using non-randomized designs and relatively small samples that were often poorly characterized. There was significant heterogeneity in the populations studied, comparison groups, and outcomes assessed. Most interventions were poorly described and varied widely in duration, frequency, and intensity.

#### Yoga for People with Rheumatic Conditions

There are several reasons the combination of physical and mental components of yoga may be well suited to people



The physical exercise associated with yoga also may build strength in the lower extremities. Three common poses (Crescent, Warrior II, and One-legged Balance) target three functionally important motor groups simultaneously—hip flexors and extensors, knee flexors and extensors, and ankle plantar flexors[23]. Notably, strengthening of these motor groups can prevent collapse of the center of mass during standing and walking[23].

In 2011, we conducted a scoping review of seven studies evaluating yoga in arthritis (five in RA and two in both osteoarthritis (OA) and RA)[35]. There was significant heterogeneity in study design, populations studied, and intervention tested. For example, although many studies included validated instruments and used blinded assessors, arthritis disease activity was assessed using a range of indicators. Outcomes ranged from changes in symptoms, function, and mobility to improvements in such measures of fitness as strength, balance, and flexibility. The type of yoga varied substantially across settings, as did dose. Funding for the studies ranged from federal or foundational grants to support in one case from a large department store. We concluded that, overall, the studies were of very low to low quality, and the heterogeneity of the studies precluded metaanalysis. Nevertheless, there was a consistent trend suggesting some evidence of improvement in pain, function, mood, energy, and self-efficacy with regular yoga practice. None of the studies reported evidence of disease worsening or increased joint symptoms, and there was some very preliminary evidence of improvement in disease activity including reductions in the number of tender and swollen joints. More recently, Cramer et al. conducted a systematic review of RCTs that evaluated yoga as an adjunctive intervention in FM (two studies), OA (three studies), RA (two studies), and carpal tunnel syndrome (CTS; one study)[36]. They also concluded that although the quality of evidence was very low to low (and hence affected the strength of recommendation), as an ancillary intervention yoga was associated with improvements in pain and disability in FM, OA, and RA. (Although the original reports of the CTS study found no evidence of the effects of yoga on CTS, reanalysis as



part of a Cochrane review revealed some evidence of benefit associated with yoga[37].) Ward et al. also completed a meta-analysis of 16 studies of yoga on selected musculoskeletal conditions (low back pain (eleven studies), RA(one), OA(two), FM(one), kyphosis(one)) judged to be of good quality. They also reported moderate treatment effects for yoga on pain (SMD –0.61; 95 % CI –0.97 to –0.26) and functional outcomes (SMD of –0.64; 95 % CI –0.89 to –0.39)[38].

We have recently completed pragmatic randomized trials of yoga in patients with arthritis and lupus who were not included in these reviews. At the Johns Hopkins Arthritis Center in Baltimore (SJB, SH, COB), Maryland, 75 adults with OA or RA (half with RA) were randomized to eight weeks of yoga or a control group receiving usual care. In brief, two 60-min classes were combined with one home practice per week. Classes consisted of gentle yoga poses including forward bends, backbends, twists, and balance poses which were completed while standing, sitting, or lying down. Modifications were provided for individuals to address affected joints, as needed, and participants were encouraged to try new skills but avoid joint discomfort. Standard props including blocks, straps, blankets, and chairs were encouraged as needed on the basis of individual limitations. Outcomes assessed included physical health perceptions, and selected indicators of physical fitness, psychological functioning, and disease activity (for those with RA). At the end of eight weeks, individuals in the yoga group, as compared with usual care, reported significantly higher ratings of physical health, mood, and physical function; improved flexibility and balance were also observed. Among participants with RA, there was a trend for swollen and tender joint counts and patient global assessment scores to improve in both groups at the end of treatment. No related adverse events were reported.

We (CM, SB) also recently implemented a similar protocol for people with systemic lupus erythematosus (SLE) seen at the McGill University Health Centers Lupus Clinic in Montreal, Canada. Fifty-seven patients were randomly assigned to yoga or usual care. The eight week yoga intervention provided 60-minute classes twice weekly that included gentle poses, and home practice. Focus groups and surveys of yoga participants conducted one week after completion of the intervention indicated participants perceived improvement of overall well-being, improved stress and pain management, healthier relationships, and better sleep. Participants expressed satisfaction with the program content and teacher. Most participants stated that they first began to notice benefits well into the program and would have preferred the duration to have been longer than eight weeks. All participants wished to continue yoga but were hesitant to try programs not designed for SLE.

Our studies offer further preliminary evidence that yoga seems to be safe, feasible, and adaptable to the needs of individuals with arthritis and lupus. Interestingly, several participants in both the arthritis and lupus studies stated that they felt yoga had helped them learn more about themselves and their bodies, and to be more accepting of and positive about the prospect of living with a rheumatic disease.

#### **Talking with Patients About Yoga**

#### **Medical Considerations**

Yoga is one component of a regular exercise program that can help improve strength, balance, and flexibility. There are, of course, general medical considerations that should be reviewed before undertaking any exercise program, including yoga (Table 2). Patients with rheumatic diseases also may have unique needs, so discussion with the treating rheumatologist and/or orthopedist is necessary to identify vulnerable joints and poses or motions that should be avoided or modified.

#### What Style of Yoga?

The optimum way for all to start may be with a gentle yoga approach with emphasis on proceeding slowly and gradually. Some forms of yoga are generally appropriate for most people with rheumatic diseases at any age whereas a few are not

Table 2 Recommendations for health-care providers to consider for rheumatic disease patients before participating in yoga

Primum non nocere: importance of principle of "non-harming" in medicine and yoga

Evaluate general health and overall endurance

Evaluate co-morbid cardiovascular and pulmonary disease (may require referral to other specialists)

Assess for severe osteoporosis (risk of fracture and/or fall)

Clearly identify vulnerable joints to the patient (e.g., joints with instability, at particular risk of injury, with limited mobility, active swelling, or underlying damage, and any joints that have been replaced). In all of these cases, the patient should be aware of the need for caution and to avoid positions that include movements contraindicated after a hip or other joint replacement. Patients should be advised to listen to their body throughout class, avoiding movements that bring on pain. Patients should always review possible problem areas and limitations with the instructor before starting the class

Review warning signs of injury and appropriate management of discomfort (e.g. rest, cold, heat)

Consider providing a letter for yoga instructor outlining general and specific medical and musculoskeletal concerns. Care providers can also agree to speak directly with the yoga instructor and provide a contact number

Engage in ongoing dialog with patient concerning their yoga experience and concerns

Consider physical and/or occupational therapist assessment of limitations/ modifications



recommended for individuals with movement limitations and chronic pain (Table 1). For example, Bikram or "hot yoga" may not be suitable both from a cardiac perspective and its increased potential for overstretching. More strenuous forms of yoga, for example Ashtanga (sometimes called "power yoga"), particularly among older individuals who are not used to exercise, should be undertaken only if there are no concerns regarding cardiovascular issues, neurological deficits, etc. In the setting of joint replacement, the treating orthopedic team should be consulted. Vinyasa yoga keeps participants moving throughout the class, sometimes quickly. Even with props and/ or modifications, the continuous movement during vinyasa yoga is often challenging for individuals who are deconditioned, or anytime fatigue is significantly increased; it is, therefore, not recommended in many instances. On the other hand, restorative yoga, which focuses on being completely supported by props with minimal physical exertion is particularly appropriate on days when individuals feel fatigued or may be having a flare.

#### Additional Considerations

For some patients, it may be advisable to avoid specific poses that are common across many yoga styles. Persons with serious painful joint involvement or damage, and particularly previous joint replacement, must be cautious and avoid yoga positions that involve movements that may be contraindicated. For example, the American Academy of Orthopedic Surgeons recommends that people who have undergone hip replacement avoid bringing the knees up higher than the hip, leaning forward while sitting, standing with toes pointed together, bending at the waist beyond ninety degrees, and kneeling [39]. Thus, after hip replacement, it is important to modify yoga poses that call for significant external rotation (e.g., cobbler), or extension of the leg backward (e.g., Warrior II).

Because seniors typically have less joint flexibility, strength, and balance and a greater prevalence of osteoarthritis and back-pain syndromes (e.g. spinal-canal stenosis, disc disease), they are at greater risk of developing musculoskeletal and neurological complications (e.g. strains, sprains, and impingements) when participating in yoga [23]. However, the needs of seniors can be adequately managed by modification of standard poses and the use of props (e.g., seated yoga) to reduce the risk of injury (Table 3). For these reasons, yoga is best learned under the supervision of qualified teachers who are well informed about and can adapt practice to individual musculoskeletal needs.

#### Helping Patients Find Qualified Yoga Instruction

Many people living with rheumatic diseases express interest in yoga, but also question whether classes offered in community settings are safe and appropriate for their needs. Although

several DVDs designed for people with arthritis are available, it is always prudent to begin with live instruction to ensure proper form and safety before practicing without supervision [14].

Currently, there are no credentialing requirements for teaching yoga in most states. However, two organizations promote standards in training and continuing education. The Yoga Alliance registers *yoga teachers* after completion of a comprehensive 200-hour program with a registered yoga training school (RYT 200). The Yoga Alliance requires a minimum number of contact hours in teaching methodology, anatomy and physiology, yoga philosophy, and practicum. Yoga teachers can then pursue a 500-hour training program (RYT 500), and can also earn a designation of E-RYT-200 or E-RYT-500 which signifies additional (at least 1,000 hours) teaching experience.

In recent years, the field of yoga therapy has emerged and distinguished itself from general yoga teaching. While yoga instructors typically teach classes to healthy populations, yoga therapists typically offer smaller groups or private sessions to individuals with such conditions as arthritis or other movement limitations. Yoga therapists are also employed by many large academic centers (e.g., UCLA, Memorial Sloan Kettering, Mayo Clinic, Boston University Medical Center). The Cleveland Clinic currently employs a full-time yoga therapist to oversee yoga classes and programming throughout the institution. The International Association of Yoga Therapists has recommended core competencies for 800 hours of training that will be required of yoga therapy training programs (beyond the initial 200 hours required for registration as a yoga teacher.) This 1,000-hour of basic training is expected to be followed by additional continuing education and may include specialization with a specific population. However, it is important to note that the title "therapist" is not protected and essentially anyone can call themselves a yoga therapist, or pay a small fee to be "certified" as a therapist. In addition, because oversight of yoga therapy training is still emerging, it is especially important that anyone with a rheumatic disease ask directly about the training, experience, and specialization of potential instructors.

It is important to recognize that there is the potential for injury with any style of yoga (and any type of exercise), especially during periods when disease activity may be increased (e.g., flares), or when exercising strenuously or for long periods of time. All patients should be advised to immediately stop engaging in any pose that brings on pain. Classes should include periods of rest, and inclusion of "resting poses" as part of regular yoga practice is always appropriate and important. Instructors should be equipped to assist the student in modifying the practice to meet their individual needs, or should recommend a class such as gentle yoga that may be more appropriate. Individuals with greater restrictions may first want to begin working privately with a



Table 3 Potential modifications and props that can be used to adapt yoga poses to specific musculoskeletal needs<sup>a</sup>

Joint	Limitation	Pose	Potential modification
Knee	Extreme flexion	Tree	Keep the foot at the opposite ankle
	Patellar weight bearing	Table(support on hands and knees)	Place blanket under knees
Hip	External rotation to edge of ROM	Easy pose (sitting crossed leg)	Blocks under knees
	Flexion beyond 90°	Extended leg	Strap around foot to reduce angle
Wrist	Extension with weight bearing	Downward dog	Place wedge under palms
Hand	Flattened palms	Prayer position	Rest hands on heart
Shoulder	Arms above shoulder height	Chair pose	Arms extended forward
Ankle	Flexion with weight bearing	Warrior I	Wedge under heel
Foot	Forced arch	Low lunge	Rest top of the foot on the floor
Spine	Lumbar flexion	Forward fold	Keep deep bend in knees
	Lumbar extension	Bridge	Support block under small of back
	Cervical extension	Upward dog	Keep neck neutral

<sup>&</sup>lt;sup>a</sup> Table reflects only a small number of the types of modification and use of props

yoga therapist to learn modifications that they can utilize in classes or during home practice.

#### **Conclusions**

Yoga has become an increasingly popular option for physical activity that can offer important health and quality-of-life benefits. Painful musculoskeletal conditions (and pain in general) are two primary reasons many people pursue yoga. Taken together, increasing evidence from studies suggests yoga is a reasonably safe and feasible option for many people living with rheumatic conditions. This holistic approach to exercise with emphasis on mindfulness and stress reduction may also offer additional opportunities to enhance psychological well-being, reduce pain, and enhance function and participation, as part of a comprehensive disease management approach.

Before engaging in yoga, individuals should first discuss this with their health care provider. Initial practice should include direct supervision by a qualified instructor, who is knowledgeable about potential joint and musculoskeletal limitations and can suggest the use of props and modifications as needed to ensure safety and comfort. However, once individuals are comfortable with the practice, yoga can be core aspect of a healthy, positive, and active lifestyle.

## Compliance with Ethics Guidelines

Conflict of Interest Susan J. Bartlett has received grant support from the National Institutes of Health (NIH) and the Arthritis Foundation and has served as a consultant for the Arthritis Foundation. Steffany H. Moonaz has received support from predoctoral NIH and Arthritis Foundation awards and served as a consultant for the NIH and the Arthritis Foundation. Clifton O. Bingham III has received grant support from the NIH and the Arthritis Foundation. Christopher Mill and Sasha Bernatsky declare that they have no conflict of interest.

**Human and Animal Rights and Informed Consent** This article does not contain any studies with animal subjects performed by any of the authors. With regard to the authors' research cited in this paper, all procedures were approved by the respective institutions' review and/or ethics boards of the lead investigators and all procedures were followed in accordance with the ethical standards of the responsible committee on human experimentation and with the Helsinki Declaration of 1975, as revised in 2000 and 2008.

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