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2022 American College of Rheumatology (ACR) Guideline for Exercise, Rehabilitation, Diet, and Additional Integrative Interventions for Rheumatoid Arthritis

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This is the author manuscript accepted for publication and has undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: [10.1002/art.42507](https://doi.org/10.1002/art.42507)

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Grant Support: This guideline project was supported by the American College of Rheumatology.

Financial Conflict: Forms submitted as required.

IRB Approval: Approval from Human Studies Committees was not required.

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Disclaimer: The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention, the National Institutes of Health, or the Department of Veterans Affairs.

Word Count (excluding abstract, references, acknowledgments, tables): 4643

Keywords: Rheumatoid Arthritis, Integrative Medicine, Physical Activity, Diet, Dietary Supplements, Rehabilitation, Physical Therapy, Occupational Therapy

ABSTRACT (250 words max for journal submission, current 245)

Objective: To develop initial American College of Rheumatology (ACR) guidelines on the use of exercise, rehabilitation, diet, and additional interventions in conjunction with disease-modifying anti-rheumatic drugs (DMARDs) as part of an integrative management approach for people with rheumatoid arthritis (RA).

Methods: An interprofessional guideline development group constructed clinically relevant Population, Intervention, Comparator, and Outcome (PICO) questions. A literature review team then completed a systematic literature review and applied the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach to rate the certainty of evidence. An interprofessional Voting Panel (n=20 participants) that included 3 persons with RA achieved consensus on the direction (for or against) and strength (strong or conditional) of recommendations.

Results: The Voting Panel achieved consensus on 28 recommendations for the use of integrative interventions in conjunction with DMARDs for the management of RA. Consistent engagement in exercise received a strong recommendation. Of 27 conditional recommendations, 4 pertained to exercise, 13 to rehabilitation, 3 to diet, and 7 to additional integrative interventions. These recommendations are specific to RA management, recognizing that other medical indications and general health benefits may exist for many of these interventions.

Discussion: This guideline provides initial ACR recommendations on integrative interventions for the management of RA to accompany DMARD treatments. The broad range of interventions included in these recommendations illustrates the importance of an interprofessional, team-based approach to RA management. The conditional nature of most recommendations requires clinicians to engage persons with RA in shared decision-making when applying these recommendations.

SIGNIFICANCE

- This is the first American College of Rheumatology clinical practice guideline addressing integrative interventions for the management of rheumatoid arthritis (RA).
- Use of integrative interventions for the management of RA should occur in concert with disease-modifying anti-rheumatic drugs according to ACR guidelines for pharmacologic treatment of RA (1).
- This guideline highlights the vital role expert members of interprofessional healthcare teams serve in providing optimal care to people with RA.
- People with RA desire awareness of different management options early in their disease course and seek counsel from their interprofessional healthcare team to decide when to employ the use of these management options.

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic, systemic, inflammatory condition, and improved outcomes occur with early diagnosis, evaluation, and management. The American College of Rheumatology (ACR) has previously published pharmacologic guidelines to aid clinicians and people with RA (1-4). In addition to pharmacological interventions, people with RA and their clinicians consider how exercise, rehabilitation, diet, and additional integrative therapies can benefit and be included in their disease management. Using the Grading of Recommendations Assessment, Development and Evaluation [GRADE] methodology, the ACR developed this first guideline to support decision-making when using specific integrative interventions in the management of RA. The interventions considered in this guideline are defined in **Table 1**; the critical outcomes were pain and physical function, and for select interventions, disease activity or work outcomes. Although people with RA may have other indications for these interventions (e.g., comorbidities), this guideline focuses specifically on managing RA.

METHODS

This guideline follows the ACR guideline development process and ACR policy guiding management of conflicts of interest and disclosures (<https://www.rheumatology.org/Practice-Quality/Clinical-Support/Clinical-Practice-Guidelines>), which includes GRADE methodology (5,6) and adheres to AGREE criteria (7). **Supplementary Appendix 1** includes a detailed description of the methods. Briefly, the Core Leadership Team (BE, BS, NB, JB, CO, GG) drafted clinical population, intervention, comparator, and outcome (PICO) questions with input from the rest of the guideline development group, and these were posted online for public comment (See **Supplementary Appendix 2**). For most questions, the critical outcomes were physical function, which refers to the ability to perform both basic and instrumental activities of daily living, and pain. Disease activity was an additional critical outcome for questions pertaining to diet and dietary supplements. Work outcomes were

additional critical outcomes for questions pertaining to vocational rehabilitation and work site evaluation and modification. The Literature Review Team performed a systematic literature review for all PICO questions, extracted relevant study data, graded the quality of evidence (high, moderate, low, very low) and produced the evidence report (see **Supplementary Appendix 3**). A Patient Panel of 12 patients with varying manifestations of RA and varying experiences with the considered interventions for RA management met virtually. This panel was moderated by a member of the Core Team (JB) and Literature Review Team (LT). The panel reviewed the evidence report (along with a summary and interpretation by the moderator) and provided patient perspectives and preferences for consideration by the Voting Panel. At a separate Voting Panel meeting held virtually, the resulting evidence was reviewed, patient perspectives considered, and recommendations formulated and voted on. Three members of the Patient Panel were also members of the Voting Panel, to ensure the Patient Panel's perspective was considered when final decisions on the recommendations were made. Rosters of the Core Leadership Team, Literature Review Team, Voting Panel, and Patient Panel are included in **Supplementary Appendix 4**. These teams included individuals with expertise in epidemiology, exercise physiology, GRADE methodology, integrative medicine, nursing, nutrition, occupational therapy, physical therapy, rheumatology, and social work.

Consensus among the Voting Panel members required $\geq 70\%$ agreement on both direction (for or against) and strength (strong or conditional) of each recommendation, as per ACR practice. According to GRADE, a recommendation is categorized as strong if the panel is very confident that the benefits of an intervention clearly outweigh the harms (or vice versa); a conditional recommendation denotes uncertainty regarding the balance of benefits and harms, such as when the evidence quality is low or very low, or when the decision is particularly sensitive to individual patient preferences, or when costs are expected to affect the decision. Thus, conditional recommendations refer to decisions in which incorporation of patient preferences and values is an essential element of shared decision-making.

Guiding Principles

Eight guiding principles (**Table 2**) were established by the Core Leadership Team to aid in the preparation of this guideline. These guiding principles specify that integrative interventions considered in this guideline should complement pharmacologic treatments, an interprofessional approach for the management of RA should be used, and shared decision-making is needed when caring for people with RA.

RESULTS/RECOMMENDATIONS

Twenty-eight recommendations were made based on a set of 28 PICO questions. The systematic literature review initially identified 8,994 manuscripts (see search strategies in **Supplementary Appendix 5**). After screening, 275 manuscripts were mapped to ≥ 1 PICO question (see flow diagram in **Supplementary Appendix 6**). The literature review did not identify any evidence fulfilling eligibility criteria for 29% (8/28) of the PICO questions.

Exercise recommendations (Table 3)

We strongly recommend consistent engagement in exercise over no exercise.

This recommendation is based on moderate certainty evidence suggesting improved physical function and pain. Aerobic, resistance, aquatic, and mind-body exercise were considered together in the evidence supporting this recommendation. The exercise type, frequency, intensity, and duration were not formally defined because the evidence on exercise interventions did not support such precision in the recommendation, and there is considerable variation in patient values, preferences, and access to different types of exercise. The specific elements of an exercise intervention should be tailored to each

person at the given time in their disease trajectory, considering their capabilities, access, and other health conditions. National physical activity guidelines can aid such instruction (8).

We conditionally recommend consistent engagement in aerobic exercise over no exercise.

This recommendation is based on very low to low certainty evidence suggesting improved physical function but moderate certainty evidence of no difference in pain. The recommendation is conditional because of the certainty of evidence and recognizing that patient preferences may vary due to RA disease activity level, the presence of joint damage or deformities, comorbidities, and the cost, access, or burden of engaging in consistent aerobic exercise.

We conditionally recommend consistent engagement in aquatic exercise over no exercise.

This recommendation is based on low certainty evidence of improvement in physical function but no difference in pain. The recommendation is conditional because of the certainty of evidence, variability in patient preferences related to comfort in water, cost, access, and burden.

We conditionally recommend consistent engagement in resistance exercise over no exercise.

This recommendation is based on very low to low certainty evidence of improvement in physical function (inferred from performance measures) and pain. The recommendation is conditional because of the certainty of evidence, variability in patient preferences related to joint damage or deformities that may limit participation, access, cost, and burden. The Voting Panel and Patient Panel emphasized the importance of appropriate prescription and supervision of resistance exercise by physical therapists or other qualified exercise professionals to prevent harm.

We conditionally recommend consistent engagement in mind-body exercise (yoga, Tai Chi, qigong) over no exercise.

This recommendation is based on very low to low certainty evidence of improvement in physical function but no difference in pain. The recommendation is conditional because of the certainty of evidence, variability in patient preferences, cost, access, and burden.

Rehabilitation recommendations (Table 4)

We conditionally recommend participation in comprehensive occupational therapy (OT) over no comprehensive OT.

We conditionally recommend participation in comprehensive physical therapy (PT) over no comprehensive PT.

These recommendations are conditional based on very low certainty evidence of improvement in pain and physical function, expected variability in patient preferences, burden, access, and cost. In these recommendations, comprehensive refers to the numerous different approaches and interventions that occupational therapists and physical therapists utilize in the assessment and management of people with RA. The comprehensive nature of these interventions also highlights the importance of identifying occupational therapists and physical therapists with expertise in tailoring these interventions to the management of RA through a shared decision-making approach. This recommendation applies throughout the RA disease course. Clinicians should discuss the opportunity to refer to OT and/or PT early in the RA disease course with the recognition that OT and/or PT interventions can be tailored to unique patient needs throughout the patient's experience with RA. Access to OT and PT services (e.g., availability, insurance coverage) may be a barrier to care. Interventions in the subsequent recommendation statements are often included in comprehensive OT and/or PT services.

For patients with hand involvement, we conditionally recommend performing hand therapy over no hand therapy exercises.

This recommendation is conditional based on low certainty evidence of pain reduction and improvement in physical function. Therapists and patients on the Voting Panel acknowledged that the evaluation of the unique needs of the person with RA with hand involvement may be best performed by an experienced hand therapist (e.g., a certified hand therapist (CHT) who is typically an occupational or physical therapist with additional training) who can guide the specific design and intensity of the intervention.

For patients with hand and/or wrist involvement and/or deformity, we conditionally recommend use of splinting, orthoses, and/or compression over no splinting, orthoses, and/or compression.

For patients with foot and/or ankle involvement, we conditionally recommend use of bracing, orthoses, and/or taping over no bracing, orthoses, and/or compression.

For patients with knee involvement, we conditionally recommend use of bracing and/or orthoses over no bracing and/or orthoses.

These recommendations are conditional based on very low certainty evidence of improvement in pain and physical function at the hand/wrist and foot/ankle. No studies pertaining to knee involvement met eligibility criteria. Although the Patient Panel discussed the discomfort and burden accompanying the periodic and regular use of these interventions, the Patient Panel and Voting Panel also recognized their potential to reduce pain and improve physical function. In addition, although these interventions are available without a prescription, the Voting Panel recommends their prescription and use under the guidance of an experienced occupational therapist or physical therapist to ensure appropriate item selection and fit.

We conditionally recommend use of joint protection techniques over no joint protection techniques.

This recommendation is conditional based on low certainty evidence of improvement in pain and function. Experienced healthcare professional guidance in joint protection techniques at various stages of a patient's experience with RA is vital for this intervention to aid the patient in maintaining physical function. The Voting Panel also stressed the importance of proper patient education in joint protection techniques by occupational or physical therapists.

We conditionally recommend use of activity pacing, energy conservation, activity modification, and/or fatigue management over no activity pacing, energy conservation, activity modification, and/or fatigue management.

There was no evidence found for this PICO question. However, these interventions are generally safe and may help preserve physical function and manage fatigue. Proper instruction in these approaches by occupational or physical therapists (e.g., ensuring no prolonged inactivity) as well as periodic reminders to employ them were suggested by the Patient Panel and Voting Panel.

We conditionally recommend use of assistive devices over no assistive devices.

We conditionally recommend use of adaptive equipment over no adaptive equipment.

We conditionally recommend use of environmental adaptations over no environmental adaptations.

In the absence of evidence addressing these PICO questions, a conditional recommendation was made in favor of using assistive devices/equipment because of the potential for meaningfully improving function and quality of life and the lack of known harms. The timing of the use of interventions,

guidance on intervention selection, and education on how to use these interventions should be considered. Involving an occupational or physical therapist can aid these processes and ensure patient safety. The Voting Panel recognized cost and burden as barriers to the use of these interventions.

For patients who are currently employed or want to become employed, we conditionally recommend use of vocational rehabilitation (training programs to support employment) over no vocational rehabilitation.

For patients who are currently employed or want to become employed, we conditionally recommend work site evaluations and/or modifications over no work site evaluations and/or modifications.

These recommendations were conditional based on the absence of evidence for vocational rehabilitation and low certainty evidence for work site evaluations and modifications. The Voting Panel recognized the following considerations in implementing worksite evaluations and modifications: 1) the employee/employer relationship regarding health-specific variables and confidentiality, 2) comfort with disclosure of RA to the employer, 3) the requirements of the Americans with Disabilities Act and the Family and Medical Leave Act, 4) the heterogeneity of employer resources and employee job responsibilities, and 5) the variable availability of experienced work and ergonomics specialists.

Diet recommendations (Table 5)

We conditionally recommend adherence to a Mediterranean-style diet over no formally defined diet.

The Mediterranean-style diet pattern emphasizes the intake of vegetables, fruits, whole grains, nuts, seeds, and olive oil; moderate amounts of low-fat dairy and fish; and limits added sugars, sodium,

highly processed foods, refined carbohydrates, and saturated fats. This recommendation is based on low to moderate certainty of evidence of improvement in pain and no difference in physical function or disease activity. The recommendation is conditional because of the evidence certainty, patient preferences, costs, access, and burden. The Voting Panel recognized the potential benefits of a Mediterranean-style diet for long-term health outcomes (e.g., longevity and cardiovascular disease) that are affected by RA disease activity and the evidence from studies in the general population (9,10). The expert role of a registered dietician as a member of the interprofessional team is recognized.

We conditionally recommend *against* adherence to a formally defined diet, other than a Mediterranean-style diet.

This recommendation is based on very low to moderate certainty evidence demonstrating no consistent, clinically meaningful benefit on physical function, pain, or disease activity specific to RA for formally defined diets other than a Mediterranean-style diet (listed in Table 1). In addition to the certainty of evidence, this recommendation is conditional because of the burden and costs that accompany adhering to a formally defined diet and patient preferences are expected to differ.

We conditionally recommend following established dietary recommendations without dietary supplements over adding dietary supplements.

This recommendation for RA management pertains to all dietary supplements considered (listed in Table 1) and is based on very low to moderate certainty evidence demonstrating no consistent, clinically meaningful benefit on physical function, pain, or disease activity specific to RA. The recommendation is conditional because of the certainty of evidence, expected variation in patient preferences, adequacy of nutrient intake through diet, lack of regulation (e.g., U.S. Food and Drug Administration), possibility of harm (e.g., interactions with medications, side effects), and costs. The

Voting Panel supported a “food first” approach but recognized the role dietary supplements may serve for bone (e.g., Vitamin D) and cardiovascular (e.g., fish oil) health, which are particularly important in people with RA (11). In this recommendation, established dietary recommendations refer to those produced by the U.S. Department of Agriculture and U.S. Department of Health & Human Services (12) and the American Heart Association (13). Recommendations on folic acid supplementation in the setting of treatment with methotrexate are included in the ACR’s pharmacologic treatment guidelines (1).

Body weight and weight loss

Given the broad spectrum of weight loss interventions, including lifestyle modification, commercial weight loss programs, pharmacologic therapies, and surgical interventions, the Voting Panel did not vote on recommendations regarding specific weight loss interventions in overweight or obese people with RA specifically for RA management. However, the Voting Panel was unanimous in its support of clinicians engaging in discussion about maintaining a healthy body weight for people with RA to optimize long-term RA and general health outcomes. In RA, obesity is associated with higher disease activity, impairments in physical function, and poorer treatment response, in addition to poor long-term health outcomes (14). General population recommendations on body weight classification and weight loss strategies, for those who are overweight or obese, can serve as a guide for these discussions (15,16).

Additional integrative intervention recommendations (Table 6)

We conditionally recommend use of a standardized self-management program over no standardized self-management program.

This recommendation is conditional based on low certainty evidence of improvement in physical function and pain. The Patient Panel described how these programs can be “life changing” and can provide motivation related to several factors that contribute to quality of life, including mental wellness

and psychological adaptation to disease experience. The availability of and access to these programs as well as their costs were noted as potential barriers.

We conditionally recommend use of cognitive behavioral therapy and/or mind-body approaches over no cognitive behavioral therapy and/or mind-body approaches.

This conditional recommendation is based on very low to low certainty evidence of no consistent improvement in pain and physical function (critical outcomes), but low to moderate certainty evidence of improvement in depression, anxiety, fatigue, and sleep (important outcomes). Although these interventions are beneficial for chronic disease management, access to experienced healthcare professionals, cost, and the burden of using these interventions were recognized barriers.

We conditionally recommend use of acupuncture over no acupuncture.

This recommendation for using acupuncture is conditional based on low certainty evidence of inconsistent improvements in pain and function. The Patient Panel generally found acupuncture to be of lower value than other considered interventions for RA management based on their disease experiences. For people with RA, the burden, cost, access, and invasiveness may impact the choice to use this intervention.

We conditionally recommend use of massage therapy over no massage therapy.

This recommendation for using massage therapy is conditional based on very low certainty evidence of improvement of pain. Massage therapy intensity and technique may affect a patient's experience; therefore, it is best delivered by a provider (e.g., massage therapist, physical therapist) with knowledge and experience of treating people with RA. Burden, cost, access, and short-term duration of benefit should be considered.

We conditionally recommend use of thermal modalities over no thermal modalities.

This recommendation for using thermal modalities, such as cryotherapy, heat, and therapeutic ultrasound, is conditional based on very low certainty evidence of improvement for pain and physical function. People with RA receive varying levels of benefit from thermal modalities, and patient preferences are expected to vary regarding the choice of a thermal modality. Persons with RA can control and administer many of these modalities at home, though others may benefit from guidance from an occupational or physical therapist.

We conditionally recommend *against* use of electrotherapy.

This recommendation *against* using electrotherapy modalities, such as transcutaneous electrical nerve stimulation (TENS) and neuro-muscular electrical nerve stimulation, for RA management is conditional based on low certainty evidence of no improvement of pain and physical function specific to RA. While some people with RA may receive benefit from these interventions (e.g., in the setting of comprehensive PT or OT), the Voting Panel recommended *against* electrotherapy because the evidence was not felt to outweigh the burden and costs.

No recommendation was made by the Voting Panel on the use of vagus nerve stimulation because this invasive procedure is not currently approved by the FDA for RA.

We conditionally recommend *against* use of chiropractic therapy.

In the absence of evidence, this recommendation *against* using chiropractic therapy (i.e., chiropractic spinal adjustment) directly for the management of RA is conditional because of the potential cervical spine complications that can occur in people with RA (17), Voting and Patient Panels' perceived lack of benefit specific to RA, burden, and costs.

Tobacco cessation

Due to existing clinical quality measures for tobacco use screening and cessation (18) and the absence of studies on tobacco cessation in RA that met eligibility criteria, the Voting Panel did not make further recommendations on individual tobacco cessation interventions for the specific management of RA beyond the clinical quality measures. The Voting Panel recognized the well-established harms of tobacco including detrimental effects on RA that include higher disease severity, poorer treatment response, and increased risk of poor long-term disease outcomes (19). Because of the trust that is frequently developed between people with RA and their clinicians and the low success rate of individual tobacco cessation counseling efforts (20), there was unanimous agreement that clinicians caring for people with RA serve an integral role in counseling on tobacco cessation (21).

DISCUSSION

This is the first ACR guideline on the use of exercise, rehabilitation, diet, and additional integrative interventions in conjunction with DMARDs for RA management. This guideline highlights the importance of an interprofessional healthcare team to provide optimal care to people with RA. The recommended interventions do not replace DMARD treatments in accordance with existing ACR pharmacologic treatment guidelines (1) but are intended to be integrated into the comprehensive management of people with RA. The recommended interventions in this new guideline intended to augment DMARD therapy were considered specifically for their efficacy for the management of RA outcomes, rather than other general health benefits or alternative medical indications. The guideline is meant to increase patient and clinician awareness, provide evidence to inform shared decision-making, improve access to the recommended interventions, and inspire much-needed future research in this area to generate higher-certainty evidence for the management of RA.

The one strong recommendation was for consistent engagement in exercise. Recommendations for exercise include multiple types (aerobic, aquatic, resistance, mind-body), which is consistent with physical activity guidelines produced by the U.S. Department of Health and Human Services (8). The specific type, frequency, intensity, and duration of exercise should be tailored to each person with the assistance of their clinicians, considering the potential burden on and capacity of each person (22). The U.S. recommendations on exercise and physical activity can serve as a guide to clinicians counseling patients (8). Because symptoms and consequences of RA may impact participation (23), more personalized exercise prescription and monitoring may be needed with the assistance of physical therapists and/or clinical exercise physiologists.

Several rehabilitation interventions as well as comprehensive OT and PT were recommended for their benefits on pain, physical function, preserving independence, remaining in work, and safety, although the certainty of evidence was low or very low. The Patient Panel consistently emphasized the importance of receiving interventions from occupational and/or physical therapists to ensure proper use and their desire for referrals to occupational and physical therapists earlier in the disease course. Early referral to these services can educate people with RA how to continue interventions independently (e.g., exercise, joint protection, energy conservation, assistive and adaptive devices) to self-manage their disease. Ensuring a sufficient workforce of occupational and physical therapists well-versed in the management of RA and access to this care are high priorities.

Dietary patterns and quality have been associated with RA risk and severity in many, though not all, epidemiologic studies (24). Of several diets evaluated in this guideline (e.g., vegan, anti-inflammatory, elimination), only a Mediterranean-style diet had sufficient evidence to be recommended, given the burden and costs that accompany adhering to a formally defined diet. Dietary supplements were heavily debated by the Voting Panel. Ultimately, there was not sufficient evidence to

recommend their use for RA management. The Voting Panel supported a “food first” approach, which emphasizes using high-quality foods to obtain necessary nutrients. Although no recommendation was made on weight loss interventions, the Voting Panel was unanimous in its support for maintaining a healthy body weight. Rheumatology clinicians should consider involving registered dietitians to assist people with RA who desire to modify their diet as part of their RA management plan.

Additional integrative interventions that were conditionally recommended included standardized self-management programs, CBT and mind body approaches, acupuncture, massage therapy, and thermal modalities. Although the evidence supporting these interventions was of very low to low certainty, these interventions possess few harms and a modest burden for many people. The Patient Panel favored standardized self-management, CBT, mind body approaches, and thermal modalities because these interventions allowed them to better cope with the chronic disease aspects of RA and/or they offered a management option that could be controlled independently, often at home.

People with RA who currently use tobacco should be supported in their tobacco cessation journey. The limited efficacy of counseling on tobacco cessation (20) illustrates why it is critical for all members of the interprofessional care team to engage in this practice, which is an existing clinical quality measure (25). There was not sufficient evidence to establish more specific recommendations for RA.

A broad range of interventions was considered in this guideline. It is unlikely that one clinician will possess the necessary expertise in all these areas, which illustrates the importance of assembling an interprofessional healthcare team to best support people with RA. The Patient Panel emphasized that rheumatology clinicians (e.g., physicians, physician assistants, nurse practitioners) are most often their first contact for therapeutic decisions. Thus, it was important to patients that their rheumatology clinician(s) be knowledgeable about integrative therapies and help guide patients to other professionals

with relevant expertise (e.g., physical and occupational therapists, dieticians, clinical exercise physiologists, psychologists, massage therapists, acupuncturists,) early in the disease course, so they can be involved in shared-decision making throughout the disease course.

RA is a chronic disease that imposes considerable costs to affected persons and society (26,27). The recommended interventions in this guideline are variably covered by health insurance, and many of the costs become the responsibility of the person with RA. We encourage health policymakers to support the coverage of these interventions to support an integrative and comprehensive approach to the management of RA. The availability of and access to these interventions was a concern of both the Patient Panel and Voting Panel, particularly for underserved populations. Improving access to and ensuring high-quality delivery of these interventions across diverse settings are important endeavors to support. In addition, the Voting Panel acknowledged that patients and/or clinicians may have implicit and/or explicit biases regarding interventions that may make them reluctant to recommend or use these interventions (28). While the evidence-based approach used in this guideline can help overcome such biases, clinicians should consider whether such biases may exist and work to reduce them.

The majority of recommendations were conditional in part because of low certainty evidence. Several factors contributed to the low certainty grading, including: 1) the limited number of studies evaluating relevant interventions; 2) lack of blinding and study attrition; 3) small sample sizes resulting in imprecision; and 4) heterogeneity of study designs (e.g., various interventions [comprehensive therapy vs. an individual component], comparators, and outcomes) that prevented pooling results through a formal meta-analysis. Many of these issues are inherent to research evaluating the considered interventions (e.g., exercise, diet). These conditional recommendations indicate that clinicians should engage in shared decision-making with patients when deciding whether to use these interventions. The low or very low certainty evidence supporting most recommendations calls for prioritizing research into

these interventions and prompted a proposed research agenda (**Table 7**). Key items include determining the efficacy, safety, optimal timing, mode of delivery, and personalization of these interventions.

There are limitations to the development of these guidelines. Studies that were conducted prior to more recent treatment eras (characterized by early diagnosis and a treat-to-target approach) were included in the evidence report and may be less generalizable than more recently completed studies. Although broad expertise was recruited and an extensive list of interventions was considered in this guideline, we could not ensure expertise in every area of integrative RA management or consider all possible integrative interventions. For example, members of the Patient Panel inquired about cannabinoids given the rising prevalence of their use in rheumatic diseases (29,30). Cannabinoids were not included in this guideline, and emerging evidence for cannabidiol, a pharmacologic therapy that is not FDA-approved for RA, is being synthesized in a living systematic review through a joint U.S. Department of Veterans Affairs and Center for Evidence-Based Policy at Oregon Health & Sciences University (31). Different modes of delivering interventions (e.g., telehealth vs. in-person) were not assessed, as this was beyond the scope of this project.

In summary, this guideline outlines initial recommendations on the management of RA with exercise, rehabilitation, diet, and additional integrative interventions. These recommendations complement existing pharmacologic treatment guidelines that instruct on the use of DMARDs and, together, can guide a shared decision-making approach between persons with RA and clinicians. Interprofessional treatment teams are crucial to implementing these recommendations. The generally low-quality evidence highlights the need for well-designed studies in the area of integrative management of RA. Policy efforts are needed to ensure access to recommended interventions for people with RA from diverse backgrounds and settings. Together, the integrative and pharmacologic

guidelines support the comprehensive management of RA in pursuit of optimal outcomes for people living with RA.

ACKNOWLEDGEMENTS

We thank the patients who (along with authors Deb Constien, Eileen Davidson, and Lawrence “Rick” Phillips) participated in the Patient Panel meeting: Grace M. Becker, Denise Cedar, Judith Flanagan, Carolyn R. Mason, Eileen Julie O’Rourke, Catherine Simons, Sharon A. Sharp, and Sumayya Spencer. We thank the ACR staff, including Regina Parker for assistance in coordinating the administrative aspects of the project and Cindy Force for assistance with manuscript preparation. We thank Janet Waters for her assistance in developing the literature search strategy, as well as performing the initial literature search and update searches. We thank Theresa Wampler Muskardin and Karen Smarr for their thoughtful review and feedback during the project.

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Tables

Table 1. Descriptions and examples of interventions included in the integrative management of rheumatoid arthritis guideline.

Intervention	Description and/or examples
<i>Exercise</i>	
Physical activity	Movement of the body requiring energy expenditure.
Exercise	Performance of physical activity in regular and structured manner to improve fitness and health.
Aerobic exercise	Exercise intended to improve cardiorespiratory fitness and muscular endurance. Examples include walking, biking or cycling, running, hiking, aerobics, rowing, swimming, using an elliptical.
Aquatic exercise	Exercise performed in water, containing elements of both aerobic and resistance exercise. Examples include swimming, water aerobics, water walking or jogging.
Resistance exercise	Exercise intended to increase muscular strength. Examples include free weights, weight machines, resistance bands, Pilates.
Mind-body exercise	Exercise that combines movement, mental focus, and controlled breathing. Examples include yoga, Tai Chi, Qigong.
<i>Rehabilitation</i>	
Comprehensive occupational therapy	Evaluation and treatment by Occupational Therapist with the goal of increasing physical function and participation. Receives patient-centered individualized treatment. Components of OT services vary and may include arthritis education, ADL evaluation and training, joint protection, activity pacing, work simplification and fatigue management, exercise (particularly for the hand and arm), splinting/orthotics, provision of assistive/adaptive devices, environmental adaptations, work and leisure counselling/rehabilitation, work-site assessment, sexual advice, relaxation, and pain and stress management training.
Comprehensive physical therapy	Evaluation and treatment by a physical therapist. Components of PT services will vary and should include exercise. May also include functional training and physical activity, energy conservation, workplace accommodations, mobility and gait training, manual therapy, self-management education, electrotherapy, application of orthoses, instruction in assistive devices, pain-management including thermal therapy.
Hand therapy exercises	Exercises of the hand to improve mobility and strength.
Bracing and orthoses	Devices to correct and support musculoskeletal function, improve joint alignment, or protect the joint. Examples include wrist and finger splints, foot or knee orthoses, compression gloves, taping.

Intervention	Description and/or examples
Joint protection techniques	Self-management approach that aims to maintain function by providing people with ways to alter work methods and movement patterns of affected joints to reduce pain, inflammation, and joint stress. Examples include changing the way of performing activities to avoid pain, resting, using alternative muscle groups.
Activity pacing	Balancing activity and rest to accomplish activities. Includes activity pacing, energy conservation, activity modification, fatigue management techniques.
Assistive devices	Devices to assist with mobility. Examples include crutches, canes, walkers, wheelchairs, tricycles, scooters.
Adaptive equipment	Devices to assist with activities of daily living. Examples include built up and/or long handled equipment, sock aide, button hook, reachers, pill cutters, cell phone holders.
Environmental adaptations	Adapting environment to improve safety. Examples include adaptations for toileting (raised toilet seat, commode, toilet safety rail), showering (tub seat, handheld shower, walk in bath), grab bars, ramps, stair lifts, home modification.
Vocational rehabilitation	Training programs to overcome barriers preventing successful employment.
Work site evaluation and modifications	Evaluating and adjusting work-site conditions and duties for safety and well-being.
<i>Dietary</i>	
Formally defined diet	Specific formally defined diets evaluated in this guideline were: anti-inflammatory, Mediterranean-style, ketogenic, paleo, gluten-free, vegetarian, vegan, intermittent fasting, elemental, elimination, raw foods, whole food plant-based.
Mediterranean-style diet	Diet pattern that emphasizes intake of vegetables, fruits, whole grains, nuts, seeds, and olive oil; moderate amounts of low-fat dairy and fish; and limits added sugars, sodium, highly processed foods, refined carbohydrates, and saturated fats.
Dietary supplement	Substances used to add nutrients, botanicals, herbs, or microbials (probiotics) to the diet. Specific supplements evaluated in this guideline were vitamin D, probiotics, fish oil and omega fatty acids, antioxidants (selenium, zinc, vitamin A, vitamin C, vitamin E), turmeric, glucosamine, γ -linolenic acid, borage seed oil, evening primrose oil, black currant seed oil, selenium, Boswellia, ginger.
Weight loss	Intentional loss of body weight. Examples include lifestyle modification through diet and/or exercise, support groups, health coaching, medically-supervised weight loss programs, branded dietary weight loss programs, weight loss surgery.
<i>Additional integrative therapies</i>	

Intervention	Description and/or examples
Self-management program	Standardized program to guide self-management. Examples include Arthritis Self-Management Program, Chronic Disease Self-Management Program, Better Choices Better Health, Tomando Control de su Salud, RA Self-Management Intervention, OPERAS (an On-demand Program to Empower Active Self-management).
Cognitive behavioral therapy	Psychological therapy to identify and change thought and behavior patterns.
Mind-body approaches	Practices engaging both mind and body functions. Examples include biofeedback, goal setting, meditation, mindfulness, breathing exercises, progressive muscle relaxation, guided imagery.
Acupuncture	Stimulation of specific body points through insertion of thin needles.
Massage therapy	Rubbing and kneading of muscles and joints with the hands. Examples include Swedish, Deep Tissue, Trigger Point.
Thermal modalities	Use of heat and cold for medical treatment. Examples include cryotherapy, heat, therapeutic ultrasound, infrared sauna, paraffin therapy, and laser therapy.
Electrotherapy	Use of electrical energy for medical treatment. Examples include transcutaneous electrical nerve stimulation (TENS), neuromuscular electrical nerve stimulation (NMES).
Vagal nerve stimulation	Implantation of a device to stimulate the vagus nerve with electrical impulses.
Chiropractic	Diagnosis and manipulation of malaligned joints, particularly the spine.
Tobacco cessation	Counseling on tobacco cessation, tobacco cessation programs (phone, mobile applications), nicotine replacement therapies, tobacco cessation medications without nicotine.

Abbreviations: ADL, activities of daily living; OT, occupational therapy; PT, physical therapy

Table 2. Guiding principles.

Integrative Rheumatoid Arthritis Guideline Guiding Principles
Rheumatoid arthritis is a chronic, systemic, inflammatory condition that requires early diagnosis, evaluation, and management to achieve optimal outcomes.
Rheumatoid arthritis should be treated with disease-modifying anti-rheumatic drugs and follow a treat-to-target management strategy, as detailed in the 2021 American College of Rheumatology (ACR) Rheumatoid Arthritis Pharmacologic Treatment Guidelines (1).
Persons with chronic diseases, like rheumatoid arthritis, seek many available therapies to maintain physical function, reduce pain, and improve their quality of life.
Treatment decisions should follow a shared decision-making process. Persons with rheumatoid arthritis present with a variety of manifestations and experiences.
Optimum rheumatoid arthritis treatment outcomes are achieved through interprofessional teams providing expert patient-centered care.
Recommendations assume no contraindications to listed management strategies.
Recommendations pertain to rheumatoid arthritis management. Recommendations do not pertain to clinical situations when patients have alternative indications for listed treatments. Other general health benefits may exist for listed treatments.
Surgical interventions are not included in this guideline because there are other guideline efforts that address large joint replacement, and small joint surgeries are not frequently a part of the current management of rheumatoid arthritis.
Disease activity and disease activity levels refer to those calculated using an ACR-endorsed RA disease activity measure (2).

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Table 3. Exercise recommendations for the management of rheumatoid arthritis.

Recommendation	Certainty of Evidence	Based on the Evidence Report of the Following PICO(s)	Page no(s) of Evidence Table(s) in Suppl. App. 3*
We strongly recommend consistent engagement in exercise is over no exercise.	Moderate	4-7	203-347
We strongly recommend consistent engagement in aerobic exercise over no exercise.	Very low to Low	4	203-245
We conditionally recommend consistent engagement in aquatic exercise over no exercise.	Low	5	246-263
We conditionally recommend consistent engagement in resistance exercise over no exercise.	Very low	6	264-320
We conditionally recommend consistent engagement in mind-body exercise over no exercise.	Very low to low	7	321-347

* [Insert link to Supplementary Appendix 3 on journal website – TBD](#)

Intervention definitions and examples are provided in Table 1.

Table 4. Rehabilitation interventions for the management of rheumatoid arthritis.

Recommendation	Certainty of Evidence	Based on the Evidence Report of the Following PICO(s)	Page no(s) of Evidence Table(s) in Suppl. App. 3*
We conditionally recommend participation in comprehensive occupational therapy over no comprehensive occupational therapy.	Very low	17	412-430
We conditionally recommend participation in comprehensive physical therapy over no comprehensive physical therapy.	Very low	18	431-446
For patients with hand involvement, we conditionally recommend performing hand therapy exercises over no hand therapy exercises.	Low	8	348-371
For patients with hand and/or wrist involvement and/or deformity, we conditionally recommend use of splinting, orthoses, and/or compression over no splinting, orthoses, and/or compression.	Very low	9	372-379
For patients with foot and/or ankle involvement, we conditionally recommend use of bracing, orthoses, and/or taping over no bracing, orthoses, and/or compression.	Very low	10	380-401
For patients with knee involvement, we conditionally recommend use of bracing and/or orthoses over no bracing and/or orthoses.	No studies met eligibility criteria	11	402
We conditionally recommend use of joint protection techniques over no joint protection techniques.	Low	12	403-406

We conditionally recommend use of activity pacing, energy conservation, activity modification, and/or fatigue management over no activity pacing, energy conservation, activity modification, and/or fatigue management.	No studies met eligibility criteria	13	408
We conditionally recommend use of assistive devices over no assistive devices.	No studies met eligibility criteria	14	409
We conditionally recommend use of adaptive equipment over no adaptive equipment.	No studies met eligibility criteria	15	410
We conditionally recommend use of environmental adaptations over no environmental adaptations.	No studies met eligibility criteria	16	411
For patients who are currently employed or desire to become employed, we conditionally recommend use of vocational rehabilitation over no work interventions.	No studies met eligibility criteria	21	503
For patients who are currently employed or desire to become employed, we conditionally recommend work site evaluations and/or modifications over no work site evaluations and/or modifications.	Low	22	504-517

* [Insert link to Supplementary Appendix 3 on journal website – TBD](#)

Intervention definitions and examples are provided in Table 1.

Table 5. Diet recommendations for the management of rheumatoid arthritis.

Recommendation	Certainty of Evidence	Based on the Evidence Report of the Following PICO(s)	Page no(s) of Evidence Table(s) in Suppl. App. 3*
We conditionally recommend adherence to a Mediterranean-style diet over no formally defined diet.	Low to moderate	1	8-78
We conditionally recommend <i>against</i> adherence to a formally defined diet, other than Mediterranean-style.	Very low to moderate	1	8-78
We conditionally recommend following established dietary recommendations without dietary supplements over adding dietary supplements.	Very low to moderate	2	79-193

* [Insert link to Supplementary Appendix 3 on journal website – TBD](#)

Intervention definitions and examples are provided in Table 1.

Table 6. Additional integrative interventions for the management of rheumatoid arthritis.

Recommendation	Certainty of Evidence	Based on the Evidence Report of the Following PICO(s)	Page no(s) of Evidence Table(s) in Suppl. App. 3*
We conditionally recommend use of a standardized self-management program over no standardized self-management program.	Low	19	447-459
We conditionally recommend use of cognitive behavioral therapy and/or mind-body approaches over no cognitive behavioral therapy and/or mind-body approaches.	Very low to low	20	460-503
We conditionally recommend use of acupuncture over no acupuncture.	Low	23	511-531
We conditionally recommend use of massage therapy over no massage therapy.	Very low	24	532-536
We conditionally recommend use of thermal modalities over no thermal modalities.	Very low	25	537-556
We conditionally recommend <i>against</i> using electrotherapy.	Low	26	557-565
We conditionally recommend <i>against</i> using chiropractic therapy.	No studies met eligibility criteria	27	566

* [Insert link to Supplementary Appendix 3 on journal website – TBD](#)

Intervention definitions and examples are provided in Table 1.

Table 7. Research agenda for the integrative management of rheumatoid arthritis.

Evaluate the efficacy and safety of integrative therapies for the management of RA. Initial evidence is needed in the areas of activity pacing, energy conservation, activity modification, fatigue management, and vocational rehabilitation. Additional strong evidence from larger, well-designed studies is needed in all other areas.
Determine the appropriate timing of different integrative interventions in the RA disease course.
Examine the delivery, education, and implementation of integrative interventions. For example, evaluating various methods of instruction and training of joint protection and activity pacing interventions.
Establish the cost-effectiveness of different integrative interventions and develop approaches for cost-effective delivery.
Identify barriers to the adoption and implementation of integrative therapies. These may include variability in access, costs, and implicit and/or explicit biases.
Describe the assembly of, communication between, and role delineation among the interprofessional care team delivering pharmacologic and integrative interventions.
Improve access to experienced healthcare professionals who provide integrative interventions.
Determine efficacy and safety of integrative interventions based on RA disease manifestations and pharmacologic therapies, e.g., modifying exercise interventions based on disease activity level or diet based on disease-modifying anti-rheumatic drugs utilized.
Tailor interventions (and their delivery) studied in the general population to persons with RA, e.g., tobacco cessation programs, exercise programs, and weight loss.
Define efficacy and safety of therapies not included in this guideline such as cannabidiol, vaping, and occupational exposures and protections as well as emerging therapies such as vagal nerve stimulation.
Evaluate dietary supplements (especially Vitamin D and Omega-3 fatty acids such as “fish oil”) in the context of dietary intake. The assessment and implementation of diets should focus on being inclusive of different cultures.
Develop vocational rehabilitation programs and work site modifications that improve the ability of persons with RA to work without negative stigma in the workplace.
Establish the efficacy and safety of integrative therapies on extra-articular manifestations and long-term RA-related outcomes. In addition to disease activity, physical function, pain, and quality of life outcomes considered in this guideline, other outcomes that should be

considered are longevity, cardiovascular disease, lung disease, cancer, osteoporosis, and infection.

Develop research methodology to study integrative therapies, e.g., defining an adequate control intervention. Publication of research standards for integrative therapies relevant to RA to guide research efforts.

Establish dedicated funding from organizations to study integrative RA therapies and their implementation.