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



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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 antirheumatic 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 individuals 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.

Conclusion. 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.

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 individuals with RA (1-4). In addition to pharmacologic interventions, individuals 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 individuals 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://rheumatology.org/clinical-practice-guidelines), which includes GRADE methodology (5,6) and adheres to AGREE criteria (7). Supplementary Appendix 1 (available on the *Arthritis Care & Research* website at https://onlinelibrary.wiley.com/doi/10.1002/acr.25117) includes a detailed description of the methods. Briefly, the Core Leadership

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Team (BRE, BJS, NAB, JLB, CAO, and 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, https://onlinelibrary.wiley.com/doi/10.1002/acr. 25117). 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, https://onlinelibrary.wiley.com/doi/10.1002/acr.25117). 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 (JLB) 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

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Table 1. Descriptions and exar	mples of interventions included in the integrative management of rheumatoid arthritis guideline
Intervention	Description and/or examples
Exercise Physical activity Exercise Aerobic exercise	Movement of the body requiring energy expenditure. Performance of physical activity in regular and structured manner to improve fitness and health. Exercise intended to improve cardiorespiratory fitness and muscular endurance. Examples include walking,
Aquatic exercise	biking or cycling, running, hiking, aerobics, rowing, swimming, using an elliptical machine. Exercise performed in water, containing elements of both aerobic and resistance exercise. Examples include
Resistance exercise	swimming, water aerobics, water walking or jogging. 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.
Rehabilitation Comprehensive occupational therapy	Evaluation and treatment by an occupational therapist with the goal of increasing physical function and participation. Receives patient-centered individualized treatment. Components of occupational therapist services vary and may include arthritis education, activities of daily living 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 counseling/rehabilitation, work site assessment, sexual advice, relaxation, pain and stress
Comprehensive physical therapy	management training. Evaluation and treatment by a physical therapist. Components of physical therapist 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 Bracing and orthoses	Exercises of the hand to improve mobility and strength. 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.
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, use of alternative muscle groups.
Activity pacing	Balancing activity and rest to accomplish activities. Includes activity pacing, energy conservation, activity modification, fatigue management techniques.
Assistive devices Adaptive equipment	Devices to assist with mobility. Examples include crutches, canes, walkers, wheelchairs, tricycles, scooters. 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 Work site evaluation and modifications	Training programs to overcome barriers preventing successful employment. Evaluating and adjusting work site conditions and duties for safety and well-being.
Dietary Formally defined diet	Specific diets include antiinflammatory, Mediterranean-style, ketogenic, paleo, gluten-free, vegetarian, vegan,
Mediterranean-style diet	intermittent fasting, elemental, elimination, raw foods, whole food plant-based. 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 to 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 include vitamin D, probiotics, fish oil and omega fatty acids, antioxidants (selenium, zinc, vitamin A, vitamin C, vitamin E), turmeric, glucosamine, y-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.
Additional integrative therapies 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, Rheumatoid Arthritis Self-Management Intervention, OPERAS (an On-demand Program to Empower Active Self-management).
Cognitive behavioral therapy Mind-body approaches	Psychological therapy to identify and change thought and behavior patterns. Practices engaging both mind and body functions. Examples include biofeedback, goal setting, meditation, mindfulness, breathing exercises, progressive muscle relaxation, guided imagery.

Table 1. (Cont'd)

Intervention	Description and/or examples
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, laser therapy.
Electrotherapy	Use of electrical energy for medical treatment. Examples include transcutaneous electrical nerve stimulation (TENS), neuro-muscular 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 (via telephone, mobile applications), nicotine-replacement therapies, tobacco cessation. medications without nicotine.

Core Leadership Team, Literature Review Team, Voting Panel, and Patient Panel are included in Supplementary Appendix 4 (https://onlinelibrary.wiley.com/doi/10.1002/acr.25117). 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 ≥70% agreement on both directions (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

Nine 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, https://onlinelibrary.wiley.com/doi/10.1002/acr. 25117). After screening, 275 manuscripts were mapped to ≥1 PICO

question (see flow diagram in Supplementary Appendix 6, https://onlinelibrary.wiley.com/doi/10.1002/acr.25117). The literature review did not identify any evidence to indicate fulfillment of the eligibility criteria for 29% (8 of 28) of the PICO questions.

Exercise recommendations (Table 3)

We strongly recommend consistent engagement in exercise over no exercise.

We recommend consistent engagement in exercise over no exercise based on moderate certainty evidence suggesting that regular exercise results in improved physical function and pain in

Table 2. Guiding principles for the integrative management of rheumatoid arthritis*

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 antirheumatic drugs and follow a treat-to-target management strategy, as detailed in the 2021 ACR Rheumatoid Arthritis Pharmacologic Treatment Guidelines (1).

Individuals 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. Individuals 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 in which 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 rheumatoid arthritis disease activity measure (32).

^{*} ACR = American College of Rheumatology.

individuals with RA. 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.

We recommend consistent engagement in aerobic exercise based on very low to low certainty evidence suggesting that it results in improved physical function but moderate certainty evidence suggesting there is no difference in pain. The recommendation is conditional because of the level of certainty of the 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 of, access to, or burden of engaging in consistent aerobic exercise.

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

We recommend consistent engagement in aquatic exercise based on low certainty evidence to indicate that it results in improvement in physical function but no difference in pain. The recommendation is conditional because of the level of certainty of the evidence, the variability in patient preferences related to comfort in engaging in water activities, and the variations in the cost of, access to, and burden of aquatic exercise.

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

We recommend consistent engagement in resistance exercise based on very low to low certainty evidence to indicate that it results in improvement in physical function (inferred from performance measures) and pain. The recommendation is conditional

because of the level of certainty of the evidence, variability in patient preferences related to joint damage or deformities that may limit participation, and variations in the access to, cost of, and burden of resistance exercise. 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 over no exercise.

We recommend consistent engagement in mind-body exercise (e.g., yoga, Tai Chi, Qigong) based on very low to low certainty evidence suggesting that it results in improved physical function but no difference in pain. The recommendation is conditional because of the level of certainty of the evidence, variability in patient preferences, and variations in the cost of, access to, and burden of this type of activity.

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.

We conditionally recommend that individuals with RA participate in comprehensive OT and PT based on very low certainty evidence to indicate that it results in improvement in pain and physical function, expected variability in patient preferences, and variations in the burden of, access to, and cost of these approaches. 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 individuals 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

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

Recommendation	Certainty of evidence	PICO questions used for the Evidence Report	Evidence Summary page nos. in Supplementary Appendix 3†
We strongly recommend consistent engagement in exercise over no exercise.	Moderate	4–7	194–344
We conditionally recommend consistent engagement in aerobic exercise over no exercise.	Very low to low	4	194–242
We conditionally recommend consistent engagement in aquatic exercise over no exercise.	Low	5	243–260
We conditionally recommend consistent engagement in resistance exercise over no exercise.	Very low	6	261–317
We conditionally recommend consistent engagement in mind-body exercise over no exercise.	Very low to low	7	318–344

^{*} Intervention definitions and examples are provided in Table 1. PICO = Population, Intervention, Comparator, and Outcome.

[†] Available on the Arthritis Care & Research website at https://onlinelibrary.wiley.com/doi/10.1002/acr.25117.

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

Recommendation	Certainty of evidence	PICO questions for the Evidence Report	Evidence Summary page nos. in Supplementary Appendix 3†
We conditionally recommend participation in comprehensive occupational therapy over no comprehensive occupational therapy.	Very low	17	409–427
We conditionally recommend participation in comprehensive physical therapy over no comprehensive physical therapy.	Very low	18	428–443
For patients with hand involvement, we conditionally recommend performing hand therapy exercises over no hand therapy exercises.	Low	8	345–368
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	369-376
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	377–398
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	399
We conditionally recommend use of joint protection techniques over no joint protection techniques.	Low	12	400–404
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	405
We conditionally recommend use of assistive devices over no assistive devices.	No studies met eligibility criteria	14	406
We conditionally recommend use of adaptive equipment over no adaptive equipment.	No studies met eligibility criteria	15	407
We conditionally recommend use of environmental adaptations over no environmental adaptations.	No studies met eligibility criteria	16	408
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	500
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	501–507

^{*} Intervention definitions and examples are provided in Table 1. PICO = Population, Intervention, Comparator, and Outcome.

shared decision-making approach. This recommendation applies throughout the RA disease course. Clinicians should discuss the opportunity to refer the patient 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 performance of hand therapy over no hand therapy exercises.

We conditionally recommend that RA patients with hand involvement undergo hand therapy exercises based on low

certainty evidence indicating that hand therapy results in pain reduction and improvement in physical function. Therapists and patients on the Voting Panel acknowledged that the evaluation of the unique needs of the RA patient with hand involvement may be best performed by an experienced hand therapist (e.g., a certified hand therapist, 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.

[†] Available on the Arthritis Care & Research website at https://onlinelibrary.wiley.com/doi/10.1002/acr.25117.

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

We conditionally recommend use of splinting, orthoses, and/or compression among individuals with hand/wrist involvement, use of bracing, orthoses, and/or taping among individuals with foot/ankle involvement, and use of bracing and/or orthoses among individuals with knee involvement. These recommendations are based on very low certainty evidence to indicate that these approaches improve pain and physical function at the hand/wrist and foot/ankle. No studies pertaining to the use of these approaches for patients with knee involvement met the 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.

We conditionally recommend use of joint protection techniques based on low certainty evidence to indicate that it results in improved 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, in order 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 to support the conditional recommendation that individuals with RA should use activity pacing, energy conservation, activity modification, and/or fatigue management. 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 recommendations for the use of assistive devices, adaptive equipment, or environmental adaptations for RA patients, a conditional recommendation was made in favor of using assistive devices/equipment because of the potential for meaningfully improving the 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.

In the absence of evidence to support use of vocational rehabilitation and low certainty evidence for use of work site evaluations and modifications, we conditionally recommend use of these approaches. The Voting Panel recognized that the following factors should be considered in implementing work site evaluations and modifications: 1) the employee/employer relationship regarding health-specific variables and confidentiality, 2) the patient's 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 and the intake of moderate amounts of low-fat dairy and fish, and limits the use of added sugars, sodium, highly processed foods, refined carbohydrates, and saturated fats. We conditionally recommend adherence to a Mediterranean-style diet 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 level of certainty of the evidence, patient preferences, and costs of, access to, and burden associated with this type of diet. 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.

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

Recommendation	Certainty of evidence	PICO questions for the Evidence Report	Evidence Summary page nos. in Supplementary Appendix 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	79–190

^{*} Intervention definitions and examples are provided in Table 1. PICO = Population, Intervention, Comparator, and Outcome.

We conditionally recommend against adherence to a formally defined diet, other than the Mediterranean-style diet, based on very low to moderate certainty evidence demonstrating no consistent, clinically meaningful benefit from following other formally defined diet strategies (other than a Mediterranean-style diet) on physical function, pain, or disease activity specific to RA (see Table 1). In addition to the level of certainty of the 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 use of dietary supplements over adding dietary supplements.

We conditionally recommend following established dietary recommendations without the use of dietary supplements for RA management. This recommendation pertains to all dietary supplements considered (as listed in Table 1) and is based on very low to moderate certainty evidence demonstrating no consistent, clinically meaningful benefit from adding dietary supplements with regard to physical function, pain, or disease activity specific to RA. The recommendation is conditional because of the level of certainty of the evidence, expected variation in patient preferences, adequacy of nutrient intake through diet, lack of regulation (e.g., by the US 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 health (e.g., fish oil), which are particularly important in individuals with RA (11). In this recommendation, established dietary recommendations refer to those produced by the US Department of Agriculture and US Department of Health and 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 weight loss interventions specifically for RA management in overweight or obese people with RA. However, the Voting Panel was unanimous in its support of clinicians engaging in discussion about maintaining a healthy body weight for individuals with RA, in order 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.

We conditionally recommend that RA patients use a standardized self-management program based on low certainty evidence to indicate that it results in improved 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.

We conditionally recommend use of cognitive behavioral therapy and/or mind-body approaches based on very low to low certainty evidence indicating 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) when individuals with RA use these approaches. Although these interventions are beneficial for chronic disease management, access to

[†] Available on the Arthritis Care & Research website at https://onlinelibrary.wiley.com/doi/10.1002/acr.25117.

Table 6. Additional integrative interventions for the management of rheumatoid arthritis*			
Recommendation	Certainty of evidence	PICO questions for the Evidence Report	Evidence Summary page nos. in Supplementary Appendix 3†
We conditionally recommend use of a standardized self-management program over no standardized self-management program.	Low	19	445–456
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	457–500
We conditionally recommend use of acupuncture over no acupuncture.	Low	23	508-528
We conditionally recommend use of massage therapy over no massage therapy.	Very low	24	529-533
We conditionally recommend use of thermal modalities over no thermal modalities.	Very low	25	534–553
We conditionally recommend <i>against</i> using electrotherapy.	Low	26	554–562
We conditionally recommend <i>against</i> using chiropractic therapy.	No studies met eligibility criteria	27	563

experienced healthcare professionals, cost, and the burden of using these interventions were recognized barriers.

We conditionally recommend use of acupuncture over no acupuncture.

We conditionally recommend use of acupuncture based on low certainty evidence indicating 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 individuals with RA, the burden, cost, access, and invasiveness of acupuncture may impact the choice to use this intervention.

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

We conditionally recommend use of massage therapy based on very low certainty evidence that it results in 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 of and experience in 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.

We conditionally recommend use of thermal modalities, such as cryotherapy, heat, and therapeutic ultrasound, based on very low certainty evidence indicating that it results in improvement in pain and physical function. Individuals with RA receive varying levels of benefit from thermal modalities, and patient preferences are expected to vary with regard to the choice of a thermal modality. Individuals 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 electrotherapy.

We conditionally recommend against use of electrotherapy modalities, such as transcutaneous electrical nerve stimulation (TENS) and neuro-muscular electrical nerve stimulation, for RA management, based on low certainty evidence indicating that there is no improvement of pain and physical function specific to RA with these modalities. While some individuals 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 as an intervention in RA.

We conditionally recommend against use of chiropractic therapy.

In the absence of evidence, we conditionally recommend against use of chiropractic therapy (i.e., chiropractic spinal adjustment) directly for the management of RA because of the potential cervical spine complications that can occur (17). The Voting Panel and Patient Panel perceived a lack of benefit from chiropractic therapy specifically for RA, and indicated that this approach carries a perceived 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 (those meeting the 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

^{*} Intervention definitions and examples are provided in Table 1. PICO = Population, Intervention, Comparator, and Outcome.

[†] Available on the Arthritis Care & Research website at https://onlinelibrary.wiley.com/doi/10.1002/acr.25117.

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 RA patients and their clinicians and the low success rate of individual tobacco cessation counseling efforts (20), there was unanimous agreement that clinicians caring for individuals 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 individuals 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 individuals with RA. The recommended interventions in this new guideline, which are intended to augment DMARD therapy, were considered specifically for their efficacy in 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 US 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 US recommendations on exercise and physical activity can serve as a guide to clinicians counseling patients (8). Because the 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 individuals

with RA as to 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, antiinflammatory, 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 dieticians to assist individuals with RA who seek to modify their diet as part of their RA management plan.

Additional integrative interventions that we conditionally recommended included standardized self-management programs, cognitive behavioral therapy 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 individuals with RA. The Patient Panel favored standardized self-management, cognitive behavioral therapy, 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.

Individuals 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 tobacco use screening and cessation in RA.

A broad range of interventions was considered in this guide-line. 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 individuals 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 that they can be involved in shared-decision making throughout the disease course.

RA is a chronic disease that imposes considerable costs on those affected as well as increased costs to 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 individual with RA. We encourage health policymakers to advocate for insurance coverage of these interventions in order 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 the 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 the following: 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 versus 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 of RA 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 use of cannabinoids as an RA treatment, 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 US Department of Veterans Affairs and Center for Evidence-Based Policy at Oregon Health &

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

Evaluate the efficacy and safety of integrative therapies for the management of rheumatoid arthritis. 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 rheumatoid arthritis 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 rheumatoid arthritis disease manifestations and pharmacologic therapies, e.g., modifying exercise interventions based on disease activity level or diet based on disease-modifying antirheumatic drugs utilized.

Tailor interventions (and their delivery) studied in the general population to individuals with rheumatoid arthritis, 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 individuals with rheumatoid arthritis to work without negative stigma in the workplace.

Establish the efficacy and safety of integrative therapies on extraarticular manifestations and long-term rheumatoid arthritis–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 rheumatoid arthritis to guide research efforts.

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

Sciences University (31). Different modes of delivering interventions (e.g., telehealth versus 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, taken together, can guide a shared decision-making approach between the individual with RA and their clinician. 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 individuals with RA from diverse backgrounds and settings. Together, these integrative and pharmacologic guidelines support the comprehensive management of RA in pursuit of optimal outcomes for people living with RA.

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