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2019 American College of Rheumatology/Arthritis Foundation Guideline for the Management of Osteoarthritis of the Hand, Hip and Knee

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Abstract

Objective. To develop an evidence-based guideline for the comprehensive management of osteoarthritis (OA) as a collaboration between the American College of Rheumatology (ACR) and the Arthritis Foundation (AF), updating the ACR 2012 recommendations for the management of hand, hip and knee OA.

Methods. We identified clinically relevant population/intervention/comparator/outcomes (PICO) questions and critical outcomes in OA. A Literature Review Team performed a systematic literature review to summarize evidence supporting the benefits and harms of available educational, behavioral, psychosocial, physical, mind-body and pharmacologic therapies for OA. Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology was used to rate the quality of the

evidence. A voting panel, including rheumatologists, physical and occupational therapists, and patients, achieved consensus on the recommendations.

Results. Based on the available evidence, either "strong" or "conditional" recommendations were made for or against the approaches evaluated. Strong recommendations were made for exercise; weight loss in patients with knee and/or hip OA who are overweight or obese; self-efficacy and self-management programs; tai chi; cane use; hand orthoses for 1st carpometacarpal (CMC) OA; tibiofemoral bracing for tibiofemoral knee OA; topical NSAIDs for knee OA; oral NSAIDs; and intra-articular corticosteroid injections for knee OA. Conditional recommendations were made for balance exercises; yoga; cognitive behavioral therapy (CBT); kinesiotaping for 1st CMC OA; orthoses for hand joints other than 1st CMC; patellofemoral bracing for patellofemoral knee OA; acupuncture; thermal modalities; radiofrequency ablation for knee OA; topical NSAIDs, intra-articular steroid injections and chondroitin sulfate for hand OA; topical capsaicin for knee OA; acetaminophen; duloxetine for knee OA; and tramadol.

Conclusion. This guideline provides direction for clinicians and patients making treatment decisions for the management of OA. Clinicians and patients should engage in shared decision making that accounts for patients' values, preferences, and comorbidities. These recommendations should not be used to limit or deny access to therapies.

Introduction

Osteoarthritis (OA) is the most common form of arthritis, affecting an estimated 302 million people worldwide (1-5) and is a leading cause of disability among older adults. The knees, hips, and hands are most commonly affected appendicular joints. OA is characterized by pathology involving the whole joint, including cartilage degradation, bone remodeling, osteophyte formation, and synovial inflammation, leading to pain, stiffness, swelling and loss of normal joint function.

As OA spans decades of a patient's life, patients with OA are likely to be treated with a number of different pharmaceutical and non-pharmaceutical interventions, often in combination. This report provides recommendations to guide patients and clinicians choosing among the available treatments. Certain principles of management apply to all patients with OA (see Comprehensive Management of OA

below and Figure 1). Some recommendations are specific to a particular joint (e.g., hip, knee, patellofemoral joint, 1st carpometacarpal joint (CMC)) or patient populations (e.g., erosive OA).

Methods

Overall methodology. This guideline follows the American College of Rheumatology (ACR) guideline development process (https://www.rheumatology.org/Practice-Quality/Clinical-Support/Clinical-Practice-Guidelines), using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology to rate the quality of the available evidence and to develop the recommendations (6). ACR policy guided management of conflicts of interest and disclosures (insert link just before publication). Supplementary Appendix 1 presents a full description of the methods.

In brief, this work involved 5 teams: 1) a Core Leadership Team that supervised and coordinated the project and drafted the clinical/PICO (population/intervention/comparator/outcomes) questions that served as the basis for the evidence report and manuscript; 2) a Literature Review Team that completed the literature screening and data abstraction and produced the evidence report (Supplementary Appendix 2); 3) an Expert Panel that had input into scoping and clinical/PICO question development; 4) a Patient Panel; and 5) an inter-professional Voting Panel that included rheumatologists, an internist, physical and occupational therapists, and patients. Supplementary Appendix 3 provides rosters of the team and panel members.

This guideline included an initial literature review limited to English language publications from inception of the databases to October 15, 2017, with updated searches conducted on August 1, 2018, and relevant papers included. Studies published after August 1, 2018, were not evaluated for this guideline. Supplementary Appendix 4 shows search terms used and databases reviewed, and Supplementary Appendix 5 highlights the study selection process. The guideline evidence base results from our own systematic review of randomized controlled trials (RCTs), rather than focusing on systematic reviews and meta-analyses published by others, as was done for the 2012 guideline. Systematic reviews of observational studies published by others were included if, in the opinion of the Voting Panel, they added critical information for formulation of a recommendation, for example, related to adverse effects that may not be seen in shorter duration RCTs. Subsequent updates of this guideline

will consider studies included here and new RCTs published since completion of the literature review for the current publication.

Although RCTs are considered the gold standard for evaluation, a number of limitations of RCTs proved particularly important in the formulation of the final recommendations: publication bias (favoring publication of positive results); adequate blinding; and the provision of active comparators and appropriate sham alternatives. Further, short duration RCTs cannot provide adequate prognostic information when applied to a complex disease, such as OA, in which pathophysiologic processes are slowly progressive over decades.

We focused on management options that are available in the United States and, for pharmacologic therapies, additionally focused on agents that are available in pharmaceutical grade formulations thus eliminating most nutraceuticals We limited our review to the English language literature. We reviewed clinicaltrials.gov to identify Phase 2 and 3 trials that may be far enough along to be FDA-approved and available by the time this guideline was published.

A hierarchy of outcome measures assessing pain and function in OA was developed based on the published literature (7,8) and is available for review in Supplementary Appendix 1.

Using GRADE, a recommendation can be either in favor of or against the proposed intervention and either strong or conditional (9,10). The strength of the recommendation is based on a 70% consensus among the Voting Panel members. Much of the evidence proved indirect (did not specifically address the PICO question as written) and of low to moderate quality (11,12). The Voting Panel made **strong recommendations** when they inferred compelling evidence of efficacy and that benefits clearly outweighed harms and burdens. Thus, a strong recommendation means that the Voting Panel was confident that the desirable effects of following the recommendation outweigh potential undesirable effects (or vice versa), so the course of action would apply to all or almost all patients, and only a small proportion of patients would not want to follow the recommendation.

The Voting Panel made **conditional recommendations** when the quality of the evidence proved low or very low and/or the balance of benefits versus harms and burdens was sufficiently close that shared decision making between the patient and the clinician would be particularly important. Conditional

recommendations are those for which the majority of informed patients would choose to follow the recommended course of action, but some would not (13,14). Thus, conditional recommendations are particularly value- and preference-sensitive and always warrant a full shared decision-making approach involving a complete and clear explication of benefits, harms, and burdens in language and in a context that patients understand (15). Where recommendations are made regarding a particular approach, details and references regarding that approach can be found in the Evidence Report (Supplementary Appendix 2).

Results/Recommendations

A. Comprehensive Management of OA

A comprehensive plan for the management of OA in an individual patient may include educational, behavioral, psychosocial and physical interventions, as well as topical, oral and intra-articular medications. Recommendations assume appropriate application of physical, psychological and/or pharmacologic therapies by an appropriate provider. Goals of management and principles for implementing those goals have broad applicability across patients. However, for some patients at some time points, a single physical, psychosocial, mind-body or pharmacologic intervention may be adequate to control symptoms; for others, multiple interventions may be used in sequence or in combination. Which interventions and the order in which interventions are used will vary from one patient to the next. An overview of a general approach to management of OA is outlined in Figure 1 for recommended options but no specific hierarchy of one option over another is implied other than on the basis of strength of the recommendation. Figure 2 summarizes the approaches that were not recommended.

Treatment decisions should take the personal beliefs and preferences of the patient, as well as their medical status, into consideration. This guideline applies to patients with OA with no specific contraindications to the recommended therapies. However, each patient should be assessed for the presence of medical conditions, such as hypertension, cardiovascular disease, heart failure, gastrointestinal bleeding risk, chronic kidney disease or other co-morbidities, that might have an impact on their risk of side effects from certain pharmacologic agents, as well as injuries, disease severity, surgical history, and access to and availability of services (transportation, distance, ability to take time off work, cost, insurance coverage) that might have an impact on the choice of physical, psychological

and mind-body approaches. It is assumed that such an assessment will be performed prior to finalization of an individual treatment plan. When choosing among pharmacologic therapies, management should begin with treatments with the least systemic exposure or toxicity.

Patients may experience a variety of additional symptoms as a result of the pain and functional limitations arising from OA and/or comorbidities. These include mood disorders, such as depression and anxiety, altered sleep, chronic widespread pain and impaired coping skills. The Patient Panel noted the broader impact of OA on these comorbidities to be of particular importance when choosing among treatment options and best addressed by a multimodal treatment plan, rather than one that is limited to the prescription of a single medication. Measures aimed at improving mood, reducing stress, addressing insomnia, managing weight and enhancing fitness may improve the patient's overall well-being and OA treatment success. Indeed, interventions that have proven beneficial in the management of chronic pain may prove useful in OA (16) even when data specific to patients with OA are limited.

Unless otherwise specified, recommendations regarding physical, psychosocial and mind-body approaches assume that the patient will be adding the intervention to usual care. For the purposes of this guideline, usual care includes the use of maximally recommended or safely tolerated doses of over the counter oral non-steroidal anti-inflammatory drugs and/or acetaminophen, as has generally been explicitly permitted in clinical trials of non-pharmacologic interventions.

B. Physical, Psychosocial and Mind-Body Approaches (Table 1)

During the GRADE analysis, clinical trials involving physical modalities and mind-body approaches were often designated as yielding low quality evidence because blinding to the active treatment was not always possible. This contributed to a preponderance of conditional recommendations for physical modalities and mind-body approaches. The delivery of instruction by physical and occupational therapists is helpful, and often essential, for the appropriate initiation and maintenance of exercise as a part of OA management. In addition to exercise, physical and occupational therapists often incorporate self-efficacy and self-management training, thermal therapies, instruction in use and fitting of splints and braces in their practices. Most patients with OA are likely to experience benefit from referral to physical therapy (PT) and/or occupational therapy (OT) at various times during the course of their disease.

1. Exercise

Exercise is **strongly recommended** for all patients with OA. However, there is considerably more evidence for the use of exercise in the treatment of knee and hip OA than for hand OA and the variety of exercise options studied is far greater. While patients and providers seek recommendations on the "best" exercise and the ideal dosage (duration, intensity and frequency), current evidence is insufficient to recommend specific exercise prescriptions. Broad recommendations suggesting one form of exercise over another are based largely on expert opinion. A substantial body of literature (see Evidence Report, Supplementary Appendix 2) supports a wide range of appropriate exercise options and suggests that the vast majority of OA patients can participate in and benefit with regard to pain and function from some form of exercise. Exercise recommendations to patients should focus on the patient's preferences and access, both of which are important barriers to participation. If a patient does not find a certain form of exercise acceptable or cannot afford to participate or arrange transportation to participate, they are not likely to get any benefit from the suggestion to pursue that exercise.

In the majority of studies that assessed the role of aerobic exercise in the management of OA, walking was the most common form of exercise evaluated, either on a treadmill or as supervised, community-based, indoor fitness walking. Other studies used supervised group cycling on stationary bicycles. Strengthening exercises have included the use of isokinetic weight machines, resistance exercise training with and without props, such as elastic bands, and isometric exercise. Neuromuscular training has been developed to address muscle weakness, reduced sensorimotor control, and functional instability specifically seen with knee OA with a series of dynamic maneuvers of increased complexity. Aquatic exercise often encompasses aspects of aerobic fitness and enhancing joint range of motion in a low impact environment.

A specific hierarchy of these various forms of exercise could not be discerned from the literature. Patient participants on the Patient and Voting Panels raised the concern that patients in pain might be hesitant to participate in exercise. There is no uniformly accepted level of pain at which a patient should or should not exercise and a common-sense approach of shared decision making between the treating clinician and the patient about when to initiate an exercise program is advisable. However, clinical trials of exercise for OA include patients with pain and functional limitations due to OA and improvements in

OA specific outcomes have been demonstrated; thus, results are likely to be generalizable to most patients with pain due to OA.

Although evidence is currently insufficient to recommend one form of exercise over another, patients will likely benefit from as specific advice as possible, rather than simple encouragement to exercise. Given the wide range of evidence-based exercise interventions shown to effectively improve pain and function in OA, all patients should be encouraged to consider some form of exercise as a central part of their treatment plan. Individual preferences, access and affordability are likely to play a role in what works best for an individual patient. Overall, exercise programs are more effective if supervised, often by physical therapists, sometimes in a class setting, rather than when performed by the individual at home. They also tend to be more effective when combined with self-efficacy and self-management interventions or weight loss programs.

Few studies have employed monitoring devices or a pre- and post-intervention assessment of cardiovascular or musculoskeletal fitness, so targets using these devices or assessments are not available. Future research is essential to establish specific exercise guidelines that will direct the patient and provider toward more individualized exercise prescriptions.

2. Balance Exercises

Balance exercises include those that improve the ability to control and stabilize body position (APTA: http://www.apta.org/BalanceFalls/). Although one might expect balance exercises to help reduce the risk of falls in patients with OA, RCTs to date have not addressed this outcome in this population, and the low quality of evidence addressing the use of balance exercises necessitates only a **conditional recommendation** for balance exercises.

3. Weight Loss

Weight loss is **strongly recommended** in patients with hip or knee OA who are overweight or obese. A dose response has been noted with regard to the amount of weight loss that will result in symptom or functional improvement (40). A loss of 5% or more of body weight can be associated with changes in clinical and mechanistic outcomes. Furthermore, clinically important benefits continue to increase with weight loss of 5-10%, 10-20% and >20%. The efficacy of weight loss for OA symptom management is enhanced by use of a concomitant exercise program.

4. Self-Efficacy and Self-Management Programs

Participation in self-efficacy and self-management programs is **strongly recommended** for all patients with OA. Although effect sizes are generally small, the benefits are consistent across studies and risks are minimal. These programs use a multi-disciplinary group-based format combining sessions of skill building (goal-setting, problem-solving, positive thinking), education about the disease and medication effects and side effects, joint protection measures, and fitness and exercise goals and approaches. Health educators, National Commission for Certification Services-certified fitness instructors, nurses, PTs, OTs, physicians and patient peers may lead the sessions that can be held in person or online. Sessions in the studies reviewed generally occurred 3 times weekly but varied from 2 to 6 times weekly.

5. Tai chi

Tai chi is **strongly recommended** for knee and hip OA. Tai chi is a traditional Chinese mind-body practice that combines meditation with slow, gentle, graceful movements, deep diaphragmatic breathing and relaxation. The efficacy of tai chi may reflect the holistic impact of this mind body practice on strength, balance and fall prevention, as well as on depression and self-efficacy.

6. Yoga

Yoga is **conditionally recommended** for those with knee OA. Due to lack of data, no recommendation can be made regarding use of yoga to help manage symptoms of hip OA. Yoga is a mind-body practice with origins in ancient Indian philosophy and typically combines physical postures, breathing techniques, and meditation or relaxation (NCCIH: https://nccih.nih.gov/health/yoga). Though far less well studied than tai chi, yoga may be helpful in OA through a similar blend of physical and psychosocial factors.

Other mind body practices could not be assessed due to insufficient evidence, as well as a lack of standard definitions of certain interventions (hypnosis, qi gong).

7. Cognitive Behavioral Therapy (CBT)

Cognitive behavioral therapy is **conditionally recommended** for all patients with OA. There is a well-established body of literature (17,18) supporting the use of CBT in chronic pain conditions, and CBT may have relevance for the management of OA. Trials have demonstrated improvement in pain, health related quality of life, negative mood, fatigue, functional capacity and disability in conditions other than

OA. In OA, limited evidence suggests that CBT may reduce pain (19). Further research is needed to establish whether or not benefits in OA are related to alteration in mood, sleep, coping or other factors that may co-occur with, result from, or be a part of the experience of OA (20).

8. Cane

Use of a cane is **strongly recommended** for knee and hip OA in those patients in whom disease in one or more joints is causing a sufficiently large impact on ambulation, joint stability or pain to warrant use of an assistive device.

9. Tibiofemoral Knee Braces

Tibiofemoral knee braces are **strongly recommended** in patients with knee OA in whom disease in one or both knees is causing a sufficiently large impact on ambulation, joint stability or pain to warrant use of an assistive device, and who are able to tolerate the associated inconvenience and burden associated with bracing.

10. Patellofemoral Braces

Patellofemoral braces are **conditionally recommended** for patients with patellofemoral knee OA in whom disease in one or both knees is causing a sufficiently large impact on ambulation, joint stability or pain to warrant use of an assistive device. The recommendation is conditional due to the variability in results across published trials and the difficulty some patients will have in tolerating the inconvenience and burden of these braces.

Optimal management with knee bracing is likely to require that clinicians are familiar with the various types of braces and where they are available and have expertise in fitting the braces. Patient Voting Panel members strongly emphasized the importance of coordination of care between primary care providers, specialists and providers of braces.

11. Kinesiotaping

Kinesiotaping is **conditionally recommended** for knee and 1st CMC joint OA. Kinesiotaping permits range of motion of the joint to which it is applied, in contrast to a brace which maintains the joint in a fixed position. Published studies have examined various products and methods of application, and blinding to use is not possible, thereby limiting the quality of the evidence.

12. Hand Orthoses: 1st CMC Joint

The use of hand orthoses is **strongly recommended** for the 1st CMC joint.

13. Hand Orthoses: Other Joints

The use of hand orthoses is **conditionally recommended** for patients with OA in other joints of the hand. A variety of mechanical supports are available, including digital orthoses, ring splints, and rigid or neoprene orthoses, some of which are intended for specifically affected joints (e.g., 1st CMC joint, individual digits, wrist) and some of which support the entire hand. In addition, gloves may offer benefit by providing warmth and compression to the joints of the hand. Data are insufficient to recommend one type of orthosis for use in the hand over another. Patients considering these interventions will likely benefit from evaluation by an occupational therapist.

14. Modified Shoes

The use of modified shoes is **conditionally recommended against** in patients with knee OA. Modifications to shoes can be intended to alter the biomechanics of the lower extremities and the gait. While optimal footwear is likely to be of considerable importance for those with hip and/or knee OA, the available studies do not define the best type of footwear to improve specific outcomes for hip or knee OA.

15. Lateral and Medial Wedged Insoles

The use of lateral and medial wedged insoles is **conditionally recommended against** in patients with hip and/or knee OA. The currently available literature does not demonstrate clear efficacy.

16. Acupuncture

Acupuncture is **conditionally recommended** for use in patients with OA. Although a large number of trials have addressed the use of acupuncture for OA, its efficacy remains controversial. Issues related to the use of appropriate blinding, the validity of sham controls, sample size, effect size and prior expectations have arisen in regard to this literature. Variability in the results of RCTs and meta-analyses is, in part, likely driven by differences in the type of controls and the intensity of the control interventions used. In addition, the benefits of acupuncture result from the large contextual effect plus small differences in outcomes between "true" and "sham" acupuncture. The latter is of the same

magnitude as the effect of full-dose acetaminophen vs. placebo. The greatest number of positive trials with the largest effect sizes have been carried out in knee OA. Positive trials and meta-analyses have also been published in a variety of other painful conditions and reported that acupuncture is effective for analgesia. While "true" magnitude of effect was difficult to discern, the risk of harm is minor, resulting in the Voting Panel providing a conditional recommendation.

17. Thermal Interventions

Use of thermal interventions (locally applied heat or cold) is **conditionally recommended** for hip, knee and hand OA. The method of delivery varies considerably in published reports, including moist heat, diathermy (electrically delivered heat), ultrasound and hot and cold packs. Studies using diathermy or ultrasound were more likely to be sham controlled than those using other heat delivery modalities. The heterogeneity of modalities and short duration of benefit for these interventions led to the conditional recommendation.

18. Paraffin

Paraffin, an additional method of heat therapy for the hands, was **conditionally recommended** for hand OA.

19. Radiofrequency Ablation

Use of radiofrequency ablation is **conditionally recommended** for knee OA. A number of studies have demonstrated potential analgesic benefits with various ablation techniques but, because of the heterogeneity of techniques and controls used and lack of long-term safety data, this recommendation is conditional.

20. Massage therapy

Massage therapy is **conditionally recommended against** in the management of knee and/or hip OA. Massage therapy encompasses a number of techniques aimed at affecting muscle and other soft tissue (NCCIH: https://nccih.nih.gov/health/massage/massageintroduction.htm#hed2). Studies addressing massage have suffered from high risk of bias, have included small numbers of patients, and have not demonstrated benefit for OA specific outcomes. Patient participants on the Patient and Voting Panels noted that some studies have shown positive outcomes and minimal risk and felt strongly that massage therapy was beneficial for symptom management (21). However, based on the available evidence

regarding OA specifically, a conditional recommendation against the use of massage for reduction of OA symptoms is made, though the Voting Panel acknowledged that massage may have other benefits.

21. Manual Therapy with Exercise

Use of manual therapy with exercise is **conditionally recommended against** over exercise alone in knee and/or hip OA. Manual therapy techniques may include manual lymphatic drainage, manual traction, massage, mobilization/manipulation, and passive range of motion and is always used in conjunction with exercise (http://guidetoptpractice.apta.org/content/1/SEC38.extract). A limited number of studies have addressed manual therapy added to exercise versus exercise alone in hip and knee OA. Although manual therapy can be of benefit for certain conditions, such as chronic low back pain, limited data in OA show little additional benefit over exercise alone when managing OA symptoms.

22. Iontophoresis

Use of iontophoresis is **conditionally recommended against** in 1st CMC joint OA. There are no RCTs evaluating iontophoresis for OA in any anatomical location.

23. Pulsed Vibration Therapy

Use of pulsed vibration therapy is **conditionally recommended against** in knee OA. Few trials have addressed pulsed vibration therapy, and, in the absence of adequate data, we recommend conditionally against its use.

24. Transcutaneous Electrical Stimulation (TENS)

Use of transcutaneous electrical stimulation is **strongly recommended against** in knee and/or hip OA. Studies examining the use of TENS have been of low quality with small size and variable controls, making comparisons across trials difficult. Studies have demonstrated lack of benefit for knee OA.

C. Pharmacologic Management (Table 2)

Randomized controlled trials of pharmacologic agents may be subject to a variety of limitations, including generalizability of their findings across patients. Publication bias may reduce the likelihood that negative trials will become part of the published literature. Statistically significant findings may

represent benefits so small that they are not clinically important to patients. We have highlighted these considerations where relevant.

1. Topical Non-Steroidal Anti-inflammatory Drugs (NSAIDs)

Use of topical NSAIDs is **strongly recommended** for **knee** OA. In keeping with the principle that medications with the least systemic exposure (i.e., local therapy) are preferable, topical NSAIDs should be considered prior to use of oral NSAIDs (22).

Practical considerations (e.g., frequent hand washing) and the lack of direct evidence of efficacy in the hand lead to a **conditional recommendation** for use of topical NSAIDs in **hand** OA.

In **hip** OA, the depth of the joint beneath the skin surface suggests topical NSAIDs are unlikely to confer benefit, and, thus, the Voting Panel did not examine use in hip OA.

2. Topical Capsaicin

Topical capsaicin is **conditionally recommended** for **knee** OA due to small effect sizes and wide confidence intervals in the available literature.

We recommended **conditionally against** the use of topical capsaicin in **hand** OA because of a lack of direct evidence to support use in hand OA, as well as a potentially increased risk of contamination of the eye with topical capsaicin used to treat hand OA.

In **hip** OA, the depth of the joint beneath the skin surface suggests topical capsaicin is unlikely to have a meaningful effect and, thus, use of topical capsaicin in hip OA was not specifically examined.

Insufficient data exists to make recommendations about the use of topical lidocaine preparations in OA.

3. Oral Non-Steroidal Anti-Inflammatory Drugs

Oral NSAIDs remain the mainstay of the pharmacologic management of osteoarthritis, and their use is **strongly recommended**. A large number of trials have established their short-term efficacy. Oral NSAIDs are the initial oral medication of choice in the treatment of osteoarthritis, regardless of anatomic location, and are recommended over all other available oral medications.

While this guideline did not address the relative merits of different NSAIDs, evidence exists suggesting that certain agents may have more favorable side effect profiles than others (23-25). Clinical considerations aimed at risk mitigation for the safe use of NSAIDs, such as appropriate patient selection, regular monitoring for the development of potential adverse gastrointestinal, cardiovascular and renal side effects and potential drug interactions were not specifically included in the GRADE process for the formulation of recommendations. Doses should be as low as possible, and NSAIDs should be continued for as short a time as possible.

4. Intra-Articular Corticosteroid Injection

The use of intra-articular corticosteroid injections is **strongly recommended** for patients with **knee** or **hip** OA. Trials of intra-articular corticosteroid injections have demonstrated short-term efficacy in knee OA.

Intra-articular corticosteroid injection is **conditionally**, rather than strongly, **recommended** for **hand** OA given the lack of evidence specific to this anatomic location. Data are insufficient to judge the choice of short-acting over long-acting preparations or the use of low rather than high doses. A recent report (26) raised the possibility that specific steroid preparations or a certain frequency of steroid injections may contribute to cartilage loss, but the Voting Panel was uncertain of the clinical significance of this finding, particularly since change in cartilage thickness was not associated with a worsening in pain, functioning or other radiographic features.

5. Ultrasound Guidance for Intra-Articular Corticosteroid Injection

When available, ultrasound guidance for steroid injection may help ensure accurate drug delivery into the joint but is not required for knee and hand joints. However, guidance with imaging is **strongly recommended** for injection into **hip** joints.

6. Intra-Articular Corticosteroid Injections Compared to Other Injections

In OA generally, intra-articular corticosteroid injection is **conditionally recommended** over other forms of intra-articular injection, including hyaluronic acid preparations. Head-to-head comparisons are few, but the evidence for efficacy of corticosteroid injections is considerably higher quality than for other agents.

7. Acetaminophen

Acetaminophen is **conditionally recommended** for patients with OA. In clinical trials, the effect sizes for acetaminophen are very small, suggesting that few of those treated experience important benefit and meta-analysis has suggested that use as monotherapy may be ineffective (27). Longer-term treatment is no better than treatment with placebo for most individuals. Members of the Patient Panel noted that, for most individuals, acetaminophen is ineffective. For those with limited pharmacologic options due to intolerance or contraindications to the use of NSAIDs, acetaminophen may be appropriate for short term and episodic use. Regular monitoring for hepatotoxicity is required for patients who use acetaminophen on a regular basis, particularly at the recommended maximum dosage of 3 gm daily in divided doses.

8. Duloxetine

Duloxetine is **conditionally recommended** for use in patients with knee OA. While studied primarily in the knee, the effects may plausibly be expected to be similar for OA of the hip or hand. While a variety of centrally acting agents (e.g., pregabalin, gabapentin, selective serotonin reuptake inhibitors, serotonin norepinephrine reuptake inhibitors and tricyclic antidepressants) have been used in the management of chronic pain, only duloxetine has adequate evidence on which to base recommendations for use in OA. However, in considering all the ways in which OA may be affecting an individual patient, shared decision making between the physician and patient may include consideration of any of these agents. Considering the utility of these agents in pain management generally, their use may be an appropriate target of future investigations specific to OA. Evidence suggests duloxetine has efficacy in the treatment of OA when used alone or in combination with NSAIDs; however, tolerability and side effect issues exist. No recommendations were made for the other centrally acting agents due to lack of direct studies of relevance in OA.

9. Tramadol

Recent work has highlighted the very modest level of beneficial effects in the long term (three months to one year) management of non-cancer pain with opioids (28). Nonetheless, there are circumstances in which tramadol or other opioids may be appropriate in the treatment of OA, including when patients may have contraindications to NSAIDs, find other therapies ineffective, or have no available surgical options. Patient Panel input demonstrated a high level of understanding concerning addiction potential,

but also included an appreciation for the role of these agents when other pharmacologic and physical options have been ineffective. However, RCT evidence addressing the use of tramadol and other opioids for periods longer than one year is not available.

Tramadol is **conditionally recommended** for use in patients with OA. Clinical trials have demonstrated some symptomatic efficacy though concerns regarding potential adverse effects remain. If an opioid is being considered, tramadol is conditionally recommended over non-tramadol opioids.

10. Non-Tramadol Opioids

Use of non-tramadol opioids is **conditionally recommended against** in patients with OA with the recognition that they may be used under certain circumstances, particularly when alternatives have been exhausted. As noted previously, evidence suggests very modest benefits of long-term opioid therapy and a high risk of toxicity and dependence. Use of the lowest possible doses for the shortest possible length of time is prudent, particularly since a recent systematic review and meta-analysis suggests that less pain relief occurs during longer trials in the treatment of non-cancer chronic pain (28).

11. Colchicine

Use of colchicine is **conditionally recommended against** in patients with OA. Two very small studies have suggested analgesic benefit, but the quality of the data was low. In addition, potential adverse effects, as well as drug interactions, may occur with use of colchicine.

12. Fish Oil

Use of fish oil is **conditionally recommended against** in patients with OA. Fish oil is the most commonly used dietary supplement in the United States (29). Despite its popularity, only one trial has addressed its potential role in OA. This study failed to show efficacy of a higher dose of fish oil over a lower dose.

13. Vitamin D

Use of vitamin D is **conditionally recommended against** in patients with OA. A number of trials in OA demonstrated small effect sizes, while others have shown no benefit and pooling data across studies yielded null results. In addition, limited and questionable health benefits from vitamin D supplementation have been suggested in other contexts (30,31).

14. Bisphosphonates

Use of bisphosphonates is **strongly recommended against** in patients with OA. Though a single small study of an oral bisphosphonate suggested a potential analgesic benefit, the preponderance of data shows no improvement for pain or functional outcomes.

15. Glucosamine

Use of glucosamine is **strongly recommended against** in patients with OA. Pharmaceutical grade preparations are available and have been studied in multiple trials. However, discrepancies in efficacy reported in studies that were industry sponsored as opposed to publicly funded have raised serious concerns about publication bias (32,33). In addition, there is a lack of a clear biologic understanding of how efficacy would vary with the type of salt studied. The data that were deemed to have the lowest risk of bias fail to show any important benefits over placebo. These recommendations represent a change from the prior conditional recommendation against the use of glucosamine. The weight of the evidence points to a lack of efficacy and large placebo effects. Nonetheless, glucosamine remains among the most commonly used dietary supplements in the United States (29) and clinicians should be aware that many patients perceive that glucosamine is efficacious. Patients also often perceive that different glucosamine formulas are associated with different degrees of efficacy and seek advice on brands and manufacturers. The potential toxicity of glucosamine is low, though some patients exposed to glucosamine may show elevations in their serum glucose (34).

16. Chondroitin Sulfate

Similarly, use of chondroitin sulfate is **strongly recommended against** in knee and hip OA, as are combination products that include glucosamine and chondroitin sulfate. However, since a single trial suggested analgesic efficacy without evidence for harm, use of chondroitin sulfate is **conditionally recommended for** use in hand OA.

17. Hydroxychloroquine

Use of hydroxychloroquine is **strongly recommended against** in patients with OA. In the subset of patients with erosive hand OA, well designed, RCTs have demonstrated no efficacy.

18. Methotrexate

Use of methotrexate is **strongly recommended against** in patients with OA. Clinical trials have demonstrated no efficacy in the subset of patients with erosive hand OA.

19. Intra-articular Hyaluronic Acid Injection

The use of intra-articular hyaluronic acid injections is **conditionally recommended against** in patients with **knee** and **1st CMC** OA. Prior systematic reviews have reported apparent benefits of hyaluronic acid injections. These reviews have not, however, taken into account the risk of bias of the individual primary studies. Our review found that benefit was restricted to the higher risk of bias studies: when limited to trials with low risk of bias, meta-analysis has found the effect size of hyaluronic acid injections compared to saline injections approaches zero (38). The finding that best evidence fails to establish a benefit, and that harm may be associated with these injections, motivated the recommendation.

Many providers want the option of using hyaluronic acid injections when corticosteroid injections or other interventions fail to adequately control local joint symptoms. In clinical practice, the choice to use hyaluronic acid injections in the knee OA patient who has had an inadequate response to non-pharmacologic therapies, topical and oral NSAIDs and intra-articular steroids, may be viewed more favorably than offering no intervention, particularly in view of the impact of the contextual effects of intra-articular hyaluronic acid injections (39). The conditional recommendation against is consistent with the use of hyaluronic acid injections, in the context of shared decision making that recognizes the limited evidence of benefit of hyaluronic acid injections, when other alternatives have been exhausted or failed to provide satisfactory benefit. The conditional recommendation against is not intended to influence insurance coverage decisions.

In contrast, the evidence of lack of benefit is higher quality with respect to hyaluronic acid injection in the hip than the knee and the use of hyaluronic acid injections is **recommended strongly against** in hip OA.

Additional agents for intra-articular use have not been evaluated in hand OA, and therefore the subsequent recommendations considered the knee and hip only.

20. Intra-articular Botulinum Toxin

The use of intra-articular botulinum toxin is **conditionally recommended against** in patients with **knee** and/or **hip** OA based on a small number of trials suggesting a lack of efficacy.

21. Prolotherapy

The use of prolotherapy is **conditionally recommended against** in patients with **knee** and/or **hip** OA. A limited number of trials involving a small number of participants have shown small effect sizes. However, injection schedules, injection sites and comparators have varied substantially between trials.

22. Platelet Rich Plasma (PRP)

The use of platelet rich plasma is **strongly recommended against** in patients with **knee** and/or **hip** OA. In contrast to intra-articular therapies already discussed, there is concern regarding the heterogeneity and lack of standardization in available preparations of platelet rich plasma, as well as techniques used, making it difficult to identify exactly what is being injected.

23. Stem Cell Injection

The use of stem cell injection is **strongly recommended against** in patients with **knee** and/or **hip** OA. There are concerns regarding the heterogeneity and lack of standardization in available preparations of stem cell injections and techniques used.

24. Biologics

Tumor necrosis factor (TNF) inhibitors and interleukin-1 receptor antagonists (IL-1 RA) are **strongly recommended against** in patients with OA. TNF inhibitors and IL-1 antagonists have been studied using both subcutaneous and intra-articular routes of administration. Efficacy has not been demonstrated, including in erosive hand OA. Therefore, given their known risks of toxicity, we strongly recommended against their use for any form of OA.

Initial observations addressing the use of anti-nerve growth factor (NGF) agents suggest significant analgesic benefits may occur but that incompletely explained important safety issues may arise. A small subset of patients treated with these agents had rapid joint destruction leading to early joint replacement. The US Food and Drug Administration (FDA) temporarily halted clinical trials of anti-NGF as a result, but trials have since resumed with ongoing collection of longer-term efficacy and safety data. As none of these agents were approved for use by the FDA and this longer-term data was not available

at the time of the literature review and Voting Panel meeting, we are unable to make recommendations regarding the use of anti-NGF therapy.

Discussion

These ACR 2019 recommendations for the management of patients with OA are based on the best available evidence of benefit, safety and tolerability of physical, educational, behavioral, psychosocial, mind-body and pharmacologic interventions, as well as the consensus judgment of clinical experts. The GRADE approach used provided a comprehensive, explicit, and transparent methodology for developing recommendations for the management of patients. The choice of any single or group of interventions may vary over the course of the disease or with patient and provider preferences and is optimally arrived at through shared decision making.

The Voting Panel made strong recommendations for patients to participate in a regular, ongoing exercise program. The literature provides support for choice from a broad menu of exercises for patients with OA. The effectiveness of an exercise program is enhanced when patient preferences and access to program are considered, as well as when they are supervised or coupled with self-efficacy, self-management and weight loss programs. Strong recommendations were also made for weight loss in patients with knee and/or hip OA who are overweight or obese; self-efficacy and self-management programs; tai chi; cane use; 1st CMC orthoses; tibiofemoral bracing; topical NSAIDs for knee OA and oral NSAIDs for hand, knee and/or hip OA; and intra-articular corticosteroid injections for knee and/or hip OA. The Voting Panel made conditional recommendations for balance exercises; yoga; CBT; kinesiotaping; orthoses for hand joints other than 1st CMC; patellofemoral bracing; acupuncture; thermal modalities; radiofrequency ablation; topical NSAIDs, intra-articular steroid injections and chondroitin sulfate for hand OA; topical capsaicin for knee OA; acetaminophen; duloxetine; and tramadol. The recommendations provide a menu of options for a comprehensive approach for optimal management of OA encompassing the use of educational, physical, behavioral, psychosocial, mind-body and pharmacological interventions. The availability, accessibility and affordability of some of these interventions vary but, in many communities, the Arthritis Foundation, as well as local hospitals and health related agencies, offer free self-efficacy and self-management programs.

For some patients with more limited disease in whom medication is required, topical NSAIDs represent an appropriate first choice. For others, particularly with hip OA or polyarticular involvement, oral NSAIDs are more appropriate. The appropriate use of other oral agents, particularly acetaminophen and opioids, will continue to evolve (35-37).

Despite the many options available, patients may continue to experience inadequate symptom control; others will experience adverse effects from the available interventions. Clinicians treating patients in these circumstances should choose interventions with a low risk of harm, but both clinicians and patients may be dissatisfied with the options and how to choose among them. Controversies in interpretation of the evidence exist, particularly with regard to the use of glucosamine and chondroitin, acupuncture and intra-articular hyaluronic acid injections. Nonetheless, the process of updating treatment guidelines permits scrutiny of the state of the literature and identification of critical gaps in our knowledge about best practices. Further, it highlights the need for ongoing, appropriately funded, high quality clinical research, as well as development of new treatment modalities, to address the human and economic impact of the most common form of arthritis.

No effective disease-modifying agents have yet been identified, though phase 2 and 3 trials are underway, and, for the time being, preventive strategies focus on weight management and injury prevention. Development of more effective therapies that permit a sophisticated and individualized approach to the patient with OA await the outcome of future investigation. Important directions for future research include gaining a more comprehensive understanding of the optimal types of exercises and the modifications that should be used based on disease location and severity; study of the intensity of exercise that would be optimal for a given individual (https://health.gov/paguidelines/second-edition/report.aspx); defining optimal footwear for patients with knee and hip OA and understanding the interaction between footwear and exercise; conducting rigorous RCTs for physical modality options in hand OA; assessing a broader array of outcomes, including fall prevention; assessing optimal use of oral, topical and injectable agents alone and in combination; obtaining a better understanding of the role of integrative medicine, including massage, herbal products, medical marijuana and additional mind-body interventions; and exploring agents with novel mechanisms of action for prevention and treatment.

In conclusion, optimal management requires a comprehensive, multi-modal approach to treating patients with hand, hip and/or knee OA offered in the context of shared decision making with patients, to choose the safest and most effective treatment possible. A large research agenda remains to be addressed, with a need for more options with greater efficacy for the millions of people worldwide with osteoarthritis.

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Addendum

Therapies that were approved after the original systematic literature review are not included in these recommendations.

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Figure 1. Recommended Therapies for the Management of Osteoarthritis.

Legend: Strongly (darker green) and conditionally (lighter green) recommended approaches to management of hand, knee, and/or hip OA. No hierarchy within categories are implied in this figure, with the recognition that the various options may be used (and reused) at various times during the course of a particular patient's disease.

[1]Exercise for knee and hip OA could include walking, strengthening, neuromuscular training, and aquatic exercise, with no hierarchy of one over another. Exercise is associated with better outcomes when supervised.

[2]Knee brace recommendations: TF brace for TF OA (strongly), PF brace for PF OA (conditionally)

[3]Hand orthosis recommendations: 1st CMC neoprene or rigid orthoses for 1st CMC OA (strongly), orthoses for joints of the hand other than the 1st CMC (conditionally)

Abbreviations: CMC, carpometacarpal; I-A, intra-articular; NSAIDs, non-steroidal anti-inflammatory drugs; PF, patellofemoral; RFA, radiofrequency ablation; TF, tibiofemoral

Figure 2. Therapies Recommended ***Against*** in the Management of Osteoarthritis.

Legend: Strongly (darker red) and conditionally (lighter red) recommended ***against*** approaches to management of hand, knee, and/or hip OA. No hierarchy within categories is implied in this figure.

Abbreviations: I-A, intra-articular; IL, interleukin; PRP, platelet rich plasma; TENS, transcutaneous electrical nerve stimulation; TNF, tumor necrosis factor-alpha

Table 1. Recommendations for **Physical, Psychosocial and Mind-Body Approaches** Management of Osteoarthritis (OA) of the Hand, Knee and Hip.

Intervention	**Joint**		
	Hand	**Knee**	**Hip**
1. Exercise			
2. Balance Training			
3. Weight Loss			
4. Self-Efficacy and Self-Management Programs			
5. Tai Chi			
6. Yoga			
7. CBT			
8. Cane			
9. Tibiofemoral Knee Braces		(Tibiofemoral)	
10. Patellofemoral Braces		(Patellofemoral)	
11. Kinesiotaping	(1st CMC)		
12. Hand Orthosis	(1st CMC)		
13. Hand Orthosis	(Other Joints)		
14. Modified Shoes			
15. Lateral and Medial Wedged Insoles			
16. Acupuncture			
17. Thermal Interventions			
18. Paraffin			
19. Radiofrequency Ablation			
20. Massage Therapy			
21. Manual Therapy with/without Exercise			
22. Iontophoresis	(1st CMC)		
23. Pulsed Vibration Therapy			
24. TENS			

Strongly Recommended
Conditionally Recommended
Strongly Recommended Against
Conditionally Recommended Against
No Recommendation

Table 2. Recommendations for **Pharmacologic** Management of Osteoarthritis (OA) of the Hand, Knee and Hip

Intervention	Joint		
	Hand	Knee	Hip
1. Topical NSAIDs			
2. Topical Capsaicin			
3. Oral NSAIDs			
4. Intra-Articular Corticosteroid Injection			
5. Ultrasound Guidance for Intra-Articular Corticosteroid Injection			
6. Intra-Articular Corticosteroid Injection Compared to Other Injections			
7. Acetaminophen			
8. Duloxetine			
9. Tramadol			
10. Non-Tramadol Opioids			
11. Colchicine			
12. Fish Oil			
13. Vitamin D			
14. Bisphosphonates			
15. Glucosamine			
16. Chondroitin Sulfate			
17. Hydroxychloroquine			
18. Methotrexate			
19. Intra-Articular Hyaluronic Acid Injection	(1st CMC)		
20. Intra-Articular Botulinum Toxin			
21. Prolotherapy			
22. PRP			
23. Stem Cell Injection			
24. Biologics (TNF inhibitors, IL-1 RAs)			

Strongly Recommended
Conditionally Recommended
Strongly Recommended Against
Conditionally Recommended Against
No Recommendation