

SUPPLEMENTARY APPENDIX 1: Methods

ACR/AF 2019 Guideline for the Management of Osteoarthritis of the Hand, Hip and Knee

Methodology Overview

This guideline followed the American College of Rheumatology (ACR) guideline development process (<http://www.rheumatology.org/Practice-Quality/Clinical-Support/Clinical-Practice-Guidelines>). This process includes using GRADE methodology (www.gradeworkinggroup.org) to rate the quality of the available evidence and to develop the recommendations (1-3). GRADE methodology specifies that panels make recommendations based on the balance of benefits and harms, the quality of the evidence (i.e., confidence in effect estimates) and patients' values and preferences. ACR policy guided disclosures and the management of conflicts of interest (<https://www.rheumatology.org/Practice-Quality/Clinical-Support/Clinical-Practice-Guidelines/Osteoarthritis>).

This work involved four teams selected by the ACR Quality of Care Committee and Guideline Subcommittee after reviewing individual and group volunteer applications to an open call for interested participants: 1) a Core Leadership Team, which supervised and coordinated the project and drafted the clinical questions, recommendation statements and manuscript; 2) a Literature Review Team, which completed the literature screening, data abstraction and synthesis; 3) an Expert Panel, which helped develop the clinical questions and decide on the project scope; and 4) a Voting Panel, which included rheumatologists, physical and occupational therapists, and two patients. Supplementary Appendix 3 presents rosters of all guideline development team members. Additionally, a Patient Panel consisting of patients with varied experiences related to osteoarthritis (OA) provided input on their values and preferences, which was reviewed before discussion of each section of the guideline (e.g., pharmacologic and non-pharmacologic) and was incorporated into discussions and formulation of recommendations. In

accordance with ACR policy, the principal investigator and the Literature Review Team leader were free of conflicts, and all teams had >50% members free of conflicts.

Framework for the Guideline Development and Scope of the Guideline

The objective of this project is to develop recommendations for the pharmacologic and non-pharmacologic management of OA of the hand, hip, and knee. At the scoping meeting, the Core Leadership Team, Voting Panel and Expert Panel decided that the guideline would focus on management options available in the United States and, for pharmacologic therapies, additionally focused on agents that are available in pharmaceutical grade formulations. Thus, nutraceuticals were not considered unless they were known to be available in pharmaceutical grade. In addition, clinicaltrials.gov was searched for Phase 2 and 3 trials to identify agents that may potentially become available by the time of publication or soon thereafter.

Systematic Synthesis of the Literature

Direct evidence in OA patient populations relating to OA questions was obtained through systematic searches of the published English-language literature, including OVID Medline, PubMed, Embase, and the Cochrane Library (including Cochrane Database of Systematic Reviews, Database of Abstracts of Reviews of Effects, Cochrane Central Register of Controlled Trials, and Health Technology Assessments) from the beginning of each database through October 15, 2017 (Supplementary Appendix 4); updated searches were conducted on August 1, 2018. Duplications were identified via DistillerSR software (<https://distillercer.com/products/distillersr-systematic-reviewsoftware/>) (Supplementary Appendix 5). All retrieved articles were screened in duplicate and the lead methodologist resolved any conflicts. For all included papers, reviewers entered extracted data describing details of the population, interventions (if any), and results into RevMan v.5.3 software (<http://tech.cochrane.org/revman>) which was used to calculate summary effect sizes (4), and evaluate risk of bias with the Cochrane risk of bias tool (<http://handbook.cochrane.org/>). RevMan files were exported into GRADEpro software to formulate a

GRADE summary of findings table (Supplementary Appendix 2) for each PICO question (5). Evidence-based models use the PICO process for framing a question; PICO elements include Population, Intervention, Comparison, and Outcome. For data not appropriate for RevMan (e.g., non-comparative data), reviewers abstracted data describing details of the population, interventions (if any), and results into Word tables. GRADE criteria provided the framework for judging the overall quality of evidence (1). When using GRADE, the overall quality of evidence rating for a given treatment comparison is based on the lowest quality rating for any critical outcome. Pain and function were identified as critical outcomes (see Table 1 and 2 below). Therefore, if the quality of evidence for pain is moderate and the quality of evidence for function is low, the overall quality of evidence rating would be low for that treatment comparison. The PICO questions and level of evidence that formed the basis for the recommendations in this guideline are outlined in Table 3 and 4.

Moving from Evidence to Recommendations

Given that GRADE methodology specifies that panels make recommendations based on the balance of benefits and harms, the quality of the evidence, and patients' values and preferences, deciding on the balance between desirable and undesirable outcomes requires estimating the relative value patients place on those outcomes. When the literature provided very limited guidance, the experience of the Voting Panel members in managing the relevant patients and problems also provided an important source of evidence. Patient values and preferences were crucial to all recommendations made, and derived from input from the members of the Patient Panel; these were particularly salient in situations with limited literature. In addition, if a systemically acting therapy (e.g., oral medication) only had evidence available for a single anatomic site (e.g., the knee), those evidence could be considered as indirect for the other anatomic sites (e.g., hand, hip) where appropriate. GRADE methodology allows for the possibility of not coming to a decision, and in such cases, a summary of the discussion is noted.

Consensus Building

During a two-day face-to-face meeting and group emails, Voting Panel members voted on the direction (for or against) and strength (conditional or strong) of the recommendations related to the PICO questions. Some recommendation statements were dropped due to lack of data or relevance, and others were combined based on level of evidence and Voting Panel discussion. Recommendations required a 70% level of agreement as used previously in other similar processes (6). If 70% agreement was not achieved during an initial vote, the panel members held additional discussions before re-voting. For all conditional recommendations, a written explanation is provided, describing the reasons for this decision.

Moving from Recommendations to Practice

These recommendations are designed to help health care providers, caregivers, and patients engage in shared decision-making regarding disease management. Level of disease activity, comorbidities, response and tolerance of prior therapies, and patient-specific factors, values and preferences should all be taken into consideration in choosing optimal therapy.

Table 1. Critical Outcomes and Outcome Measures for Hand OA:

Outcomes: Critical	Pain	Function: Self-Reported	Function: Performance Based
Outcomes Measures (sorted alphabetically):	AUSCAN	AUSCAN	AHFT
	DASH	Cochin	COPM
	MHQ	DASH	GAT
	PRWE	FIHOA	Grip Strength
	QuickDASH	MHQ	JFHT
	VAS	PRWE	MAM
		QuickDASH	Pinch Strength
AHFT=Arthritis Hand Function Test AUSCAN=Australian Canadian Osteoarthritis Hand Index; Cochin=Cochin Hand Function Scale; COPM=Canadian Occupational Performance Measure ; DASH=Disabilities of the Arm, Shoulder and Hand Questionnaire; FIHOA=Functional Index for Hand			

Osteoarthritis (aka Dreiser Functional Hand Index); GAT=Grip Ability Test; JHFT=Jebsen Hand Function Test; MHQ=Michigan Hand Outcomes Questionnaire; MAM=Manual Ability Measure; PRWE=Patient Rated Wrist Evaluation; VAS=Visual Analog Scale

Table 2. Critical Outcomes and Outcome Measures for Hip and Knee OA:

Outcomes: Critical	Pain	Function: Self-Reported	Function: Performance Based
Outcomes Measures (sorted per established hierarchy):	(after Juhl 2012): (1) WOMAC pain subscale (Likert/100mm) or KOOS or HOOS (2) Pain during activity (VAS) (3) Pain during walking (VAS) (4) Global knee pain (VAS) (5) Pain at rest (VAS) (6) SF-36 (bodily pain (BP) subscale) (7) HAQ (pain subscale), Lequesne algofunctional index (pain subscale), AIMS (pain subscale), Knee-Specific Pain Scale (KSPS), McGill Pain Questionnaire (pain intensity) (8) Pain at night (VAS), pain during activity (NRS), pain on walking (NRS), number of painful days (days)	(after Juhl 2012): (1) WOMAC subscale function (Likert/100mm) or KOOS or HOOS (2) SF-36 (subscales physical function (PF) (3) Physical composite score (PCS) based on SF-36, SF-12, or SF-8 (4) HAQ (disability subscale), PDI (pain disability index), ASES (disability subscale)	(after Dobson 2013): (1) sit-to-stand (30-sec chair stand test) (2) walking short distances (4x10m fast paced walk) [gait speed] (3) stair negotiation (no test recommended) (4) ambulatory transitions (timed up and go) (5) aerobic capacity/walking long distances (6-min walk test)
<p>AIMS=Arthritis Impact Measurement Scale; ASES=Arthritis Self Efficacy Scale; HAQ=Health Assessment Questionnaire; HOOS=Hip Disability and Osteoarthritis Outcome Score; KOOS=Knee Injury and Osteoarthritis Outcome Score; NRS=Numerical Rating Scale; VAS=Visual Analog Scale; WOMAC=Western Ontario and McMaster Universities Osteoarthritis Index</p> <p>Dobson F, Hinman RS, Roos EM, Abbott JH, Stratford P, Davis AM, Buchbinder R, Snyder-Mackler L, Henrotin Y, Thumboo J, Hansen P, Bennell KL. OARSI recommended performance-based tests to assess physical function in people diagnosed with hip or knee osteoarthritis. <i>Osteoarthritis and Cartilage</i> 2013;21(8):1042-1052.</p> <p>Juhl C, Lund H, Roos E, Zhang W, Christensen R. A hierarchy of patient-reported outcomes for meta-analysis of knee osteoarthritis trials: empirical evidence from a survey of high impact journals. <i>Arthritis</i> 2012;136-245.</p>			

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Table 3. PICOs and levels of evidence for physical, psychosocial and mind body approach recommendations for the management of osteoarthritis (OA) of the hand, knee and hip.

RECOMMENDATION	LEVEL OF EVIDENCE	PICO #
Exercise		
Strongly recommend exercise for all patients with OA.	Moderate	1 (H/K)
	Moderate	2 (H/K)
	Moderate	3 (H/K)
	Moderate	4 (H/K)
	Moderate	5 (H/K)
	Low (hip); very low (knee)	6 (H/K)
	Low (hip); very low (knee)	7 (H/K)
	Low (hip); very low (knee)	8 (H/K)
	Low (hip); very low (knee)	9 (H/K)
	Very low	10 (H/K)
	Low	11 (H/K)
	Very low	12 (H/K)
	Very low	13 (H/K)
	Low	14 (H/K)
	Very low	16 (H/K)
	Low	17 (H/K)
	Very low	18 (H/K)
	Very low	19 (H/K)
	Very low	20 (H/K)
	Low	21 (H/K)
	Very low	22 (H/K)
Very low	23 (H/K)	
Very low	30 (H)	
Moderate (hip); low (knee)	39 (H)	
Low		
Very low		
Weight loss		
Strongly recommend weight loss for patients with hip and/or knee OA who are overweight.	Moderate	26 (H/K)
	Moderate	36 (H/K)
Self-efficacy and self-management programs		
Strongly recommendation participation in self-efficacy and self-management programs for all patients with OA.	Moderate	24 (H/K)
	Very low	37 (H/K)
	Very low	34 (H)

<i>Mind-body interventions</i>		
Strongly recommend tai chi for patients with knee and hip OA.	Moderate	28 (H/K)
Conditionally recommend yoga for patients with knee OA.	Moderate	28 (H/K)
<i>Cognitive behavioral therapy</i>		
Conditionally recommend cognitive behavioral therapy for all patients with OA.	Low	25 (H/K)
<i>Supportive devices</i>		
Strongly recommend use of a cane for knee and hip OA in those patients in whom disease progression in one or more joints is having a sufficiently large impact on ambulation, joint stability and/or pain to warrant use of an assistive device.	Moderate	29 (H/K)
Strongly recommend tibiofemoral knee braces for knee OA patients in whom disease progression in one or both knees is having a sufficiently large impact on ambulation, joint stability and/or pain to warrant use of an assistive device and are able to tolerate the associated inconvenience and burden.	Moderate	105 (H/K)
Conditionally recommend patellofemoral braces for patients with patellofemoral knee OA in whom disease progression in one or both knees is having a sufficiently large impact on ambulation, joint stability and/or pain to warrant use of an assistive device and are able to tolerate the associated inconvenience and burden.	Low	106 (H/K)
Conditionally recommend kinesiotaping for patients with knee and 1st carpometacarpal joint OA.	Low Very low	107 (H/K) 49 (H)
Strongly recommend the use of hand orthoses in the 1 st CMC joint for patients with hand OA.	Low Low Very low Very low	46 (H) 47(H) 48 (H) 50 (H)
Conditionally recommend the use of hand orthoses for patients with OA in other joints of the hand.	Very low Very low Low Very low	37 (H) 38 (H) 51 (H) 52 (H)
Conditionally recommend against the use of modified shoes for patients with hip and/or knee OA.	Low	104 (H/K)
Conditionally recommend against the use of lateral and medial wedged insoles for patients with hip and/or knee OA.	Low	103 (H/K)
<i>Acupuncture</i>		
Conditionally recommend the use of acupuncture in patients with OA.	Low (hip); low (knee) Very low	27 (H/K) 36 (H)
<i>Other physical modalities</i>		
Conditionally recommend the use of thermal interventions (locally applied heat or cold) for patients with hip, knee and/or hand OA.	Low Low Low	30 (H/K) 31 (H/K) 32 (H)

Conditionally recommend the use of paraffin for patients with hand OA.	Low	31 (H)
Conditionally recommend the use of radiofrequency ablation for patients with knee OA.	Moderate	102 (H/K)
Conditionally recommend against the use of massage therapy for management of OA.	Low	34 (H/K)
Conditionally recommend against the use of manual therapy with exercise over exercise alone in the management of OA.	Low Low	35 (H/K) 38 (H/K)
Conditionally recommend against the use of iontophoresis in patients with 1st carpometacarpal joint OA.	Very low Very low Very low	13 (H) 24 (H) 45 (H)
Conditionally recommend against the use of pulsed vibration therapy in patients with knee OA.	Low	33 (H/K)
Strongly recommend against the use of transcutaneous electrical stimulation (TENS) in all patients with OA.	Low	32 (H/K)

Abbreviations: (H/K), Hip/Knee; (H) Hand

Table 4. PICOs and level of evidence for pharmacologic recommendations for the management of osteoarthritis (OA) of the hand, knee and hip.

RECOMMENDATION	LEVEL OF EVIDENCE	PICO #
Topical preparations		
Strongly recommend the use of topical NSAIDs in patients with knee OA.	Moderate Low	96 (H/K) 98 (H/K)
Conditionally recommend the use of topical NSAIDs in patients with hand OA.	Low Very low	11 (H) 22 (H)
Conditionally recommend the use of topical capsaicin in patients with knee OA.	Moderate Very low Very low	97 (H/K) 99 (H/K) 101 (H/K)
Conditionally recommend against the use of topical capsaicin in patients with hand OA.	Very low Very low Very low	12 (H) 23 (H) 28 (H)
Non-steroidal anti-inflammatory drugs		
Strongly recommend the use of NSAIDs in all patients with OA.	Moderate Low Moderate	56 (H/K) 76 (H/K) 1 (H)
Intra-articular corticosteroid injections		
Strongly recommend the use of intra-articular corticosteroid injections in patients with knee or hip OA.	Low Very low Low Moderate Very low	39 (H/K) 40 (H/K) 46 (H/K) 54 (H/K) 55 (H/K)
Conditionally recommend the use of intra-articular corticosteroid injections in patients with hand OA.	Low Very low	25 (H) 44 (H)
Strongly recommend guidance with imaging for injection into hip joints.	Low	109 (H/K)
Conditionally recommend intra-articular corticosteroid injection, in OA generally, over other forms of intra-articular injection, including hyaluronic acid preparations.	Low Moderate Moderate	46 (H/K) 47 (H/K) 51 (H/K)
Acetaminophen		
Conditionally recommend the use of acetaminophen in patients with OA.	Low Very low Very low	57 (H/K) 2 (H) 14 (H)
Duloxetine		
Conditionally recommend the use of duloxetine in patients with knee OA.	Moderate Very low	59 (H/K) 78 (H/K)
Opioids		
Conditionally recommend the use of tramadol in patients with OA.	Moderate Low Very low Very low	62 (H/K) 81 (H/K) 95 (H/K) 8 (H)

	Very low Very low	19 (H) 27 (H)
Conditionally recommend against the use of non-tramadol opioids in patients with OA.	Low Very low Very low Very low	63 (H/K) 82 (H/K) 7 (H) 18 (H)
Colchicine		
Conditionally recommend against the use of colchicine in patients with OA.	Very low Very low	67 (H/K) 86 (H/K)
Fish oil		
Conditionally recommend against the use of fish oil in patients with OA.	Moderate Very low	72 (H/K) 91 (H/K)
Vitamin D		
Conditionally recommend against the use of vitamin D in patients with OA.	Low Very low	71 (H/K) 90 (H/K)
Bisphosphonates		
Strongly recommend against the use of bisphosphonates in patients with OA.	Moderate Very low Very low	58 (H/K) 77 (H/K) 3 (H)
Glucosamine and chondroitin sulfate		
Strongly recommend against the use of glucosamine in patients with OA.	Moderate Low Very low Very low	68 (H/K) 87 (H/K) 4 (H) 15 (H)
Strongly recommend against the use of chondroitin sulfate in patients with knee OA, as are combination products that include glucosamine and chondroitin sulfate.	Moderate Moderate Moderate Moderate Very low	69 (H/K) 70 (H/K) 88 (H/K) 89 (H/K) 6 (H)
Conditionally recommend the use of chondroitin sulfate in patients with hand OA.	Low Very low	5 (H) 16 (H)
Hydroxychloroquine		
Strongly recommend against the use of hydroxychloroquine in patients with OA.	Moderate	40 (H)
Methotrexate		
Strongly recommend against the use of methotrexate in patients with OA.	Very low Very low Very low	66 (H/K) 85 (H/K) 42 (H)
Other intra-articular agents		
Conditionally recommend against the use of intra-articular hyaluronic acid injections in patients with knee and 1 st CMC OA.	Low Moderate Very low Low	41 (H/K) 47 (H/K) 26 (H) 29 (H)
Strongly recommend against the use of intra-articular hyaluronic acid injections in patients with hip OA.	Low	46 (H/K)

Conditionally recommend against the use of intra-articular botulinum toxin in patients with OA.	Very low Moderate	45 (H/K) 51 (H/K)
Conditionally recommend against the use of prolotherapy in patients with OA.	Low Very low	44 (H/K) 50 (H/K)
Strongly recommend against the use of platelet-rich plasma in patients with OA.	Low Low	42 (H/K) 48 (H/K)
Strongly recommend against the use of stem-cell injections in patients with OA.	Low Very low	43 (H/K) 49 (H/K)
<i>Biologic agents</i>		
Strongly recommend against the use of tumor necrosis factor (TNF) inhibitors and interleukin-1 (IL-1) receptor antagonists in patients with OA.	Very low	74 (H/K)
	Low	75 (H/K)
	Very low	93 (H/K)
	Very low	94 (H/K)
	Very low	41 (H)
	Very low	43 (H)

Abbreviations: (H/K), Hip/Knee; (H) Hand