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# American College of Rheumatology (ACR) Guideline for the Pharmacologic and Non-Pharmacologic Management of Osteoarthritis of the Hand, Hip and Knee

***Project Plan – September 2017***

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## ORGANIZATIONAL LEADERSHIP AND SUPPORT

This project of the American College of Rheumatology (ACR) has the broad objective of developing an evidence-based clinical practice guideline for the pharmacologic and non-pharmacologic management of osteoarthritis (OA) of the hand, hip and knee.

## BACKGROUND

OA is a joint disorder characterized by structural pathology that involves the whole joint, including cartilage lesions, bone remodeling, osteophyte formation, and joint inflammation, among others, leading to symptoms and loss of normal joint function. OA typically becomes symptomatic later in life, usually after age 50, though it may start earlier, such as when joint injury has occurred or in familial forms. It is the most common form of arthritis worldwide, affecting an estimated 250 million people; about 80% of people over 65 having radiographic evidence of OA. Further, OA is a leading cause of disability among older adults worldwide. While any joint can be affected, weight bearing joints (hips, knees) and hands are most commonly involved. The symptoms of OA may initially be intermittent and activity-related, but often progress to more persistent symptoms punctuated by flares over time.

In addition to aging, several risk factors can increase the likelihood of OA. Women are more likely than men to develop OA. Obesity may increase risk through physical stress on joints, as well as via adipokine-mediated inflammation. Occupations in which excessive joint loading occurs (e.g., athletes, jobs involving frequent squatting, heavy lifting), and repeated microtrauma or overt joint injury are also major risk factors.

The main symptoms of OA are joint pain, stiffness in the morning or after periods of inactivity, limited range of motion, and swelling. These symptoms can lead to functional limitations and disability. Diagnosis can typically be made on the basis of symptoms and physical examination alone. Radiographic findings include joint space narrowing, osteophytes, sclerosis, and subchondral cysts; however, the early pathologic features of OA are not visualized by radiographs.

There are multiple non-pharmacologic, pharmacologic, and surgical treatments. Weight loss, avoidance of excessive joint use or joint injury, physical therapy, aerobic, strengthening, balance and aquatic exercise, orthoses, assistive devices, vitamins, dietary supplements, and thermal treatments are a few of the non-pharmacologic therapies available. Pharmacologic treatments include medications aimed

primarily at reducing pain, such as NSAIDs and intra-articular injections. Orthopedic surgery is usually reserved for more severely disabled patients who have failed medical and nonpharmacological therapies.

**OBJECTIVES**

The objective of this project is to develop recommendations for the pharmacologic and non-pharmacologic management of OA of the hand, hip, and knee. Specifically, we aim to:

1. Evaluate the evidence regarding the benefits and harms of oral, topical, injectable, and intra-articular agents in the management of symptomatic hand, hip, and knee OA.
2. Evaluate the evidence regarding the benefits and harms of exercise, physical therapy (for knee and hip), occupational therapy (for hand), assistive devices and other non-pharmacologic modalities in the management of symptomatic hand, hip and knee OA.
3. Develop recommendations based on the best available evidence for patients with symptomatic hand, hip, or knee OA.
4. Determine whether there are any differences in treatment recommendations for particular subtypes of hand or knee OA where treatments may be subtype-specific (e.g., 1$^{st}$ CMC OA, unicompartmental knee OA, PFOA).

**METHODS**

*Identification of Studies*

Literature search strategies, based on PICO questions (Population/patients, Intervention, Comparator, and Outcomes; *see Appendix A*) will be developed by the principal investigators, systematic literature review leader, and a research librarian, with input from the Core Team. The search strategies will be peer reviewed by another medical librarian using Peer Review of Electronic Search Strategies (PRESS) (1). Searches will be performed in OVID Medline (1946 +), Embase (1974 +), the Cochrane Library, and PubMed (mid-1960s +).

The search strategies will be developed using the controlled vocabulary or thesauri language for each database: Medical Subject Headings (MeSH) for OVID Medline, PubMed and Cochrane Library; and Emtree terms for Embase. Text words will also be used in OVID Medline, PubMed, and Embase, and keyword/title/abstract words in the Cochrane Library.

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*Search Limits*

Only English language articles will be retrieved.

*Grey Literature*

The websites of appropriate agencies, such as the Agency for Healthcare Research and Quality (AHRQ), will be searched for peer-reviewed reports not indexed by electronic databases.

*Literature Search Update*

Literature searches will be updated just before the voting panel meeting to ensure completeness.

*Inclusion/Exclusion Criteria*

See PICO questions (*Appendix A*), which outline the defined patient population, interventions, comparators and outcomes.

*Management of Studies and Data*

References and abstracts will be imported into bibliographic management software (Reference Manager) (2), duplicates removed, and exported to Distiller SR, a web-based systematic review manager (3). Screening and data abstraction forms will be created in Distiller SR. Search results will be divided among reviewers and two reviewers will screen each title/abstract, with disagreements at the title/abstract screening stage defaulting to inclusion for full manuscript review. Following the same dual review process, disagreements at the full manuscript screening stage will be discussed and adjudicated by the literature review leadership, if necessary.

*Phases*

1. A search for randomized controlled trials and observational studies about interventions aimed at the pharmacologic and non-pharmacologic management of OA of the hand, hip and knee will be performed to determine existing studies covering outcomes of interest. Subsequently, identified studies will be assessed using the RevMan (4) and GRADE Pro tools (5).

2. Chosen studies will be assessed for risk of bias using modified versions of the Cochrane Risk of Bias tool (6) and the Newcastle-Ottawa Scale (7).
3. Additionally, recently published systematic reviews covering outcomes of interest will also be sought and used for reference cross-checking.

*GRADE Methodology*

GRADE methodology (8) will be used in this project to grade available evidence and facilitate development of recommendations. The certainty in the evidence (also known as 'quality' of evidence) will be graded as high, moderate, low or very low. The strength of recommendations will be graded as strong or conditional. The strength of recommendations will not depend solely on the certainty in the evidence, but also on patient preferences and values, and the weight between benefits and harms. A series of articles that describe the GRADE methodology can be found on the GRADE working group's website: www.gradeworkinggroup.org.

*Analysis and Synthesis*

The literature review team will analyze and synthesize data from included studies that address the PICO questions. An evidence profile, including a GRADE Summary of Findings table, will be prepared for each PICO question using Review Manager (RevMan) (2) and GRADEprofiler (GRADEpro) software (5). The Summary of Findings table contains the benefits and harms for each outcome across studies, the assumed and corresponding risk for comparators and interventions (95% CI), the absolute risk and relative effect (95% CI), the number of participants/number of studies, and the certainty in the evidence for each critical and important outcome (i.e., high, moderate, low or very low).

The evidence profile documents the overall certainty in the evidence for each critical and important outcome across studies and summarizes the rationale of the GRADE criteria for downgrading (risk of bias, inconsistency, indirectness, imprecision and publication bias), or upgrading the certainty in a body of evidence (large magnitude of effect, dose-response gradient, and all plausible confounding that would reduce a demonstrated effect).

*Development of Recommendation Statements*

PICO questions will be revised into drafted recommendation statements. Using the GRADE Evidence Profiles and Summaries of Findings tables, the voting panel, consisting of 10 rheumatologists, one

occupational therapist, one physical therapist, and two patient representatives, will consider the drafted recommendation statements in two stages. The first assessment will be done individually, and the results will be anonymous; this vote will only be used to determine where consensus might or might not already exist and develop the voting panel meeting agenda. At the face-to-face voting panel meeting, chaired by the principal investigators, the panelists will discuss the evidence in the context of their clinical experience and expertise to arrive at consensus on the final recommendations. The voting panel meeting discussions will be supported by the literature review leader, the GRADE expert, and selected members of the literature review team, who will attend the meeting to provide details about the evidence, as requested. Voting panel discussions and decisions will be informed by a separately convened patient panel, which will meet in the days before the voting panel meeting, to provide unique patient perspectives on the drafted recommendations based on their experiences and the available literature.

**PLANNED APPENDICES (AT MINIMUM)**

A. Final literature search strategies
B. GRADE evidence profiles and summary of findings tables for each PICO question

**AUTHORSHIP**

Authorship of the guideline will include: principal investigator, Dr. Sharon L. Kolasinski, as the lead author; Dr. James Reston, literature review leader; Drs. Marc Hochberg, Tuhina Neogi and Carol Oatis, content experts; and Dr. Gordon Guyatt, GRADE expert. Members of the literature review team and voting panel will also be authors. The PI will determine final authorship, dependent on the efforts made by individuals throughout the guideline development process, using international authorship standards as guidance.

**DISCLOSURES/CONFLICTS OF INTEREST**

The ACR's disclosure and COI policies for guideline development will be followed for this project. These can be found in the ACR Guideline Manual on this page of the ACR web site, under Policies & Procedures. *See Appendix B for participant disclosures.*

## REFERENCES

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## APPENDIX A – PICO Questions

### Hand:

| 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 |

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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

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| Patient | I# | Intervention | Comparison | Outcomes : Harms |
|---|---|---|---|---|
| **Symptomatic hand OA** | 1 | oral NSAIDs | no treatment | gastrointestinal (perforations, ulcer, bleed) SAEs, cardiovascular (MI, CVA) SAEs, other SAEs |
| | 2 | acetaminophen | no treatment | hepatotoxicity, SAEs |

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| | | | | |
|---|---|---|---|---|
| | 3 | bisphosphonates | no treatment | SAEs |
| | 4 | glucosamine | no treatment | SAEs |
| | 5 | chondroitin | no treatment | SAEs |
| | 6 | glucosamine + chondroitin | no treatment | SAEs |
| | 7 | non-tramadol opioids | no treatment | SAEs |
| | 8 | tramadol | no treatment | SAEs |
| | 9 | duloxetine | no treatment | SAEs |
| | 11 | topical NSAIDs | no treatment | skin reaction, SAEs |
| | 12 | topical capsaicin | no treatment | skin reaction, SAEs |
| | 13 | iontophoresis | no treatment | increased pain, injury, other SAEs |
| | | | | |

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| | | | | |
|---|---|---|---|---|
| | 14 | acetaminophen | oral NSAIDs | hepatotoxicity, SAEs |
| | 15 | glucosamine | oral NSAIDs | SAEs |
| | 16 | chondroitin | oral NSAIDs | SAEs |
| | 17 | glucosamine + chondroitin | oral NSAIDs | SAEs |
| | 18 | non-tramadol opioids | oral NSAIDs | SAEs |
| | 19 | tramadol | oral NSAIDs | SAEs |
| | 20 | duloxetine | oral NSAIDs | SAEs |
| | 21 | anti-nerve growth factor | oral NSAIDs | osteonecrosis, rapidly progressive OA, need for total joint arthroplasty, neurological SAEs, other SAEs |
| | 22 | topical NSAIDs | oral NSAIDs | skin reaction, SAEs |
| | 23 | topical capsaicin | oral NSAIDs | skin reaction, SAEs |

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| | | | | |
|---|---|---|---|---|
| | | | | |
| | 24 | iontophoresis | oral NSAIDs | increased pain, injury, other SAEs |
| | | | | |
| | 25 | intra-articular corticosteroids | oral NSAIDs | increased pain, septic arthritis, other SAEs |
| | 26 | intra-articular hyaluronic acid | oral NSAIDs | increased pain, septic arthritis, other SAEs |
| | | | | |
| | 27 | tramadol | non-tramadol opioids | SAEs |
| | | | | |
| | 28 | topical capsaicin | topical NSAIDs | skin reaction, SAEs |
| | | | | |

| | | | | |
|---|---|---|---|---|
| | | | | |
| | 29 | intra-articular hyaluronic acid | intra-articular corticosteroids | increased pain, septic arthritis, other SAEs |
| | | | | |
| | 30 | hand exercise + usual care | usual care (maximally tolerable therapeutic doses of acetaminophen or oral NSAIDs) | increased pain, injury, other SAEs |
| | 31 | paraffin + usual care | usual care (maximally tolerable therapeutic doses of acetaminophen or oral NSAIDs) | increased pain, injury, other SAEs |
| | 32 | therapeutic heat (including ultrasound) + usual care | usual care (maximally tolerable therapeutic doses of acetaminophen or oral NSAIDs) | increased pain, injury, other SAEs |

| | | | | |
|---|---|---|---|---|
| | 33 | therapeutic cooling + usual care | usual care (maximally tolerable therapeutic doses of acetaminophen or oral NSAIDs) | increased pain, injury, other SAEs |
| | 34 | patient education + usual care | usual care (maximally tolerable therapeutic doses of acetaminophen or oral NSAIDs) | increased pain, injury, other SAEs |
| | 35 | OT/hand therapy + usual care (includes joint stabilization, joint protection, work simplification, assistive devices, pain management; orthoses + exercise may be included as part of comprehensive | usual care (maximally tolerable therapeutic doses of acetaminophen or oral NSAIDs) | increased pain, injury, other SAEs |

| | | | | |
|---|---|---|---|---|
| | | OT/hand therapy) | | |
| | 36 | acupuncture + usual care | usual care (maximally tolerable therapeutic doses of acetaminophen or oral NSAIDs) | increased pain, injury, other SAEs |
| | 37 | digital orthosis + usual care | usual care (maximally tolerable therapeutic doses of acetaminophen or oral NSAIDs) | increased pain, injury, other SAEs |
| | 38 | glove + usual care (edema, compression, nylon, spandex or neoprene therapeutic glove) | usual care (maximally tolerable therapeutic doses of acetaminophen or oral NSAIDs) | increased pain, injury, other SAEs |
| | | | | |
| | 39 | strengthening | stretching/ROM | increased pain, injury, other SAEs |

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| | | | | |
| **Symptomatic erosive hand OA** | 40 | HCQ + NSAIDs + usual care | oral NSAIDs | SAEs, gastrointestinal (perforations, ulcer, bleed) SAEs, cardiovascular (MI, CVA) SAEs |
| | 41 | TNF-I + NSAIDs + usual care | oral NSAIDs | serious infections, cancer, other SAEs, gastrointestinal (perforations, ulcer, bleed) SAEs, cardiovascular (MI, CVA) SAEs |
| | 42 | MTX + NSAIDs + usual care | oral NSAIDs | hepatotoxicity, serious infections, other SAEs, gastrointestinal (perforations, ulcer, bleed) SAEs, cardiovascular (MI, CVA) SAEs |
| | 43 | IL-1 + NSAIDs+ usual care | oral NSAIDs | serious infections, cancer, other SAEs, gastrointestinal (perforations, ulcer, bleed) SAEs, cardiovascular (MI, CVA) SAEs |
| | | | | |
| **1st CMC** | 44 | usual care | intra-articular corticosteroids | increased pain, injury, other SAEs |
| | 45 | iontophoresis + usual care | intra-articular corticosteroids | increased pain, injury, other SAEs |

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| | | | | |
|---|---|---|---|---|
| | | | | |
| | 46 | rigid hand-base spica + usual care | usual care (maximally tolerable therapeutic doses of acetaminophen or oral NSAIDs) | increased pain, injury, other SAEs |
| | 47 | neoprene hand-base spica + usual care | usual care (maximally tolerable therapeutic doses of acetaminophen or oral NSAIDs) | increased pain, injury, other SAEs |
| | 48 | glove + usual care (edema, compression, nylon, spandex or neoprene therapeutic glove) | usual care (maximally tolerable therapeutic doses of acetaminophen or oral NSAIDs) | increased pain, injury, other SAEs |
| | 49 | kinesiotape + usual care | usual care (maximally tolerable therapeutic doses of acetaminophen | increased pain, injury, other SAEs |

| | | | | |
|---|---|---|---|---|
| | | | or oral NSAIDs) | |
| | | | | |
| | 50 | orthosis + usual care | kinesiotape | increased pain, injury, other SAEs |
| | | | | |
| **Symptomatic wrist OA** | 51 | rigid cock-up splint + usual care | usual care (maximally tolerable therapeutic doses of acetaminophen or oral NSAIDs) | increased pain, injury, other SAEs |
| | 52 | neoprene cock-up splint + usual care | usual care (maximally tolerable therapeutic doses of acetaminophen or oral NSAIDs) | increased pain, injury, other SAEs |

**Hip and Knee:**

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| **Outcomes: Critical** | **Pain** | **Function: Self-Reported** | **Function: Performance Based** |
|---|---|---|---|
| **Outcomes Measures::** | **(after Juhl 2012):**<br><br>(1) WOMAC pain subscale (Likert/100mm) or KOOS or HOOS<br>(2) Pain during activity (VAS)<br>(3) Pain during walking (VAS)<br>(4) Global knee pain (VAS)<br>(5) Pain at rest (VAS)<br>(6) SF-36 (bodily pain (BP) subscale)<br>(7) HAQ (pain subscale), Lequesne algofunctional index (pain subscale), AIMS (pain subscale), Knee-Specific Pain Scale (KSPS), McGill Pain Questionnaire (pain intensity)<br>(8) Pain at night (VAS), pain during activity (NRS), pain on walking (NRS), number of | **(after Juhl 2012):**<br><br>(1) WOMAC subscale function (Likert/100mm) or KOOS or HOOS<br>(2) SF-36 (subscale physical function (PF)<br>(3) Physical composite score (PCS) based on SF-36, SF-12, or SF-8<br>(4) HAQ (disability subscale), PDI (pain disability index), ASES (disability subscale) | **(after Dobson 2013):**<br><br>(1) sit-to-stand (30-sec chair stand test)<br>(2) walking short distances (4x10m fast paced walk) [gait speed]<br>(3) stair negotiation (no test recommended)<br>(4) ambulatory transitions (timed up and go)<br>(5) aerobic capacity/walking long distances (6-min walk test) |

| | | | |
|---|---|---|---|
| | painful days (days) | | |

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

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| Patient | I# | Intervention | Comparison | Outcomes (see below) |
|---|---|---|---|---|

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| | | | | |
|---|---|---|---|---|
| **Symptomatic knee or hip OA** | 1 | aerobic exercise + usual care | usual care (maximally tolerable therapeutic doses of acetaminophen or oral NSAIDs) | increased pain, injury, SAEs |
| | 2 | strength training + usual care | usual care (maximally tolerable therapeutic doses of acetaminophen or oral NSAIDs) | increased pain, injury, SAEs |
| | 3 | neuromuscular training + usual care | usual care (maximally tolerable therapeutic doses of acetaminophen or oral NSAIDs) | increased pain, injury, SAEs |
| | 4 | aquatic exercise + usual care | usual care (maximally tolerable therapeutic doses of acetaminophen or oral NSAIDs)) | increased pain, injury, SAEs |
| | 5 | balance training + usual care | usual care (maximally | increased pain, injury, SAEs |

| | | | | |
|---|---|---|---|---|
| | | | tolerable therapeutic doses of acetaminophen or oral NSAIDs) | |
| | 6 | daily walking + usual care | usual care (maximally tolerable therapeutic doses of acetaminophen or oral NSAIDs) | increased pain, injury, SAEs |
| | | | | |
| | 7 | strength training + usual care | aerobic exercise + usual care (maximally tolerable therapeutic doses of acetaminophen or oral NSAIDs) | increased pain, injury, SAEs |
| | 8 | neuromuscular training + usual care | aerobic exercise usual care (maximally tolerable therapeutic doses of acetaminophen or oral | increased pain, injury, SAEs |

| | | | | |
|---|---|---|---|---|
| | | | NSAIDs) | |
| | 9 | aquatic exercise + usual care | aerobic exercise + usual care (maximally tolerable therapeutic doses of acetaminophen or oral NSAIDs) | increased pain, injury, SAEs |
| | 10 | balance training + usual care | aerobic exercise + usual care (maximally tolerable therapeutic doses of acetaminophen or oral NSAIDs) | increased pain, injury, SAEs |
| | 11 | daily walking + usual care | aerobic exercise + usual care (maximally tolerable therapeutic doses of acetaminophen or oral NSAIDs) | increased pain, injury, SAEs |
| | | | | |

| | | | | |
|---|---|---|---|---|
| | 12 | neuromuscular training + usual care | strength training + usual care (maximally tolerable therapeutic doses of acetaminophen or oral NSAIDs) | increased pain, injury, SAEs |
| | 13 | aquatic exercise + usual care | strength training + usual care (maximally tolerable therapeutic doses of acetaminophen or oral NSAIDs) | increased pain, injury, SAEs |
| | 14 | balance training + usual care | strength training + usual care (maximally tolerable therapeutic doses of acetaminophen or oral NSAIDs) | increased pain, injury, SAEs |
| | 15 | daily walking + usual care | strength training + usual care (maximally tolerable therapeutic doses of | increased pain, injury, SAEs |

| | | | | |
|---|---|---|---|---|
| | | | acetaminophen or oral NSAIDs) | |
| | | | | |
| | 16 | aquatic exercise + usual care | neuromuscular training + usual care (maximally tolerable therapeutic doses of acetaminophen or oral NSAIDs) | increased pain, injury, SAEs |
| | 17 | balance training + usual care | neuromuscular training + usual care (maximally tolerable therapeutic doses of acetaminophen or oral NSAIDs) | increased pain, injury, SAEs |
| | 18 | daily walking + usual care | neuromuscular training + usual care (maximally tolerable therapeutic doses of acetaminophen or oral | increased pain, injury, SAEs |

| | | | | |
|---|---|---|---|---|
| | | | NSAIDs) | |
| | | | | |
| | 19 | balance training + usual care | aquatic exercise + usual care (maximally tolerable therapeutic doses of acetaminophen or oral NSAIDs) | increased pain, injury, SAEs |
| | 20 | daily walking + usual care | aquatic exercise + usual care (maximally tolerable therapeutic doses of acetaminophen or oral NSAIDs) | increased pain, injury, SAEs |
| | | | | |
| | 21 | daily walking + usual care | balance training + usual care (maximally tolerable therapeutic doses of acetaminophen or oral | increased pain, injury, SAEs |

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| | | | | |
|---|---|---|---|---|
| | | | NSAIDs) | |
| | | | | |
| | 22 | unsupervised exercise **(simply advised to exercise)** + usual care | supervised exercise (with prescribed specific program) + usual care (maximally tolerable therapeutic doses of acetaminophen or oral NSAIDs) | increased pain, injury, SAEs |
| | 23 | unsupervised **prescribed** exercise + usual care | supervised exercise (with prescribed specific program) + | increased pain, injury, SAEs |
| | | | | |
| | 24 | self-efficacy/self-management + usual care | usual care (maximally tolerable therapeutic doses of acetaminophen or oral NSAIDs) | increased pain, injury, SAEs |

| | | | | |
|---|---|---|---|---|
| | 25 | cognitive behavioral therapy + usual care | usual care (maximally tolerable therapeutic doses of acetaminophen or oral NSAIDs) | increased pain, injury, SAEs |
| | 26 | weight loss + usual care | usual care (maximally tolerable therapeutic doses of acetaminophen or oral NSAIDs) | increased pain, injury, SAEs |
| | 27 | acupuncture + usual care | usual care (maximally tolerable therapeutic doses of acetaminophen or oral NSAIDs) | increased pain, injury, SAEs |
| | 28 | mind body practices + usual care | usual care (maximally tolerable therapeutic doses of acetaminophen or oral NSAIDs) | increased pain, injury, SAEs |
| | 29 | cane + usual care | usual care (maximally | increased pain, injury, SAEs |

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| | | | tolerable therapeutic doses of acetaminophen or oral NSAIDs) | |
| | 30 | therapeutic heat (including ultrasound) + usual care | usual care (maximally tolerable therapeutic doses of acetaminophen or oral NSAIDs) | increased pain, injury, SAEs |
| | 31 | therapeutic cooling + usual care | usual care (maximally tolerable therapeutic doses of acetaminophen or oral NSAIDs) | increased pain, injury, SAEs |
| | 32 | TENS + usual care | usual care (maximally tolerable therapeutic doses of acetaminophen or oral NSAIDs) | increased pain, injury, SAEs |
| | 33 | pulsed vibration therapy + usual care | usual care (maximally tolerable therapeutic doses | increased pain, injury, SAEs |

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| | | | of acetaminophen or oral NSAIDs) | |
| | 34 | massage therapy + usual care | usual care (maximally tolerable therapeutic doses of acetaminophen or oral NSAIDs) | increased pain, injury, SAEs |
| | 35 | manual therapy + exercise + usual care | usual care (maximally tolerable therapeutic doses of acetaminophen or oral NSAIDs) | increased pain, injury, SAEs |
| | | | | |
| | 36 | weight loss + any type of exercise | exercise alone | increased pain, injury, SAEs |
| | 37 | self-efficacy + any type of exercise | exercise alone | increased pain, injury, SAEs |
| | 38 | manual therapy + any type of exercise | exercise alone | increased pain, injury, SAEs |

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| | 39 | intra-articular corticosteroids | oral NSAIDs | increased pain, septic arthritis, other SAEs |
| | 40 | long-acting intra-articular corticosteroids | oral NSAIDs | increased pain, septic arthritis, other SAEs |
| | 41 | intra-articular hyaluronic acid | oral NSAIDs | increased pain, septic arthritis, other SAEs |
| | 42 | intra-articular platelet rich plasma | oral NSAIDs | increased pain, septic arthritis, other SAEs |
| | 43 | intra-articular mesenchymal stem cells | oral NSAIDs | increased pain, septic arthritis, other SAEs |
| | 44 | intra-articular prolotherapy | oral NSAIDs | increased pain, septic arthritis, other SAEs |
| | 45 | intra-articular botulinum toxin | oral NSAIDs | increased pain, septic arthritis, other SAEs |
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| | 46 | intra-articular saline | intra-articular corticosteroid | increased pain, septic arthritis, other SAEs |

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| | 47 | intra-articular hyaluronic acid | intra-articular corticosteroid | increased pain, septic arthritis, other SAEs |
| | 48 | intra-articular platelet rich plasma | intra-articular corticosteroid | increased pain, septic arthritis, other SAEs |
| | 49 | intra-articular mesenchymal stem cells | intra-articular corticosteroid | increased pain, septic arthritis, other SAEs |
| | 50 | intra-articular prolotherapy | intra-articular corticosteroid | increased pain, septic arthritis, other SAEs |
| | 51 | intra-articular botulinum toxin | intra-articular corticosteroid | increased pain, septic arthritis, other SAEs |
| | 52 | intra-articular anesthetic | intra-articular corticosteroid | increased pain, septic arthritis, other SAEs |
| | 53 | intra-articular corticosteroids + intra-articular anesthetic | intra-articular corticosteroid | increased pain, septic arthritis, other SAEs |
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| | 54 | long-acting intra-articular corticosteroid | short-acting intra-articular corticosteroid | increased pain, septic arthritis, other SAEs |
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| | 55 | high dose (> 50 mg) intra-articular corticosteroid | low-dose (≤ 50 mg) intra-articular corticosteroid | increased pain, septic arthritis, other SAEs |
| | | | | |
| | 56 | oral NSAIDs | no treatment | gastrointestinal (perforations, ulcer, bleed) SAEs, cardiovascular (MI, CVA) SAEs, other SAEs |
| | 57 | acetaminophen | no treatment | hepatotoxicity, SAEs |
| | 58 | bisphosphonates | no treatment | SAEs |
| | 59 | duloxetine | no treatment | SAEs |
| | 60 | other serotonin norepinephrine reuptake inhibitors | no treatment | SAEs |

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| | 61 | tricyclic anti-depressants | no treatment | SAEs |
| | 62 | tramadol | no treatment | SAEs |
| | 63 | non-tramadol opioids | no treatment | SAEs |
| | 64 | gabapentin | no treatment | SAEs |
| | 65 | pregabalin | no treatment | SAEs |
| | 66 | MTX | no treatment | hepatotoxicity, serious infections, other SAEs |
| | 67 | colchicine | no treatment | SAEs |
| | 68 | glucosamine | no treatment | SAEs |
| | 69 | chondroitin | no treatment | SAEs |
| | 70 | glucosamine + chondroitin combination | no treatment | SAEs |

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|---|---|---|---|---|
| | 71 | vitamin D | no treatment | SAEs |
| | 72 | fish oil | no treatment | SAEs |
| | 73 | anti-nerve growth factor | no treatment | osteonecrosis, rapidly progressive OA, need for total joint arthroplasty, neurological SAEs, other SAEs |
| | 74 | TNF-I | no treatment | serious infections, cancer, other SAEs |
| | 75 | IL-1 | no treatment | serious infections, cancer, other SAEs |
| | | | | |
| | 76 | acetaminophen | oral NSAIDs | hepatotoxicity, SAEs |
| | 77 | bisphosphonates | oral NSAIDs | SAEs |
| | 78 | duloxetine | oral NSAIDs | SAEs |
| | 79 | other serotonin norepinephrine reuptake inhibitors | oral NSAIDs | SAEs |

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|---|---|---|---|---|
| | 80 | tricyclic anti-depressants | oral NSAIDs | SAEs |
| | 81 | tramadol | oral NSAIDs | SAEs |
| | 82 | non-tramadol opioids | oral NSAIDs | SAEs |
| | 83 | gabapentin | oral NSAIDs | SAEs |
| | 84 | pregabalin | oral NSAIDs | SAEs |
| | 85 | MTX | oral NSAIDs | hepatotoxicity, serious infections, other SAEs |
| | 86 | colchicine | oral NSAIDs | SAEs |
| | 87 | glucosamine | oral NSAIDs | SAEs |
| | 88 | chondroitin | oral NSAIDs | SAEs |
| | 89 | glucosamine + chondroitin combination | oral NSAIDs | SAEs |

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|---|---|---|---|---|
| | 90 | vitamin D | oral NSAIDs | SAEs |
| | 91 | fish oil | oral NSAIDs | SAEs |
| | 92 | anti-nerve growth factor | oral NSAIDs | osteonecrosis, rapidly progressive OA, need for total joint arthroplasty, neurological SAEs, other SAEs |
| | 93 | TNF-I | oral NSAIDs | serious infections, cancer, other SAEs |
| | 94 | IL-1 | oral NSAIDs | |
| | | | | |
| | 95 | tramadol | non-tramadol opioids | SAEs |
| | | | | |
| **Symptomatic knee OA ONLY** | 96 | topical NSAIDs | no treatment | skin reaction, SAEs |
| | 97 | topical capsaicin | no treatment | skin reaction, SAEs |
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|---|---|---|---|---|
| | 98 | topical NSAIDs | oral NSAIDs | skin reaction, SAEs |
| | 99 | topical capsaicin | oral NSAIDs | skin reaction, SAEs |
| | 100 | topical lidocaine | oral NSAIDs | skin reaction, SAEs |
| | | | | |
| | 101 | topical capsaicin | topical NSAIDs | skin reaction, SAEs |
| | | | | |
| | 102 | ablation + usual care | usual care (maximally tolerable therapeutic doses of acetaminophen or oral NSAIDs) | increased pain, injury, SAEs |
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| **Symptomatic UNICOMPARTMENTAL knee OA ONLY** | | | | |

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| | 103 | wedge insoles (lateral for medial OA; medial for lateral OA) + usual care | usual care (maximally tolerable therapeutic doses of acetaminophen or oral NSAIDs) | increased pain, injury, SAEs |
| | 104 | modified shoe + gait retraining + usual care | usual care (maximally tolerable therapeutic doses of acetaminophen or oral NSAIDs) | increased pain, injury, SAEs |
| | 105 | modified shoe + gait retraining + usual care | usual care (maximally tolerable therapeutic doses of acetaminophen or oral NSAIDs) | increased pain, injury, SAEs |
| | 106 | unloader knee brace + usual care | usual care (maximally tolerable therapeutic doses of acetaminophen or oral NSAIDs) | increased pain, injury, SAEs |
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| **Symptomatic PATELLOFEMORAL (PF) OA ONLY** | 107 | PF brace + usual care | usual care (maximally tolerable therapeutic doses of acetaminophen or oral NSAIDs) | increased pain, injury, SAEs |
| | 108 | PF taping + usual care | usual care (maximally tolerable therapeutic doses of acetaminophen or oral NSAIDs) | increased pain, injury, SAEs |

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**APPENDIX B – Participant Disclosures**

In order for the College to most effectively further its mission and to otherwise maintain its excellent reputation in the medical community and with the public, it is important that confidence in the College's integrity be maintained. The cornerstone of the ACR's Disclosure Policy is disclosure of actual and potential conflicts so that they can be evaluated by the College in order to avoid undue influence of potential conflicts. The purpose of the ACR's Disclosure Policy is identification of relationships which may pose actual or potential conflicts. These actual or potential conflicts can then be evaluated by the College so that adjustments can be made that will avoid any undue influence. This policy is based on the principle that, in many cases, full disclosure of the actual or potentially conflicting relationship will of itself suffice to protect the integrity of the College and its interests.

| Participants | Role | Primary employer | Sources of personal income (salary information from primary employer is not required): | Intellectual Property | Research Grants/Contracts | Investments to include medical industry and nonmedical industry | Organizational Benefit | Activities with other organizations | Family or other relations |
|---|---|---|---|---|---|---|---|---|---|
| Sharon L Kolasinski MD, FACP, FACR | Core Team/PI | University of Pennsylvania | American College of Physicians; Current Rheumatology Reports | N/A | N/A | N/A | N/A | N/A | N/A |
| Carol Oatis, PT, PhD | Core Team/Content Expert | Arcadia University | Wolters Kluwer | N/A | NIAMS; PCORI | N/A | N/A | N/A | N/A |
| Marc Hochberg, MD, MPH | Core Team/Content Expert | University of Maryland Baltimore; Department of Veterans Affairs; Elsevier | Bioiberica SA; Bristol Myers Squibb; EMD Serono; Galapagos; IBSA; Novartis Pharma AG; Pfizer; Samumed LLC | N/A | National Institutes of Health | Theralogix LLC | N/A | U.S. Bone and Joint Initiative | N/A |
| Tuhina Neogi, MD, PhD, FRCPC | Core Team/Content Expert | Boston Univ Sch of Med | Pfizer; EMD-Merck Serono | N/A | NIH/NIAMS; AF | N/A | N/A | OARSI; Osteoarthritis & Cartilage | N/A |
| James Reston, MD | Core Team/Lit Review Leader | ECRI | N/A | N/A | N/A | N/A | N/A | N/A | N/A |
| Gordon Guyatt, MD | Core Team/GRADE Expert | McMaster University | N/A | N/A | N/A | N/A | N/A | N/A | N/A |
| Anne-Marie Malfait, MD, PhD | Expert Panel | Rush University Medical Center | Osteoarthritis and Cartilage, Assoc Editor; Arthritis Rheumatology, Assoc Editor; Galapagos (consulting) | N/A | NIAMS | N/A | N/A | ACR; OARSI | N/A |
| ChenChen Wang, MD, MSc | Expert Panel | Tufts Medical Center | N/A | N/A | NIH; VA | N/A | N/A | N/A | N/A |
| Edward Herzig, MD | Voting Panel / ACR Board of Directors Liaison | Self employed | MediSync; IRA and 457B | N/A | N/A | N/A | N/A | Mercy Jealth Regional Board; Mercy Health Select | N/A |
| Jas Singh, MD, MPH | Expert Panel | Birmingham VA Med Ctr; University of Alabama at Birmingham | American College of Rheumatology; Horizon Pharmaceuticals/DINORA | N/A | PCORI; NIAMS; AHRQ; VA | N/A | N/A | OMERACT; Editorial Board, JCR; Editorial Board, BMC MSD; VA Field Advisory committee | N/A |
| Leena Sharma, MD | Expert Panel | Northwestern University Feinberg School of Medicine | N/A | N/A | NIH/NIAMS | N/A | N/A | N/A | N/A |
| Nancy Baker ScD, MPH, OTR/l | Expert Panel | University of Pittsburgh | USBJI; Cleveland Clinic; ARHP; Boston University | N/A | NIOSH; ACR | N/A | N/A | USBJI; AOTF | N/A |
| Nancy Lane, MD | Expert Panel | University of California | Novartis- psoriatic arthritis; Amgen-osteoporosis; Eli Lilly-osteoporosis | N/A | NIH; CIRM | N/A | N/A | Seminars in Arthritis and Rheumatism; Nature Rheumatology Reviews | N/A |
| Richard Loeser, MD | Expert Panel | University of North Carolina | Unity Biotechnology; American College of Rheumatology; Up to Date | N/A | NIAMS; NIA; Arhtitis Foundation | N/A | N/A | Osteoarthritis and Cartilage | N/A |
| Steve Messier, PhD | Expert Panel | Wake Forest University | Nestle; NIAMS AMSC Study Section | N/A | NIH/NIAMS; Department of Defense | N/A | N/A | OARSI; Med Sci Sports Ex; Osteoarthritis Cartilage | N/A |
| Svetlana Krasnokutsky Samuels, MD | Expert Panel | NYU Langone School of Medicine | Horizon Pharmaceuticals; Ironwood Pharmaceuticals | N/A | Rheumatology Research Foundation | N/A | N/A | Americal College of Physicians | N/A |
| Thomas Schnitzer , MD, PhD | Expert Panel | Northwestern University | Regeneron; Genentech; Lilly; Flexion; Sanofi; Astellas; Plexxikon; Pfizer | N/A | NIH/NIDCR; NIH/NCCAM; NIH/NIAMS; U.S Army Medical Research and Materiel Command; Department of Defense; CDMRP Peer Reviewed Orthopaedic Research Program Expansion Award; Pfizer; Regeneron; Axsome; | N/A | N/A | N/A | N/A |
| Yvonne Golightly, PT, MS, PhD | Expert Panel | University of North Carolina | N/A | N/A | NIH/NIAMS; CDC; NIH/NIAMS | N/A | N/A | Osteoarthritis and Cartilage; Arthritis Care & Research | N/A |
| Amit Shah, MD | Lit Review Team | American College of Rheumatology | N/A | N/A | N/A | N/A | N/A | N/A | N/A |
| Anna K. Shmagel, MD | Lit Review Team | University of Minnesota | N/A | N/A | NIH | N/A | USBJI | N/A | N/A |
| Devyani Misra, MD | Lit Review Team | Boston University School of Medicine | N/A | N/A | Rheumatology Research Foundation; NIH/Boston University CTSI; Boston University CTSI | N/A | N/A | N/A | N/A |
| Mariko Ishimori | Lit Review Team | Cedars Sinai Medical Center | N/A | N/A | NIH/NCATS; NIH/NIAID; NIH/NIAMS; EULAR | N/A | Pfizer; ACR/Amgen | Lupus LA; OMERACT | N/A |
| Marat Turgunbaev, MD | Lit Review Team | American College of Rheumatology | N/A | N/A | | N/A | N/A | N/A | N/A |
| Amanda E. Nelson, MD MSCR RhMSUS | Voting Panel | University of North Carolina at Chapel Hill | QuantiaMD; Health Press Limited; GlaxoSmithKline | N/A | NIAMS ; NIAMS; NIAMS; CDC; RRF | N/A | N/A | OARSI; BMC Journals; NCRA; OAAA; ACR | N/A |
| Barton Wise, MD | Voting Panel | UC Davis | Hamcock, Daniel, Johnson & Nagle | N/A | NIH/NIAMS | N/A | N/A | N/A | N/A |
| C Kent Kwoh, MD | Voting Panel | University of Arizona | Novartis; Astellas; Thusane; EMD Serono; Pharmacy Benefits Manager | N/A | NIH; EMD; Abbvie | N/A | N/A | N/A | N/A |
| Carla Scanzello, MD, PhD | Voting Panel | Corporal Michael J. Crescenz VA Medical Center (CMCVAMC); University of Pennsylvania, Perleman School of Medicine | Bayer, Inc; | N/A | NIH/NIAMS; VA ORD; Baxalta US, Inc | N/A | N/A | N/A | N/A |
| Carole Dodge, OT, CHT | Voting Panel | Michigan Medicine, University of Michigan | N/A | N/A | NIH | N/A | N/A | N/A | N/A |
| Daniel White, PT, ScD | Voting Panel | University of Delaware | Midbridge; AC&R | N/A | NIH/CTR | N/A | N/A | University of Toronto; Peking University | N/A |
| David Felson, MD, MPH | Voting Panel | Boston University | Arthritis and Rheumatology; University of Manchester, England; Zimmmer, Knee Creations (discontinued) | N/A | NIH/NIA; NIH/NIAMS; Arthritis Research UK | N/A | N/A | N/A | N/A |
| Gillian Hawker, MD, MSc | Voting Panel | University of Toronto; Self-employed | N/A | N/A | Canadian Institutes of Health Research; Arthritis Alliance of Canada | N/A | N/A | Executive Committee, Arthritis Alliance of Canada | N/A |
| Joel Block, MD | Voting Panel | Rush University Medical Center | Daiichi Sankyo, Inc.; Agios, Inc.; Pri-Med Institute | N/A | Novartis; Pfizer; Janssen; Abbvie | N/A | N/A | OA Research Society Intl; Orthopaedic Research Soc | Spouse: Past-President, IL Chapter, Am Acad Peds. |

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| Jonathon Samuels, MD | Voting Panel | NYU | Novartis | N/A | Geisinger | N/A | N/A | N/A | N/A |
| Leigh Callahan, PhD | Voting Panel | University of North Carolina | Eli Lilly; West Virginia University/School of Public Health | N/A | NIH/NIAMS; PCORI; CDC | N/A | N/A | Arthritis Foundation; Rheumatology Research Foundation; FDA; United States Bone and Joint Initiative | N/A |
| William F. Harvey, MD, MSc, FACR | Voting Panel | Tufts Medical Center Physicians Org | UpToDate | N/A | NIH; Samumed; Abbvie | UpToDate | N/A | N/A | N/A |