

## Cross-sectional analysis of recommendations for the treatment of hip and knee osteoarthritis in clinical guidelines

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## **Cross-sectional analysis of recommendations for the treatment of hip and knee osteoarthritis in clinical guidelines**

(1) **Running head:** Appraisal of osteoarthritis guidelines

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## Abstract

**Objective:** To compare guideline recommendations for hip and knee osteoarthritis (OA) and their level of evidence.

**Data Sources:** Medline, Embase, the Cochrane library, and websites of professional societies were searched in June 2020 using key words such as knee or hip osteoarthritis, degenerative arthritis, guideline, and practice guideline.

**Study Selection:** General treatment guidelines for OA of the hip or knee published in English. After 461 abstracts were screened, 31 publications (17 guidelines from 10 professional societies) were included for analysis.

**Data Extraction:** Three reviewers assessed the quality of the guidelines according to the Appraisal of Guidelines for Research & Evaluation (AGREE) II tool. The rating of evidence and strength of recommendation was extracted and standardized into the Grading of Recommendations Assessment, Development and Evaluation (GRADE) criteria.

**Data Synthesis:** Of the 17 guidelines included, 6 (35%) were of high quality, 10 (59%) of moderate quality, and one (6%) of low quality. Guidelines published after 2017 were of good quality. Although guidelines generally agreed on a non-surgical multimodal concept including patient education, exercise, and weight loss in obese, some recommendations remained vague and the level of evidence varied widely. In pharmacological treatment, oral non-steroidal anti-inflammatory drugs were the mainstay for pain management. Guidelines published after 2017 were more cautious in their recommendation for the use of paracetamol and strong opioids.

Disagreement was observed for chondroitin sulfate, glucosamine, and intraarticular hyaluronic acid injections. Recommendations were conflicting for the use of insoles, braces, and transcutaneous electrical stimulation (TENS). The main indications for hip/knee arthroplasty were severe, persisting pain and loss of function despite non-surgical treatment. No guideline defined a minimum time of conservative treatment before surgery.

**Conclusions:** We found a wide variation in evidence and strength of recommendations for OA treatment. Recommendations on when to refer patients for surgery remained unclear.

**Keywords:** Osteoarthritis, treatment guidelines, knee, hip

### List of abbreviations

AAOS	American Academy of Orthopedic Surgery
ACOEM	American College of Occupational and Environmental Medicine

ACR	American College of Rheumatology
AGREE	Appraisal of Guidelines for Research & Evaluation II
E	level of evidence
ESCEO	European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases
GRADE	Grading of Recommendations Assessment, Development and Evaluation
IAHA	intra-articular injection of hyaluronic acid
NICE	National Institute for Health and Care Excellence
NSAID	non-steroidal anti-inflammatory drug
OA	osteoarthritis
OARSI	Osteoarthritis Research Society International
OECD	Organisation for Economic Co-operation and Development
PANLAR	Pan-American League of Rheumatology Associations
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
R	strength of recommendations
RCT	randomized-controlled trial
TENS	transcutaneous electrical stimulation
THA	total hip arthroplasty
TKA	total knee arthroplasty
UKA	Unicompartmental knee arthroplasty
VA/DoD	Department of Veterans Affairs / Department of Defense

WOMAC	Western Ontario and McMaster Universities OA index
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## Introduction

Osteoarthritis (OA) affects more than 300 million people worldwide and is a major source of pain, disability, and socioeconomic costs (1-3). The clinically most relevant affected joints include knee and hip (4, 5). OA of the knee accounted for approximately 85% of the OA burden worldwide (1). Disability related to OA is expected to further increase with an ageing population and growing number of obesity, two major risk factors for OA (1, 2). To improve pain and function in patients with OA, treatment options include a wide variety of pharmacological, non-pharmacological, and surgical options (2).

With technological advancement and gain of new evidence, standard of care changes (6). Today, total knee (TKA) or hip arthroplasty (THA) are highly effective to improve function (7, 8) and are performed earlier in life in patients with milder loss of mobility and less symptoms (8-10). However, up to 20% of patients were dissatisfied after TKA and in younger patients the lifetime revision risk is considerable (2, 7, 8). Therefore, non-surgical treatment should also aim to decelerate progression of OA to delay total joint replacement (2, 7).

The use of non-pharmacological (e.g., exercise, walking aids, insoles) and pharmacological (e.g., pain medications) treatment options often depend on preferences of the treating physician and patient (2, 7). Studies have shown a wide variation in the use of TKA and THA across countries, indicating differences in practice patterns (11). Using validated clinical appropriateness criteria for THA and TKA (12-14), approximately 14% to 20% of THA (12, 13) and 34% to 68% (14) of

TKA are considered inappropriate. The underlying reasons are not well understood. Treatment guidelines should assist the decision process and address uncertainty about the strength of evidence for or against a recommendation (2). Differences in guideline recommendations may explain variations in treatment of hip and knee OA. Therefore, the aim of this study was to systematically compare recommendations and the strength of evidence of guidelines for treatment of hip and knee OA including changes over time.

## Methods

### Study design

Cross-sectional analysis of clinical guidelines for the treatment of knee and hip OA. We conducted a systematic review to identify all relevant guidelines following the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (15).

### Systematic Literature Review

We searched the following databases from the inception until June 15, 2020: Medline (via PubMed), the Cochrane library and Embase (via EBSCO). We used the Medical Subject Heading (MeSH) search terms for osteoarthritis and the free text search for osteoarthritis. The full search is depicted in the **supplementary material (Table S1)**. In addition to the systematic search, we also searched the webpages of relevant



professional societies, the bibliographies of review articles, editorials, and guidelines to identify additional guidelines.

### **Eligibility criteria**

Included were treatment guidelines for OA of the hip and / or knee published in English. We excluded monothematic guidelines that focused on only one of the therapeutic options because such guidelines are of less use for clinical decision-making during the continuum of care for patients with osteoarthritis and are often used by specialists. In case of various guidelines from the same society and/or several publications, we included the most recent or the most relevant guideline and used the other guideline(s) to extract additional important recommendations or methodological aspects not included in the main guideline.

### **Study procedure**

Two reviewers (JS, DB) independently screened all titles and abstracts of the identified references for inclusion and read potentially relevant references in full text. Recommendations were extracted using a predefined spreadsheet to cover the following domains: General recommendations, non-pharmacological and pharmacological treatment, and when to consider surgery. The rating of evidence and strength of recommendation was extracted and standardized (**supplementary material, Tables S2 and S3**) into the Grading of Recommendations Assessment, Development and Evaluation (GRADE) criteria (16) with the level of evidence (E) high, moderate, low, or very low and the strength of recommendation (R) strong,

conditional, conditional against, or strong against. In case of disagreement between the two reviewers, the final grading was discussed within the research team until all authors agreed to a final version.

### **Quality of guidelines**

Three reviewers (DB, FL, and MW) independently assessed the quality of guidelines using the Appraisal of Guidelines for Research & Evaluation II (AGREE II) tool (17) for an overall assessment and the following six domains (total 23 items): scope and purpose (3 items), stakeholder involvement (3 items), rigor of development (8 items), clarity of presentation (3 items), applicability (4 items), and editorial independence (2 items). Each item was rated on a 7-point scale (1: not mentioned to 7: fully complied). We calculated the mean rating for each domain using the individual ratings of the reviewers. A quality score for each of the six AGREE II domains and the overall assessment was calculated by summing up all the scores of the individual items in a domain and scaling the total as a percentage of the maximum possible score for that domain. Quality of a domain was categorized into good (score 80 - 100 %), moderate (score 50 - 80 %), and poor (score <50 %).

### **Statistical analyses**

We summarized continuous and categorical variables with number and percentage, mean and standard deviation or median and interquartile range.

## Results

### Systematic literature review

Of 461 screened references (**Figure 1**), 100 references were read in full-text, whereof 17 guidelines from 10 professional societies (4 North American, 2 European, 1 British, 1 Turkish, and 2 international) were included (31 publications). Main reasons for exclusion were other publication types (e.g., comments, letters to the editor, articles on applicability of guidelines; n=53) and monothematic guidelines limited to only one therapeutic option (e.g., acupuncture, physiotherapy, arthroscopy, rehabilitation; n=6).

### Overview and quality of the guidelines

**Table 1** provides a summary of the publications (for more details see **supplementary material Table S4**). Most guidelines covered hip and knee OA (n = 8), 5 covered only knee OA and 3 only hip OA. The overall quality was mainly moderate (n=10, 58.8%) (18-26, 51) or good (n=6, 35.3%) (27-32). In one guideline, the quality was rated to be poor (5.9%) (33). The quality of the guidelines improved over time. Guidelines published after 2017 were of good overall quality (29-32).

### Guideline recommendations for non-pharmacological treatment of knee OA

All guidelines recommended patient education (R: strong, n=8, E: very low to high, **Table 2**) including information about the disease, medication effects and side effects, joint protection measures, fitness and exercise goals, and self-management (23, 25,

28, 29). Two guidelines (30, 31) included education in a “core set” of non-pharmacological interventions together with weight loss and exercise programs. Exercise was recommended by most guidelines (R: strong, E: very low to high, n=8; R: conditional, E: moderate, n=1). Exercise programs that included supervised muscle strengthening and aerobic exercise several times a week were considered more effective than unsupervised (28-30). There was insufficient evidence to recommend one specific type of exercise over another and most guidelines did not indicate intensity and duration of exercise programs (22, 28-30). A Cochrane systematic review on exercise for OA of the knee published in 2015 (34) influenced guideline recommendations. Although the effect size of exercise was considered small, positive effects on pain, function, and quality of life was sustainable for 2-6 months in several studies (34). Aquatic exercise was recommended by 2 guidelines (R: conditional, E: moderate (31) to strong strong (19)). While the VA/DoD 2014 guideline recommended aquatic exercise (E: moderate), the VA/DoD 2020 guideline downgraded and restricted the recommendation to patients who are unable to tolerate land-based therapies (51).

Most guidelines issued a strong recommendation for weight reduction in overweight (E: low (31) to high (19, 30)). After the Department of Veterans Affairs / Department of Defense (VA/DoD) guideline 2014 (22) conditionally recommended referral to a weight management program (E: moderate), the updated recommendation (2020) was more general (51). A secondary analysis of a randomised-controlled trial (RCT) on weight loss in obese, elderly patients showed improved function and less pain in knee OA with more weight loss (35) and influenced the American College of Rheumatology (ACR) (2019) recommendation to lose >5% of total body weight (29).

However, risk of diet programs in very elderly remained controversial because of risk of sarcopenia (30, 36).

Whereas guidelines mainly recommended the use of appropriate footwear, recommendations for insoles and braces were contradictory. Although the ACR (2019) guideline conditionally recommended against modified shoes, the authors acknowledged the importance of appropriate footwear but criticized the lack of studies to address this question. Three guidelines recommended for (19, 20, 23) and two guidelines against the use (29)(25) of insoles with a wide variation in the level of evidence. Despite the publication of a meta-analysis in 2013 that found no effect of lateral or medial wedged insoles on knee pain (37) two guidelines recommended the use (R: strong (19) or conditional (20), E: high quality (19)) and one conditionally recommended against the use (29). Three guidelines recommended tibiofemoral braces (R: strong (28, 29, 51)), while the American Academy of Orthopedic Surgery (AAOS) (2013) issued an inconclusive recommendation.

The recommendations for the use of cold / heat, traditional acupuncture and transcutaneous electrical stimulation (TENS) were inconsistent. TENS was recommended by two guidelines (R: strong (19), conditional (28)) and recommended against by two guidelines (R: strong against, E: very low (31) to low (29)).

Recommendations for local use of heat / cold also differed (R: strong for (19) to strong against (31)). Although most guidelines (23, 28, 31) recommended against the use of acupuncture (R: conditional to strong, E: low to high), the ACR (2019) guideline (29) recommended it due to the low risk of harm (R: conditionally, E: low) and the VA/DoD 2020 (51) issued no recommendation due to the low level of evidence. The use of assistive devices such as walking aids was recommended by

most guidelines (R: strong (19, 25, 29) to conditional (20, 28, 31), E: very low to moderate). The VA/DoD recommended in 2014 to train patients in the use of assistive devices (22) but did not address assistive devices in 2020 (51).

### **Guideline recommendations for non-pharmacological treatment of hip OA**

All guidelines recommended patient education (R: strong (n=4), conditional (n=2), E: low to moderate (n=4) (20, 29, 31, 32), high (n=1) (25)) and exercise (R: strong (n=6), conditional (n=2), E: moderate (20, 22, 29, 31, 32) to high (25)). The core principles of exercise therapy were aerobic exercise (e.g., walking, cycling, and swimming) and muscle strengthening to reduce pain and improve function, without specific recommendations on intensity or duration (18, 25, 29, 38, 51). Guidelines recommended weight loss (R: strong (20, 25, 28, 29) to conditional (51), E: very low (25, 31) to moderate (20, 29)). Again, the potentially negative effects (e.g., sarcopenia) of weight loss in frail individuals (31) was highlighted.

The use of insoles was not (29) or conditionally recommended (32). Appropriate footwear (25, 28) or modified shoes were recommended (E: low (29) or very low (25, 28)). The use of TENS was strongly recommended against (29, 31) and recommendations for acupuncture were conditional for (29, 32), indeterminated (51), or against (28, 31) (E: low to very low).

Local heat or cold to relief pain was recommended due to low costs and a good safety profile (E: very low (32) to moderate (20, 28, 29)), but with one guideline recommending strongly against the use (31). Assistive devices (e.g. canes) were recommended (R: conditional to strong, E: weak (39) to strong (20, 28)). The use of

crutches should be limited to acute injuries (R: conditional, E: very low (32)) because chronic use may paradoxically result in increased disability (32).

### **Guideline recommendations for pharmacological treatment of knee OA**

Topical treatment with NSAID (20, 29, 31, 51) (E: moderate to high) and capsaicin (R: conditional, E: very low to moderate) was recommended by several guidelines (28, 29, 51)), while one guideline conditionally recommended against capsaicin (31) (**Table 3**).

Paracetamol was strongly recommended due to a favorable side effect profile by most guidelines published until 2017 (19, 20, 22, 40-42), mainly based on results from a systematic review published in 2009 (26). The AAOS in 2013 downgraded the recommendation to inconclusive because of low evidence (23) and the National Institute for Health and Care Excellence (NICE) in 2014 issued a caution that efficacy of paracetamol was smaller than previously thought (28, 43). After the publication of a network meta-analysis in 2015 that found no role for single-agent paracetamol with comparable safety profile to non-steroidal anti-inflammatory drug (NSAID) (44, 45), in newer guidelines paracetamol was only recommended as a short pain relief in daily doses of <3-4 g (19, 29-32). The VA/DoD 2020 guideline recommended the use of the lowest effective dose for the shortest possible duration (51).

Oral NSAIDs or Cox-2 inhibitors were recommended by all guidelines (R: strong (19, 20, 29, 30) to moderate (28, 31, 51); E: moderate to high) in carefully selected patients due to their risk profile (e.g., gastrointestinal and renal side effects).

For refractory pain, weak opioids (tramadol) were recommended by most guidelines (E: very low (29) to high (19, 30)). Most guidelines recommended against the use of strong opioids (R: conditionally (23, 29, 51) to strong (31)), especially if comorbidities are present. Strong opioids may be considered in patients with refractory pain and contraindications to other treatments (e.g., NSAIDs, surgery) (28, 30). The VA/DoD guideline changed its conditional recommendation for opioids of 2014 to a conditional recommendation against in 2020 (E: low) (22, 51).

The use of glucosamine and chondroitin sulfate is controversial and a network meta-analysis of 10 randomized controlled trials found no effect on pain and structure (46). Whereas two guidelines advocated the use of prescription crystalline glucosamine sulfate due to its structure-modifying effect (20, 30), three guidelines (28, 29, 31) recommended against the use (E: low).

Most guidelines recommended (R: strong (19, 29) or conditionally (20, 30, 51), E: low) the use of intra-articular injection of glucocorticoids for short-term effect. The VA/DoD (2014) recommended to avoid joint injections if surgery is anticipated within three months (E: expert opinion (51)).

Evidence on the efficacy of intra-articular injection of hyaluronic acid (IAHA) evolved over time. After the publication of a network-meta-analysis in 2012, that found no clinically significant effect of IAHA in blinded trials (47), NICE (2014), AAOS (2013) and ACR (2019) recommended against the use of IAHA. The European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO) (2019) and OARSI (2019) conditionally recommended the use in patients with pain despite the use of NSAID and because of a more favorable long-term safety profile than repeated intraarticular corticosteroid injections (E: weak).



### **Guideline recommendations for pharmacological treatment of hip OA**

Topical treatment with NSAIDs was recommended by the NICE (2014) guideline (R: moderate) and not recommended by the American College of Occupational and Environmental Medicine (ACOEM) (R: conditional against, E: very low (32)). The use of topical capsaicin was recommended in one guideline (R conditional (32)) and not recommended by OARSI 2019 (R: strong against (31)). Given the low potential for adverse events with most supplements and very low level of evidence the VA/DoD guideline in 2020 did not issue a recommendation against or for (51).

Similar to knee OA, recommendations evolved over time for the use of paracetamol. More recently published guidelines either recommended against the use (31) or only in selected patients with limited pharmacological options for short term analgesia (29, 32, 51). Oral NSAID remain the mainstay for pain management in all guidelines (R: strong (20, 24, 27, 29, 32, 51), E: moderate to high).

Weak opioids (tramadol) were recommended by most guidelines for refractory pain (R: conditional, n=4 to strong, n=1), E: very low (18, 29) to strong (24)). Three guidelines published until 2014 (22, 24, 28) recommended strong opioids in refractory pain (R: conditional, E: moderate to high). More recent guidelines recommended against the use (R: conditionally (29, 51) and strongly (31), E: very low to low), especially if comorbidities are present.

Three guidelines (28, 29, 31) recommended against the use of glucosamine or chondroitin sulfate (R: strong); two guidelines recommended the use (R: conditional (18, 24)).

Intra-articular glucocorticoid injections were recommended to improve function and reduce pain in the short-term in most guidelines (R: strong (18, 29) and conditional (31)), E: low (29, 51) to high (18)). Preferably, injections should be guided by ultrasound (29) and avoided in the 3 months before joint replacement (51).

Guidelines published before 2012 (24, 48) recommended the use of intra-articular injection of hyaluronic acid (R: conditional); more recent guidelines recommended against the use (R: strong (18, 28, 29) or conditional (31, 51)).

### **Guideline recommendations when to consider surgery in knee OA**

Guidelines agreed, that surgery should only be considered after failed conservative treatment (**Table 4**).

High tibial osteotomy was recommended in younger, active patients with malalignment (R: conditional (19, 23, 48, 49), E: low (23) to strong (19, 26)). A network meta-analysis published in 2018 found better short-term functional improvement for osteotomy and UKA while results for total knee arthroplasty were better in the long-term (50). Although unicompartmental knee arthroplasty (UKA) was recommended for elderly (R: strong, n=2, E: moderate (48) to high (19)), the ESCEO (2019) guideline recommended to further investigate UKA (30) due to higher revision but lower complication rates including mortality compared with TKA.

TKA was recommended in patients with failed conservative treatment (R: strong (19, 30, 48, 49), E: low (48) to high (19)). Two guidelines issued a conditional recommendation for TKA: The NICE (2014) because no clear criteria exist, when to refer for surgery and because the timing for surgery remains an individual decision,

and the Pan-American League of Rheumatology Associations (PANLAR) due to the moderate evidence (20, 28). Treatment failure was defined as persistent pain, functional limitations with impairment in activities of daily living, and impaired quality of life despite adequate conservative treatment (19, 28, 30). The VA/DoD guideline 2014 recommended to use validated measures to assess pain severity and function (i.e., Western Ontario and McMaster Universities OA index (WOMAC) scores for pain and stiffness (22)) without providing specific cut-off values when surgery may be necessary. Most guidelines considered it a responsibility of the referring physician to ensure that the patient was offered at least the “core set” of non-surgical treatment including patient information, exercise, weight loss and analgesic treatment. Although no guideline defined a specific time frame, NICE (2014) strongly recommended to consider joint surgery before prolonged functional limitation and severe pain is established (28). According to the AAOS (2015) an eight month delay of TKA does not worsen outcomes (R: moderate, E: moderate) (27).

Radiological findings were not considered to be important for the decision to recommend surgery as radiological findings do not correlate with pain and functional limitations (19, 28).

Most guidelines highlighted the need for careful selection of patients and consideration of benefits and risks in an interdisciplinary discussion involving the patient for decision making (28). Factors that may be associated with less improvement after TKA included high body mass index, diabetes, chronic pain or psychological problems (27). However, modifiable or patient-specific factors (including age, sex, smoking, obesity and comorbidities) should not be barriers to

referral for joint surgery because these patients might even have a greater benefit (22, 28).

### **Guideline recommendations when to consider surgery in hip OA**

Osteotomy was recommended in three guidelines in symptomatic younger patients, especially if dysplasia or alignment abnormalities are present (R: conditional, E: very low to moderate (24, 32, 48)).

All guidelines recommended THA (R: strong (32, 48, 49) or conditional (20, 22, 24), E: low (24, 28, 48) to high (32)) in patients with persisting pain and/or functional deficits affecting activities of daily living, work, or quality of life despite conservative treatment. According to the NICE (2014) guideline difficulties climbing stairs and putting on shoes or socks were significant limitations that require referral for THA (28). No guideline defined a minimal duration and intensity of conservative treatment until it may be considered to have failed. The ACOEM (2019) guideline suggested “a prolonged treatment period” (32). Some guidelines (24, 48) emphasized, that THA is highly cost-effective, while NICE highlighted, that the economic benefit is mainly based on reduction of societal costs (28). Decision for referral to surgery should be based on clinical assessment, i.e., pain and functional deficits, rather than radiological findings (32). Although x-rays were recommended for diagnosis and to document progress of hip OA (32), the importance of radiological changes (joint damage, deformity, dysplasia) for THA was controversial. Whereas earlier guidelines supported the use of radiographic changes as criteria to consider surgery together with clinical evaluation (24, 49), newer guidelines based indication for surgery mainly

on refractory clinical symptoms (22, 32). Although pre-operative x-rays (< 6 months) were recommended (R: strong (22)), the routine use of computed tomography (32) or magnetic resonance imaging was not recommended (R: conditional against, E: very low (22, 32)).

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## Discussion

In the analysis of guidelines issued by 10 professional societies we found differences in the interpretation of the available evidence and recommendations for the treatment of hip and knee OA. The guideline quality improved over time and guidelines published after 2017 were of good quality. More recent guidelines addressed the clinical applicability of recommendations by providing flowcharts to assist the decision process and included comorbidities and risk factors in their treatment recommendations (22, 30, 31, 51). The quality of evidence for recommendations was considered to be low or very low for many treatments. This is surprising given the prevalence of OA and the frequency of arthroplasty. Even in guidelines published in 2019 that assessed the same evidence, we observed controversial recommendations in particular for specific pharmacological (i.e., intrarticular hyaluronic acid, glucosamine or chondroitine sulfate) and non-pharmacological treatments (i.e., the use of acupuncture, TENS, insoles, and braces). Further, the recommendations for a core set of exercise, education and weight loss were often vague and difficult to translate into specific treatment plans. In particular, the recommendations on how long and intensive conservative exercise treatments should be performed before treatment failure can be assumed, was not further specified.

Joint biomechanics influences joint degeneration and thus progression of OA while muscles play an important role in dynamic joint stability and absorption of loading (52). According to recently published systematic reviews, resistance and strengthening training over 8 to 15 weeks in 2-3 sessions per week was found to

have best effect on pain reduction and improvement of physical function in patients with knee OA (53, 54). Treatment duration of less than 8 weeks and less than three times per week was not efficacious. Studies reported insufficient information to assess the optimal number of repetitions, maximum strength, or frequency of sets. Lower levels of physical activity (> 45 minutes/week of moderate-intensity) were associated with improved or sustained high function up to 6 months after cessation of a defined program (5). Therefore, conservative treatment including resistance and strengthening training of at least 8 weeks should be completed before TKA is considered. According to a German consensus statement, the duration of the preceding conservative therapy was defined as at least 3-6 months (55). For hip OA, fewer studies assessed the efficacy and required intensity of exercise. According to a recommendation of the Ottawa panel, weekly strengthening exercises is strongly recommended over 8 (to 24) weeks (21).

Regional variation in the treatment of knee and hip OA beyond demographic, cultural, and socioeconomic factors have been observed between and within countries (11). Many factors may explain such variation including access to care, patient's and physician's preferences, involvement of shared decision-making, mistrust in the efficacy of physical therapy and enthusiasm for surgery (56, 57). Physician's preferences are influenced by various factors including adherence to guidelines for non-surgical treatment, personal experiences, peers, lack of standardized conservative treatment pathways and financial incentives (11, 58). Guidelines should provide clinicians a guidance on how to advise their patients the most effective treatment choice to reduce pain, improve function, and delay progression of OA. The

gap between guideline recommendations and clinical practice has been previously recognized. Potential barriers for health-care professionals to implement guidelines into clinical practice include trivialization, prioritization of co-morbidities, lack of knowledge, personal beliefs, and dissonant patient expectations (73). Vague recommendations in clinical guidelines further add to the perceived unpreparedness of physicians and other therapists, which may be one reason why adherence to guidelines has been found to be low while algorithm-based clinical scenarios could be more user-friendly (58, 59).

### **Study limitations**

The main limitation of the current study was, that we only considered guidelines published in English. While guidelines published in the original language of a country may be more detailed on what is recommended in a country, it is reasonable to assume that they are influenced by guidelines published by international groups or large professional societies. Further, we did not include guidelines that assessed only one treatment modality, which are more detailed and able to provide more refined recommendations. However, the aim of the current study was to assess the spectrum of treatment options throughout the continuum of care which is covered in general guidelines that inform physicians on the variety of treatment options. In contrast, monothematic guidelines address one treatment option, will usually be consulted by specialists in a field and add little help to decide which therapeutic option to choose. Despite the frequency of the clinical problem, the evidence available to issue recommendations was surprisingly of limited quality. Therefore, future research



should aim at addressing clinically controversial or unclear evidence on how hip and knee OA should be treated in clinical practice. Further, treatment guidelines need to address uncertainty and provide more specific recommendations for clinical practice.

### **Clinical implications**

Although we observed wide variations across guidelines in some recommendations, the core principles for the treatment of patients with osteoarthritis of the hip and knee include patient education and exercise therapy. Aerobic exercise and muscle strengthening to reduce pain and improve function should be recommended early on. Various pharmacological and non-pharmacological options exist to tailor pain management according to individual needs and should primarily be used to allow patients to stay active. Primary care physicians should work together with allied health professionals with expert knowledge in the respective fields to improve efficacy of chosen treatments. Future high-quality studies should clarify the areas identified of uncertain evidence in this study.

### **Conclusions**

Although treatment guidelines agreed on the importance of non-pharmacological treatments in knee and hip OA, i.e., education, exercise and weight loss, the recommendations remained vague. Conflicting recommendations with regards to non-pharmacological treatments, chondroitin sulfate, and intraarticular hyaluronic acid injection are difficult to interpret for clinicians. The use of non-pharmacological and pharmacological treatments of uncertain efficacy should be discussed with the

patient and the efficacy appraised. It remains unclear, when to recommend joint replacement surgery.

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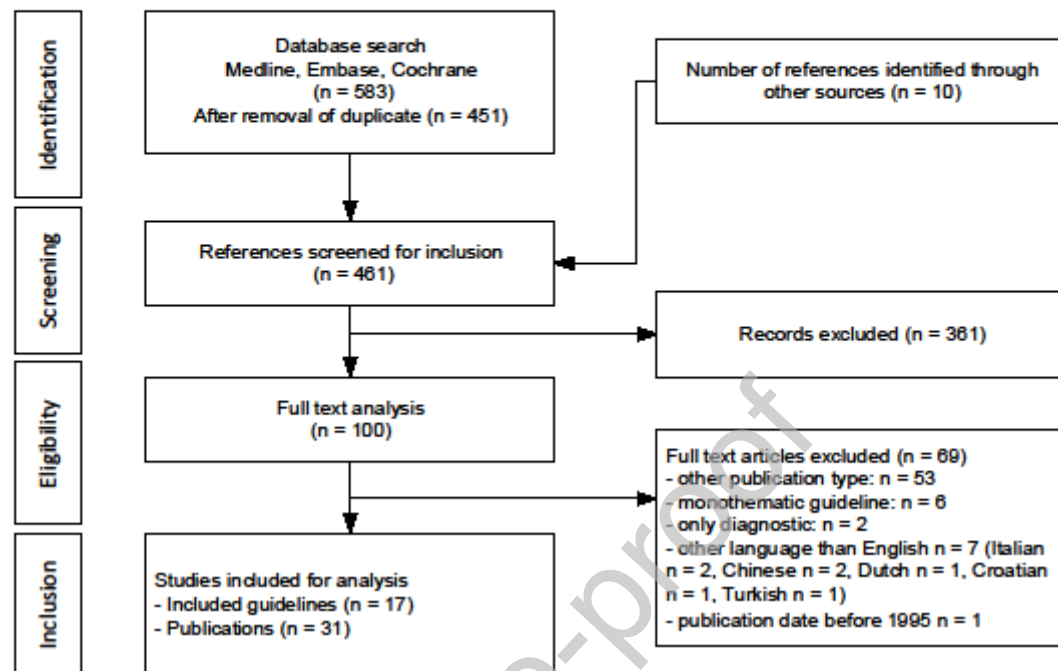
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## Figures legends

**Figure 1: Flowchart systematic literature review**



**Table 1:** Quality analysis assessment of the guidelines with domains according to AGREE II (17). Quality of a domain was defined as good if the score was >80 - 100 %, moderate if the score was between 50 - 80 %, and poor if the score was <50 % (\*\*\*, good; \*\*, moderate; \*, poor). 1, Scope and purpose; 2, Stakeholder involvement; 3, Rigor of development; 4, Clarity of presentation; 5, Applicability; 6, Editorial independence; OQ, Overall quality

Society, year	Coverage	1	2	3	4	5	6	OQ
Department of Veterans Affairs/Department of Defense (VA/DoD, 2020 (51))	Hip / knee	***	***	**	***	**	**	***
American College of Rheumatology (ACR, 2019 (29))	Hip / knee	***	***	***	***	*	**	***
European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO, 2019 (30))	Knee	***	**	**	***	*	***	***
Osteoarthritis Research Society International (OARSI, 2019 (31))	Hip / knee	***	***	***	***	**	***	***
American College of Occupational and Environmental Medicine (ACOEM, 2019 (32))	Hip / groin	***	***	***	***	**	***	***
American Academy of Orthopedic Surgery (AAOS, 2017 (18))	Hip	***	***	***	***	***	***	**
Turkish league against rheumatism (TLAR, 2017 (19, 60))	Knee	**	*	**	**	*	**	**
European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and	Knee	**	*	*	**	*	**	*

Musculoskeletal Diseases (ESCEO, 2016 (33, 61))								
Pan-American League of Rheumatology Associations (PANLAR, 2016 (20))	Hip / knee	**	**	**	**	*	***	**
American Academy of Orthopedic Surgery (AAOS, 2015 (27))	Knee	***	**	***	**	*	***	***
Department of Veterans Affairs/Department of Defense (VA/DoD, 2014 (22))	Hip / knee	***	**	**	***	*	*	**
National Institute for Health and Care Excellence (NICE, 2014 (28))	Hip / knee	***	**	***	***	**	**	***
American Academy of Orthopedic Surgery (AAOS, 2013 (23))	Knee	***	**	***	***	**	***	**
European League Against Rheumatism (EULAR, 2013 (25))	Hip / knee	***	***	**	***	*	***	**
American College of Rheumatology (ACR, 2012 (62))	Hip / knee	**	**	**	**	*	*	**
Osteoarthritis Research Society International (OARSI, 2009 (26))	Hip / knee	***	**	***	***	**	**	**
European League Against Rheumatism (EULAR, 2005 (24))	Hip	**	*	**	***	*	*	**

**Table 2: Guideline recommendations (↑↑, strong for; ↑?, conditional for; ↓?, conditional against; ↓↓, strong against) with level of evidence (⊕⊕⊕⊕, very low; ⊕⊕⊕⊙, low; ⊕⊕⊕⊙, moderate; ⊕⊕⊕⊕, high) of non-pharmacological treatment for knee and hip OA.**

Guideline &	Education	Exercise	Weight loss	Insoles (I), footwear (F), braces (B)	TENS	Heat/cold	Traditional acupuncture	Assistive devices (walking aids, canes)
<b>Knee OA</b>								
VA/DoD 2020 (51)	N.S.	⊕⊕⊙ ⊙ / ↑?	⊕⊕⊕⊙ / ↑?	N.S.	⊕⊕⊙ ⊙ / n.r.	N.S.	⊕⊕⊕⊙ / n.r.	N. S.
ACR 2019 (29)	⊕⊕⊙ ⊙ to ⊕⊕⊕ ⊙ / ↑↑	⊕⊕⊙ ⊙ to ⊕⊕⊕ ⊙ / ↑↑	⊕⊕⊕⊙ / ↑↑	Tibio-femoral B: ⊕⊕⊕ ⊙ / ↑↑, patella-femoral B: ⊕⊕⊙ ⊙ / ↑?, F: ⊕⊕⊙	⊕⊕⊙ ⊙ / ↓↓	⊕⊕⊙ ⊙ / ↑?	⊕⊕⊕⊙ / ↑?	⊕⊕⊕ ⊙ / ↑↑

				$\odot / \downarrow?$ , I: $\oplus \oplus \odot$ $\odot / \downarrow$				
ESCEO 2019 (30)	$\oplus \oplus \odot$ $\odot /$ $\uparrow \uparrow$	$\oplus \oplus \oplus$ $\oplus /$ $\uparrow \uparrow$	$\oplus \oplus \oplus \oplus /$ $\uparrow \uparrow$	N.S.	N.S.	N.S.	N.S.	N.S.
OARSI 2019 (31)	$\oplus \oplus \oplus$ $\odot /$ $\uparrow \uparrow$	$\oplus \oplus \oplus$ $\odot /$ $\uparrow \uparrow$	$\oplus \odot \odot \odot /$ $\uparrow \uparrow$	F: $\oplus \oplus \odot$ $\odot /$ $\downarrow \downarrow$ , B: $\oplus \odot \odot$ $\odot$ to $\oplus \oplus \oplus$ $\odot / \downarrow?$ to $\downarrow \downarrow$	$\oplus \odot \odot$ $\odot /$ $\downarrow \downarrow$	$\oplus \odot \odot$ $\odot / \uparrow?$ to $\downarrow \downarrow$	$\oplus \oplus \odot \odot /$ $\downarrow?$	$\oplus \odot \odot$ $\odot / \uparrow?$
TLAR 2017 (19)	$\oplus \oplus \oplus$ $\oplus /$ $\uparrow \uparrow$	$\oplus \oplus \oplus$ $\oplus /$ $\uparrow \uparrow$	$\oplus \oplus \oplus \oplus /$ $\uparrow \uparrow$	I: $\oplus \oplus \oplus$ $\oplus / \uparrow \uparrow$	$\oplus \oplus \oplus$ $\odot /$ $\uparrow \uparrow$	$\oplus \odot \odot$ $\odot /$ $\uparrow \uparrow$	N.S.	$\oplus \oplus \oplus$ $\odot /$ $\uparrow \uparrow$
PANLAR 2016 (20)	$\oplus \oplus \oplus$ $\oplus /$ $\uparrow \uparrow$	$\oplus \oplus \oplus$ $\oplus /$ $\uparrow \uparrow$	N.S.	I: $\oplus \oplus \oplus$ $\oplus / \uparrow?$ , B: $\oplus \oplus \oplus$ $\oplus / \uparrow?$	N.S.	$\oplus \oplus \oplus$ $\oplus / \uparrow?$	N.S.	$\oplus \oplus \oplus$ $\odot / \uparrow?$

NICE 2014 (28)	↑↑	↑↑	↑↑	F: ↑↑, B: ↑?	↑?	↑?	↓?	↑?
EULAR 2013 (25)	⊕⊕⊕ ⊕ / ↑↑	⊕⊕⊕ ⊕ / ↑↑	⊕⊕⊕⊕ / ↑↑	I: ⊕⊕⊕ ⊙ / ↓?, F: ⊕⊕⊕ ⊙ / ↑↑	N.S.	N.S.	N.S.	⊕⊕⊕ ⊙ / ↑↑
AAOS 2013 (23)	⊕⊕⊕ ⊕ / ↑↑	⊕⊕⊕ ⊕ / ↑↑	⊕⊕⊕⊕ / ↑?	B: ⊕⊕⊕ ⊙ / n.r., I: ⊕⊕⊕ ⊙ / ↑?	⊕⊕⊕ ⊙ / n.r.	N.S.	⊕⊕⊕⊕ / ↓↓	N.S.
<b>Hip OA</b>								
VA/DoD 2020 (51)	N.S.	⊕⊕⊕ ⊙ / ↑?	⊕⊕⊕⊕ / ↑?	N.S.	N.S.	N.S.	⊕⊕⊕⊕ / no recommendati on	N.S.
ACR 2019 (29)	⊕⊕⊕ ⊙ to ⊕⊕⊕ ⊙ / ↑↑	⊕⊕⊕ ⊙ to ⊕⊕⊕ ⊙ / ↑↑	⊕⊕⊕⊕ / ↑↑	F: ⊕⊕⊕ ⊙ / ↓?, I: ⊕⊕⊕ ⊙ / ↓?	⊕⊕⊕ ⊙ / ↓↓	⊕⊕⊕ ⊙ / ↑?	⊕⊕⊕⊕ to ⊕⊕⊕⊕ / ↑?	⊕⊕⊕ ⊙ / ↑↑
ACOEM 2019 (32)	⊕⊕⊕ ⊙ / ↑?	⊕⊕⊕ ⊙ / ↑?	N.S.	⊕⊕⊕ ⊙ / ↑?	⊕⊕⊕ ⊙ / n.r.	⊕⊕⊕ ⊙ / ↑?	⊕⊕⊕⊕ / ↑?	⊕⊕⊕ ⊙ / ↑?

OARSI 2019 (31)	⊕⊕⊕ ⊖ / ↑↑	⊕⊕⊕ ⊖ / ↑↑	⊕⊖⊖⊖ / ↑?, with comorbiditi es: ↓?	N.S.	⊕⊖⊖ ⊖ / ↓↓	⊕⊖⊖ ⊖ / ↑? to ↓↓	⊕⊖⊖⊖ / ↑?	⊕⊖⊖ ⊖ / ↑?
PANLAR 2016 (20)	⊕⊕⊕ ⊖ / ↑↑	⊕⊕⊕ ⊖ / ↑↑	⊕⊕⊕⊖ / ↑↑	Orthoses : ⊕⊕⊕ ⊖ / ↑?	⊕⊕⊕ ⊖ / ↑?	⊕⊕⊕ ⊖ / ↑?	N.S.	⊕⊕⊕ ⊖ / ↑?
NICE 2014 (28)	↑↑	↑↑	↑↑	F: ↑↑, B: ↑?	↑?	↑?	↓?	↑?
EULAR 2013 (25)	⊕⊕⊕ ⊕ / ↑↑	⊕⊕⊕ ⊕ / ↑↑	⊕⊖⊖⊖ / ↑↑	I: ⊕⊖⊖ ⊖, F: ⊕⊖⊖ ⊖ / ↑↑	N.S.	N.S.	N.S.	⊕⊕⊖ ⊖ / ↑↑

**Abbreviations:** AAOS, American Academy of Orthopedic Surgery; ACR, American College of Rheumatology; ACOEM, American College of Occupational and Environmental Medicine; EULAR, European League Against Rheumatism; NICE, National Institute for Health and Care Excellence; OARSI, Osteoarthritis Research Society International; PANLAR, Pan-American League of Rheumatology Associations; TLAR, Turkish League Against Rheumatism; VA/DoD, Department of Veterans Affairs/Department of Defense; ESCEO, European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases; TENS, transcutaneous electrical nerve stimulation; N.S., not specified by the



guideline; n.r., no recommendation issued by the guideline; & most recently published or most relevant guideline

**Table 3: Guideline recommendations (↑↑, strong for; ↑?, conditional for; ↓?, conditional against; ↓↓, strong against) with level of evidence (⊕⊕⊕⊕, very low; ⊕⊕⊕⊖, low; ⊕⊕⊕⊖, moderate; ⊕⊕⊕⊕, high) of pharmacological therapies for knee and hip OA.**

Guideline *	Topical NSAID	Topical capsaicin	Paracetamol	Oral NSAID	Weak opioids	Strong opioids	Glucosamine or chondroitin sulfate	Intra-articular glucocorticoid injection	Intra-articular hyaluronic acid injection
<b>Knee OA</b>									
VA/DoD 2020 (51)	⊕⊕⊕⊕ ⊖ / ↑↑	⊕⊕⊖ ⊖ / ↑?	⊕⊕⊖ ⊖ / ↑?	⊕⊕⊖ ⊖ / ↑?	⊕⊖⊖ ⊖ / ↓?	⊕⊖⊖⊖ / ↓?	⊕⊖⊖⊖ / n.r.	⊕⊕⊖⊖ / ↑?	⊕⊕⊖ ⊖ / ↑?
ACR 2019 (29)	⊕⊕⊖ ⊖ to ⊕⊕⊕ ⊖ / ↑↑	⊕⊖⊖ ⊖ to ⊕⊕⊕ ⊖ / ↑?	⊕⊖⊖ ⊖ / ↑?	⊕⊕⊕ ⊖ / ↑↑	⊕⊖⊖ ⊖ / ↑?	⊕⊖⊖⊖ to ⊕⊕⊖⊖ / ↓?	⊕⊖⊖⊖ to ⊕⊕⊕⊖ / ↓↓	⊕⊕⊖⊖ / ↑↑	⊕⊖⊖ ⊖ to ⊕⊕⊕ ⊖ / ↓?

ESCEO	⊕⊕⊕	N.S.	⊕⊕⊕	⊕⊕⊕	⊕⊕⊕	⊕⊕⊕⊖	⊕⊕⊖⊖	⊕⊕⊖⊖	⊕⊕⊖
2019	⊖ /		⊕ / ↓?	⊕ /	⊕ /	to	to	to	⊖ to
(30)	↑↑		long-term, ↑?	↑↑	↑?	⊕⊕⊕⊕	⊕⊕⊕⊕	⊕⊕⊕⊖	⊕⊕⊕
			short-term			/ ↑?	/ ↑↑	/ ↑?	⊖ / ↑?
OARSI	⊕⊕⊕	⊕⊕⊖	⊕⊕⊖	⊕⊕⊕	N.S.	⊕⊖⊖⊖	Glucosam	⊕⊖⊖⊖	⊕⊕⊖
2019	⊕ /	⊖ /	⊖ / ↓?	⊖ /		to	ine:	/ ↑?	⊖ / ↑?
(31)	↑↑	↓?		↑?		⊕⊕⊖⊖	⊕⊖⊖⊖		
						/ ↓?, if	/ ↓↓,		
						comorbidi	chondroit		
						ties: ↓↓	in:		
							⊕⊖⊖⊖		
							/ ↓?		
TLAR	⊕⊕⊕	N.S.	⊕⊕⊕	⊕⊕⊕	⊕⊕⊕	N.S.	N.S.	⊕⊕⊕⊕	⊕⊕⊕
2017	⊕ /		⊕ / ↑↑	⊕ /	⊕ /			/ ↑↑	⊕ /
(19)	↑↑			↑↑	↑↑				↑↑
PANLA	⊕⊕⊕	⊕⊕⊕	⊕⊕⊕	⊕⊕⊕	⊕⊕⊖	N.S.	⊕⊕⊕⊕	⊕⊕⊕⊖	⊕⊕⊕
R 2016	⊕ /	⊖ /	⊖ / ↑↑	⊕ /	⊖ /		/ ↑↑	/ ↑?	⊖ / ↑?
(20)	↑↑	↑?		↑↑	↑?				
NICE	↑?	↑?	↑?	↑?	N.S.	↑?	↓↓	⊕⊕⊖⊖	↓↓
2014								/ ↑?	
(28)									
AAOS	N.S.	N.S.	N.S.	⊕⊕⊕	N.S.	⊕⊖⊖⊖	Glucosam	⊕⊕⊖⊖	⊕⊕⊕
2013				⊕ /		/ ↓?	ine:	/ n.r.	⊕ /

(23)				↑↑			⊕⊕⊕⊖ / ↓?		↓↓
<b>Hip OA</b>									
VA/Do D 2020 (51)	n.r.	⊕⊖⊖ ⊖ / n.r.	⊕⊕⊖ ⊖ / ↑?	⊕⊕⊖ ⊖ / ↑?	⊕⊖⊖ ⊖ / ↓?	⊕⊖⊖⊖ / ↓?	⊕⊖⊖⊖ / n.r.	⊕⊕⊖⊖ / ↑?	⊕⊕⊖ ⊖ / ↓?
ACR 2019 (29)	N.S.	N.S.	⊕⊖⊖ ⊖ / ↑?	⊕⊕⊕ ⊖ / ↑↑	⊕⊖⊖ ⊖ / ↑?	⊕⊖⊖⊖ to ⊕⊕⊖⊖ / ↓?	⊕⊕⊕⊖ to ⊕⊖⊖⊖ / ↓↓	⊕⊕⊖⊖ / ↑↑	⊕⊕⊖ ⊖ / ↓↓
OARSI 2019 (31)	N.S.	⊕⊖⊖ ⊖ / ↓↓	⊕⊕⊖ ⊖ / ↓?	⊕⊕⊕ ⊖ / ↑?	N.S.	⊕⊖⊖⊖ to ⊕⊕⊖⊖ / ↓?, if comorbidi ties: ↓↓	⊕⊖⊖⊖ / ↓↓	⊕⊕⊕⊖ / ↑?	⊕⊕⊕ ⊖ / ↓?
ACOEM 2019 (32)	⊕⊖⊖ ⊖ / ↓?	⊕⊖⊖ ⊖ / ↑?	⊕⊕⊕ ⊖ to ⊕⊕⊕ ⊕ / ↑?	⊕⊕⊕ ⊕ / ↑↑	⊕⊖⊖ ⊖ / ↑?	N.S.	⊕⊖⊖⊖ / n.r.	⊕⊕⊕⊖ / ↑?	⊕⊖⊖ ⊖ / ↓?
AAOS 2017 (18)	N.S.	N.S.	N.S.	⊕⊕⊕ ⊕ / ↑↑	N.S.	N.S.	Glucosam ine: ⊕⊕⊕⊖ / ↑?	⊕⊕⊕⊕ / ↑↑	⊕⊕⊕ ⊕ / ↓↓
PANLA R 2016	N.S.	N.S.	⊕⊕⊕ ⊖ / ↑↑	⊕⊕⊕ ⊖ /	⊕⊕⊕ ⊖ /	N.S.	N.S.	⊕⊕⊕⊖ / ↑?	⊕⊕⊕ ⊖ / ↑?

(20)				↑↑	↑?				
NICE 2014 (28)	↑?	N.S.	↑?	↑?	N.S.	↑?	↓↓	↑?	↓↓
EULAR 2005 (24)	N.S.	N.S.	⊕⊕⊕ ⊕ / ↑↑	⊕⊕⊕ ⊕ / ↑↑	⊕⊕⊕ ⊕ / ↑↑	⊕⊕⊕⊕ / ↑?	⊕⊕⊕⊙ / ↑?	⊕⊕⊕⊙ / ↑?	⊕⊕⊙ ⊙ / ↑?

**Abbreviations:** AAOS: American Academy of Orthopedic Surgery; ACR: American

College of Rheumatology; ACOEM: American College of Occupational and

Environmental Medicine; EULAR: European League Against Rheumatism; NICE:

National Institute for Health and Care Excellence; OARSI: Osteoarthritis Research

Society International; PANLAR: Pan-American League of Rheumatology

Associations; TLAR: Turkish League Against Rheumatism; VA/DoD: Department of

Veterans Affairs/Department of Defense; ESCEO, European Society for Clinical and

Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases;

NSAID, Nonsteroidal anti-inflammatory drug; N.S., not specified by the guideline; n.r.,

no recommendation issued by the guideline; \* most recently published or most

relevant guideline

**Table 4: Strength of evidence (⊕⊕⊕⊕, very low; ⊕⊕⊕⊙, low; ⊕⊕⊕⊙, moderate; ⊕⊕⊕⊕, high) and strength of recommendation (↑↑, strong for; ↑?, conditional for; ↓?, conditional against; ↓↓, strong against) for considering surgery in knee and hip OA according to most recent guidelines**

Guideline, year	Osteotomy*	Unicompartmental knee arthroplasty	Total joint arthroplasty, criteria: pain (p), functional impairment (f), radiological changes (r), and failed / futile non-surgical therapy (t)
<b>Knee</b>			
European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO), 2019 (30)	N.S.	N.S.	p, f, t: ↑↑
Turkish league against rheumatism (TLAR), 2017 (19)	⊕⊕⊕⊕ / ↑?	⊕⊕⊕⊕ / ↑? (for elderly)	p, f, t: ⊕⊕⊕⊕ / ↑↑
Pan-American League of Rheumatology	N.S.	N.S.	p, f: ⊕⊕⊕⊙ / ↑?

Associations (PANLAR), 2016 (20)			
National Clinical Guideline Centre (NICE), 2014 (28)	N.S.	N.S.	p, f, t: ↑?
American Academy of Orthopaedic Surgeons (AAOS), 2013 (23)	⊕⊕⊖⊖ / ↑?	N.S.	N.S.
Osteoarthritis Research Society International (OARSI), 2006/2009 (48)	⊕⊕⊕⊖ - ⊕⊕⊕⊕ / ↑?	⊕⊕⊕⊖ / ↑↑	p, f, t: ⊕⊕⊖⊖ / ↑↑
American College of Rheumatology (ACR), 2000 (49)	↑?	N.S.	p, f, t: ↑↑
<b>Hip</b>			
American College of Occupational and Environmental Medicine, 2019 (32)	⊕⊖⊖⊖ / ↑?	N/A	p, f, r, t: ⊕⊕⊕⊕ / ↑↑
Pan-American League of Rheumatology Associations (PANLAR), 2016 (20)	N.S.	N/A	p, f: ⊕⊕⊕⊖ / ↑?

Department of Veterans Affairs / Department of Defense, 2014 (22)	N.S.	N/A	p, f, r, t: ↑?
National Clinical Guideline Centre (NICE), 2014 (28)	N.S.	N/A	p, f, t: ⊕⊕⊖⊖ / ↑? (expert opinion)
Osteoarthritis Research Society International (OARSI), 2006/2009 (26, 48)	⊕⊕⊕⊖ / ↑?	N/A	p, f, t: ⊕⊕⊖⊖ / ↑↑
European League Against Rheumatism (EULAR), 2005 (24)	⊕⊕⊖⊖ / ↑?	N/A	p, f, r, t: ⊕⊕⊖⊖ / ↑?
American College of Rheumatology (ACR), 2000 (49)	N.S.	N/A	p, f, r, t: ↑↑

\*Knee: High tibial osteotomy in younger, active patients with malalignment. N/A, not applicable. N.S., not specified by the guideline