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ABSTRACT

Background: Numerous scientific organisations have developed evidence-based recommendations aiming to optimise the management of osteoarthritis (OA). Uptake, however, has been suboptimal. The purpose of this exercise was to harmonize the recent recommendations and develop a user-friendly treatment algorithm to facilitate translation of evidence into practice.

Methods: We updated a previous systematic review on clinical practice guidelines (CPGs) for OA management. The guidelines were assessed using the Appraisal of Guidelines for Research and Evaluation for quality and the standards for developing trustworthy CPGs as established by the National Academy of Medicine (NAM). Four case scenarios and algorithms were developed by consensus of a multidisciplinary panel.

Results: Sixteen guidelines were included in the systematic review. Most recommendations were directed toward physicians and allied health professionals, and most had multi-disciplinary input. Analysis for trustworthiness suggests that many guidelines still present a lack of transparency. A treatment algorithm was developed for each case scenario advised by recommendations from guidelines and based on panel consensus.

Conclusion: Strategies to facilitate the implementation of guidelines in clinical practice are necessary. The algorithms proposed are examples of how to apply recommendations in the clinical context, helping the clinician to visualise the patient flow and timing of different treatment modalities.

Key-words: osteoarthritis, management, guidelines.

INTRODUCTION

In recent years the American College of Rheumatology (ACR)[1], Osteoarthritis Research Society International (OARSI)[2], American Academy of Orthopaedic Surgeons (AAOS)[3], National Institute for Health and Care Excellence (NICE)[4], European League against Rheumatism (EULAR)[5] and others have developed recommendations through Clinical Practice Guidelines (CPGs) to optimise the treatment of hand, hip and/or knee osteoarthritis (OA) based on a variable combination of expert consensus and systematic review of clinical research evidence. These guidelines have many commonalities, however, uptake has been suboptimal[6,7].

A task force led by the US Chronic Osteoarthritis Management Initiative (COAMI) Work Group of the US Bone and Joint Initiative examined the potential issues and barriers involved in the translation of CPGs to clinical practice[8]. The authors found that information about guideline applicability such as items regarding facilitators and barriers to guideline use, practical advice concerning guideline implementation, resource implications and monitoring/auditing criteria was often not included. A critical review of guidelines published in 2007 stated that in order to improve applicability and to increase uptake by end users, stakeholder opinions and barriers to use need to be taken into account during guideline development[9]. Furthermore, effective delivery of treatments requires clear procedural details of the essential elements of treatment, including how and when they are best administered, but unfortunately, these details are often lacking[10].

A general practitioner survey of adherence to EULAR 2000 recommendations found that the majority of the physicians were aware of OA guidelines (79%) and almost all of them agreed with the recommendations (97%), but only 54% adhered to the pharmacological and non-pharmacological recommendations[11]. These findings suggest a deficiency of methods to operationalize and disseminate the existing recommendations in target populations across specialties, particularly in general practice. With this insight, the 2014 version of the NICE guideline offered implementation tools and resources to help users put the recommendations into practice; hopefully this advancement will be adopted in future guidelines[4]. The current study offers a different view, as we based our strategy on examples of clinical scenarios in order to bring the recommendations to the reality of clinical practice.

The purposes of this exercise were: (i) to harmonize the recent guidelines, searching for common ground among the recommended treatment options for OA and (ii) to develop user-friendly management algorithms for common case scenarios as a method to discuss, prioritise and put into a complex setting/context the different individual recommendations, aiming to facilitate the translation of evidence-based recommendations into practice. The target

audience is professionals across countries involved with the primary care of OA but also relevant to secondary care professionals.

MATERIALS AND METHODS

To accomplish our research objectives we coordinated the exercise in five distinct phases:

(1) *Participants* - invitation of health professionals in the field of OA (OA panel and systematic review panel, described below) and two people living with symptoms of knee OA (public involvement);

(2) *Systematic review update* - update of the appraisal of existing guidelines[8];

(3) *Trustworthy guidelines assessment* - assessment of selected guidelines according to the standards for developing trustworthy clinical practice guidelines as established by the National Academy of Medicine (NAM)[12] to improve guideline quality;

(4) *Case scenarios* - development of four case scenarios reflecting persons with hand, hip and knee OA considering the inclusion of comorbidities and different stages of disease management in order to represent common clinical situations

(5) *Algorithms* - development of management algorithms for each case scenario applying the evidence-based recommendations and the expertise of the panel consensus.

Participants

OA Panel

We established a comprehensive panel in order to cover multidisciplinary and transcultural aspects of OA management with an international focus. The role of this panel was to appraise the existing pooled evidence base and develop case scenarios and their respective algorithms. The panel consisted of 15 health professionals in the field of OA (physiotherapists, general practitioners, rheumatologists and orthopaedists) from 8 countries (Chinese, Portuguese, Swedish and predominantly English speaking) across different continents (America, Oceania, Europe and Asia). For further details, including conflicts of interest see Appendix.

Systematic Review Panel

A subset of the OA panel (AG, AN, JJ, KA and YG) corresponded to the previous authors of a comprehensive systematic review on clinical practice guidelines for OA management[8]. The role of this panel was to provide a critical appraisal of existing treatment guidelines through the update of their previous systematic review by including the most recent guidelines and respective recommendations.

Trustworthy Guidelines Assessors

The 16 guidelines were assessed regarding all the criteria and sub-criteria proposed by the NAM for developing trustworthy clinical practice guidelines[12]. The evaluation was made by two assessors (SM and TL). DH acted as moderator in case of disagreement between the assessors.

Public involvement

Two people with knee OA from Australia were involved in giving feedback throughout the process. They participated in the case scenario formulation, algorithm construction and manuscript development. All comments were considered and incorporated. The participants approved the final version of this manuscript and agreed with its content. All the communications were made via in person meeting or email.

Systematic Review Update

The design of the systematic review was developed using the guidelines of the *Preferred Reporting Items for Systematic Reviews and Meta-Analyses* (PRISMA). The PRISMA statement includes a 27-item checklist for use as a basis for reporting systematic reviews[13]. The methodology used here was consistent with the previous work and is presented as supplementary material. A protocol was not registered for this review.

Our goal was to update the findings of a previous comprehensive systematic review on clinical practice guidelines for OA management. Our search time frame was restricted to January 1st, 2013 to October 1st 2014 to overlap the search of this previous comprehensive review, which investigated this topic from January 1st 2000 to April 1st 2013[8]. We searched Medline and the Agency for Healthcare Research & Quality (AHRQ) Guidelines Clearinghouse using the keywords “osteoarthritis and practice management”. Our search terms differed from the previous review in order to create a more sensitive search given the short time frame between reviews.

The overall quality of each included guideline was assessed using the AGREE II instrument (Appraisal of Guidelines for Research and Evaluation, 2nd edition; www.agreetrust.org). Since the methodological approach to the updates to previous guidelines did not change, the scores from the previous versions were maintained.

Trustworthy Guidelines Assessment

In March 2011, the NAM established standards for developing Trustworthy Clinical Practice Guidelines (CPGs), in order to examine the quality and trustworthiness of clinical practice guidelines and how they can be improved to enhance healthcare quality and patient outcomes[12]. The NAM standards include eight criteria items: establishing transparency, management of conflict of interest, guideline development group composition, clinical practice guideline–systematic review intersection, establishing evidence foundations for and rating strength of recommendations, articulation of recommendations, external review and updating.

The guidelines used in the updated systematic review were assessed regarding all the criteria and sub-criteria. The evaluation was conducted by two assessors (SM and SL). In the first meeting, a table with the NAM standards and the electronic copy of the guidelines were provided. After both assessors independently evaluated the compliance of all guidelines to NAM criteria and completed the table, a second meeting was scheduled in order to verify disagreements. All conflicting answers were discussed until a consensus was reached between the two assessors. The remaining conflicting answers were discussed with a moderator (DH) at a third meeting in order to produce a final consensus. After this meeting, valid answers for trustworthy CPG were established.

Case Scenarios

The OA panel produced four case scenarios for the most affected joints: hand (1), knee (2) and hip OA (1). Aspects like symptoms, comorbidities and previous treatment response were included in the scenario in order to be consistent with what occurs in clinical practice. DH developed the first draft. All authors and the two consumers with OA provided feedback through email over four rounds and they discussed all issues until consensus was reached. DH produced the final version.

Algorithms

The algorithm development consisted of four steps. First, we only selected the recommendations that were consistent across the guidelines, in other words, we excluded controversial recommendations (i.e. a

recommendation advised by one guideline and advised against by another). To do this we extracted the results of the updated systematic review and created a list of homogeneous recommendations.

Second, with the recommendations' list in hand we selected the appropriated treatment options for each scenario, considering the comorbidities and treatment contra-indications.

The third step was the review and feedback process through email, in which we collected and incorporated all suggestions of co-authors. The OA panel commented on the treatment options and structure of the algorithms. The group discussed all aspects of discordance until a consensus was reached, thus the algorithms were developed using guideline consistency plus expert consensus. The drafts of each algorithm were presented to the consumers with OA for feedback and their comments incorporated. DH resolved the discrepancies and the OA panel approved the final version.

The last step was the design elaboration. The arrangement of the algorithm was strategically created to facilitate clinical interpretation. We organised the algorithm structuring the non-pharmacological and pharmacological interventions in parallel and surgical options at the bottom since optimal management for OA requires a combination of conservative non-drug and drug treatments, with surgery reserved for severe clinical disease with structural changes[17]. The intention is to encourage clinicians to offer first non-invasive interventions always cognisant of symptom severity and the level of disability of the patient. Clinical practice varies but in general nonpharmacologic and pharmacologic options are used simultaneously[14].

RESULTS

Systematic Review Update

After duplicate citations were removed, we screened 101 unique citations (n=84 Medline and n=17 AHRQ) along with the 16 citations included from the previous review. Full-text review occurred for 22 manuscripts. Reasons for exclusion of a guideline after full-text review were: 1) not meeting inclusion criteria (guideline was not OA-specific [n=1][15] or 2) a guideline was outdated by a more recently available update or revised version [n=5][16,17,18,19,20]. After screening and full text review, we included a total of 16 articles describing guidelines for OA management (Figure 1). The majority of the included articles were consistent with the previous review (n=15) with two updates (MQIC[21] and NICE[4]), two revisions (EULAR Hip and Knee[5] and OARSI Knee[2]) and one additionally identified guideline (Italian

Society for Rheumatology[22]). Five were from the United States[1,3,21,23,24] one from Canada[25], eight from Europe[4,5,22,26,27,28,29,30] one from Asia[31], and one multinational[2]. Most recommendations were directed toward doctors and allied health professionals, and most had multi-disciplinary input from general practitioners, rheumatologists, orthopaedic surgeons, and physiotherapists. Also, a few guidelines received feedback from patient representatives. The various grading scales used by the individual societies for their recommendations are summarized in Table 1 (supplementary material).

AGREE II

Scaled AGREE II scores were derived from the two independent reviewers' scores as a percentage of the maximum possible score. The 6 domain scores are listed separately. The OARSI guidelines scored highest on the overall assessment (75%), followed by the AAOS, ACR, MOVE, and NICE guidelines (all 67%). The highest domain scores were for scope and purpose (description of overall objectives, health questions covered, and target population) and rigor of development (use of systematic methods, clear criteria for study selection, strengths and limitations of evidence described, methods of formulating recommendations described, risks and benefits considered, clear link between recommendation and supporting evidence, external review, and procedure for updates). The lowest domain scores were for applicability. This domain includes items about facilitators and barriers to guideline use, practical advice regarding guideline implementation, resource implications, and monitoring/auditing criteria, which were not often included in the OA guidelines. Several guidelines also did not adequately discuss issues related to editorial independence.

The summary of recommendations regarding non-pharmacological interventions can be found in the supplementary material as Table 2 (education and self-management), Table 3 (exercise and weight loss), Table 4 (assistive devices), Table 5 (alternative and complementary modalities), Table 6 (surgical interventions) and Table 7 (pharmacological recommendations).

Trustworthy Guidelines Assessment

All CPGs detailed the development process; however, information regarding the funding source was missing from some. According to NAM standards, the management of Conflicts of Interest (COI) needs to be performed prior to selection of the Guideline Development Group (GDG), and whenever possible the GDG chair should not have a COI.

However, there was only one guideline (AAOS) which completely followed these criteria. Other guidelines presented the authors' COI but included no information about whether COI were declared prior to formation of the GDG.

The GDGs were frequently composed of a multidisciplinary group of experts; however, only a few included patient representatives or advocates in the development process. Strategies and incentives to increase the effective participation of patient representatives were only used by two GDGs (OARSI and EULAR 2013). Most CPGs were based on systematic reviews, but did not inform whether the articles met the standards set by the NAM's Committee, and no guideline produced their own systematic review.

Regarding the recommendations, most of the CPGs established an evidence foundation, rated evidence strength and the majority articulated them in a standardized form. Only a few CPGs had an external and confidential review process and provided the opportunity for the general public for comment on the draft version prior to final guideline release. The updating process was poorly documented or not presented in the majority of CPGs. All guidelines should document the proposed date and conditions for future review, and regularly monitor the literature base to identify the emergence of new relevant evidence that could potentially affect the validity of the CPG.

Algorithm development

The algorithm was developed for each case scenario consistent with the evidence from the consensus recommendations within the guidelines (Case Scenario 1, 2, 3 and 4). In order to improve clarity for the general reader we provided the criteria for which we would make a diagnosis of OA. Therefore, for each case, we added the common signs and symptoms based on Map of Medicine Healthguides[32]. We also included a warning box to check for comorbidities with examples of the most frequent conditions.

As suggested by the OA panel, the algorithm includes more conservative or less costly treatment approaches prior to more invasive, expensive or potentially harmful interventions, such as: A) Referral to physiotherapist or occupational therapist: the first approach should be group activity/exercise programs available at the patient's community or home exercise program and the referral criteria for therapy should be "if in the clinicians' judgment the patient is weak, stiff or has other functional deficits". B) Assistive devices and orthoses with the condition "if ADL is impaired". C) Braces and footwear/insoles only "if malalignment". D) Invasive interventions like intra-articular injections with the criteria "If not effective (prior pharmacological treatment), consider referral to specialist for invasive treatment options". E) Opioid therapy, "if the patient has severe and disabling pain, consider opioid for short term use only and

insist on non-pharmacological interventions" and F) Surgery "if disabling symptoms and if already exhausted all other options including pharmacological and non-pharmacological interventions".

For patients with concurrent conditions such as upper GI problems, peptic ulcer and chronic kidney disease we excluded oral non selective nonsteroidal anti-inflammatory drug (NSAID), except in the case 1 where the patient has a past history of upper GI problems; for this case we consider NSAID or cyclooxygenase-2 inhibitors (COX-2), both added to a proton-pump inhibitors (PPI) for gastroprotection in case of failure of acetaminophen treatment. For others, we recommended continued intermittent acetaminophen and topical NSAIDs. Depending on effect and after consideration of potential for harm we recommended considering a COX2 +PPI for other cases where there is concern over GI toxicity. We excluded topical NSAID for the hip case since we believed the drug is incapable of reaching the joint with therapeutic effect. We also excluded drugs previously used by patients that were not effective for them (e.g. In the hip -case 2 algorithm we excluded acetaminophen from the algorithm since the patient reported not experiencing any benefit from intermittent dosing of over the counter acetaminophen).

Other important input from the panel was the suggestion, based on clinical judgment, to include a post-operative physical therapy program. This was not explicitly included in the guidelines but was considered essential by the panel, since the treatment and follow-up of patients does not finish immediately after surgery.

The guidelines recommended psychological interventions for patients with hip and knee OA. We gave an example of an intervention (cognitive behavioural therapy) and the specific purpose of this kind of intervention: "for assistance with pain coping or psychological symptoms if appropriate". The recommendation from guidelines "weight loss, if overweight" was slightly adapted and instead of referring to a dietician, we included instruction for the patient to join a weight loss program available in community, since not all patients may have access to dieticians. This type of program focuses on nutrition and physical activity education. The panel considered that some recommendations were not specific and clear enough to be used in the algorithm, such as lifestyle changes, joint protection, and regular contact to promote self-care.

It is worth noting that for the recommendations used during the construction of the algorithm for the hip case, we extrapolated the evidence from knee OA management. The reason for this is that guidelines related to hip OA are usually produced in combination with knee OA and studies involving hip OA only are scarce.

DISCUSSION

The purpose of this exercise were: (i) to harmonize the recent guidelines, searching for common ground among the recommended treatment options for OA and (ii) to develop user-friendly management algorithms for common case scenarios as a method to discuss, prioritise and put into a complex setting/context the different individual recommendations, aiming to facilitate the translation of evidence-based recommendations into practice. We updated a systematic review and based on recent evidence based recommendations we built an algorithm to address each case scenario.

Regarding the trustworthy guidelines assessment, future CPGs should follow the standards proposed by the NAM in order to ensure the quality of the processes supporting development of CPGs. Our analysis suggests that many guidelines still present a lack of transparency, particularly with regards to the management of conflict of interest, external review process and information about planned future updates. It is important to note that all the guidelines used in this paper were not specifically designed to achieve the NAM standards, thus we cannot apply to them the rigour of how the criteria were addressed. The key message is to incentivize future guidelines to address these standards in order to improve quality and transparency.

In the updated systematic review, a limited number of additional articles were identified to those included in the previous review by Nelson and colleagues[8]. Two guidelines were updated, two reviewed and one new guideline introduced. Once again, it is evident that the majority of interventions are consistently recommended across guidelines, such as education, exercise, and weight loss. Some were still conflicting like acupuncture, glucosamine/chondroitin supplementation and intra-articular hyaluronans. The main reason highlighted in guidelines for disagreements is the lack of efficacy of these interventions. The focus of guideline dissemination should be for interventions where there is consistent strong and reliable clinical support. Our results are broadly consistent with recently published systematic appraisals of guidelines in the literature[33].

Due to their general consistency, most of the recommendations can be applied in clinical practice. However, at present there is insufficient uptake[6,7]. Consistent with this concern, our results demonstrate that the lowest domain scores in the AGREE II were for applicability of guidelines. This domain includes important points like discussion of facilitators and barriers to application, provision of advice for practical use, consideration of resource implications, and monitoring/auditing criteria. Poor results in AGREE II were also shown in a 2014 systematic review of non-pharmacological management of OA[34]. This lack of focus on the applicability of a CPG seems contradictory to the primary purpose of the guideline in guiding and improving clinical practice. Fortunately, the most recent guidelines

seem to better address the domains of the AGREE II[8]. With this in mind, this algorithm exercise is an example of practical use of recommendations in common clinical scenarios to facilitate the practical use of guidelines. In addition, the algorithms establish some criteria to consider for the triage or judicious use of some interventions. Future guidelines could use this methodology in order to facilitate the implementation of recommendations. It is important to note that the AGREE scores reported are based upon the independent views of 2 reviewers and that others may have differing opinions.

While people with severe OA symptoms may warrant a combination of treatment modalities, e.g. exercise, pharmacological and potentially surgical interventions, people with mild to moderate OA symptoms should consider non pharmacologic management in the first instance[35,36]. Guidelines routinely advocate their use but studies suggest that their use in clinical practice is sub-optimal[37]. Our hope is that this study provides guidance on how to extract the information present in guidelines in a logical manner and consequently improve the management of patients with OA. The algorithm is also a visualization of what is often times overly comprehensive guidelines with extensive text that may limit interpretation and ready dissemination.

There is a great need for further work in the rational allocation of health resources which besides the clinical judgement must take into account health economic aspects. Therefore, it is important to establish the best way of combining the current evidence on the treatment of osteoarthritis, facilitating this way the construction of an efficient treatment plan and improving the cost-effectiveness of these interventions. With this in mind, the European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (ESCEO) group proposed a set of disease-specific recommendations on the conduct and reporting of economic evaluations in OA that could help the standardization and comparability of studies that evaluate therapeutic strategies of OA in terms of costs and effectiveness[38].

In this paper, we aimed to rationalise the recommended treatment options considering an ideal management. We are aware that some options indicated are not available for the entire international population, however we considered it important to present what would be the best treatment scenario for each case. We believe that clinicians should opt for the non-pharmacological options prior to the pharmacological pathway; however we know that in the clinical practice this is not the reality. Thus, we chose to organise both treatments in parallel but here we state this hierarchy would represent a better sequence.

In addition, it is important to note that some interventions must be better studied in order to reduce the number of contradictory and inconclusive recommendations among the guidelines. As example, for the hand OA case, due to inconsistency within the guidelines we did not recommend acetaminophen and intra-articular corticosteroid injections. In our case, we solved the conflicts with help of the OA panel. A recent systematic review and meta-analysis[39] showed that paracetamol provides minimal short term benefit for people with osteoarthritis. Thus, we decided to offer it as one of the last options on the algorithms. Future guidelines should include this important finding since paracetamol is often the first option among the pharmacological options.

Another significant point is that we lack full understanding of who will get the most benefit and least harm for each treatment. On the algorithms we intentionally left the surgical options at the end with a warning that all the other options must be already exhausted before offering the option of surgery. The reason for this is that in spite of universal recommendations for total joint replacement (TJR) in severe cases of OA unresponsive to other therapies, there is insufficient high-quality evidence to support (or quantify) its benefit over the other treatments and there are certainly associated adverse events.

Information that is not presented in any guideline is the follow-up period after a joint replacement. We considered it relevant to include this step in all algorithms as: “individualised exercise program aiming for personalized goals for strength, ROM and function regarding the replaced joint and other joints at risk”. We believe this is a crucial step in the rehabilitation process and future guidelines should pay more attention to it. Furthermore, we provided in each algorithm a box with clinical signs and symptoms and another with comorbidities check-list. We expect with this to encourage clinicians to diagnose OA based on clinical findings rather than radiological and always consider the comorbidities that the patient might have in order to carefully plan the treatment strategy.

There are some important limitations of this work that warrant mention. Firstly, these algorithms are the work of a select group of health professional researchers and do not necessarily reflect the opinions of the organizations that they come from, nor those of others in the field of OA. Another limitation is that only one general practitioner was involved, whereas they are the primary end users. Whilst we appraised and disclosed conflicts of interest, independence from competing interests can never be guaranteed and this paper should be appraised with that caveat in mind. In addition, not all contexts globally are consistent with regards to access to certain interventions, resource implications and barriers to care, so some of the algorithms/interventions may not be optimal or applicable for certain countries. Finally, only guidelines published in English were reviewed, leading to a potential publication

bias. We planned to update this paper in three years after it is published or when new evidence suggests the need for modification of clinically important recommendations.

CONCLUSIONN

In summary, the relative consensus within the guidelines suggests that rather than a lack of quality, there is a failure in the application of the recommendations in clinical practice. The algorithms proposed are examples of how to discuss, prioritise and put into a complex setting/context the different individual recommendations, aiming to facilitate the translation of evidence-based recommendations into practice.

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CONTRIBUTIONS

All authors have made *substantial contributions to:* (1) the conception and design of the study, or acquisition of data, or analysis and interpretation of data; (2) drafting the article or revising it critically for important intellectual content and; (3) final approval of the version submitted.

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COMPETING INTEREST

All the conflicts of interest are declared in the Appendix 1.

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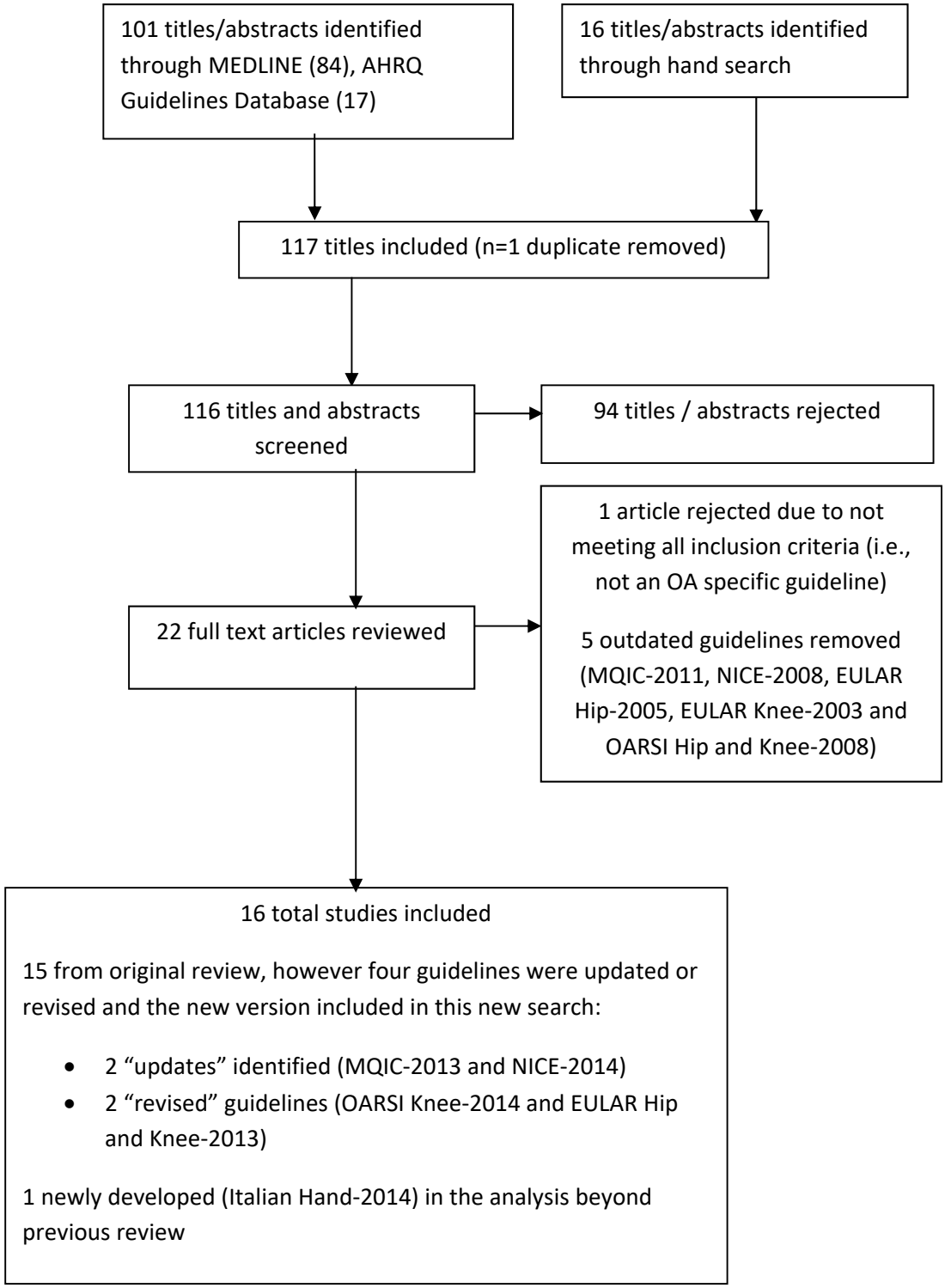
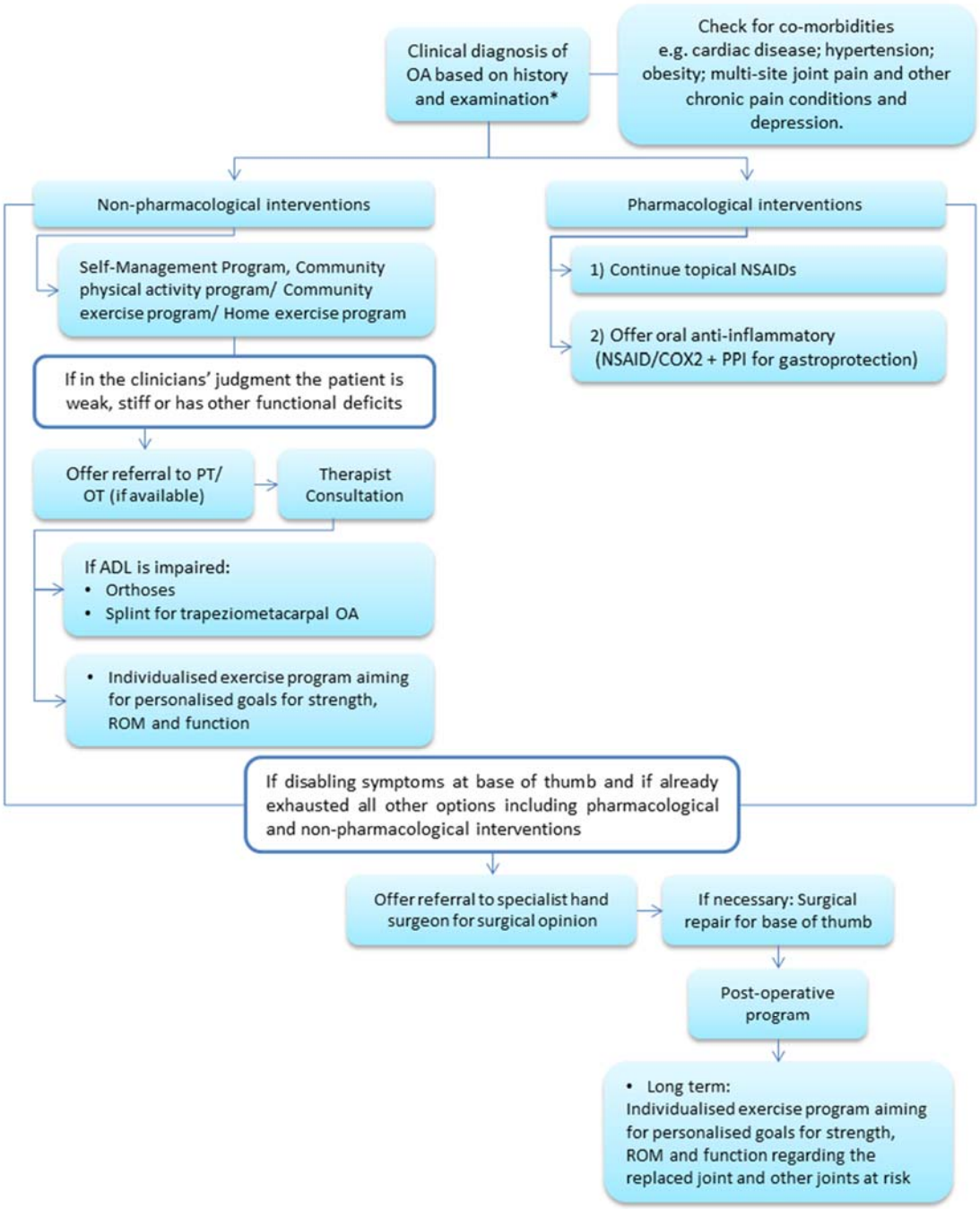
Figure 1. Flow Diagram for Study Inclusion.



Hand – Case 1



***Signs and symptoms**

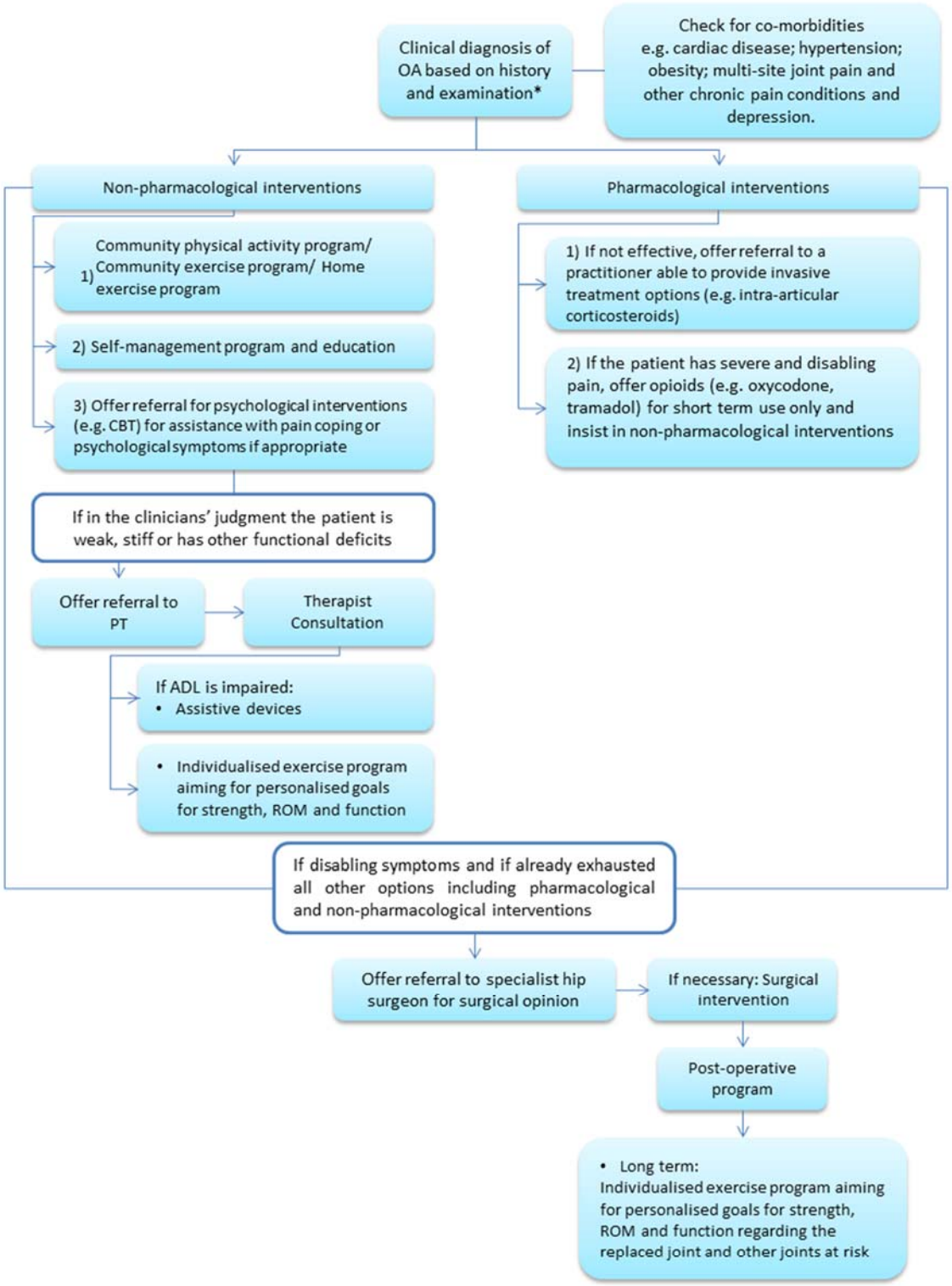
- Joint pain
- Impaired activities of daily living, such as opening jars, turning keys, lifting saucepans and writing
- Diminished grip and pinch strength
- Wasting of the thenar muscles
- Stiffness
- Decreased joint mobility
- Joint swelling
- Crepitus
- Bony nodules
- Ulnar or radial deviation of the finger distal to a distal interphalangeal joint
- 'Squaring' at the first carpometacarpal joint in advanced hand OA

http://healthguides.mapofmedicine.com/choices/map/osteoarthritis1.html

Case Scenario 1 - Hand

An overweight sedentary 60 year old female with symptomatic hand OA presents to her primary care provider for treatment. She has a past history of upper GI problems and depression. She has had pain in several finger joints including the base of thumb for several months. At this point she has not begun any formal medical treatment for this problem but has tried heat and over the counter and topical NSAID treatments.

Hip – Case 2



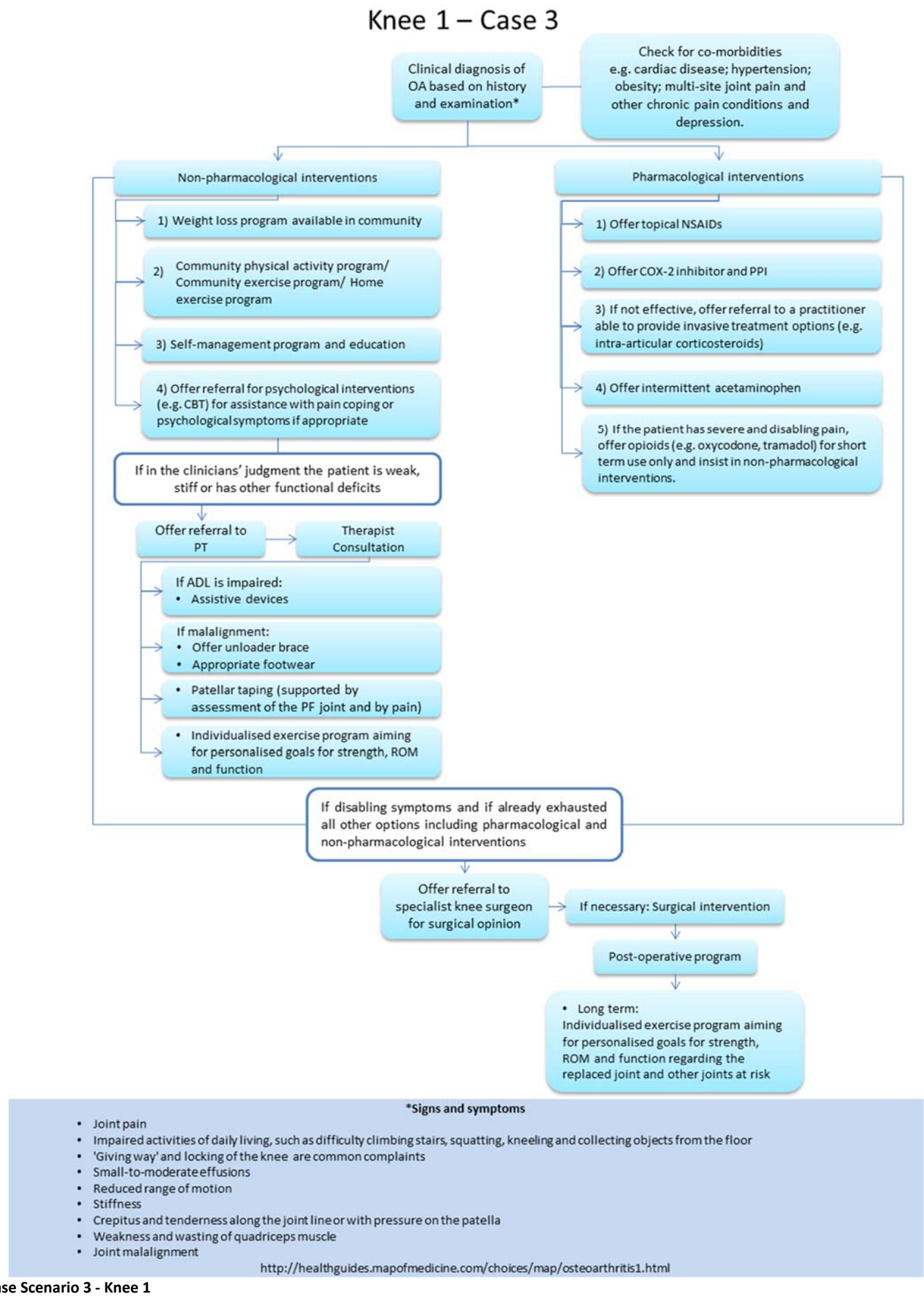
***Signs and symptoms**

- Joint pain typically felt maximally deep in the anterior groin, but may be referred over a wide area such as the upper buttock and anterior thigh
- Impaired activities of daily living, such as difficulty putting on shoes and socks, and getting in and out of cars
- Antalgic gait – a lurch towards the affected hip with less time spent weight bearing on that side; the pelvis is held normally
- Trendelenburg gait, due to wasting and weakness of the gluteal and anterior thigh muscles in later stages of OA
- Decreased joint mobility: painful restriction of internal rotation with the hip flexed is usually the first sign to develop, followed by reduced flexion
- Stiffness
- Crepitus

http://healthguides.mapofmedicine.com/choices/map/osteoarthritis1.html

Case Scenario 2 - Hip

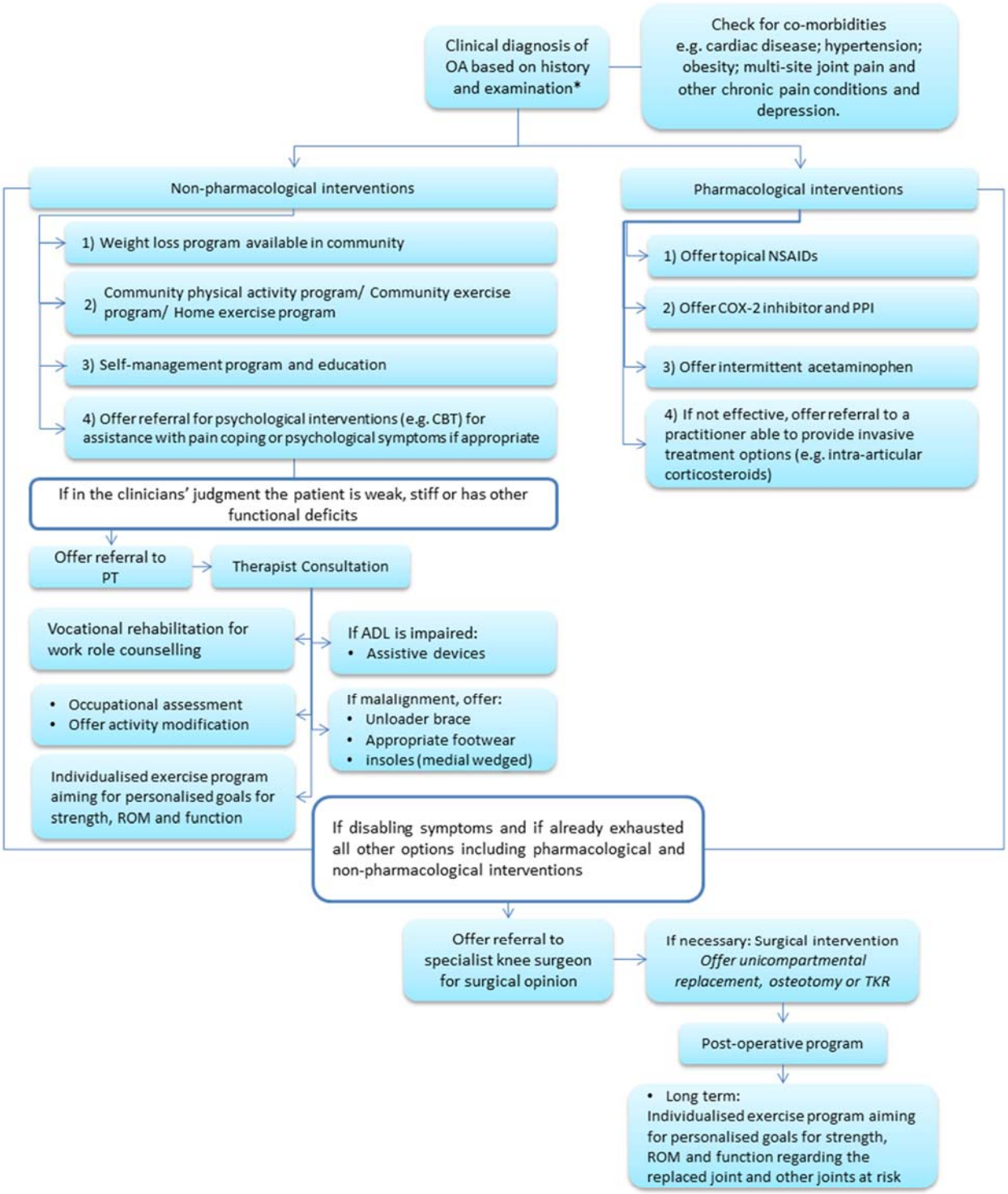
A 56 year old male with symptomatic hip OA presents to his primary care provider for treatment. He has angina currently well controlled on medication and chronic kidney disease (GFR ~30mls/ minute). He is normal weight and experiences pain over the lateral aspect of his hip on movement with hip internal rotation limited to 5 degrees with pain. He has not experienced any benefit from intermittent dosing of over the counter (OTC) acetaminophen.



Case Scenario 3 - Knee 1

An obese 55 year old sedentary female with symptomatic knee OA presents to her primary care provider for treatment. She has depression, sleep apnoea and hypertension currently well controlled on medication and has previously had a peptic ulcer. She experiences pain in and around one knee (including pain in PF joint) and has not had an adequate response to either intermittent dosing of OTC acetaminophen, OTC NSAIDs, or OTC nutritional supplements (e.g., chondroitin sulfate, glucosamine). She has involvement in both the medial tibiofemoral and patellofemoral compartments.

Knee 2 – Case 4



***Signs and symptoms**

- Joint pain
- Impaired activities of daily living, such as difficulty climbing stairs, squatting, kneeling and collecting objects from the floor
- 'Giving way' and locking of the knee are common complaints
- Small-to-moderate effusions
- Reduced range of motion
- Stiffness
- Crepitus and tenderness along the joint line or with pressure on the patella
- Weakness and wasting of quadriceps muscle
- Joint malalignment

http://healthguides.mapofmedicine.com/choices/map/osteoarthritis1.html

Case Scenario 4 - Knee 2

An overweight 48 year old male with symptomatic knee OA (and mild hip OA) presents to his primary care provider for treatment 15 years following a lateral meniscectomy. He has no cardiovascular comorbidities but does have a history of prior peptic ulcer. He works in the building industry in a physically demanding role. He experiences pain in and around the knee and has not had an adequate response to either intermittent dosing of OTC acetaminophen, NSAIDs, or nutritional supplements (e.g., chondroitin sulfate, glucosamine). Opioid drugs whilst helpful made him nauseated and drowsy. He has radiological involvement in the lateral tibiofemoral compartment and marked quadriceps weakness.

APPENDIX 1. Panel members and their conflicts of interest

Expert Panel			
Name	**Expertise**	**Location**	**Conflict of Interest**
Kim L Bennell	Physiotherapist	Australia	- Received royalties from an Osteoarthritis Shoe (ASICS Pty Ltd) and payment from Physitrack for endorsement of an on line exercise programming system. - Received grants from the National Health and Medical Research Council, the Australian Research Council and the Medibank Health Foundation. - Holds a Fellowship from the National Health and Medical Research Council
Philip G Conaghan	NICE Guidelines lead author, rheumatologist	England	- The author has been on advisory boards or attended speaker meetings for Abbvie, BMS, Janssen, Merck, Roche, Novartis and UCB on the topics of inflammatory arthritis. The author also declared that based on his knowledge only Merck has an OA product on the UK market and his work for them involved an epidemiological study of treatments for OA and was not related in any way to Merck's product.
Linda Fernandes	EULAR Guidelines lead author, Physiotherapist	Denmark	- The author declared that she was a co-funder (2012) of a small company developing a mobile exercise application (Ther-ex) to inspire people with OA to a more physically active lifestyle. The app is available on the App Store and Google Play in Denmark and Sweden at the cost of 3 euros to fund the cost of development.
Marc C Hochberg	ACR Guidelines lead author, rheumatologist	USA	- The author declared that during the past 12 months, he has served as a consultant to Bioiberica S.A., Eli Lilly, EMD Serono S.A., Iroko Pharmaceutical Co., Moebius Medical Co., Novartis Pharma A.G., Pfizer Inc., Samumed LLC, and Theralogix LLC. - The author also declared that during the past 12 months, he has served on committees of the European Society for Clinical and Economic Outcomes in Osteoarthritis and Osteoporosis (ESCEO) that have published recommendations on the management of knee OA (Bruyere O, et al: Semin Arthritis Rheum. 2014;44(3):253-63).
David J Hunter	Rheumatologist	Australia	- The author declared that he received royalty payments from DJO for a patellofemoral brace and funding from Flexion Therapeutics, NESTLE for conducting research. - The author participated as expert/co-author in most recent OARSI version of OA guidelines.

Stefan Lohmander	Orthopaedic surgeon	Sweden	- The author declared that received honorarium for consultations on early phase development of novel drugs for osteoarthritis from Abbvie, Flexion, Galapagos, Medivir and Teijin. Each less than $5000. - The author participated as expert/co-author in most recent OARSI version of OA guidelines. Editor-in-chief of Osteoarthritis and Cartilage.
Timothy E McAlindon	OARSI guidelines lead author, rheumatologist	USA	- The author is a consultant for Flexion Therapeutics, Sanofi, Abbvie, McNeil, Samumed, Bioventus, Fidia and receives lecture fees from BioIberica. - The author declared being a board member of OARSI and chair of OARSI guideline development group. - The author also declared having clinical trial contract and/or research involvement with NIH/NIAMS, AHRQ, Allergan, Abbvie, Samumed, Sanofi, Fidia, NCCAM/NIH, Novartis and Human Genome Sciences.
Martin Underwood	General Practitioner	Canada	- The author has received travel expenses, accommodation costs and waiver of conference fees from OARSI to allow him to attend guideline development group meetings. - His employers receive a fee from NICE for his chairing of the NICE accreditation advisory committee and they have received income for author's time as a co-applicant for a project on the use of acupuncture for OA knee. - The author was a member of the group that developed the OARSI guidelines. He has chaired guideline development groups for NICE (back pain and headaches) that have made positive recommendations for acupuncture. He has been involved in research funded by UK National Institute of Health Research (NIHR) on acupuncture for knee pain. He chairs the NICE accreditation advisory committee. He was a member of the NICE, 2008, OA guideline development group. He was a co-applicant on a , subsequently rejected, proposal being considered for funding by NIHR on the use of chondroitin for hand OA at the time this work was done.
Jianhao Lin	Orthopaedic surgeon	China	None
Authors of both the Expert Panel and the Systematic Review Panel			
Adam Goode	Physiotherapist	USA	None
Amanda Nelson	Rheumatologist	USA	- The author receives book royalties from Health Press Ltd (for Fast Facts: Osteoarthritis). - She receives research grant from NIAMS and is member of the Editorial Board of Osteoarthritis and Cartilage.

Joanne Jordan	Rheumatologist	USA	Consultant for ProActiva, Samumed, Algynomics, Abbvie, Flexion; Research support from Centers for Disease Control and Prevention and National Institute of Arthritis, Musculoskeletal and Skin Diseases; Deputy Editor for Clinical Science for Osteoarthritis and Cartilage; Board of Directors of American College of Rheumatology
Kelli Allen	Health Services Research, Exercise and Sport Science	USA	Editorial Board for Osteoarthritis and Cartilage
Yvonne Golightly	Physiotherapist	USA	Editorial Board for Osteoarthritis and Cartilage
Trustworthy Guidelines Assessors			
Name	**Formation**		**Conflict of Interest**
Sichang Liu	Medical student		None
Sarah Meneses	Physiotherapist, PhD student		None
People with OA			
Anne Ashford			
Yarie Nikolic			

Organization	Recommendation grading descriptions
OARSI	Recommendations graded by expert consensus. Panelists ranked the appropriateness of each treatment on a nine point scale, in which a median appropriateness score in the range 1-3 is considered 'inappropriate' (Not App), 4-6 'uncertain' (Unc), and 7-9 'appropriate' (App).
AAOS 2013	Graded as Strong (S, high quality evidence), Moderate (M, moderate quality), Limited (L, low quality), Inconclusive (I), or Consensus (C). NR=not recommended
ACR	Recommendations graded by expert consensus. A strong recommendation (SR) required high-quality evidence and a large gradient of difference between desirable and undesirable treatment effects. A conditional recommendation (CR) was based on absence of high-quality evidence and/or evidence of only a small gradient of difference between desirable and undesirable treatment effects. CNR=conditionally not recommended
MOVE	Recommendations graded: A (Category I evidence), B (Category II evidence or extrapolated from category I evidence), C (Category III evidence or extrapolated from category I or II evidence), or D (Category IV evidence or extrapolated from category II or III evidence).
NICE	Treatments were recommended (R) based on grading of evidence and formal consensus.
EULAR-Hand	Level of evidence graded as Ia: meta-analysis of RCTs, Ib: Randomized controlled trial (RCT), IIa: Controlled, non-randomized, IIb: quasi-experimental study, III: non-experimental/descriptive, or IV: expert committee report/opinion/clinical experience. Recommendations were graded on a VAS scale 0-100mm (0=not recommended at all, 100mm=fully recommended) and an A-E ordinal scale (A=fully recommended, B=strongly recommended, C = moderately recommended, D=weakly recommended, and E=not recommended).
EULAR-Hip and Knee	Level of evidence graded as Ia: meta-analysis of RCTs, Ib: Randomized controlled trial (RCT), IIa: Controlled, non-randomized, IIb: quasi-experimental study, III: non-experimental/descriptive, or IV: expert committee report/opinion/clinical experience. Level of agreement was determined from anonymously voting by experts on a 0 (total disagreement) and 10 (total agreement) for each recommendation.
APTA-OS	Recommendations graded: A (Strong evidence or preponderance of level I/II studies, with at least 1 level I study), B (Moderate evidence, single high-quality RCT or preponderance of level II studies), C (Weak evidence, single level II study or preponderance of level III/IV studies, including expert consensus, D (Conflicting evidence), E (Theoretical Evidence, preponderance of evidence from animal/cadaver studies, conceptual models/principles, or basic sciences), F (Expert Opinion).
Dutch	Recommendations graded: 1 (One A1 study or at least two A2 studies), 2 (One A2 study or at least two B studies), 3 (One B study or at least two B studies), 4 (Expert Opinion). A1 = Meta-analyses which include at least 2 RCTs quality level A2 that show consistent results. A2 = RCTs of a good methodological quality (Randomized double-blind controlled studies) with a sufficient power and consistency. B=RCTs of a moderate methodological quality with insufficient power, or non-randomized, cohort of patient-control group study involving intergroup comparisons. NR=not recommended
Ottawa	Recommendations graded A (strongly recommended), B (recommended), C+ (suggested), C (neutral), D (neutral), D+ (suggest not to use) and D- (strongly not recommended)
SOFMER (Gelis)	Recommendations graded: A (Category I evidence), B (Category II evidence or extrapolated from category I evidence), C (Category III evidence or extrapolated from category I/II evidence), D (Category IV evidence or extrapolated from category II/III evidence); validated by multidisciplinary expert reading committee.
SOFMER (Mazieres)	Recommendations graded: A (Category I evidence), B (Category II evidence or extrapolated from category I evidence), C (Category III evidence or extrapolated from category I/II evidence), D (Category IV evidence or extrapolated from category II/III evidence) and validated by expert panel.
ACCP	Recommendations were by expert panel consensus (no SOR given).
ACPMAB	Recommendations suggested by roundtable expert discussion and consensus (no SOR given).
MQIC	R=recommended based on expert consensus; A = randomized controlled trials; B = controlled trials, no randomization; C = observational studies; D = opinion of expert panel
Italian Hand	Recommendations developed by a multidisciplinary team of experts using the same methodology of the 2006 EULAR Hand guideline development above.

Supplementary Table 1 – Recommendation grading descriptions – updated from Nelson et al (2014) Error! Bookmark not defined..

Supplementary Table 2. Non-pharmacologic recommendations: Education and self-management – updated from Nelson et al (2014) Error! Bookmark not defined.

Organization*	Self management and education	Regular contact to promote self care	Joint protection	Evaluate ability to perform ADLs	Psychosocial Interventions	Individualized Treatment
OARSI – Knee**	App (8), (9), (9), (9)					
AAOS	S					
ACR (Hand)			CR	CR		
ACR (Knee)	CR				CR	
ACR (Hip)	CR				CR	
MOVE	A	A				D
NICE	R	R		R		R
EULAR-Hand			IV (59)			IV (84)
EULAR-Hip and Knee	Ib, mixed		Ib, mixed	Ib, mixed	Ib, mixed	Ib, mixed; Ib, knee
APTA-OS	B (I, II)					
Dutch	2					
Ottawa						
SOFMER (Gelis)						
SOFMER (Mazieres)		C				C
ACCP						
ACPMAB	R					
MQIC	R		R			
Italian			IV (80)			IV (97)

**** Appropriateness scores () listed in order of knee OA without comorbidities, with comorbidities, multisite OA without comorbidities and with comorbidities.**

*Grading systems described in Table 1

Supplementary Table 3. Non-pharmacologic recommendations: Exercise and weight loss – updated from Nelson et al (2014) Error! Bookmark not defined.

Organization*	Low impact aerobic exercise	Range of motion/ flexibility	Quadriceps strengthening	Supervised exercise with manual therapy	Balance	Manual therapy alone	Endurance/ strengthening	Exercise after TJR	Consider PT/OT referral	Weight Loss if overweight
OARSI-Knee**	App (8), (8), (8), (8)						App (8), (8), (8), (7)			App (8), (8), (8), (9)
	Ib hip-water (96)									
AAOS	S			I		I	S			M
ACR (Hand)										
ACR (Knee)	SR			CR	NR	NR				SR
ACR (Hip)	SR			CR						SR
MOVE	A (knee) C (hip)						D			
NICE	R		R	R			R		R	R
EULAR-Hand	IV (59)	IV (59)								
EULAR-Hip and Knee	Ia, knee, aerobic ; Ia, mixed, water-based; Ia, knee, delivery mode, Ia hip/knee overall exercise	Ia, mixed	Ia, knee							III, hip; Ia, knee
APTA-OS		B (II)		B (I, IV)	C		B (II)			
Dutch	1			2				2		
Ottawa	A						A			
SOFMER (Gelis)										
SOFMER (Mazieres)	C									
ACCP										
ACPMAB										
MQIC	R	R (B)					R		R	R
Italian	IV (80)	IV (80)								

**** Appropriateness scores () listed in order of knee OA without comorbidities, with comorbidities, multisite OA without comorbidities and with comorbidities**

*Grading systems described in Table 1.

Supplementary Table 4. Non-pharmacologic recommendations: Assistive devices, orthosis, braces, taping and insoles– updated from Nelson et al (2014) Error! Bookmark not defined..

Organization*	Patellar taping	Brace with varus/valgus as indicated	Free-floating interpositional device for unicompartmental knee OA	Heel wedges (medial or lateral as indicated)	Assistive devices to improve ADLs	Walking aids as needed	Splints for trapeziometacarpal OA	Appropriate footwear/ insoles
OARSI-Knee		App (7), (7), (7), (7)				App (7), (7), Unc (6), (6)		I, IV (77)
AAOS		I	NR-C	NR-M				
ACR (Hand)					CR		CR	
ACR (Knee)	CR			CR		CR		
ACR (Hip)						CR		
MOVE								
NICE		R			R	R	R	R
EULAR-Hand							IV (67)	
EULAR-Hip and Knee				Ib***	III, hip and knee [for chair height, hand rails, shower, etc	III, knee and hip		IIb, knee
APTA-OS					C	C		
Dutch	2							
Ottawa								
SOFMER (Gelis)				B				
SOFMER (Mazieres)								
ACCP								
ACPMAB								
MQIC					R	R		
Italian							Ib ; IV (73)	

**** Appropriateness scores () listed in order of knee OA without comorbidities, with comorbidities, multisite OA without comorbidities and with comorbidities**

***** Rejected**: lateral-wedged insole for medial knee pain, Ib

*Grading systems described in Table 1

Supplementary Table 5. Non-pharmacologic recommendations: Alternative modalities and thermo and electrophysical agents – updated from Nelson et al (2014) Error!

Bookmark not defined.

Organization*	Acupuncture	Tai Chi	Thermal modalities	TENS (if not surgical candidate)	Therapeutic ultrasound	NMES (Strengthening/function)	Balneotherapy / Spa therapy
OARSI	Unc (5), (4.5), (4.5), (4.5)		Ia (64)	Unc (5), (5), Not App (3), (3)	Unc (4), (4), Not App (3), (3)	Not App (3), (3), (3), (3)	Unc (5), (6), (6), (7)
AAOS	NR-S			I	I		
ACR (Hand)			CR				
ACR (Knee)	CR	CR	CR	CR			
ACR (Hip)			CR				
MOVE							
NICE	NR		R	R			
EULAR-Hand			IV (77)		IV (25)		
EULAR-Hip and Knee							
APTA-OS							
Dutch					NR (2)		
Ottawa							
SOFMER (Gelis)							
SOFMER (Mazieres)							
ACCP							
ACPMAB	R	R					
MQIC							
Italian			Ib; IV (71)		Ib; IV (71)		

**** Appropriateness scores () listed in order of knee OA without comorbidities, with comorbidities, multisite OA without comorbidities and with comorbidities**

*Grading systems described in Table 1

Supplementary Table 6. Non-pharmacologic recommendations: Surgical interventions – updated from Nelson et al (2014) Error! Bookmark not defined.

Organization*	Needle lavage	Arthroscopy with debridement	Arthroscopic partial meniscectomy	Osteotomy for isolated PFJ OA	Osteotomy/partial replacement for unicompartmental OA	Surgical repair of trapeziometacarpal OA	Osteotomy for hip OA	Joint replacement	Joint fusion in replacement failure
OARSI – Knee**									
AAOS	NR-M	NR-S	I		L				
ACR (Hand)									
ACR (Knee)									
ACR (Hip)									
MOVE									
NICE		NR						R	
EULAR-Hand						III (68)			
EULAR-Hip and Knee									
APTA-OS									
Dutch									
Ottawa									
SOFMER (Gelis)									
SOFMER (Mazieres)									
ACCP									
ACPMAB									
MQIC									
Italian						III (85)			

**** OARSI recommends referral for consideration of surgery if more conservative treatment modalities are ineffective**

*Grading systems described in Table 1

Supplementary Table 7. Pharmacologic recommendations – updated from Nelson et al (2014) Error! Bookmark not defined.

Organization*	Acetaminophen or paracetamol (<4g/day)	Oral NSAID-Non-selective	Oral NSAID (Cox-2 Inhibitors)	Topical NSAID	Glucosamine and/or chondroitin	Gastroprotection for high risk patients [TT]	Tramadol	Capsaicin	Opioids[§]	Duloxetine	Diacerhein	Avocado Soybean unsaponifiables	Intra-articular corticosteroids	Intra-articular hyaluronic acid	Herbal Remedies	Risedronate
OARSI-Knee**	App (7), (6), (7), (6)	App (7), App (7.5)	App (7), App (7)	App (8), App (7), Unc (6), Unc (6)	Not App (3), (3), (3), (3)			App (7), Unc (6), (6), (6)	Unc (5), (4), (5), (6)	App (7), Unc (6), App (7), (7)	Unc (4), (4), (4), (4)	Unc (4), (4), (5), (5)	App (7), (7), (7), (7)	Unc (5), (4), Not app (3), (3)	Unc, (5), (5), (5), (5)	Not App (3), (3), (3), (3)
OARSI Moderate Comorbidity Risk***		Unc (5), Unc (4)	Unc (6), Not App (7),													
OARSI High Comorbidity Risk***		Not app (2), Not App (2)	Not App (3), Not App (3)			App, App										
AAOS	I	S		S	NR-S		S		I				I	NR-S		
ACR (Hand)		CR[&]		CR		CR	CR	CR	CNR				CNR			
ACR (Knee)	CR	CR[&]		CR	CNR		CR	CNR	SR	CR[§]			CR			
ACR (Hip)	CR	CR[&]			CNR		CR		SR				CR			
MOVE																
NICE	R	R	R	R	NR	R	R	R	R				R	NR		
EULAR-Hand	IV (87)	Ia (81)		Ia (75)	Ib (63)	Ia (81)		Ia (75)			IV (63)	IV (63)	Ib (60)	IIb (63)		
APTA-OS		R (I)			NR (I)								R (I)			
Dutch																
Ottawa																
SOFMER (Gelis)																
SOFMER (Mazieres)																
ACCP	R	R[&]				R										
ACPMAB		R				R										
MQIC	R	R	R			R (D)	R	R	R				R	R		
Italian		Ia, IV(86)		IIb; IV (71)	Ib-IV(72)						Ib-V(72)	Ib-IV(72)	III(82)	Ib-IV(72)		

**** Appropriateness scores () listed in order of knee OA without comorbidities, with comorbidities, multisite OA without comorbidities and with comorbidities**

***** Appropriateness scores () listed in order of knee OA with comorbidities and multisite OA with comorbidities**

*Grading systems described in Table 1. [TT]COX-2, topical over oral NSAID, or add PPI or other agent; [§]for cases refractory to other modalities; [#] Inconclusive; [&] after acetaminophen

Systematic Review Update (complete methodology)

The design of the systematic review was developed using the guidelines of the *Preferred Reporting Items for Systematic Reviews and Meta-Analyses* (PRISMA). The PRISMA statement includes a 27-item checklist for use as a basis for reporting systematic reviews[1]. The methodology used here was consistent with the previous work. A protocol was not registered for this review.

Our goal was to update the findings of a previous comprehensive systematic review on clinical practice guidelines for OA management. Our search time frame was restricted to January 1st, 2013 to October 1st 2014 to overlap the search of this previous comprehensive review, which investigated this topic from January 1st 2000 to April 1st 2013[2]. We searched Medline and the Agency for Healthcare Research & Quality (AHRQ) Guidelines Clearinghouse using the keywords "osteoarthritis and practice management". Our search terms differed from the previous review in order to create a more sensitive search given the short time frame between reviews. The validity and reliability for assessment of practice guidelines by the AGREE II has been established[3,4]. The instrument includes 23 items covering six quality domains: 1) scope and purpose, 2) stakeholder involvement, 3) rigor of development, 4) clarity of presentation, 5) applicability, and 6) editorial independence; two additional assessment items (Overall Guideline Assessment) are included for the evaluator to make an overall judgment of the practice guideline. Each item is scored on a scale of 1-7, with a 1 assigned for items with no clear discussion, a 7 for exceptional quality of reporting, and 2-6 for items not fully meeting the AGREE II criteria. There are no strict cutoffs designating quality using this tool, but it allows comparison between guidelines. Two authors (KDA and YMG) first read the entire AGREE II user's manual, and then independently assessed all included guidelines. Since the same two authors conducted the scoring in the previous review, those scores were maintained and newly developed and revised guidelines were scored. Since the methodological approach to the updates to previous guidelines did not change, the scores from the previous versions were maintained. Scoring was conducted (by AEN and APG) according to the instrument protocol, and consisted of adding the scores of items in a domain for both reviewers and standardizing the total score out of 100%.

Bibliographies of all identified guidelines were reviewed and participants from the systematic review panel were questioned for any additional available relevant references. Citations from online databases and hand searches were combined together and duplicates were removed. A two-step process was utilized to screen and review articles. First, two authors independently screened titles and abstracts of all identified citations (AG and AN). To be included at this step, the title and abstract needed to describe a clinical practice guideline that was "revised", "updated" or developed to focus on OA of the hip, knee, or hand or a combination of sites, and covered either pharmacologic or non-pharmacologic management. Citations were excluded during this step if they evaluated isolated interventions or were editorial pieces. We considered a "revised" guideline as one in which the original organization or specialty produced a new version of the original guideline with a new methodological approach in the guideline development. We considered an update to an original guideline as one in which the original organization or specialty produced a brief change in the wording definition or change in the recommendation status without conducting a full revision or changing the methodological approach from the original version. To operationally define a developed clinical practice guideline, we followed the NAM definition as a "systematically developed statement to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances"[12]. The full-text of an article was retrieved and included if one of the two reviewers indicated a "yes" to article inclusion during the screening process. In the second step, the same two authors conducted a full-text review of articles selected from the screening process. To be included at this stage, these two authors came to consensus of full-text inclusion by discussion. Full-text articles were excluded if the guideline was not specific to OA or was specific to a joint site other than hand/knee/hip, or did not meet our operational definition of a guideline (e.g. comments on other guidelines, guideline development without specific recommendations made, Figure 1). If an updated or revised guideline from the same organization was retained after full review and consensus agreement, the previous version of the guideline was removed.

Data were extracted from included articles (excel spreadsheet containing categories agreed upon by all authors) by one author (APG) and over-read by a second (AEN). Discrepancies in extracted data were resolved by discussion. These files were then reviewed and edited by other co-authors (YMG, KDA, JMJ). The extracted data included: publication year, country, specialties involved, and whether a systematic review was performed. Similar recommendations across guidelines were collapsed (e.g. many specific types of exercise to "low impact aerobic exercise") to ease reporting and interpretation.

The overall quality of each included guideline was assessed using the AGREE II instrument (Appraisal of Guidelines for Research and Evaluation, 2nd edition; www.agreetrust.org). The validity and reliability for assessment of practice guidelines by the AGREE II has been established[14,15]. The instrument includes 23 items covering six quality domains: 1) scope and purpose, 2) stakeholder involvement, 3) rigor of development, 4) clarity of presentation, 5) applicability, and 6) editorial independence; two additional assessment items (Overall Guideline Assessment) are included for the evaluator to make an overall judgment of the practice guideline. Each item is scored on a scale of 1-7, with a 1 assigned for items with no clear discussion, a 7 for exceptional quality of reporting, and 2-6 for items not fully meeting the AGREE II criteria. There are no strict cutoffs designating quality using this tool, but it allows comparison between guidelines. Two authors (KDA and YMG) first read the entire AGREE II user's manual, and then independently assessed all included guidelines. Since the same two authors conducted the scoring in the previous review, those scores were maintained and newly developed and revised guidelines were scored. Since the methodological approach to the updates to previous guidelines did not change, the scores from the previous versions were maintained. Scoring was conducted (by AEN and APG) according to the instrument protocol, and consisted of adding the scores of items in a domain for both reviewers and standardizing the total score out of 100%.

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