

Review

Appraisal of quality and analysis of the similarities and differences between osteoarthritis Clinical Practice Guideline recommendations: A systematic review



Bimbi Gray # * ¹, Alison Gibbs † ‡ ², Jocelyn L. Bowden # ¹, Jillian P. Eyles # ¹, Sandra Grace § ³, Kim Bennell ¶, Rinie Geenen ||, Sharon Kolasinski ## ⁴, Christian Barton † ‡ ⁵, Philip G. Conaghan ††, Timothy McAlindon ‡‡, Olivier Bruyere §§, Quentin Géczy # ¹, David J. Hunter # ¹

Sydney Musculoskeletal Health, Kolling Institute, Faculty of Medicine and Health, The University of Sydney and the Northern Sydney Local Health District, Sydney, NSW, Australia

† La Trobe Sports and Exercise Medicine Research Centre, La Trobe University, Bundoora, Australia

‡ School of Allied Health, Human Services and Sport, La Trobe University, Bundoora, Australia

§ Faculty of Health, Southern Cross University, Lismore, NSW, Australia

¶ Centre for Health, Exercise and Sports Medicine, Department of Physiotherapy, The University of Melbourne, Melbourne, Victoria, Australia, Level 7, Alan Gilbert Building, Carlton, VIC 3052, Australia

|| Utrecht University, Department of Psychology, Heidelberglaan 1, 3584 CS Utrecht, the Netherlands

Division of Rheumatology, University of Pennsylvania

†† Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds & NIHR Leeds Biomedical Research Centre, Leeds, United Kingdom

‡‡ Tufts University School of Medicine and Tufts Medical Center, 800 Washington Street Boston, MA 02111, USA

§§ WHO Collaborating Center for Public Health aspects of musculo-skeletal health and ageing, Division of Public Health, Epidemiology and Health Economics, University of Liège, Belgium

ARTICLE INFO

Article history:

Received 14 September 2023

Accepted 27 February 2024

Keywords:

Osteoarthritis
Clinical practice guideline
Evidence-to-practice
Implementation

SUMMARY

Objective: Clinical Practice Guidelines (CPGs) aim to support management of hip and knee osteoarthritis (OA), but recommendations are often conflicting and implementation is poor, contributing to evidence-to-practice gaps. This systematic review investigated the contextual and methodological factors contributing to conflicting recommendations for hip and knee OA.

Method: Our systematic review appraised CPGs for managing hip and knee OA in adults ≥ 18 years (PROSPERO CRD42021276635). We used AGREE-II and AGREE-REX to assess quality and extracted data on treatment gaps, conflicts, biases, and consensus. Heterogeneity of recommendations was determined using Weighted Fleiss Kappa (K). The relationship between (K) and AGREE-II/AGREE-REX scores was explored.

Results: We identified 25 CPGs across eight countries and four international organisations. The ACR, EULAR, NICE, OARSI and RACGP guidelines scored highest for overall AGREE-II quality (83%). The highest overall AGREE-REX scores were for BMJ Arthroscopy (80%), RACGP (78%) and NICE (76%).

CPGs with the least agreement for pharmacological recommendations were ESCEO and NICE (−0.14), ACR (−0.08), and RACGP (−0.01). The highest agreements were between RACGP and NICE (0.53), RACGP and ACR (0.61), and NICE and ACR (0.91). Decreased internal validity determined by low-quality AGREE

* Corresponding author.

E-mail addresses: bimbi.gray@sydney.edu.au (B. Gray), a.gibbs@latrobe.edu.au (A. Gibbs), jocelyn.bowden@sydney.edu.au (J.L. Bowden), jillian.eyles@sydney.edu.au (J.P. Eyles), sandra.grace@scu.edu.au (S. Grace), r.geenen@uu.nl (R. Geenen), sharon.kolasinski@penncmedicine.upenn.edu (Sharon Kolasinski), c.barton@latrobe.edu.au (C. Barton), p.conaghan@leeds.ac.uk (P.G. Conaghan), tmcalindon@tuftsmedicalcenter.org (T. McAlindon), olivier.bruyere@uliege.be (O. Bruyere), qg6670@uni.sydney.edu.au (Q. Géczy), david.hunter@sydney.edu.au (D.J. Hunter).

¹ Level 10, Kolling Building, Reserve Road, St Leonards, NSW, 2065, Australia.

² Physiotherapy Department, Eastern Health, Box Hill Hospital, 8 Arnold Street, Box Hill, 3128, Victoria, Australia.

³ Level 2, Z Block, Military Rd, Lismore, NSW, 2480, Australia.

⁴ Penn Musculoskeletal Center, 3737 Market Street, Philadelphia, PA, USA

⁵ HS3 Room 521, La Trobe University Bundoora, VIC 3068, Australia.

<https://doi.org/10.1016/j.joca.2024.02.890>

1063–4584/© 2024 The Author(s). Published by Elsevier Ltd on behalf of Osteoarthritis Research Society International. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>).

scores (<60%) in editorial independence were associated with less agreement for pharmacological recommendations.

Conclusion: There were associations between guideline quality and agreement scores. Future guideline development should be informed by robust evidence, editorial independence and methodological rigour to ensure a harmonisation of recommendations. End-users of CPGs must recognise the contextual factors associated with the development of OA CPGs and balance these factors with available evidence.

© 2024 The Author(s). Published by Elsevier Ltd on behalf of Osteoarthritis Research Society International. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>).

Introduction

Osteoarthritis (OA) is one of the most common chronic diseases worldwide, with disease prevalence projected to increase with population aging, obesity, inactivity and joint injury.^{1–3} OA is the 18th highest contributor to global disability of 369 conditions assessed in the Global Burden of Disease study.⁴ The significant morbidity and disability of OA is impacted by health care professional and consumer perceptions that surgery and medications are first-line care. These perceptions contribute to mounting costs both to consumers and healthcare systems.^{5–7} The lack of evidence-based care contributes to the overall burden of disease, with discordant care exemplified by rates of opioid and acetaminophen use and persistently high rates of arthroscopic surgery increasing alongside pain severity.⁸

Clinical Practice Guidelines (CPGs) developed by various international organisations aim to aid clinical decision making and inform evidence-based management. However, the benefits of CPGs are only as good as their quality, internal validity, and applicability for end-users.⁹ High quality CPGs are developed by a panel of experts through systematic review of current evidence to form consensus-based recommendations. By convention, randomised controlled trials (RCTs) are the foundation for CPG development.¹⁰ CPG developers frequently use a range of other types of contextual knowledge to form consensus when evidence from RCTs is unavailable, inconsistent or inappropriate.¹¹ Developing CPGs based on the best available evidence is a determinant for their trustworthiness.¹⁰ However, the trust in CPG recommendations is jeopardised when non-systematic methodologies are used to synthesise evidence with potential for bias of results, with over- or under-representation of treatment effects supporting the recommendations.¹²

Different recommendations for OA management between CPGs potentially add to confusion and inappropriate care for OA.¹³ OA CPGs provide recommendations for physical and lifestyle management, pharmacological management, surgical management, or a combination of these strategies. Current OA CPGs provide unified guidance for a 'core set' of care recommendations, namely, provision of exercise and physical activity, weight-management and education for OA self-management. However, there is discrepancy between CPG recommendations outside this core set, particularly for select pharmacological (e.g. paracetamol and opioids) and adjunctive treatments, such as acupuncture, transcutaneous electrical nerve stimulation (TENS), manual therapy, and massage.¹⁴ Although variation in recommendations may be due to the age of the CPGs and changing evidence, it also prompts enquiry about how CPGs are developed, particularly in relation to rigour of development, editorial independence and applicability. In particular, there is some ambiguity about the internal validity of CPG design, namely the consensus process and how this contributes to variability in guideline recommendations and consensus forming when evidence is lacking or conflicting.

The primary aim of this systematic review was to understand why OA CPG recommendations differ. To that aim, we investigated the causes of heterogeneity of recommendations by identifying potential biases, conflicts and consensus methods associated with the formulation of OA CPGs. This is the first systematic review to take these factors into account. By trying to explain the disparities between CPGs, it extends findings of a partnered study which reviewed the recommendations from high-quality CPGs.¹⁴

Methods

Search strategy and selection criteria

The systematic review protocol was prospectively registered (PROSPERO CRD42021276635, 2 October, 2021), adhering to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.¹⁵ Guided by the Cochrane Handbook for Systematic Reviews,¹⁶ a librarian-assisted literature search was conducted using the Medical Subject Heading (MeSH) search term and related terms to "osteoarthritis" and "clinical practice guidelines". The search strategy included a preliminary search of MEDLINE and CINAHL databases (4 August, 2020), with the final keywords and index terms incorporated. The initial search was conducted (7 August, 2021), and updated (7 August, 2022) in PubMed, MEDLINE, Web of Science, the Cumulative Index to Nursing and Allied Health Literature (CINAHL), Sport Discus and the Physiotherapy Evidence Database (PEDro). Further searches to guideline repositories (Clinical Practice Guidelines Portal, Guidelines International Network, Turning Research Into Practice (TRIP), Cochrane, orthoguidelines.org, Epistemonikos, Guideline Central and the National Institute for Health and Care Excellence (NICE)) were conducted. Grey literature and hand searching of reference lists was conducted. All searches were updated on 27 October, 2022.

All CPGs published in English, relating to any aspect of hip and knee OA management other than arthroplasty in people age 18+ years were included. Publications were defined as a CPG using the Institute of Medicine definition, as "statements that include recommendations, intended to optimise patient care, that are informed by systematic review of the evidence and an assessment of the benefits and harms of alternative care options."¹⁷ CPGs were excluded if OA was not listed as the major clinical presentation or where arthroplasty was the only recommendation. Stand-alone systematic reviews, narrative reviews, consensus statements, CPGs replaced by more updated versions, and CPGs relating to radiographic diagnosis, or prevention of OA were also excluded. All CPGs which had not been updated were included to provide comprehensive representation of international guidelines.

Study selection

Search results were imported into Endnote by one reviewer (AG). Two independent reviewers (AG, BG) conducted title, abstract and

full text screening using Covidence Systematic Review software (Veritas Health Innovation, Melbourne, Australia). CPGs selected for inclusion were determined through consensus between AG and BG with consultation with third and fourth reviewers (DH, CB) as necessary.

Data appraisal: quality assessment of CPGs

The quality of CPGs was appraised using the Appraisal of Guidelines for Research and Evaluation (AGREE) II instrument.¹⁸ The AGREE-II instrument is internationally validated to assess 23 items across six domains: scope and purpose, stakeholder involvement, rigour of development, clarity of presentation, applicability and editorial independence of CPG. Two independent reviewers (AG, BG) conducted the AGREE-II appraisal using the “My AGREE Plus” online platform.¹⁹ Each CPG was rated using a 7-point Likert score from 1 (lowest quality) to 7 (highest quality) for the 23 items across all domains.¹⁸ We established domain score thresholds using the AGREE-II methodology. The AGREE-II instrument does not have predetermined threshold scores to indicate quality, therefore, a consensus on threshold criteria was determined before evaluations began. To assess quality of domains, we utilised threshold criteria from previous guideline appraisals and considered a score of 60% of the maximum possible score as high quality.^{20,21} The domains decided a priori, by consensus for determining high quality CPGs were *stakeholder involvement*, *rigour of development*, and *editorial independence*. These domains were selected to evaluate whether heterogeneity between CPGs might be influenced by the development process. Domain scores were calculated as percentages, and an overall assessment score rated quality separately.

To complement the AGREE-II, the AGREE-REX tool²² was used to assess the quality and internal validity of the CPG recommendations. The AGREE-REX was completed by two reviewers (BG, QG) to further assess the credibility, trustworthiness and implementability of the CPGs. The AGREE-REX consists of 9 items across 3 domains: *clinical applicability*, *values and preferences*, and *implementability*. Scores were rated using a 7-point Likert scale from 1 (lowest quality) to 7 (highest quality). The AGREE-REX scores were then calculated and CPGs with overall scores > 60% were defined as high quality.

Data extraction and data items

To ensure we explored full constituent bias from commercial entities involved in the development of the CPGs, data attributed to conflicts, biases, consensus methods and gaps between evidence and recommendations were extracted. Two reviewers (BG, AG) independently extracted study details and findings from each included CPG into purpose-designed spreadsheets. Further methodological detail outlining the data items and data extraction process have been published previously.¹⁴ To ensure the accuracy of CPG data, we were guided by the expertise and views from the lead authors of the major CPGs (PC, KB, RG, SK, OB, TM).

Effect measures and synthesis methods

To determine the extent of agreement between guideline recommendations, the Weighted Fleiss Kappa coefficient measure was calculated for all recommendations using SPSS (IBM SPSS Statistics for Windows, version 28). The Kappa (K) coefficient estimates the proportion of agreement between CPGs over and above chance agreement to determine where lack of concordance between organisations exists. The (K) considers both the direction and strength of agreement based on recommendation rating. First, all recommendations were graded on a scale; -2 (strongly against

recommendation) to +2 (strongly for recommendation). Then the (K) score was calculated, ranging from -1 to +1, with a negative value indicating less agreement than expected by chance, with -1 indicating no observed agreement. A (K) greater than 0 suggests better-than-chance agreement for two or more CPGs. The scale used for the (K) included weights (-2 to +2) corresponding to the strength of agreement or disagreement.²³ Due to the similarity of recommendations, scope and purpose, subgroup analysis was performed on the OARSI, ESCEO, RAGCP, NICE, ACR, and AAOS-Knee non-surgical CPGs. We used the (K) “pairwise-rater” analysis for all possible pairs of these CPGs. To specify the weights to be applied for lack of agreement (distance), quadratic weight analysis was used, which is based on non-linear weights penalising bigger proximities with higher power (quadratic).²⁴ With consideration to the differences in the quality of development between guidelines, the subgroup analysis aimed to identify how variations in internal validity may influence agreement levels. This approach provided a comprehensive understanding of the factors contributing to agreement or disagreement among guidelines with seemingly similar recommendations.

Results

A total of 20,227 papers were identified. We removed duplicates and reviewed titles and abstracts of 12,612 papers and screened 125 full text papers. Twenty-five CPGs met the inclusion criteria, with publication dates ranging from 2007 to 2022. Results from the literature search are summarised in Fig. 1.

Data extraction and Risk of Bias (AGREE-II and AGREE-REX) were conducted for six guidelines from the United States of America,^{25–30} six from Canada,^{31–36} and one each from Australia,³⁷ France,³⁸ Turkey,³⁹ China,⁴⁰ Singapore,⁴¹ Malaysia,⁴² South America,⁴³ The Netherlands,⁴⁴ and the United Kingdom.⁴⁵ Two additional guidelines developed by European professional societies,^{46,47} and two developed by international organisations^{48,49} were included for data extraction and quality appraisal.

Most (92%) of CPG recommendations were targeted at physicians and allied health professionals as end-users, with 44% of CPGs targeting patients. Two CPGs specified policy makers as target users. The composition, discipline, and relevant expertise of the guideline development group varied between organisations; 14 CPGs included patient representatives in the development of the recommendations (Table 1). The description of grades of recommendation differed between guideline organisations, as did the methodology for formulating the recommendations and how consensus for recommendations was achieved (Table 1). Twelve guidelines provided strategies for implementing recommendations, although the approaches to implementation varied widely (Table 1).^{25,27–30,37,44–49}

Summary of recommendations

The ‘core set’ of recommendations was consistently comprised of patient education/self-management, physical activity/exercise and weight management, as well as unanimous discouragement of arthroscopy. In contrast, many guidelines did not report on the same set of pharmacological and adjunctive interventions. There was variation in how CPGs stratified recommendations for OA joints: seven CPGs included recommendations for OA generally and five CPGs provided recommendations for both knee and hip. There were ten CPGs for knee OA and three were specific for hip OA. The systems used by CPG organisations to grade the strength of recommendations and the terminology used to classify the strength of recommendations were inconsistent between CPGs.

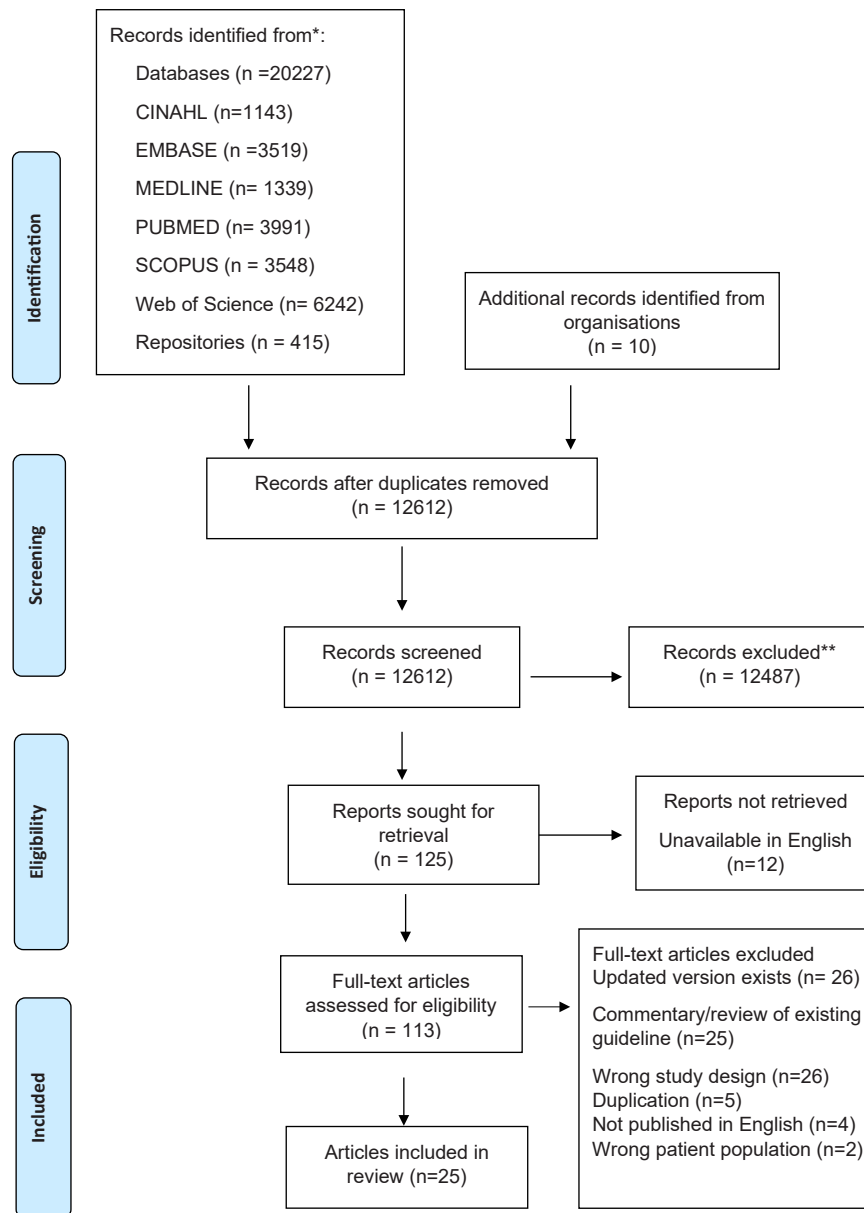


Fig. 1

Flowchart showing article identification, inclusion and exclusion.

Quality assessment

The six AGREE-II domain scores are listed separately and as an overall domain score (Table II). The ACR, EULAR, NICE, OARSI and RACGP guidelines scored highest on overall assessment (83%), followed by American PT Hip, BMJ Arthroscopy, and VA/DOD (75%). The highest domain scores were for *scope and purpose* and the lowest domain scores were for *applicability*, the intraclass correlation (ICC) values indicate “good” to “excellent” reliability 0.81 (95% CI 0.51–0.92) and 0.96 (95%CI 0.90–0.98), respectively. The domain scores with greatest variation between the guidelines were *stakeholder involvement* (ICC 0.87 (95% CI 0.70–0.94)), *rigour of*

development (ICC 0.94 95%CI 0.84–0.98) and *editorial independence* (ICC 0.87 (95% CI 0.70–0.94)) (Table II).

The AGREE-REX scores are provided in Table III. The highest scores for quality of recommendation for the *clinical applicability* domain (quality of evidence, applicability to target users and applicability to patients and population) were for RACGP (92%) and NICE (89%) (ICC 0.83 (95% CI 0.45–0.86)).

For the *values and preferences* domain (values and preferences of target users, patient population, policy decision makers and guideline developers), The US Veterans Affairs/Department of Defence (VA/DoD) scored highest (84%) (ICC 0.85 (95% CI 0.63–0.93)). The NICE and RACGP guidelines scored highest (75%) on the evaluation of

Clinical practice guideline appraisal-AGREE II							
Clinical practice guideline	Domain 1 scope and purpose (%)	Domain 2 stakeholder involvement (%)	Domain 3 rigour of development (%)	Domain 4 clarity of presentation (%)	Domain 5 applicability (%)	Domain 6 editorial independence (%)	Overall score (%)
AAOS Hip	64	36	80	53	52	50	67
AAOS Knee non-arthroplasty	61	33	72	50	35	50	50
AAOS-Knee surgical	58	36	80	53	35	50	50
ACR	92	86	80	92	38	75	83
APTA	83	72	74	78	31	75	75
BMJ Arthroscopy	67	75	76	92	73	88	75
China	61	56	60	58	2	50	50
Dutch (KNGF)	58	78	75	53	56	38	58
ESCEO	69	67	57	72	50	46	59
EULAR	78	78	72	64	27	63	83
France	81	72	40	61	19	38	50
Malaysia	75	72	66	67	58	54	50
NICE	86	81	89	83	69	79	83
OARSI	92	72	71	83	19	71	83
Ottawa hip	83	33	52	42	2	58	50
Ottawa Knee	56	50	52	72	4	63	50
Part 1 - Mind body							
Ottawa Knee	56	56	45	69	21	58	58
Part 2 Strength							
Ottawa knee	50	53	49	69	4	58	58
Part 3 Aerobic							
Ottawa overweight/obese	58	47	36	14	2	25	33
PANLAR	44	56	27	61	8	54	42
PEER	53	58	52	53	33	50	58
RACGP	97	83	93	94	63	63	83
Singapore	33	33	16	58	44	0	25
TLAR	47	50	52	75	6	25	58
VA/DoD	86	89	73	72	73	42	75
Intraclass correlation coefficient (ICC) between raters							
ICC (95% CI)	0.81 (0.51- 0.92)	0.87 (0.70-0.94)	0.94 (0.84-0.98)	0.79 (0.51-0.91)	0.96 (0.90-0.98)	0.87 (0.70-0.94)	

Clinical Practice Guideline abbreviations: American Academy of Orthopaedic Surgeons (AAOS); The American College of Rheumatology (ACR); American Physical Therapy Association (APTA); British Medical Journal (BMJ); Royal Dutch Society for Physical Therapy (KNGF); European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO); European Alliance of Associations for Rheumatology (EULAR); French Society of Rheumatology (France); National Institute for Health and Care Excellence (NICE); University of Ottawa, Canada (Ottawa); Pan-American League of Associations for Rheumatology (PANLAR); Canadian College of Family Physicians (PEER); Royal Australian College of General Practitioners (RACGP); Singapore Ministry of Health (Singapore); Turkish League Against Rheumatism (TLAR); *The US Veterans Affairs/Department of Defence (VA/DoD)*.

Intraclass correlation coefficient (ICC) values less than 0.5 are indicative of poor reliability, values between 0.5 and 0.75 indicate moderate reliability, values between 0.75 and 0.9 indicate good reliability, and values greater than 0.90 indicate excellent reliability.

Table II

AGREE-II quality appraisal scores for osteoarthritis clinical practice guidelines.

the *implementability* domain (evaluation of purpose and local application and adoption) (ICC 0.76 (95% CI 0.46–0.89)).

Agreement between clinical practice guideline recommendations

The (K) pairwise analysis was conducted for all recommendation categories to assess agreement. K was calculated pairwise between the hip CPGs and then separately for the knee CPGs. There was total agreement on the key recommendations, including patient education, self-management, physical activity and exercise, and arthroscopy. Pharmacological and adjunctive therapy recommendations presented the greatest level of heterogeneity among CPGs (Figs. 2 and 3). The guideline pairs with the least agreement (K) for the pharmacological recommendations were between ESCEO and the NICE (–0.14), ESCEO and ACR (–0.08) and ESCEO and RACGP (–0.01)

guidelines (Fig. 2). The guideline pairs with the greatest level of agreement (K) for the pharmacological recommendations were between NICE and ACR (0.91), RACGP and ACR (0.61) and RACGP and NICE (0.53).

The (K) for adjunctive therapies demonstrated less agreement between RACGP and ACR (–0.52) and between NICE and ACR (–0.50). The greatest level of agreement for adjunctive therapies was between RACGP and NICE for the hip (0.90) and knee (0.75) recommendations (Fig. 3).

Correlating the level of agreement (K) alongside the agreement scores (AGREE II/AGREE-REX) we demonstrate the level of concordance with recommendations between CPGs of higher or lower quality. For the pharmacological recommendations, the (K) and median AGREE-II domain scores for *editorial independence* demonstrated an association between a low-quality score from ESCEO and

Clinical practice guideline appraisal-AGREE-REX			
Clinical practice guideline	Domain 1 clinical applicability (%)	Domain 2 values & preferences (%)	Domain 3 implementability (%)
AAOS Hip	78	52	67
AAOS Knee non- arthroplasty	78	52	58
AAOS- Knee surgical	75	63	63
ACR	72	44	38
APTA	75	60	54
BMJ Arthroscopy	83	69	71
China	58	31	17
Dutch (KNGF)	75	46	50
ESCEO	64	23	29
EULAR	83	67	67
France	39	25	33
Malaysia	58	35	54
NICE	89	67	75
OARSI	81	56	58
Ottawa-therapeutic exercise HIP	42	10	33
Ottawa Knee Part 1- Mind body	50	23	33
Ottawa Knee Part 2 Strength	64	27	29
Ottawa knee Part 3 Aerobic	61	25	29
Ottawa overweight/obese	50	15	38
PANLAR	47	38	29
PEER	72	56	58
RACGP	92	67	75
Singapore	42	17	38
TLAR Knee	72	36	50
VA/DoD	78	74	63
Intraclass correlation coefficient (ICC) between raters			
ICC (95% CI)	0.83 (0.45–0.86)	0.85 (0.63–0.93)	0.76 (0.46–0.89)

Clinical Practice Guideline abbreviations: American Academy of Orthopaedic Surgeons (AAOS); The American College of Rheumatology (ACR); American Physical Therapy Association (APTA); British Medical Journal (BMJ); Royal Dutch Society for Physical Therapy (KNGF); European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO); European Alliance of Associations for Rheumatology (EULAR); French Society of Rheumatology (France); National Institute for Health and Care Excellence (NICE); University of Ottawa, Canada (Ottawa); Pan-American League of Associations for Rheumatology (PANLAR); Canadian College of Family Physicians (PEER); Royal Australian College of General Practitioners (RACGP); Singapore Ministry of Health (Singapore); Turkish League Against Rheumatism (TLAR); *The US Veterans Affairs/Department of Defence (VA/DoD)*.

Intraclass correlation coefficient (ICC) values less than 0.5 are indicative of poor reliability, values between 0.5 and 0.75 indicate moderate reliability, values between 0.75 and 0.9 indicate good reliability, and values greater than 0.90 indicate excellent reliability.

Table III

Osteoarthritis and Cartilage

AGREE REX quality appraisal scores for osteoarthritis clinical practice guidelines.

showed 'less agreement' with the RACGP (−0.01), NICE (−0.14), the and ACR (−0.08) guidelines for the pharmacological recommendations. Conversely, the NICE and ACR guidelines demonstrated a high level of agreement (0.91) and high quality AGREE-II score in the same domain (79% and 75% respectively) (Fig. 4). The CPGs with higher AGREE-II quality scores demonstrated greater agreement of recommendations.^{26,37,45,47,48}

A further relationship was established with a low AGREE-II applicability score for the ESCEO CPG (50%) and correlation of less agreement (K), between the NICE (−0.14) and ACR (−0.08) pharmacological recommendations (Fig. 4).

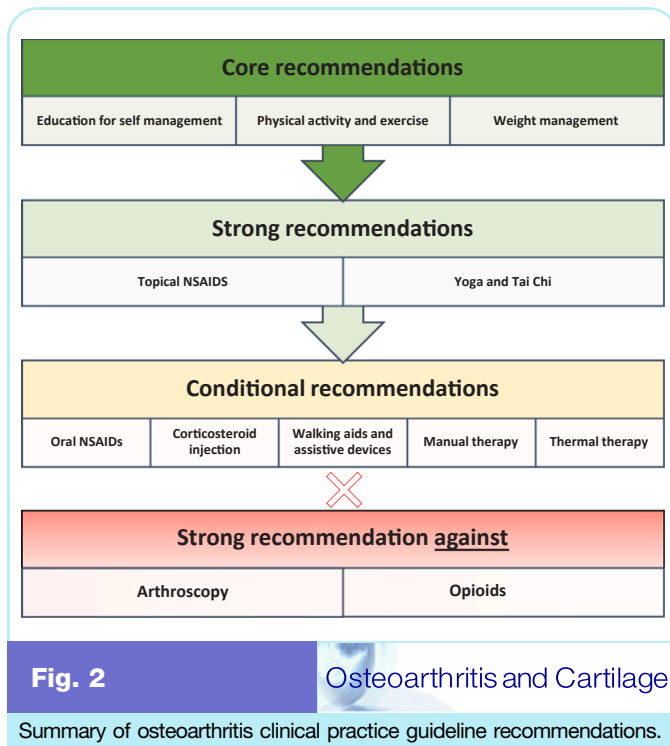
The overall AGREE-REX quality appraisal also demonstrated parallels between a low-quality guideline and less agreement, with the ESCEO guideline presenting as the outlier for the pharmacological recommendations (Fig. 5).

Discussion

This systematic review appraised the quality of 25 current international OA CPGs, and analyzed the differences and similarities

between CPG recommendations. There are several existing systematic reviews analysing the difference between OA CPG recommendations.^{14,50–55} However, this is the first study to specifically explore the reasons why the recommendations differ. As assessed by the validated AGREE-II and AGREE-REX instruments, our results show that the quality of the CPGs and their individual recommendations vary widely across guidelines both overall and by domain. Of note, the CPGs with higher quality scores overall demonstrated greater agreement of recommendations.^{26,37,45,47,48} In terms of the specific recommendations, most CPGs agreed on a 'core set' of OA treatments (education for self-management, physical activity/exercise, and weight management). Similarly, all guidelines recommended against the use of arthroscopy.

The CPGs with less rigorous development and less editorial independence, as determined by the AGREE instrument, are more likely to recommend pharmacologic interventions that are not in agreement with higher quality CPGs (Figs. 4 and 5). The connection between CPGs of higher quality with increased internal validity, as determined by the AGREE instrument, and a greater consensus in recommendations emphasises the importance of CPG quality in



fostering consistency. Internal validity, in this context, refers to the robustness and reliability of the guideline's development process. Those guidelines that adhere to more rigorous development processes and maintain editorial independence are more likely to align with current evidence recommendations, highlighting the crucial role played by guideline development processes.

However, despite these positive correlations, there were considerable variation and discordance between the remainder of the recommendations, regardless of their treatment focus (i.e. physical, lifestyle, or pharmacological). The discordance between the CPGs ultimately leads to confusion for the end-user, widening the evidence-to-practice-gap for OA. Understanding why and how the differences in recommendations have arisen is an important step towards resolving them. We discuss these findings below with reference to the difference in guideline quality, their recommendations, and how this may impact the variability of care recommended.

One explanation for the discordance between CPG recommendations is the lack of standardisation and adherence to GRADE methodology, resulting in low quality CPG development. In addition, even when GRADE methodology is applied, the subjectivity of the “values and judgements” may create a divergence from robust systems of evaluating evidence and is open to influence from individual opinions or intellectual bias of the panel members. We recognise that the gathering and weighting of expert opinion is part of the consensus process for the final formulation of CPG recommendations, regardless of how rigorously CPG developers apply GRADE criteria and critical literature review. Thus, there may be a time during the CPG formulation process that the expert opinion of some may be heard more loudly than that of others or may outweigh the balance of evidence. Further research is required to investigate this phenomenon. This

also highlights the need to improve and diversify stakeholder involvement for future CPG development, being sure to include broad representation of health professionals and the perspectives of people with OA. Future CPG development needs to focus on the rigour of development, with greater objectivity applied to the consensus process, free of vested interest, intellectual bias and providing explicit links between recommendations and supporting evidence.

Impact of the quality of the CPGs and recommendations

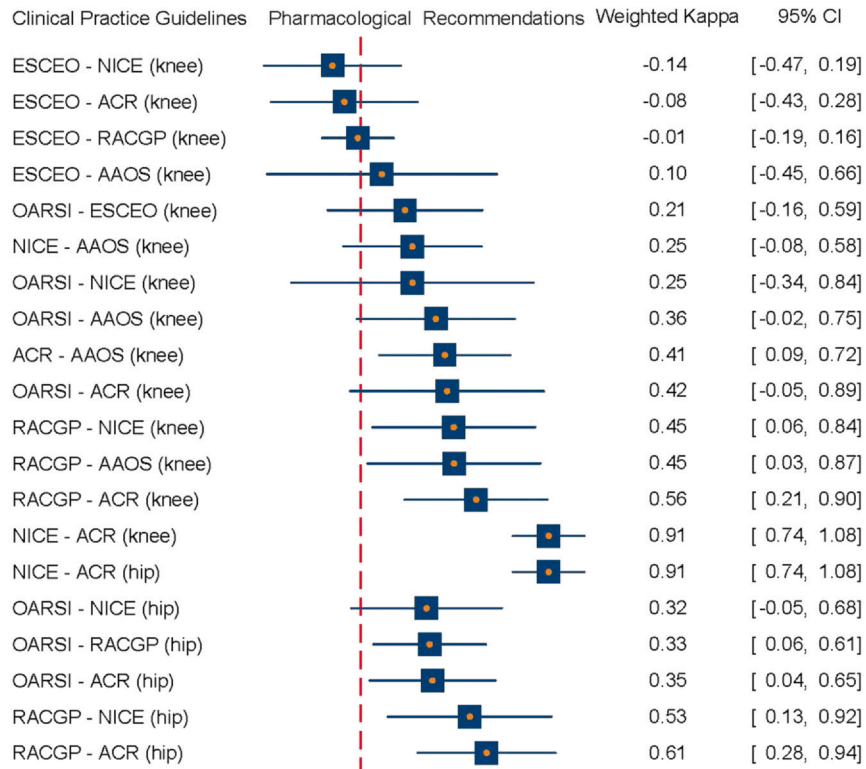
Reduced applicability of CPGs exacerbates the disconnect between evidence- to-practice for OA.¹⁴ Consistently low AGREE-II and AGREE-REX scores were observed for the evaluation of the usefulness of tools and resources provided for the implementation of recommendations across all OA CPGs. Strategies for implementation and guidance on how to improve the local application of CPG recommendations were not reinforced by the CPGs. The decreased applicability of OA CPGs further emphasises the necessity for better stakeholder involvement from CPG organisations. It is crucial to have active engagement and collaboration with stakeholders throughout the development and implementation of CPGs to ensure that recommendations are relevant, practical and effective in improving patient outcomes.⁵⁶

Strengths and limitations

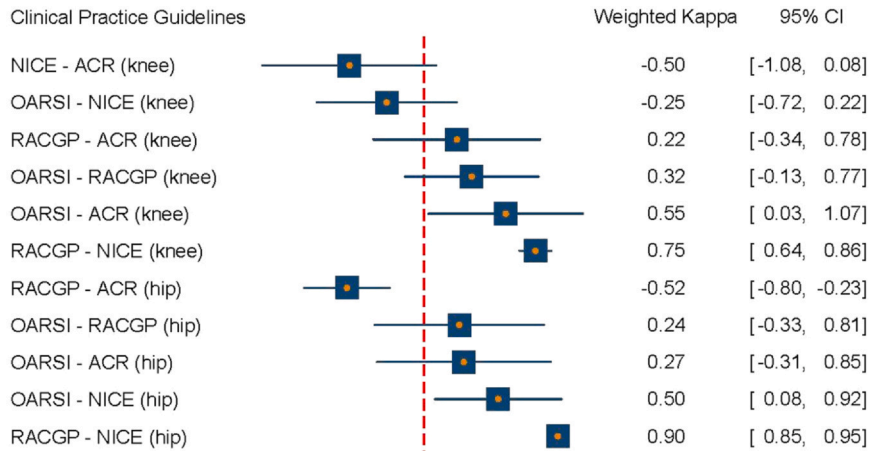
We applied a broad search strategy including multiple databases, professional organisations and guideline repositories. The inclusion of all current international OA CPGs relating to physical, lifestyle, pharmacological management and arthroscopy, irrespective of their quality rating, is a major strength of the study as it ensures full representation of the available CPGs. Including the views and expertise of the chairs of the ACR, ESCEO, EULAR, NICE, OARSI, and RACGP, OA CPGs is another strength of this study as involving these major stakeholders in this study will likely lead to improved methodologies in the development of future CPGs through these organisations. Exclusion of guidelines not published in English was a limitation; however, no translated versions were available. Many CPGs did not include the same grouping of recommendations which contributed to a significant amount of missing data in certain categories. With consideration to the data sample, the absence of consistency between the sampled CPGs hinders the provision of clear insights into the specific agreement on each recommendation, offering only a broader, higher-level overview of consensus among guidelines. Therefore, due to the relatively low sample size of homogenous CPGs, results should be viewed cautiously. Several CPGs did not disclose conflicts of interest, thereby hindering a confident investigation into whether potential conflicts of interests were linked to the observed discrepancies.

Implications for practice and future guideline development

This study examines the reasons for variations in CPG recommendations for knee and hip OA and provides valuable insights for healthcare professionals seeking to improve management for individuals with OA. Healthcare professionals should approach CPG recommendations with discernment, recognising the potential variations highlighted in this study. For organisations developing CPGs, we highlight the need for more rigorously developed guidelines and



a



b

Fig. 3

Weighted Kappa pairwise analysis, direction and magnitude of agreement between the recommendations for pharmacological and adjunctive therapy recommendations between CPGs. The (K) for each possible guideline pairing was applied to determine the direction and magnitude of agreement between the recommendations for Pharmacological and adjunctive therapy recommendations. The direction indicates whether the guidelines agree or disagree, while the magnitude reflects the strength of that agreement. The recommendations were on a scale of 'no observed agreement' -1, to 'perfect agreement' +1.

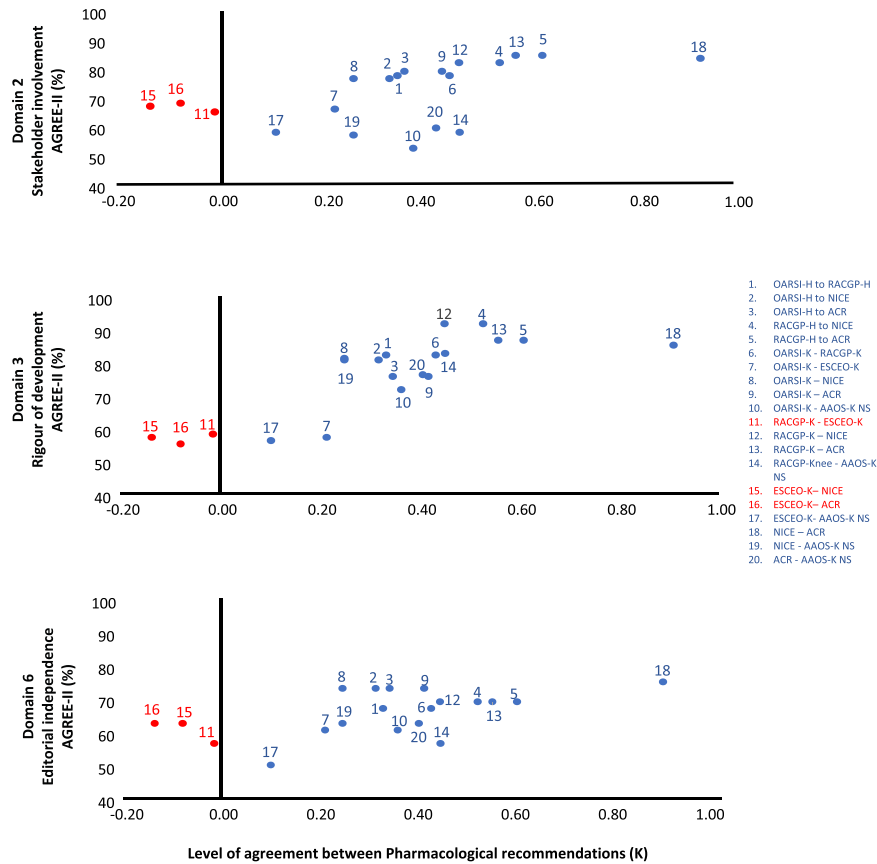


Fig. 4

Association of agreement with pharmacological recommendations (weighted kappa) and quality (median AGREE II scores). The dotted line represents the 0 axis, illustrating change of direction of agreement. Scores >0 show increasingly greater agreement, <0 increasingly less agreement. Clinical Practice Guideline abbreviations: American Academy of Orthopaedic Surgeons (AAOS); The American College of Rheumatology (ACR); European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO); European Alliance of Associations for Rheumatology (EULAR); National Institute for Health and Care Excellence (NICE); Royal Australian College of General Practitioners (RACGP)^{24,25,35,43,44,46}. Hip (H); Knee (K). Non-Surgical (NS).

regular revisions, particularly in areas where pharmacological and adjunctive recommendations show significant discordance or may evolve rapidly. A challenge for CPG development is the availability of the evidence required for recommendations to be made, in particular, the absence of high quality RCTs for certain pharmacological and adjunctive therapies. Future CPGs require specific recommendations for hip OA as many recommendations are based on evidence from knee OA. We call all organisations developing CPG to action, to improve methodological rigour and editorial independence to foster trust in the recommendations provided.

Additionally, we recommend journals apply the AGREE instrument (or an equivalent tool) for assessing all submitted CPGs as a first step in the review procedure to align with the practice observed in high-quality journals, similar to the inclusion of a CONSORT checklist when submitting a clinical trial report.

End-users of CPGs must also recognise that panel members, in addition to their expertise, may bring preconceived notions,

prejudices and biases to the table that influence their rating of recommendations, and CPGs must be viewed in this context. Further research is required to investigate effective strategies for translation and dissemination of CPG recommendations, thus harmonising evidence-to-practice management of OA.

Contributors

BG, JPE, JLB, SG and DJH designed the study. BG and AG designed and ran the literature search extracted the data and conducted the risk of bias screening using AGREE PLUS. BG coordinated the study and wrote the report. BG, AG, JLB, JPE, SG, CB and DJH provided critical conceptual input, analysed and interpreted data, and critically revised the manuscript. All authors gave feedback on draughts of this paper and read and approved the final manuscript.

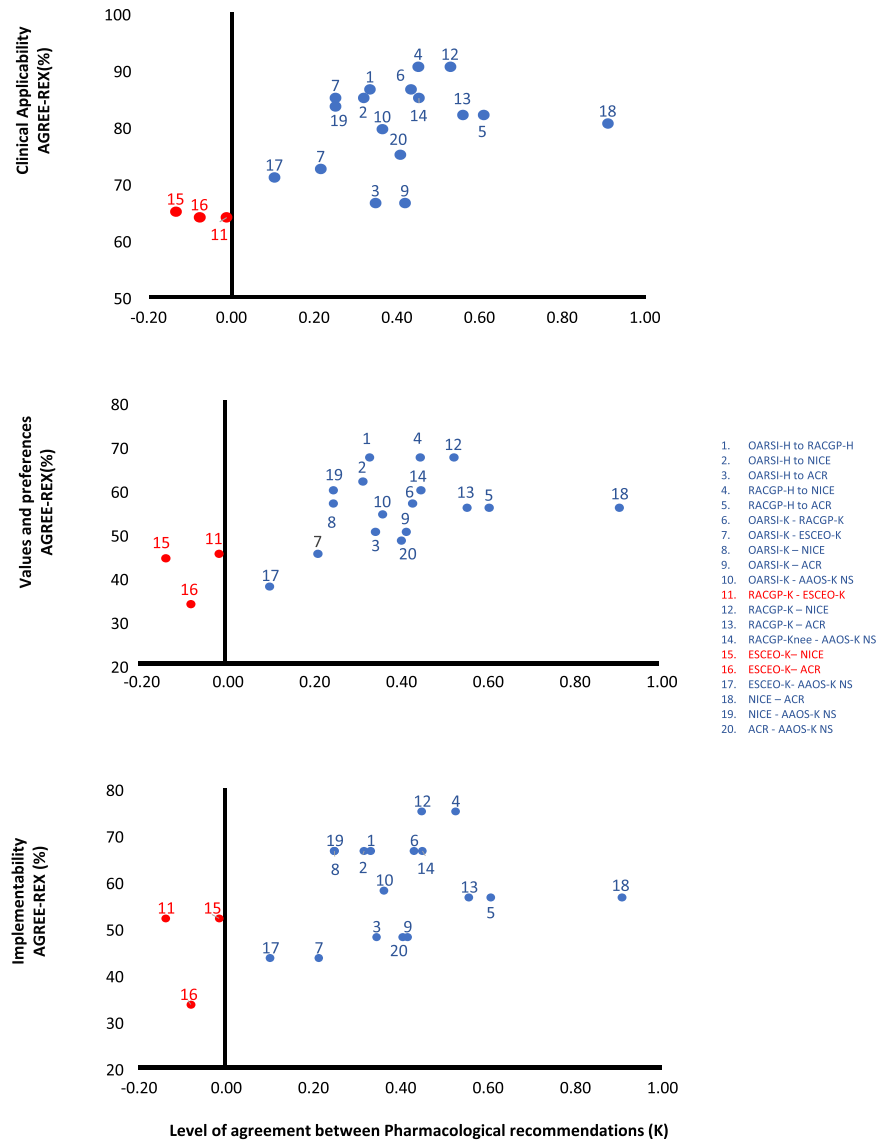


Fig. 5

Association of agreement with pharmacological recommendations (weighted kappa) and quality (median AGREE REX scores). The dotted line represents the 0 axis, illustrating change of direction of agreement. Scores >0 show increasingly greater agreement, <0 increasingly less agreement. Clinical Practice Guideline abbreviations: American Academy of Orthopaedic Surgeons (AAOS); The American College of Rheumatology (ACR); European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO); European Alliance of Associations for Rheumatology (EULAR); National Institute for Health and Care Excellence (NICE); Royal Australian College of General Practitioners (RACGP).^{24,25,35,43,44,46} Hip (H); Knee (K). Non-Surgical (NS).

Declaration of Competing Interest

DJH provides consulting advice to Pfizer, Lilly, Merck Serono, and TLC bio. KLB receives royalties from Wolters Kluwer. DJH and KLB are supported by National Health and Medical Research Council (NHMRC) Investigator Grants. AG has received payments from La Trobe University for tutoring physiotherapists involved in GLAD training. CJB is co-lead for the GLAD Australia programme and receives no income from the programme. PGC has received consulting or speaker fees from AbbVie, AstraZeneca, Eli Lilly, Galapagos, GlaxoSmithKline, Grunenthal, Janssen, Levicept, Merck, Novartis,

Pfizer, Regeneron, Stryker and UCB. JPE receives royalties from Wolters Kluwer. TEM provides consulting advice to Organogenesis, KolonTissueGene, Remedium-Bio, and Noven. OB has received consultancy or speaker fees from Amgen, Aptissen, Biophytis, IBSA, Mylan, Novartis, Orifarm, Sanofi, UCB and Viatrix.

The other authors declare no competing interests.

Acknowledgements

We gratefully acknowledge the contribution from the chairs of the ACR, ESCEO, EULAR, NICE, OARSI, and RACGP, OA CPGs. We also

acknowledge the contribution from Venkatesha (biostatistician) from the Sydney Musculoskeletal Health, Kolling Institute, University of Sydney, Australia for their assistance throughout the process of this review. PGC was a member of the development group for the NICE guideline on osteoarthritis (NG226) and is funded in part by the National Institute for Health and Care Research (NIHR) Leeds Biomedical Research Centre. The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health and Social Care. No funding was received for this study.

Data sharing

The data supporting the findings of this study is available from the corresponding author upon reasonable request.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at [doi:10.1016/j.joca.2024.02.890](https://doi.org/10.1016/j.joca.2024.02.890).

References

- Cui A, Li H, Wang D, et al. Global, regional prevalence, incidence and risk factors of knee osteoarthritis in population-based studies. *EClinicalMedicine* 2020;29-30, 100587. <https://doi.org/10.1016/j.eclinm.2020.100587>
- Briggs AM, Shiffman J, Shawar YR, et al. Global health policy in the 21st century: challenges and opportunities to arrest the global disability burden from musculoskeletal health conditions. *Best Pract Res Clin Rheumatol* 2020;34(5), 101549. <https://doi.org/10.1016/j.berh.2020.101549>
- Safiri S, Kolahi AA, Smith E, et al. Global, regional and national burden of osteoarthritis 1990-2017: a systematic analysis of the Global Burden of Disease Study 2017. *Ann Rheum Dis* 2020;79(6): 819–28. <https://doi.org/10.1136/annrheumdis-2019-216515>
- Abrams EM, Akombi B, Alam S, et al. Global burden of 369 diseases and injuries in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet* 2020;396(10258):1204–22. [https://doi.org/10.1016/S0140-6736\(20\)30925-9](https://doi.org/10.1016/S0140-6736(20)30925-9)
- Ackerman IN, Bohensky MA, Zomer E, et al. The projected burden of primary total knee and hip replacement for osteoarthritis in Australia to the year 2030. *BMC Musculoskelet Disord* 2019;20(1), 90. <https://doi.org/10.1186/s12891-019-2411-9>
- Ferket BS, Feldman Z, Zhou J, et al. Impact of total knee replacement practice: cost effectiveness analysis of data from the Osteoarthritis Initiative. *BMJ* 2017;356, 1131. <https://doi.org/10.1136/bmj.j1131>
- Bennell KL, Bayram C, Harrison C, et al. Trends in management of hip and knee osteoarthritis in general practice in Australia over an 11-year window: a nationwide cross-sectional survey. *Lancet Reg Health West Pac* 2021;12, 100187. <https://doi.org/10.1016/j.lanwpc.2021.100187>
- Nalamachu SR, Robinson RL, Viktrup L, et al. Multimodal treatment patterns for osteoarthritis and their relationship to patient-reported pain severity: a cross-sectional survey in the United States. *J Pain Res* 2020;13:3415–25. <https://doi.org/10.2147/JPR.S285124>
- Moleman M, Jerak-Zuiderent S, van de Bovenkamp H, et al. Evidence-basing for quality improvement; bringing clinical practice guidelines closer to their promise of improving care practices. *J Eval Clin Pract* 2022(6):1003–26. <https://doi.org/10.1111/jep.13659>
- Guidelines CoSfDTCP. *Clinical Practice Guidelines We Can Trust*. National Academies Press; 2011.
- Lewin S, Glenton C, Munthe-Kaas H, et al. Using qualitative evidence in decision making for health and social interventions: an approach to assess confidence in findings from qualitative evidence syntheses (GRADE-CERQual). *PLoS Med* 2015;12(10), e1001895. <https://doi.org/10.1371/journal.pmed.1001895>
- Lunny C, Ramasubbu C, Puil L, et al. Over half of clinical practice guidelines use non-systematic methods to inform recommendations: a methods study. *PLoS One* 2021;16(4), e0250356. <https://doi.org/10.1371/journal.pone.0250356>
- Allen KD, Golightly YM, White DK. Gaps in appropriate use of treatment strategies in osteoarthritis. *Best Pract Res Clin Rheumatol* 2017;31(5):746–59. <https://doi.org/10.1016/j.berh.2018.05.003>
- Gibbs AJ, Gray B, Wallis JA, et al. Recommendations for the management of hip and knee osteoarthritis: a systematic review of clinical practice guidelines. *Osteoarthritis Cartil* 2023;S1063-4584(23):00832–4. <https://doi.org/10.1016/j.joca.2023.05.015>
- Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *Syst Rev* 2021;10(1), 89. <https://doi.org/10.1136/bmj.n71>
- Higgins JPT. *Cochrane Handbook for Systematic Reviews of Interventions*. Second ed. Hoboken, NJ: Wiley-Blackwell.; 2019.
- Institute of medicine committee on standards for systematic reviews of comparative effectiveness R. In: Eden J, Levit L, Berg A, Morton S, editors. *Finding What Works in Health Care: Standards for Systematic Reviews* Washington (DC): National Academies Press (US) Copyright 2011 by the National Academy of Sciences; 2011. <https://doi.org/10.17226/13059>
- Brouwers MC, Kho ME, Browman GP, et al. AGREE II: advancing guideline development, reporting and evaluation in health care. *Can. Med. Assoc. J.* 2010;182(18):E839–42. <https://doi.org/10.1503/cmaj.090449>
- AGREE NSC. The AGREE II Instrument [Electronic Version]. Published 2013. Accessed October 22, 2022.
- Brosseau L, Rahman P, Toupin-April K, et al. A systematic critical appraisal for non-pharmacological management of osteoarthritis using the appraisal of guidelines research and evaluation II instrument. *PLoS One* 2014;9(1), e82986. <https://doi.org/10.1371/journal.pone.0082986>
- Tittlemier BJ, Wittmeier KD, Webber SC. Quality and content analysis of clinical practice guidelines which include non-pharmacological interventions for knee osteoarthritis. *J Eval Clin Pract* 2021;27(1):93–102. <https://doi.org/10.1111/jep.13391>
- Brouwers MC, Spithoff K, Kerkvliet K, et al. Development and validation of a tool to assess the quality of clinical practice guideline recommendations. *JAMA Netw Open* 2020;3(5), e205535. <https://doi.org/10.1001/jamanetworkopen.2020.5535>
- McHugh ML. Interrater reliability: the kappa statistic. *Biochem Med* 2012;22(3):276–82.
- Fleiss JL. Measuring nominal scale agreement among many raters. *Psychol Bull* 1971;76(5):378–82. <https://doi.org/10.1037/h0031619>
- Cibulka MT, Bloom NJ, Ensey KR, et al. Hip pain and mobility deficits-hip osteoarthritis: revision 2017. *J Orthop Sports Phys Ther* 2017;47(6):A1–37. <https://doi.org/10.2519/jospt.2017.0301>
- Kolasinski SL, Neogi T, Hochberg MC, et al. 2019 American College of rheumatology/arthritis foundation guideline for the management of osteoarthritis of the hand, hip, and knee. *Arthritis Care Res* 2020;72(2):149–62. <https://doi.org/10.1002/art.41142>
- American Academy of Orthopaedic Surgeons Management of Osteoarthritis of the Knee (Non-Arthroplasty) Evidence-Based Clinical Practice Guideline; 2021. Accessed October 2, 2022.
- Surgical Management of Osteoarthritis of the Knee Evidence-Based Clinical Practice Guideline; 2015. Accessed October 2, 2022.

29. American Academy of Orthopaedic Surgeons Management of Osteoarthritis of the Hip Evidence-Based Clinical Practice Guideline; 2017. Accessed October 2, 2022.
30. The US Veterans Affairs/Department of Defence (VA/DoD). The Non-Surgical Management of Hip & Knee Osteoarthritis; 2020. <https://www.healthquality.va.gov/guidelines/cd/oa/index.asp>. Accessed October 2, 2022.
31. Brosseau L, Wells GA, Tugwell P, et al. Ottawa panel evidence-based clinical practice guidelines for the management of osteoarthritis in adults who are obese or overweight. *Phys Ther* 2011;91(6):843–61. <https://doi.org/10.2522/ptj.20100104>
32. Brosseau L, Wells GA, Pugh AG, et al. Ottawa Panel evidence-based clinical practice guidelines for therapeutic exercise in the management of hip osteoarthritis. *Clin Rehabil* 2016;30(10):935–46. <https://doi.org/10.1177/0269215515606198>
33. Brosseau L, Taki J, Desjardins B, et al. The Ottawa panel clinical practice guidelines for the management of knee osteoarthritis. Part one: introduction, and mind-body exercise programs. *Clin Rehabil* 2017;31(5):582–95. <https://doi.org/10.1177/0269215517691083>
34. Brosseau L, Taki J, Desjardins B, et al. The Ottawa panel clinical practice guidelines for the management of knee osteoarthritis. Part two: strengthening exercise programs. *Clin Rehabil* 2017;31(5):596–611. <https://doi.org/10.1177/0269215517691084>
35. Brosseau L, Taki J, Desjardins B, et al. The Ottawa panel clinical practice guidelines for the management of knee osteoarthritis. Part three: aerobic exercise programs. *Clin Rehabil* 2017;31(5):612–24. <https://doi.org/10.1177/0269215517691085>
36. Korownyk CS, Montgomery L, Young J, et al. PEER simplified chronic pain guideline: management of chronic low back, osteoarthritic, and neuropathic pain in primary care. *Can. Fam. Physician*. 2022;68(3):179–90. <https://doi.org/10.46747/cfp.6803179>
37. Royal Australian College of General Practitioners. Guideline for the Management of Knee and Hip Osteoarthritis. RACGP. <https://www.racgp.org.au/download/Documents/Guidelines/Musculoskeletal/guideline-for-the-management-of-knee-and-hip-oa-2nd-edition.pdf>. Published 2018. Accessed 2021.
38. Sellam J, Courties A, Eymard F, et al. Recommendations of the French Society of Rheumatology on pharmacological treatment of knee osteoarthritis. *JT Bone Spine* 2020;87(6):548–55. <https://doi.org/10.1016/j.jbspin.2020.09.004>
39. Tuncer T, Cay FH, Altan L, et al. 2017 update of the Turkish League Against Rheumatism (TLAR) evidence-based recommendations for the management of knee osteoarthritis. *Rheumatol Int* 2018;38(8):1315–31. <https://doi.org/10.1007/s00296-018-4044-y>
40. Zhang Z, Huang C, Jiang Q, et al. Guidelines for the diagnosis and treatment of osteoarthritis in China (2019 edition). *Ann Trans Med* 2020;8(19), 1213. <https://doi.org/10.21037/atm-20-4665>
41. Ministry of Health Singapore. Osteoarthritis of the Knees Clinical Practice Guideline; 2007. https://www.moh.gov.sg/docs/librariesprovider4/guidelines/cpg_oa-knees_booklet.pdf. Accessed October 2, 2022.
42. Ministry of Health Malaysia. Management of Osteoarthritis Clinical Practice Guideline; 2013. <https://www.moh.gov.my/moh/attachments/8933.pdf>. Accessed October 2, 2022.
43. Rillo O, Riera H, Acosta C, et al. PANLAR consensus recommendations for the management in osteoarthritis of hand, hip, and knee. *J Clin Rheumatol* 2016;22(7):345–54. <https://doi.org/10.1097/RHU.0000000000000449>
44. Doormaal MCM, Meerhoff GA, Vliet Vlieland TPM, Peter WF. A clinical practice guideline for physical therapy in patients with hip or knee osteoarthritis. *Musculoskelet Care* 2020;18(4):575–595. <https://doi.org/10.1002/msc.1492>
45. NICE. Osteoarthritis in over 16s: diagnosis and management. National Institute for Health and Clinical Excellence. <https://www.nice.org.uk/guidance/ng226> Published 2022. Accessed November 11, 2022.
46. Bruyère O, Honvo G, Veronese N, et al. An updated algorithm recommendation for the management of knee osteoarthritis from the European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO). *Semin Arthritis Rheum* 2019;49(3):337–50. <https://doi.org/10.1016/j.semarthrit.2019.04.008>
47. Geenen R, Overman CL, Christensen R, et al. EULAR recommendations for the health professional's approach to pain management in inflammatory arthritis and osteoarthritis. *Ann Rheum Dis* 2018;77(6):797–807. <https://doi.org/10.1136/annrheumdis-2017-212662>
48. Bannuru RR, Osani MC, Vaysbrot EE, et al. OARSI guidelines for the non-surgical management of knee, hip, and polyarticular osteoarthritis. *Osteoarthritis Cartil* 2019;27(11):1578–89. <https://doi.org/10.1016/j.joca.2019.06.011>
49. Siemieniuk RAC, Harris IA, Agoritsas T, et al. Arthroscopic surgery for degenerative knee arthritis and meniscal tears: a clinical practice guideline. *BMJ* 2017;357, j1982. <https://doi.org/10.1136/bmj.j1982>
50. Meneses SR, Goode AP, Nelson AE, et al. Clinical algorithms to aid osteoarthritis guideline dissemination. *Osteoarthritis Cartil* 2016;24(9):1487–99. <https://doi.org/10.1016/j.joca.2016.04.004>
51. Nelson AE, Allen KD, Golightly YM, et al. A systematic review of recommendations and guidelines for the management of osteoarthritis: the chronic osteoarthritis management initiative of the U.S. bone and joint initiative. *Semin Arthritis Rheum* 2014;43(6):701–12. <https://doi.org/10.1016/j.semarthrit.2013.11.012>
52. Hagen KB, Smedslund G, Østerås N, Jamtvedt G. Quality of community-based osteoarthritis care: a systematic review and meta-analysis. *Arthritis Care Res* 2016;68(10):1443–52. <https://doi.org/10.1002/acr.22891>
53. Oral A, Arman S, Tarakci E, et al. A systematic review of clinical practice guidelines for persons with osteoarthritis. A “Best Evidence for Rehabilitation” (be4rehab) paper to develop the WHO’s Package of Interventions for Rehabilitation. *Int J Rheum Dis* 2022;25(4):383–93. <https://doi.org/10.1111/1756-185X.14292>
54. Phillips M, Bhandari M, Grant J, et al. A systematic review of current clinical practice guidelines on intra-articular hyaluronic acid, corticosteroid, and platelet-rich plasma injection for knee osteoarthritis: an international perspective. *Orthop J Sports Med* 2021;9(8), 23259671211030272. <https://doi.org/10.1177/23259671211030272>
55. Conley B, Bunzli S, Bullen J, et al. What are the core recommendations for osteoarthritis care? A systematic review of clinical practice guidelines. *Arthritis Care Res* 2023;2010. <https://doi.org/10.1002/acr.25101>
56. Chua J, Hansen P, Briggs AM, et al. Stakeholders’ preferences for osteoarthritis interventions in health services: a cross-sectional study using multi-criteria decision analysis. *Osteoarthritis Cartil* 2020;2(4), 100110–100110. <https://doi.org/10.1016/j.ocarto.2020.100110>