National Institute for Health and Care Excellence

Draft for consultation

Osteoarthritis: assessment and management (update)

[A] Additional benefit of imaging in the diagnosis of osteoarthritis

NICE guideline <number>

Evidence reviews underpinning recommendations 1.1.1 to 1.1.2 in the NICE guideline

April 2022

Draft for Consultation

NICE accredited
www.nice.org.uk/accreditation

Disclaimer

The recommendations in this guideline represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, professionals are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or service users. The recommendations in this guideline are not mandatory and the guideline does not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian.

Local commissioners and/or providers have a responsibility to enable the guideline to be applied when individual health professionals and their patients or service users wish to use it. They should do so in the context of local and national priorities for funding and developing services, and in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities. Nothing in this guideline should be interpreted in a way that would be inconsistent with compliance with those duties.

NICE guidelines cover health and care in England. Decisions on how they apply in other UK countries are made by ministers in the Welsh Government, Scottish Government, and Northern Ireland Executive. All NICE guidance is subject to regular review and may be updated or withdrawn.

Copyright

© NICE 2022. All rights reserved. Subject to Notice of rights.

ISBN:

Contents

1 Additional benefit of imaging in the diagnosis of osteoarthritis 5
1.1 Review question 5
What is the clinical and cost-effectiveness of using imaging in the diagnosis of osteoarthritis in people with suspected osteoarthritis? 5
1.1.1 Introduction 5
1.1.2 Summary of the protocol 5
1.1.3 Methods and process 6
1.1.4 Effectiveness evidence 7
1.1.5 Summary of studies included in the effectiveness evidence 7
1.1.6 Summary of the effectiveness evidence 7
1.1.7 Economic evidence 8
1.1.8 Summary of included economic evidence 9
1.1.9 Economic model 9
1.1.10 Unit costs 9
1.1.11 Economic evidence statements 9
1.1.12 The committee's discussion and interpretation of the evidence 9
1.1.13 Recommendations supported by this evidence review 11
1.1.14 References 12
Appendices 16
Appendix A – Review protocols 16
Appendix B – Literature search strategies 25
B.1 Clinical search literature search strategy 25
B.2 Health Economics literature search strategy 29
Appendix C – Effectiveness evidence study selection 34
Appendix D – Effectiveness evidence 35
Appendix E – Forest plots 36
Appendix F – GRADE tables 37
Appendix G – Economic evidence study selection 38
Appendix H – Economic evidence tables 39
Appendix I – Health economic model 40
Appendix J – Excluded studies 41
Clinical studies 41
Health Economic studies 42

1 Additional benefit of imaging in the diagnosis of osteoarthritis

1.1 Review question

What is the clinical and cost-effectiveness of using imaging in the diagnosis of osteoarthritis in people with suspected osteoarthritis?

1.1.1 Introduction

In the absence of red flag signs or symptoms, the diagnosis of osteoarthritis can be achieved through clinical assessment (history taking and examination). Imaging findings do not always correlate well with the patient's symptoms, particularly in the early stages of osteoarthritis, and management is not dictated by imaging results alone. There is no gold standard for the clinical diagnosis of osteoarthritis and multiple clinical and research focussed definitions of the condition have been developed and some patients expect imaging to confirm a diagnosis. Imaging continues to be frequently used despite uncertainties about the benefit this adds to the diagnosis, the resource implications and potential for delays in commencing management. X-ray is the most common imaging used for knee osteoarthritis, however magnetic resonance imaging (MRI) is now being used more commonly to examining soft tissues and to pick up more subtle bony changes. Some healthcare professionals may use ultrasound for more superficial joints (for example: finger, toe). In some parts of the country, primary care has direct access to MRI and ultrasound scans. The aim of this review is to establish if there is additional benefit in using any imaging as an adjunct to clinical examination to diagnose osteoarthritis. This review does not seek to define when imaging is indicated in the natural history of osteoarthritis.

1.1.2 Summary of the protocol

For full details see the review protocol in Appendix A.

Table 1: PICO characteristics of review question

Population	Inclusion: • Adults (age ≥16 years) with clinically suspected osteoarthritis affecting any joint. Exclusion: • Children (age <16 years). • People previously diagnosed with osteoarthritis before the study • Spinal osteoarthritis
Interventions	Diagnosis based on: • Clinical assessment without imaging • Clinical assessment with CT imaging • Clinical assessment with CT after X-ray or ultrasound • Clinical assessment with MRI imaging • Clinical assessment with MRI imaging after X-ray or ultrasound • Clinical assessment with x-ray • Clinical assessment with ultrasound
Comparisons	• Compared to each other (clinical-effectiveness)
Outcomes	Primary outcomes (critical outcomes) Stratify by ≤/>3 months (longest time-point in each):

	• Health-related quality of life [validated patient-reported outcomes, continuous data prioritised] • Pain [validated patient-reported outcomes, continuous data prioritised] • Physical function [validated patient-reported outcomes, continuous data prioritised] Secondary outcomes (important outcomes) • Psychological distress [validated patient-reported outcomes, continuous data prioritised] • Healthcare utilisation (prescribing, investigations, hospitalisation or health professional visit) [dichotomous data prioritised] • Any alternative diagnosis [dichotomous data prioritised]
Study design	RCTs or systematic reviews of RCTs. Non-randomised evidence including: 1. Prospective and retrospective cohort studies 2. Case control studies (if no other evidence identified)

1.1.3 Methods and process

This evidence review was developed using the methods and process described in Developing NICE guidelines: the manual. Methods specific to this review question are described in the review protocol in appendix A and the methods document.

Declarations of interest were recorded according to NICE's conflicts of interest policy.

1.1.4 Effectiveness evidence

1.1.4.1 Included studies

No relevant clinical studies comparing diagnosis based on different imaging techniques to each other were identified.

This review aimed to investigate the diagnostic effectiveness rather than the diagnostic accuracy of techniques. This was as the committee agreed that there was no gold standard test that would be used to diagnose osteoarthritis, as osteoarthritis is a clinical syndrome and may or may not have imaging features associated with it. Given this, the committee decided to investigate if there was additional benefit to using imaging on long-term outcomes for people with osteoarthritis. No studies fulfilled this criterion while reporting outcomes included in the protocol.

See also the study selection flow chart in Appendix C.

1.1.4.2 Excluded studies

See the excluded studies list in Appendix J.

1.1.5 Summary of studies included in the effectiveness evidence

No evidence was identified for this review.

1.1.6 Summary of the effectiveness evidence

No evidence was identified for this review.

1.1.7 Economic evidence

1.1.7.1 Included studies

No health economic studies were included.

1.1.7.2 Excluded studies

No relevant health economic studies were excluded due to limited applicability or methodological limitations.

See also the health economic study selection flow chart in Appendix G.

1.1.8 Summary of included economic evidence

There was no economic evidence found.

1.1.9 Economic model

This area was not prioritised for new cost-effectiveness analysis

1.1.10 Unit costs

Relevant unit costs are provided below to aid consideration of cost effectiveness.

Resource	Unit costs	Source
CT scan	£94	NHS Reference Costs 2019/20[36]
MRI scan	£173	
Plain film imaging (including x-ray)	£56	
Ultrasound	£75	

1.1.11 Economic evidence statements

- No relevant economic evaluations were identified.

1.1.12 The committee's discussion and interpretation of the evidence

1.1.12.1. The outcomes that matter most

The critical outcomes were quality of life, pain and physical function. These were considered critical due to their relevance importance to people with osteoarthritis. The Osteoarthritis Research Society International (OARSI) consider that pain and physical function were the most important outcomes for evaluating interventions. Quality of life gives a broader perspective on the person's wellbeing, allowing for examination of the biopsychosocial impact of interventions. Psychological distress, healthcare utilisation and any alternative diagnosis were included as important outcomes.

Mortality was not considered in this review. Osteoarthritis as a disease process is not considered to cause mortality by itself and mortality is an uncommon outcome from osteoarthritis interventions. The committee agreed that the intervention from this review were unlikely to cause mortality rates to change. Given this, the committee did not feel that mortality required a specific outcome.

The committee considered if a diagnostic accuracy review was appropriate. During discussion of the protocol, it was agreed that there was no consistent gold standard test that could be used for a diagnostic accuracy review (as people may have findings consistent with osteoarthritis on imaging but not have clinical symptoms of osteoarthritis, and people may have no findings on imaging yet have clinical symptoms of osteoarthritis). Therefore, a test-and-treat review was conducted. However, no outcome data was available for this review.

1.1.12.2 The quality of the evidence

No evidence was identified for this review.

1.1.12.3 Benefits and harms

No evidence was identified for this review. Therefore, the committee discussion was based on expert opinion.

The committee considered the potential benefits and harms of imaging. The committee considered that imaging findings consistent with osteoarthritis may not indicate that someone's clinical symptoms are due to osteoarthritis. Current practice in the United Kingdom considers osteoarthritis as a clinical syndrome consisting of activity-related joint pain with morning stiffness that lasts no longer than 30 minutes (or no morning joint-related stiffness) that generally occurs in people 45 years or over.

Based on the absence of evidence, the committee agreed that imaging is unlikely to provide benefit for diagnosing osteoarthritis. Based on these factors the committee agreed recommending that there is no evidence to support the use of imaging in addition to clinical assessment for people with osteoarthritis unless there are atypical features or features that suggest an alternative or additional diagnosis such as other inflammatory arthritis (for example, rheumatoid arthritis) and malignancy. These conditions are less common than osteoarthritis but can have significant consequences if they are not identified. Atypical features could include: a history of trauma, prolonged morning joint-related stiffness, rapid worsening of symptoms and the presence of a hot swollen joint. While the committee agreed these features could prompt further investigation (including imaging) they also noted that imaging may not always be the optimal investigation in these cases.

Overall, the committee agreed that it is widely accepted that diagnosis is achieved through clinical assessment, that imaging proffers no benefit and that there was no evidence to change current practice. They also agreed that further research is not warranted and no research recommendation has been made.

1.1.12.4 Cost effectiveness and resource use

No economic evaluations were identified for inclusion in this review

NHS reference costs data suggested that the cost of imaging ranges between £56 and £173, with the cheapest option being x-ray imaging and the most expensive being an MRI scan. Imaging is currently used routinely in the diagnosis of osteoarthritis. Given the incidence of osteoarthritis, a change in practice would potentially cause a substantial cost impact in either direction.

In the absence of evidence of clinical effectiveness or cost effectiveness the committee did not recommend imaging for the diagnosis of osteoarthritis. The committee's recommendation should result in a reduction in NHS resource use and ultimately be a cost saving measure.

1.1.12.5 Other factors the committee took into account

The committee noted that there is NICE guidance relating to some of the differential diagnoses that may be relevant when assessing people with osteoarthritis. These may contain recommendations for imaging and other investigations (including blood tests) that could be used. These include:

- Rheumatoid arthritis in adults: management (NG100)
- Suspected cancer: recognition and referral (NG12)
- Gout: diagnosis and management (in development)

The committee agreed that a research recommendation was not required in this area. While studies were not identified in the review, the committee agreed through consensus that there was limited value to be gained from the use of imaging in the diagnosis of osteoarthritis, as osteoarthritis is defined as a clinical syndrome of joint pain accompanied by varying degrees of functional limitation and reduced quality of life. The committee noted that observational evidence indicated that people with imaging features related to osteoarthritis may be symptomatic and may not develop symptoms. Given this, further research is unlikely to change understanding in this area.

The committee noted that the osteoarthritis research in general did not appear to represent the diverse community of people who can have osteoarthritis. While future research is not recommended in this area, they agreed that any future research should be representative of the population, including people from different family backgrounds, and socioeconomic backgrounds, disabled people, and people of different ages and genders. This should be done to consider the different experiences of people from diverse communities to ensure that the approach taken can be made equitable for everyone.

1.1.13 Recommendations supported by this evidence review

This evidence review supports recommendations 1.1.1 to 1.1.2. Other evidence supporting these recommendations can be found in Evidence Review A.

1.1.14 References

1. Abedin J, Antony J, McGuinness K, Moran K, O'Connor NE, Rebholz-Schuhmann D et al. Predicting knee osteoarthritis severity: comparative modeling based on patient's data and plain X-ray images. Scientific Reports. 2019; 9(1):5761

2. Agoda-Koussema LK, Oniankitan O, Abalo GA, Ouro-Kefia DD, Awobanou KM, N'Dakena KG. [Contribution of the x-ray to the diagnosis of the non traumatic knee's pain in the teaching hospitals Tokoin and campus of Lome]. [French]. Le Mali Medical. 2012; 27(1):37-41

3. Alvarez C, Chicheportiche V, Lequesne M, Vicaut E, Laredo JD. Contribution of helical computed tomography to the evaluation of early hip osteoarthritis: a study in 18 patients. Joint, Bone, Spine: Revue du Rhumatisme. 2005; 72(6):578-584

4. Amitai I, Werner S, Schicke B, Burmester GR, Minet O, Zabarylo U et al. Comparison of photo optical imaging with musculoskeletal ultrasound and clinical examination in the assessment of inflammatory activity in proximal interphalangeal joints in rheumatoid arthritis and osteoarthritis. Journal of Rheumatology. 2015; 42(9):1595-1602

5. Atar MO, Ozcakar L, Gencturk Z, Aytur Y. Serum endothelin-1 levels, radiographic and ultrasonographic evaluations, and clinical parameters in patients with knee and/or hand osteoarthritis. Journal of Back and Musculoskeletal Rehabilitation. 2019; 32(4):549-554

6. Badel T, Marotti M, Savic-Pavicin I, Zadravec D, Kern J. Radiographic validation of manual functional analysis of temporomandibular joint osteoarthritis. Acta Clinica Croatica. 2012; 51(1):35-42

7. Baker JF, Caborn DN, Schlierf TJ, Fain TB, Smith LS, Malkani AL. Isolated patellofemoral joint arthroplasty: Can preoperative bone scans predict survivorship? Journal of Arthroplasty. 2020; 35(1):57-60

8. Boegard TL, Rudling O, Petersson IF, Jonsson K. Distribution of MR-detected cartilage defects of the patellofemoral joint in chronic knee pain. Osteoarthritis and Cartilage. 2003; 11(7):494-498

9. Brandt KD, Heilman DK, Slemenda C, Katz BP, Mazzuca S, Braunstein EM et al. A comparison of lower extremity muscle strength, obesity, and depression scores in elderly subjects with knee pain with and without radiographic evidence of knee osteoarthritis. Journal of Rheumatology. 2000; 27(8):1937-1946

10. Brealey SD. Influence of magnetic resonance imaging of the knee on GPs' decisions: A randomised trial. British Journal of General Practice. 2007; 57(541):622-629

11. Cai G, Cicuttini F, Aitken D, Laslett LL, Zhu Z, Winzenberg T et al. Comparison of radiographic and MRI osteoarthritis definitions and their combination for prediction of tibial cartilage loss, knee symptoms and total knee replacement: a longitudinal study. Osteoarthritis and Cartilage. 2020; 28(8):1062-1070

12. Chen S, Lin S, Li Y, Liu Y. Characteristics of musculoskeletal ultrasound versus x-ray in their differential diagnosis of knee osteoarthritis. International Journal of Clinical and Experimental Medicine. 2020; 13(11):8734-8739

13. Chen YJ, Chen CH, Wang CL, Huang MH, Chen TW, Lee CL. Association between the severity of femoral condylar cartilage erosion related to knee osteoarthritis by ultrasonographic evaluation and the clinical symptoms and functions. Archives of Physical Medicine and Rehabilitation. 2015; 96(5):837-844

14. Chiba D, Tsuda E, Maeda S, Sasaki E, Takahashi I, Nakaji S et al. Evaluation of a quantitative measurement of suprapatellar effusion by ultrasonography and its association with symptoms of radiographic knee osteoarthritis: a cross-sectional observational study. Arthritis Research & Therapy. 2016; 18:181

15. Emshoff R, Rudisch A. Validity of clinical diagnostic criteria for temporomandibular disorders: clinical versus magnetic resonance imaging diagnosis of temporomandibular joint internal derangement and osteoarthrosis. Oral Surgery Oral Medicine Oral Pathology Oral Radiology & Endodontics. 2001; 91(1):50-55

16. Ezzat AM, Cibere J, Koehoorn M, Li LC. Association between cumulative joint loading from occupational activities and knee osteoarthritis. Arthritis Care and Research. 2013; 65(10):1634-1642

17. Gluckert K, Blank-Schal A, Hofmann G, Kladny B, Willauschus W, Wirtz P. Possibilities for early detection of arthroses using imaging procedures. [German]. Der orthopade. 1990; 19(1):50-57

18. Haghighi A, Arani ND, Kianmehr N, Mofidi M, Farjadnia M, Rajae E et al. Is there a correlation between the clinical, radiological and ultra-sonographic findings of osteoarthritis of the knee? International Journal of Pharmaceutical and Clinical Research. 2017; 9(5):368-373

19. Hirsch G, O'Neill TW, Kitas G, Sinha A, Klocke R. Accuracy of injection and short-term pain relief following intra-articular corticosteroid injection in knee osteoarthritis - an observational study. BMC Musculoskeletal Disorders. 2017; 18(1):44

20. Ip S, Sayre EC, Guermazi A, Nicolaou S, Wong H, Thorne A et al. Frequency of bone marrow lesions and association with pain severity: results from a population-based symptomatic knee cohort. Journal of Rheumatology. 2011; 38(6):1079-1085

21. Javaid MK, Kiran A, Guermazi A, Kwoh CK, Zaim S, Carbone L et al. Individual magnetic resonance imaging and radiographic features of knee osteoarthritis in subjects with unilateral knee pain: the health, aging, and body composition study. Arthritis and Rheumatism. 2012; 64(10):3246-3255

22. Keen HI, Wakefield RJ, Conaghan PG. A systematic review of ultrasonography in osteoarthritis. Annals of the Rheumatic Diseases. 2009; 68(5):611-619

23. Kim CK, Park KW. Characteristic appearance of facet osteoarthritis of the lower lumbar spine on planar bone scintigraphy with a high negative predictive value for metastasis. Clinical Nuclear Medicine. 2008; 33(4):251-254

24. Kim J, Lee HH, Kang Y, Kim TK, Lee SW, So Y et al. Maximum standardised uptake value of quantitative bone SPECT/CT in patients with medial compartment osteoarthritis of the knee. Clinical Radiology. 2017; 72(7):580-589

25. Kinds MB, Welsing PM, Vignon EP, Bijlsma JW, Viergever MA, Marijnissen AC et al. A systematic review of the association between radiographic and clinical osteoarthritis of hip and knee. Osteoarthritis and Cartilage. 2011; 19(7):768-778

26. Kroon FPB, van Beest S, Ermurat S, Kortekaas MC, Bloem JL, Reijnierse M et al. In thumb base osteoarthritis structural damage is more strongly associated with pain than synovitis. Osteoarthritis and Cartilage. 2018; 26(9):1196-1202

27. Laursen JO. Treatment of full-thickness cartilage lesions and early OA using large condyle resurfacing prosthesis: UniCAP(R). Knee Surgery, Sports Traumatology, Arthroscopy. 2016; 24(5):1695-1701

28. Macri EM, Neogi T, Jarraya M, Guermazi A, Roemer F, Lewis CE et al. Can MRI-defined osteoarthritis features explain anterior knee pain in individuals with, or at risk for, knee osteoarthritis? The MOST Study. Arthritis Care and Research. 2021; 25

29. Magnusson K, Kumm J, Turkiewicz A, Englund M. A naturally aging knee, or development of early knee osteoarthritis? Osteoarthritis and Cartilage. 2018; 26(11):1447-1452

30. Matsos M, Harish S, Zia P, Ho Y, Chow A, Ioannidis G et al. Ultrasound of the hands and feet for rheumatological disorders: influence on clinical diagnostic confidence and patient management. Skeletal Radiology. 2009; 38(11):1049-1054

31. Menz HB, Munteanu SE, Marshall M, Thomas MJ, Rathod-Mistry T, Peat GM et al. Identification of Radiographic Foot Osteoarthritis: Sensitivity of Views and Features Using The La Trobe Radiographic Atlas. Arthritis Care and Research. 2021; 16

32. Mortada M, Zeid A, Al-Toukhy MA, Ezzeldin N, Elgawish M. Reliability of a proposed ultrasonographic grading scale for severity of primary knee osteoarthritis. Clinical Medival Insights Arthritis Musculoskeletal Disorders. 2016; 9:161-166

33. Nalamachu S, Robinson RL, Viktrup L, Cappelleri JC, Bushmakin AG, Tive L et al. Pain severity and healthcare resource utilization in patients with osteoarthritis in the United States. Postgraduate Medicine. 2020; 02:02

34. National Institute for Health and Care Excellence. Developing NICE guidelines: the manual [updated October 2020]. London. National Institute for Health and Care Excellence, 2014. Available from: http://www.nice.org.uk/article/PMG20/chapter/1%20Introduction%20and%20overview

35. Neiman M, Neiman OH, Aharoni D, Liberman B, Adar E, Eshed I. Magnetic resonance arthrography of the hip: Prevalence of diagnoses not suspected by the referring physician and correlation with clinical examination and pain score. Acta Radiologica. 2016; 57(5):595-601

36. NHS England and NHS Improvement. National Cost Collection Data Publication 2019-2020. London. 2020. Available from: https://www.england.nhs.uk/wp-content/uploads/2021/06/National-Cost-Collection-2019-20-Report-FINAL.pdf

37. Pan F, Tian J, Cicuttini F, Jones G, Aitken D. Differentiating knee pain phenotypes in older adults: a prospective cohort study. Rheumatology. 2019; 58(2):274-283

38. Park JW, Song HH, Roh HS, Kim YK, Lee JY. Correlation between clinical diagnosis based on RDC/TMD and MRI findings of TMJ internal derangement. International Journal of Oral and Maxillofacial Surgery. 2012; 41(1):103-108

39. Roberts TT, Singer N, Hushmendy S, Dempsey IJ, Roberts JT, Uhl RL et al. MRI for the evaluation of knee pain comparison of ordering practices of primary care physicians and orthopaedic surgeons. Journal of Bone and Joint Surgery - American Volume. 2015; 97(9):709-714

40. Roux CH, Mazieres B, Verrouil E, Rat AC, Fardellone P, Fautrel B et al. Femoro-tibial knee osteoarthritis: One or two X-rays? Results from a population-based study. Joint, Bone, Spine: Revue du Rhumatisme. 2016; 83(1):37-42

41. Sheridan GA, Bisseru A, Glynn AA. The utility of MRI scans for a painful knee in the elderly patient. Irish Journal of Medical Science. 2021; 190(1):363-366

42. Smink AJ, Bierma-Zeinstra SM, Schers HJ, Swierstra BA, Kortland JH, Bijlsma JW et al. Non-surgical care in patients with hip or knee osteoarthritis is modestly consistent

with a stepped care strategy after its implementation. International Journal for Quality in Health Care. 2014; 26(4):490-498

43. Thomas E, Peat G, Mallen C, Wood L, Lacey R, Duncan R et al. Predicting the course of functional limitation among older adults with knee pain: do local signs, symptoms and radiographs add anything to general indicators? Annals of the Rheumatic Diseases. 2008; 67(10):1390-1398

44. Wang Q, Runhaar J, Kloppenburg M, Boers M, Bijlsma JWJ, Bierma-Zeinstra SMA et al. Diagnosis of early stage knee osteoarthritis based on early clinical course: data from the CHECK cohort. Arthritis Research & Therapy. 2021; 23(1):217

45. Wang Y, Teichtahl AJ, Abram F, Hussain SM, Pelletier JP, Cicuttini FM et al. Knee pain as a predictor of structural progression over 4 years: data from the Osteoarthritis Initiative, a prospective cohort study. Arthritis Research & Therapy. 2018; 20(1):250

46. Whittaker JL, Toomey CM, Woodhouse LJ, Jaremko JL, Nettel-Aguirre A, Emery CA. Association between MRI-defined osteoarthritis, pain, function and strength 3-10 years following knee joint injury in youth sport. British Journal of Sports Medicine. 2018; 52(14):934-939

47. Yoong P, Guirguis R, Darrah R, Wijeratna M, Porteous MJ. Evaluation of ultrasound-guided diagnostic local anaesthetic hip joint injection for osteoarthritis. Skeletal Radiology. 2012; 41(8):981-985

48. Zhu Z, Laslett LL, Jin X, Han W, Antony B, Wang X et al. Association between MRI-detected osteophytes and changes in knee structures and pain in older adults: a cohort study. Osteoarthritis and Cartilage. 2017; 25(7):1084-1092

Appendices

Appendix A – Review protocols

Review protocol for Additional benefit of imaging in the diagnosis of osteoarthritis

ID	Field	Content
0.	PROSPERO registration number	CRD42020221796
1.	Review title	1.1 What is clinical and cost-effectiveness of using imaging in the diagnosis of osteoarthritis in people with suspected osteoarthritis?
2.	Review question	1.1 What is the clinical and cost-effectiveness of using imaging in the diagnosis of osteoarthritis in people with suspected osteoarthritis?
3.	Objective	To determine if there is a additional benefits to be gained from using imaging studies (in addition to clinical assessment) in the diagnostic process for people with suspected osteoarthritis.
4.	Searches	The following databases will be searched: • Cochrane Central Register of Controlled Trials (CENTRAL) • Cochrane Database of Systematic Reviews (CDSR) • Embase • MEDLINE Searches will be restricted by: • English language • Human studies • Letters and comments are excluded Other searches: • Inclusion lists of relevant systematic reviews will be checked by the reviewer. The searches may be re-run 6 weeks before final submission of the review and further studies retrieved for inclusion if relevant.

		The full search strategies for MEDLINE database will be published in the final review.
5.	Condition or domain being studied	Suspected osteoarthritis (of any joint) in adults
6.	Population	Inclusion: • Adults (age ≥16 years) with clinically suspected osteoarthritis affecting any joint. Exclusion: • Children (age <16 years). • People previously diagnosed with osteoarthritis before the study • Spinal osteoarthritis Stratify by site of osteoarthritis: • Hip • Knee • Ankle • Foot • Toe • Shoulder • Elbow • Wrist • Hand • Thumb • Finger • Temporomandibular joint (TMJ) • Multisite To note that where evidence for other rare forms of osteoarthritis is identified the committee will stratify into a group they are most similar to.
7.	Intervention/Test	Diagnosis based on: • Clinical assessment without imaging • Clinical assessment with CT imaging • Clinical assessment with CT after X-ray or ultrasound • Clinical assessment with MRI imaging • Clinical assessment with MRI imaging after X-ray or ultrasound • Clinical assessment with x-ray • Clinical assessment with ultrasound
8.	Comparator/Reference standard/Confounding factors	• Compared to each other (clinical-effectiveness)

9.	Types of study to be included	• Systematic reviews of RCTs • RCTs • Non-randomised evidence including: 1. Prospective and retrospective cohort studies 2. Case control studies (if no other evidence identified)
10.	Other exclusion criteria	• Non-English language studies • Conference abstracts will be excluded as it is expected there will be sufficient full text published studies available. • Single arm non-randomised studies
11.	Context	N/A
12.	Primary outcomes (critical outcomes)	Stratify by ≤/>3 months (longest time-point in each): • Health-related quality of life [validated patient-reported outcomes, continuous data prioritised] • Pain [validated patient-reported outcomes, continuous data prioritised] • Physical function [validated patient-reported outcomes, continuous data prioritised]
13.	Secondary outcomes (important outcomes)	• Psychological distress [validated patient-reported outcomes, continuous data prioritised] • Healthcare utilisation (prescribing, investigations, hospitalisation or health professional visit) [dichotomous data prioritised] • Any alternative diagnosis [dichotomous data prioritised] *The COMET database was searched and several core outcome sets were identified for specific sites of osteoarthritis (including hand, knee and hip). The committee took these into account when defining outcomes:* https://onlinelibrary.wiley.com/doi/full/10.1002/acr.22868 https://www.ncbi.nlm.nih.gov/pubmed/26136489 https://www.ncbi.nlm.nih.gov/pubmed/30647185 The committee did not include stiffness or global scores as Delphi discussions by the OMERACT group have found these to not be as important to people with osteoarthritis or clinicians. The outcomes included were universal for all groups allowing for broader comparisons.

14.	Data extraction (selection and coding)	EndNote will be used for reference management, sifting, citations and bibliographies. All references identified by the searches and from other sources will be screened for inclusion. 10% of the abstracts will be reviewed by two reviewers, with any disagreements resolved by discussion or, if necessary, a third independent reviewer. The full text of potentially eligible studies will be retrieved and will be assessed in line with the criteria outlined above. A standardised form will be used to extract data from studies (see Developing NICE guidelines: the manual section 6.4). Study investigators may be contacted for missing data where time and resources allow.
15.	Risk of bias (quality) assessment	Risk of bias will be assessed using the appropriate checklist as described in Developing NICE guidelines: the manual. • Systematic reviews: Risk of Bias in Systematic Reviews (ROBIS) • Randomised Controlled Trial: Cochrane RoB (2.0) • Non randomised study, including cohort studies: Cochrane ROBINS-I • Case control study: CASP case control checklist 10% of all evidence reviews are quality assured by a senior research fellow. This includes checking: • papers were included /excluded appropriately • a sample of the data extractions • correct methods are used to synthesise data • a sample of the risk of bias assessments Disagreements between the review authors over the risk of bias in particular studies will be resolved by discussion, with involvement of a third review author where necessary.
16.	Strategy for data synthesis	• Pairwise meta-analyses will be performed using Cochrane Review Manager (RevMan5). • GRADEpro will be used to assess the quality of evidence for each outcome, taking into account individual study quality and the meta-analysis results. The 4 main quality elements (risk of bias, indirectness, inconsistency and imprecision) will be appraised for each outcome. Publication bias is tested for when there are more than 5 studies for an outcome.

		The risk of bias across all available evidence was evaluated for each outcome using an adaptation of the 'Grading of Recommendations Assessment, Development and Evaluation (GRADE) toolbox' developed by the international GRADE working group http://www.gradeworkinggroup.org/ • Where meta-analysis is not possible, data will be presented and quality assessed individually per outcome. • WinBUGS will be used for network meta-analysis, if possible given the data identified. Heterogeneity between the studies in effect measures will be assessed using the I^2 statistic and visually inspected. An I^2 value greater than 50% will be considered indicative of substantial heterogeneity. Sensitivity analyses will be conducted based on pre-specified subgroups using stratified meta-analysis to explore the heterogeneity in effect estimates. If this does not explain the heterogeneity, the results will be presented pooled using random-effects.
17.	Analysis of sub-groups	• Age (≤/> 45 years)
18.	Type and method of review	☒ Intervention ☐ Diagnostic ☐ Prognostic ☐ Qualitative ☐ Epidemiologic ☐ Service Delivery ☐ Other (please specify)
19.	Language	English
20.	Country	England
21.	Anticipated or actual start date	23/08/2019
22.	Anticipated completion date	25/08/2021
23.	Stage of review at time of this submission	Review stage / Started / Completed Preliminary searches ☐ ☐ Piloting of the study selection process ☐ ☐ Formal screening of search results against eligibility criteria ☐ ☐

		Data extraction	☐	☐
		Risk of bias (quality) assessment	☐	☐
		Data analysis	☐	☐
24.	Named contact	5a. Named contact National Guideline Centre 5b Named contact e-mail [Guideline email]@nice.org.uk [Developer to check with Guideline Coordinator for email address] 5e Organisational affiliation of the review National Institute for Health and Care Excellence (NICE) and the National Guideline Centre		
25.	Review team members	From the National Guideline Centre: Carlos Sharpin [Guideline lead] Julie Neilson [Senior systematic reviewer] George Wood [Systematic reviewer] David Wonderling [Senior health economist] Joseph Runicles [Information specialist] Amber Hernaman [Project manager]		
26.	Funding sources/sponsor	This systematic review is being completed by the National Guideline Centre which receives funding from NICE.		
27.	Conflicts of interest	All guideline committee members and anyone who has direct input into NICE guidelines (including the evidence review team and expert witnesses) must declare any potential conflicts of interest in line with NICE's code of practice for declaring and dealing with conflicts of interest. Any relevant interests, or changes to interests, will also be declared publicly at the start of each guideline committee meeting. Before each meeting, any potential conflicts of interest will be considered by the guideline committee Chair and a senior member of the development team. Any decisions to exclude a person from all or part of a meeting will be documented. Any changes to a member's declaration of interests will be recorded in the minutes of the meeting. Declarations of interests will be published with the final guideline.		

28.	Collaborators	Development of this systematic review will be overseen by an advisory committee who will use the review to inform the development of evidence-based recommendations in line with section 3 of Developing NICE guidelines: the manual. Members of the guideline committee are available on the NICE website: https://www.nice.org.uk/guidance/indevelopment/gid-ng10127	
29.	Other registration details		
30.	Reference/URL for published protocol		
31.	Dissemination plans	NICE may use a range of different methods to raise awareness of the guideline. These include standard approaches such as: • notifying registered stakeholders of publication • publicising the guideline through NICE's newsletter and alerts • issuing a press release or briefing as appropriate, posting news articles on the NICE website, using social media channels, and publicising the guideline within NICE.	
32.	Keywords	Healthcare utilisation; Imaging; MRI; Osteoarthritis; Ultrasound; X-ray	
33.	Details of existing review of same topic by same authors		
34.	Current review status	☒	Ongoing
		☐	Completed but not published
		☐	Completed and published
		☐	Completed, published and being updated
		☐	Discontinued
35..	Additional information	N/A	
36.	Details of final publication	www.nice.org.uk	

1

2 **Table 2: Health economic review protocol**

Review question	All questions – health economic evidence
Objectives	To identify health economic studies relevant to any of the review questions.
Search criteria	• Populations, interventions and comparators must be as specified in the clinical review protocol above.

	• Studies must be of a relevant health economic study design (cost–utility analysis, cost-effectiveness analysis, cost–benefit analysis, cost–consequences analysis, comparative cost analysis). • Studies must not be a letter, editorial or commentary, or a review of health economic evaluations. (Recent reviews will be ordered although not reviewed. The bibliographies will be checked for relevant studies, which will then be ordered.) • Unpublished reports will not be considered unless submitted as part of a call for evidence. • Studies must be in English.
Search strategy	A health economic study search will be undertaken for all years using population-specific terms and a health economic study filter – see appendix B below.
Review strategy	Studies not meeting any of the search criteria above will be excluded. Studies published before 2005, abstract-only studies and studies from non-OECD countries or the USA will also be excluded. Studies published in 2005 or later, that were included in the previous guidelines, will be reassessed for inclusion and may be included or selectively excluded based on their relevance to the questions covered in this update and whether more applicable evidence is also identified. Each remaining study will be assessed for applicability and methodological limitations using the NICE economic evaluation checklist which can be found in appendix H of Developing NICE guidelines: the manual (2014).[34] **Inclusion and exclusion criteria** • If a study is rated as both 'Directly applicable' and with 'Minor limitations' then it will be included in the guideline. A health economic evidence table will be completed and it will be included in the health economic evidence profile. • If a study is rated as either 'Not applicable' or with 'Very serious limitations' then it will usually be excluded from the guideline. If it is excluded then a health economic evidence table will not be completed and it will not be included in the health economic evidence profile. • If a study is rated as 'Partially applicable', with 'Potentially serious limitations' or both then there is discretion over whether it should be included. **Where there is discretion** The health economist will make a decision based on the relative applicability and quality of the available evidence for that question, in discussion with the guideline committee if required. The ultimate aim is to include health economic studies that are helpful for decision-making in the context of the guideline and the current NHS setting. If several studies are considered of sufficiently high applicability and methodological quality that they could all be included, then the health economist, in discussion with the committee if required, may decide to include only the most applicable studies and to selectively exclude the remaining studies. All studies excluded on the basis of applicability or methodological limitations will be listed with explanation in the excluded health economic studies appendix below. The health economist will be guided by the following hierarchies. *Setting:* • UK NHS (most applicable).

	• OECD countries with predominantly public health insurance systems (for example, France, Germany, Sweden). • OECD countries with predominantly private health insurance systems (for example, Switzerland). • Studies set in non-OECD countries or in the USA will be excluded before being assessed for applicability and methodological limitations. *Health economic study type:* • Cost–utility analysis (most applicable). • Other type of full economic evaluation (cost–benefit analysis, cost-effectiveness analysis, cost–consequences analysis). • Comparative cost analysis. • Non-comparative cost analyses including cost-of-illness studies will be excluded before being assessed for applicability and methodological limitations. *Year of analysis:* • The more recent the study, the more applicable it will be. • Studies published in 2005 or later (including any such studies included in the previous guidelines) but that depend on unit costs and resource data entirely or predominantly from before 2005 will be rated as 'Not applicable'. • Studies published before 2005 (including any such studies included in the previous guidelines) will be excluded before being assessed for applicability and methodological limitations. *Quality and relevance of effectiveness data used in the health economic analysis:* • The more closely the clinical effectiveness data used in the health economic analysis match with the outcomes of the studies included in the clinical review the more useful the analysis will be for decision-making in the guideline.

1

Appendix B – Literature search strategies

- What is clinical and cost-effectiveness of using imaging in the diagnosis of osteoarthritis in people with suspected osteoarthritis?

The literature searches for this review are detailed below and complied with the methodology outlined in Developing NICE guidelines: the manual.[34]

For more information, please see the Methodology review published as part of the accompanying documents for this guideline.

B.1 Clinical search literature search strategy

Searches were constructed using a PICO framework where population (P) terms were combined with Intervention (I) and in some cases Comparison (C) terms. Outcomes (O) are rarely used in search strategies for interventions as these concepts may not be well described in title, abstract or indexes and therefore difficult to retrieve. Search filters were applied to the search where appropriate.

Table 3: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline (OVID)	1946 – 17 November 2021	Randomised controlled trials Systematic review studies Observational studies Exclusions (animals studies, letters, comments)
Embase (OVID)	1974 – 17 November 2021	Randomised controlled trials Systematic review studies Observational studies Exclusions (animals studies, letters, comments)
The Cochrane Library (Wiley)	Cochrane Reviews to 2021 Issue 11 of 12 CENTRAL to 2021 Issue 11 of 12	None

Medline (Ovid) search terms

1.	exp osteoarthritis/
2.	(osteoarthriti* or osteo-arthriti* or osteoarthrotic or osteoarthros*).ti,ab.
3.	(degenerative adj2 arthritis).ti,ab.
4.	coxarthrosis.ti,ab.
5.	gonarthrosis.ti,ab.
6.	or/1-5
7.	letter/
8.	editorial/
9.	news/
10.	exp historical article/
11.	Anecdotes as Topic/
12.	comment/

13.	case report/
14.	(letter or comment*).ti.
15.	or/7-14
16.	randomized controlled trial/ or random*.ti,ab.
17.	15 not 16
18.	animals/ not humans/
19.	exp Animals, Laboratory/
20.	exp Animal Experimentation/
21.	exp Models, Animal/
22.	exp Rodentia/
23.	(rat or rats or mouse or mice or rodent*).ti.
24.	or/17-23
25.	6 not 24
26.	limit 25 to English language
27.	Magnetic Resonance Imaging/
28.	(mri* or nmr* or magnetic resonance).ti,ab.
29.	tomography, x-ray computed/ or tomography, x ray/
30.	((radiograph* or compute*) adj3 tomograph*).ti,ab.
31.	(echogra* or echotomogra* or sonograph* or ultrasound or ultrasonogra* or x-ray).ti,ab.
32.	(ultrasonic adj2 (tomogra* or imag* or diagnos*)).ti,ab.
33.	((CT or CAT) adj2 (imag* or scan* or diagnos*)).ti,ab.
34.	or/27-33
35.	26 and 34
36.	randomized controlled trial.pt.
37.	controlled clinical trial.pt.
38.	randomi#ed.ti,ab.
39.	placebo.ab.
40.	randomly.ti,ab.
41.	Clinical Trials as topic.sh.
42.	trial.ti.
43.	or/36-42
44.	Meta-Analysis/
45.	exp Meta-Analysis as Topic/
46.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
47.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
48.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
49.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
50.	(search* adj4 literature).ab.
51.	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
52.	cochrane.jw.
53.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
54.	or/44-53
55.	Epidemiologic studies/

56.	Observational study/
57.	exp Cohort studies/
58.	(cohort adj (study or studies or analys* or data)).ti,ab.
59.	((follow up or observational or uncontrolled or non randomi#ed or epidemiologic*) adj (study or studies or data)).ti,ab.
60.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort* or data)).ti,ab.
61.	Controlled Before-After Studies/
62.	Historically Controlled Study/
63.	Interrupted Time Series Analysis/
64.	(before adj2 after adj2 (study or studies or data)).ti,ab.
65.	exp case control studies/
66.	case control*.ti,ab.
67.	Cross-sectional studies/
68.	(cross sectional and (study or studies or review or analys* or cohort* or data)).ti,ab.
69.	or/55-68
70.	35 and (43 or 54 or 69)

Embase (Ovid) search terms

1.	exp osteoarthritis/
2.	(osteoarthriti* or osteo-arthriti* or osteoarthrotic or osteoarthros*).ti,ab.
3.	(degenerative adj2 arthritis).ti,ab.
4.	coxarthrosis.ti,ab.
5.	gonarthrosis.ti,ab.
6.	or/1-5
7.	letter.pt. or letter/
8.	note.pt.
9.	editorial.pt.
10.	case report/ or case study/
11.	(letter or comment*).ti.
12.	or/7-11
13.	randomized controlled trial/ or random*.ti,ab.
14.	12 not 13
15.	animal/ not human/
16.	nonhuman/
17.	exp Animal Experiment/
18.	exp Experimental Animal/
19.	animal model/
20.	exp Rodent/
21.	(rat or rats or mouse or mice or rodent*).ti.
22.	or/14-21
23.	6 not 22
24.	Limit 23 to English language
25.	nuclear magnetic resonance imaging/
26.	(mri* or nmr* or magnetic resonance).ti,ab.
27.	x-ray computed tomography/

28.	*computer assisted tomography/
29.	((radiograph* or compute*) adj3 tomograph*).ti,ab.
30.	(echogra* or echotomogra* or sonograph* or ultrasound or ultrasonogra* or x-ray).ti,ab.
31.	(ultrasonic adj2 (tomogra* or imag* or diagnos*)).ti,ab.
32.	((CT or CAT) adj2 (imag* or scan* or diagnos*)).ti,ab.
33.	or/25-32
34.	24 and 33
35.	random*.ti,ab.
36.	factorial*.ti,ab.
37.	(crossover* or cross over*).ti,ab.
38.	((doubl* or singl*) adj blind*).ti,ab.
39.	(assign* or allocat* or volunteer* or placebo*).ti,ab.
40.	crossover procedure/
41.	single blind procedure/
42.	randomized controlled trial/
43.	double blind procedure/
44.	or/35-43
45.	systematic review/
46.	meta-analysis/
47.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
48.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
49.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
50.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
51.	(search* adj4 literature).ab.
52.	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
53.	cochrane.jw.
54.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
55.	or/45-54
56.	Clinical study/
57.	Observational study/
58.	family study/
59.	longitudinal study/
60.	retrospective study/
61.	prospective study/
62.	cohort analysis/
63.	follow-up/
64.	cohort*.ti,ab.
65.	63 and 64
66.	(cohort adj (study or studies or analys* or data)).ti,ab.
67.	((follow up or observational or uncontrolled or non randomi#ed or epidemiologic*) adj (study or studies or data)).ti,ab.
68.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort* or data)).ti,ab.
69.	(before adj2 after adj2 (study or studies or data)).ti,ab.

70.	exp case control study/
71.	case control*.ti,ab.
72.	cross-sectional study/
73.	(cross sectional and (study or studies or review or analys* or cohort* or data)).ti,ab.
74.	or/56-62,65-73
75.	34 and (44 or 55 or 74)

Cochrane Library (Wiley) search terms

#1.	MeSH descriptor: [Osteoarthritis] explode all trees
#2.	(osteoarthriti* or osteo-arthriti* or osteoarthrotic or osteoarthros*):ti,ab
#3.	(degenerative near/2 arthritis):ti,ab
#4.	coxarthrosis:ti,ab
#5.	gonarthrosis:ti,ab
#6.	(or #1-#5)
#7.	MeSH descriptor: [Magnetic Resonance Imaging] explode all trees
#8.	(mri* or nmr* or magnetic resonance):ti,ab
#9.	MeSH descriptor: [Tomography, X-Ray Computed] explode all trees
#10.	MeSH descriptor: [Tomography, X-Ray] explode all trees
#11.	((radiograph* or compute*) near/3 tomograph*):ti,ab
#12.	(echogra* or echotomogra* or sonograph* or ultrasound or ultrasonogra* or x-ray):ti,ab
#13.	(ultrasonic near/2 (tomogra* or imag* or diagnos*)):ti,ab
#14.	((CT or CAT) near/2 (imag* or scan* or diagnos*)):ti,ab
#15.	(or #7-#14)
#16.	#6 and #15

B.2 Health Economics literature search strategy

Health economic evidence was identified by conducting a broad search relating to a Gout population in NHS Economic Evaluation Database (NHS EED – this ceased to be updated after March 2015) and the Health Technology Assessment database (HTA – this ceased to be updates after March 2018). NHS EED and HTA databases are hosted by the Centre for Research and Dissemination (CRD). Additional searches were run on Medline and Embase for health economics studies and quality of life studies. Searches for quality of life studies were run for general information.

Table 4: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline	1 January 2014 – 17 November 2021	Health economics studies Quality of life studies Exclusions (animals studies, letters, comments)
Embase	1 January 2014 – 17 November 2021	Health economics studies Quality of life studies Exclusions (animals studies, letters, comments)
Centre for Research and Dissemination (CRD)	HTA - Inception – 31 March 2018	None

Database	Dates searched	Search filter used
	NHSEED - Inception to 31 March 2015	

Medline (Ovid) search terms

1.	exp osteoarthritis/
2.	(osteoarthriti* or osteo-arthriti* or osteoarthrotic or osteoarthros*).ti,ab.
3.	(degenerative adj2 arthritis).ti,ab.
4.	coxarthrosis.ti,ab.
5.	gonarthrosis.ti,ab.
6.	or/1-5
7.	letter/
8.	editorial/
9.	news/
10.	exp historical article/
11.	Anecdotes as Topic/
12.	comment/
13.	case report/
14.	(letter or comment*).ti.
15.	or/7-14
16.	randomized controlled trial/ or random*.ti,ab.
17.	15 not 16
18.	animals/ not humans/
19.	exp Animals, Laboratory/
20.	exp Animal Experimentation/
21.	exp Models, Animal/
22.	exp Rodentia/
23.	(rat or rats or mouse or mice or rodent*).ti.
24.	or/17-23
25.	6 not 24
26.	limit 25 to English language
27.	Economics/
28.	Value of life/
29.	exp "Costs and Cost Analysis"/
30.	exp Economics, Hospital/
31.	exp Economics, Medical/
32.	Economics, Nursing/
33.	Economics, Pharmaceutical/
34.	exp "Fees and Charges"/
35.	exp Budgets/
36.	budget*.ti,ab.
37.	cost*.ti.

38.	(economic* or pharmaco?economic*).ti.
39.	(price* or pricing*).ti,ab.
40.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
41.	(financ* or fee or fees).ti,ab.
42.	(value adj2 (money or monetary)).ti,ab.
43.	or/27-42
44.	quality-adjusted life years/
45.	sickness impact profile/
46.	(quality adj2 (wellbeing or well being)).ti,ab.
47.	sickness impact profile.ti,ab.
48.	disability adjusted life.ti,ab.
49.	(qal* or qtime* or qwb* or daly*).ti,ab.
50.	(euroqol* or eq5d* or eq 5*).ti,ab.
51.	(health utility* or utility score* or disutilit* or utility value*).ti,ab.
52.	(hui or hui1 or hui2 or hui3).ti,ab.
53.	(health* year* equivalent* or hye or hyes).ti,ab.
54.	discrete choice*.ti,ab.
55.	rosser.ti,ab.
56.	(willingness to pay or time tradeoff or time trade off or tto or standard gamble*).ti,ab.
57.	(sf36* or sf 36* or short form 36* or shortform 36* or shortform36*).ti,ab.
58.	(sf20 or sf 20 or short form 20 or shortform 20 or shortform20).ti,ab.
59.	(sf12* or sf 12* or short form 12* or shortform 12* or shortform12*).ti,ab.
60.	(sf8* or sf 8* or short form 8* or shortform 8* or shortform8*).ti,ab.
61.	(sf6* or sf 6* or short form 6* or shortform 6* or shortform6*).ti,ab.
62.	or/44-61
63.	26 and (43 or 62)

Embase (Ovid) search terms

1.	exp osteoarthritis/
2.	(osteoarthriti* or osteo-arthriti* or osteoarthrotic or osteoarthros*).ti,ab.
3.	(degenerative adj2 arthritis).ti,ab.
4.	coxarthrosis.ti,ab.
5.	gonarthrosis.ti,ab.
6.	or/1-5
7.	letter.pt. or letter/
8.	note.pt.
9.	editorial.pt.
10.	case report/ or case study/
11.	(letter or comment*).ti.
12.	or/7-11

13.	randomized controlled trial/ or random*.ti,ab.
14.	12 not 13
15.	animal/ not human/
16.	nonhuman/
17.	exp Animal Experiment/
18.	exp Experimental Animal/
19.	animal model/
20.	exp Rodent/
21.	(rat or rats or mouse or mice or rodent*).ti.
22.	or/14-21
23.	6 not 22
24.	Limit 23 to English language
25.	health economics/
26.	exp economic evaluation/
27.	exp health care cost/
28.	exp fee/
29.	budget/
30.	funding/
31.	budget*.ti,ab.
32.	cost*.ti.
33.	(economic* or pharmaco?economic*).ti.
34.	(price* or pricing*).ti,ab.
35.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
36.	(financ* or fee or fees).ti,ab.
37.	(value adj2 (money or monetary)).ti,ab.
38.	or/25-37
39.	quality adjusted life year/
40.	"quality of life index"/
41.	short form 12/ or short form 20/ or short form 36/ or short form 8/
42.	sickness impact profile/
43.	(quality adj2 (wellbeing or well being)).ti,ab.
44.	sickness impact profile.ti,ab.
45.	disability adjusted life.ti,ab.
46.	(qal* or qtime* or qwb* or daly*).ti,ab.
47.	(euroqol* or eq5d* or eq 5*).ti,ab.
48.	(qol* or hql* or hqol* or h qol* or hrqol* or hr qol*).ti,ab.
49.	(health utility* or utility score* or disutilit* or utility value*).ti,ab.
50.	(hui or hui1 or hui2 or hui3).ti,ab.
51.	(health* year* equivalent* or hye or hyes).ti,ab.
52.	discrete choice*.ti,ab.

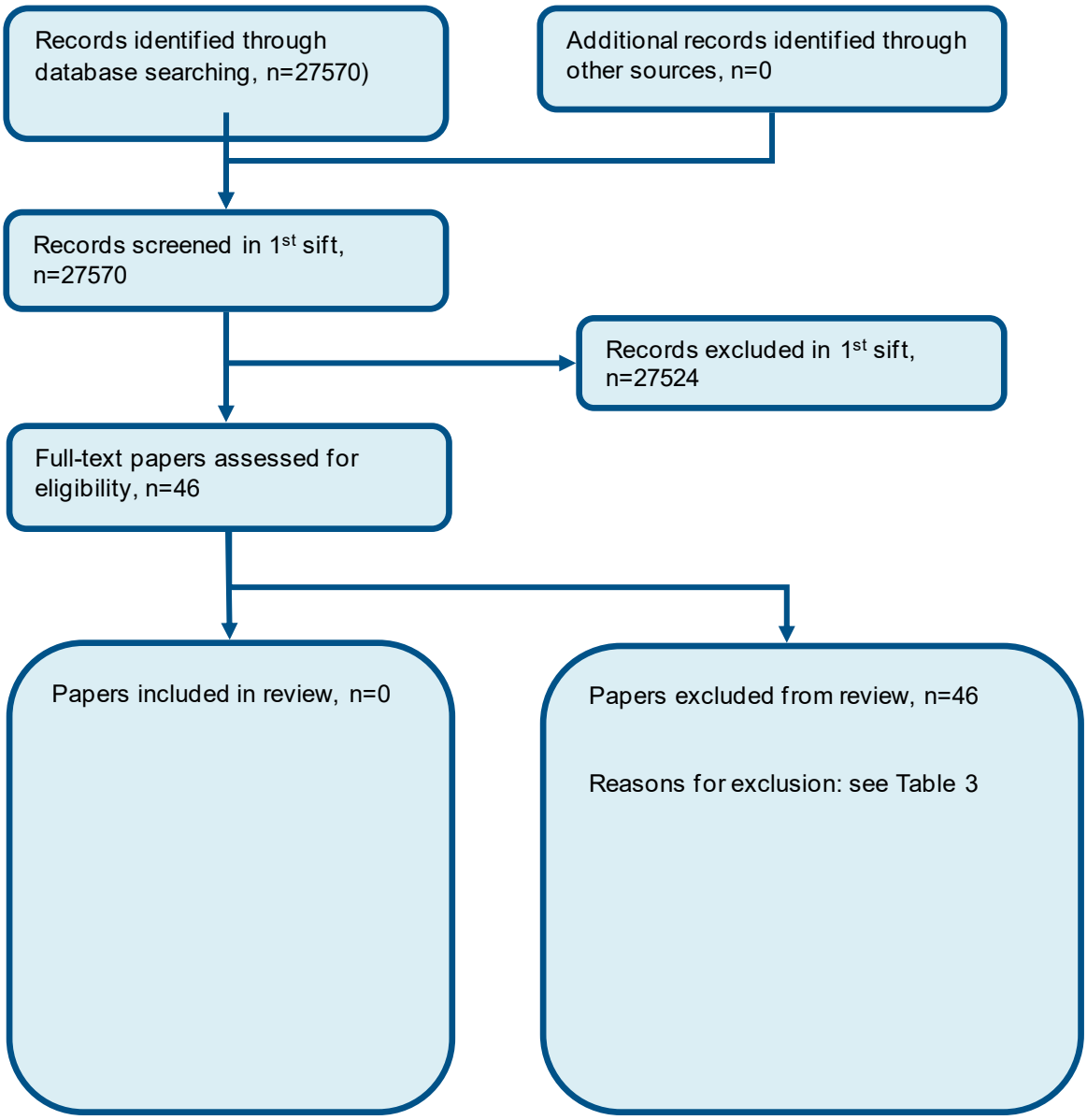
53.	rosser.ti,ab.
54.	(willingness to pay or time tradeoff or time trade off or tto or standard gamble*).ti,ab.
55.	(sf36* or sf 36* or short form 36* or shortform 36* or shortform36*).ti,ab.
56.	(sf20 or sf 20 or short form 20 or shortform 20 or shortform20).ti,ab.
57.	(sf12* or sf 12* or short form 12* or shortform 12* or shortform12*).ti,ab.
58.	(sf8* or sf 8* or short form 8* or shortform 8* or shortform8*).ti,ab.
59.	(sf6* or sf 6* or short form 6* or shortform 6* or shortform6*).ti,ab.
60.	or/39-59
61.	24 and (38 or 60)

NHS EED and HTA (CRD) search terms

#1.	MeSH DESCRIPTOR Osteoarthritis EXPLODE ALL TREES
#2.	((osteoarthriti* or osteo-arthriti* or osteoarthrotic or osteoarthros*))
#3.	((degenerative adj2 arthritis))
#4.	(coxarthrosis)
#5.	(gonarthrosis)
#6.	#1 OR #2 OR #3 OR #4 OR #5
#7.	(#6) IN NHSEED
#8.	(#6) IN HTA

Appendix C – Effectiveness evidence study selection

Figure 1: Flow chart of clinical study selection for the review of additional benefit of imaging in the diagnosis of osteoarthritis



Appendix D – Effectiveness evidence

No studies were included.

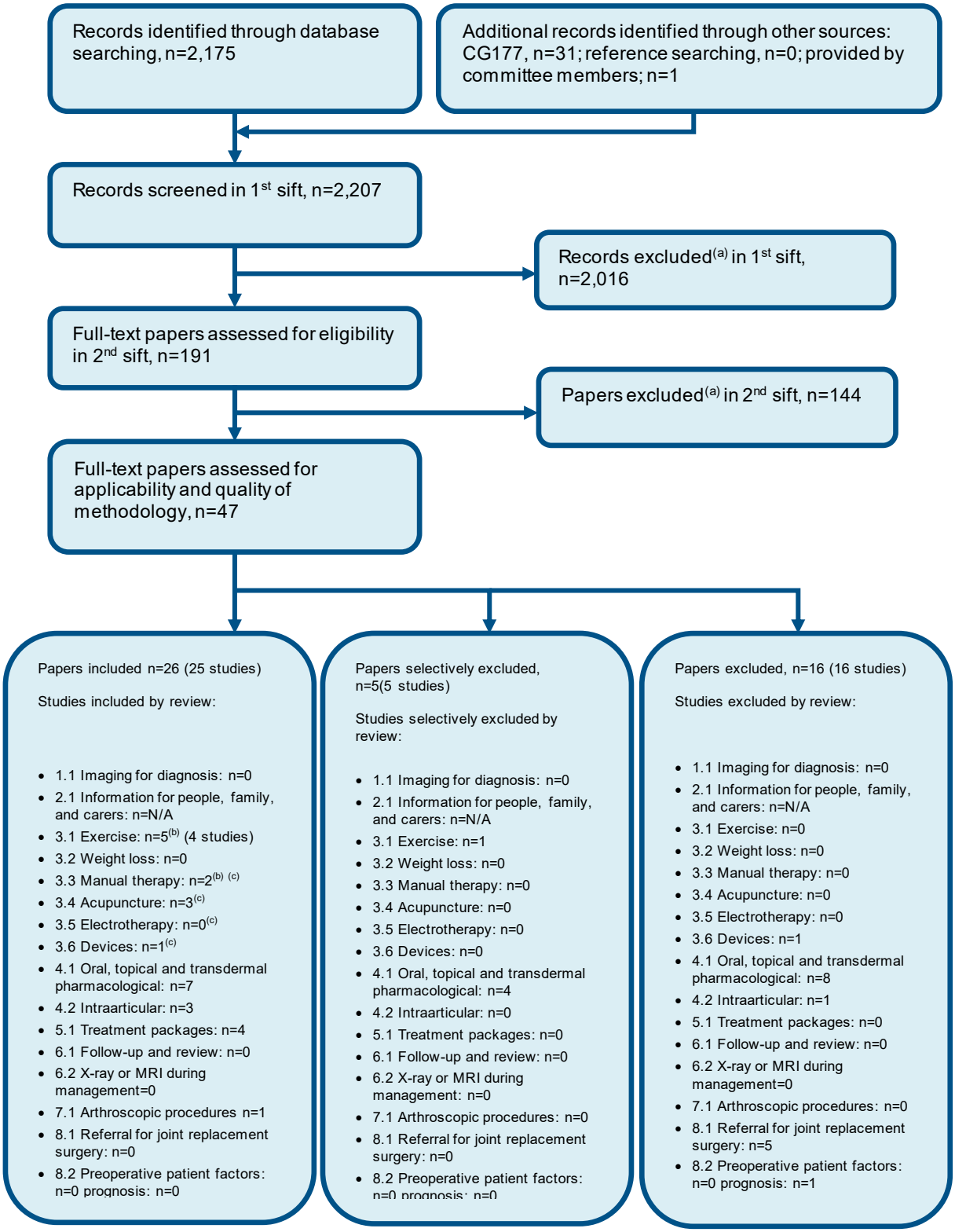
Appendix E – Forest plots

No studies were included.

Appendix F – GRADE tables

No studies were included.

Appendix G – Economic evidence study selection



(a) Non-relevant population, intervention, comparison, design or setting; non-English language.
(b) Two articles identified were applicable to Q3.1 and Q3.3, for the purposes of this diagram they have been included under Q3.1 only.
(c) One article identified was applicable to Q3.3, Q3.4, Q3.5 and Q3.6, for the purposes of this diagram it has been included under Q3.3 only.

Appendix H – Economic evidence tables

There were no health economic studies found in the review

Appendix I – Health economic model

No original economic modelling was undertaken.

Appendix J – Excluded studies

Clinical studies

Table 5: Studies excluded from the clinical review

Reference	Reason for exclusion
Abedin 2019[1]	Incorrect comparison (comparing different models of diagnosis using the same imaging modality)
Agoda-Koussema 2012[2]	Not in English.
Alvarez 2005[3]	Non-comparative study.
Amitai 2015[4]	Included people with rheumatoid arthritis. Diagnostic accuracy study.
Atar 2019[5]	Incorrect comparison (comparing serum endothelin levels with clinical/sonographic measurements)
Badel 2012[6]	Incorrect comparison. Diagnostic accuracy study.
Baker 2020[7]	Incorrect comparison (comparing bone scan to magnetic resonance imaging). No usable outcomes.
Boegard 2003[8]	Incorrect comparison. Cross-sectional study comparing people with and without radiographic evidence of osteoarthritis.
Brandt 2000[9]	Incorrect comparison (comparing people with radiographic knee osteoarthritis to people without radiographic knee osteoarthritis).
Breasley 2007[10]	Excludes people with osteoarthritis.
Cai 2020[11]	Incorrect comparison (comparing people with osteoarthritis on knee radiograph, osteoarthritis on magnetic resonance imaging, both and neither to each other)
Chen 2015[13]	Incorrect comparison (compares people with ultrasound grades of osteoarthritis)
Chen 2020[12]	Incorrect population (including people with knee osteoarthritis confirmed by arthroscopy and healthy participants)
Chiba 2016[14]	Incorrect comparison (compared people with different grades of radiographic knee osteoarthritis with the presence of effusion on ultrasound)
Emshoff 2001[15]	Diagnostic accuracy study. No usable outcomes.
Ezzat 2013[16]	Incorrect comparison (compared people with and without radiographic, symptomatic and magnetic resonance imaging evidence of osteoarthritis when all participants had all of the types of imaging)
Gluckert 1990[17]	Not in English
Haghighi 2017[18]	Incorrect comparison (investigated a correlation between ultrasound, radiographic and symptomatic osteoarthritis using the same imaging on all participants)
Hirsch 2017[19]	Incorrect comparison (investigates the use of imaging guidance for intra-articular injections)
Ip 2011[20]	Incorrect comparison (compares people with different severities of radiographic osteoarthritis to magnetic resonance imaging findings where all people had both imaging techniques performed).
Javaid 2012[21]	Incorrect comparison (compares people with radiographic osteoarthritis to magnetic resonance imaging findings where all people had both imaging techniques performed).
Keen 2009[22]	Systematic review with a different PICO to that in the protocol (investigating ultrasound scoring systems).
Kim 2008[23]	Incorrect intervention (bone scan).

Reference	Reason for exclusion
Kim 2017[24]	Incorrect comparison (investigates findings on SPECT/CT).
Kinds 2011[25]	Systematic review with a different PICO to that in the protocol (investigating radiographic severity in people with symptomatic osteoarthritis)
Kroon 2018[26]	Wrong study type (cross-sectional study)
Laursen 2016[27]	Incorrect comparison (imaging post-surgical prosthesis insertion)
Macri 2021[28]	Wrong study type (cross-sectional study)
Magnusson 2018[29]	Incorrect comparison (all participants had imaging at the start of the study)
Matsos 2009[30]	Incorrect comparison (includes people without osteoarthritis)
Menz 2021[31]	Wrong study type (cross-sectional study)
Mortada 2016[32]	Incorrect comparison (investigating diagnostic accuracy in people who had all had ultrasound scans)
Nalamachu 2020[33]	Wrong study type (cross-sectional study)
Neiman 2016[35]	Incorrect intervention (magnetic resonance arthrography obtained with all participants including people without osteoarthritis)
Pan 2019[37]	Incorrect comparison (investigating different phenotypes of knee pain. All people had imaging).
Park 2012[38]	Wrong population (includes people with temporomandibular joint disorders, not just osteoarthritis)
Roberts 2015[39]	Incorrect comparison (compares people evaluated by primary care physicians and people evaluated by staff orthopaedic surgeons).
Roux 2016[40]	Incorrect comparison (compares semi-flexed x-ray to anteroposterior extended and semi-flexed x-ray).
Sheridan 2021[41]	Incorrect population (including people with meniscal tears as well as people with knee osteoarthritis)
Smink 2014[42]	Incorrect comparison (investigating the implementation of a stepped care sequence).
Thomas 2008[43]	No relevant outcomes (reports dichotomous outcomes for values that the protocol specifies should be reported as continuous outcomes).
Wang 2018[45]	Incorrect comparison (compares people with and without radiographic knee osteoarthritis).
Wang 2021[44]	Incorrect intervention (predictors for early stage arthritis- all people had imaging)
Whittaker 2018[46]	Incorrect comparison (compares people with and without magnetic resonance imaging osteoarthritis).
Yoong 2012[47]	Incorrect comparison (investigating image guided intra-articular injections).
Zhu 2017[48]	Incorrect comparison (compares people with different severities of imaging, all people had magnetic resonance imaging).

Health Economic studies

Published health economic studies that met the inclusion criteria (relevant population, comparators, economic study design, published 2005 or later and not from non-OECD country or USA) but that were excluded following appraisal of applicability and methodological quality are listed below. See the health economic protocol for more details.

None.