# National Institute for Health and Care Excellence

Draft for consultation

# Osteoarthritis: assessment and management (update)

[M] Evidence reviews for the clinical and costeffectiveness of imaging during the management of osteoarthritis

NICE guideline <number>

Evidence reviews underpinning recommendation 1.5.4 and research recommendations in the NICE guideline

**April** 2022

**Draft for Consultation** 



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## 1 Imaging to inform management of2 osteoarthritis

#### 1.1 Review question

- 4 What is the clinical and cost-effectiveness of using radiological investigations (x-ray,
- 5 ultrasound, MRI, CT) to inform management choices for people with osteoarthritis?

#### 1.1.1 Introduction

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- 7 People with osteoarthritis may have ongoing issues that are not completely managed by the
- 8 interventions prescribed. While there are times where imaging is clearly indicated (e.g. with a
- 9 history or worsening symptoms triggered by trauma) it is not apparent whether it provides
- any benefit using it more widely as management plans are made predominantly on the basis
- 11 of symptoms and function. There is concern about the resource impact for the NHS if
- imaging is widely used without leading to a change in the person's management.
- 13 Current practice for people with osteoarthritis is to undertake imaging if the patient reports
- worsening symptoms, wants to assess for deterioration and to image prior to referral. Some
- 15 clinicians may be more likely to use imaging than others, further, once patients have had
- imaging once, they are more likely to have it again in the future.
- 17 This review aims to determine whether there is any benefit in using imaging to aid clinicians
- in decision making regarding choices for the management of osteoarthritis.

#### 19 **1.1.2 Summary of the protocol**

#### 20 Table 1: PICO characteristics of review question

#### **Population** Adults (age ≥16 years) with osteoarthritis affecting any joint Exclusion: • Children (age <16 years) • People with conditions that may make them susceptible to osteoarthritis or often occur alongside osteoarthritis (including: crystal arthritis, inflammatory arthritis, septic arthritis, hemochromatosis, haemophilic arthropathy, diseases of childhood that may predispose to osteoarthritis, and malignancy). • Studies with an unclear population (e,g, proportion of participants with osteoarthritis unclear) Spinal osteoarthritis Interventions Imaging before a surgical or non-surgical intervention (for example: imaging used to determine whether an intra-articular injection should be performed, using any criteria provided in the study) X-ray before o A surgical intervention o A non-surgical intervention · Ultrasound before o A surgical intervention o A non-surgical intervention MRI before A surgical intervention

	∘ A non-surgical intervention
	CT before
	○ A surgical intervention
	∘ A non-surgical intervention
	The radiological interventions will be analysed separately, as will surgical and non-surgical interventions for each imaging type.
Comparisons	No imaging before a non-surgical/surgical intervention (decision made purely on clinical presentation)
	Confounding factors (if including non-randomised evidence):
	Age
	· ·
	Baseline symptoms such as pain and/or function  Baseline SMI (security the shapes of SMI)
	Baseline BMI (or weight in the absence of BMI)
Outcomes	Primary outcomes (critical outcomes):
	Stratify by ≤/>3 months (longest time-point in each):
	<ul> <li>Health-related quality of life [validated patient-reported outcomes, continuous data prioritised]</li> </ul>
	Pain [validated patient-reported outcomes, continuous data prioritised]
	<ul> <li>Physical function [validated patient-reported outcomes, continuous data prioritised]</li> </ul>
	Changes to planned management [dichotomous data prioritised]
	Secondary outcomes (important outcomes):
	<ul> <li>Psychological distress [validated patient-reported outcomes, continuous data prioritised]</li> </ul>
	Osteoarthritis flares [validated patient-reported outcomes, continuous data prioritised]
	Number of adverse events [dichotomous data prioritised]
Study design	Systematic reviews of RCTs
	• RCTs
	If insufficient RCT evidence is available, non-randomised studies will be
	considered, including:
	Prospective and retrospective cohort studies
	Case control studies (if no other evidence identified)

1 For full details see the review protocol in Appendix A.

#### 1.1.3 Methods and process

- 3 This evidence review was developed using the methods and process described in
- 4 <u>Developing NICE guidelines: the manual</u>. Methods specific to this review question are
- described in the review protocol in Appendix A and the methods document.
- 6 Declarations of interest were recorded according to NICE's conflicts of interest policy.

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#### 1 1.1.4 Effectiveness evidence

#### 2 1.1.4.1 Included studies

- 3 No relevant clinical studies comparing imaging used before management to no imaging used
- 4 before management.
- 5 Some studies that were excluded compared imaging used before management to no imaging
- 6 used before management. However, in these cases the population did not necessarily have
- 7 osteoarthritis, and instead had a range of conditions (such as ligamentous injuries) and were
- 8 therefore excluded.
- 9 See also the study selection flow chart in Appendix C.

#### 10 1.1.4.2 Excluded studies

11 See the excluded studies list in Appendix J.

#### 1.1.5 Summary of studies included in the effectiveness evidence

13 No evidence was identified for this review

#### 14 **1.1.6 Summary of the effectiveness evidence**

No evidence was identified for this review.

#### 16 1.1.7 Economic evidence

#### 17 1.1.7.1 Included studies

18 No health economic studies were included.

#### 19 1.1.7.2 Excluded studies

- 20 No relevant health economic studies were excluded due to limited applicability or
- 21 methodological limitations.
- See also the health economic study selection flow chart in Appendix G.

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#### 1 1.1.8 Summary of included economic evidence

There was no economic evidence found.

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- 1 1.1.9 Economic model
- 2 This area was not prioritised for new cost-effectiveness analysis.

#### 1 **1.1.10 Unit costs**

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

Resource	Unit costs	Source
CT scan	£94	NHS Reference Costs
MRI scan	£173	2019/20 <sup>52</sup>
Plain film imaging (including x-ray)	£56	
Ultrasound	£75	

#### 3 1.1.11 Economic evidence statements

No relevant economic evaluations were identified.

#### 5 1.1.12 The committee's discussion and interpretation of the evidence

#### 1.1.12.1. The outcomes that matter most

- 7 The critical outcomes were quality of life, pain and physical function. These were considered
- 8 critical due to their importance to people with osteoarthritis. The Osteoarthritis Research
- 9 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
- 12 interventions. Changes to planned management was included as a measure of the effect of
- doing imaging. If imaging was important to informing management, the committee expected
- that there would be changes to planned management before imaging was available.
- 15 Psychological distress, osteoarthritis flares and number of adverse events were considered
- 16 as important outcomes.
- 17 The committee considered osteoarthritis flares to be important in the lived experience and
- management of osteoarthritis. However, these were also considered difficult to measure with
- 19 no clear consensus on their definition. The Flares in OA OMERACT working group have
- 20 proposed an initial definition and domains of OA flares through a consensus exercise; "it is a
- transient state, different from the usual state of the condition, with a duration of a few days,
- characterized by onset, worsening of pain, swelling, stiffness, impact on sleep, activity,
- functioning, and psychological aspects that can resolve spontaneously or lead to a need to
- adjust therapy.". However, this has been considered to have limitations and has not been
- widely adopted. Therefore, the committee included the outcome accepting any reasonable
- definition provided by any studies discussing the event.
- 27 Mortality was considered as a composite of serious adverse events rather than as a discrete
- 28 outcome and categorised as an important outcome. Osteoarthritis as a disease process is
- 29 not considered to cause mortality by itself and mortality is an uncommon outcome from
- 30 osteoarthritis interventions.

#### 31 1.1.12.2 The quality of the evidence

32 No evidence was identified for this review.

#### 33 1.1.12.3 Committee consideration of advantages and disadvantages

- No evidence was identified for this review. The committee discussed how imaging is
- 35 currently used. The previous version of the guideline did not make a recommendation
- regarding using imaging for the management of osteoarthritis. Current practice is varied.

- 1 While osteoarthritis is diagnosed clinically, in some cases clinicians may request imaging to
- 2 confirm that there is no new alternative diagnosis which may change management decisions.
- 3 Imaging is required to confirm the structural severity of osteoarthritis changes where is can
- 4 be used to inform preoperative planning (including the size of surgical implants). In this way
- 5 imaging is seen as essential for surgical planning. The committee discussed when this
- 6 imaging should take place. Current practice is inconsistent across the country, with some
- 7 areas requiring imaging to be completed before referral to a surgeon, while in other areas the
- 8 surgeon will request imaging after the referral has been accepted. The majority of this
- 9 imaging will employ X-rays.
- 10 There was no evidence to determine if imaging would be useful for non-surgical
- 11 management decisions. The committee's consensus agreement was that imaging would not
- be beneficial for non-surgical management as it would be unlikely to change decisions
- regarding management while adding additional costs and potential risks. With the previous
- thoughts on surgical planning and the committee's consensus on non-surgical management
- decisions the committee agreed recommendation 1.5.4.
- 16 Imaging may be used to guide interventional procedures. This was not considered in this
- 17 review question (see 4.2 the clinical and cost-effectiveness of intra-articular injections for
- people with osteoarthritis for more information) but was noted as an important area where
- imaging may be required. Imaging may be more important for different joints. For smaller,
- 20 more complicated joints (such as foot and hand), imaging may be more important for
- 21 investigating progression and planning for injection. However, for larger joints (such as hip
- and knee) this may not be required.
- 23 The committee noted that evidence was needed in this area to gain more information about
- 24 when imaging could be useful. While the committee agreed that there was unlikely to be a
- benefit from imaging for non-surgical management, there was no evidence to base this on.
- Due to this, they recommended further research into the use of management in primary care
- to guide non-surgical management (see Appendix K.1).
- 28 Finally, the committee noted the inconsistency across the country of when imaging is
- 29 performed when considering surgery. Therefore, they recommended investigating the clinical
- and cost-effectiveness of imaging when performed in different clinical settings, including
- 31 primary, intermediary and secondary care to determine where the most effective setting is to
- 32 complete imaging for surgical management (see Appendix K.2).

#### 1.1.12.4 Cost effectiveness and resource use

- 34 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,
- 36 with the cheapest option being x-ray imaging and the most expensive being an MRI scan.
- 37 In the absence of evidence of clinical effectiveness or cost effectiveness the committee did
- 38 not recommend imaging in the management of osteoarthritis, other than as an essential
- 39 component of preoperative assessment.

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#### 1.1.12.5 Other factors the committee took into account

- The committee noted that osteoarthritis research in general does not appear to represent the
- 42 diverse population of people with osteoarthritis. They agreed that any further 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.
- 45 Future work 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. With
- 47 this in mind the committee sub-grouped their research recommendation by these protected

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- 1 characteristics where appropriate while suggesting that people from each group should be
- 2 included in the research to ensure that it is applicable to the entire population

#### 3 1.1.13 Recommendations supported by this evidence review

- 4 This evidence review supports recommendation 1.5.4 and the research recommendation on
- 5 Imaging for Management. Other evidence supporting these recommendations can be found
- 6 in evidence review M.

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#### 1.1.14 References

1

- 2 1. Akdemir G, Van Der Bijl A, De Lange-Brokaar B, Huizinga T, Allaart C, Kloppenburg M. Magnetic resonance imaging outcomes in patients with chronic or recurrent gonarthritis treated with intra-articular infliximab or corticosteroid injections. Annals of the Rheumatic Diseases. 2015; 2):882-883
- Aronowitz JG, Harmsen WS, Schleck CD, Sperling JW, Cofield RH, Sanchez-Sotelo J. Radiographs and computed tomography scans show similar observer agreement when classifying glenoid morphology in glenohumeral arthritis. Journal of Shoulder and Elbow Surgery. 2017; 26(9):1533-1538
- 10 3. Atchia I, Kane D, Reed MR, Isaacs JD, Birrell F. Efficacy of a single ultrasound-11 guided injection for the treatment of hip osteoarthritis. Annals of the Rheumatic 12 Diseases. 2011; 70(1):110-116
- Baum T, Joseph GB, Arulanandan A, Nardo L, Virayavanich W, Carballido-Gamio J et al. Association of magnetic resonance imaging-based knee cartilage T2 measurements and focal knee lesions with knee pain: data from the Osteoarthritis Initiative. Arthritis Care and Research. 2012; 64(2):248-255
- 5. Benli Kucuk E, Ozyemisci Taskiran O, Tokgoz N, Meray J. Effects of isokinetic, isometric, and aerobic exercises on clinical variables and knee cartilage volume using magnetic resonance imaging in patients with osteoarthritis. Turkiye Fiziksel Tip ve Rehabilitasyon Dergisi. 2018; 64(1):8-16
- 21 6. Bevers K, Zweers MC, Vriezekolk JE, Bijlsma JW, den Broeder AA. Are
  22 ultrasonographic signs of inflammation predictors for response to intra-articular
  23 glucocorticoids in knee osteoarthritis? Clinical and Experimental Rheumatology.
  24 2014; 32(6):930-934
- Blackburn WD, Jr., Bernreuter WK, Rominger M, Loose LL. Arthroscopic evaluation of knee articular cartilage: a comparison with plain radiographs and magnetic resonance imaging. Journal of Rheumatology. 1994; 21(4):675-679
- 8. Boegard T. Radiography and bone scintigraphy in osteoarthritis of the knee-comparison with MR imaging. Acta Radiologica - Supplementum. 1998; 418:7-37
- Boegard T, Rudling O, Dahlstrom J, Dirksen H, Petersson IF, Jonsson K. Bone
   scintigraphy in chronic knee pain: comparison with magnetic resonance imaging.
   Annals of the Rheumatic Diseases. 1999; 58(1):20-26
- 33 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
- 35 11. Bridgman S, Richards PJ, Walley G, MacKenzie G, Clement D, McCall I et al. The 36 effect of magnetic resonance imaging scans on knee arthroscopy: randomized 37 controlled trial. Arthroscopy. 2007; 23(11):1167-1173.e1161
- 38 12. Broderick LS, Turner DA, Renfrew DL, Schnitzer TJ, Huff JP, Harris C. Severity of 39 articular cartilage abnormality in patients with osteoarthritis: Evaluation with fast spin-40 echo MR vs arthroscopy. American Journal of Roentgenology. 1994; 162(1):99-103
- 41 13. Buendia-Lopez D, Medina-Quiros M, Fernandez-Villacanas Marin MA. Clinical and radiographic comparison of a single LP-PRP injection, a single hyaluronic acid injection and daily NSAID administration with a 52-week follow-up: a randomized controlled trial. Journal of Orthopaedics and Traumatology. 2018; 19(1):3
- 45
   46
   Case JP, Baliunas AJ, Block JA. Lack of efficacy of acetaminophen in treating
   symptomatic knee osteoarthritis: a randomized, double-blind, placebo-controlled

- 1 comparison trial with diclofenac sodium. Archives of Internal Medicine. 2003; 163(2):169-178
- Chao J, Wu C, Sun B, Hose MK, Quan A, Hughes TH et al. Inflammatory
   characteristics on ultrasound predict poorer longterm response to intraarticular
   corticosteroid injections in knee osteoarthritis. Journal of Rheumatology. 2010;
   37(3):650-655
- 7 16. Collins JE, Losina E, Marx RG, Guermazi A, Jarraya M, Jones MH et al. Early MRIbased Changes in Patients with Meniscal Tear and Osteoarthritis. Arthritis Care and Research. 2020; 72(5):630-640
- 10 17. Cubukcu D, Ardic F, Karabulut N, Topuz O. Hylan G-F 20 efficacy on articular cartilage quality in patients with knee osteoarthritis: clinical and MRI assessment. Clinical Rheumatology. 2005; 24(4):336-341
- 13 18. Ding C, Zhang Y, Hunter D. Use of imaging techniques to predict progression in osteoarthritis. Current Opinion in Rheumatology. 2013; 25(1):127-135
- Dutton AQ, Yeo SJ, Yang KY, Lo NN, Chia KU, Chong HC. Computer-assisted
   minimally invasive total knee arthroplasty compared with standard total knee
   arthroplasty. A prospective, randomized study. Journal of Bone & Joint Surgery American Volume. 2008; 90(1):2-9
- 20. Eymard F, Chevalier X, Conrozier T. Obesity and radiological severity are associated with viscosupplementation failure in patients with knee osteoarthritis. Journal of Orthopaedic Research. 2017; 35(10):2269-2274
- 22 21. Feczko P, Engelmann L, Arts JJ, Campbell D. Computer-assisted total knee 23 arthroplasty using mini midvastus or medial parapatellar approach technique: A 24 prospective, randomized, international multicentre trial. BMC Musculoskeletal 25 Disorders. 2016; 17:19
- 22. Gaffney K, Ledingham J, Perry JD. Intra-articular triamcinolone hexacetonide in knee
   osteoarthritis: factors influencing the clinical response. Annals of the Rheumatic
   Diseases. 1995; 54(5):379-381
- 29 23. Gudbergsen H, Boesen M, Christensen R, Astrup A, Bliddal H. Radiographs and low field MRI (0.2T) as predictors of efficacy in a weight loss trial in obese women with knee osteoarthritis. BMC Musculoskeletal Disorders. 2011; 12:56
- 32 24. Gudbergsen H, Boesen M, Lohmander LS, Christensen R, Henriksen M, Bartels EM 33 et al. Weight loss is effective for symptomatic relief in obese subjects with knee 34 osteoarthritis independently of joint damage severity assessed by high-field MRI and 35 radiography. Osteoarthritis and Cartilage. 2012; 20(6):495-502
- Gudbergsen H, Lohmander LS, Jones G, Christensen R, Bartels EM, Danneskiold-Samsoe B et al. Correlations between radiographic assessments and MRI features of knee osteoarthritis--a cross-sectional study. Osteoarthritis and Cartilage. 2013; 21(4):535-543
- 40 26. Guermazi A, Kalsi G, Niu J, Crema MD, Copeland RO, Orlando A et al. Structural
  41 effects of intra-articular TGF-beta1 in moderate to advanced knee osteoarthritis: MRI42 based assessment in a randomized controlled trial. BMC Musculoskeletal Disorders.
  43 2017; 18(1):461
- 44 27. Guermazi A, Kraines J, Aydemir A, Wax S, Crema M, Hochberg MC et al. Structural 45 effects of intra-articular sprifermin in symptomatic radiographic knee osteoarthritis: A 46 post-hoc analysis of cartilage morphology over the 2-year treatment-period of a 5-

- year randomized, placebo-controlled, phase II study. Arthritis and rheumatology. 2018; 70 (Supplement 9):465-466
- 3 28. Han W, Aitken D, Zheng S, Wluka AE, Zhu Z, Blizzard L et al. Association between 4 quantitatively measured infrapatellar fat pad high signal intensity alteration and MRI-5 assessed progression of knee osteoarthritis. Arthritis Care and Research. 2019; 6 71(5):638-646
- 7 29. Hayashi D, Roemer FW, Guermazi A. Imaging of osteoarthritis Recent research developments and future perspective. British Journal of Radiology. 2018; 91(1085):20170349
- 30. Hellio le Graverand MP, Clemmer RS, Redifer P, Brunell RM, Hayes CW, Brandt KD et al. A 2-year randomised, double-blind, placebo-controlled, multicentre study of oral selective iNOS inhibitor, cindunistat (SD-6010), in patients with symptomatic osteoarthritis of the knee. Annals of the Rheumatic Diseases. 2013; 72(2):187-195
- Henricsdotter C, Ellegaard K, Klokker L, Bartholdy C, Bandak E, Bartels EM et al.
   Changes in ultrasound assessed markers of inflammation following intra-articular
   steroid injection combined with exercise in knee osteoarthritis: exploratory outcome
   from a randomized trial. Osteoarthritis and Cartilage. 2016; 24(5):814-821
- Hochberg M, Guermazi A, Guehring H, Aydemir A, Wax S, Fleuranceau-Morel P et al. Efficacy and safety of intra-articular sprifermin in symptomatic radiographic knee osteoarthritis: Prespecified analysis of 3-year data from a 5-year randomized, placebo-controlled, phase ii study. Osteoarthritis and Cartilage. 2018; 26 (Suppl 1):S26-S27
- 33. Hoeksma HL, Dekker J, Ronday HK, Breedveld FC, Van den Ende CH. Manual
   therapy in osteoarthritis of the hip: outcome in subgroups of patients. Rheumatology.
   25. 2005; 44(4):461-464
- 34. Hoppe S, Mainzer JD, Frauchiger L, Ballmer PM, Hess R, Zumstein MA. More
   accurate component alignment in navigated total knee arthroplasty has no clinical
   benefit at 5-year follow-up. Acta Orthopaedica. 2012; 83(6):629-633
- Hunter DJ, Beavers DP, Eckstein F, Guermazi A, Loeser RF, Nicklas BJ et al. The Intensive Diet and Exercise for Arthritis (IDEA) trial: 18-month radiographic and MRI outcomes. Osteoarthritis and Cartilage. 2015; 23(7):1090-1098
- 36. Jang SH, Lee SC, Lee JH, Nam SH, Cho KR, Park Y. Comparison of ultrasound (US)-guided intra-articular injections by in-plain and out-of-plain on medial portal of the knee. Rheumatology International. 2013; 33(8):1951-1959
- 35 37. Joseph GB, Baum T, Carballido-Gamio J, Nardo L, Virayavanich W, Alizai H et al.
  36 Texture analysis of cartilage T2 maps: individuals with risk factors for OA have higher
  37 and more heterogeneous knee cartilage MR T2 compared to normal controls--data
  38 from the osteoarthritis initiative. Arthritis Research & Therapy. 2011; 13(5):R153
- 39 38. Khan RJ, Lam LO, Breidahl W, Blakeney WG. Magnetic resonance imaging features 40 of preserved vs divided and repaired piriformis during total hip arthroplasty: a 41 randomized controlled trial. Journal of Arthroplasty. 2012; 27(4):551-558
- 42 39. Kim YH, Park JW, Kim JS. Computer-navigated versus conventional total knee 43 arthroplasty a prospective randomized trial. Journal of Bone & Joint Surgery -44 American Volume. 2012; 94(22):2017-2024
- 45 40. Knoop J, Dekker J, van der Leeden M, van der Esch M, Klein JP, Hunter DJ et al. Is 46 the severity of knee osteoarthritis on magnetic resonance imaging associated with 47 outcome of exercise therapy? Arthritis Care and Research. 2014; 66(1):63-68

- Lequesne M, Maheu E, Cadet C, Dreiser RL. Structural effect of avocado/soybean unsaponifiables on joint space loss in osteoarthritis of the hip. Arthritis and Rheumatism. 2002; 47(1):50-58
- 4 42. Lutzner J, Krummenauer F, Wolf C, Gunther KP, Kirschner S. Computer-assisted and conventional total knee replacement: A comparative, prospective, randomised study with radiological and CT evaluation. Journal of Bone and Joint Surgery Series B. 2008; 90(8):1039-1044
- Macri EM, Neogi T, Jarraya M, Guermazi A, Roemer F, Lewis CE et al. Can MRIdefined osteoarthritis features explain anterior knee pain in individuals with, or at risk for, knee osteoarthritis? The MOST Study. Arthritis Care and Research. 2021; 25
- 44. Mazzuca SA, Brandt KD. Is knee radiography useful for studying the efficacy of a
   disease-modifying osteoarthritis drug in humans? Rheumatic Diseases Clinics of
   North America. 2003; 29(4):819-830
- 45. Mazzuca SA, Brandt KD, Chakr R, Lane KA. Varus malalignment negates the
   structure-modifying benefits of doxycycline in obese women with knee osteoarthritis.
   Osteoarthritis and Cartilage. 2010; 18(8):1008-1011
- 46. Melville DM, Taljanovic MS, Scalcione LR, Eble JM, Gimber LH, DeSilva GL et al.
   Imaging and management of thumb carpometacarpal joint osteoarthritis. Skeletal
   Radiology. 2015; 44(2):165-177
- 47. Menashe L, Hirko K, Losina E, Kloppenburg M, Zhang W, Li L et al. The diagnostic
   performance of MRI in osteoarthritis: a systematic review and meta-analysis.
   Osteoarthritis and Cartilage. 2012; 20(1):13-21
- 48. 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
- 49. Moystad A, Mork-Knutsen BB, Bjornland T. Injection of sodium hyaluronate compared
   to a corticosteroid in the treatment of patients with temporomandibular joint
   osteoarthritis: a CT evaluation. Oral Surgery Oral Medicine Oral Pathology Oral
   Radiology & Endodontics. 2008; 105(2):e53-60
- Nam D, Nunley RM, Berend KR, Lombardi AV, Barrack RL. The impact of custom cutting guides on patient satisfaction and residual symptoms following total knee arthroplasty. Knee. 2016; 23(1):144-148
- 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
- NHS England and NHS Improvement. National Cost Collection Data Publication
   2019-2020. London. 2020. Available from: <a href="https://www.england.nhs.uk/wp-content/uploads/2021/06/National-Cost-Collection-2019-20-Report-FINAL.pdf">https://www.england.nhs.uk/wp-content/uploads/2021/06/National-Cost-Collection-2019-20-Report-FINAL.pdf</a>
- Odding E, Valkenburg HA, Algra D, Vandenouweland FA, Grobbee DE, Hofman A.
   Associations of radiological osteoarthritis of the hip and knee with locomotor disability in the Rotterdam Study. Annals of the Rheumatic Diseases. 1998; 57(4):203-208
- 43 54. Pelletier JP, Roubille C, Raynauld JP, Abram F, Dorais M, Delorme P et al. Disease44 modifying effect of strontium ranelate in a subset of patients from the Phase III knee
  45 osteoarthritis study SEKOIA using quantitative MRI: reduction in bone marrow lesions
  46 protects against cartilage loss. Annals of the Rheumatic Diseases. 2015; 74(2):42247 429

- Pessis E, Chevrot A, Drape JL, Leveque C, Sarazin L, Minoui A et al. Study of the joint space of the hip on supine and weight-bearing digital radiographs. Clinical Radiology. 1999; 54(8):528-532
- 56. Petursson G, Fenstad AM, Gothesen O, Dyrhovden GS, Hallan G, Rohrl SM et al.
  Computer-assisted compared with conventional total knee replacement: A multicenter parallel-group randomized controlled trial. Journal of Bone & Joint Surgery American Volume. 2018; 100(15):1265-1274
- Phan CM, Link TM, Blumenkrantz G, Dunn TC, Ries MD, Steinbach LS et al. MR imaging findings in the follow-up of patients with different stages of knee osteoarthritis and the correlation with clinical symptoms. European Radiology. 2006; 16(3):608-618
- 11 58. Plant MJ, Borg AA, Dziedzic K, Saklatvala J, Dawes PT. Radiographic patterns and 12 response to corticosteroid hip injection. Annals of the Rheumatic Diseases. 1997; 13 56(8):476-480
- 14 59. Quatman CE, Hettrich CM, Schmitt LC, Spindler KP. The clinical utility and diagnostic performance of magnetic resonance imaging for identification of early and advanced knee osteoarthritis: a systematic review. American Journal of Sports Medicine. 2011; 39(7):1557-1568
- 18 60. Raynauld JP, Martel-Pelletier J, Abram F, Dorais M, Haraoui B, Choquette D et al.
  19 Analysis of the precision and sensitivity to change of different approaches to assess
  20 cartilage loss by quantitative MRI in a longitudinal multicentre clinical trial in patients
  21 with knee osteoarthritis. Arthritis Research & Therapy. 2008; 10(6):R129
- 22 61. Raynauld JP, Martel-Pelletier J, Bias P, Laufer S, Haraoui B, Choquette D et al.
  23 Protective effects of licofelone, a 5-lipoxygenase and cyclo-oxygenase inhibitor,
  24 versus naproxen on cartilage loss in knee osteoarthritis: a first multicentre clinical trial
  25 using quantitative MRI. Annals of the Rheumatic Diseases. 2009; 68(6):938-947
- 26 62. Rozendaal RM, Uitterlinden EJ, van Osch GJ, Garling EH, Willemsen SP, Ginai AZ et 27 al. Effect of glucosamine sulphate on joint space narrowing, pain and function in 28 patients with hip osteoarthritis; subgroup analyses of a randomized controlled trial. 29 Osteoarthritis and Cartilage. 2009; 17(4):427-432
- 30 63. Saarakkala S, Waris P, Waris V, Tarkiainen I, Karvanen E, Aarnio J et al. Diagnostic performance of knee ultrasonography for detecting degenerative changes of articular cartilage. Osteoarthritis and Cartilage. 2012; 20(5):376-381
- 33 64. Samuel AM, Jain H. Scintigraphic changes of osteoarthritis: An analysis of findings during routine bone scans to evaluate the incidence in an Indian population. Indian Journal of Nuclear Medicine. 2012; 27(2):73-80
- 36 65. Sato H, Fujii T, Yamada N, Kitamori H. Temporomandibular joint osteoarthritis: a 37 comparative clinical and tomographic study pre- and post-treatment. Journal of Oral 38 Rehabilitation. 1994; 21(4):383-395
- 39 66. Sawitzke AD, Shi H, Finco MF, Dunlop DD, Bingham CO, 3rd, Harris CL et al. The 40 effect of glucosamine and/or chondroitin sulfate on the progression of knee 41 osteoarthritis: a report from the glucosamine/chondroitin arthritis intervention trial. 42 Arthritis and Rheumatism. 2008; 58(10):3183-3191
- 43 67. Schaefer LF, Nikac V, Lynch JA, Duryea J. Quantitative measurement of cartilage 44 volume is possible using two-dimensional magnetic resonance imaging data sets. 45 Osteoarthritis and Cartilage. 2018; 26(7):920-923
- 46 68. Shapiro SA, Arthurs JR, Heckman MG, Bestic JM, Kazmerchak SE, Diehl NN et al. Quantitative t2 mri mapping and 12-month follow-up in a randomized, blinded,

- placebo controlled trial of bone marrow aspiration and concentration for osteoarthritis of the knees. Cartilage. 2019; 10(4):432-443
- 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
- 5 70. Sibbitt WL, Band PA, Kettwich LG, Chavez-Chiang NR, DeLea SL, Bankhurst AD. A randomized controlled trial evaluating the cost-effectiveness of sonographic guidance for intra-articular injection of the osteoarthritic knee. Journal of Clinical Rheumatology. 2011; 17(8):409-415
- 9 71. Siramanakul C, Sriphirom P. Comparison of clinical and radiographic outcomes 10 between minimally invasive lateral approach and mini-midvastus approach in total 11 knee arthroplasty. Journal of the Medical Association of Thailand. 2012; 95 (Suppl 12 10):S53-57
- 72. Song IH, Althoff CE, Hermann KG, Scheel AK, Knetsch T, Burmester GR et al.
   Contrast-enhanced ultrasound in monitoring the efficacy of a bradykinin receptor 2
   antagonist in painful knee osteoarthritis compared with MRI. Annals of the Rheumatic Diseases. 2009; 68(1):75-83
- Tindall EA, Sharp JT, Burr A, Katz TK, Wallemark CB, Verburg K et al. A 12-month, multicenter, prospective, open-label trial of radiographic analysis of disease progression in osteoarthritis of the knee or hip in patients receiving celecoxib. Clinical Therapeutics. 2002; 24(12):2051-2063
- 74. Todesca A, Garro L, Penna M, Bejui-Hugues J. Conventional versus computer-navigated TKA: a prospective randomized study. Knee Surgery, Sports
   Traumatology, Arthroscopy. 2017; 25(6):1778-1783
- 75. Vasilakis I, Solomou E, Vitsas V, Fennema P, Korovessis P, Siamblis DK. Correlative
   analysis of MRI-evident abductor hip muscle degeneration and power after minimally
   invasive versus conventional unilateral cementless THA. Orthopedics. 2012;
   35(12):e1684-1691
- 76. Vincken PW, ter Braak BP, van Erkel AR, Bloem RM, van Luijt PA, Coene LN et al.
   Only MR can safely exclude patients from arthroscopy. Skeletal Radiology. 2009;
   38(10):977-982
- 77. Wacker FK, Konig H. Quantitative evaluation of magnetic resonance imaging in longterm therapy: a pilot study in patients with osteoarthritis of the knee. Acta Pharmaceutica (Zagreb, Croatia). 1993; 43(4):253-260
- 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
- Wang Y, Hall S, Hanna F, Wluka AE, Grant G, Marks P et al. Effects of Hylan G-F 20 supplementation on cartilage preservation detected by magnetic resonance imaging in osteoarthritis of the knee: a two-year single-blind clinical trial. BMC Musculoskeletal Disorders. 2011; 12:195
- Wei W, Lambach B, Jia G, Kaeding C, Flanigan D, Knopp MV. A Phase I clinical trial of the knee to assess the correlation of gagCEST MRI, delayed gadolinium-enhanced MRI of cartilage and T2 mapping. European Journal of Radiology. 2017; 90:220-224
- 44 81. Wenham CY, Hensor EM, Grainger AJ, Hodgson R, Balamoody S, Dore CJ et al. A 45 randomized, double-blind, placebo-controlled trial of low-dose oral prednisolone for 46 treating painful hand osteoarthritis. Rheumatology. 2012; 51(12):2286-2294

## DRAFT FOR CONSULTATION [Imaging for Management]

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1 82. Westesson PL, Brooks SL. Temporomandibular joint: Relationship between MR 2 evidence of effusion and the presence of pain and disk displacement. American 3 Journal of Roentgenology. 1992; 159(3):559-563 4 83. Wildi LM, Raynauld JP, Martel-Pelletier J, Abram F, Dorais M, Pelletier JP. 5 Relationship between bone marrow lesions, cartilage loss and pain in knee osteoarthritis: results from a randomised controlled clinical trial using MRI. Annals of 6 7 the Rheumatic Diseases. 2010; 69(12):2118-2124 8 84. Wittoek R, Jans L, Lambrecht V, Carron P, Verstraete K, Verbruggen G. Reliability 9 and construct validity of ultrasonography of soft tissue and destructive changes in erosive osteoarthritis of the interphalangeal finger joints: A comparison with MRI. 10 11 Annals of the Rheumatic Diseases. 2011; 70(2):278-283 12 85. Wu XD, Xiang BY, Schotanus MGM, Liu ZH, Chen Y, Huang W. CT- versus MRI-13 based patient-specific instrumentation for total knee arthroplasty: A systematic review 14 and meta-analysis. Surgeon Journal of the Royal Colleges of Surgeons of Edinburgh 15 & Ireland. 2017; 15(6):336-348 16 86. Yokozeki H, Igarashi M, Karube S, Shiraki M, Kurokawa T. The relation between osteoporosis of the spine and osteoarthritis of the knee. A study using dual energy X-17 18 ray absorptiometry and radiographs. International Orthopaedics. 1995; 19(5):282-284 87. Yoong P, Guirguis R, Darrah R, Wijeratna M, Porteous MJ. Evaluation of ultrasound-19 guided diagnostic local anaesthetic hip joint injection for osteoarthritis. Skeletal 20 Radiology. 2012; 41(8):981-985 21 22 88. Yue Y, Collaku A. Correlation of pain reduction with fmri bold response in osteoarthritis patients treated with paracetamol: Randomized, double-blind, crossover 23 24 clinical efficacy study. Pain Medicine. 2018; 19(2):355-367

## **Appendices**

### 2 Appendix A – Review protocols

Review protocol for the clinical and cost-effectiveness of imaging during the management of osteoarthritis

ID	Field	Content CRD42021236834		
0.	PROSPERO registration number			
1.	Review title	What is the clinical and cost-effectiveness of using radiological investigations (for example: x-ray, ultrasound, MRI) to inform management choices for people with osteoarthritis?		
2.	Review question	6.2 What is the clinical and cost-effectiveness of using radiological investigations (x-ray, ultrasound, MRI, CT) to inform management choices for people with osteoarthritis?		
3.	Objective	To determine whether there is any benefit in using imaging to aid clinicians in decision making regarding choices for the management of osteoarthritis.		
4.	Searches	The following databases (from inception) 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 committee meeting and further studies retrieved for inclusion if relevant.	
		The full search strategies will be published in the final review. Medline serach strategy to be quality assured using the PRESS evidence-based checklist (see methods chapter for full details).	
5.	Condition or domain being studied	People, aged 16 years and over, with osteoarthritis (of any joint)	
6.	Population	Inclusion:	
		Adults (age ≥16 years) with osteoarthritis affecting any joint	
		Exclusion:	
		Children (age <16 years)	
		• People with conditions that may make them susceptible to osteoarthritis or often occur alongside osteoarthritis (including: crystal arthritis, inflammatory arthritis, septic arthritis, hemochromatosis, haemophilic arthropathy, diseases of childhood that may predispose to osteoarthritis, and malignancy).	
		• Studies with an unclear population (e,g, proportion of participants with osteoarthritis unclear)	
		Spinal osteoarthritis	
7.	Intervention/Exposure/Test	Imaging before a surgical or non-surgical intervention (for example: imaging used to determine whether an intra-articular injection should be performed, using any criteria provided in the study)	
		X-ray before	
		∘ A surgical intervention	
		○ A non-surgical intervention	

T				
	Ultrasound before			
	○ A surgical intervention			
	○ A non-surgical intervention			
	MRI before			
	○ A surgical intervention			
	○ A non-surgical intervention			
	CT before			
	○ A surgical intervention			
	○ A non-surgical intervention			
	The radiological interventions will be analysed separately, as will surgical and non-surgical interventions for each imaging type.			
Comparator/Reference standard/Confounding factors	No imaging before a non-surgical/surgical intervention (decision made purely on clinical presentation)			
	Confounding factors (if including non-randomised evidence):			
	• Age			
	Baseline symptoms such as pain and/or function			
	Baseline BMI (or weight in the absence of BMI)			
Types of study to be included	Systematic reviews of RCTs			
	• RCTs			
	If insufficient RCT evidence is available, non-randomised studies will be considered, including:  3. Prospective and retrospective cohort studies  4. Case control studies (if no other evidence identified)			
	Studies will only be included if all of the key confounders have been accounted for in a multivariate analysis. In the absence of multivariate analysis, studies that account for key confounders with univariate analysis or matched groups will be considered.			
Other exclusion criteria	Image-guided procedures			
	Non-English language studies			
	standard/Confounding factors  Types of study to be included			

		Conference abstracts will be excluded as it is expected there will be sufficient full text published studies available.
11.	Context	Adults with osteoarthritis before any intervention in primary or secondary care
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]  • Changes to planned management [dichotomous data prioritised]
13.	Secondary outcomes (important outcomes)	<ul> <li>Psychological distress [validated patient-reported outcomes, continuous data prioritised]</li> <li>Osteoarthritis flares [validated patient-reported outcomes, continuous data prioritised]</li> <li>Number of adverse events [dichotomous]</li> </ul>
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 <u>Developing NICE guidelines: the manual</u> section 6.4).
		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.
		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  For intervention reviews the following checklists will be used according to the study design being assessed:  • 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
16.	Strategy for data synthesis	<ul> <li>Pairwise meta-analyses will be performed using Cochrane Review Manager (RevMan5). Fixed-effects (Mantel-Haenszel) techniques will be used to calculate risk ratios for the binary outcomes where possible. Continuous outcomes will be analysed using an inverse variance method for pooling weighted mean differences.</li> <li>Heterogeneity between the studies in effect measures will be assessed using the I² statistic and visually inspected. An I² 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.</li> </ul>
		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 Crading of Recommendations Assessment. Development and Evaluation (CRADE) tealback developed by
		<ul> <li>'Grading of Recommendations Assessment, Development and Evaluation (GRADE) toolbox' developed by the international GRADE working group <a href="http://www.gradeworkinggroup.org/">http://www.gradeworkinggroup.org/</a></li> <li>Where meta-analysis is not possible, data will be presented and quality assessed individually per outcome.</li> </ul>
		WinBUGS will be used for network meta-analysis, if possible given the data identified.

17.	Analysis of sub-groups	Subgroup analysis to be conducted if heterogeneity in the meta-analysis is present:		
		<ul> <li>Multimorbidity (high versus low morbidity score; as defined by study, measured by validated instruments e.g. Charlson Comorbidity Index</li> </ul>		
		Age (≤/> 75 years)		
		• Jo	int site	
		<ul> <li>Class of intervention (oral, topical or transdermal medicines, intra-articular injections, exercise, manual therapy, acupuncture, electrotherapy, devices, treatment package, combination of treatments)</li> <li>Type of non-surgical interventions</li> </ul>		
18.	Type and method of review	$\boxtimes$	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				
		5b Named contact e-mail			
		[Guideline email]@nice.org.uk			
		[Developer to check with Guideline Coordinator for email address]			
		5e Organisational aff	filiation of th	e 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]	
		Muksitur Rahman [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 <a href="Developing NICE guidelines: the manual">Developing NICE guidelines: the manual</a> . Members of the guideline committee are available on the NICE website: <a href="https://www.nice.org.uk/guidance/indevelopment/gid-ng10127">https://www.nice.org.uk/guidance/indevelopment/gid-ng10127</a>	
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	Adults; Flare; Imaging; Management; MRI; Osteoarthritis; Plain film radiography; Referral; Ultrasound		
33.	Details of existing review of same topic by same authors			
34.	Current review status	$\boxtimes$	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		

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#### 1 Table 2: Health economic review protocol

identify health economic studies relevant to any of the review questions.  opulations, interventions and comparators must be as specified in the clinical review protocol above.  tudies must be of a relevant health economic study design (cost—utility analysis, cost-effectiveness analysis, cost—benefit nalysis, cost—consequences analysis, comparative cost analysis).  tudies must not be a letter, editorial or commentary, or a review of health economic evaluations. (Recent reviews will be ordered though not reviewed. The bibliographies will be checked for relevant studies, which will then be ordered.)  npublished reports will not be considered unless submitted as part of a call for evidence.  tudies must be in English.  ealth economic study search will be undertaken for all years using population-specific terms and a health economic study filter—appendix B below.  dies not meeting any of the search criteria above will be excluded. Studies published before 2005, abstract-only studies and
tudies must be of a relevant health economic study design (cost–utility analysis, cost-effectiveness analysis, cost–benefit nalysis, cost–consequences analysis, comparative cost analysis). tudies must not be a letter, editorial or commentary, or a review of health economic evaluations. (Recent reviews will be ordered though not reviewed. The bibliographies will be checked for relevant studies, which will then be ordered.) npublished reports will not be considered unless submitted as part of a call for evidence. tudies must be in English. ealth economic study search will be undertaken for all years using population-specific terms and a health economic study filter – appendix B below.
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appendix B below.
dies not meeting any of the search criteria above will be excluded. Studies published before 2005, abstract-only studies and
dies from non-OECD countries or the USA will also be excluded.
dies published in 2005 or later, that were included in the previous guidelines, will be reassessed for inclusion and may be uded or selectively excluded based on their relevance to the questions covered in this update and whether more applicable dence is also identified.
ch remaining study will be assessed for applicability and methodological limitations using the NICE economic evaluation checklist ch can be found in appendix H of Developing NICE guidelines: the manual (2014). <sup>51</sup>
lusion and exclusion criteria
a study is rated as both 'Directly applicable' and with 'Minor limitations' then it will be included in the guideline. A health economic vidence table will be completed and it will be included in the health economic evidence profile.
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 xcluded then a health economic evidence table will not be completed and it will not be included in the health economic evidence rofile.
a study is rated as 'Partially applicable', with 'Potentially serious limitations' or both then there is discretion over whether it should e included.
in the second se

#### 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.

#### Appendix B – Literature search strategies

 What is the clinical and cost-effectiveness of using radiological investigations (for example: x-ray, ultrasound, MRI) to inform management choices for people with osteoarthritis?

The literature searches for this review are detailed below and complied with the methodology outlined in Developing NICE guidelines: the manual.<sup>51</sup>

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 an Osteoarthritis population. All results were then sifted for each question. 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  Exclusions (animals studies, letters, comments)
Embase (OVID)	1974 – 17 November 2021	Randomised controlled trials Systematic review 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

	(Ovia) scarcii terme
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.	randomized controlled trial.pt.
28.	controlled clinical trial.pt.
29.	randomi#ed.ti,ab.
30.	placebo.ab.
31.	randomly.ti,ab.
32.	Clinical Trials as topic.sh.
33.	trial.ti.
34.	or/27-33
35.	Meta-Analysis/
36.	exp Meta-Analysis as Topic/
37.	(meta analy* or metanaly* or meta regression).ti,ab.
38.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
39.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
40.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
41.	(search* adj4 literature).ab.
42.	(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.
43.	cochrane.jw.
44.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
45.	or/35-44
46.	26 and (34 or 45)

#### Embase (Ovid) search terms

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 not English language
25.	random*.ti,ab.
26.	factorial*.ti,ab.
27.	(crossover* or cross over*).ti,ab.
28.	((doubl* or singl*) adj blind*).ti,ab.
29.	(assign* or allocat* or volunteer* or placebo*).ti,ab.
30.	crossover procedure/
31.	single blind procedure/
32.	randomized controlled trial/
33.	double blind procedure/
34.	or/25-33
35.	systematic review/
36.	meta-analysis/
37.	(meta analy* or metanaly* or meta regression).ti,ab.
38.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
39.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
40.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
41.	(search* adj4 literature).ab.
42.	(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.
43.	cochrane.jw.
44.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
45.	or/35-44
46.	24 and (34 or 45)

#### Cochrane Library (Wiley) search terms

•	Soomane Eistary (vincy) scaron 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)

#### **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,
Embase	1 January 2014 – 17 November 2021	letters, comments) Health economics studies Quality of life studies  Exclusions (animals studies, letters, comments)
Centre for Research and Dissemination (CRD)	HTA - Inception – 31 March 2018 NHSEED - Inception to 31 March 2015	None

#### Medline (Ovid) search terms

Medine (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)

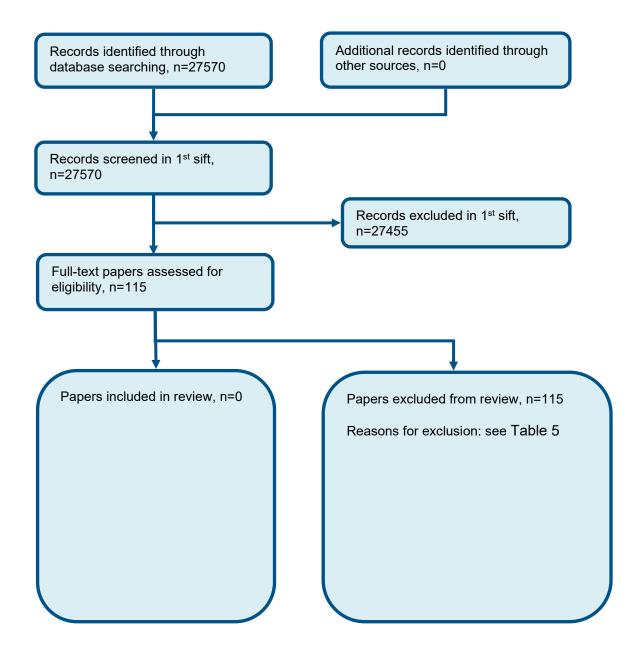
### NHS EED and HTA (CRD) search terms

#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 imaging to inform management for people with osteoarthritis



# Appendix D – Effectiveness evidence

No studies were included.

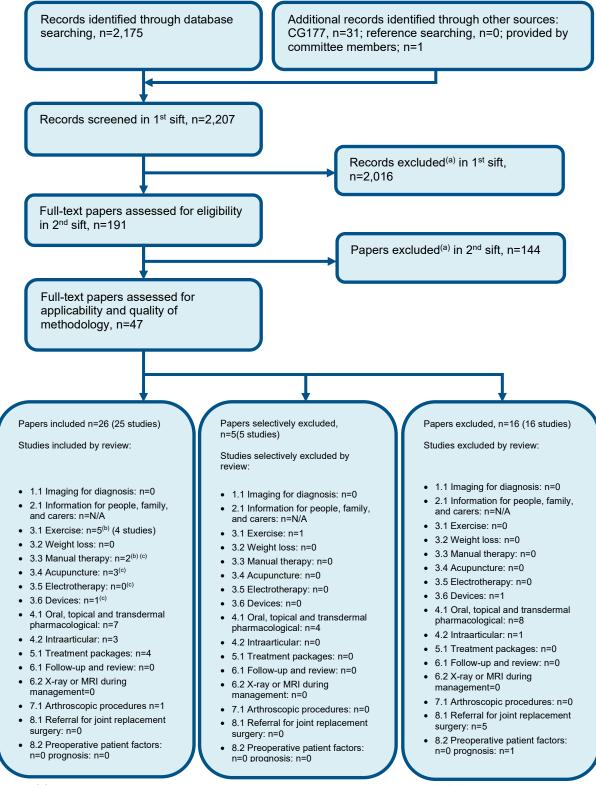
# **Appendix E – Forest plots**

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

Study	Exclusion reason
Akdemir 2015 <sup>1</sup>	Abstract only
Aronowitz 2017 <sup>2</sup>	Inappropriate comparison (all people received all imaging techniques)
Atchia 2011 <sup>3</sup>	Inappropriate comparison (no imaging-related comparison).
Baum 2012 <sup>4</sup>	Inappropriate comparison (no imaging-related comparison).
Benli kucuk 2018 <sup>5</sup>	Inappropriate comparison (no imaging-related comparison).
Bevers 2014 <sup>6</sup>	Wrong study type (non-comparative)
Blackburn 1994 <sup>7</sup>	Incorrect interventions (combination of X-ray, MRI and arthroscopic examination compared to X-ray and arthroscopic examination, no intervention being delivered).
Boegard 1998 <sup>8</sup>	Conference abstract only
Boegard 1999 <sup>9</sup>	Inappropriate comparison (compares people with radiographic imaging features to people without radiographic imaging features)
Brealey 2007 <sup>10</sup>	Not review population (people who did not have osteoarthritis, comparing referral after MRI with orthopaedic referral without MRI).
Bridgman 2007 <sup>11</sup>	Not review population (people who may not have had osteoarthritis, comparing arthroscopy after MRI with arthroscopy without MRI).
Broderick 1994 <sup>12</sup>	Inappropriate comparison (compares imaging to arthroscopy).
Buendia-lopez 2018 <sup>13</sup>	Inappropriate comparison (no imaging-related comparison).
Case 2003 <sup>14</sup>	Inappropriate comparison (no imaging-related comparison).
Chao 2010 <sup>15</sup>	Inappropriate comparison (no imaging-related comparison).
Collins 2020 <sup>16</sup>	Inappropriate comparison (no imaging-related comparison).
Cubukcu 2005 <sup>17</sup>	Inappropriate comparison (no imaging-related comparison).
Ding 2013 <sup>18</sup>	Systematic review: literature search not sufficiently rigorous
Dutton 2008 <sup>19</sup>	Incorrect interventions (compares computer assisted arthroplasty to non-computer assisted arthroplasty).
Eymard 2017 <sup>20</sup>	Inappropriate comparison (no imaging-related comparison).
Feczko 2016 <sup>21</sup>	Inappropriate comparison (no imaging-related comparison).
Gaffney 1995 <sup>22</sup>	Inappropriate comparison (no imaging-related comparison).
Gudbergsen 2011 <sup>23</sup>	Inappropriate comparison (no imaging-related comparison).
Gudbergsen 2012 <sup>24</sup>	Wrong study type (non-comparative)
Gudbergsen 2013 <sup>25</sup>	Inappropriate comparison (compares radiographic assessment to MRI features)
Guermazi 2017 <sup>26</sup>	Inappropriate comparison (no imaging-related comparison).
Guermazi 2018 <sup>27</sup>	Abstract only
Han 2019 <sup>28</sup>	Inappropriate comparison (compares different MRI signals)
Hayashi 2018 <sup>29</sup>	Systematic review: literature search not sufficiently rigorous
Hellio le graverand 2013 <sup>30</sup>	Inappropriate comparison (no imaging-related comparison).
Henricsdotter 201631	Inappropriate comparison (no imaging-related comparison).
Hochberg 2018 <sup>32</sup>	Abstract only
Hoeksma 2005 <sup>33</sup>	Inappropriate comparison (no imaging-related comparison).

Study	Exclusion reason
Hoppe 2012 <sup>34</sup>	Wrong study type (non-comparative).
Hunter 2015 <sup>35</sup>	Inappropriate comparison (no imaging-related comparison).
Jang 2013 <sup>36</sup>	Incorrect interventions (compares image-guided procedure to non-image guided procedure).
Joseph 2011 <sup>37</sup>	Not review population (healthy participants).
Khan 2012 <sup>38</sup>	Incorrect interventions (different arthroplasty techniques).
Kim 2012 <sup>39</sup>	Incorrect interventions (computer-guided arthroplasty)
Knoop 2014 <sup>40</sup>	Inappropriate comparison (compares MRI to x-ray)
Lequesne 2002 <sup>41</sup>	Inappropriate comparison (no imaging-related comparison).
Lutzner 2008 <sup>42</sup>	Inappropriate comparison (no imaging-related comparison).
Macri 2021 <sup>43</sup>	Wrong study type (cross-sectional study)
Mazzuca 2003 <sup>44</sup>	Systematic review: literature search not sufficiently rigorous
Mazzuca 2010 <sup>45</sup>	Inappropriate comparison (no imaging-related comparison).
Melville 2015 <sup>46</sup>	Systematic review: literature search not sufficiently rigorous
Menashe 2012 <sup>47</sup>	Systematic review is not relevant to review question or unclear PICO
Menz 2021 <sup>48</sup>	Wrong study type (cross-sectional study)
Moystad 2008 <sup>49</sup>	Inappropriate comparison (no imaging-related comparison).
Nam 2016 <sup>50</sup>	Incorrect interventions (MRI-based custom cutting guide systems for total knee arthroplasty).
Odding 1998 <sup>53</sup>	Inappropriate comparison (compares people with and without radiographic knee osteoarthritis).
Pelletier 2015 <sup>54</sup>	Inappropriate comparison (no imaging-related comparison).
Pessis 1999 <sup>55</sup>	Wrong study type (non-comparative study).
Petursson 2018 <sup>56</sup>	Incorrect interventions (computer-guided arthroplasty).
Phan 2006 <sup>57</sup>	Inappropriate comparison (compares different amounts of radiographic osteoarthritis to healthy participants).
Plant 1997 <sup>58</sup>	People with conditions that may make them susceptible to osteoarthritis or often occur alongside osteoarthritis (including: crystal arthritis, inflammatory arthritis, septic arthritis, hemochromatosis, haemophilic arthropathy, diseases of childhood that may predispose to osteoarthritis, and malignancy).
Quatman 2011 <sup>59</sup>	Systematic review is not relevant to review question or unclear PICO
Raynauld 2008 <sup>60</sup>	Inappropriate comparison (no imaging-related comparison).
Raynauld 2009 <sup>61</sup>	Inappropriate comparison (no imaging-related comparison).
Rozendaal 2009 <sup>62</sup>	Inappropriate comparison (no imaging-related comparison).
Saarakkala 2012 <sup>63</sup>	Inappropriate comparison (compares ultrasound to arthroscopy).
Samuel 2012 <sup>64</sup>	Wrong study type (non-comparative)
Sato 1994 <sup>65</sup>	Wrong study type (non-comparative)
Sawitzke 2008 <sup>66</sup>	Inappropriate comparison (no imaging-related comparison).
Schaefer 2018 <sup>67</sup>	Inappropriate comparison (compares different results from MRI).
Shapiro 2019 <sup>68</sup>	Inappropriate comparison (no imaging-related comparison).
Sheridan 2021 <sup>69</sup>	Incorrect population (including people with meniscal tears as well as people with knee osteoarthritis)
Sibbitt 2011 <sup>70</sup>	Inappropriate comparison (image-guided technique compared to no image-guidance).

Study	Exclusion reason
Siramanakul 2012 <sup>71</sup>	Inappropriate comparison (no imaging-related comparison).
Song 2009 <sup>72</sup>	Inappropriate comparison (no imaging-related comparison).
Tindall 2002 <sup>73</sup>	Inappropriate comparison (no imaging-related comparison).
Todesca 2017 <sup>74</sup>	Incorrect interventions (computer-guided arthroplasty).
Vasilakis 2012 <sup>75</sup>	Inappropriate comparison (no imaging-related comparison).
Vincken 2009 <sup>76</sup>	Inappropriate comparison (compares abnormal MRI to normal MRI results)
Wacker 199377	Inappropriate comparison (no imaging-related comparison).
Wang 2011 <sup>79</sup>	Inappropriate comparison (no imaging-related comparison).
Wang, 2021 <sup>78</sup>	Incorrect intervention (predictors for early stage arthritis- all people had imaging.)
Wei 2017 <sup>80</sup>	Not review population. Inappropriate comparison (compares different types of MRI technique).
Wenham 201281	Inappropriate comparison (no imaging-related comparison).
Westesson 199282	Wrong study type (non-comparative)
Wildi 2010 <sup>83</sup>	Inappropriate comparison (no imaging-related comparison).
Wittoek 201184	Inappropriate comparison (compares ultrasound and MRI).
Wu 2017 <sup>85</sup>	Systematic review is not relevant to review question or unclear PICO
Yokozeki 199586	Incorrect interventions (dual-energy absorptiometry to check for osteoporosis).
Yoong 201287	Wrong study type (non-comparative)
Yue 2018 <sup>88</sup>	Inappropriate comparison (no imaging-related comparison).

#### **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.

# Appendix K - Research recommendations - full details

### K.1 Research recommendation 1

What is the clinical and cost effectiveness of imaging for informing non-surgical management (for example, exercise, weight loss) in primary care for people with osteoarthritis?

### K.1.1 Why this is important

Imaging has been used previously to both diagnose and assess the structural severity of osteoarthritis. However, it is acknowledged that imaging findings of osteoarthritis correlate poorly with symptoms of osteoarthritis. Therefore, these recommendations have proposed that osteoarthritis should be defined clinically without the need for imaging. However, clinicians often still request imaging for a variety of reasons, including to support management decisions. No evidence was found to support this in this review and whilst the use of imaging to support surgical decision making is essential, the role of imaging to support decision making for conservative management is unclear. Therefore, this research recommendation would aim to investigate the potential uses of imaging to support management decisions in a primary care setting.

#### K.1.2 Rationale for research recommendation

Importance to 'patients' or the population	Many people believe an x-ray will show the cause of their joint pain, without understanding x-rays can only show bones and not most of the structures where pain may arise. More advanced imaging techniques which detect soft tissue has not improved the ability to determine where pain is coming from in the joint. Repeated imaging over an extended period can potentially cause harm (for example, from accumulated radiation dose exposure) and has additional impact on the daily life of the individual (for example: attendances to imaging departments) which may not be required. Therefore, identifying the appropriate time and indication to perform imaging will lessen the risks of such harm occurring.
Relevance to NICE guidance	Imaging to assist making management decisions has been explored in this review but no evidence was identified. If a particular subgroup of osteoarthritis which had benefit from a specific therapy could only be identified with imaging, then this would indicate a benefit from imaging. Therefore, additional evidence would support the development of this guidance in future.
Relevance to the NHS	Inappropriate imaging has significant impact on resources in the NHS (for example: additional trained staff required to perform imaging, costs of equipment and maintenance, costs of infrastructure, extended waiting times for imaging). This impact may depend on the type of imaging being used, where conventional x-rays may result in a smaller impact than facilities

	such as ultrasound and MRI. Therefore, identifying the appropriate uses for imaging would allow for better regulation of these impacts.
National priorities	This is not an area of national priority.
Current evidence base	There is currently no evidence identified that answers this question (based on the protocol included for this review).
Equality considerations	The committee noted that osteoarthritis research in general does not appear to represent the diverse population of people with osteoarthritis. They agreed that any further 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. Future work 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.

### K.1.3 Modified PICO table

Population	Inclusion:
	<ul> <li>Adults (age ≥16 years) with osteoarthritis affecting any joint</li> </ul>
Intervention	Imaging before a non-surgical intervention for example:
	• Exercise
	Weight loss
	The type of imaging should be stratified by:
	• X-ray
	Ultrasound
	• MRI
	• CT
	The type of non-surgical intervention should be stratified by the type of imaging and considered in a subgroup analysis.
Comparator	No imaging before a non-surgical intervention
Outcome	Reported at least at 3 months and a long term follow up period after 3 months (for example: 1 year):
	<ul> <li>Health-related quality of life [validated patient- reported outcomes, continuous data]</li> </ul>
	<ul> <li>Pain [validated patient-reported outcomes, continuous data]</li> </ul>

	<ul> <li>Physical function [validated patient-reported outcomes, continuous data</li> <li>Changes to planned management [dichotomous data]</li> <li>Psychological distress [validated patient-reported outcomes, continuous data]</li> <li>Osteoarthritis flares [validated patient-reported outcomes, continuous data]</li> <li>Number of adverse events [dichotomous data]</li> <li>Cost incurred stratified by type of imaging</li> </ul>
	[continuous data]
Study design	Randomised controlled trial
Timeframe	Long term (preferably 1 year or longer)
Additional information	Subgroup analysis:
	The class of non-surgical intervention
	Multimorbidity (high versus low morbidity score)
	Age
	Joint site

### K.2 Research recommendation 2

What is the clinical and cost effectiveness of imaging for use at different parts of the care pathway (for example, primary care, intermediary care, secondary care) before surgery for people with osteoarthritis?

#### K.2.1 Why this is important

Imaging is required for surgical planning when considering a joint replacement surgery for a person with osteoarthritis. However, current practice is unclear as to when this should take place. In some cases, the orthopaedic surgeon would prefer to request their own imaging to ensure they have all the appropriate information they need, while in other cases, orthopaedic surgeons prefer to see accompanying imaging to support the referral before accepting the referral. Determining the most appropriate timing for imaging to take place will reduce duplication in tasks leading to potential resource savings while ensuring everyone has all the information, they require to best inform decisions regarding surgery.

#### K.2.2 Rationale for research recommendation

	radiation dose exposure) and has additional impact on the daily life of the individual (for example: attendances to imaging departments) which may not be required. Therefore, reducing the chance of duplication of imaging would be useful for managing this. If the need for imaging proves to be a key gatekeeper for referral, identifying the most appropriate time for it to occur would reduce the chance of referrals being refused and support the person to see the relevant healthcare professional in a timely manner.
Relevance to NICE guidance	The answer to this could help support decision making as to whether imaging for osteoarthritis should take place outside of secondary care for the consideration of surgery (the committee noted that imaging should not be used regularly in primary care) and thereby help support this guidance in the future, where there is currently no evidence.
Relevance to the NHS	Current practice in the NHS is inconsistent regarding this matter. Use of different imaging modalities (including MRI) may increase the cost. This research could help strategic planning to optimise referrals for surgery and allow them to be completed in a more efficient manner.
National priorities	This is not an area of national priority.
Current evidence base	There was no evidence in this area identified in this review.
Equality considerations	The committee noted that osteoarthritis research in general does not appear to represent the diverse population of people with osteoarthritis. They agreed that any further 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. Future work 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.

### K.2.3 Modified PICO table

Population	Inclusion:  • Adults (age ≥16 years) with osteoarthritis affecting any joint
	Exclusion:
	• Children (age <16 years)
	<ul> <li>People with conditions that may make them susceptible to osteoarthritis or often occur alongside osteoarthritis (including: crystal</li> </ul>

	arthritis, inflammatory arthritis, septic arthritis, hemochromatosis, haemophilic arthropathy, diseases of childhood that may predispose to osteoarthritis, and malignancy).  • Spinal osteoarthritis
Intervention	The imaging required by a surgeon for decision making for that joint (in most cases an X-ray, but may include MRI or CT) requested in:  • Primary care (general practice)  • Intermediary care (intermediate musculoskeletal assessment centre)
Comparator	<ul> <li>Secondary care (orthopaedic surgery clinic)</li> <li>Imaging requested in a different service (for example: primary care compared to intermediary care, intermediary care compared to secondary care, primary care compared to secondary care)</li> </ul>
Outcome	<ul> <li>Health-related quality of life [validated patient-reported outcomes, continuous data]</li> <li>Changes to planned management [dichotomous data]</li> <li>Time to surgery [continuous data]</li> <li>Number of adverse events [dichotomous data]</li> <li>Costs of service use [continuous data]</li> <li>Further imaging required [dichotomous data]</li> </ul>
Study design	Randomised controlled trial (a cluster randomised design may be appropriate here)
Timeframe	Short term (up to time to surgery)
Additional information	None