Prevalence of knee osteoarthritis features on magnetic resonance imaging in asymptomatic uninjured adults: a systematic review and meta-analysis

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ABSTRACT

Background Knee magnetic resonance imaging (MRI) is increasingly used to inform clinical management. Features associated with osteoarthritis are often present in asymptomatic uninjured knees; however, the estimated prevalence varies substantially between studies. We performed a systematic review with meta-analysis to provide summary estimates of the prevalence of MRI features of osteoarthritis in asymptomatic uninjured knees.

Methods We searched six electronic databases for studies reporting MRI osteoarthritis feature prevalence (i.e., cartilage defects, meniscal tears, bone marrow lesions, osteophytes) in asymptomatic uninjured knees. Summary estimates were calculated using random-effects meta-analysis (and stratified by mean age: <40 vs. ≥40 years). Meta-regression explored heterogeneity.

Results We included 63 studies (5,397 knees of 4,751 adults). The overall pooled prevalence of cartilage defects was 24% (95%CI 15-34%) and meniscal tears was 10% (7-13%), with significantly higher prevalence with age: cartilage defect <40 years 11% (6-17%) and ≥40 years 43% (29-57%); meniscal tear <40 years 4% (2-7%) and ≥40 years 19% (13-26%). The overall pooled estimate of bone marrow lesions and osteophytes was 18% (12-24%) and 25% (14-38%), respectively, with prevalence of osteophytes (but not bone marrow lesions) increasing with age. Significant associations were found between prevalence estimates and MRI sequences used, physical activity, radiographic osteoarthritis, and risk of bias.

Conclusions Summary estimates of MRI osteoarthritis feature prevalence among asymptomatic uninjured knees were 4-14% in adults aged <40 years to 19-43% in adults ≥40 years. These imaging findings should be interpreted in the context of clinical presentations and considered in clinical decision making.

Key Words: magnetic resonance imaging, asymptomatic, osteoarthritis, cartilage, knee

WHAT IS ALREADY KNOWN ON THIS SUBJECT?

- Increasing availability of MRI has resulted in a rapid rise in its utilisation to help inform clinical management of patients with knee symptoms, yet the overall clinical benefit of the current use of knee MRI is uncertain.
- Community-based studies have reported a high prevalence of knee osteoarthritis features detected by MRI, but these cohorts include people with knee pain and history of knee injury, a well-established risk factor for the accelerated development of knee osteoarthritis.

WHAT ARE THE NEW FINDINGS?

- The prevalence of knee osteoarthritis features on MRI in otherwise healthy, asymptomatic, uninjured knees is high – up to 43% in adults aged ≥40 years.
- Prevalence rates generally increase with age and are influenced by other factors such as physical activity levels and type of MRI sequences used.

INTRODUCTION

Magnetic resonance imaging (MRI) is the most reliable non-invasive diagnostic technique to assess internal derangement of the knee joint. Increasing MRI availability has resulted in a rapid rise in its utilisation to help inform clinical management of patients with knee symptoms.[1 2] Over $14 billion is spent on diagnostic imaging in the United States annually,[3] yet the overall clinical benefit of the current use of knee MRI is uncertain.[4 5] Findings such as meniscal tears, cartilage defects, bone marrow lesions (BMLs), osteophytes and other features suggestive of knee osteoarthritis (OA) are often interpreted as causes of pain and symptoms, triggering medical and surgical interventions.[6 7] However, the relationship between MRI features of OA and knee pain is imprecise.[8]

In patients with knee OA, there is moderate evidence that MRI-assessed BMLs and effusion/synovitis are associated with knee pain, but conflicting or limited evidence for other MRI findings.[8] Features associated with OA have also been observed on MRI in asymptomatic uninjured knees[9-11], suggesting that MRI-assessed OA features may not necessarily be the source of pain in symptomatic patients. However, estimates of the prevalence of MRI features of OA in asymptomatic uninjured knees vary across studies, from 0 to 75%.[9 10] Given the large number of adults undergoing MRI to investigate the cause of knee symptoms, a reliable estimate of the prevalence of MRI features of OA in asymptomatic uninjured knees is important to inform efforts to diagnose and treat knee symptoms across the lifespan. Therefore, the aim of this systematic review and meta-analysis was to determine the prevalence of, and factors contributing to, MRI features of OA in asymptomatic uninjured knees.

METHODS

Search strategy and selection criteria

This systematic review conforms to the Preferred Reporting Items for Systematic reviews and Meta-Analysis (PRISMA) guidelines and is registered with PROSPERO (CRD42016053969). Study investigators searched for studies reporting the prevalence of MRI features of knee OA in asymptomatic adult knees (i.e., mean age ≥18 years with no knee symptoms during any activity) with no history of injury or surgery in EMBASE, Medline, CINAHL, SPORTDiscus, Web of Science and Scopus from inception to the day of the search on October 24, 2017. The searches combined terms related to knee, asymptomatic, MRI, and pathology, without language restriction, and adjusted according to individual database specifications (Appendix eMethods 1).

Primary outcomes were individual MRI features assessed semi-quantitatively and included in the definition of MRI-defined knee OA[12]: i) cartilage defects, defined as partial- or full-thickness cartilage lesions; ii) meniscal tears, defined as high signal extending to an articular surface; iii) BMLs, defined as areas of ill-delineated signal within trabecular bone (hypointense on T1-weighted images, hyperintense on T2-weighted fat-suppressed images); and iv) osteophytes, defined as presence of osteo-cartilagenous protrusions at articular margins. Secondary outcomes were other MRI features previously associated with knee OA (defined in detail in Appendix eMethods 2): effusion-synovitis, subchondral cysts, ligament tears, subchondral sclerosis/attrition, and infrapatellar fat pad synovitis/edema. Two authors (AGC, HFH) independently assessed all titles and abstracts of identified reports for eligibility. Reference lists of all publications considered for inclusion were hand-searched recursively until no additional eligible publications were identified. When eligibility could not be

confirmed from title and abstract, full-texts were reviewed and study investigators contacted as required. If authors were able to provide data from the subset of asymptomatic participants without prior index knee injury or surgery, these were included, otherwise the article was excluded. Only full-text published articles were eligible. No publication was excluded based on language or study design. Detailed eligibility criteria are described in Appendix eMethods 3.

Data extraction

The following information was independently extracted from the included studies by two investigators (AGC, JJS): number of participants/knees, participant characteristics (e.g., age, sex, body mass index (BMI), sporting/physical activity level), MRI sequences, outcome definition (i.e., specific diagnostic criteria), and reported prevalence of whole knee, as well as compartment-specific (i.e., tibiofemoral and patellofemoral), abnormalities. The publication with the most participants (or most OA features assessed) was used when several publications utilised the same population.

Risk of bias assessment

Two reviewers (AGC, BEØ) independently assessed risk of bias using a 13-item checklist developed specifically for this review assessing quality of reporting, sample representativeness and size, comparability between respondents and non-respondents, distribution of confounders, and ascertainment of MRI features of OA (Appendix eMethods 4). As per the Cochrane Handbook for Systematic Reviews recommendations, we customised specific items from the Downs and Black checklist for randomised and non-randomised studies,[13] and a population-based prevalence study checklist.[14] Items related to

113 randomisation, intervention, and others not relevant for the current review were excluded.
114 Items were scored as adequate, inadequate or unable to determine. Discrepancies were
115 resolved by discussion.
116
117 **Data synthesis and analysis**
118 Prevalence estimates of the primary outcomes at a per-knee level were calculated by
119 pooling the study-specific estimates using random-effects proportion meta-analysis that
120 accounted for between-study heterogeneity (Stata v.14.2 *metaprop* command).[15] Freeman-
121 Tukey arcsine transformation was used to normalise variance. Binomial proportion 95%
122 confidence intervals (CIs) for individual studies were calculated around study-specific and
123 pooled prevalences based on the score-test statistic.[16] Due to the incidence of degenerative
124 changes generally increasing substantially after 40 years of age,[17] prevalence estimates of
125 the primary outcomes were calculated separately for studies with a mean age of <40 years
126 and for those with a mean age ≥40 years. Secondary outcomes were often inconsistently
127 defined and thus, descriptively synthesised. Between-study heterogeneity was evaluated for
128 each primary outcome using standard Q-tests and the I^2 statistic (i.e., the percentage of
129 variability in prevalence estimates that is due to heterogeneity rather than chance, 0%=no
130 inconsistency, 100%=maximal inconsistency).[18] We further explored between-study
131 heterogeneity by comparing results from studies grouped according to several study level
132 characteristics (detailed in Appendix eMethods 3) using stratified meta-analysis and meta-
133 regression. Study level characteristics assessed were age, sex, MRI sequences employed
134 (summarised in Appendix eTable 1), participation in weight-bearing sports, radiographic
135 knee OA, sample size, and overall risk of bias. The prevalence estimates of primary
136 compartment-specific outcomes (i.e., tibiofemoral and patellofemoral cartilage defects,

BMLs, osteophytes; medial and lateral meniscal tears) were pooled wherever reported, and differences between compartments assessed with a two-proportion z-test. Publication bias of the primary outcomes secondary to small study effects was assessed using funnel plots and the Egger test when meta-analysis included ≥10 studies. We also conducted sensitivity analyses excluding studies reporting the prevalence of primary outcomes from both knees of each participant to account for potential within-person correlations. All analyses were performed using Stata v.14.2 with a significance threshold of $P<0.05$.

RESULTS

Study characteristics

Forty-six cross-sectional[9 11 19-62] and 17 longitudinal studies[10 63-78] involving a total of 4,751 individuals (5,397 knees) were included in this review (Figure 1, Table 1). Thirty-two took place in North America, 11 in Australia, 12 in Europe, 7 in Asia, and 2 in Africa. The median number of participants and knees per study was 27 (range, 4-836) and 40 (range, 4-836), respectively. The diagnostic criteria used by the studies are summarised in Appendix eTable 1. Out of 13 possible points on the risk of bias scoring criteria, 5 studies scored 0-4 points, 26 scored 5-7 points, 25 scored 8-10 points and 7 scored 11-13 points (details in Appendix eTable 2 and eFigure 1).

FIGURE ONE HERE

TABLE ONE HERE

Prevalence of articular cartilage defects

Forty-two studies (4,322 knees from 3,446 participants) reported the prevalence of cartilage defects with an overall pooled prevalence estimate of 24% (95%CI 15-34%; I^2=97.8%). Studies with a mean age <40 years and ≥40 years had a pooled prevalence of 11% (6-17%) and 43% (29-57%), respectively, with significant evidence of between-study heterogeneity (I^2=84.6% and 98.5%, respectively) (Figure 2). The prevalence of cartilage defects significantly increased with age (slope=14.4% increase per 10-years; 95% CI 9.0-19.9%, p<0.001) (Appendix eFigure 2) and a higher proportion of females (slope=4.3% increase per 10% increase in proportion of females; 95% CI 1.3-7.3%, p=0.006). Heterogeneity was not accounted for by other factors evaluated except: i) risk of bias score in studies with a mean age <40 years, where a lower risk of bias resulted in a higher prevalence (p=0.03; Appendix eFigure 3; and ii) sample size in studies with a mean age ≥40 years, where a sample of ≥50 knees resulted in a significantly higher prevalence (55% (95% CI 39-71%)) than samples of <50 knees (15% (0-42%)) (p=0.014) (Appendix eTable 3).

FIGURE TWO HERE

Prevalence of meniscal tears

Forty-four studies (3,761 knees from 2,817 participants) reported prevalence of meniscal tears with an overall pooled prevalence estimate of 10% (95%CI 7-13%; I^2=87.2%). Studies with a mean age <40 years and ≥40 years had a pooled prevalence of 4% (2-7%) and 19% (13-26%), respectively, with significant evidence of between-study heterogeneity (I^2=60.2% and 92.9%, respectively) (Figure 3). The prevalence of meniscal tears significantly increased with age (slope=3.2% increase per-10 years, 95%CI 0.2-6.1%, p=0.036) (Appendix eFigure 2) and a higher proportion of females (slope=0.2% increase per 10% increase in proportion of

females; 95%CI -1.4 to 1.8%, p=0.797). Prevalence of meniscal tears did not differ by any other study level characteristic except MRI sequences used in studies with a mean age <40 years, where use of optimal MRI sequences resulted in a significantly lower pooled prevalence (3% (0-7%)) than studies using suboptimal MRI sequences (7% (4-10%)) (p=0.034) (Appendix eTable 3).

FIGURE THREE HERE

Prevalence of bone marrow lesions

Thirty-four studies (4,089 knees from 3,255 participants) reported BML prevalence with an overall pooled prevalence estimate of 18% (95%CI 12-24%; I^2=95.6%). Studies with mean age <40 years and ≥40 years had a pooled prevalence of 14% (6-24%) and 21% (14-31%), respectively, with significant evidence of between-study heterogeneity (I^2=91.2% and 96.8%, respectively) (Figure 5). While BML prevalence was not associated with age (slope=4.3% increase per 10-years; 95%CI -0.4 to 9.1%, p=0.076) (Appendix eFigure 2) or percentage of females (slope=1.2% increase per 10% increase in proportion of females; 95%CI -1.5 to 3.9%, p=0.370), the large heterogeneity in those aged <40 years was partly explained by participation in weight-bearing sports. Studies of athletes playing weight-bearing sports resulted in a pooled estimate of 30% (17-45%) compared to general population studies of 3% (0-11%) (p<0.001) (Appendix eTable 3). MRI sequences employed also partly explained the heterogeneity in all studies, with a significantly higher pooled prevalence in studies using optimal sequences (<40 years p=0.027; ≥40 years p=0.002) (Appendix eTable 3). In studies with a mean age ≥40 years, a significantly higher prevalence was also observed in studies

specifically excluding knees with radiographic OA (p<0.001) and in studies with a sample size ≥50 knees (p=0.029) (Appendix eTable 3).

FIGURE FOUR HERE

Prevalence of osteophytes

Eighteen studies (3,257 knees from 2,499 participants) reported osteophyte prevalence with an overall pooled prevalence estimate of 25% (95% CI 14-38%; I^2=98.2%). Studies with a mean age <40 years and ≥40 years had a pooled prevalence of 8% (0-25%) and 37% (22-53%), respectively, with significant evidence of between-study heterogeneity (I^2=94.3% and 98.6%, respectively) (Figure 5). The prevalence of osteophytes significantly increased with age (slope=10.2% increase per-10 years, 95% CI 1.7-18.7%, p=0.021) (Appendix eFigure 2) but not with a higher proportion of females (slope=-0.1% increase per 10% increase in proportion of females; 95%CI -4.8 to 6.5%, p=0.756). Although the relatively small number of studies precluded evaluation of some study level characteristics, in studies with a mean age ≥40 years prevalence of osteophytes was significantly higher in studies that specifically excluded knees with radiographic OA (p=0.046) (Appendix eTable 3).

FIGURE FIVE HERE

Compartment-specific outcomes

There were no significant differences between the prevalence of tibiofemoral and patellofemoral abnormalities (Appendix eTable 4). In studies with a mean age ≥40 years,

medial meniscal tears (14% (95% CI 8-20%)) were significantly more common than lateral meniscal tears (5% (2-8%)) (p=0.009) (Appendix eTable 4).

Prevalence of secondary outcomes, sensitivity analysis and publication bias

The prevalence of secondary outcomes was generally assessed in fewer studies, with a large range of feature definitions (details in Appendix eTable 5). Prevalence of effusion/effusion-synovitis and subchondral cysts ranged from 0-92% (21 studies) and 0-24% (6 studies), respectively. Prevalence of ligament tears was 0% for 16 of the 20 studies, with the remaining four studies reporting 1-30% of mostly anterior cruciate or collateral ligament partial tears. Infrapatellar fat pad synovitis and edema prevalence was 16-80% (3 studies) and 9-75% (2 studies), respectively. One study reported the prevalence of subchondral sclerosis/attrition, with a prevalence of 31%. Sensitivity analyses, excluding 21 studies of bilateral knees, resulted in almost identical prevalence of OA features as the full analyses (≤5% difference). Visual inspection of funnel plots stratified by age (<40 years and ≥40 years) revealed minimal asymmetry, with some evidence of small studies effect only for meniscal tears (Egger test <40 years of age p=0.027; ≥40 years of age p=0.037; Appendix eFigure 4).

DISCUSSION

This systematic review and meta-analysis of 63 studies involving 5,397 knees demonstrated that OA features on MRI are common in asymptomatic uninjured knees and are generally associated with age. In young adults aged <40 years, the pooled prevalence of asymptomatic OA features ranged from 4-14%, with pooled prevalence estimates of 19-43% in older adults. These findings assist both clinical providers and patients to interpret the importance of

structural changes noted on MRI reports throughout the lifespan. Since more than one-third of the older population will exhibit these knee OA related features, medical and/or surgical interventions targeting these imaging findings may not alleviate pain in patients with knee symptoms.

Clinical implications

Current management of OA related features and atraumatic knee pain should centre on improving symptoms and functional limitations, and not be driven by imaging findings.[79 80] The high rate of asymptomatic older adults (aged ≥40 years) with knee OA features on MRI, helps to explain why interventions for these, such as arthroscopy, are no more efficacious in reducing symptoms than sham surgery.[81] Imaging features also do not predict non-surgical treatment outcomes.[79] The explosion of clinical MRI use and expenditure, by as much as 30% annually, over the past two decades[1 2] has not resulted in improved treatment decisions or outcomes for people with knee pain in general practice settings.[82] Alarmingly, in cases of back pain, undergoing early MRI has led to inferior outcomes.[83] Future research should investigate whether explaining the normal rates of imaging features of OA, to symptomatic patients presenting with imaging changes on MRI can improve outcomes and decrease the need for analgesic prescriptions, similar to that observed in the lumbar spine.[84]

The prevalence of MRI findings and older age

The prevalence of most knee OA related features increased with older age, which partially explained the heterogeneity between studies. This increase of approximately 10-15% per-decade for osteophytes and cartilage defects, and 3% per-decade for meniscal tears, suggests these features reflect normal age-related changes. Indeed, meta-regression shows

that approximately three-quarters of asymptomatic adults aged 70 years will have a cartilage lesion. A similarly high pooled prevalence of intraarticular abnormalities has also been observed in asymptomatic spines (disk/facet degeneration)[85] and hips (cartilage/labral defects).[86] Evidence purporting an increased risk of future radiographic OA in the presence of cartilage[87] and meniscal pathology[88] indicates that some of these asymptomatic OA features may not be entirely benign. As radiographic OA was already established in some knees in this review, it is possible that structural abnormalities observed were already part of the pathological OA process. However, higher rates of structural abnormalities were not evident in studies that potentially included knees with radiographic OA (i.e., did not specifically exclude radiographic OA). Indeed, radiographic OA was also common in many asymptomatic knees, and can also reflect normal aging processes.[89]

Bone marrow lesions and the association with physical activity

Bone marrow lesions were the most common feature in younger adults and were not associated with age. Participation in weight-bearing sports contributed to the observed heterogeneity in BML prevalence in younger adults. The consequences of these BMLs in young athletes are not known. However, the transient nature of BMLs means that even after knee injury, when BMLs are common, most resolve without sequelae.[90] While BMLs associated with established OA are an important source of knee pain, they display distinct biochemical properties from those associated with sports-related impact.[91]

The influence of MRI sequences acquired

The prevalence of OA features in the current review was influenced by the type of MRI sequences employed, reflecting variation in diagnostic accuracy with different MRI

techniques.[92] While MRI is the gold-standard imaging technique for diagnosing OA-related pathology,[93] studies using non-optimal sequences to assess BMLs, such as gradient echo sequences, which are particularly prone to susceptibility artefacts,[93] reported significantly lower rates. The pooled prevalence of meniscal tears in younger adults extends observations from a previous systematic review (without meta-analysis) describing the same prevalence (4%) of meniscal tears in asymptomatic, but not exclusively uninjured, athletes (mean age 20-47 years).[94]

Strengths and limitations

The studies included in this review used a large variety of outcome assessment tools to define MRI features. Although there were too many to assess their individual influence on prevalence rates, all methods to assess primary outcomes resulted in equivalent cut-off criteria. Thresholds to define presence of secondary outcomes were more variable and prevented meta-analysis. The detection bias associated with less experienced readers having more errors,[95] was reflected in risk of bias scores, with the addition of a specific item assessing reader experience. Risk of bias scores partly contributed to cartilage lesion prevalence between-study heterogeneity. In many studies, the asymptomatic uninjured controls were part of a comparator group for diseased cases; the general lack of publication bias (except for meniscal tears) confirms that prevalence rates reported were not a key determinant of publication.

Limitations of this review include the heterogeneity between studies that remained unexplained by the variables examined. Unexplained factors, such as the inherent subjective nature of grading MRIs, irrespective of experience, may contribute to OA feature prevalence.

The influence of BMI was unable to be assessed as half of the studies did not report BMI. When whole knee data was not available, the highest prevalence from either compartment was analysed as the whole knee feature rate. While likely underrepresenting overall prevalence, this conservative approach ensured a minimum rate was reported, as lesions in one compartment are known to increase the risk of lesions in the other compartment.[96] Of the studies that reported compartment-specific abnormalities, prevalence of tibiofemoral and patellofemoral lesions were similar, while medial meniscal tears were significantly more common than lateral meniscal tears. Finally, the meta-regression analyses relied on aggregated published data, which may have underestimated the association of MRI features with older age and female sex.

CONCLUSION

In this systematic review, summary estimates of the prevalence of MRI features suggestive of OA among otherwise healthy asymptomatic uninjured knees ranged from 4 to 14% in young adults to 19 to 43% in older adults aged ≥40 years. These imaging findings must be interpreted in the context of clinical presentations and considered in clinical decision making.

CONTRIBUTORS

AGC, BEØ and KMC desgined the study. AGC and HFH completed all searches, study selection (including inclusion and exclusion of abstracts). AGC and JJS completed all data extraction. AGC and BEØ completed all risk of bias assessment. AG completed all critical appraisals of magnetic resonance imaging sequences. AGC, BEØ and KMC planned the analyses, AGC did the meta-analyses and meta-regressions, and all authors interpreted the data. AGC wrote the initial draft and all authors critically revised the manuscript for important intellectual content approved the final version of the manuscript. AGC is the guarantor.

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COMPETING INTERESTS

AG is president of Boston Imaging Core Lab, LLC, and a consultant to Merck Serono, Genzyme, OrthoTrophix, and TissueGene. These sources had no involvement in study design, interpretation of data, writing of the manuscript or the decision to submit the manuscript for publication. All other authors declare no competing interests.

ETHICAL APPROVAL

Not required.

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603

FIGURE LEGENDS

Figure 1. Flow diagram for identifying studies

Figure 2. Meta-analysis of the prevalence of cartilage defects

Figure 3. Meta-analysis of the prevalence of meniscal tears

Figure 4. Meta-analysis of the prevalence of bone marrow lesions

Figure 5. Meta-analysis of the prevalence of osteophytes

613 TABLES

Table 1: Summary of included studies investigating the prevalence of MRI assessed knee OA features prevalence in asymptomatic uninjured populations

Study	Cohort*	Subjects (knees), No.	Women, No. (%)	Age, years**	BMI, kg/m²**	MRI (T)	Risk of bias score
Alharis & Hameed,[19] 2012		80 (80)	38 (48%)	40-60	NR	0.2	7
Antony et al,[59] 2016	Childhood Determinants of Adult Health Study	119 (119)†	56 (47%)¶	35±3 (31-41)‖	25.7±4.3‖	1.5	11
Baranyay et al,[20] 2007	Melbourne Collaborative Cohort Study	297 (297)	186 (63%)	58±6 (40-69)	25.2±3.8	1.5	13
Beattie et al,[9] 2005		44 (44)	33 (75%)	41±14 (20-68)	25.4±4.4	1.0	7
Berry et al,[29] 2010		153 (153)	124 (81%)	47±9 (25-60)	32±9	1.5	6
Boden et al,[30] 1992		74 (74)	41 (55%)	34 (16-65)	NR	1.5	8
Brennan et al,[63] 2010	Geelong Osteoporosis Study	142 (142)	142 (100%)	42±5 (30-49)	27.3±6.3	1.5	11
Brunner et al,[31] 1989	Basketballers/Footballers	5 (10)†	NR	NR (collegiate)	NR	0.5/1.5	6
Calixto et al,[32] 2016		85 (85)	50 (59%)	50±9	24.0±3.4	3.0	8
Culvenor et al,[44] 2015		20 (20)	7 (35%)	30±7 (21-44)	22.8±1.8	3.0	7
Davies-Tuck et al,[45] 2008		20 (20)	20 (100%)	61±6	25.3±4.2	1.5	7
Ding et al,[46] 2005		99 (99)†	62 (63%)	45±7 (26-61)	25.8±3.8	1.5	8
Dong et al,[47] 2017		20 (20)	6 (30%)	35±11	23.5±3.0	1.5	5
Dore et al,[64] 2013	Tasmanian Older Adult Cohort Study	97 (97)†	39 (40%)	65±7 (55-81)	27.3±4.0	1.5	10
Emad et al,[48] 2012		20 (40)	12 (60%)	41±7	31.7±6.3	1.5	3
Fleming et al,[78] 2013		24 (24)	5 (21%)	25±7	25.5±4.8	3.0	3
Foppen et al,[65] 2013		29 (55)†	0 (0%)	24 (23-25)‖	NR	3.0	8
Fukuta et al,[57] 2002		115 (115)	60 (52%)	48 (13-78)	NR	0.5	7
Fukuta et al,[49] 2009		43 (43)	34 (79%)	62 (40-79)	NR	0.5	7
Guermazi et al,[58] 2012	Framingham Osteoarthritis Study	434 (434)†	220 (51%)	63±8 (51-89)	27.3±4.8	1.5	12
Guymer et al,[11] 2007	Victorian Electoral Role	176 (176)	176 (100%)	52±7 (40-67)	27.1±5.5	1.5	12
Hagemann et al,[66] 2008	Runners	10 (10)	3 (30%)	37 (32-44)	NR	1.5	8
Jerosch et al,[60] 1996		66 (126)‡	32 (48%)	16-62‡	NR	1.0	8
Kaplan et al,[61] 2005	Basketballers	20 (40)	0 (0%)	26 (21-36)	NR	1.5	8
Kaukinen et al,[62] 2016	Oulu Knee Osteoarthritis Study	63 (63)	38 (60%)	55±14	24.8±3.2	3.0	8
Kornaat & Van de Velde,[67] 2014	Runners	16 (32)	3 (19%)	23±3	20.4±1.1	1.5	9
Kornick et al,[50] 1990		54 (59)∫	31 (48%)	(20-74)∫	NR	1.5	9
Krampla et al,[68] 2001	Runners	6 (6)†	0 (0%)	37±8 (27-46)	NR	1.0	9
Kumar et al,[51] 2013		27 (42)	9 (33%)	28±4 (20-35)	22.7±2.1	3.0	6

Table 1: Summary of included studies investigating the prevalence of MRI assessed knee OA features prevalence in asymptomatic uninjured populations (continued)

Study	Cohort*	Subjects (knees), No.	Women, No. (%)	Age, years**	BMI, kg/m²**	MRI (T)	Risk of bias score
Kursunoglu-Brahme et al,[69] 1990	Runners	10 (10)	5 (50%)	(20-35)	NR	1.5	5
Landsmeer et al,[70] 2016	Prevention of Knee Osteoarthritis in Overweight Females Study	300 (473)†	300 (100%)	56±3 (50-60)	32.2±4.3	1.5	9
La Prade et al,[52] 1994		54 (54)	29 (54%)	29±5 (19-39)	NR	1.0	5
Li et al,[53] 2009		200 (200)	72 (36%)	31 (20-40)	NR	1.5	8
Ludman et al,[54] 1999	General	14 (26)	5 (36%)	20 (18-23)	NR	1.5	8
	Gymnasts	14 (24)	4 (29%)	20 (18-22)			
Major & Helms,[55] 2002	Basketballers	17 (33)†	5 (29%)	NR (collegiate)	NR	1.5	7
Marik et al,[56] 2016		9 (9)	3 (33%)	40±18 (23-69)	22.1±2.6	7	4
Morgenroth et al,[33] 2014		14 (14)	NR	55±2 (35-65)	84.6±3.2††	1.5	5
Negendank et al,[34] 1990	General	18 (36)	18 (56%)	43±16	67.4±14.5	1.0	9
	Contralateral meniscal tear	20 (20)	4 (20%)	41±12	79.3±14.5		
Nozaki et al,[35] 2004		57 (86)	37 (65%)	43 (18-79)	NR	0.3	4
Pan et al,[71] 2011	Osteoarthritis Initiative healthy control cohort	95 (95)	58 (61%)	55±8 (45-78)	24.2±2.9	3.0	11
Pappas et al,[10] 2016	Basketballers	24 (24)	12 (50%)	(18-22)	NR	3.0	9
Peers et al,[41] 2014	Basketballers	10 (10)	10 (100%)	20 (19-22)	NR	3.0	8
	Swimmers	10 (10)	10 (100%)	20 (19-23)			
Reinig et al,[72] 1991	Footballers	17 (17)	0 (0%)	(19-21)	NR	NR	6
Rennie & Finlay,[42] 2006		23 (36)	5 (22%)	26 (15-41)	NR	1.5	5
Schiphof et al,[73] 2014	Rotterdam Study	424 (836)†	424 (100%)	55±4	26.3±4.3	1.5	10
Schweitzer et al,[43] 1995		25 (50)	7 (28%)	25 (20-46)	NR	1.5	5
Shellock et al,[36] 1991	Runners	23 (23)	15 (65%)	40 (25-55)	NR	1.5	9
Shellock & Mink,[74] 1991	Runners	4 (4)†	2 (50%)‖	37±4 (33-43)‖	NR	1.5	5
Shellock et al,[37] 2003	Triathletes	13 (13)	5 (38%)	48 (37-66)	NR	1.5	9
Souza et al,[38] 2013		19 (19)	8 (42%)	39±10	23.5±3.4	3.0	6
Sowers et al,[39] 2011	Michigan Study of Women's Health Across the Nation Study	159 (259)†	159 (100%)	57±3	29.9±6.3	1.5/3.0	11
Sritanyaratana et al,[40] 2014		20 (20)	5 (25%)	32 (23-45)	NR	3.0	3

Table 1: Summary of included studies investigating the prevalence of MRI assessed knee OA features prevalence in asymptomatic uninjured populations (continued)

Study	Cohort*	Subjects (knees), No.	Women, No. (%)	Age, years**	BMI, kg/m²**	MRI (T)	Risk of bias score
Stahl et al,[75] 2008	General	12 (12)	4 (33%)	37±11	75.8±12.6††	3.0	9
	Runners	10 (10)	6 (60%)	31±5	68.6±10.0††		
Su et al,[76] 2013		16 (16)	8 (50%)	33 (23-57)	24.4 (20-29)	3.0	6
Tarhan et al,[24] 2003		16 (29)	12 (75%)	28±5 (46-77)	28.2±3.7	0.23	6
van der Heijden et al,[25] 2006		70 (70)	41 (59%)	23±6 (14-40)	22.3±3.0	3.0	9
Walczak et al,[26] 2008	Basketballers	14 (25)†	0 (0%)	26 (20-36)	NR	0.3/0.7/1.5	6
Wang et al,[23] 2012		38 (38)	18 (47%)	42±7 (30-55)	25.2±4.1	1.5	7
Wang et al,[21] 2015		16 (16)	4 (25%)	34±10 (18-63)	24.5±2.3	3.0	7
Wang et al,[22] 2017		30 (30)	11 (37%)	28±5 (18-40)	23.4±3.3	1.5/3.0	6
Wei et al,[77] 2017	Footballers	13 (25)	0 (0%)	20±1 (18-22)	34.2±3.2	3.0	6
Whittaker et al,[27] 2017	Alberta Youth Prevention of Early Osteoarthritis Study	73 (146)	45 (62%)	23±3 (15-27)	23.6±2.6	1.5	9
Zanetti et al,[28] 2003	Contralateral meniscal tear	100 (100)	41 (41%)	43 (18-73)	NR	1.0/1.5	8

BMI, body mass index; MRI, magnetic resonance imaging; NR, not reported.

* Participants are healthy volunteers from the general population unless otherwise indicated

† subset of whole cohort without previous knee injury or surgery

‡ after excluding participant group aged <16 years

ʃ number of people/knees estimated after excluding participants aged 10-20 years

¶ estimated from total sample reported in original publication

|| values represent total sample reported in original publication

** Mean ± standard deviation (range)

††body mass, as BMI not reported

Appendix: web extra material

eMethods 1. Systematic search strategy used

MEDLINE	Knee [MeSH] OR knee [tiab] OR Knee joint [MeSH] OR tibiofemoral [tiab] OR Patellofemoral joint [MeSH] OR Patellofemoral [tiab] **AND** Asymptomatic Diseases [MeSH] OR asymptomatic [tiab] OR control [tiab] OR pain free [tiab] OR Healthy Volunteers [MeSH] OR healthy [tiab] OR uninjured [tiab] **AND** Magnetic Resonance Imaging [MeSH] OR MRI [tiab] OR magnetic resonance imaging [tiab] OR MR imaging [tiab] **AND** Cartilage [MeSH] OR Articular Cartilage [MeSH] OR Hyaline Cartilage [MeSH] OR cartilage [tiab] OR chondral [tiab] OR Menisci, Tibial [MeSH] OR meniscal [tiab] OR meniscus [tiab] OR subchondral [tiab] OR bone marrow [MeSH] OR bone marrow [tiab] OR Osteophyte [MeSH] OR osteophyte [tiab] OR effusion [tiab] OR Synovitis [MeSH] OR synovitis [tiab] OR Ligaments [MeSH] OR ligament [tiab] OR Sclerosis [MeSH] OR sclerosis [tiab] OR attrition [tiab] OR Cysts [MeSH] OR cyst [tiab] OR fat pad [tiab]
Embase	Knee [MeSH] OR knee [tiab] OR tibiofemoral [tiab] OR Patellofemoral joint [MeSH] OR Patellofemoral [tiab] **AND** Asymptomatic Disease [MeSH] OR asymptomatic [tiab] OR Control [MeSH] OR control [tiab] OR pain free [tiab] OR healthy [tiab] OR uninjured [tiab] **AND** Nuclear magnetic Resonance Imaging [MeSH] OR MRI [tiab] OR magnetic resonance imaging [tiab] OR MR imaging [tiab] **AND** Cartilage [MeSH] OR Articular Cartilage [MeSH] OR Hyaline Cartilage [MeSH] OR cartilage [tiab] OR chondral [tiab] OR Knee meniscus [MeSH] OR meniscal [tiab] OR meniscus [tiab] OR Subchondral bone plate [MeSH] OR subchondral [tiab] OR bone marrow [MeSH] OR bone marrow [tiab] OR Osteophyte [MeSH] OR osteophyte [tiab] OR Effusion [MeSH] OR effusion [tiab] OR Synovitis [MeSH] OR synovitis [tiab] OR Ligament [MeSH] OR ligament [tiab] OR Sclerosis [MeSH] OR sclerosis [tiab] OR attrition [tiab] OR Cyst [MeSH] OR cyst [tiab] OR fat pad [tiab]
CINAHL **Scopus** **Web of Science** **SPORTDiscus**	Knee OR tibiofemoral OR patellofemoral **AND** Asymptomatic OR “pain free” OR control OR healthy OR uninjured **AND** MRI OR magnetic resonance OR MR imaging **AND** Cartilage OR chondral OR meniscal OR meniscus OR “bone marrow” OR subchondral OR osteophyte OR effusion OR synovitis OR ligament OR sclerosis OR attrition OR cyst OR “fat pad”

eMethods 2. Details of secondary outcomes

Based on established imaging criteria:[1]

1. *Joint effusion/synovitis* defined as presence of increased fluid-equivalent signal within the knee joint cavity on fluid-sensitive sequences;
2. *Subchondral cysts* defined as presence of well-delineated lesions of fluid-equivalent signal in the subarticular bone (with no internal marrow tissue or trabecular bone) on T1-weighted non-fat suppressed sequence and fluid-sensitive sequence;
3. *Ligament tears* defined as at least a partial tear of the cruciate or collateral ligaments,
4. *Subchondral sclerosis/attrition* defined as subchondral bone alteration of increased density assessed as ill-defined low-signal intensity in the subchondral bone on fluid-sensitive and T1-weighted sequences.

Infrapatellar fat pad synovitis defined as the presence of diffuse hyperintense signal within the fat pad on fat suppressed fluid sensitive sequences.

eMethods 3. Detailed eligibility criteria and subgroup stratification

Types of studies

Only full-text published articles were eligible (i.e., conference abstracts and unpublished data were excluded). No restrictions were placed on study design or language. In studies involving follow-up MRI assessments, baseline prevalence data were used wherever possible. Potentially eligible studies published in languages other than English (i.e., after screening English abstract) were translated with the assistance of a native speaker (resulting in one Chinese article being included). The authors of papers identified that did not specifically state that participants with a history of knee injury, surgery or pain were excluded, were contacted to clarify the population. If authors were able to provide data from participants without prior index knee injury/surgery/ symptoms, these were included, otherwise the paper was excluded. Data reported for quantitative outcome measures (e.g., volume, thickness, extrusion), compositional measures (e.g., T1rho, T2) or histochemical measures of knee structures were excluded. Data reporting structural change as an acute response to activity (e.g., immediately post-running) were excluded (but baseline data prior to bout of activity were eligible).

When eligible studies did not report complete whole knee (or compartment-specific) data (e.g., only patellofemoral lesions; medial or lateral meniscal tears reported separately), we included whole knee or compartment-specific data from other publications of the same cohort or contacted the authors requesting additional data. When whole knee data was not reported, and additional data was not provided upon request, we used data from the compartment with the highest prevalence as the rate of whole knee abnormality.

Participants/population

Inclusion criteria: Adults (i.e., mean age ≥18 years) with no index knee symptoms during any activity and no history of index knee injury or surgery were included. When studies did not specifically report whether participants with previous (or current) knee injury, surgery or symptoms were excluded, or if a portion of uninjured asymptomatic participants were included but prevalence data not reported separately, authors were contacted requesting prevalence data on only those without a history (or current) knee injury, surgery or symptoms (and studies were included if able to provide this data).

Exclusion criteria: Studies primarily evaluating children and adolescents (i.e., mean age <18 years) were excluded due to difficulties differentiating normal tissue development from pathology.[2,3] The planned exclusion of participants with radiographic knee OA changed slightly from what was outlined in the review protocol. Many eligible studies did not acquire concurrent radiographs and therefore the presence of radiographic knee OA was not assessed in these studies (and potential participants with radiographic knee OA unable to be excluded). We instead conducted sensitivity analyses based on whether participants with radiographic knee OA were specifically excluded. We contacted authors of studies that included some asymptomatic uninjured participants with radiographic knee OA, and requested the prevalence of MRI abnormalities in only those without radiographic knee OA. This additional data was included in meta-analysis whenever possible. As per our *a prior* protocol, we specifically excluded studies from the Multicentre Osteoarthritis Study (MOST)[4] and Osteoarthritis Initiative (OAI)[5] databases (except the healthy control sub-cohort) as these participants were recruited primarily based on the presence of radiographic OA, knee symptoms, and previous knee injury/surgery.

Subgroup stratification criteria

1. *MRI sequences used:* MRI sequences employed to assess each knee abnormality were classified as optimal (representing the most sensitive sequences) or non-optimal (known to be less sensitive) based on current best-practice recommendations. For the assessment of cartilage defects, optimal sequences were considered water sensitive sequences, such as proton density weighted, intermediate-weighted and T2-weighted with or without fat suppression.[6] For meniscal tears, optimal sequences were considered intermediate-weighted with or without fat-suppression.[7] For BML assessment, optimal sequences were considered water sensitive sequences such as T2, intermediate-weighted, proton density weighted with fat suppression, T1-weighted with fat-suppression and contrast-enhanced and short tau inversion recovery (STIR).[8] For osteophytes, any MRI sequence is appropriate, as osteophytes are excrescence of the normal bone that can be visualised on any sequence.
2. *Participation in weight-bearing sports:* Study cohorts were classified as participating in weight-bearing sports if the study specifically recruited non-water sport athletes (e.g., college basketballers). If participant level sporting details were not provided, a study cohort was considered as participating in weight-bearing sports when ≥50% of participants reported playing level I/II sports (e.g., basketball, football, racket sports, skiing) as per Hefti et al.[9]
3. *Radiographic knee OA:* Studies were classified as either specifically excluding participants with radiographic knee OA or not.

Sample size: Studies were classified as either small (<50 participants) or large (≥50 participants).

eMethods 4. Risk of bias checklist

13-item checklist developed from two previously published quality assessment scales and one additional item specific to this review.

Questions derived from Downs and Black checklist for randomized and non-randomized studies:[10]

1. Is the primary hypothesis/aim of the study to evaluate knee MRI pathology prevalence in asymptomatic people?
2. Are the main outcomes to be measured clearly described in the introduction or methods section?
3. Are the characteristics of the patients included in the study clearly described?
4. Is the population of interest clearly described?
5. Are the distributions of principal confounders in each group of subjects to be compared clearly described?
6. Are the main findings of the study clearly described?
7. Was the sample size included in the analysis adequate (i.e., ≥50)?
8. Were the subjects asked to participate in the study representative of the entire population from which they were recruited?
9. Were those subjects who were prepared to participate representative of the entire population from which they were recruited?
10. Were the main outcome measures used accurate (valid and reliable)?

Questions derived from Hoy et al. checklist for population-based prevalence studies:[11]

11. Was an acceptable case definition used in the study?
12. Was the same mode of data collection used for all subjects?

Additional question specific to current review:

13. Was the person(s) scoring the MRI scans described and suitably qualified (i.e., radiologist, or reliable trained observer)?

Each item is scored as adequate (1), unclear (0) or inadequate (0). Scores range from 0 to 13, assessing risk of bias in several domains: reporting bias, performance bias, selection bias, and information/detection bias.

eTable 1. Evaluation of MRI sequences and diagnostic criteria employed

Author	Features assessed & criteria	Sequences	Optimal?
Alharis & Hameed,[12] 2012	*Meniscus:* abnormal signal to articular surface	(1) T2 weighted (with and without fat suppression – Spectral Pre saturation by Inversion Recovery [SPIR]) (2) T1 weighted	Meniscus: Yes
Antony et al,[13] 2016	*Cartilage*: focal defect [a]	(1) T1 weighted fat saturation 3D spoiled gradient recall acquisition in steady state (2) Proton density weighted fat saturated 2D fast spin echo	Cartilage: Yes
	BML: increased signal adjacent to subchondral bone	(1) Proton density weighted fat saturated 2D fast spin echo	BML: Yes
Baranyay et al,[14] 2007	*Cartilage*: focal defect [a] *BML*: increased signal adjacent to subcortical bone *Osteophyte*: present	(1) T2 weighted fat saturated (2) T1 weighted fat suppressed 3D gradient recall acquisition in the steady state	Cartilage: Yes BML: Yes Osteophyte: Yes
Beattie et al,[15] 2005	*Cartilage*: focal defect [a] *Meniscus*: abnormal signal reaching articular surface *BML*: present *Osteophyte*: present	(1) 3D gradient echo	Cartilage: No Meniscus: No BML: No Osteophyte: Yes
Berry et al,[16] 2010	*Cartilage*: focal defect [a] *Osteophyte*: present	(1) T1 weighted fat saturation 3D gradient recall acquisition in steady state (2) Fat saturated, fast spin echo 3D, T2 weighted	Cartilage: Yes Osteophyte: Yes
	BML: present	(1) Fat saturated, fast spin echo 3D, T2 weighted	BML: Yes
Boden et al,[17] 1992	*Meniscus*: Crues [b] *BML*: ≥minimal subchondral signal *Osteophyte*: present	(1) Gradient echo technique (2) T2 weighted (3) Proton density weighted	Meniscus: No BML: No Osteophyte: Yes
Brennan et al,[18] 2010	*Cartilage*: focal defect [a] *BML*: present *Osteophyte*: present	(1) T1 weighted fat suppressed 3D gradient recall acquisition in steady state (2) T2 weighted fat saturated acquisition (1) T2 weighted coronal fat saturated acquisition	Cartilage: Yes BML: Yes Osteophyte: Yes
Brunner et al,[19] 1989	*Meniscus*: Modified Crues [b]	(1) Spin echo sequences	Meniscus: No
Calixto et al,[20] 2016	*Meniscus*: Modified WORMS	(1) 3D fast spin echo CUBE	Meniscus: Yes
Culvenor et al,[21] 2015	*Cartilage*: MOAKS *Meniscus*: MOAKS *Osteophyte*: MOAKS *BML*: MOAKS	(1) 3D proton-density VISTA sequence (2) Short tau inversion recovery (STIR) (3) Proton density turbo spin echo sequence (1) Short tau inversion recovery (STIR) (2) Proton density turbo spin echo sequence	Cartilage: Yes Meniscus: Yes Osteophyte: Yes BML: Yes
Davies-Tuck et al,[22] 2008	*Meniscus*: abnormal signal reaching articular surface	(1) T1 weighted fat suppressed 3D gradient recall	Meniscus: No
Ding et al,[23] 2005	*Cartilage*: focal defect [a]	(1) T1 weighted fat saturation 3D gradient recall acquisition in the steady state	Cartilage: No
Dong et al,[24] 2017	*Cartilage*: WORMS *BML*: increased bone marrow signal intensity	(1) T2 proton density weighted fat suppression fast spin echo (2) T1 weighted fast spin echo (3) T2 weighted proton density fat suppressed fast spin echo (4) T2 proton density fat suppressed fast spin echo	Cartilage: Yes BML: Yes
Dore et al,[25] 2013	*Cartilage*: focal defect [a]	(1) T1 weighted fat saturation 3D gradient recalled acquisition in steady state	Cartilage: No
	BML: increased signal adjacent subchondral bone	(1) T2 weighted fat saturation 2D fast spin echo	BML: Yes
	Osteophyte: Knee OA Scoring System	(1) T1 weighted fat saturation 3D gradient recalled acquisition in steady state (2) T2 weighted fat saturation 2D fast spin echo	Osteophyte: Yes
Emad et al,[26] 2012	*Cartilage*: Erosions *BML*: increased bone marrow signal intensity	(1) T1 weighted spin echo (2) T2 weighted (3) Short tau inversion recovery (STIR)	Cartilage: Yes BML: Yes

Fleming et al,[27] 2013	*Cartilage:* WORMS *Meniscus:* WORMS *BML:* WORMS *Osteophyte:* WORMS	(1) T1 weighted water-excitation 3D fast low-angle shot (FLASH) (2) Intermediate weighted turbo spin echo (3) Intermediate weighted turbo spin echo with fat saturation	Cartilage: Yes Meniscus: Yes BML: Yes Osteophyte: Yes
Foppen et al,[28] 2013	*Cartilage*: International Prophylaxis Study Group score	(1) 3D water only selection gradient echo (2) Proton density spectral adiabetic inversion recovery (SPAIR)	Cartilage: Yes
Fukuta et al,[29] 2009	*Meniscus*: Crues [b]	(1) T1 weighted proton density (2) T2 weighted spin echo	Meniscus: Yes
Fukuta et al,[30] 2002	*Meniscus*: Crues [b] *BML*: low signal on T1-weighted and proton density	(1) T1 weighted sagittal spin echo (2) T2 weighted proton density	Meniscus: No BML: No
Guermazi et al,[31] 2012	*Cartilage*: WORMS *Meniscus*: WORMS *BML*: WORMS Osteophyte: WORMS	(1) Proton density weighted fat saturated turbo spin echo (2) T1 weighted spin echo without fat saturation	Cartilage: Yes Meniscus: Yes BML: Yes Osteophyte: Yes
Guymer et al,[32] 2007	*Cartilage*: focal defect [a] *BML*: increased signal adjacent subcortical bone	(1) T1 weighted fat suppressed 3D gradient recall acquisition in steady state (2) T2 weighted fat saturated	Cartilage: Yes BML: Yes
Hagemann et al,[33] 2008	*Cartilage*: focal defect [a] *Meniscus*: Mink [b] *BML*: bone marrow contusion	(1) T1 weighted fast spin echo (2) T2 weighted fast spin echo fat saturated	Cartilage: Yes Meniscus: Yes BML: Yes
Jerosch et al,[34] 1996	*Meniscus*: Modified Crues [b]	(1) T1 weighted spin-echo (2) Partial-saturation (3) Short time inversion recovery (STIR)	Meniscus: Yes
Kaplan et al,[35] 2005	*Cartilage*: Modified Outerbridge *Meniscus*: Crues [b]	(1) Turbo spin-echo	Cartilage: No Meniscus: No
Kaukinen et al,[36] 2016	*Cartilage*: MOAKS *Meniscus*: MOAKS *BML*: MOAKS *Osteophyte*: MOAKS	(1) T2 weighted spin echo (2) T2 weighted dual echo steady-state, (3) Proton density weighted SPACE fat suppressed turbo spin echo (4) Proton density weighted turbo spin echo and (5) T1 weighted turbo spin echo	Cartilage: Yes Meniscus: Yes BML: Yes Osteophyte: Yes
Kornaat & Van de Velde,[37] 2014	*BML*: Knee OA Scoring System	(1) T2 weighted fat suppressed (2) 3D SPACE (Sampling Perfection with Application optimized Contrasts using different flip angle Evolution) fat suppressed	BML: Yes
Kornick et al,[38] 1990	*Meniscus*: Crues [b]	(1) Spin echo	Meniscus: No
Krampla et al,[39] 2001	*Meniscus*: Crues [b]	(1) T1 weighted fast spin echo	Meniscus: No
	BML: high signal on T2 or low signal on T1	(1) T2 weighted gradient echo DESS 3D	BML: No
Kumar et al,[40] 2013	*Cartilage*: Modified WORMS *Meniscus*: Modified WORMS	(1) T2 weighted fat saturated fast spin echo	Cartilage: Yes Meniscus: Yes
Kursunoglu-Brahme et al,[41] 1990	*Meniscus*: Crues [b]	(1) T1 weighted (2) Proton density (3) T2 weighted	Meniscus: No
Landsmeer et al,[42] 2016	*Cartilage*: MOAKS *Meniscus*: MOAKS *BML*: MOAKS *Osteophyte*: MOAKS	(1) Non fat suppressed proton density weighted (2) T2 weighted Spectral Pre saturation by Inversion Recovery (SPIR) (3) Dual spin echo sequence (4) 3D water selective (WATS) with fat saturation	Cartilage: Yes Meniscus: Yes BML: Yes Osteophyte: Yes
LaPrade et al,[43] 1994	*Meniscus*: Crues [b] *BML*: subchondral bone bruise	(1) T1 weighted spin echo (2) Proton density spin echo (3) T2 weighted spin echo	Meniscus: No BML: No

Li et al,[44] 2009	*Cartilage*: Noyes	(1) Fat suppression disturbance phase gradient echo (fat suppressed spoiled gradient) (2) Fat suppression proton density weighted (fat suppressed prototype)	Cartilage: Yes
Ludman et al,[45] 1999	*Meniscus*: Crues [b]	(1) T1 weighted spin echo (2) Proton density spin echo (3) T2 weighted spin echo	Meniscus: No
Major & Helms,[46] 2002	*Cartilage*: focal defect [a]	(1) T2 weighted fast spin echo fat suppression	Cartilage: Yes
	Meniscus: abnormal signal to articular surface	(1) Proton density spin echo fat suppressed	Meniscus: Yes
Marik et al,[47] 2016	*Cartilage*: ICRS	(1) Proton density turbo spin echo	Cartilage: Yes
Morgenroth et al,[48] 2014	*Cartilage*: WORMS *Meniscus*: WORMS *BML*: WORMS *Osteophyte*: WORMS	(1) Proton density (2) T2 weighted spectral inversion recovery fat saturation (SPIR) (3) 3D gradient echo water selective cartilage (4) T1 weighted (5) Proton density SPIR	Cartilage: Yes Meniscus: Yes BML: Yes Osteophyte: Yes
Negendank et al,[49] 1990	*Meniscus*: Modified Lotysch [b]	(1) T1 weighted (2) 3D slab excitation gradient recalled echo (FLASH).	Meniscus: No
Nozaki et al,[50] 2004	*Meniscus*: Modified Crues [b]	(1) T1 weighted (2) Gradient echo	Meniscus: No
Pan et al,[51] 2011	*Cartilage*: WORMS *Meniscus*: WORMS *BML*: WORMS *Osteophyte*: WORMS	(1) Intermediate weighted 2D fast spin echo (2) 2D intermediate weighted fast spin echo sequence with fat suppression (3) 3D dual-echo steady state sequence with selective water excitation	Cartilage: Yes Meniscus: Yes BML: Yes Osteophyte: Yes
Pappas et al,[52] 2016	*Cartilage*: Modified Noyes *Meniscus*: Crues [b] *BML*: present	(1) Proton density (2) T2 weighted	Cartilage: Yes Meniscus: Yes BML: Yes
Peers et al,[53] 2014	*Cartilage*: Modified ICRS	(1) T1 rho	Cartilage: No
Reinig et al,[54] 1991	*Meniscus*: Modified Lotysch [b]	(1) T1 weighted spin echo (2) Gradient recalled echo	Meniscus: No
Rennie & Finlay,[55] 2006	*Meniscus*: high signal to articular surface	(1) T1-weighted spin echo (2) T2-weighted gradient echo	Meniscus: No
Schiphof et al,[56] 2014	*Meniscus*: Knee OA Scoring System *BML*: Knee OA Scoring System *Osteophyte*: Knee OA Scoring System	(1) Dual echo fast spin echo proton density weighted (2) Fast spin echo T2 weighted with fat suppression (3) Spoiled gradient echo sequence with fat suppression (4) Fast imaging employing steady state acquisition (FIESTA)	Meniscus: Yes BML: Yes Osteophyte: Yes
	Cartilage: Knee OA Scoring System	(1) Dual echo fast spin echo proton density weighted (2) Fast imaging employing steady state acquisition (FIESTA)	Cartilage: Yes
Schweitzer et al,[57] 1995	*BML*: present	(1) Intermediate weighted fat suppressed spin echo (2) T2 weighted fast spin echo (3) Intermediate weighted spin echo (4) T2 weighted fat suppressed fast spin echo	BML: Yes
Shellock et al,[58] 1991	*Meniscus*: Crues [b]	(1) T1 weighted (2) Proton density-weighted (3) T2-weighted	Meniscus: No

Shellock & Mink,[59] 1991	*Meniscus*: Crues	(1) T1 weighted (2) Proton density weighted (3) T2 weighted (4) Short T1 inversion recovery	Meniscus: No
Shellock et al,[60] 2003	*Cartilage*: Mink *Meniscus*: Mink [b] *BML*: poorly marginate signal intensity changes	(1) T2 weighted spin echo (2) Proton density weighted (3) T2 weighted turbo spin echo (4) Proton density weighted turbo spin echo with fat saturation (5) Inversion recovery	Cartilage: Yes Meniscus: Yes BML: Yes
Souza et al,[61] 2013	*Cartilage*: WORMS *Meniscus*: WORMS	(1) T2-weighted fat saturated fast spin echo sequence	Cartilage: Yes Meniscus Yes
Sowers et al,[62] 2011	*Cartilage*: focal defect [a] *Meniscus*: Crues [b] *BML*: present *Osteophyte*: present	(1) Fast spin echo proton density with fat saturation (2) Spin echo proton density (3) 3D spoiled gradient echo (SPGR) with fat saturation	Cartilage: Yes Meniscus: Yes BML: Yes Osteophyte: Yes
Sritanyaratana et al,[63] 2014	*Cartilage*: BLOKS *Meniscus*: BLOKS *BML*: BLOKS *Osteophyte*: BLOKS	(1) Fat suppressed T2 weighted fast spin echo (2) Spoiled gradient recalled least squares estimation (IDEAL) fat-water separation (3) Fat suppressed 3D intermediate weighted fast spin echo	Cartilage: Yes Meniscus: Yes BML: Yes Osteophyte: Yes
Stahl et al,[64] 2008	*Cartilage*: WORMS	(1) Fat saturated intermediate weighted fast spin echo (2) T1 weighted 3D high-spatial-resolution volumetric fat suppressed spoiled gradient echo (3) 3D FIESTA-C (fast imaging employing steady state acquisition with constructive interference in steady state, CISS)	Cartilage: Yes
	Meniscus: Modified WORMS *Osteophyte*: WORMS	(1) T1 weighted fast spin echo (2) T2 weighted fat-suppressed fast spin echo	Meniscus: Yes Osteophyte: Yes
	BML: WORMS	(1) Fat saturated intermediate weighted fast spin echo sequence	BML: Yes
Su et al,[65] 2013	*Cartilage*: Modified WORMS *Meniscus*: Modified WORMS	(1) T2 weighted fat saturated fast spin echo (2) 3D fat suppressed spoiled gradient echo	Cartilage: Yes Meniscus: Yes
Tarhan et al,[66] 2003	*Effusion*: distension of suprapatellar recess	(1) T2 weighted	Effusion: Yes
van der Heijden et al,[67] 2016	*Cartilage*: MOAKS *Meniscus*: MOAKS *Osteophyte*: MOAKS *BML*: MOAKS	(1) Fast spin echo proton density weighted (2) T2 weighted sequences with fat suppression (3) 3D high resolution sagittal fat-saturated spoiled gradient echo	Cartilage: Yes Meniscus: Yes Osteophyte: Yes BML: Yes
Walczak et al,[68] 2008	*Cartilage*: focal defect [a] *Meniscus*: high signal to articular surface *BML*: present	(1) T2 weighted or proton density fast spin echo (2) T2 weighted fast spin echo (3) Inversion recovery fast spin echo (4) Proton density fast spin echo (5) Dual equivalent T2-weighted fast spin echo	Cartilage: Yes Meniscus: Yes BML: Yes
Wang et al,[69] 2012	*Cartilage*: focal defect	(1) T1 weighted fat suppressed 3D gradient recall acquisition in the steady state	Cartilage: No
Wang et al,[70] 2015	*Cartilage*: WORMS	(1) Proton density weighted without fat saturation (2) Proton density weighted fast spin echo with fat saturation	Cartilage: Yes
Wang et al,[71] 2017	*Cartilage*: ICRS	(1) T1 weighted 3D gradient recall (2) T1 weighted (3) Proton density weighted	Cartilage: No
	BML: present	(1) Proton density weighted fat saturated spin echo	BML: Yes
Wei et al,[72] 2017	*Cartilage*: Outerbridge	(1) Proton density weighted turbo spin echo with/without fat saturation	Cartilage: Yes

		(2) T1 weighted turbo spin echo (3) 3D steady state free precession (water excitation pulse)	
Whittaker et al,[73] 2017	*Cartilage*: MOAKS *Meniscus*: MOAKS *BML*: MOAKS *Osteophyte*: MOAKS	(1) Proton density (2) Proton density fat saturated (3) 3D gradient echo FIESTA	Cartilage: Yes Meniscus: Yes BML: Yes Osteophyte: Yes
Zanetti et al,[74] 2003	*Cartilage*: Modified Noyes *Meniscus*: abnormal signal to articular surface *BML*: high signal on T2 fat-suppressed or low signal on T1	(1) Intermediate weighted (2) T2 weighted turbo spin-echo (3) T1 weighted spin-echo (4) T2 weighted turbo spin-echo with fat suppression (5) Short tau inversion recovery (STIR)	Cartilage: Yes Meniscus: Yes BML: Yes

MRI, magnetic resonance imaging; BML, bone marrow lesion; WORMS, Whole-Organ Magnetic Resonance Imaging Score; MOAKS, Magnetic resonance imaging Osteoarthritis Knee Score; OA, osteoarthritis; ICRS, International Cartilage Research Society

[a] focal cartilage defect = partial- or full-thickness cartilage defect

[b] Meniscal tear defined as ≥grade 3 on Crues, Mink and Modified Lotysch systems (i.e., abnormal hyperintensity extending to at least one articular surface)

eTable 2. Risk of bias assessment results

Study	Item number													Total
	1	2	3	4	5	6	7	8	9	10	11	12	13	
Alharis & Hameed,[12] 2012	1	1	0	0	0	1	1	U	U	1	1	1	0	7
Antony et al,[13] 2016	1	1	1	1	1	1	1	1	U	1	1	1	0	11
Baranyay et al,[14] 2007	1	1	1	1	1	1	1	1	1	1	1	1	1	13
Beattie et al,[15] 2005	1	1	1	0	0	1	0	U	U	0	1	1	1	7
Berry et al,[16] 2010	0	0	1	1	0	1	1	U	U	0	U	1	1	6
Boden et al,[17] 1992	1	1	1	0	0	0	1	U	U	1	1	1	1	8
Brennan et al,[18] 2010	0	1	1	1	1	1	1	1	U	1	1	1	1	11
Brunner et al,[19] 1989	1	1	0	1	0	1	0	U	U	0	1	0	1	6
Calixto et al,[20] 2016	0	1	1	0	0	1	1	U	U	1	1	1	1	8
Culvenor et al,[21] 2015	0	1	1	0	0	1	0	U	U	1	1	1	1	7
Davies-Tuck et al,[22] 2008	0	1	1	U	0	1	0	U	U	1	1	1	1	7
Ding et al,[23] 2005	0	1	1	0	1	1	1	U	U	1	1	1	0	8
Dong et al,[24] 2017	0	1	0	0	0	0	0	U	U	1	1	1	1	5
Dore et al,[25] 2013	0	1	1	1	0	1	1	1	U	1	1	1	1	10
Emad et al,[26] 2012	0	1	0	0	0	1	0	U	U	0	0	1	0	3
Fleming et al,[27] 2013	0	0	1	0	0	0	0	U	U	1	0	1	0	3
Foppen et al,[28] 2013	1	1	1	1	0	1	0	U	U	0	1	1	1	8
Fukuta et al,[30] 2002	1	1	1	0	0	0	1	U	U	1	1	1	0	7
Fukuta et al,[29] 2009	1	1	1	0	0	0	1	U	U	1	1	1	0	7
Guermazi et al,[31] 2012	1	1	1	1	1	1	1	1	U	1	1	1	1	12
Guymer et al,[32] 2007	1	1	1	1	1	1	1	1	U	1	1	1	1	12
Hagemann et al,[33] 2008	1	1	1	1	0	1	0	U	U	0	1	1	1	8
Jerosch et al,[34] 1996	1	1	1	0	0	0	1	U	U	1	1	1	1	8
Kaplan et al,[35] 2005	1	1	1	1	0	0	0	U	U	1	1	1	1	8
Kaukinen et al,[36] 2016	0	1	1	U	0	1	1	U	U	1	1	1	1	8
Kornaat & Van de Velde,[37] 2014	1	1	1	1	0	1	0	U	U	1	1	1	1	9
Kornick et al,[38] 1990	1	1	1	0	1	0	1	U	U	1	1	1	1	9
Krampla et al,[39] 2001	1	1	1	1	0	1	0	1	U	0	1	1	1	9
Kumar et al,[40] 2013	0	1	1	0	0	1	0	U	U	1	U	1	1	6
Kursunoglu-Brahme et al,[41] 1990	1	1	0	0	0	1	0	U	U	0	0	1	1	5
Landsmeer et al,[42] 2016	1	1	1	1	0	1	1	U	U	1	U	1	1	9
LaPrade et al,[43] 1994	1	0	1	U	0	1	1	U	U	0	U	1	0	5
Li et al,[44] 2009	1	1	1	0	0	1	1	U	U	0	1	1	1	8
Ludman et al,[45] 1999	1	1	0	1	0	1	0	U	U	1	1	1	1	8
Major & Helms,[46] 2002	1	1	0	1	0	1	0	U	U	0	1	1	1	7
Marik et al,[47] 2016	0	1	0	0	0	0	0	U	U	1	0	1	1	4
Morgenroth et al,[48] 2014	0	1	1	U	0	0	0	U	U	1	0	1	1	5
Negendank et al,[49] 1990	1	1	0	0	1	1	1	U	U	1	1	1	1	9
Nozaki et al,[50] 2004	0	1	0	0	0	0	1	U	U	0	1	1	0	4
Pan et al,[51] 2011	1	1	1	1	0	1	1	1	U	1	1	1	1	11
Pappas et al,[52] 2016	1	1	1	1	0	1	0	U	U	1	1	1	1	9
Peers et al,[53] 2014	0	1	1	1	0	1	0	U	U	1	1	1	1	8
Reinig et al,[54] 1991	1	1	0	1	0	1	0	U	U	0	1	1	0	6
Rennie & Finlay,[55] 2006	0	0	1	0	0	1	0	U	U	0	1	1	1	5
Schiphof et al,[56] 2014	0	1	1	1	0	1	1	1	U	1	1	1	1	10
Schweitzer et al,[57] 1995	0	1	0	0	0	1	1	U	U	0	1	0	1	5
Shellock et al,[58] 1991	1	1	1	1	0	1	0	U	U	1	1	1	1	9
Shellock & Mink,[59] 1991	1	0	0	1	0	1	0	U	U	0	0	1	1	5
Shellock et al,[60] 2003	1	1	1	1	0	1	0	U	U	1	1	1	1	9
Souza et al,[61] 2013	0	1	1	U	0	0	0	U	U	1	1	1	1	6
Sowers et al,[62] 2011	1	1	1	1	0	1	1	1	1	1	1	0	1	11
Sritanyaratana et al,[63] 2014	0	0	0	0	0	0	0	U	U	1	U	1	1	3
Stahl et al,[64] 2008	1	1	1	1	0	1	0	U	U	1	1	1	1	9
Su et al,[65] 2013	0	1	1	0	0	0	0	U	U	1	1	1	1	6
Tarhan et al,[66] 2003	0	1	1	0	0	1	0	U	U	0	1	1	1	6
van der Heijden et al,[67] 2016	0	1	1	1	0	1	1	U	U	1	1	1	1	9
Walczak et al,[68] 2008	1	1	1	1	0	1	0	U	U	0	U	0	1	6
Wang et al,[69] 2012	0	1	1	0	0	1	0	U	U	1	1	1	1	7
Wang et al,[70] 2015	0	1	1	0	0	1	0	U	U	1	1	1	1	7
Wang et al,[71] 2017	0	1	1	0	0	1	1	U	U	1	1	0	1	6
Wei et al,[72] 2017	0	1	1	1	0	1	0	U	U	0	1	0	1	6
Whittaker et al,[73] 2017	0	1	1	1	0	1	1	U	U	1	1	1	1	9
Zanetti et al,[74] 2003	1	1	1	1	0	1	1	U	U	0	1	0	1	8

1, adequate; U, unclear; 0, inadequate

eTable 3. Meta-analyses stratified by study level characteristics*

	Number of studies	Number of knees with pathology	Total number of knees	Prevalence of pathology, % (95% confidence interval)	P value
Articular cartilage lesions					
Mean age <40 years					
MRI sequences					0.210
Optimal	19	132	906	9% (4-16)	
Suboptimal	3	22	90	21% (5-43)	
Impact sports					0.536
Yes	14	74	544	12% (5-21)	
No	8	80	452	8% (1-19)	
Radiographic OA					0.226
Excluded	5	22	221	6% (1-14)	
Not excluded	17	132	775	12% (6-20)	
Sample size					0.657
<50	18	62	461	10% (4-17)	
≥50	4	92	535	14% (4-29)	
Mean age ≥40 years					
MRI sequences					0.081
Optimal	15	1650	3064	50% (35-66)	
Suboptimal	4	62	262	18% (0-51)	
Impact sports					NA
Yes	1	0	13	0% (0-23)	
No	18	1712	3313	46% (31-60)	
Radiographic OA					0.338
Excluded	8	1176	2311	51% (29-73)	
Not excluded	11	536	1015	36% (17-58)	
Sample size					**0.014**
<50	6	26	144	15% (0-42)	
≥50	13	1686	3182	55% (39-71)	
Meniscal tears					
Mean age <40 years					
MRI sequences					**0.034**
Optimal	15	41	587	3% (0-7)	
Suboptimal	14	36	398	7% (4-10)	
Impact sports					0.146
Yes	16	39	517	2% (0-6)	
No	13	38	468	7% (4-10)	
Radiographic OA					0.189
Excluded	4	32	205	10% (2-23)	
Not excluded	25	45	780	3% (1-6)	
Sample size					0.588
<50	24	34	576	3% (1-6)	
≥50	5	43	409	7% (2-16)	
Mean age ≥40 years					
MRI sequences					0.831
Optimal	13	362	2510	19% (11-27)	
Suboptimal	8	53	266	19% (10-30)	
Impact sports					0.395
Yes	2	2	20	9% (0-28)	
No	19	413	2756	20% (13-27)	
Radiographic OA					0.622
Excluded	8	297	2235	18% (10-28)	
Not excluded	13	118	541	20% (11-30)	
Sample size					0.820
<50	11	52	287	19% (10-31)	
≥50	10	363	2489	19% (11-28)	
Bone marrow lesions					
Mean age <40 years					
MRI sequences					**0.027**
Optimal	14	148	616	18% (9-29)	
Suboptimal	4	6	175	2% (0-12)	
Impact sports					**0.002**
Yes	11	119	409	26% (13-41)	
No	7	35	382	3% (0-11)	
Radiographic OA					0.832
Excluded	2	28	170	15% (10-21)	
Not excluded	16	126	621	15% (6-28)	
Sample size					0.896
<50	12	55	274	14% (3-31)	
≥50	6	99	517	14% (4-29)	
Mean age ≥40 years					
MRI sequences					**0.002**
Optimal	15	1031	3180	24% (15-34)	
Suboptimal	2	13	118	8% (4-14)	
Impact sports					NA
Yes	0	NA	NA	NA	

No	17	1044	3298	21% (14-31)	
Radiographic OA					**<0.001**
Excluded	6	901	2182	43% (33-53)	
Not excluded	11	143	1116	11% (6-17)	
Sample size					**0.029**
<50	4	7	111	6% (0-20)	
≥50	13	1037	3187	26% (17-36)	
Osteophytes					
Mean age <40 years					
MRI sequences					NA
Optimal	7	61	376	8% (0-25)	
Suboptimal	0	NA	NA	NA	
Impact sports					0.206
Yes	5	59	272	12% (0-38)	
No	2	2	94	1% (0-6)	
Radiographic OA					0.757
Excluded	2	14	170	7% (3-12)	
Not excluded	5	47	206	10% (0-40)	
Sample size					0.183
<50	4	3	86	1% (0-9)	
≥50	3	58	290	19% (0-56)	
Mean age ≥40 years					
MRI sequences					NA
Optimal	12	1043	2881	37% (22-53)	
Suboptimal	0	NA	NA	NA	
Impact sports					NA
Yes	0	NA	NA	NA	
No	12	1043	2881	37% (22-53)	
Radiographic OA					**0.046**
Excluded	6	926	2187	49% (26-71)	
Not excluded	6	117	694	23% (13-34)	
Sample size					0.800
<50	2	22	58	37% (25-50)	
≥50	10	1021	2823	35% (19-53)	

* Meta-analysis performed when subgroup has ≥2 studies, and overall number of studies ≥5. MRI, magnetic resonance imaging; OA, osteoarthritis; NA, not applicable. Bold p-values represent statistical significance ($p<0.05$).

- *MRI sequences:* MRI sequences employed to assess each knee abnormality were classified as optimal (representing the most sensitive sequences) or non-optimal (known to be less sensitive) based on current best-practice recommendations (as per eTable 1).

- *Impact sports:* Cohorts were classified as participating in impact/weight-bearing sports if the study specifically recruited non-water sport athletes (as per eMethods 3).

- *Radiographic OA:* Studies were classified as specifically excluding subjects with radiographic knee OA or not.

Sample size: Studies were classified as either small (<50 participants) or large (≥50 participants).

eTable 4. Pooled prevalence rates of compartment-specific tibiofemoral and patellofemoral pathology, and medial and lateral meniscal tears

	Number of studies	Number of knees with pathology	Total number of knees	Prevalence of pathology, % (95% confidence interval)	P value
Articular cartilage lesions					
Mean age <40 years					0.140
Patellofemoral	19	67	673	8% (4-12)	
Tibiofemoral	20	53	677	4% (1-8)	
Mean age ≥40 years					0.633
Patellofemoral	13	1156	2973	33% (20-48)	
Tibiofemoral	15	1256	3167	38% (24-54)	
Meniscal tears					
Mean age <40 years					0.080
Medial	24	45	786	3% (1-5)	
Lateral	24	18	786	1% (0-2)	
Mean age ≥40 years					**0.009**
Medial	15	231	2300	14% (8-20)	
Lateral	15	108	2300	5% (2-8)	
Bone marrow lesions					
Mean age <40 years					0.722
Patellofemoral	14	69	481	8% (1-18)	
Tibiofemoral	17	86	651	10% (4-18)	
Mean age ≥40 years					0.057
Patellofemoral	7	632	2202	25% (16-34)	
Tibiofemoral	13	587	3138	15% (10-20)	
Osteophytes					
Mean age <40 years					0.875
Patellofemoral	7	43	302	3% (0-24)	
Tibiofemoral	6	11	232	2% (0-7)	
Mean age ≥40 years					0.599
Patellofemoral	7	642	2195	33% (17-51)	
Tibiofemoral	10	818	2771	27% (14-43)	

Bold p-values represent statistical significance ($p<0.05$).

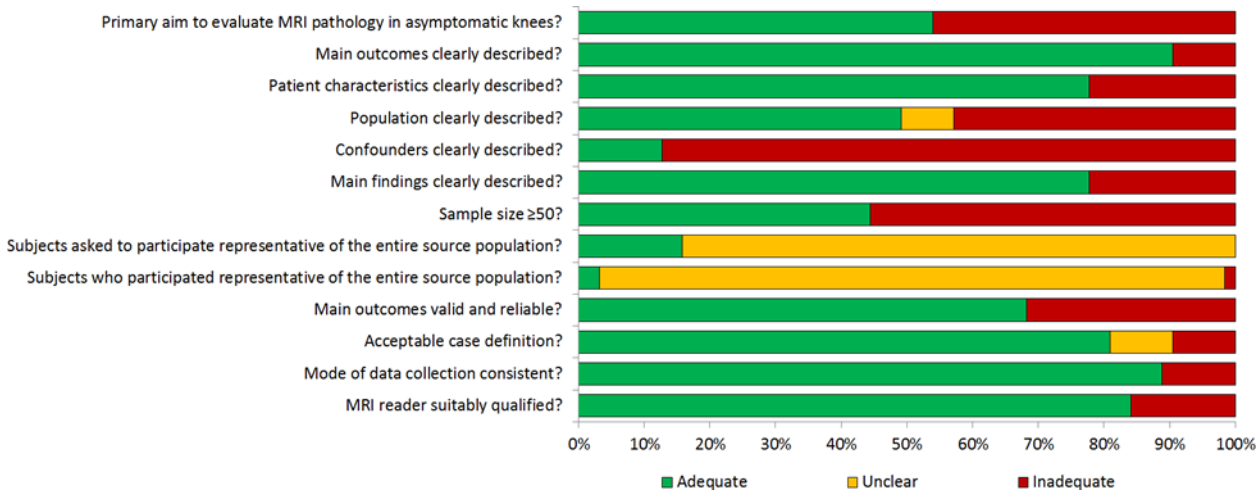
eTable 5. Prevalence of secondary outcomes

Effusion/synovitis (n=1,461)		Ligament Tear (n=1,444)		Subchondral Cyst (n=909)		Infrapatellar fat pad pathology (n=323)	
Mean age	Effusion-synovitis (≥mild WORMS/MOAKS)	Mean age	ACL/PCL/LCL/MCL	Mean age		Mean age	Synovitis (≥mild MOAKS)
23	7% (4-12)[73]	19	0% (0-10)[46]	24	0% (0-7)[28]	23	71% (63-77)[73]
30	10% (3-30)[21]	19	0% (0-28)[19]	34	0% (0-15)[64]	30	80% (58-92)[21]
33	0% (0-19)[65]	20	0% (0-14)[52]	41	14% (6-27)[15]	55	16% (9-27)[36]
34	0% (0-15)[64]	23	0% (0-3)[73]	55	24% (17-34)[51]		
55	6% (3-13)[51]	27	0% (0-28)[41]	57	24% (19-29)[62]		Edema (any)
55	33% (23-46)[36]	30	0% (0-16)[21]	63	18% (15-22)[31]	20	75% (55-88)[52]
56	7% (1-31)[48]	34	0% (0-15)[64]				
63	35% (31-40)[31]	37	30% (11-60)[33]				Edema (≥moderate MOAKS)
		37	0% (0-49)[59]			23	9% (4-17)[67]
	Effusion-synovitis (≥moderate WORMS/MOAKS)	39	0% (0-17)[61]				
		48	8% (1-33)[60]				
23	16% (9-26)[67]	57	0% (0-1)[62]				
65	62% (52-71)[25]						
			ACL/LCL/MCL				
	Small effusion	34	0% (0-5)[17]				
19	33% (20-50)[46]						
20	8% (2-26)[52]		LCL/MCL				
27	0% (0-28)[41]	43	0% (0-4)[74]				
	Moderate-large effusion		ACL/PCL				
26	19% (10-35)[55]	23	0% (0-5)[67]				
34	7% (3-15)[17]	41	0% (0-8)[15]				
		55	0% (0-6)[36]				
	At least small effusion	63	1% (0-2)[31]				
26	32% (17-52)[68]						
48	92% (67-99)[60]						
			ACL only				
		26	8% (3-28)[55]				
	Fluid in/distention of patellar recesses	28	0% (0-7)[43]				
37	80% (49-94)[33]						
57	58% (52-64)[62]						
37	0% (0-49)[59]						
59	24% (12-42)[66]						

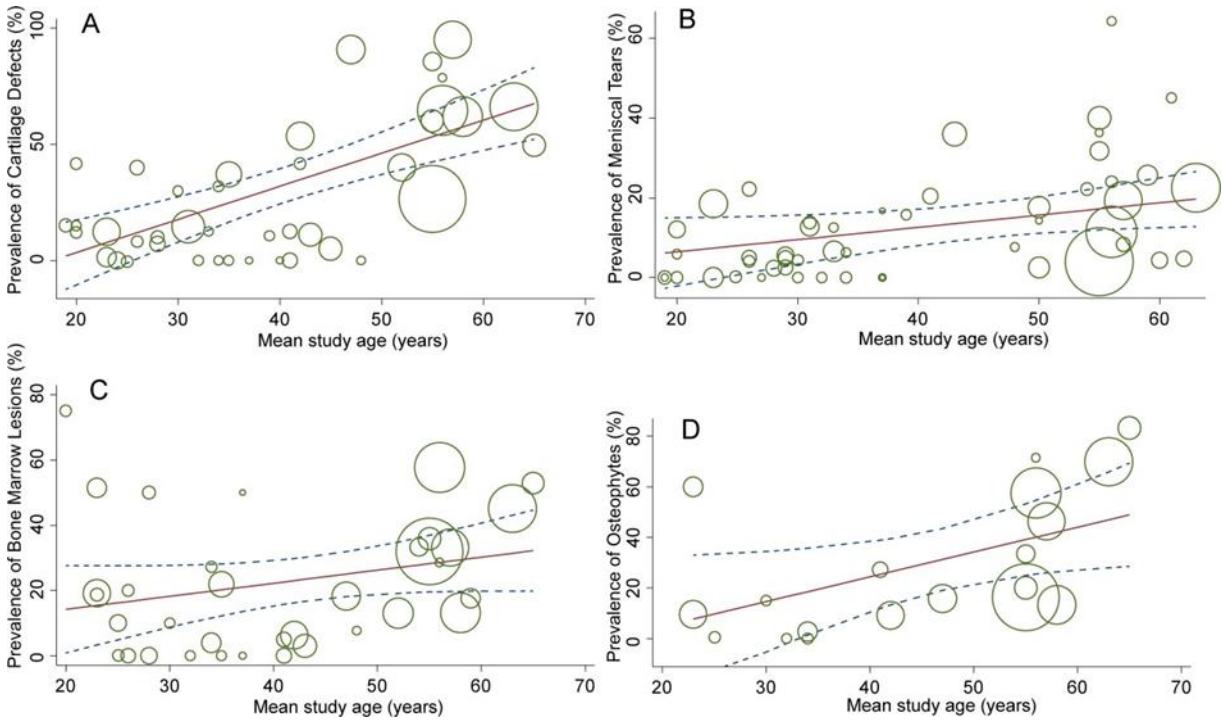
WORMS, Whole-organ magnetic resonance imaging score; MOAKS, Magnetic resonance imaging osteoarthritis knee score; ACL, anterior cruciate ligament; PCL, posterior cruciate ligament; LC; lateral collateral ligament; MCL, medial collateral ligament; n, number of knees.

One study with a mean age of 63 years (n=434) reported a prevalence of subchondral attrition of 30% (26-35%)[31]

eFigure 1. Risk of bias summary graph

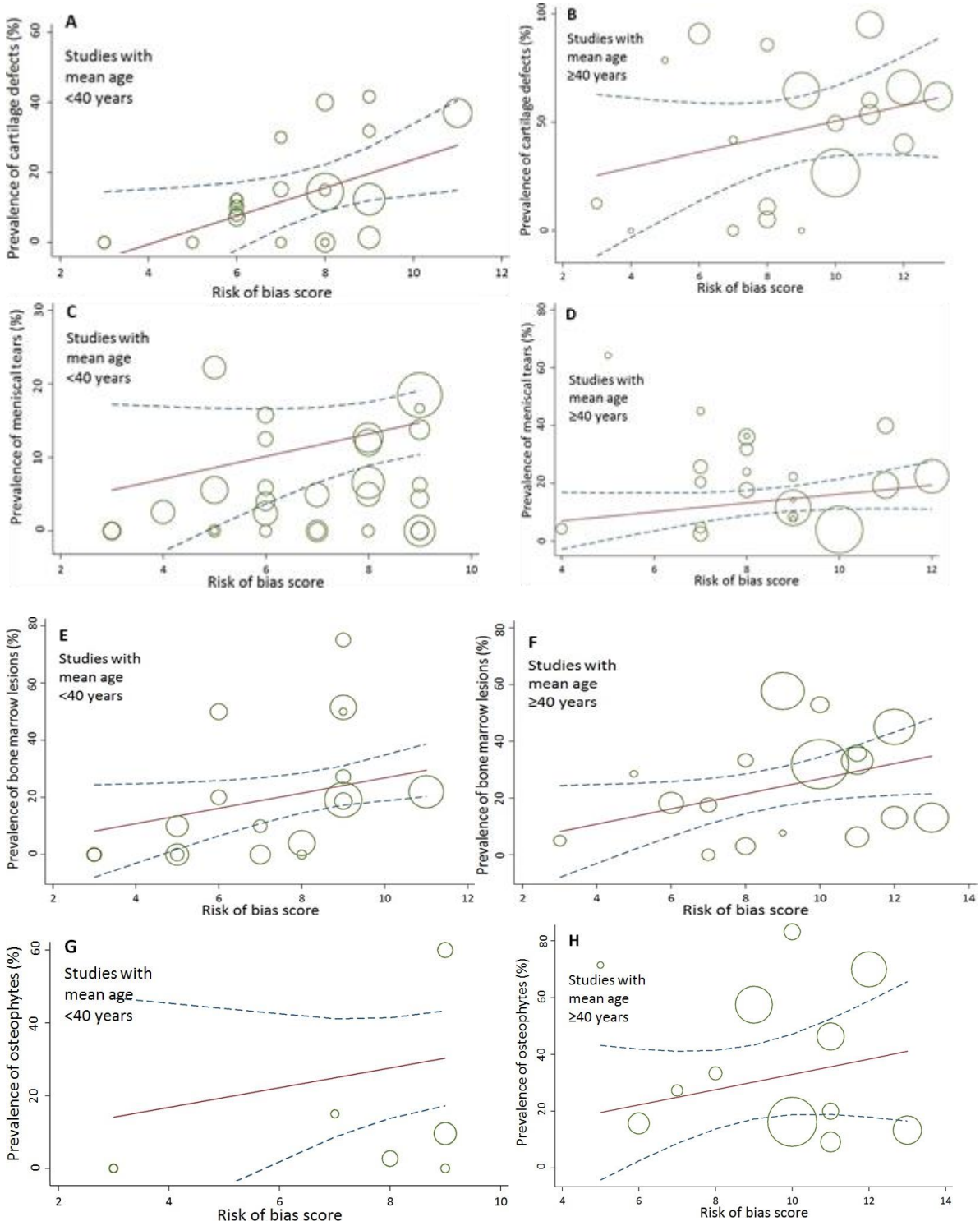


eFigure 2. Weighted random-effects meta-regression analyses according to age



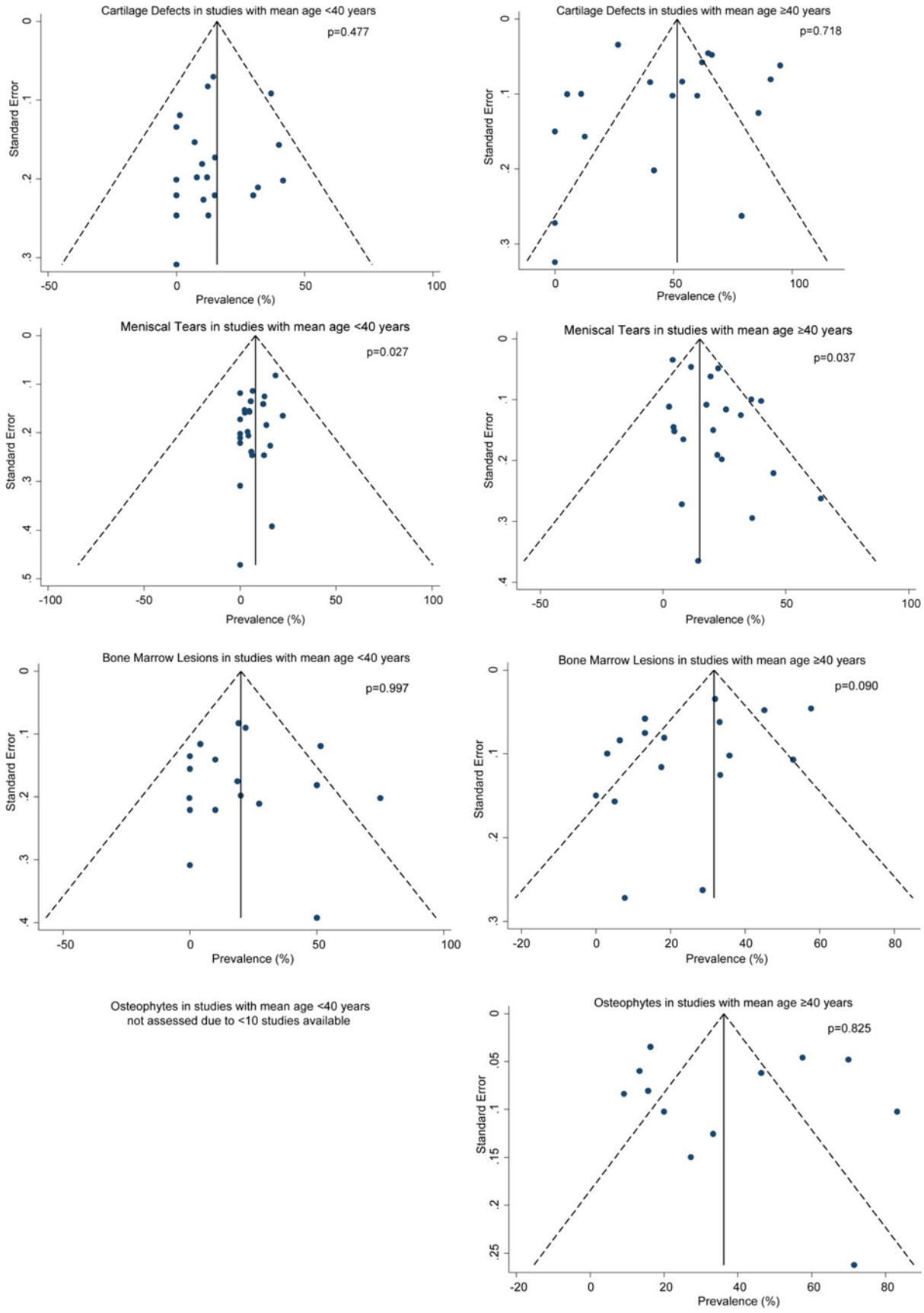
Legend: The area of each circle is inversely proportional to the random effects variance of the prevalence. The fitted random-effects regression line (solid line) is shown with 95% confidence intervals (dashed lines). **A)** Cartilage defects (slope 14.4% (9.0%-19.9%) increase per 10-years; p<0.001); **B)** Meniscal Tears (slope 3.2% (0.2%-6.1%) increase per 10-years; p=0.036); **C)** Bone Marrow Lesions (slope 4.3% (-0.4% to 9.1%) increase per 10-years; p=0.076); **D)** Osteophytes (slope 10.2% (1.7%-18.7%) increase per 10-years; p=0.021).

eFigure 3. Weighted random-effects meta-regression analyses according to risk of bias score



Legend: The area of each circle is inversely proportional to the random effects variance of the prevalence. The fitted random-effects regression line (solid line) is shown with 95% confidence intervals (dashed lines). **A)** Cartilage defects <40 years of age (slope 4.0% (0.4 to 7.6%) increase per 1-unit; p=0.030; **B)** Cartilage defects ≥40 years of age (slope 3.6% (-2.1 to 9.2%) increase per 1-unit; p=0.200;
C) Meniscal tears <40 years of age (slope 1.1% (-2.6 to 4.7%) increase per 1-unit; p=0.544); **D)** Meniscal tears ≥40 years of age (slope 0.3% (-3.2 to 3.8%) increase per 1-unit; p=0.854);
E) Bone marrow lesions <40 years of age (slope 4.1% (-0.3 to 8.5%) increase per 1-unit; p=0.066);
F) Bone marrow lesions ≥40 years of age (slope 1.7% (-2.3 to 5.7%) increase per 1-unit; p=0.371);
G) Osteophytes <40 years of age (slope 3.8% (-6.5 to 14.2%) increase per 1-unit; p=0.384);
H) Osteophytes ≥40 years of age (slope -0.6% (-8.4 to 7.3%) increase per 1-unit; p=0.868.

eFigure 4. Assessment of small study effects by funnel plot and Egger test



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