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Review

# The relationship between meniscal pathologies, cartilage loss, joint replacement and pain in knee osteoarthritis: a systematic review

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SUMMARY

*Objective:* We conducted a systematic review in order to understand the relationship between imaging-visualised meniscus pathologies, hyaline cartilage, joint replacement and pain in knee osteoarthritis (OA).
*Design:* A search of the Medline, Excerpta Medica database (EMBASE) and Cochrane library databases was performed for original publications reporting association between imaging-detected meniscal pathology (extrusion or tear/damage) and longitudinal and cross-sectional assessments of hyaline articular cartilage loss [assessed on magnetic resonance imaging (MRI)], incident joint replacement and pain (longitudinal and cross-sectional) in knee OA. Each association was qualitatively characterised by a synthesis of data from each analysis, based upon study design and quality scoring (including risk of bias assessment and adequacy of covariate adjustment using Cochrane recommended methodology).
*Results:* In total 4,878 abstracts were screened and 82 publications were included (comprising 72 longitudinal analyses and 49 cross-sectional). Using high quality, well-adjusted data, meniscal extrusion and meniscal tear/damage were associated with longitudinal progression of cartilage loss, cross-sectional cartilage loss severity and joint replacement, independently of age, sex and body mass index (BMI). Medial and lateral meniscal tears were associated with cartilage loss when they occurred in the body and posterior horns, but not the anterior horns. There was a lack of high quality, well-adjusted meniscal pathology and pain publications and no clear independent association between meniscal extrusion or tear/damage with pain severity, progression in pain or incident frequent knee symptoms.
*Conclusion:* Meniscal features have strong associations with cartilage loss and joint replacement in knee OA, but weak associations with knee pain.
Systematic review PROSPERO registration number: CRD 42020210910



## Introduction

Osteoarthritis (OA) is the commonest form of arthritis and a major cause of disability and chronic pain. OA confers a large burden on both individuals and health economies[1,2]. While hyaline cartilage loss is the hallmark pathology, knee OA usually involves multiple tissues including menisci[3].

Studies using radiographs have long reported a relationship between meniscal damage (sometimes assessed at arthroscopy) and radiographic progression[4]. Structural severity and disease progression can be quantified by radiographic joint space narrowing, however, this construct consists of articular cartilage loss, meniscal extrusion and maceration[5]. In knee OA, magnetic resonance imaging (MRI) enables the most comprehensive evaluation of soft tissue structures, with ultrasound visualising to a lesser degree.

The aim of this work was therefore to comprehensively review the literature on imaging-visualised meniscal pathologies in knee OA, describing their relationships with longitudinal progression

*Abbreviations:* NR, not reported; (C), cross-sectional measurement; (L), longitudinal measurement; SQ, semiquantitative.

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**Abbreviations**

| | |
|---|---|
| BMI | body mass index |
| EMBASE | Excerpta Medica database |
| KL | Kellgren Lawrence |
| MRI | magnetic resonance imaging |
| NA | no association |
| OA | osteoarthritis |
| PRISMA | Preferred Reporting Items for Systematic Reviews and Meta-Analyses |
| TKR | total knee replacement |
| WOMAC | Western Ontario and McMaster Universities arthritis index |

and cross-sectional severity of hyaline cartilage damage, joint replacement and pain.

## Methods

### *Systematic literature search*

A systematic literature search of Medline (from 1950), Excerpta Medica database [EMBASE (from 1980)] and the Cochrane library databases until April 2022 was performed. Supplementary Table 1 shows the full description of the search terms used. An abbreviation of the full search terms used was 'knee' and 'osteoarthritis' and 'meniscus' manifestations of OA, 'MRI', 'CT' and 'US'. The final search was restricted to humans. Language was not restricted and abstracts were included. Fig. 1 lists the exclusion criteria. The inclusion criteria were *in vivo* observational studies of human populations with clinical and/or radiographic OA, which included an imaging description of meniscal pathology and its relationship with pain, structural severity/progression or joint replacement. Analyses describing the relationship between OA imaging meniscal pathology and structural severity (cross-sectional) or progression (prospective cohorts) in populations without clinical and radiographic OA were included to incorporate early structural features of joint degeneration. The outcome measures of structural severity or progression included cartilage defects, cartilage thickness, cartilage volume and delayed gadolinium-enhanced MRI of cartilage (dGEMRIC) and other MRI-defined early cartilage degeneration measures. Other outcome measures included joint replacement and any pain measures (including incident knee pain, knee pain progression and pain severity in cross-sectional analysis).

Articles identified by the preliminary search were screened by two reviewers (AG and AB) for relevance and for references not identified by the preliminary search, although no additional citations were found. A third reviewer (PC) resolved discordances in opinion. We applied the methods for reporting meta-analyses of observational studies in epidemiology that are recommended by the Cochrane collaboration[6,7], which has been used in previous joint imaging systematic literatures reviews for OA[8].

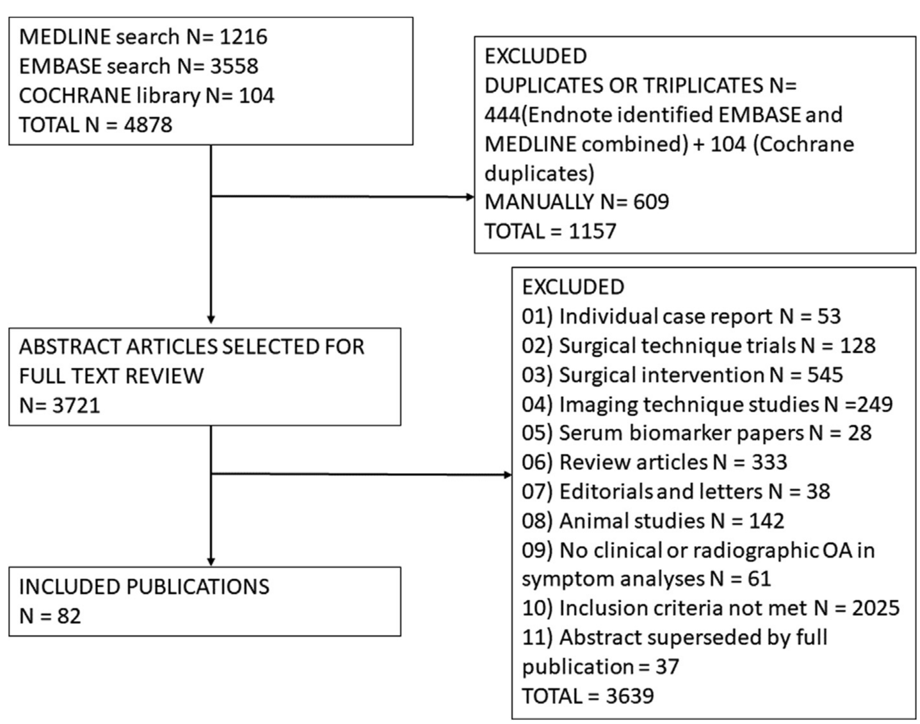


**Fig. 1** Osteoarthritis and Cartilage

PRISMA diagram describing literature flow.

*Data extraction*

Two reviewers (AG and AB) performed data extraction as described in the Supplementary Methods 'data extraction' (see Additional file 1.doc – Multimedia component 6). Extracted data on meniscal tears described if the tear was medial and lateral or anterior, middle and posterior (or combined) where data was available. Meniscal extrusion data described if the location was medial or lateral when available.

*Quality assessment*

The quality of each observational analysis was independently assessed by two reviewers (AG, CM), as described in Supplementary Methods 'Quality assessment' (see Additional file 1.doc – Multimedia component 6) and Table IV.

*Best evidence synthesis*

Statistical pooling of the data was considered inappropriate due to the heterogeneous study populations, methodological quality, meniscal pathology feature described or OA outcome measurements. Therefore a qualitative summary of the evidence for each meniscal feature (e.g. tear) and its association with structural progression and severity, joint replacement or pain is provided at the end of each results section, based upon the study design, adequacy of adjustment for confounders (age, body mass index (BMI) and sex) and quality score as described in the Supplementary Methods 'Best evidence synthesis' (see Additional file1.doc – Multimedia component 6). This methodology has been used previously[8]. For example, cohort analyses were scored using a 17 point checklist assessing risk of bias in the selected study population, risk of bias in methods assessing the joint imaging features, the suitability of statistical analysis and covariate adjustment. In quality scoring, an appropriate statistical analysis of longitudinal cohort data was considered to be logistic or linear regression.

Certain publications measured more than one predictor or outcome of interest, and some publications described both cross-sectional and longitudinal data of interest, "analysis" was therefore used as a broad term to describe the range of study evaluations. Analyses which investigated the association between multiple meniscal features (e.g., tear and extrusion) and OA pain or structural progression outcomes were considered as a single analysis for each meniscal feature. Included analyses that established a significant association between meniscal pathology, structural progression and severity, joint replacement and pain were described as positive (+) or negative (−) accordingly. If no association or inconclusive findings were described, this was reported as no association (NA).

An association of a meniscus pathology with a longitudinal OA outcome (structural progression, longitudinal change in pain, incident pain or joint replacement) was determined from cohort analyses only (summarised in Table III). If a cohort analysis was of above average quality and found a statistically significant association between a meniscal feature and a longitudinal outcome after adjustment for at least age, sex and body mass index (referred to in the text as 'well-adjusted') this association was described as an association independent of age, sex and BMI. This is because these three factors are important determinants in not only the incidence and prevalence of OA[9,10], but also the risk of structural progression[11–13], symptom progression[14] and total knee replacement (TKR) incidence[15] (the three main outcomes of this literature review). These three criteria were determined for all longitudinal analyses and if any of these were not fulfilled, the association was referred to simply as an association. The validity of cross-sectional and case–control associations was assessed in a similar manner but cohort analyses were used primarily to describe meniscal associations.

## Results

*Systematic literature search and selection*

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) diagram in Fig. 1 describes the literature flow. Following exclusion of duplicates and triplicates, 3,721 articles met the search criteria. After applying inclusion/exclusion criteria, 82 articles were included for data extraction and quality scoring.

*Data extraction from included publications*

121 statistical association analyses were performed in 82 included publications. Only one outcome (which could be pain, TKR or structural progression) was examined in 79 publications (which may have been cross-sectional, longitudinal or both and may have assessed one or multiple meniscal features); three publications examined multiple outcomes (e.g., structural progression as well as TKR incidence) (see Appendix and Tables I and II). In 111 out of 121 analyses the mean age was above 50 years. Most analyses ($n = 108$) described both genders; three analyses included females only[16–18], no analyses used male patients only and there was an undisclosed gender ratio in seven analyses[19–23]. One full text publication was inaccessible and one publication was not in English and therefore English abstract data only was used for these (with no available age, gender or demographic data). Knee OA was defined using clinical and radiographic criteria and is described in Supplementary Table 2 (see also Additional file1.doc – Multimedia component 6). Meniscal features were analysed with MRI in 114 analyses and ultrasound in six analyses, with most of these having clinical or radiographic knee OA. Six analyses described structural associations without clinical or radiographic knee OA[19,24–28]. 15 structural analyses described cartilage progression in relation to an individual meniscus subregion (the anterior horn, middle/body or posterior horn). 14 of these were in relation to subregional tear and one in relation to subregional extrusion. No analyses measured pain outcomes in relation to a meniscal subregion pathology.

*Quality assessment of analyses*

Concordance of opinion in quality scoring was observed in 1,343 (97%) of the 1,385 scoring items assessed (recorded in Tables V–VII). The majority of discordant scoring was for study design (criterion 17) and appropriate statistical analysis (criterion 19). Quality scores were converted to percentages of the maximum scores for each class of paper. The mean (range) quality score was 53% (15-85%), 54% (24-76%) and 57% (38-75%) for cross-sectional, cohort and case–control analyses respectively.

*Relationship between meniscal extrusion and structural progression*

The association of meniscal extrusion with structural progression (longitudinal quantitative and semi-quantitative cartilage loss) and structural severity (cross-sectional quantitative and semi-quantitative cartilage loss) are described in Tables I and III.

This section included 30 publications providing 20 cohort analyses, nine cross-sectional analyses and two case–control analyses using MRI and two analyses using cross-sectional ultrasound. Of the 20 cohort analyses measuring the association between meniscal extrusion and structural progression[22,23,25,27,29–44], nine were high quality and well-adjusted analyses[23,25,27,29–33,35]. Six of these

| Author | Feature (method) | Structural progression outcome | Adjustment for confounders | Association (magnitude) crude | Association (magnitude) Adjusted | Association | Quality (score %) |
|---|---|---|---|---|---|---|---|
| **MRI meniscal extrusion − cohort analyses (ME-C)** | | | | | | | |
| Sharma *et al.* 2008[23] | Baseline SQ medial and lateral meniscal extrusion WORMS (C) | Quantitative cartilage loss over 2 years in the ipsilateral tibiofemoral cartilage plates (L) | Age, sex and BMI (*1)<br>Or<br>Age, sex, BMI, medial meniscal damage, medial meniscal extrusion, varus malalignment, and lateral Laxity (*2) | NR | Medial tibia<br>Cartilage volume loss OR 1.99 (1.36, 2.91) *1<br>1.21 (0.79, 1.87) (all covariates) *2<br>cartilage thickness loss<br>OR 1.81 (1.23, 2.65) *1<br>1.27 (0.78, 2.06) (all covariates) *2<br>Medial weight-bearing femur<br>cartilage volume loss OR 1.68 (1.15, 2.44) *1<br>1.28 (0.84, 1.96) (all covariates) *2<br>cartilage thickness loss OR 1.93 (1.35, 2.77) *1<br>1.46 (0.97, 2.20) *2<br>Lateral tibia<br>cartilage volume loss OR 2.11 (1.28, 3.47) *1<br>1.41 (0.80, 2.48) (all covariates) *2<br>cartilage thickness loss<br>OR 2.25 (1.36, 3.73) *1<br>1.33 (0.74, 2.40) (all covariates) *2<br>Lateral weight-bearing femur<br>cartilage volume loss OR 2.30 (1.38, 3.85) *1<br>1.22 (0.66, 2.27) (all covariates) *2<br>cartilage thickness loss OR 1.93 (1.21, 3.06) *1<br>0.95 (0.52, 1.75) (all covariates) *2 | + | 76% (high) |
| Wang *et al.* 2010[29] | Baseline medial meniscal extrusion (C) | Annual quantitative medial tibial cartilage loss on manual segmentation (L) | Age, sex, BMI, baseline tibial plateau bone area and cartilage volume | OR −1.2 (−3.8, 1.4), $P = 0.37$ | OR −1.1 (−4.7, 2.5) $P = 0.56$ | NA | 71% (high) |
| Ding *et al.* 2007[27] | Baseline SQ medial meniscal extrusion (C) | Knee cartilage volume (quantitative by semi-automated segmentation) over 2 years (L)<br>Knee cartilage SQ defects over 2 years (L) | Adjusted for change in cartilage defect score adjusted for age, sex, offspring/control status, BMI and past knee injury, baseline tibial bone area and osteophytes. | NR for cartilage defects<br>Medial tibiofemoral cartilage volume change OR −1.42 (−2.66 to −0.17) | Change over 2 years: Medial tibiofemoral cartilage defects OR 1.56 (0.88–2.77),<br>Medial femoral cartilage defects OR 2.59 (1.14, 5.86)<br>Lateral tibiofemoral cartilage defects OR 1.80 (1.05, 3.08)<br>Medial tibiofemoral cartilage volume change over 2 years OR −1.44 (−2.76 to −0.12) | −<br>Meniscal extrusion is associated with baseline cartilage defects, increase in defects over 2 years and volume loss<br>Nb these defect associations were lost after adjusting for bone area/osteophytes but | 65% (high) |

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|---|---|---|---|---|---|---|---|
| | | | | | | became significant for volume | |
| Teichtahl *et al.* 2017[30] | SQ baseline meniscal extrusion (C) | Quantitative tibial plateau cartilage volume loss at 72 months (L)<br><br>TKR at 72 months (L) | Age<br>Sex<br>BMI<br>Presence of BMLs at baseline | NR | The presence of medial and lateral meniscal extrusion at baseline with ROA was associated with total knee replacement at 72 months<br><br>Medial OR 1.8 (1.3, 2.5). $P = 0.001$<br>Lateral OR 1.6 (1.1, 2.6), $P = 0.04$<br><br>The presence of lateral meniscal extrusion at baseline with ROA was not associated with total knee replacement at 72 months OR 1.30 (0.66, 2.58), $P = 0.45$<br><br>In patients with ROA, baseline meniscal extrusion associated with:<br>greater ipsi-compartmental tibial cartilage loss:<br>medial tibia: −2.1% vs −1.5% per annum, $P < 0.001$<br>lateral tibia: −2.6% vs −1.6% per annum, $P < 0.001$.<br><br>Similar findings among patients without ROA in the medial compartment only. ME associated with:<br>Greater cartilage loss (medial tibia −2.1% vs 1.2%, $P < 0.001$)<br><br>TKR (Medial ME: OR 1.8%, 95% CI 1.3–2.5%, $P = 0.001$, Lateral ME: OR 1.6%, 95% CI 1.1–2.6%, $P = 0.004$) | + meniscal extrusion is associated with cartilage loss and TKR | 65% (high) |
| Liu 2020[31] | Medial meniscal extrusion (MME) at baseline (C) | WORMS SQ cartilage damage progression over 4 years (L) | Model 1: age, sex, knee side, BMI, race, and K&L scores<br><br>Model 2: age, sex, knee side, BMI, race, K&L scores and baseline meniscal injury | NR | <u>Model 1</u><br><br><u>MME was statistical significantly associated with:</u><br><br>Medial compartmental cartilage damage progression OR 1.23 (1.01, 1.50); $P = 0.035$<br><br>Medial tibial cartilage damage progression OR 1.28 (1.00, 1.63)<br><br><u>MME was not associated with:</u><br><br>Medial femur cartilage damage progression OR 1.21 (0.99, 1.49); $P = 0.067$<br><br>Whole knee cartilage damage progression OR 1.13 (0.93, 1.36); $P = 0.209$<br><br><u>Model 2</u><br><br>MME was not associated with any structural cartilage progression after including adjustment for baseline meniscal injury | +/NA<br><br>After adjusting for baseline meniscal injury there was no association between MME and cartilage damage progression | 65% (high) |
| Raynauld *et al.* 2011[49] | Meniscal extrusion at baseline (C) | TKR incidence after 4–7 years (L) | Age, sex, BMI and WOMAC pain | Univariate analysis<br><br><u>Baseline prediction</u><br>Medial meniscal extrusion | Multivariate analysis<br><br><u>Baseline variables only</u> | + | 65% (high) |

(*continued on next page*)

**Table I** (*continued*)

| Author | Feature (method) | Structural progression outcome | Adjustment for confounders | Association (magnitude) crude | Association (magnitude) Adjusted | Association | Quality (score %) |
|---|---|---|---|---|---|---|---|
| | | | | $P = 0.013$, OR 4.06 (1.35, 12.23) | Medial meniscal extrusion OR 3.07 (95% CI 0.91, 10.33) $P = 0.070$<br><br>Baseline variables and 2 year changes in BMI and WOMAC<br><br>Medial meniscal extrusion OR 3.894 (95% CI 1.230 to 12.326) $P = 0.021$ | | |
| Berthiaume *et al.* 2005[22] | Baseline SQ medial meniscal extrusion (C) (Anterior, middle and posterior) | Medial and global compartment cartilage volume loss over 2 years (L) | Nil | Mann Whitney. Non-parametric two sample tests<br><br>Severe medial anterior horn extrusion vs no extrusion is significantly associated with greater medial compartment and global cartilage volume loss (both $P < 0.001$)<br><br>Multilinear regression<br><br>Medial anterior horn extrusion is significantly associated with global cartilage loss (regression coefficient 714.4; $P = 0.01$) and medial cartilage loss (regression coefficient 399.5; $P = 0.01$)<br><br>Medial middle horn extrusion is significantly associated with global cartilage loss (regression coefficient 614.8; $P = 0.02$) and medial cartilage loss (regression coefficient 329.6; $P = 0.03$)<br><br>Lateral middle and anterior meniscal horn extrusion were significantly associated with loss of cartilage for the second year ($P = 0.01$, data not shown).<br><br>Nobody had posterior horn extrusion | NR | + | 59% (high) |
| Pelletier *et al.* 2007[32] | Baseline SQ medial meniscal extrusion (C) | Quantitative MRI medial femoral and tibial change in cartilage volume in 24 months (modified | Nil<br><br>Age, sex, BMI, WOMAC, JSW, BMLs, meniscal tear | Univariate Spearman $P = 0.007$ to 0.0001<br><br>NR | NR<br><br>Stepwise forward multivariate regression $\beta$ coefficient $-0.28$ | + | 59% (high) |

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|---|---|---|---|---|---|---|---|
| | | WORMS) (L) | | | (SE 0.10)$P = 0.004$ | | |
| Sharma *et al.*, 2014[25] | Baseline SQ Meniscal extrusion (C) | 12–48-month incident TF or PF SQ cartilage damage (L) | Age, sex, BMI, previous knee injury or surgery, hand OA, physical activity | NR | OR (95% CI)<br>1.72 (0.63–4.71)$P > 0.05$ | NA | 59% (high) |
| Hart *et al.* 2018[33] | Meniscal SQ extrusion (lateral and medial) (WORMS) at the 60 month visit (C) | Patellofemoral (PF) joint SQ cartilage damage (lateral or medial, WORMS) change between the 60 and 84 month visits (L) | Age, sex, BMI and history of previous knee injury or surgery | NR | Medial or lateral Meniscal extrusion vs no extrusion was associated with:<br><br><u>Longitudinal</u> progression in ipsicompartmental cartilage damage in the lateral but not the medial PF joint compartment<br>lateral OR 1.7 (1.2, 2.5) medial OR 1.0 (0.7, 1.4) | + | 59% (high) |
| Roubille *et al.* 2015[34] | SQ medial meniscal extrusion at baseline (C) | Quantitative change in cartilage volume at 36 months (L) | Nil | Comparing those with and without meniscal extrusion at baseline, extrusion was associated with greater cartilage loss at:<br><br>36 months$P = 0.034$ global knee; $P = 0.0005$ medial compartment | NR | + | 59% (high) |
| Roubille *et al.* 2015[35] | SQ medial meniscal extrusion at baseline (C) | qMRI cartilage volume change at 12 months and 24 months (L) | Age, sex, BMI, WOMAC pain score, cartilage volume (for lateral subregions, which were different at baseline), and JSW at T0 | Comparing those with and without meniscal extrusion at baseline, extrusion was associated with greater cartilage loss at:<br><br>12 months<br>Global and medial compartment cartilage<br>$P < 0.001$<br><br>24 months$P = 0.01$ global knee; $P < 0.001$ medial compartment | Comparing those with and without meniscal extrusion at baseline, extrusion was associated with greater cartilage loss at:<br><br>24 months$P = 0.179$ global knee; $P = 0.021$ medial compartment | − | 59% (high) |
| Eathakkattu Antony *et al.* 2016[36] | Baseline SQ meniscal extrusion (C) | Tibial cartilage volume loss over 10.7 years (L) | Age, sex, BMI and radiographic KOA status | NR | $\beta = 0.28\%$, $P < 0.01$<br><br>Linear regression | + | 53% (low) |
| Eathakkattu Antony *et al.*, 2016[50]<br>(caution this is a different abstract) | Baseline SQ meniscal extrusion (C) | Ipsilateral total knee replacement within 10.7 years (L) | age, sex, body mass index (BMI), baseline WOMAC knee pain and radiographic KOA status. Other MRI structural pathologies | NR | NR | NA | 53% (low) |
| Hafezi-Najad 2015[51] | WORMS and BLOKS average medial and lateral meniscal extrusion score at baseline (C) and change over 2 years (L) | Knee replacement incidence over 6.2 years (L) | <u>First adjustment:</u> Age, sex and BMI<br><br><u>Second adjustment:</u><br>Age, gender, BMI, maximum baseline radiographic Kellgren—Lawrence (KL) score, Physical Activity Scale for the Elderly (PASE) and Western Ontario McMaster Questionnaire (WOMAC) | <u>Baseline</u><br><br>BLOKS Average meniscal extrusion score HR 3.76 (1.30–10.92)<br><br>WORMS Average meniscal extrusion score 0.83 (0.31–2.24)<br><br><u>24 month change in</u> | <u>Baseline</u><br>BLOKS Average meniscal extrusion score<br>Adjusted HR-1<br>3.70 (1.20–11.36)<br>Adjusted HR-2<br>4.19 (1.08–16.19)<br><br>WORMS Average meniscal extrusion score<br>Adjusted HR-1<br>0.74 (0.26–2.05)<br>Adjusted HR-2<br>0.59 (0.21–1.67) | + for baseline BLOKS meniscal extrusion vs incident TKR but not for WORMS baseline or longitudinal change in BLOKS or WORMS | 53% (low) |

(*continued on next page*)

**Table I** (*continued*)

| Author | Feature (method) | Structural progression outcome | Adjustment for confounders | Association (magnitude) crude | Association (magnitude) Adjusted | Association | Quality (score %) |
|---|---|---|---|---|---|---|---|
| | | | | BLOKS Average meniscal extrusion score HR 0.46 (0.02–11.60)<br><br>WORMS Average meniscal extrusion score 0.34 (0.01–10.43) | 24 month change<br><br>BLOKS Average meniscal extrusion score Adjusted HR-1<br><br>0.46 (0.02–10.95)<br>Adjusted HR-2<br>0.34 (0.00–28.90)<br><br>WORMS Average meniscal extrusion score Adjusted HR-1<br>0.30 (0.01–9.77)<br>Adjusted HR-2<br>0.42 (0.02–10.50) | | |
| Hunter *et al.* 2006[37] | Baseline medial and lateral meniscal subluxation (C) | SQ WORMS ipsicompartmental tibiofemoral cartilage loss over 30 months (L) | Age, body mass index (BMI), tibial width, and sex | NR | Odds ratios<br><br>**Medial meniscus**<br><br>Medial subluxationSecond<br><br>quartile 0.9 (0.4–1.9) $P = 0.847$Third quartile 3 3.2 (1.5–6.9) $P = 0.003$Fourth quartile 2.4 (.1–5.0) $P = 0.026$<br>Trend $P = 0.002$<br><br>Anterior subluxationSecond<br><br>quartile 1.3 (0.6–2.7) $P = 0.557$Third quartile 1.7 (0.8–3.6) $P = 0.275$Fourth quartile 3.2 (1.6–6.2) $P = 0.001$<br>Trend $P = 0.001$<br><br>**Lateral meniscus**<br><br>Lateral subluxationSecond<br><br>quartile 1.7 (0.6–5.0) $P = 0.355$Third quartile 3.0 (1.3–7.0) $P = 0.009$Fourth quartile 4.6 (2.0–10.8) $P = 0.001$<br>Trend $P < 0.0001$<br><br>Anterior subluxationSecond<br><br>quartile 2.6 (0.9–7.3) $P = 0.080$Third quartile 2.9 (1.2–7.0) $P = 0.015$Fourth quartile 2.2 (0.7–7.5) $P = 0.204$<br>Trend $P = 0.052$ | +<br><br>Medial meniscal medial and anterior subluxation are associated with ipsicompartmental progressive cartilage loss.<br><br>Lateral meniscal lateral subluxation but not anterior subluxation is associated with ipsicompartmental progressive cartilage loss | 53% (low) |
| Klein 2016[38] | Baseline Meniscus Extrusion Score SQ WORMS (C) | Baseline and 48 month follow up of medial compartmental cartilage thickness (L) | Age, sex, BMI and cartilage thickness at baseline | Meniscus extrusion positively correlated with future cartilage loss. ($P = 0.0001$, Kruskal–Wallis)<br><br>Comparing those with and without medial meniscal extrusion, the presence of extrusion was associated | Multivariable regression analysis: medial compartment cartilage thickness loss was associated with baseline meniscal extrusion (present/absent). Coefficient −0.33 (95%CI −0.47, −0.20), $P < 0.001$ | + | 53% (low) |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | | | | with greater cartilage loss ($P < 0.0001$, unpaired *t*-test) | | | |
| Roemer 2022[44] | Presence of MOAKS meniscal extrusion at baseline (C) | Medial and lateral quantitative tibiofemoral compartments cartilage loss over 24 months (L) | Age, sex and BMI | NR | Medial compartment:<br><br>Mean adjusted difference −0.09 mm, 95% CI: [−0.13, −0.04] mm $P < 0.001$<br><br>Lateral compartment:<br>Mean adjusted difference −0.16 (−0.22, −0.10) $P < 0.001$ | + | 53% (low) |
| Wu 2022[52] | Presence or absence of meniscal extrusion at baseline (C) | Presence or absence of TKR over 108 months (L) | NR | $r = 0.252$<br>Standard error 0.11$P < 0.0001$ | $r = 0.313$<br>Standard error 0.1$P = 0.0036$ | + | 53% (low) |
| Buck *et al.*, 2011[39] | Quantitative medial meniscal subluxation (extrusion) and percentage of meniscal covering at baseline (C) | Loss of cartilage thickness (ΔthCtAB) over 24 months (L) | Nil | Meniscal subluxation was associated with longitudinal loss of cartilage thickness but only in central weight-bearing medial femorotibial cartilage (cMFTC)<br>Kendall's Tau −0.181 ($P = 0.04$)<br><br>Lower meniscal covering was associated with<br><br>longitudinal loss of cartilage thickness Kendall's tau 0.194 and $P$ 0.031 but not in a specific subregion | NR | + | 47% (low) |
| Roemer 2022[43] | MOAKS change in SQ medial meniscal extrusion grade from baseline to 24 months (L) | Two-year difference in medial femoro-tibial compartment cartilage thickness change (L) | Age, sex and BMI | NR | 1 grade: mean adjusted difference −0.15 mm, 95% CI: [−0.20, −0.10] mm $P < 0.001$<br><br>2/3 grades: mean adjusted difference −0.26 mm, 95% CI: [−0.33, −0.18] mm $P < 0.001$<br><br>Any grade change: −0.18 mm, 95% CI: [−0.22, −0.14] mm $P < 0.001$ | + | 47% (low) |
| Roemer *et al.*, 2012[40] | Baseline SQ medial and lateral<br>Meniscal extrusion (C) | Progression in ipsilateral SQ cartilage defects (WORMS) over 6-month TFJ (L) | Age, sex, BMI, glucosamine treatment, prevalent cartilage damage | NR | Meniscal extrusion<br><br>OR (95% CI) 3.60 (1.29–10.07) $P = 0.015$ | +<br><br>Even after adjustment for baseline cartilage, extrusion remains associated cf damage | 41% (low) |
| Roemer *et al.* 2009[41] | Baseline SQ<br><br>(WORMS) medial and lateral meniscal extrusion (C) | Progression in SQ cartilage defects (WORMS) over 30-months TFJ (L) | Age, sex, race, BMI, meniscal alignment | Baseline presences of meniscal extrusion vs no meniscal extrusion was associated with both:<br><br><u>Slow cartilage loss</u><br><br>(WORMS<5 in all subregions at 30 months)<br>OR 2.45 (1.40, 4.27)<br><br><u>Fast cartilage loss</u><br>(WORMS ≥5 in at least one | Baseline presences of meniscal extrusion vs no meniscal extrusion was associated with both:<br><br><u>Slow cartilage loss</u><br><br>(WORMS<5 in all subregions at 30 months)<br>OR 2.02 (1.12, 3.63)$P = 0.02$<br><br><u>Fast cartilage loss</u><br>(WORMS ≥5 in at least one subregion at follow-up) | + | 41% (low) |

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**Table I** (*continued*)

| Author | Feature (method) | Structural progression outcome | Adjustment for confounders | Association (magnitude) crude | Association (magnitude) Adjusted | Association | Quality (score %) |
|---|---|---|---|---|---|---|---|
| | | | | subregion at follow-up) OR 4.77 (1.86, 12.2) | OR 3.62 (1.34, 9.82)$P = 0.01$ | | |
| Choi *et al.* 2014[42] | Quantitative medial meniscal subluxation (Meniscal subluxation index; MSI, the ratio of meniscal overhang to meniscal width in mid-coronal image) at baseline (C) | SQ cartilage degeneration at the medial femoral condyle over 2 years (L) | Nil | Increasing medial meniscal subluxation was associated with incident severe cartilage degeneration (normal cartilage at baseline). The probability of cartilage degeneration to grade 3 or 4 after 2 years was dependent on the MSI:<br><br>0.38 = 44%<br>0.4 = 50%<br>0.6 = 99% | NR | + | 41% (low) |
| **Meniscal extrusion − cross sectional analyses (ME-CS)** | | | | | | | |
| Crema 2012[47] | SQ medial or lateral meniscal extrusion WORMS (C) | Prevalent ipsi-compartmental WORMS (≥2) cartilage damage of medial or lateral TFJ (C) | Age, sex, body mass index, knee malalignment, effusion | NR | Medial tibiofemoral compartment<br><br>OR 1.8 (1.4, 2.2)$P < 0.05$<br><br>Lateral tibiofemoral compartment<br><br>OR 2.0 (1.3, 2.9)$P < 0.05$ | + | 69% (high) |
| Wang *et al.* 2010[29] | Baseline SQ medial and lateral meniscal extrusion (C) | Tibial cartilage volume (medial and lateral) (C) | Age, sex, BMI and baseline tibial plateau bone area | Univariate regression analysis<br><br>media meniscal extrusion vs medial tibial cartilage volume<br><br>OR −60.6 (−250.6, 129.3)$P = 0.53$<br><br>Lateral meniscal extrusion vs Lateral tibial cartilage volume<br><br>OR −852.7 (−1155.0, −550.4)$P < 0.001$ | Multivariate analysis<br><br>media meniscal extrusion vs medial tibial cartilage volume<br><br>OR −350.3 (−541.8, −158.8)$P < 0.001$<br><br>Lateral meniscal extrusion vs Lateral tibial cartilage volume<br><br>OR −762.8 (−1108.1, −417.6) $P < 0.001$ | −<br><br>Meniscal extrusion is associated with ipsicompartmental lower cartilage volume | 65% (high) |
| Ding *et al.* 2007[27] | Baseline SQ medial meniscal extrusion (C) | Knee cartilage SQ defects at baseline (C) | Adjusted for change in cartilage defect score adjusted for age, sex, offspring/control status, BMI and past knee injury, baseline tibial bone area and osteophytes | NR for cartilage defects<br><br>Medial tibiofemoral cartilage volume change OR −1.42 (−2.66 to −0.17) | Baseline: Medial tibiofemoral cartilage defects OR 2.45 (1.36–4.40)<br><br>Lateral tibiofemoral cartilage defects OR 1.80 (1.05, 3.08) | −<br><br>ME is associated with baseline cartilage defects | 62% (high) |
| Hart *et al.* 2018[33] | Meniscal SQ extrusion (medial and lateral) (WORMS) at the 60 month visit (C) | Patellofemoral (PF) joint SQ cartilage damage (lateral or medial, WORMS) at the 60 month visits (C) | Age, sex, BMI and history of previous knee injury or surgery | NR | Medial or lateral Meniscal extrusion vs no extrusion was associated with:<br><br>cross-sectional ipsicompartmental cartilage damage in the PF joint compartment | + | 62% (high) |

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| | | | | | medial OR 1.2 (1.1, 1.3)<br>lateral OR 1.3 (1.1, 1.5) | | |
| Roubille *et al.* 2015[34] | SQ medial meniscal extrusion at baseline (C) | Quantitative change in cartilage volume at baseline (C) | Nil | Comparing those with and without meniscal extrusion at baseline, extrusion was not associated with greater cartilage loss at:<br><br>Baseline*P*<br><br>= 0.395 global knee<br>*P* = 0.682 medial compartment | NR | NA | 62% (high) |
| Takahashi 2015[45] | WORMS medial meniscus extrusion SQ (C) | MRI medial tibiofemoral cartilage T1 ρ relaxation time (C) | Nil | The presence of medial meniscus extrusion was associated with evidence of cartilage damage in 6 defined regions within the medial TFJ<br><br>ROI 1 *P* = 0.008<br>ROI 2 *P* = 0.026<br>ROI 3 *P* = 0.026<br>ROI 4 *P* = 0.026<br>ROI 5 *P* = 0.002<br>ROI 6 *P* = 0.002 | NR | + | 54% (high) |
| Ozdemir 2019[46] | Medial meniscal extrusion in non−weight-bearing and weight-bearing positions by ultrasound scan. Difference of these values (ΔMME)© | Cartilage damage of medial TFJ on MRI (adapted WORMS SQ) (C) | Nil | Weight bearing MME is significantly greater with increasing cartilage loss for grades 1−4, *P* = 0.001<br><br>ΔMME in mm is significantly greater with increasing cartilage loss for grades 1−4, *P* = 0.001 | NR | +<br><br>Non-weight bearing MME was significantly greater only in advanced medial TFJ cartilage loss. Weight-bearing MME and ΔMME were significantly greater with increasing medial TFJ cartilage loss | 54% (high) |
| Paparo *et al.* 2014[102] | The difference between Medial meniscal extrusion (ΔMME) between supine and standing positions© | Medial TFJ cartilage loss SQ (WORMS) (C) | Nil | ΔMME was significantly associated with medial TFJ cartilage loss *P* = 0.0449, *β* 0.1195 (SE 0.006) | NR | + | 46% (low) |
| Arepati 2021[103] | SQ MRI medial meniscus extrusion (MME) and anterior meniscus extrusion (AME) (C) | MRI WORMS cartilage destruction (C) | Age, sex and BMI | NR | Versus no medial and anterior extrusion group:<br><br>MME (−) and AME (+) − OR 1.70 (1.04–2.79), *P* = 0.035<br><br>MME (+) and AME (−) − OR 2.10 (1.31−3.38), *P* = 0.002<br><br>MME (+) and AME (+) − OR 5.30 (3.45−8.14)*P* = 0.001 | + | 46% (low) |
| Lerer 2004[104] | | Qualitative assessment of medial compartment | Nil | Medial meniscal extrusion ≥3 mm was more prevalent | NR | + | NB low quality |

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**Table I** (*continued*)

| Author | Feature (method) | Structural progression outcome | Adjustment for confounders | Association (magnitude) crude | Association (magnitude) Adjusted | Association | Quality (score %) |
|---|---|---|---|---|---|---|---|
| | Quantitative Medial meniscal extrusion in mm (C) | articular cartilage loss (C) | | in knees with moderate to severe medial compartment articular cartilage loss than those without this degree of extrusion 69% (27/39)*P*<br><br>< 0.0001 95% | | Meniscal extrusion of ≥3 mm was more prevalent than >3 mm in knees with more advanced cartilage loss | paper, statistics are inappropriate and relative risk has not been included here because of this<br><br>38% (low) |
| Alaam 2021[69] | Sonographer defined US meniscal extrusion (C) | Sonographer defined US femoral cartilage degeneration (C) | Nil | Meniscal extrusion correlated significantly with femoral cartilage degeneration ($P < .001$) | NR | + | 23% (low) |
| **MRI meniscal extrusion – case control analyses (ME-CC)** | | | | | | | |
| Roemer *et al.* 2015[54] | Baseline SQ meniscal extrusion MOAKS (C) | Incidence of total knee replacement 1 year later (L) | Nested case control study within the OAI cohort.<br><br>1:1 matched<br><br>case–control design (Age, sex, radiographic disease status) | Meniscal extrusion ≥5 mm vs extrusion <5 mm or no extrusion<br><br>Medial<br>OR, 1.00 (0.60, 1.67)<br><br>Lateral<br>OR, 1.42 (0.54, 3.75) | NR | NA | 75% (high) |
| Roth 2020[53] | Quantitative progression in MRI-assessed medial meniscal extrusion in the 2 years before joint replacement (L) | Incidence of knee replacement after 2 years (L) | Nested case control study within the OAI cohort.<br><br>1:1 matched<br>case–control design (Age, sex, radiographic disease status)<br><br>Adjusted for<br>Baseline BMI and pain at T-2 years | NR | Significantly greater odds of knee replacement with greater increase in maximal medial extrusion<br><br>OR 1.40 [1.12, 1.75]*P*<br><br>-value < 0.005 | + | 63% (high) |
| Sharma 2019[48] | 3D MRI medial meniscal extrusion measures (C) | Medial femorotibial cartilage thickness loss above 102 μm over 12 months (L) | Matched based on radiographic stage, WOMAC pain, BMI, height and sex | NR | Extrusion area (%) Cohen's *D* 0.24, $P = 0.20$<br><br>Mean extrusion distance Cohen's *D* 0.38, $P = 0.09$<br><br>Max. extrusion distance Cohen's *D* 0.66, $P = 0.01$<br><br>Mean extrusion 5 central slices Cohen's *D* 0.58, $P = 0.01$<br><br>Mean extrusion 1 central slice Cohen's *D* 0.62, $P = 0.01$ | + | 56% (high) |
| Sharma 2022[105] | Quantitative MRI 3D medial and lateral meniscus extrusion (C) | Quantitative MRI cartilage thickness loss vs non-progressors over 12 months (L) | Matched 1:1 by the same sex, baseline Kellgren Lawrence grade, body height, BMI and WOMAC pain scores | NR | Medial meniscus<br><br>Mean extrusion 5 central slices Cohen's *D* 0.58, $P < 0.01$<br><br>Mean extrusion central slice 0.62, $P < 0.01$ | + for medial side | 44% (low) |

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| | | | | | Max. extrusion distance Cohen's $D$ 0.62, $P < 0.01$<br><br><u>Lateral meniscus</u><br><br>Mean extrusion 5 central slices Cohen's $D$ 0.22, $P = 0.41$<br><br>Mean extrusion central slice 0.06, $P < 0.83$<br><br>Max. extrusion distance Cohen's $D$ 0.09, $P = 0.68$ | | |
| **MRI meniscal tear/damage − cohort analyses (MT-C)** | | | | | | | |
| Sharma *et al.* 2008[23] | Baseline SQ medial and lateral meniscal damage WORMS (C) | Quantitative cartilage loss over 2 years in the ipsilateral tibiofemoral cartilage plates (L) | Age, sex and BMI (*1)<br><br>Or<br><br>Age, sex, BMI, medial meniscal damage, medial meniscal extrusion, varus malalignment, and lateral<br><br>Laxity (*2) | NR | <u>Medial tibia</u><br><br>cartilage volume loss<br><br>OR 1.57 (1.29, 1.91) *1<br>1.29 (1.02, 1.64) (all covariates) *2<br><br>cartilage thickness loss<br><br>OR 1.40 (1.16, 1.69) *1<br>1.07 (0.84, 1.37) (all covariates) *2<br><br><u>Medial weight-bearing femur</u><br><br>cartilage volume loss OR 1.32 (1.09, 1.60) *1<br>1.10 (0.87, 1.38) (all covariates) *2<br><br>cartilage thickness loss OR 1.39 (1.16, 1.68) *1<br>1.19 (0.94, 1.50) (all covariates) *2<br><br><u>Lateral tibia</u><br><br>cartilage volume loss OR 1.54 (1.26, 1.87) *1<br>1.45 (1.14, 1.85) (all covariates) *2<br><br>cartilage thickness loss<br>OR 1.69 (1.39, 2.06) *1<br>1.62 (1.28, 2.06) (all covariates) *2<br><br><u>Lateral weight-bearing femur</u><br><br>cartilage volume loss OR 1.78 (1.43, 2.20) *1<br>1.62 (1.27, 2.07) (all covariates) *2<br>cartilage thickness loss OR 1.75 (1.42, 2.17) *1<br>1.66 (1.30, 2.12) (all covariates) *2 | + | 76% (high) |
| Raynauld *et al.*, 2006[11] | Baseline SQ medial and lateral meniscal tear (C) | 24 month progression in MRI-assessed quantitative loss in cartilage volume (L) | Age, sex, body mass index, Western Ontario McMaster Osteoarthritis Index (WOMAC) pain at baseline | Baseline severe MM tear associated with “fast” vs “slow” global cartilage volume loss<br>ANOVA $P < 0.001$<br>ANOVA $P = 0.005$<br><br>Lateral tears were not associated with “fast” vs “slow” cartilage volume loss<br>ANOVA $P = 0.28$ | NR<br><br>Multivariate linear regression<br><br>Severe medial meniscal tear was not associated with medial TFJ cartilage volume loss at 24 months<br>(authors conclude this is due to strong collinearity with extrusion which was associated) | + | 71% (high) |

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**Table I** (*continued*)

| Author | Feature (method) | Structural progression outcome | Adjustment for confounders | Association (magnitude) crude | Association (magnitude) Adjusted | Association | Quality (score %) |
|---|---|---|---|---|---|---|---|
| Roemer *et al.* 2012[59] | Baseline SQ medial and lateral meniscal damage (C) | SQ (WORMS) ipsicompartmental tibiofemoral cartilage loss (in the femur or tibia) over 30 months (L) | Age, sex and body mass index | NR | When comparing severe meniscal tear and damage (grades 3 and 4) to no meniscal tear or damage<br><br>Ipsicompartmental medial cartilage loss was more likely<br>OR 4.4 (2.2, 8.7) ($P < 0.05$)<br><br>Ipsicompartmental lateral cartilage loss was more likely<br>OR 3.8 (1.1, 13.0)<br>($P < 0.05$) | +<br><br>No associations were seen with lower grades of meniscal damage/tear | 65% (high) |
| Chang 2011[55] | SQ measurement of medial and lateral meniscal tears using WORMS at baseline (C) | Semi-automated tibial and weight-bearing femoral cartilage thickness loss over 2 years in the medial and lateral compartments (L) | Age, sex, body mass index, tear in the other two segments (and extrusion where described*). | NR | MEDIAL COMPARTMENT TEAR VS MEDIAL TIBIAL CARTILAGE<br><br>**Body tear** was not associated with cartilage loss in the internal or posterior subregions but was with cartilage loss in the<br><br>Central subregion<br>OR 3.80 (1.47–9.78)* ($P < 0.01$)<br><br>External subregion<br>OR 8.04 (2.99–21.66)* ($P < 0.0001$)<br><br>Anterior subregion<br>OR 2.76 (1.23–6.21)* ($P < 0.05$)<br><br>**Posterior horn tear** was only associated with cartilage loss in the posterior subregion<br>OR 2.65 (1.23–5.71)* ($P < 0.05$)<br><br>MEDIAL COMPARTMENT TEAR VS MEDIAL FEMORAL CARTILAGE<br><br>**Body tear** was only associated with cartilage loss in the external femoral subregion<br>OR 2.61 (1.20–5.66) ($P < 0.05$)<br><br>**Posterior horn tear** was not associated with femoral cartilage loss<br><br>LATERAL COMPARTMENT TEAR VS LATERAL TIBIAL CARTILAGE<br><br>**Body tear** was not associated with cartilage loss in the internal subregion but was with cartilage loss in the<br><br>Central subregion<br>OR 3.81 (1.12–13.0) ($P < 0.05$)<br><br>External subregion<br>OR 3.99 (1.01–15.85.66) ($P < 0.05$)<br><br>Anterior subregion | +<br><br>Anterior horn tears in either medial or lateral compartments had no association with ipsicompartmental cartilage loss in any region<br><br>MEDIAL<br><br>Medial body tear is associated with cartilage loss in external tibial and femoral subregions and in adjacent central and anterior tibial subregions.<br>Medial posterior horn tear is associated with cartilage loss of posterior tibial and no other subregion. (the above are independent of age, sex, BMI, tears in the other two meniscal segments<br>LATERAL<br>body tear was associated with cartilage loss in the external and adjacent central, anterior, and posterior<br><br>tibial subregions<br><br>posterior horn tear with cartilage loss in external tibial subregion | 62% (high) |

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|---|---|---|---|---|---|---|---|
| | | | | | OR 3.24 (1.02–10.35) ($P < 0.05$)<br><br>Posterior subregion<br>OR 6.47 (1.74–24.05) ($P < 0.01$)<br><br>**Posterior horn tear** was only associated with cartilage loss in the external subregion<br>OR 3.94 (1.26–12.38) ($P < 0.05$)<br><br>LATERAL COMPARTMENT TEAR VS LATERAL FEMORAL CARTILAGE<br><br>There were no associations of this nature within this compartment | | |
| Raynauld *et al.* 2011[49] | Meniscal tear at baseline (C) and 2 year change from baseline (L) | TKR incidence after 4–7 years (L) | Age, sex, BMI and WOMAC pain | Univariate analysis<br><br>Baseline prediction<br><br>TKR was associated with severe medial tear $P = 0.004$, OR 5.69 (1.75, 18.50) but not:<br><br>Lateral tear $P = 0.132$<br>Severe lateral tear $P = 0.976$<br>Medial tear $P = 0.072$ | Multivariate analysis<br><br>Baseline variables only<br><br>Severe medial meniscal tear OR 4.62 (95% CI 1.24 to 17.30) $P = 0.02$<br><br>Baseline variables and 2 year changes in BMI and WOMAC<br><br>Severe medial meniscal tear OR 5.35 (95% CI 1.54, 18.63) $P = 0.008$ | + baseline tears are associated with incident TKR | 62% (high) |
| Berthiaume 2005[22] | Baseline medial or lateral SQ meniscal tear or degeneration (C) | Medial and global compartment cartilage volume loss over 2 years (L) | Nil | Mann Whitney. Non-parametric two sample tests<br><br>Severe medial tear vs no tear significant association with greater medial compartment and global cartilage volume loss (global cartilage $P = 0.002$; medial cartilage $P < 0.0001$)<br><br>No significant differences in cartilage volume losses were seen among the groups with lateral meniscal tear.<br><br>Multilinear regression analysis<br>Medial meniscal tear is not significantly associated with global cartilage loss (regression coefficient 28.2; $P = 0.83$) and medial cartilage loss (regression coefficient 30.5; $P = 0.70$) | NR | Both + and NA | 59% (high) |
| Crema *et al.* 2010[16] | SQ BLOKS medial meniscus morphology at baseline (C) | Subregional cartilage loss in medial tibiofemoral compartment over 24 | Model 1 = adjusted for age, BMI &<br><br>Model 2 = adjusted for age, BMI & medial meniscal | NR | Whole meniscus<br><br>for complex tear and maceration vs no meniscal disease | + | 59% (high) |

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**Table I** (*continued*)

| Author | Feature (method) | Structural progression outcome | Adjustment for confounders | Association (magnitude) crude | Association (magnitude) Adjusted | Association | Quality (score %) |
|---|---|---|---|---|---|---|---|
| | | months (L) | extrusion<br><br>(NB all patients were female) | | Model 1: Reported greater total medial tibia and central medial femur cartilage loss 0.101 mm ($P = 0.01$)<br><br>Model 2: Reported greater medial tibial cartilage loss 0.04 mm ($P = 0.04$)<br><br>Subregional meniscal tears<br><br>for single body tears vs no meniscal disease or meniscal signal change<br><br>Models 1 & 2 reported greater cartilage loss<br><br>For posterior horn complex tear and maceration vs no meniscal disease or meniscal signal change Model 2 reported greater cartilage loss of 0.074 mm ($P = 0.03$) at the External medial tibia | | |
| Pelletier 2007[32] | Baseline SQ medial and lateral meniscal tear (C) | Quantitative MRI medial femoral and tibial change in cartilage volume in 24 months (modified WORMS) (L) | Nil<br><br>Age, sex, BMI, WOMAC, JSW, BMLs, meniscal extrusion | Univariate Spearman $P = 0.0001$ to 0.007<br><br>NR | NR<br><br>Stepwise forward multivariate regression<br><br>Medial tear<br>$\beta$ coefficient −0.16<br>(SE 0.09) $P = 0.08$<br><br>Lateral tear<br>$\beta$ coefficient +0.15<br>(SE 0.09) $P = 0.08$ | NA | 59% (high) |
| Sharma 2014[25] | Baseline SQ meniscal tear (C) | 12–48-month incident TF or PF SQ cartilage damage (L) | Age, sex, BMI, previous knee injury or surgery, hand OA; physical activity | NR | OR (95% CI)<br>1.05 (0.39–2.82) $P > 0.05$ | NA | 59% (high) |
| Guermazi *et al.* 2013[56] | Baseline isolated medial posterior root tear (C)<br><br>Baseline SQ WORMS meniscal tear (grade 1 or above) without root involvement (C) | Incidence or progression of SQ WORMS cartilage damage over 30 months (L) | Age, sex, BMI malalignment, clinic site, malalignment | Comparing knees with Isolated medial posterior meniscal root tear vs no tear is associated with incident and progressive medial tibiofemoral cartilage loss.<br><br>RR 2.35 (1.40–3.94)<br><br>Comparing knees with meniscal tears (without isolated medial posterior meniscal root tear) vs no tear is associated with incident and progressive medial tibiofemoral cartilage loss.<br><br>RR 2.10 (1.55–2.85) | Comparing knees with Isolated medial posterior meniscal root tear vs no tear is associated with incident and progressive medial tibiofemoral cartilage loss.<br><br>RR 2.03 (1.18–3.48)<br><br>Comparing knees with meniscal tears (without isolated medial posterior meniscal root tear) vs no tear is associated with incident and progressive medial tibiofemoral cartilage loss<br><br>RR 1.84 (1.32–2.58) | +<br><br>Meniscal tears are associated with cartilage loss | 59% (high) |
| Hart 2018[33] | | | | NR | | + | 59% (high) |

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| | Medial and lateral meniscal SQ tear (lateral and medial) (WORMS) at the 60 month visits (C) | Patellofemoral (PF) joint SQ cartilage damage (lateral or medial, WORMS) change between the 60 and 84 month visits (L) | Age, sex, BMI and history of previous knee injury or surgery | | Medial or lateral Meniscal tear grade 3–4 vs no tear was associated with:<br><br>longitudinal progression in ipsicompartmental cartilage damage in the lateral but not the medial PF joint compartment<br><br>lateral OR 1.7 (1.1, 2.7) medial OR 0.7 (0.4, 1.1) | | |
| Khan 2016[26] | Progression in SQ meniscal damage/tear over 8 years(L) | Progression in Cartilage volume loss (medial tibiofemoral) over 8 years (L) | Age, sex, BMI, offspring control status, change in BMLs, meniscal extrusion, baseline radiographic OA status | NR | *β* (95% CI)<br><br>Medial tibiofemoral cartilage<br><br>−176 (−302 to −49)*P*<br><br>< 0.05) | +<br><br>Association not present fo lateral compartment or total knee cartilage | 56% (high) |
| Eathakkattu Antony *et al.*, 2016 (caution this is a different abstract)[50] | Baseline SQ meniscal tear (C) | Ipsilateral total knee replacement within 10.7 years (L) | Age, sex, body mass index (BMI), baseline WOMAC knee pain and radiographic KOA status. Other MRI structural pathologies | NR | NR | + | 53% (low) |
| Hafezi-Najad 2015[51] | Medial and lateral meniscal WORMS and BLOKS average tear score at baseline © and change over 2 years (L) | Knee replacement incidence over 6.2 years (L) | First adjustment: Age, sex and BMI<br><br>Second adjustment:<br><br>Age, sex, BMI, maximum baseline radiographic Kellgren–Lawrence (KL) score, Physical Activity Scale for the Elderly (PASE) and Western Ontario McMaster Questionnaire (WOMAC) | Baseline<br><br>BLOKS Average meniscal tear score HR 1.10 (0.78 −1.55)<br><br>WORMS Average meniscal tear score HR 1.10 (0.51 −2.36)<br><br>24 month change<br><br>BLOKS Average meniscal tear score HR 1.57 (0.66 −3.69)<br><br>WORMS Average meniscal tear score HR 1.74 (0.40 −7.53) | Baseline<br><br>BLOKS Average meniscal tear score<br>Adjusted HR-1<br>1.15 (0.80–1.66)<br>Adjusted HR-2<br>1.09 (0.72–1.66)<br><br>WORMS Average meniscal tear score<br>Adjusted HR-1<br>1.19 (0.54–2.65)<br>Adjusted HR-2<br>0.92 (0.41–2.06)<br><br>24 month change<br><br>BLOKS Average meniscal extrusion score<br>Adjusted HR-1<br>1.50 (0.61–3.71)<br>Adjusted HR-2<br>1.84 (0.70–4.84)<br><br>WORMS Average meniscal extrusion score<br>Adjusted HR-1<br>1.63 (0.36–7.31)<br>Adjusted HR-2<br>1.69 (0.39–7.30) | NA | 53% (low) |
| Hunter *et al.* 2006[37] | Baseline medial and lateral meniscal damage SQ WORMS (C) | SQ WORMS ipsicompartmental tibiofemoral cartilage loss over 30 months (L) | Age, body mass index (BMI), tibial width, and sex | NR | Odds ratios<br><br>**Medial meniscus**Second<br><br>quartile 3.4 (1.8–6.2) *P* < 0.0001Third<br><br>quartile 3.9 (2.2–7.0) *P* < 0.0001Fourth<br><br>quartile 6.3 (3.1–12.6) *P* < 0.0001<br><br>Trend *P* < 0.0001 | +<br><br>Meniscal damage is associated with progressive ipsicompartmental cartilage loss | 53% (low) |

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**Table I** (*continued*)

| Author | Feature (method) | Structural progression outcome | Adjustment for confounders | Association (magnitude) crude | Association (magnitude) Adjusted | Association | Quality (score %) |
|---|---|---|---|---|---|---|---|
| | | | | | **Lateral meniscus**Second quartile 2.5 (1.1–6.0) $P = 0.037$Third quartile 4.5 (2.1–9.9) $P = 0.0002$Fourth quartile 4.2 (1.6–11.2) $P = 0.004$<br>Trend $P < 0.0001$ | | |
| Klein 2016[38] | Baseline meniscus damage Score SQ WORMS and presence/ absence of tear (C) | Baseline and 48 month follow up of medial compartmental cartilage thickness (L) | Age, sex, BMI and cartilage thickness at baseline | Meniscus damage positively correlated with future cartilage loss. ($P = 0.0001$, Kruskal–Wallis)<br>Comparing those with and without medial meniscal damage ≥3, damage >3 was associated with greater cartilage loss (−4.8% vs −9.2%, respectively; $P = 0.05$, unpaired *t*-test) | Multivariable regression analysis: medial compartment cartilage thickness loss was not associated with baseline meniscal tear (present vs absent). Coefficient 0.65 (95% CI −0.06, 0.19), $P = 0.32$ | + unadjusted, NA for adjusted | 53% (low) |
| Roemer 2022[44] | Presence of MOAKS meniscal tear at baseline (C) | Medial and lateral tibiofemoral compartments quantitative cartilage loss over 24 months (L) | Age, sex and BMI | NR | Medial compartment:<br>Mean adjusted difference −0.08 mm, 95% CI: [−0.12, −0.04] mm $P < 0.001$<br>Lateral compartment:<br>Mean adjusted difference −0.13 (−0.17, −0.09) $P < 0.001$ | + | 53% (low) |
| Madan-Sharma *et al.*,2008[57] | Baseline presence of meniscal tear (C) | 24 month progression in SQ OARSI medial TFJ radiographic JSN and cartilage loss (L) | Age, sex, BMI, family effect | | | | 47% (low) |
| | | All patients | | RR 4.1 (1.3–13.1) | RR 3.57 (1.1–10.0) | + | |
| | | Knees KL < 2 | | NR | RR 1.19 (0.14–6.92) | NA | |
| | | Knees KL > 2 | | RR 8.91 (1.1–22.8) | RR 8.91 (1.1–22.8) | + | |
| Roemer 2022[43] | MOAKS change in medial meniscal tear/ damage from baseline to 24 months (L) | Two-year difference in medial femoro-tibial compartment cartilage thickness change (L) | Age, sex and BMI | NR | 1 grade: mean adjusted difference −0.10 mm, 95% CI: [−0.16, −0.04] mm $P = 0.001$<br>2 grades: mean adjusted difference −0.28 mm, 95% CI: [−0.37, −0.18] mm $P < 0.001$<br>Any grade change: −0.14 mm, 95% CI: [−0.20, −0.09] mm $P < 0.001$ | + | 47% (low) |
| Roemer *et al.* 2009[41] | Baseline SQ (WORMS) meniscal tear (C) | Progression in SQ cartilage defects (WORMS) over 30-months TFJ (L) | Age, sex, race, BMI, meniscal alignment | Baseline presences of meniscal tear vs no meniscal tear was associated with both:<br>Slow cartilage loss | Baseline presences of meniscal tear vs no meniscal tear was associated with both:<br>Slow cartilage loss<br>(WORMS<5 in all subregions at 30 months) OR 3.25 (1.70, 6.25)*P* | + | 41% (low) |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | | | | (WORMS<5 in all subregions at 30 months)<br>OR 3.15 (1.73, 5.72)<br><br>Fast cartilage loss (WORMS ≥5 in at least one subregion at follow-up)<br>OR 4.53 (1.76, 11.7) | $< 0.001$<br><br>Fast cartilage loss (WORMS ≥5 in at least one subregion at follow-up)<br>OR 3.19 (1.13, 9.03)$P = 0.03$ | | |
| Biswal 2002[58] | Baseline presence of meniscal tear or damage (medial or lateral) (C) | Progression in SQ cartilage loss over at least 1 year (L) | Nil | 22% vs 14% of cartilage lesions progressed in the presence and in the absence of meniscal tears respectively*t*<br><br>-test<br>($P \leq 0.018$). | NR | + | Low quality*t*<br><br>test retrospective cohort based upon risk of meniscal tear<br><br>24% (low) |
| **Meniscal tear/damage – cross-sectional analyses (MT-CS)** | | | | | | | |
| Hart 2018[33] | Meniscal SQ tear (lateral and medial) (WORMS) at the 60 month visits (C) | Patellofemoral (PF) joint SQ cartilage damage (lateral or medial, WORMS) at the 60 month visits (C) | Age, sex, BMI and history of previous knee injury or surgery | NR | Medial or lateral Meniscal tear grade 3–4 vs no tear was associated with:<br><br>cross-sectional ipsicompartmental cartilage damage in the PF joint compartment<br><br>medial OR 1.1 (1.0,1.2)<br>lateral OR 1.2 (1.0, 1.4) | + | 62% (high) |
| Ding *et al.* 2007[60] | Baseline presence or absence of meniscal tear in the medial or lateral TFJ (C) | Baseline SQ cartilage defect score and quantitative cartilage volume in the ipsicompartmental TFJ (C) | Age, sex, OA family history, BMI, cartilage volume, bone area, cartilage defect score, and radiographic change | NR | Medial anterior horn tear<br><br>Medial tibial cartilage volume OR 1.53 (95% CI 0.61, 3.86); $P = 0.365$<br><br>Medial femoral cartilage volume OR 0.88 (95% CI 0.55, 1.39); $P = 0.574$<br><br>Medial TFJ cartilage defect score OR 1.91 (95% CI 1.30, 2.80); $P = 0.020$<br><br>Medial body tear<br><br>Medial tibial cartilage volume OR 1.24 (95% CI 0.61, 2.54); $P = 0.554$<br><br>Medial femoral cartilage volume OR 0.88 (95% CI 0.63, 1.24); $P = 0.466$<br><br>Medial TFJ cartilage defect score OR 1.38 (95% CI 1.03, 1.85); $P = 0.029$<br><br>Posterior horn tear<br><br>Medial tibial cartilage volume OR 1.45 (95% CI 0.66, 3.19); $P = 0.357$<br><br>Medial femoral cartilage volume OR 0.88 (95% CI 0.63, 1.23); $P = 0.452$<br><br>Medial TFJ cartilage defect score OR 1.33 (95% CI 1.00, 1.76); $P = 0.048$ | +<br>The presence of any meniscal tear is associated with ipsicompartmental TFJ cartilage defects except for lateral anterior and posterior horn tears.<br><br>Ipsicompartmental meniscal tears are not associated with TFJ cartilage volume in the medial compartment but are in the lateral compartment | 62% (high) |

(*continued on next page*)

**Table I** (*continued*)

| Author | Feature (method) | Structural progression outcome | Adjustment for confounders | Association (magnitude) crude | Association (magnitude) Adjusted | Association | Quality (score %) |
|---|---|---|---|---|---|---|---|
| | | | | | Lateral anterior horn tear<br><br>Lateral tibial cartilage volume OR 0.33 (95% CI 0.15, 0.69); $P = 0.004$<br><br>Lateral femoral cartilage volume OR 0.53 (95% CI 0.31, 0.92); $P = 0.025$<br><br>Lateral TFJ cartilage defect score OR 1.18 (95% CI 0.87, 1.60); $P = 0.283$<br><br>Lateral body tear<br><br>Lateral tibial cartilage volume OR 0.51 (95% CI 0.28, 0.94); $P = 0.031$<br><br>Lateral femoral cartilage volume OR 0.92 (95% CI 0.61, 1.39); $P = 0.696$<br><br>Lateral TFJ cartilage defect score OR 1.53 (95% CI 1.12, 2.08); $P = 0.007$<br><br>Lateral posterior horn tear<br><br>Lateral tibial cartilage volume OR 0.22 (95% CI 0.10, 0.50); $P < 0.001$<br><br>Lateral femoral cartilage volume OR 0.50 (95% CI 0.28, 0.87); $P = 0.014$<br><br>Lateral TFJ cartilage defect score OR 1.35 (95% CI 0.99, 1.84); $P = 0.057$ | | |
| Crema *et al.* 2014[17] | Baseline SQ medial meniscal tear (BLOKS) (C) | Delayed gadolinium-enhanced magnetic resonance imaging of cartilage (dGEMRIC) indices in the medial tibial and femoral cartilage. Analyses performed at baseline and at 1 year but no longitudinal analysis is made(C) | Concomitant ACL tear | Analysis of covariance (Difference in dGEMRIC index, mean ± S.E.M. ms) for Advanced meniscal damage Grade 3 (complex tears/ maceration) vs Grade 0 (no tear or damage)<br><br>Central medial femur<br>−120.3 ± 35.2 $P = 0.04$<br><br>Medial tibial plateau<br>−47.4 ± 31.6 $P = 0.94$<br><br>Posterior medial femur<br>−22.2 ± 33.7 $P = 1.00$ | NR | −<br><br>There is only an association of cartilage degeneration (lower dGEMRIC) with the most severe meniscal damage in the central medial femur. There is no association in any other cartilage or at any other meniscal disease grade | 62% (high) |
| Hangaard *et al.* 2018[62] | dGEMRIM T1 relaxation times of lateral meniscus at baseline (C) | dGEMRIC T1 relaxation times of lateral femoral cartilage at baseline (C) | Nil | Comparing dGEMRIC and dGEMRIM in the lateral compartment revealed a low but significant correlation | NR | +<br><br>Association between dGEMRIC and dGEMRIM in the lateral compartment | 62% (high) |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | | | | ($R = 0.26$ and $P = 0.02$) | | | |
| Souza *et al.* 2013[63] | Medial meniscus lesion T1 rho relaxation time (C) | T1 rho cartilage relaxation time in the medial femoral condyle (C) | Nil | Relative to knees with mild SQ cartilage defects, those with extensive cartilage defects had a significantly higher T1 rho relaxation time of the medial meniscus at the posterior and the anterior horn | NR | + | 62% (high) |
| Van Tiel *et al.* 2014[64] | MRI dGEMERIM of the medial and lateral meniscus at baseline (C) | MRI medial and lateral TFJ cartilage dGEMERIC at baseline (C) | Nil | <u>Medial compartment weight-bearing femoral condyle</u><br><br>Anterior $r = 0.94$ (0.84, 0.98)<br>Posterior $r = 0.78$ (0.17, 0.96)<br><br><u>Medial compartment weight-bearing tibial plateau</u><br><br>Anterior $r = 0.87$ (0.66, 0.95)<br>Posterior $r = 0.78$ (0.18, 0.96)<br><br>Weaker but significant association in the lateral compartment for the same measures | NR | +<br>ipsicompartmental meniscal damage is associated with tibiofemoral joint cartilage damage | 62% (high) |
| Zarins *et al.* 2010[65] | Posterior horn medial meniscus WORMS SQ tear score at baseline (C) | MRI quantitative cartilage thickness and volume, T1p and T2 relaxation times at baseline in the TFJ (C) | Nil | Amongst knees with meniscal tear grade 2–4 compared with no tear, there was significantly lower<br><br>Medial tibial cartilage thickness $P = 0.027$,<br><br>Medial tibial cartilage volume $P = 0.024$<br><br>But there was no such significant difference observed in lateral tibial, lateral femoral or medial femoral cartilage plates | NR | −<br>Greater cartilage tear is associated with greater cartilage loss | 62% (high) |
| Pelletier 2007[32] | Baseline SQ medial meniscal tear (C) | Quantitative MRI medial femoral and tibial cartilage volume (modified WORMS) I | Nil | Fisher exact test*P*<br><br>$= 0.002–0.02$ | NR | + | 62% (high) |
| Friedrich *et al.* 2009[61] | Presence of meniscal tear at baseline (C) | Quantitative T2 cartilage values at baseline (C) | Age, sex, BMI, Kellgren–Lawrence score, and the presence of anterior cruciate ligament tears | NR | After adjustment for covariates, patients with any meniscal tear (median ± interquartile range, 50.1 ± 6.1 ms) had significantly ($P = 0.021$) higher T2 values of cartilage than those without meniscal tears (45.7 ± 4.8 ms) | + | 54% (high) |

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**Table I** (*continued*)

| Author | Feature (method) | Structural progression outcome | Adjustment for confounders | Association (magnitude) crude | Association (magnitude) Adjusted | Association | Quality (score %) |
|---|---|---|---|---|---|---|---|
| Posadzy 2020[66] | Development of a new right medial or lateral meniscal tear at baseline (C) | WORMS SQ cartilage abnormalities at baseline (C) | Matched for BMI, sex, race, and age | NR | Comparing those with a new tear vs controls without tears at baseline, cartilage damage was greater amongst new meniscal tear knees than controls:<br><br>Globally<br><br>Total knee MAX score coef 0.47 (0.01, 0.93); $P = 0.044$<br><br>In the medial compartment<br><br>MAX score medial compartment (medial femoral condyle + medial tibia) coef 0.69; (0.35, 1.04); $P < 0.001$<br><br>But not in the lateral TFJ or patellofemoral compartment:<br><br>MAX score lateral compartment coef 0.25 (−0.01, 0.53) $P = 0.066$<br><br>MAX score patellofemoral coef 0.25; (−0.22, 0.74); $P = 0.297$<br><br>There is significantly greater cartilage damage seen in non-horizontal tear compared to knees either with horizontal tears or controls (no tears). There is no significance in cartilage damage between knees with horizontal tears and controls | +<br><br>At the time of meniscal tear, greater hyaline cartilage damage is observed compared to knees without meniscal tears | 54% (high) |
| Takahashi *et al.* 2015[45] | WORMS medial meniscus tear SQ (C) | MRI medial tibiofemoral cartilage T1p relaxation time (C) | Nil | The presence of cartilage damage in 6 specified regions of interest (ROI) in the medial TFJ was associated with tear/damage to:<br><br>WORMS Medial anterior root and horn<br>ROI 2 $P < 0.001$<br><br>ROI 3 $P < 0.001$<br><br>WORMS Medial middle body<br><br>ROI 2 $P < 0.001$<br>ROI 3 $P < 0.001$<br>ROI 5 $P = 0.021$<br><br>WORMS Medial posterior root and horn<br><br>ROI 2 $P = 0.002$<br>ROI 3 $P < 0.001$<br>ROI 4 $P = 0.014$ | NR | + | 54% (high) |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | | | | ROI 5 $P = 0.002$<br>ROI 6 $P < 0.001$<br><br>Medial posterior meniscal radial tear<br><br>ROI 1 $P = 0.013$<br>ROI 2 $P < 0.001$<br>ROI 3 $P < 0.001$<br>ROI 4 $P = 0.025$<br>ROI 5 $P = 0.010$<br>ROI 6 $P = 0.003$ | | | |
| Sato *et al.* 2014[19] | Posterior horn WORMS scores and posterior radial meniscal tear at baseline (C) | T2 values of medial and lateral femorotibial joint cartilage (C) | Age and KL | NR | WORMS not associated with T2 medial TFJ cartilage values<br><br>Posterior radial meniscal tear associated with T2 cartilage values in the medial and lateral femorotibial cartilage $P < 0.05$ | +<br><br>Very limited results provided | 46% (low) |
| Krych 2020[67] | A displaced flap tear of the medial meniscus (DFTMM) or medial meniscal posterior root tear (MMPRT) (C) | SQ cartilage score (Outerbridge score) of the medial femoral condyle and medial tibial plateau (C) | Nil | Comparing femoral modified Outerbridge scores of MMPRT with the DFTMM, MMPRT has a significantly increased mean score (3.72 vs 2.68, $P < 0.0001$). | NR | +<br><br>Posterior root tears are associated with more cartilage damage than flap tears | 46% (low) |
| Rangeng *et al.* 2016[68] | SQ meniscus injury on MRI (C) | MRI cartilage defects (C) | Age, sex and BMI | NR | Lateral meniscus injury was associated with:<br><br>Lateral tibiofemoral cartilage defect (OR = 1.41, $P = 0.014$)<br><br>Lateral femoral cartilage defect (OR = 1.57, $P = 0.002$) | +<br><br>No mention of the medial compartment in this abstract | 31% (low) |
| Alaam 2021[69] | Sonographer defined US meniscal degeneration (C) | Sonographer defined US femoral cartilage degeneration (C) | Nil | Meniscal degeneration correlated significantly with femoral cartilage degeneration ($P < .001$) | NR | + | 23% (low) |
| Herrmann 1990[20] (abstract only) | Medial meniscal tear at baseline (C) | Femoral and tibial changes of the cartilage at baseline (C) | Nil | There was no correlation between the degenerative changes of the medial meniscus and femoral or tibial changes of the cartilage | NR | NA | 15% (low) |
| **MRI meniscal tear/damage– case control analyses (MT-CC)** | | | | | | | |
| Russell 2017[28] | Posterior meniscal horn lesion at baseline (C) | T1p and T2 cartilage relaxation times at baseline and 2 years in the medial femur and medial tibia (L) | Age, BMI, sex | T1p medial femur $P = 0.02$<br><br>T1p medial tibia $P = 0.03$<br><br>T2 medial femur $P = 0.02$<br><br>T2 medial tibia $P = 0.03$ | 15 knees with posterior meniscal horn lesions were compared to 15 knees with no meniscal lesions after careful matching for age, BMI, sex.<br><br>Elevated T1p of the lateral tibia and elevated T2 of the medial tibia and lateral tibia at 1 and 2 years were seen in those with meniscal lesions compared to controls without. | + | 75% (high) |
| Roemer *et al.* 2015[54] | Baseline SQ meniscal maceration MOAKS (C) | Incidence of total knee replacement 1 year later (L) | Nested case control study within the OAI cohort.<br><br>1:1 matched<br><br>case–control design (Age, | Severe vs little or no meniscal maceration Medial body<br><br>OR, 1.84 (1.16, 2.92)<br><br>No association for medial | NR | NA | 75% (high) |

(continued on next page)

**Table I** (*continued*)

| Author | Feature (method) | Structural progression outcome | Adjustment for confounders | Association (magnitude) crude | Association (magnitude) Adjusted | Association | Quality (score %) |
|---|---|---|---|---|---|---|---|
| | | | sex, radiographic disease status) | anterior or posterior horn or any region of lateral meniscus | | | |
| Guermazi *et al.* 2015[75] | Baseline Meniscal damage of TFJ (SQ WORMS) (C) | Quantitative ipsi-compartmental cart thinning of TFJ (L) | Age, sex, body mass index, alignment axis (degrees) and baseline KL grade | NR | Aor 3.94 [2.09–7.43]$P < 0.0001$ | + | 63% (high) |
| Roth 2020[53] | Quantitative progression in MRI-assessed medial meniscal narrowing in the 2 years before joint replacement (L) | Incidence of knee replacement after 2 years (L) | Nested case control study within the OAI cohort.<br><br>1:1 matched<br><br>case–control design (Age, sex, radiographic disease status)<br>Adjusted for<br>Baseline BMI and pain at T-2 years | NR | Significantly greater odds of knee replacement with greater medial meniscal narrowing<br><br>OR 2.01 [1.23, 3.26]$P$-value $< 0.005$<br><br>No association with medial meniscal thickness change or volume (NB thickness tended to increase but volume remained constant before joint replacement) | + | 63% (high) |
| Posadzy 2020[66] | Development of a new right medial or lateral meniscal tear at baseline (C) | WORMS SQ cartilage damage progression over 4 years (L) | Matched for BMI, sex, race, and age | NR | Comparing those with a tear at baseline vs controls without tears over 4 years<br><br>There was no difference in cartilage damage progression between these 2 groups globally or within any knee compartment, except in the patellofemoral joint where controls had greater cartilage damage<br><br>When comparing horizontal tears vs controls<br><br>Greater lateral TFJ compartment progression was observed −0.25 (−0.50, −0.005) $P = 0.045$<br><br>When comparing non-horizontal tears vs controls<br><br>Greater global cartilage damage progression was observed coef 0.37 (0.03, 0.72) $P = 0.033$<br><br>There was no significant difference in cartilage progression between horizontal and non-horizontal tears. | + Non-horizontal meniscal tears are associated with global cartilage damage progression (but not in individual TFJ compartments)<br><br>Horizontal tears were not associated with significant in cartilage damage except in the lateral TFJ compartment | 56% (high) |
| Matsubara 2015[76] | MRI WORMS medial and lateral meniscal tear at baseline (C) | MRI subregional T1ρ values on the femoral condyle and tibial plateau at baseline vs healthy controls (C) | Nil | Femoral Condyle<br><br>Superficial (−30° to 0°)$P < 0.05$<br><br>Deep (−30° to 0°)$P < 0.05$<br><br>Superficial (0°–30°)$P < 0.05$<br><br>Deep (0°–30°)$P < 0.05$<br><br>Superficial (30°–60°)$P < 0.05$ | NR | +<br><br>The presence of meniscal tear appears to be associated with greater T1ρ cartilage values | 56% (high) |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | | | | Deep (30°–60°) $P = 0.08$<br><br>Superficial (60°–90°) $P = 0.29$<br><br>Deep (60°–90°) $P = 0.15$<br><br><u>Tibial plateau</u><br><br>Superficial (anterior) $P < 0.05$<br><br>Deep (anterior) $P = 0.28$<br><br>Superficial (posterior) $P < 0.05$<br><br>Deep (posterior) $P = 0.55$ | | | |
| Roemer 2012[40] | Baseline SQ meniscal damage (WORMS) (C) | Progression in ipsilateral SQ cartilage defects (WORMS) over 6-month TFJ (L) | Age, sex, BMI, glucosamine treatment,<br><br>Age, sex, BMI, glucosamine treatment, prevalent cartilage damage | NR | Meniscal damage<br>OR (95% CI)<br>3.72 (1.56–8.89) $P = 0.003$<br><br>OR (95% CI)<br>1.92 (0.74–4.97) $P = 0.177$ | NA<br><br>Association lost after adjusting for baseline cartilage damage | 50% (low) |
| Cao 2012[73]<br><br>(Unable to locate full text) | SQ meniscal tear (Stoller) score (C) | T2 mapping values of TFJ cartilage (C) | Nil | There was positive correlation between the Stoller scores and the T2 values of cartilage ($r = 0.34$); | NR | + | 44% (low) |
| Heilmeier 2017[21] | Presence of meniscal tear at baseline (C) | Total knee replacement 4–7 years later (L) | Nil | $P > 0.05$ | NR | NA | 44% (low) |
| Cohen 2012[74] | Baseline qualitative meniscal tear (C) | Progression of SQ TFJ cartilage loss between 2 MRI scans of broad interval range (3–57 months) (L) | Nil | Horizontal OR 0.505 (0.040–6.720) $P = 1.000$<br><br>Oblique OR 0.250 (0.061–1.062) $P = 0.093$<br><br>Vertical OR 0.462 (0.093–2.402) $P = 0.450$<br><br>Radial OR 19.174 (1.599–210.901) $P = 0.017$<br><br>Complex OR 2.533 (0.636–10.128) $P = 0.277$<br><br>No association with anterior horn or body but significant association with posterior horn ($P = 0.031$) | NR | Radial and posterior horn + | 38% (low) |

**Table I**

Osteoarthritis and Cartilage

Knee structural associations by feature and quality grade

| Author | Feature (method) | Knee pain outcome | Adjustment for confounders | Association (magnitude) crude | Association (magnitude) adjusted | Association | Quality score (%) |
|---|---|---|---|---|---|---|---|
| **MRI meniscal extrusion – Cohort analyses (ME-C)** | | | | | | | |
| Eathakkattu Antony *et al.* 2016[36] (abstract) | SQ meniscal extrusion at baseline (C) | Total WOMAC scores and pain over 10.7 years (L) | Age, sex, BMI and radiographic KOA status | NR | $\beta = 3.21$, $P < 0.01$<br><br>Linear mixed-effects models | + | 53% (low) |
| Antony 2017[72] | Presence or absence of baseline meniscal extrusion (C) | WOMAC knee pain clinically meaningful change over 2 years (L) | Age, sex, and BMI | OR 1.44 (1.00, 2.08) | OR 1.44 (0.99, 2.09) | NA | 53% (low) |
| Kwoh 2017[77] | New onset meniscal extrusion over 48 months MOAKS SQ (L) | Incident frequent knee pain (L) | Age, sex, and BMI | NR | OR 2.36; 95%CI: 1.30, 4.27 | + | 41% (low) |
| Kwoh 2020[78] | Quantitative medial meniscal extrusion at baseline (C) | Incident frequent knee symptoms (i.e., pain, aching or stiffness on most days during the past 30 days) and KL grade ≥2 at 10 years (L) | Nil | Comparing extrusion >3 mm vs knees <2 mm the HR of developing symptomatic and radiographic knee OA was 3.08 (1.70, 5.58) $P < 0.0001$ | NR | + | 41% (low) |
| **Meniscal extrusion – Cross-sectional analyses (ME-CS)** | | | | | | | |
| Oo 2020[79] | US SQ medial meniscus extrusion (C) | NRS pain and KOOS pain (C) | Age, sex, BMI, duration of disease, and radiographic Kellgren–Lawrence grade | NRS<br>$\beta$ coefficient<br>0.71 (0.02, 1.40) $P < 0.05$<br><br>KOOS pain<br>$\beta$ coefficient −8.11<br>(−14.90, −1.31) $P < 0.05$ | NRS<br>$\beta$ coefficient 1.01 (0.22, 1.80) $P < 0.05$<br><br>KOOS pain<br>$\beta$ coefficient −10.84<br>(−18.57, −3.10) $P < 0.05$ | + Medial meniscal extrusion was significantly associated with cross-sectional pain | 69% (high) |
| Roubille *et al.* 2014[80] | Presence of meniscal extrusion (C) | Neuropathic pain measure (PainDETECT score trichotomised into unlikely, uncertain and likely neuropathic pain) (C) | Nil | Medial meniscal extrusion $P = 0.006$; lateral meniscal extrusion $P = 0.023$ | NR | + Meniscal extrusion in either compartment is associated with neuropathic pain | 62% (high) |
| Kaukinen 2016[71] | Presence of baseline meniscal extrusion (anywhere, medial, lateral or anterior) (C) | Presence of pain and location of pain (patellar, medial, lateral, posterior and diffuse) (C) | Sex, age, BMI and the presence of any severe cartilage loss, any BMLs, any osteophytes and/or any Hoffa's synovitis | Extrusion anywhere and presence of pain<br><br>RR 2.42 (CI 1.70–3.44<br><br>Significant association also seen in medial, lateral and anterior extrusion.<br><br>Medial and posterior knee pain are associated with medial and anterior meniscal extrusion.<br><br>Anterior extrusion<br>RR 3.47 (CI 1.73–6.98) | Extrusion anywhere, medial lateral and anterior were no longer significantly associated with the presence of pain after adjustment<br><br>Extrusion anywhere<br>RR 1.27 (CI 0.83–1.94)<br><br>Anterior meniscal extrusion and medial knee pain are significantly associated RR 2.78 (CI 1.14–6.75). There is no other significant association of focal extrusion with focal pain | No association between meniscal extrusion and presence of pain after adjustment.<br><br>+<br><br>After adjustment, anterior extrusion remained associated with medial knee pain | 54% (high) |
| Antony 2017[72] | Presence or absence of baseline meniscal extrusion (C) | WOMAC knee pain at baseline (C) | Age, sex, and BMI | OR 1.34 (0.93, 1.93) | OR 1.13 (0.78, 1.67) | NA | 54% (high) |
| Wu 2012[106] | Protrusion of medial meniscus (MMP) on US at baseline (C) | VAS Score on motion and at rest | Age, sex, BMI, Kellgren/Lawrence grade, and other US features | NR | VAS in motion<br>$\beta$-coefficients: −1.19<br>95% CI: (−27.63, 5.65)*P* | No association between medial meniscal | 46% (low) |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | | WOMAC score and WOMAC index<br><br>Spontaneous medial knee pain | | | = 0.195<br><br>VAS at rest<br>$\beta$-coefficients: −0.56<br>95% CI: (−19.73, 7.98)$P$ = 0.406<br><br>WOMAC pain<br>$\beta$-coefficients: −0.18<br>95% CI: (−5.14, 1.47)$P$ = 0.276<br><br>WOMAC index<br>$\beta$-coefficients: −1.14<br>95% CI: (−22.81, 2.00)$P$ = 0.100<br><br>Spontaneous medial knee pain<br>Grade 1<br>OR 2.4 (0.4–13.7)$P$ = 0.334<br><br>Grade 2<br>OR 3.4 (0.5–21.4)$P$ = 0.198<br><br>Grade 3<br>Or 4.4 (0.4–46.1)$P$ = 0.221 | protrusion (MMP) and knee pain | |
| Baert 2014[18] | Presence of meniscal extrusion at baseline (C) | KOOS pain and KOOS weight bearing pain at baseline (C) | Nil | KOOS pain$\beta$ = −0.040<br><br>KOOS weight bearing pain$\beta$ = −0.059 | NR | NA | 46% (low) |
| Aoki 2017[81] | MOAKS Baseline medial meniscal extrusion (C) | Japanese Knee Osteoarthritis Measure (JKOM) pain and stiffness score (C) | Nil | JKOM category II (pain and stiffness) ($r$ = 0.294, $P$ = 0.009) | NR | +<br><br>There is an association between pain and stiffness and meniscal extrusion | 46% (low) |
| Huang 2020[82] | Quantitative medial meniscus extrusion (C) | Presence of pain (C) | Nil | The medial meniscal extrusion width was significantly greater in those with knee pain compared to those without knee pain | NR | + | 46% (low) |
| Momoeda 2021[85] | MRI medial meniscus extrusion (MME) and anterior meniscus extrusion (AME) (C) | VAS pain (C) | Age, sex and BMI | NR | VAS scale has higher risk in MME and AME group, compared with group with no MME and AME ($\beta$ = 1.56 (95% CI: 1.08–2.25, $P$ = 0.017) | + | 46% (low) |
| Kwoh 2011[83] | Presence or absence of meniscal extrusion at baseline (C) | Crude presence of any pain and specific location of knee pain using knee pain map at baseline (C) | Age, sex and BMI<br><br>Then other MRI abnormalities | NR | Local Medial Joint Line Pain relative risk ratio 1.08 (CI 0.47, 2.49)<br><br>Regional Medial Pain relative risk ratio 8.77 (CI 2.18, 35.23) | + Meniscal extrusion was associated with medial (joint line and regional) and global pain after adjustment | 38% (low) |

(*continued on next page*)

**Table II** (*continued*)

| Author | Feature (method) | Knee pain outcome | Adjustment for confounders | Association (magnitude) crude | Association (magnitude) adjusted | Association | Quality score (%) |
|---|---|---|---|---|---|---|---|
| | | | | | Global Pain relative risk ratio 3.46 (CI 1.00, 12.05)<br><br>Medial regional pain was associated with meniscal extrusion CI 6.76 (1.57, 29.05) | | |
| Kijima 2015[84] | US quantitative medial meniscus extrusion at baseline (C) | Presence or absence of pain (C) | NR | Average medial meniscal extrusions (MMEs) of the<br><br>knees with and without pain were 7.58 and 5.88 mm, respectively;<br><br>knees with pain had greater MMEs than knees without pain ($P = 0.0005$) | NR | +<br><br>MME is associated with knee pain | 38% (low) |
| **MRI meniscal extrusion − Case-control analyses (ME-CC)** | | | | | | | |
| Collins 2016[86] | MOAKS SQ medial meniscus extrusion at baseline (C) and change over 24 months (L) | Progression in (WOMAC) pain score over 24 months (L) | Sex, race, and baseline age, body mass index, Kellgren/Lawrence grade, Western Ontario and McMaster Universities Osteoarthritis Index pain score, pain medication use, and minimum joint space width, | NR | Baseline meniscal extrusion<br><br>Reference no extrusion<br><br>Grade 1 (2–2.9-mm extrusion) OR 1.5 (95% CI 0.9–2.4)<br><br>Grade 2 (3–4.9-mm extrusion) OR 1.8 (95% CI 1.1–3.1)<br><br>Grade 3 (0.5-mm extrusion) OR 3.3 (95% CI 1.6–6.8)<br><br>Worsening of medial meniscal extrusion<br><br>OR 4.3 (95% CI 2.6–7.1) | + Both baseline and worsening medial meniscal extrusion over 24 months was associated with progression in knee pain over 24 months | 63% (high) |
| Wenger 2012[87] | Quantitative MRI medial and lateral meniscal extrusion in both knees within an individual with bilateral radiographic knee OA but only unilateral pain (C) | The presence or absence of frequent knee pain over 12 months (L) | Analyses are within individuals, therefore adjusted for age, BMI and sex | NR | Medial meniscus<br><br>mean external extrusion $P = 0.441$<br><br>maximal external extrusion $P = 0.422$<br><br>extrusion in the most central slice $P = 0.038$<br><br>extrusion in the central five slices $P = 0.024$<br><br>Lateral meniscus<br><br>mean external extrusion $P = 0.001$<br><br>maximal external extrusion | +<br><br>In the body of the medial and lateral meniscus there is significantly greater (by paired *t*-test) meniscal disease in painful knees vs painless knees (within an individual) with bilateral knee OA | 56% (high) |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | | | | | $P = 0.778$<br><br>extrusion in the most central slice $P = 0.020$<br><br>extrusion in the central five slices $P = 0.026$ | | |
| **MRI meniscal tear/damage − Cohort analyses (MT-C)** | | | | | | | |
| Khan 2016[26]<br><br>Previously known as Aitken 2013 Abstract | Progression in SQ meniscal damage/tear over 8 years (L) | Progression in WOMAC pain over 8 years (L) | Age, sex, BMI, offspring control status, change in BMLs, meniscal extrusion, baseline radiographic OA status, history of knee injury, change in effusion and cartilage defects | $\beta$ (95% CI)<br><br>+2.87 (+1.84 - +3.90)$P < 0.05$ | $\beta$ (95% CI)<br>+2.81 (+1.40 to +4.22) $P < 0.05$<br><br>Subscales of pain were also all associated with meniscal damage | + | 56% (high) |
| Eathakkattu Antony *et al.* 2016[36] (abstract) | SQ meniscal tear at baseline (C) | Total WOMAC scores and pain over 10.7 years (L) | Age, sex, BMI and radiographic KOA status | NR | NR | NA | 53% (low) |
| Antony 2017[72] | Presence or absence of baseline meniscal tear or maceration (C) | WOMAC knee pain clinically meaningful change over 2 years (L) | Age, sex, and BMI | Maceration OR 1.10 (0.73, 1.66)<br><br>Any tear OR 0.82 (0.58, 1.15) | Maceration OR 1.02 (0.66, 1.57)<br><br>Any tear OR 0.82 (0.58, 1.17) | NA | 53% (low) |
| Kwoh 2017[77] | New onset meniscal tear/maceration over 48 months MOAKS SQ (L) | Incident frequent knee pain (L) | Age, sex, and BMI | NR | OR 3.72; 95%CI: 1.88, 7.36 | + | 41% (low) |
| **MRI meniscal tear/damage − Cross-sectional analyses (MT-CS)** | | | | | | | |
| Torres 2006[88] | WORMS meniscus subluxation and tear at baseline (C) | Visual analogue scale pain (C) | Age and BMI | <u>Meniscal tears</u><br>RR 3.33 (0.90, 5.77)<br><br><u>Meniscal subluxation</u><br><br>Grade 1 vs 0 RR 0 (−11.88, 11.88)<br><br>Grade 2 vs 0 RR 15.00 (−0.32, 30.32) | <u>Meniscal tears</u><br>RR 1.99 (0.60, 3.38)<br><br><u>Meniscal subluxation</u><br><br>Grade 1 vs 0 RR −2.96 (−10.39, 4.46)<br><br>Grade 2 vs 0 RR 2.22 (−6.89, 11.33) | +<br><br>Positive association between meniscal tear presence and median VAS pain but no association with meniscal subluxation | 85% (high) |
| Carotti 2017[70] | Baseline WORMS meniscal lesion score (C) | Baseline Italian WOMAC pain and VAS (C) | Age, sex, disease duration, educational level, BMI, and K/L grades | NR | Coefficient = 15.17, SE = 10.74$T = 1.412$$P = 0.1602$ | NA | 69% (high) |
| Roubille *et al.* 2014[80] | Presence of meniscal tear (C) | Neuropathic pain measure (PainDETECT score trichotomised into unlikely, uncertain and likely neuropathic pain) (C) | Nil | Medial meniscal tear $P = 0.347$; Lateral meniscal tear $P = 0.011$ | NR | + Neuropathic pain is associated with lateral but not medial meniscal tears | 62% (high) |
| Zarins 2010[65] | MRI medial and lateral meniscal T1p and T2 relaxation times at baseline (C) | WOMAC pain at baseline (C) | Nil | Anterior horn medial meniscus T1p coefficient −0.341 $P = 0.793$, **T2 0.259 *P* = 0.042**<br><br>Posterior horn medial meniscus **T1p coefficient 0.503 *P* < 0.001, T2 coefficient 0.526 *P* < 0.001**<br><br>Anterior horn lateral meniscus **T1p coefficient 0.319 *P* = 0.014, T2 coefficient 0.396 *P* = 0.002** | NR | + Positive association between T1p and T2 relaxation times of the medial and lateral meniscus with pain | 62% (high) |

(*continued on next page*)

**Table II** (*continued*)

| Author | Feature (method) | Knee pain outcome | Adjustment for confounders | Association (magnitude) crude | Association (magnitude) adjusted | Association | Quality score (%) |
|---|---|---|---|---|---|---|---|
| | | | | Posterior horn lateral meniscus **T1p coefficient 0.419 *P* < 0.001, T2 coefficient 0.414 P < 0.001** | | | |
| Kaukinen 2016[71] | Presence of baseline meniscal tear and maceration (anywhere, medial, lateral or anterior) (C) | Presence of pain and location of pain (patellar, medial, lateral, posterior and diffuse) (C) | Sex, age, BMI and the presence of any severe cartilage loss, any BMLs, any osteophytes and/or any Hoffa's synovitis | Meniscal tear anywhere and pain RR 1.54 (CI 1.13–2.11)<br><br>Meniscal maceration anywhere and pain RR 2.30 (CI 1.72–3.07)<br><br>Lateral knee pain and posterior meniscal tear RR 3.05 (CI 1.02 –9.09)<br><br>Medial knee pain and medial meniscal maceration RR 2.98 (CI 1.54–5.74) | Meniscal tear anywhere and pain RR 1.11 (CI 0.85–1.46)<br><br>Meniscal maceration anywhere and pain RR 1.17 (CI 0.88–1.57)<br><br>Lateral knee pain and posterior meniscal tear RR 2.98 (CI 1.09 –8.17)<br><br>Medial knee pain and medial meniscal maceration RR 2.20 (CI 1.01–4.79) | No association for tear/ maceration with pain presence after adjustment<br>+<br>+ There is an association between lateral knee pain and posterior meniscal tear, and medial knee pain and medial meniscal maceration after adjustment | 54% (high) |
| Antony 2017[72] | Presence or absence of baseline meniscal tear or maceration (C) | WOMAC knee pain at baseline (C) | Age, sex, and BMI | Maceration OR 2.35 (1.54, 3.58)<br><br>Any tear OR 1.02 (0.73, 1.44) | Maceration OR 2.82 (1.79, 4.43)<br><br>Any tear OR 1.30 (0.91, 1.86) | + for maceration but no association with tear | 54% (high) |
| Baert 2014[18] | Presence of meniscal tear, maceration and increased signal at baseline (C) | KOOS pain and KOOS weight bearing pain at baseline (C) | Nil | <u>Presence of increased signal</u><br>KOOS pain$\beta = -0.360$ $P = 0.015$<br>KOOS weight bearing pain$\beta = -0.331$ $P = 0.027$<br><u>Presence of tear</u><br><br>KOOS pain$\beta$<br><br>$= 0.182$<br><br>KOOS weight bearing pain$\beta = 0.057$<br><br><u>Presence of maceration</u><br><br>KOOS pain$\beta = 0.039$<br><br>KOOS weight bearing pain$\beta = -0.183$ | NR | NA<br><br>No association between maceration or tear and knee pain but increased meniscal signal was associated with knee pain | 46% (low) |
| Kwoh 2011[83] | Presence or absence of meniscal damage at baseline (C) | Crude presence of any pain and specific location of knee pain using knee pain map at baseline (C) | Age, sex and BMI<br><br>Then for other MRI abnormalities | NR | Local Medial Joint Line Pain relative risk ratio 1.46 (CI 0.56, 3.77)<br><br>Regional Medial Pain relative risk ratio CI 3.72 (1.10, 12.60)<br><br>Global Pain relative risk ratio CI 2.65 (0.77, 9.11)<br><br>Not significant when adjusted for meniscal extrusion (no RRR documented) | +<br>Meniscal damage was associated with medial (joint line and regional) and global pain after adjustment | 38% (low) |
| Bhattacharyya[107] | Presence of meniscal tear at baseline (C) | Knee pain VAS at baseline (C) | Nil | Knee pain VAS pain $P = 0.67$ | NR | NA | 38% (low) |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Rangeng 2016[68] | SQ medial and lateral meniscus injury on MRI (C) | Pain score (C) | Age, sex and BMI | NR | Medial meniscal injury was associated with pain score<br><br>OR = 6.08, $P = 0.004$ | + | 31% (low) |
| Yegane 2011[89] (Abstract only – full text not in English) | MRI meniscal degeneration at baseline (C) | Quantified knee pain at baseline (C) | Nil | $P = 0.036$ | NR | + There is an association between meniscal degeneration and pain | 15% (low) |
| **MRI meniscal tear/damage – Case-control analyses (MT-CC)** | | | | | | | |
| Englund *et al.*, 2007[90] | Baseline SQ meniscal tear (Collapsed WORMS score) (C) | Development of frequent knee pain over 15 months (L) | Age, sex, BMI, malalignment, change in pain medication | NR | The pooled Mantel-Haenszel odds ratio estimate was null (1.1, 95% CI 0.65–2.0) | NA | 63% (high) |
| Collins 2016[86] | MOAKS SQ medial meniscus damage at baseline (C) and change over 24 months (L) | Progression in (WOMAC) pain score over 24 months (L) | Sex, race, and baseline age, body mass index, Kellgren/Lawrence grade, Western Ontario and McMaster Universities Osteoarthritis Index pain score, pain medication use, and minimum joint space width, | NR | Meniscus morphology at baseline<br><br>Grade 1 tear OR 1.3 (95% CI 0.9–2.1)<br>Grade 2 tear OR 0.8 (95% CI 0.5–1.5)<br><br>Worsening in any meniscal region<br><br>OR 3.8 (95% CI 2.4–6.1) | + Worsening medial meniscal damage over 24 months was associated with progression in knee pain over 24 months but baseline meniscal damage was not | 63% (high) |

**Table II**



Knee pain associations by feature and quality score

| Meniscal feature | | Structural and pain associations | | |
|---|---|---|---|---|
| | | Knee structure | Knee pain | Knee joint replacement |
| **Extrusion** | **Association** | **Progression** | **Not applicable** | **TKR** |
| | **Number of cohort analyses** | 6 out of 9 | No appropriate analyses* | 2 out of 2 |
| | **Mean number of participants** | 789 | Not applicable | 123 |
| | **Mean length of follow up** | 32 months | Not applicable | 6 years |
| | **Mean age** | 60.6 | Not applicable | 60.8 |
| **All tear** | **Association** | **Progression** | **LPP** | **TKR** |
| | **Number of cohort analyses** | 8 out of 10 | 1 out of 1 | 1 out of 1 |
| | **Mean number of participants** | 489 | 331 | 123 |
| | **Mean length of follow up** | 34 months | 8 years | 4–7 years |
| | **Mean age** | 61.3 | 47 | 60.3 |
| **Tear subregion** | **Anterior horn association** | **Progression (0)** (0 out of 2) | No appropriate analyses* | No appropriate analyses* |
| | **Body association** | **Progression** (2 out of 2) | No appropriate analyses* | No appropriate analyses* |
| | **Posterior horn association** | **Progression** (2 out of 2) | No appropriate analyses* | No appropriate analyses* |

Total knee replacement (TKR), longitudinal pain progression (LPP).
Association insignificant after covariate adjustment (0).
* Only high quality well-adjusted cohort analyses were included (appropriate analyses).
† Approximate mean age, sample size and follow up calculated as data was unable to be acquired from some publications.

**Table III**

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A summary table describing meniscal associations with joint replacement, structural progression and pain in knee OA high quality, well-adjusted cohort analyses*,†

nine analyses identified an association between meniscal extrusion and cartilage structural progression[23,27,30,32,33,35].

Seven out of 11 cross-sectional analyses were high quality[27,29,33,34,45–47] (four of which were also well-adjusted[27,29,33,47]) and six of the seven cross-sectional analyses found an association between meniscal extrusion and structural severity[27,29,33,45–47], although two of these were not well-adjusted[45,46]. The analyses showing association included pre-radiographic and radiographic OA and examined extrusion of medial and lateral menisci.

There were two case control analyses measuring extrusion and structural progression, only one of which was high quality but not well-adjusted and demonstrated an association between meniscal extrusion and structural progression (progressive cartilage loss)[48].

*Summary*: Based on the literature reviewed, meniscal extrusion was associated with structural progression and structural severity of knee OA, independently of age, sex and BMI.

### *Relationship between meniscal extrusion and total knee replacement*

The association of meniscal extrusion with joint replacement is described in Tables I and III.

This section included seven publications providing five cohort and two case control analyses all using MRI.

Five cohort analyses investigated the association between meniscal extrusion and TKR[30,49–52]. Two of these were high quality and well-adjusted[30,49]. Both analyses identified that the presence of meniscal extrusion (of the medial and lateral or combined medial and lateral menisci by semi-quantitative scoring) was associated with increased risk of incident TKR when following up patients for 6–7 years[30,49]. Only one (low quality) analysis investigated whether longitudinal progression in meniscal extrusion was associated with incident TKR[51]. This found that neither progressive meniscal extrusion (combined medial and lateral semi-quantitative scoring – BLOKS and WORMS) nor longitudinal progression in semi-quantitative cartilage disease or bone marrow lesions (BLOKS and WORMS) were associated with incident TKR over 2 years[51].

Both case control analyses measuring meniscal extrusion and TKR were of high quality. One of these, which was well-adjusted, demonstrated a positive association between meniscal extrusion and incident TKR over 2 years[53,54]. No association between meniscal extrusion and incident TKR was reported in the other case control analysis, but this did not adjust for BMI and the observation period was only 1 year[54].

*Summary:* Based on the literature reviewed, high quality prospective cohort studies showed meniscal extrusion was associated with risk of TKR in knee OA.

### *Relationship between meniscal tear or damage and structural progression*

The association of meniscal tear with structural progression (longitudinal quantitative and semi-quantitative cartilage loss) and structural severity (cross-sectional quantitative and semi-quantitative cartilage loss) are described in Tables I and III.

This section included 38 publications providing 18 cohort, 15 cross-sectional and seven case–control analyses all using MRI and one cross-sectional analysis using ultrasound. Of the 18 cohort analyses measuring the association between meniscal tear and structural progression[11,16,22–26,32,33,37,38,41,43,44,55–58], ten were high quality and well-adjusted[11,16,23–26,32,33,55,56].

Amongst the ten prospective cohorts with high quality, well-adjusted analyses, the presence of and increasing baseline meniscal

**Table IV**

Quality scoring tool

| Item | Criterion | CC | CH | CS |
|---|---|---|---|---|
| Study population | | | | |
| 1 | Recruitment from the general population | 1 | 1 | 1 |
| 2 | Selection occurred before disease onset or at a uniform point. A uniform point was considered to be equal baseline grade of structural progression (e.g., Kellgren Lawrence grade) or an analysis within the same osteoarthritic joint | 1 | 1 | 1 |
| 3 | Cases and controls drawn were from the same population | 1 | | |
| 4 | Participation rate >80% for cohort studies (retrospective cohort studies score zero automatically) | | 1 | |
| 5 | Sufficient description of baseline characteristics – must include age, sex and BMI (or height and weight) | 1 | 1 | 1 |
| 6 | Baseline characteristics comparable between cases and controls – must include age, sex and BMI (or height and weight) | 1 | | |
| Assessment of Imaging-detected subchondral bone risk factor or feature | | | | |
| 7 | Risk factor/feature assessed with a standardised method (e.g., WORMS BML scoring or an automated calculation of meniscus but not a subjective opinion of a radiologist on the presence of bone attrition) | 1 | 1 | 1 |
| 8 | Risk factor/feature assessment was identical (performed the same way) in the studied population(s) | 1 | 1 | 1 |
| 9 | Risk factor/feature was assessed prior to the outcome (structural progression or pain). A score of zero was allocated if the methods did not describe this. | 1 | 1 | 1 |
| Assessment of joint OA outcome (pain or structural progression) | | | | |
| 10 | Outcome assessment was identical in the studied population(s) | 1 | 1 | 1 |
| 11 | Outcomes were assessed reproducibly (intraclass correlation coefficient >0.81 with a standardised assessment). If multiple outcomes were measured the mean reproducibility score was used. | 1 | 1 | 1 |
| 12 | Outcome classification was standardised (e.g., the WOMAC pain score but not a subjective opinion of a patient's pain) | 1 | 1 | 1 |
| Study design | | | | |
| 13 | Prospective study design used | | 1 | |
| 14 | Follow up time >1 year | 1 | 1 | |
| 15 | Information provided on completers vs withdrawls in cohorts (without prospective trial data cohorts automatically score zero) | | 1 | |
| 16 | Outcome evaluators were blinded to feature (risk factor) | 1 | 1 | 1 |
| 17 | Analysis of relationship between feature and outcome was planned prospectively | 1 | 1 | 1 |
| Analysis and data presentation | | | | |
| 18 | The frequency of most important outcomes were given | 1 | 1 | 1 |
| 19 | appropriate analysis techniques used (statistical or comparative techniques) | 1 | 1 | 1 |
| Maximum Score | | 16 | 17 | 13 |

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tear (anterior, middle or posterior aspects of the medial or lateral meniscus) by semi-quantitative scoring was associated with structural progression (MRI cartilage loss) in eight cohort analyses[16,23,26,32,33,55,56,59]. In the one analysis demonstrating no association, the meniscal tear location was not defined[25]. Longitudinal medial tibiofemoral compartment cartilage structural progression over 8 years was associated with worsening semi-quantitative meniscal tear scoring for the combined medial and lateral menisci over 8 years[26]. Only two of the 16 cohort analyses did not support the association of meniscal tear with structural progression[25,38].

Of the 16 cross-sectional analyses, 15 found an association between meniscal tear and cartilage structural severity[17,19,32,33,45,60–69]. 11 of these were high quality but only 3 well-adjusted[70–72]. All but one cross-sectional analysis, which was low quality, found an association between meniscal tear and cartilage structure severity[20].

Six case control analyses out of seven found an association between meniscal tear and cartilage structural progression[28,66,73–76]. Two of these were high quality and well-adjusted[28,75]. The one case control analysis which did not find an association between meniscal tear and cartilage structural progression was low quality[40].

Considering meniscal sub-regions, three high quality, well-adjusted, cohort analyses[16,55,56], seven cross-sectional[19,45,60,63–65,67] (four of which were high quality[60,63–65]) and two case control analyses[28,74] (only one high quality[28]) analysed posterior root tears as a discrete predictive feature, with all of these analyses demonstrating an association with structural progression or severity. In two high quality, well-adjusted, cohort analyses, the location of the meniscal tear and its association with structural progression was analysed. While medial meniscal tears in the body and posterior regions are associated with structural progression, no association with anterior tears was observed[16,55]. This same pattern was also observed in the lateral meniscus[55]. Structural progression and structural severity were associated with tears in the body and posterior horn of medial and lateral menisci in cohort, case control analyses and cross-sectional respectively[16,19,28,45,55,56,60,63–65,67,74].

*Summary*: Based on the literature reviewed, medial and lateral meniscal tears were associated with structural progression and structural severity of knee OA when they occurred in the body and posterior horns, but not the anterior horns.

*Relationship between meniscal tear and total knee replacement*

The association of meniscal tear with TKR is described in Tables I and III.

This section included six publications providing three cohort and three case control analyses, all using MRI.

Three cohort analyses measured the association between meniscal tear and TKR incidence, only one of which was high-quality and well-adjusted. In two cohort analyses (one high quality and one low quality), the presence of and increasing baseline

**Table V**

Quality scoring results cross-sectional analyses

| No. | Cross-sectional study | Quality scoring criteria | | | | | | | | | | | | | | | | | | | Total | % |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | | |
| 1 | Torres 2006[88] | 1 | 1 | | | 1 | | 1 | 1 | 0 | 1 | 1 | 1 | | | | 1 | 0 | 1 | 1 | 11 | 85 |
| 2 | Crema 2012[47] | 1 | 0 | | | 1 | | 1 | 1 | 1 | 1 | 0 | 1 | | | | 0 | 0 | 1 | 1 | 9 | 69 |
| 3 | Oo 2020[79] | 0 | 1 | | | 1 | | 1 | 1 | 0 | 1 | 0 | 1 | | | | 1 | 0 | 1 | 1 | 9 | 69 |
| 4 | Russell 2017[28] | 1 | 1 | | | 0 | | 1 | 1 | 1 | 1 | 0 | 1 | | | | 0 | 0 | 1 | 1 | 9 | 69 |
| 5 | Carotti 2017[70] | 0 | 1 | | | 1 | | 1 | 1 | 0 | 1 | 0 | 1 | | | | 1 | 0 | 1 | 1 | 9 | 69 |
| 6 | Wang *et al.* 2010[29] | 0.5 | 0 | | | 1 | | 1 | 1 | 0 | 1 | 1 | 0 | | | | 1 | 0 | 1 | 1 | 8.5 | 65 |
| 7 | Ding *et al.* 2007[27] | 0 | 0 | | | 1 | | 1 | 1 | 0 | 1 | 1 | 1 | | | | 0 | 0 | 1 | 1 | 8 | 62 |
| 8 | Hart *et al.* 2018[33] | 0 | 0 | | | 1 | | 1 | 1 | 0 | 1 | 1 | 1 | | | | 0 | 0 | 1 | 1 | 8 | 62 |
| 9 | Sharma *et al.* 2014[25] | 0 | 1 | | | 1 | | 1 | 1 | 0 | 1 | 0 | 1 | | | | 0 | 0 | 1 | 1 | 8 | 62 |
| 10 | Crema *et al.* 2014[17] | 0 | 1 | | | 1 | | 1 | 1 | 0 | 1 | 0 | 1 | | | | 0 | 0 | 1 | 1 | 8 | 62 |
| 11 | Roubille *et al.* 2014[80] | 0 | 1 | | | 1 | | 0 | 1 | 0 | 1 | 0 | 1 | | | | 1 | 0 | 1 | 1 | 8 | 62 |
| 12 | Hangaard *et al.* 2018[62] | 0 | 1 | | | 1 | | 0 | 1 | 0 | 1 | 1 | 1 | | | | 0 | 0 | 1 | 1 | 8 | 62 |
| 13 | Souza *et al.* 2013[63] | 1 | 0 | | | 1 | | 1 | 1 | 0 | 1 | 0 | 1 | | | | 0 | 0 | 1 | 1 | 8 | 62 |
| 14 | Van Tiel *et al.* 2014[64] | 0 | 1 | | | 1 | | 1 | 1 | 0 | 1 | 0 | 1 | | | | 0 | 0 | 1 | 1 | 8 | 62 |
| 15 | Zarins *et al.* 2010[65] | 1 | 0 | | | 1 | | 1 | 1 | 0 | 1 | 0 | 1 | | | | 0 | 0 | 1 | 1 | 8 | 62 |
| 16 | Roubille *et al.* 2015[34] | 0 | 1 | | | 1 | | 1 | 1 | 0 | 1 | 0 | 1 | | | | 0 | 0 | 1 | 1 | 8 | 62 |
| 17 | Pelletier 2007[32] | 0 | 0 | | | 1 | | 1 | 1 | 0 | 1 | 0 | 1 | | | | 1 | 0 | 1 | 1 | 8 | 62 |
| 18 | Kaukinen 2016[71] | 0 | 0 | | | 1 | | 1 | 1 | 0 | 1 | 0 | 1 | | | | 0 | 0 | 1 | 1 | 7 | 54 |
| 19 | Antony 2017[72] | 0 | 0 | | | 1 | | 0 | 1 | 0 | 1 | 1 | 1 | | | | 0 | 0 | 1 | 1 | 7 | 54 |
| 20 | Friedrich *et al.* 2009[61] | 0 | 0 | | | 1 | | 1 | 1 | 0 | 1 | 0 | 1 | | | | 0 | 0 | 1 | 1 | 7 | 54 |
| 21 | Posadzy 2020[66] | 0 | 0 | | | 1 | | 0 | 1 | 0 | 1 | 1 | 1 | | | | 0 | 0 | 1 | 1 | 7 | 54 |
| 22 | Takahashi *et al.*[45] | 0 | 0 | | | 0 | | 1 | 1 | 0 | 1 | 1 | 1 | | | | 0 | 0 | 1 | 1 | 7 | 54 |
| 23 | Ozdemir 2019[46] | 0 | 0 | | | 1 | | 1 | 1 | 0 | 1 | 0 | 1 | | | | 0 | 0 | 1 | 1 | 7 | 54 |
| 24 | Ding *et al.* 2007[60] | 0.5 | 0 | | | 1 | | 0 | 1 | 0 | 1 | 1 | 0 | | | | 0 | 0 | 1 | 1 | 6.5 | 50 |
| 25 | Wu 2012[106] | 0 | 0 | | | 1 | | 0 | 1 | 0 | 1 | 0 | 1 | | | | 0 | 0 | 1 | 1 | 6 | 46 |
| 26 | Krych 2020[67] | 0 | 1 | | | 0 | | 0 | 1 | 0 | 1 | 0 | 1 | | | | 0 | 0 | 1 | 1 | 6 | 46 |
| 27 | Huang 2020[82] | 1 | 0 | | | 1 | | 1 | 1 | 0 | 1 | 0 | 0 | | | | 0 | 0 | 0 | 1 | 6 | 46 |
| 28 | Baert 2014[18] | 0 | 0 | | | 1 | | 1 | 1 | 0 | 1 | 0 | 1 | | | | 0 | 0 | 0 | 1 | 6 | 46 |
| 29 | Aoki 2017[81] | 1 | 0 | | | 0 | | 1 | 1 | 0 | 1 | 0 | 1 | | | | 0 | 0 | 0 | 1 | 6 | 46 |
| 30 | Sato *et al.* 2014[19] | 0 | 1 | | | 0 | | 1 | 1 | 0 | 1 | 0 | 1 | | | | 0 | 0 | 0 | 1 | 6 | 46 |
| 31 | Paparo *et al.* 2014[102] | 0 | 0 | | | 0 | | 1 | 1 | 0 | 1 | 1 | 1 | | | | 0 | 0 | 0 | 1 | 6 | 46 |
| 32 | Arepati 2021[103] | 0 | 0 | | | 0 | | 1 | 1 | 0 | 1 | 0 | 1 | | | | 0 | 0 | 1 | 1 | 6 | 46 |
| 33 | Momoeda 2021[85] | 1 | 1 | | | 0 | | 0 | 1 | 0 | 1 | 0 | 1 | | | | 0 | 0 | 0 | 1 | 6 | 46 |
| 34 | Kwoh 2011[83] | 0 | 0 | | | 0 | | 1 | 1 | 0 | 1 | 0 | 1 | | | | 0 | 0 | 0 | 1 | 5 | 38 |
| 35 | Kijima 2015[84] | 0 | 0 | | | 0 | | 1 | 0 | 0 | 1 | 0 | 1 | | | | 0 | 0 | 1 | 1 | 5 | 38 |
| 36 | Bhattacharyya[107] | 0 | 0 | | | 0 | | 0 | 1 | 0 | 1 | 0 | 1 | | | | 0 | 0 | 1 | 1 | 5 | 38 |
| 37 | Lerer 2004[104] | 0 | 0 | | | 0 | | 1 | 1 | 0 | 1 | 0 | 0 | | | | 0 | 0 | 1 | 1 | 5 | 38 |
| 38 | Rangeng *et al.* 2016[68] | 0 | 0 | | | 0 | | 1 | 1 | 0 | 1 | 0 | 0 | | | | 0 | 0 | 0 | 1 | 4 | 31 |
| 39 | Alaam 2021[69] | 0 | 0 | | | 0 | | 0 | 1 | 0 | 1 | 0 | 0 | | | | 0 | 0 | 1 | 0 | 3 | 23 |
| 40 | Yegane 2011[89] | 0 | 0 | | | 0 | | 0 | 1 | 0 | 1 | 0 | 0 | | | | 0 | 0 | 0 | 0 | 2 | 15 |
| 41 | Herrmann 1990[20] (abstract only) | 0 | 0 | | | 0 | | 0 | 1 | 0 | 1 | 0 | 0 | | | | 0 | 0 | 0 | 0 | 2 | 15 |
| | | | | | | | | | | | | | | | | | | | | Mean | 6.8 | 52 |
| | | | | | | | | | | | | | | | | | | | | Max. | 13 | |

meniscal tear (either medial or unspecified meniscus by semi-quantitative scoring) was associated with increased incident TKR risk[49,50]. The high quality, well-adjusted, analysis investigated whether longitudinal meniscal tear progression was associated with incident TKR or structural progression. Incident TKR during a 7 year observation period was associated with meniscal tear progression during 2 years after baseline[49]. In the low quality cohort analysis, incident TKR during a 6 year observation period was not associated with progression in WORMS and BLOKS combined medial and lateral tear progression over 2 years[51]. This was in pre-radiographic and radiographic OA patients.

Of the three case control analyses, one high quality, well-adjusted, case control analysis found an association between meniscal tear and incident TKR[53], whereas two poorly-adjusted case control analyses (one of which was high quality) did not[21,54].

*Summary*: Based on the literature reviewed, meniscal tear was associated with incident TKR in knee OA, independently of age, sex and BMI.

### *Relationship between meniscal extrusion and pain*

The association of meniscal extrusion with knee pain progression, pain severity and incident knee pain are described in Tables II and III.

This section included 16 publications providing four cohort, 11 cross-sectional, two case control analyses. Three analyses used ultrasound and 14 used MRI meniscus assessment.

Overall, four cohort analyses investigated the association of meniscal extrusion (medial and lateral or unspecified) with knee pain. No analyses were high quality. Of the well-adjusted cohort

**Table VI**

Quality scoring results cohort analyses

| No. | Cohort study | Quality scoring criteria | | | | | | | | | | | | | | | | | | | Total | % |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | | |
| 1 | Sharma *et al.* 2008[23] | 1 | 1 | | 1 | 0 | | 1 | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 0 | 0 | 1 | 1 | 13 | 76 |
| 2 | Wang *et al.* 2010[29] | 1 | 0 | | 0 | 1 | | 1 | 1 | 0 | 1 | 1 | 1 | 1 | 0 | 1 | 1 | 0 | 1 | 1 | 12 | 71 |
| 3 | Raynauld *et al.*2006[11] | 0 | 0 | | 1 | 1 | | 1 | 1 | 0 | 1 | 1 | 1 | 1 | 0 | 1 | 1 | 0 | 1 | 1 | 12 | 71 |
| 4 | Ding *et al.* 2007[27] | 0 | 0 | | 0 | 1 | | 1 | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 0 | 0 | 1 | 1 | 11 | 65 |
| 5 | Roemer *et al.* 2012[59] | 1 | 0 | | 0 | 1 | | 1 | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 1 | 1 | 11 | 65 |
| 6 | Teichtahl *et al.* 2017[30] | 0 | 1 | | 0 | 1 | | 1 | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 1 | 1 | 11 | 65 |
| 7 | Liu 2020[31] | 0 | 0 | | 0 | 1 | | 1 | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 0 | 1 | 0 | 1 | 1 | 11 | 65 |
| 8 | Raynauld *et al.* 2011[49] | 1 | 1 | | 0 | 1 | | 1 | 1 | 0 | 1 | 0 | 1 | 1 | 1 | 0 | 0 | 0 | 1 | 1 | 11 | 65 |
| 9 | Chang 2011[55] | 0.5 | 1 | | 0 | 1 | | 1 | 1 | 0 | 1 | 0 | 0 | 1 | 1 | 1 | 0 | 0 | 1 | 1 | 10.5 | 62 |
| 10 | Berthiaume 2005[22] | 0 | 1 | | 1 | 0 | | 1 | 1 | 0 | 1 | 0 | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 1 | 10 | 59 |
| 11 | Crema *et al.* 2010[16] | 0 | 1 | | 1 | 1 | | 1 | 1 | 0 | 1 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 1 | 1 | 10 | 59 |
| 12 | Guermazi *et al.* 2013[56] | 1 | 0 | | 1 | 1 | | 0 | 1 | 0 | 1 | 0 | 1 | 1 | 0 | 0 | 1 | 0 | 1 | 1 | 10 | 59 |
| 13 | Roubille *et al.* 2015[35] | 0 | 0 | | 0 | 1 | | 1 | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 1 | 1 | 10 | 59 |
| 14 | Sharma *et al.* 2014[25] | 0 | 1 | | 0 | 1 | | 1 | 1 | 0 | 1 | 0 | 1 | 1 | 1 | 0 | 0 | 0 | 1 | 1 | 10 | 59 |
| 15 | Hart *et al.* 2018[33] | 0 | 0 | | 0 | 1 | | 1 | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 1 | 1 | 10 | 59 |
| 16 | Pelletier *et al.* 2007[32] | 0 | 0 | | 1 | 1 | | 1 | 1 | 0 | 1 | 0 | 1 | 1 | 1 | 0 | 0 | 0 | 1 | 1 | 10 | 59 |
| 17 | Roubille *et al.* 2015[34] | 0 | 1 | | 0 | 1 | | 1 | 1 | 0 | 1 | 0 | 1 | 1 | 1 | 0 | 0 | 0 | 1 | 1 | 10 | 59 |
| 18 | Khan 2016[26] | 0.5 | 0 | | 0 | 0 | | 1 | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 1 | 1 | 9.5 | 56 |
| 19 | Eathakkattu Antony *et al.* 2016[50] | 1 | 0 | | 0 | 0 | | 1 | 1 | 0 | 1 | 0 | 1 | 1 | 1 | 0 | 1 | 0 | 0 | 1 | 9 | 53 |
| 20 | Eathakkattu Antony *et al.* 2016[36] | 1 | 0 | | 0 | 0 | | 1 | 1 | 0 | 1 | 0 | 1 | 1 | 1 | 0 | 0 | 0 | 1 | 1 | 9 | 53 |
| 21 | Hafezi-Najad 2015[51] | 0 | 0 | | 0 | 1 | | 1 | 1 | 0 | 1 | 0 | 1 | 1 | 1 | 0 | 0 | 0 | 1 | 1 | 9 | 53 |
| 22 | Hunter *et al.* 2006[37] | 0 | 0 | | 0 | 1 | | 1 | 1 | 0 | 1 | 0 | 1 | 1 | 1 | 0 | 0 | 0 | 1 | 1 | 9 | 53 |
| 23 | Antony 2017[72] | 0 | 0 | | 0 | 1 | | 0 | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 1 | 1 | 9 | 53 |
| 24 | Klein 2016[38] | 0 | 0 | | 0 | 1 | | 1 | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 1 | 9 | 53 |
| 25 | Roemer 2022[44] | 0 | 0 | | 0 | 1 | | 1 | 1 | 0 | 1 | 0 | 1 | 1 | 1 | 0 | 0 | 0 | 1 | 1 | 9 | 53 |
| 26 | Wu 2022[52] | 0 | 0 | | 0 | 1 | | 1 | 1 | 0 | 1 | 0 | 1 | 1 | 1 | 0 | 0 | 0 | 1 | 1 | 9 | 53 |
| 27 | Madan-Sharma *et al.* 2008[57] | 0 | 0 | | 0 | 1 | | 1 | 1 | 0 | 1 | 1 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 1 | 8 | 47 |
| 28 | Buck *et al.*, 2011[39] | 0 | 0 | | 1 | 0 | | 1 | 1 | 0 | 1 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 1 | 1 | 8 | 47 |
| 29 | Roemer 2022[43] | 0 | 0 | | 0 | 1 | | 1 | 1 | 0 | 1 | 0 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 1 | 8 | 47 |
| 30 | Kwoh 2017[77] | 0 | 0 | | 0 | 0 | | 1 | 1 | 0 | 1 | 0 | 0 | 1 | 1 | 0 | 1 | 0 | 0 | 1 | 7 | 41 |
| 31 | Roemer *et al.* 2012[40] | 0 | 0 | | 0 | 1 | | 1 | 1 | 0 | 1 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 7 | 41 |
| 32 | Roemer *et al.* 2009[41] | 0 | 0 | | 0 | 1 | | 1 | 1 | 0 | 1 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 7 | 41 |
| 33 | Bloecker 2015[108] | 0 | 0 | | 0 | 1 | | 1 | 1 | 0 | 1 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 7 | 41 |
| 34 | Choi *et al.* 2014[42] | 0 | 1 | | 0 | 1 | | 1 | 1 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 1 | 7 | 41 |
| 35 | Kwoh 2020[78] | 0 | 0 | | 0 | 0 | | 1 | 1 | 0 | 1 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 1 | 1 | 7 | 41 |
| 36 | Biswal 2002[58] | 0 | 0 | | 0 | 0 | | 0 | 1 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 1 | 4 | 24 |
| | | | | | | | | | | | | | | | | | | | | Mean | 9.3 | 54 |
| | | | | | | | | | | | | | | | | | | | | Max. | 17 | |

analyses, one found an association between unspecified meniscal extrusion and WOMAC pain progression[36] with a follow up period of 10 years. Another found no association between medial and lateral meniscal extrusion and clinically meaningful change in WOMAC pain over 2 years, but almost achieved statistical significance[72]. Two low quality cohort analyses (one well-adjusted) found an association between unspecified meniscal extrusion and incident frequent knee pain[77,78].

Of the four high quality cross-sectional analyses of meniscal extrusion and pain, three were also well-adjusted cross-sectional analyses describing the association between meniscal extrusion and knee pain severity[71,72,79]. For two of these, medial meniscal extrusion by ultrasound[79] and medial and lateral MRI-defined meniscal extrusion[71] was associated with quantitative and qualitative knee pain severity respectively. However, medial and lateral MRI-defined meniscal extrusion was not associated with WOMAC pain in the remaining high quality, well-adjusted study[72]. Overall, eight out of 11 cross-sectional analyses found an association between meniscal extrusion and knee pain severity[71,79–85].

Only two case–control analyses measured the association between meniscal extrusion and knee pain progression[86,87]. Both were high quality and well-adjusted and found a positive association.

*Summary*: Based on the literature reviewed, acknowledging the lack of high quality evidence, meniscal extrusion appeared to be associated with longitudinal change in WOMAC knee pain independently of age, sex and BMI, but not clinically meaningful change in pain. Meniscal extrusion was cross-sectionally associated with pain severity in knee OA.

### *Relationship between meniscal tear/damage and pain*

The association of meniscal tear/damage with knee pain progression, pain severity and incident knee pain are described in Tables II and III.

This section included 16 publications providing four cohort, 11 cross-sectional and two case control analyses all using MRI.

Of the four cohort analyses, only one was a high quality, well-adjusted analysis, demonstrating an association between meniscal

| No. | Case control study | Quality scoring criteria | | | | | | | | | | | | | | | | | | | Total | % |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | | |
| 1 | Roemer *et al.* 2015[54] | 0 | 0 | 1 | | 1 | 1 | 1 | 1 | 0 | 1 | 1 | 1 | | 1 | | 1 | 0 | 1 | 1 | 12 | 75 |
| 2 | Russell 2017[28] | 1 | 1 | 1 | | 0 | 1 | 1 | 1 | 1 | 1 | 0 | 1 | | 1 | | 0 | 0 | 1 | 1 | 12 | 75 |
| 3 | Roth 2020[53] | 0 | 1 | 1 | | 1 | 0 | 1 | 1 | 0 | 1 | 0 | 0 | | 1 | | 1 | 0 | 1 | 1 | 10 | 63 |
| 4 | Guermazi *et al.* 2015[75] | 0 | 0 | 1 | | 1 | 0 | 1 | 1 | 0 | 1 | 1 | 1 | | 1 | | 0 | 0 | 1 | 1 | 10 | 63 |
| 5 | Englund *et al.* 2007[90] | 0 | 0 | 1 | | 1 | 0 | 1 | 1 | 0 | 1 | 0 | 1 | | 1 | | 1 | 0 | 1 | 1 | 10 | 63 |
| 6 | Collins 2016[86] | 0 | 0 | 1 | | 1 | 0 | 1 | 1 | 0 | 1 | 0 | 1 | | 1 | | 1 | 0 | 1 | 1 | 10 | 63 |
| 7 | Wenger 2012[87] | 0 | 1 | 1 | | 1 | 1 | 1 | 1 | 0 | 1 | 0 | 0 | | 0 | | 0 | 0 | 1 | 1 | 9 | 56 |
| 8 | Sharma 2019[48] | 0 | 1 | 1 | | 0 | 1 | 1 | 1 | 0 | 1 | 1 | 1 | | 0 | | 0 | 0 | 1 | 0 | 9 | 56 |
| 9 | Posadzy 2020[66] | 0 | 0 | 1 | | 1 | 1 | 0 | 1 | 0 | 1 | 1 | 1 | | 0 | | 0 | 0 | 1 | 1 | 9 | 56 |
| 10 | Matsubara 2015[76] | 0 | 1 | 1 | | 1 | 0 | 1 | 1 | 0 | 1 | 1 | 0 | | 0 | | 0 | 0 | 1 | 1 | 9 | 56 |
| 11 | Roemer 2012[40] | 0 | 0 | 1 | | 1 | 0 | 1 | 1 | 0 | 1 | 0 | 1 | | 0 | | 0 | 0 | 1 | 1 | 8 | 50 |
| 12 | Heilmeier 2017[21] | 0 | 0 | 1 | | 0 | 0 | 1 | 1 | 0 | 1 | 0 | 1 | | 1 | | 0 | 0 | 0 | 1 | 7 | 44 |
| 13 | Cao[73] | 0 | 0 | 1 | | 0 | 0 | 1 | 1 | 0 | 1 | 0 | 1 | | 0 | | 0 | 0 | 1 | 1 | 7 | 44 |
| 14 | Sharma 2022[105] | 0 | 1 | 1 | | 1 | 0 | 0 | 1 | 0 | 1 | 0 | 0 | | 0 | | 0 | 0 | 1 | 1 | 7 | 44 |
| 15 | Cohen 2012[74] | 0 | 0 | 1 | | 0 | 0 | 0 | 1 | 0 | 1 | 0 | 0 | | 1 | | 0 | 0 | 1 | 1 | 6 | 38 |
| | | | | | | | | | | | | | | | | | | | | Mean | 9 | 56 |
| | | | | | | | | | | | | | | | | | | | | Max. | 16 | |

**Table VII**

Osteoarthritis and Cartilage

Quality scoring results case–control analyses

tear (medial and lateral) and longitudinal change in knee pain[26]. This was from the Offspring cohort study (mean age 47 years). Two low quality cohort analyses (both with a mean age of 63 years) found no association[36,72]. Another low quality, well-adjusted cohort analysis found a positive association between meniscal tear and incident frequent knee pain[77].

Out of the 11 cross-sectional analyses measuring meniscal tear and pain, three were high quality and well-adjusted[70–72]. Two out of these three found an association between meniscal tear and knee pain severity[71,72]. Overall eight out of 11 cross-sectional analyses demonstrated an association between meniscal tear and pain severity[65,68,71,72,80,83,88,89].

Two high quality, well-adjusted case control analyses investigated meniscal tear and knee pain[86,90], with a positive association only found in one[86].

*Summary*: Based on the literature reviewed, meniscal tears were not clearly associated with progression in knee pain. Meniscal tear was associated with incident frequent knee pain in a poor quality study. Meniscal tears were cross-sectionally associated with knee pain severity.

## Discussion

This is the first systematic literature review to describe the association between meniscal pathologies and knee OA structural progression and severity, TKR and knee OA-related pain, using modern imaging that directly assessed meniscal and cartilage pathology. Based on the reviewed available literature, meniscal extrusion and meniscal tear were associated with cartilage structural progression and TKR incidence independently of age, sex and BMI. However there was a more uncertain association between meniscal pathology and knee pain progression, pain severity and pain incidence.

The anterior and posterior meniscal horns have anatomical differences in their dimensions and attachments[91] and the increased risk of damage to the posterior horn compared to the anterior horn may be related to this, its reduced mobility and the increased load during flexion compared to the anterior horn[92,93]. This may cause each meniscus segment to have a different effect on force distribution to adjacent cartilage when they are damaged, resulting in differing levels of cartilage damage associated with each segment. Chang *et al.* demonstrated that the anterior meniscal segment overlies a smaller proportion of articular cartilage, therefore meniscal damage may affect a smaller area of cartilage, compared to the body which overlies a larger proportion of articular cartilage[55]. Two analyses also demonstrated an association between posterior root tears and OA cartilage progression[45,56], although root tears are recognised as a different type of pathology to horn tears[56]. Previous evidence has suggested that posterior root repair reduces the risk of OA cartilage loss[94]. One possibility why posterior root tear confers a greater risk of OA cartilage progression may be due to disrupted circumferential fibres causing abnormal weight distribution, decreased tibiofemoral contact area and increasing peak contact pressure through a loss of hoop tension, leading to hyaline articular cartilage damage and meniscal extrusion[95–97].

This systematic review demonstrated both meniscal tear and extrusion are independently associated (of age, sex and BMI) with TKR incidence. This review also identified that meniscal extrusion is a risk factor for knee OA cartilage structural progression independently of age, sex and BMI. Unlike the literature on meniscal tears, there was little data on subregional meniscal extrusion and its association with cartilage structural progression. There was only one such analysis[22], which demonstrated a positive association between anterior horn and body extrusion with OA cartilage progression. However it should be noted that many meniscal tears are degenerative and part of the multi-tissue pathology of OA which may contribute to biomechanical adversity which in itself may contribute to structural progression.

Degenerative meniscal tears have been associated with incident frequent symptoms of knee OA amongst patients without radiographic knee OA[25]. In this review, however, there were few high quality, well-adjusted prospective analyses measuring meniscal pathology and pain in knee OA. Of the analyses reviewed, there was no clear association between meniscal pathology and pain severity cross-sectionally or pain longitudinally (pain progression or incident pain). This is supported by data suggesting meniscal repair does not improve long term OA knee pain[98].

Multiple pain scoring tools were used but no clear pattern of association was demonstrated between an individual scoring method and meniscal pathology. 19 clinical studies measuring knee pain were excluded due to lack of participants with radiographic knee OA. There were no longitudinal studies measuring the relationship between subregional meniscal tear and OA knee pain.

Considering possible limitations of this study, the range of quality scores were broad (see Quality assessment of analyses) for the selected cross-sectional and longitudinal analyses, suggesting that the scoring system employed could discern quality differences between analyses. High quality analyses were therefore not artificially created from a pool of generally low quality analyses. However, analyses that included participants with predominantly pre-radiographic OA were grouped together with those that included participants with predominantly radiographic OA, which may not fully take into account potential differences in the mechanisms driving OA incidence and progression. The marked heterogeneity in the analyses precluded a meta-analysis or effect size calculation. Another limitation may relate to the use of TKR as an outcome measure, which has certain limitations including the effect of patient willingness, differences in opinion between orthopaedic specialists, availability of health service provision and health insurance. As all MRI studies measured extrusion in a supine, non weight-bearing position, this may underestimate the true incidence of meniscal extrusion. Meniscus positioning may be altered by weight-bearing in asymptomatic individuals[99] and under loading conditions in knee OA subjects[100]. Few studies used meniscal ultrasound measurements, of these only one study[46] measured meniscal extrusion on weight bearing and its association with OA structural severity. No ultrasound studies measured the association between weight-bearing meniscal pathology and pain. OA is a typically weight-bearing condition and further weight-bearing imaging studies may reveal further insights into the structure pain relationship of knee OA[101].

Meniscal pathology was associated with structural progression and severity of knee OA and TKR risk. Medial and lateral meniscal tears were associated with cartilage progression loss when they occurred in the body and posterior horns, but not anterior horns. There was a weak association between meniscal pathology and pain in knee OA.

## Contributions

AG carried out the literature search, eligibility assessment, extraction of data, quality assessment, along with drafting and revising of the manuscript content. AB carried out conception and design, eligibility assessment, extraction of data, quality assessment, along with drafting and revising of the manuscript content. SM and CM carried out conception and design. ER carried out extraction and presentation of data. SK carried out conception and design. PC carried out conception and design, quality assessment and revising the manuscript for content. All authors reviewed the final version of the manuscript.

## Conflict of interest statement

AG reports no conflicts. AB reports no conflicts. SM reports no conflicts. CM reports no conflicts. ER reports no conflicts. SK reports no conflicts. PGC reports speakers' bureaus or consultancies for Abbvie, Astra Zeneca, BMS, Centrexion, EMD Serono, Flexion Therapeutics, Galapagos, Gilead, Novartis, Pfizer, Samumed and Stryker.

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## Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.joca.2022.08.002.

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