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Review

Which patellofemoral joint imaging features are associated with patellofemoral pain? Systematic review and meta-analysis

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SUMMARY

Objectives: To review the association between patellofemoral joint (PFJ) imaging features and patellofemoral pain (PFP).
Design: A systematic review of the literature from AMED, CiNAHL, Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, PEDro, EMBASE and SPORTDiscus was undertaken from their inception to September 2014. Studies were eligible if they used magnetic resonance imaging (MRI), computed tomography (CT), ultrasound (US) or X-ray (XR) to compare PFJ features between a PFP group and an asymptomatic control group in people <45 years of age. A pooled meta-analysis was conducted and data was interpreted using a best evidence synthesis.
Results: Forty studies (all moderate to high quality) describing 1043 people with PFP and 839 controls were included. Two features were deemed to have a large standardised mean difference (SMD) based on meta-analysis: an increased MRI bisect offset at 0° knee flexion under load (0.99; 95% CI: 0.49, 1.49) and an increased CT congruence angle at 15° knee flexion, both under load (1.40 95% CI: 0.04, 2.76) and without load (1.24; 95% CI: 0.37, 2.12). A medium SMD was identified for MRI patella tilt and patellofemoral contact area. Limited evidence was found to support the association of other imaging features with PFP. A sensitivity analysis showed an increase in the SMD for patella bisect offset at 0° knee flexion (1.91; 95% CI: 1.31, 2.52) and patella tilt at 0° knee flexion (0.99; 95% CI: 0.47, 1.52) under full weight bearing.
Conclusion: Certain PFJ imaging features were associated with PFP. Future interventional strategies may be targeted at these features.
PROSPERO registration number: CRD 42014009503.

Introduction

Patellofemoral pain (PFP) refers to pain experienced either from the anterior or retro-patellar region and typically occurs in adolescents and younger adults[1]. Knee pain affects up to 30% of adolescents[2] with as much as 50% attributed to PFP[3]. Whilst one in six adults consulting their general practitioner with knee pain will be diagnosed with PFP[4]. Currently, unfavourable recovery rates in PFP are known to be as much as 40% up to one year following treatment[5]. The degree of unfavourable recovery is important given the growing concern that PFP, if not successfully managed, may be a potential precursor to patellofemoral osteoarthritis (PFOA)[6].

The exact pathogenesis of PFP remains unknown and thus its management remains inconsistent[7]. Many factors have been previously associated with PFP, including biomechanical, structural and clinical features[7]. It is widely believed that abnormalities of the structure and the function of the patellofemoral joint (PFJ) is the underlying cause of PFP[8]. The prevailing theory is that PFP is caused by abnormal tracking and alignment of the patella leading to irritation of richly innervated PFJ structures like subchondral bone, lateral retinaculum or synovium[9]. The structure of the PFJ has more recently become the subject of increased interest since the PFJ was established as the most common compartment for knee OA[10,11].

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Currently there is a paucity of evidence to support the link between PFP and PFOA[12], however, reported similarities in their clinical impairments and functional limitations, such as stair descent, would infer a relationship[6]. Furthermore, Utting *et al.*[13] reported that over 20% of people undergoing surgery for isolated PFOA recalled experiencing PFP symptoms as an adolescent.

Historically, the PFJ has been visualised using X-rays in a static, non-weight bearing position. Over the last 20 years, imaging has revolutionised the understanding of the knee as a whole[14] with advances in structure visualisation, kinematic applications and loading capabilities[15]. More recently, a variety of modern imaging modalities have been used to assess PFJ structure[16], but no consensus exists on which of these image modalities should be used or the key features to image.

This systematic review aimed to establish which PFJ imaging features are associated with PFP compared to asymptomatic individuals.

Methods

Protocol and registration

This systematic review was performed using a predetermined protocol in accordance with the PRISMA statement[17]. The study protocol was registered with PROSPERO, registration number CRD 42014009503.

Search strategy and study selection

A primary electronic search of AMED, CiNAHL, Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, PEDro, EMBASE and SPORTDiscus was undertaken from their inception to September 2014. Additionally, a secondary electronic search of unpublished and trial registry databases was performed. This included: OpenGrey, the WHO International Clinical Trials Registry Platform, Current Controlled Trials and the UK National Research Register Archive. The electronic search was complemented by hand searching the references of the retrieved articles. The search terms used for Medline (also used for the other databases) are in Supplementary Material.

Eligibility criteria

The selection of studies was made using the titles and abstracts, independently screened by two reviewers (BD, FP). Potential studies had the full text retrieved and were screened against the eligibility criteria. Studies were eligible if: (1) they included human participants under 45 years (mean age of participants) diagnosed with PFP; (2) magnetic resonance imaging (MRI), computed tomography (CT), ultrasound (US) or X-ray (XR) was used to image the PFJ and local structures; (3) a comparison of PFP cases and a healthy control group was provided; (4) they were published in English. For the purposes of this study, PFP was determined using previously published clinical criteria[18]. Studies that included participants diagnosed of PFP, anterior knee pain or chondromalacia patellae were all considered. If a study included participants with arthroscopically confirmed chondromalacia patellae outside the currently accepted clinical presentation of PFP[18] then these studies were excluded. Studies including other conditions such patella tendinopathy and patella dislocation were also excluded if the PFP could not be analysed separately.

Data extraction was initially piloted by two reviewers (BD, FP) before the formal extraction was undertaken. Two reviewers (BD, FP) then used a standardised, piloted form to extract data regarding study characteristics, participant characteristics, imaging procedures, settings and outcome data results. A third reviewer (TS) was used to resolve disagreements in eligibility, data extraction or quality assessment.

Quality assessment

The methodological quality of the included studies was assessed by the same two reviewers (BD, FP). A modified version of the Down & Black's Checklist[19] was used with original 27 items reduced to 17 items as described previously[20] (Supplementary Material), as not all items were applicable for all non-randomised studies. All included studies were classified using the following quality rating bandings which have been used previously in conjunction with Downs & Blacks checklist[21]: low (<33.3%), moderate (33.4–66.7%) and high (≥66.8%)[22].

Data analysis

Study heterogeneity was assessed using the extraction tables. If there were no heterogeneity between studies in relation to population, assessment procedure or outcome measurement method, a meta-analysis was conducted to compare between case and control groups for each PFJ feature calculating the standardised mean difference (SMD). SMD was categorised as small (SMD ≥ 0.2), medium (SMD ≥ 0.5) and large (SMD ≥ 0.8)[23]. Statistical heterogeneity was assessed using I-squared and Chi-squared tests. When I-squared was greater than 20% and Chi-squared less than $P = 0.10$, a random-effects model was used. When I-squared was less than 20% and Chi-squared was greater than $P = 0.10$, a fixed-effect model was adopted. When substantial heterogeneity was present, a narrative synthesis of the literature was presented. Both the narrative synthesis and the meta-analysis were interpreted using a best evidence synthesis[24] (Table I[25]) determined by the results of the risk-of-bias assessment and the methodological quality of the included studies[26,27].

Results

Study selection

Fig. 1 summarizes the results of the search strategy. The search identified 5,290 papers, with 3,852 after duplications were removed. Following screening of the title and abstract, 3,702 of these were excluded. Subsequent full text assessment identified 46 papers describing 40 studies. Five studies[28–38] reported the same

Table I
Best evidence synthesis

1.) Strong evidence is provided by generally consistent findings in multiple high-quality cohort studies.
2.) Moderate evidence is provided by general consistent findings in one high-quality cohort study and two or more high quality case–control studies or in three or more high-quality case–control studies.
3.) Limited evidence is provided by (general consistent) findings in a single cohort study, in one or two case–control studies or in multiple cross-sectional studies.
4.) Conflicting evidence is provided by conflicting findings (i.e., <75% of the studies reported consistent findings).
5.) No evidence is provided when no studies could be found.

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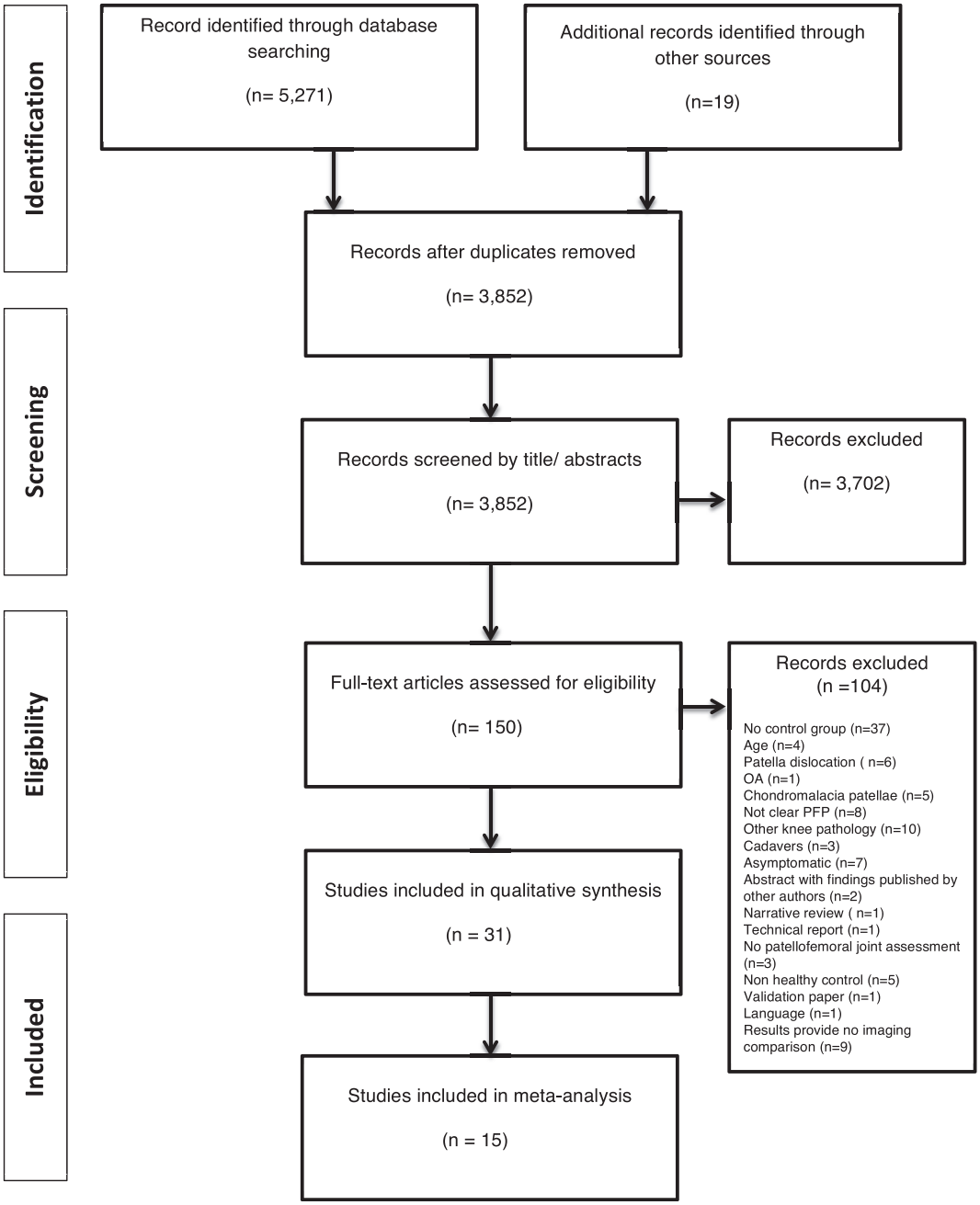

Fig. 1. Study selection flow diagram.

study population in more than one paper. These papers described different outcomes so were analysed independently, although the risk of bias assessment was conducted on only 40 studies to prevent the overestimation of effects.[39]

Study characteristics

The study characteristics are presented in Table II. Of the 40 studies included, 22 used MRI[28–38,40–56], of which five included kinematic MRI[41,43,46,55,56], eight used CT[57–64], six used US[65–70] and five used XR[60,71–74]. The review included 1043 PFP subjects and 839 control subjects. The mean age was 27.0 years (range: 14–40.7 years), with 74.3% women in the case group and 69.0% in the control group. The duration of symptoms was reported in only ten of the 40 studies[30,31,37,38,40,47,55,60,63,65,67,73]. The duration of symptoms ranged from two[47] to 168 months[63]. All studies presented cross-sectional data except for two studies[41,50]. Pain was established in the PFP cohort most commonly from: reproducible pain in greater than two functional activities[28–34,38,40–43,45–47,51,65,66,68,70,75]. This was further quantified by five studies that only recruited participants with a Visual Analogue Scale (VAS) score greater than 3/10 on these provocation activities[30,31,42,43,47,51]. A further four studies used the Anterior Knee Pain (Kujala) score to quantify pain and dysfunction of their PFP cohort[38,40,41,49]. In ten studies it was unclear how pain was measured[44,48,54,57,58,60,62,63,67,72]. Imaging reliability data was presented in 43% (20/46) of the included studies[30,33–35,38,40,43,46,47,49,51,53,59,65,66,74–76] (Supplementary Material) and most of these studies used a single observer. Based on the

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Table II
Sample sizes and population characteristics for each included paper

Study	Study design	Follow up	Country of origin e.g., UK, USA	Population e.g., students, athletes	Sample size	Age (years)	Female %	Mean duration of symptoms (months)
Aglietti *et al.*, 1983	Case–control	No	USA	UTD	Case = 53 Control = 150	22	Case = 60.3 Control = 50%	UTD
Bretcher & Powers, 2002a Bretcher & Powers, 2002b	Case–control	No	USA	Orthopaedic referrals	Case = 10 Control = 10	34.6	Case = 50% Control = 50%	UTD
Botanlioglu *et al.*, 2013	Case–control	No	Turkey	UTD	Case = 11 Control = 22	29.5	Case = 100 Control = 50%	UTD
Callaghan & Oldham, 2004	Case–control	No	UK	Orthopaedic & Rheumatology referrals	Case = 57 Control = 10	32.6	Case = 61% Control = 60%	34
Chen & Powers, 2014	Case–control	No	USA	Orthopaedic referrals & university students	Case = 20 Control = 20	27	Case = 100% Control = 100%	UTD
Chen *et al.*, 2012	Case–control	No	Taiwan	Orthopaedic referrals	Case = 26 Control = 26	27.8	Case = 81% Control = 81%	UTD
Chiu *et al.*, 2012	Case–control	8 weeks	Hong Kong	UTD	Case = 9 Control = 6	33.1	Case = 55.6 Control = 50	UTD
Connolly *et al.*, 2009	Case–control	No	Canada	Sports Medicine Physician referrals	Case = 10 Control = 10	27	Case = 100% Control = 100%	UTD
Draper *et al.*, 2006	Case–control	No	USA	UTD	Case = 34 Control = 16	28.8	Case = 64.7% Control = 50%	UTD
Draper *et al.*, 2009	Case–control	No	USA	Orthopaedic & Sports Medicine referrals	Case = 23 Control = 13	29.4	Case = 100% Control = 100%	UTD
Eckhoff *et al.*, 1994	Case–control	No	USA	Failed conservative management	Case = 20 Control = 20	UTD	UTD	UTD
Farrokhi *et al.*, 2011a Farrokhi *et al.*, 2011b	Case–control s	No	USA	UTD	Case = 10 Control = 10	27.4	Case = 100% Control = 100%	87.6 1
Felicio *et al.*, 2011a Felicio *et al.*, 2012b Felicio *et al.*, 2014c	Case–control	No	Brazil	UTD	Case = 19 Control = 20	22.5	Case = 100% Control = 100%	UTD
Guzzanti *et al.*, 1994	Case–control	No	Italy	Adolescents	Case = 27 Control = 20	14	Case = 77.8 Control = 50	UTD
Haim *et al.*, 2006	Case–control	No	Israel	Military soldiers	Case = 61 Control = 25	21.8	Case = 0% Control = 0%	19
Harman *et al.*, 2002	Case–control	No	Turkey	UTD	Case = 17 Control = 10	29.4	Case 0% Controls 0%	UTD
Ho *et al.*, 2014 Ho *et al.*, 2014b	Case–control	No	USA	UTD	Case = 10 Control = 10	25.5	Case = 100% Control = 100%	UTD
Joensen *et al.*, 2001	Case–control	No	Denmark	Athletes	Case = 24 Control = 17	21.6	Case = 37.5 Control = 35.3	UTD
Jones *et al.*, 1995	Case–control	No	USA	Failed conservative management	Case = 40 Control = 10	UTD	Case = UTD Control = 50%	UTD
Kim *et al.*, 2014	Case–control	No	South Korea	Orthopaedic referrals	Case = 51 Control = 44	27.4	Case = 47% Control = 50%	UTD
Laprade & Culham, 2003	Case–control	No	Canada	Military	Case = 33 Control = 33	30.9	Case = 33.3 Control = 33.3	UTD
Jan *et al.*, 2009	Case–control	No	Taiwan	Orthopaedic referrals	Case = 54 Control = 54	40.7	Case = 75.9 Control = 75.9	UTD
Metin Cubuk *et al.*, 2000	Case–control	No	Turkey	Orthopaedic referrals	Case = 42 Control = 40	27	Case = 100% Control = 100%	11
Muneta *et al.*, 1994	Case–control	No	Japan	UTD	Case = 60 Control = 19	21	Case = 100 Control = 100	UTD
Pal *et al.*, 2013c	Case–control	No	USA	University Orthopaedic and Sport Medicine referrals	Case = 37 Control = 15	29.7	Case = 54.1% Control = 53.3%	3–132
Pattyn *et al.*, 2011 Pattyn *et al.*, 2013c	Case–control	No	Belgium	Hospital Orthopaedic Surgeon referrals	Case = 46 Control = 30	23.3	Case = 54.3 Control = 56.7	17.37
Pinar *et al.*, 1994	Case–control	No	Turkey	UTD	Case = 26 Control = 14	29	Case = 78.5	UTD
Powers, 2000b	Case–control	NAD	USA	Orthopaedics referrals & university students	Case = 23 Control = 12	27.9	Control = UTD	UTD
Ribeiro *et al.*, 2010	Case–control	NAD	Brazil	UTD	Case = 12 Control = 12	22.5	Case = 100% Control = 100%	UTD
Salsich & Perman, 2007	Case–control	No	USA	UTD	Case = 21 Control = 21	25	Case = 76.2 Control = 66.7	UTD
Salsich & Perman, 2013	Case–control	No	USA	Multiple sources – including community dwelling population	Case = 27 Control = 29	25.6	Case = 77.8 Control = 65.5	>2
Schoots *et al.*, 2013	Case–control	No	Netherlands	Sports medicine & Orthopaedic referrals	Case = 10 Control = 10	29.3	Case = 60% Control = 60%	>6
Schutzer *et al.*, 1986	Case–control	No	USA	UTD	Case = 24 Control = 10	19	Case = 91.7 Control = 70	3–168
Souza *et al.*, 2010	Case–control	No	USA	Orthopaedic referrals & community dwelling population	Case = 15 Control = 15	29.9	Case = 100% Control = 100%	UTD
Taskiran *et al.*, 1998	Case–control	No	Turkey	UTD	Case = 10 Controls = 9	27	Case = 100% Control = 88.9	UTD

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Table II (*continued*)

Study	Study design	Follow up	Country of origin e.g., UK, USA	Population e.g., students, athletes	Sample size	Age (years)	Female %	Mean duration of symptoms (months)
Teng *et al.*, 2014	Case–control	No	USA	UTD	Case = 18 Control = 18	27.3	Case = 100% Control = 100%	UTD
Thuiller *et al.*, 2013	Case–control	No	USA	Sports Medicine referrals	Case = 20 Control = 10	31.3	Case = 60 Control = 50	UTD
Tuncyurek *et al.*, 2010	Case–control	No	Turkey	Orthopaedics referrals	Case = 23 Control = 9	31.3	Case = 52 Control = 78	UTD
Wilson *et al.*, 2009	Case–control	No	USA	UTD	Case = 7 Control = 7	30.6	Case = 71.4 Control = 57.1	UTD
Witzonzi & Goraj, 1999	Case–control	No	Poland	UTD	Case = 10 Control = 10	19.1	Case = 100% Control = 80%	8–60

UTD = Unable to detect.

reported intraclass correlation coefficients (ICC) a pooling of the data was available for MRI bisect offset, patella tilt, patellofemoral contact area, with Insall-Salvati ratio and sulcus angle showing mean ICCs of 0.92, 0.85, 0.90, 0.96, 0.82 respectively. Inter-observer reliability data was only presented in seven studies[38,41,49,50,59,71,74].

Quality assessment

A summary of the quality assessment results are presented in Table III. Based on the categorisations used[22], 23 studies were judged as high quality ([30–38,40–51,65–67,69,71,73,74]), with the remaining 17 studies considered of moderate quality[28,29,52–64,68,70,72]. The criteria of best performance using the modified Downs & Black checklist were 1, 2, 3 and 4, which were satisfied by all the included studies. The criteria that the included studies performed most poorly were 9, 10, 11, 15 and 17 (Supplementary Material). Criteria 9, 10 and 15 pertained to the documentation of population in which participants are recruited. Only half the studies clearly documented from where their participants were recruited e.g., hospital, military *etc*. Criterion 11 posed: *was an attempt made to blind those measuring the outcome*. Only 17.5% (7/40) of the studies we were able to determine whether the person/s interpreting the images were blinded to group allocation. Criteria 17 posed: *did the study have sufficient power to detect clinically important effect*. Only 17.5% (7/40) of studies[40,42,47,48,65,69,71] clearly documented how they calculated their sample size.

Based on published guidelines[77], funnel plots were not employed due to no one feature having more than ten studies and so reducing the likelihood of distinguishing real asymmetry.

Synthesis of results

MRI features (patellofemoral contact area, patellar tilt, patellar bisect offset, patellar cartilage T2 relaxation times and sulcus angle) and CT features (congruence angle) were the only imaging features that yielded homogenous data appropriate for meta-analysis. These features are demonstrated schematically in Fig. 2. If discrepancies were noted in either the knee loading status, assessments of the imaging feature or knee flexion angle, then features were not considered for meta-analysis. The results of the meta-analyses are displayed in Table IV.

MRI

Of the twenty-two studies that used MRI, sixteen studies[30–38,40–51,78] were judged as high quality. Controlling for the knee loading status, assessment of the imaging feature and knee flexion angle, patella bisect offset at 0° with load demonstrated the largest SMD (0.99; 95% CI: 0.49, 1.49; moderate evidence) based on five high quality[41,43,46,47,51] and one moderate quality[53] study (Fig. 3). This was the only MRI feature which presented with a large SMD[23]. Five other features demonstrated a medium SMD[23]. These included: patella bisect offset at 20° with load (0.73; 95% CI: 0.29, 1.17; limited evidence)[41,47,53,67], patella tilt at 0° with load (0.63: 95% CI: 0.37, 0.90; moderate evidence)[41,43,46,47,51,53], patella bisect offset at 40° with load (0.61; 95% CI: −0.09, 1.31; limited evidence)[41,47,53], patellofemoral contact area at 20° with load (−0.53; 95% CI: −1.01, −0.06; limited evidence)[47,50] and patella bisect offset at 60° with load (0.50; 95% CI 0.02, 0.98; limited evidence)[41,53].

A small SMD was found for the pooling of sulcus angle at 0° with load (0.44; 95% CI: −0.17, 1.05; limited evidence)[46,53], sulcus angle at 30° without load (0.43; 95% CI: −0.48, 1.35; limited evidence)[34,52], patella tilt at 20° with load (0.35; 95% CI: 0.02, 0.69; moderate evidence)[41,47,50,53], patella tilt at 30° without load (0.25; 95% CI: −0.24, 0.75; limited evidence)[34,52], T2 Relaxation time at 0° with without load (−0.01; 95% CI: −0.35, 0.34; limited evidence)[31,48]. The data for patellofemoral joint reaction force (PFJRF) was considered inappropriate for pooling as its outputs were produced via computational modelling, with imaging as only one component. For the data not amenable to pooling, there was limited evidence to support a difference between PFP and a control group with regards to: congruence angle at 20°[55] and 30°[52] without load; T1 value of the lateral patellofemoral cartilage without load[48]; articular lesions of the patella[44]; peak PFJRF; and patella cartilage thickness in males[49]. There was conflicting evidence to support a difference in patella cartilage thickness in women[30,36,45,49] and no evidence to support differences in patella tendon morphology[54].

US

US was used to assess PFP imaging features in four studies[65–67,69]. These were all judged as high quality. Pooling of data was not appropriate due to the variety of outcome features analysed and the different assessment techniques used. For the data not amenable to pooling, there was limited evidence, from single studies, to support a difference between PFP and control group in terms of: a reduction in vastus medialis oblique (VMO) contraction ratio and capacity[68]; an increase in VMO electrical mechanical delay and a reduction in vastus lateralis (VL) delay[66]; and a difference in VMO fibre angle, insertion level and volume[69].

CT

CT was employed in eight studies, all of which were judged as moderate quality. Pooling of data was limited for congruence angle[57,58,63,64]; patella tilt angle[57,58,63,64]; sulcus angle[57,64] since studies either: did not provide adequate data[64]; it was unclear

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Table III
Quality assessment ratings using the Modified Down's and Blacks checklist

Study	Q1 (/1)	Q2 (/1)	Q3. (/1)	Q4. (/1)	Q5. (/2)	Q6. (/1)	Q7. (/1)	Q8. (/1)	Q9 (/1)	Q10. (/1)	Q11. (/1)	Q12. (/1)	Q13. (/1)	Q14. (/1)	Q15. (/1)	Q16. (/1)	Q17. (/1)	Total	% Score	
Aglietti *et al*., 1983	1	1	1	1	1	1	1	0	UTD	UTD	UTD	1	1	1	UTD	1	0	11	/18	**61.1**
Botanlioglu *et al*., 2013	1	1	1	1	1	1	1	1	UTD	UTD	UTD	1	1	UTD	UTD	1	0	11	/18	**61.1**
Bretcher & Powers, 2002	1	1	1	1	1	0	1	1	1	1	UTD	1	1	0	1	0	0	12	/18	**66.7**
Bretcher & Powers, 2002b																				
Callaghan & Oldham, 2004	1	1	1	1	2	1	1	1	1	1	UTD	1	1	1	1	1	1	17	/18	**94.4**
Chen & Powers, 2014	1	1	1	1	1	1	1	1	1	1	UTD	1	1	1	UTD	1	1	15	/18	**83.3**
Chen *et al*., 2012	1	1	1	1	1	1	1	1	1	1	UTD	1	1	1	UTD	0	0	13	/18	**72.2**
Chiu *et al*., 2012	1	1	1	1	1	1	1	1	UTD	UTD	1	1	1	1	1	0	0	13	/18	**72.2**
Connolly *et al*., 2009	1	1	1	1	1	1	1	0	1	1	UTD	1	1	1	1	1	0	14	/18	**77.8**
Draper *et al*., 2006	1	1	1	1	2	1	1	1	UTD	UTD	UTD	1	1	1	1	1	0	14	/18	**77.8**
Draper *et al*., 2009	1	1	1	1	2	1	1	1	1	1	UTD	1	1	1	1	1	0	16	/18	**88.9**
Eckhoff *et al*., 1994	1	1	1	1	0	0	1	0	0	0	UTD	UTD	1	1	UTD	0	0	7	/18	**38.9**
Farrokhi *et al*., 2011a	1	1	1	1	2	1	1	1	UTD	UTD	UTD	1	1	1	1	1	0	14	/18	**77.8**
Farrokhi *et al*., 2011b																			/18	
Felicio *et al*., 2011a	1	1	1	1	2	1	1	1	UTD	UTD	UTD	1	1	1	1	1	0	14	/18	**77.8**
Felicio *et al*., 2012b																			/18	
Felicio *et al*., 2014c																			/18	
Guzzanti *et al*., 1994	1	1	1	1	1	1	1	0	UTD	UTD	UTD	1	1	1	UTD	1	0	11	/18	**61.1**
Haim *et al*., 2006	1	1	1	1	2	1	1	1	1	1	0	1	1	1	1	1	0	16	/18	**88.9**
Harman *et al*., 2002	1	1	1	1	0	1	0	0	UTD	UTD	UTD	1	0	1	UTD	0	0	7	/18	**38.9**
Ho *et al*., 2014	1	1	1	1	2	1	1	1	UTD	UTD	UTD	1	1	1	1	1	0	14	/18	**77.8**
Ho *et al*., 2014b																				
Joensen *et al*., 2011	1	1	1	1	2	0	1	0	1	1	1	1	1	1	1	1	0	15	/18	**83.3**
Jones *et al*., 1995	1	1	1	1	0	1	1	0	UTD	UTD	UTD	1	1	UTD	1	0	0	9	/18	**50**
Kim *et al*., 2014	1	1	1	1	1	1	1	1	1	1	UTD	1	1	UTD	1	0	0	13	/18	**72.2**
Laprade & Culham, 2003	1	1	1	1	2	1	1	1	1	1	1	1	1	1	1	0	1	17	/18	**94.4**
Jan *et al*., 2009	1	1	1	1	2	1	1	1	1	1	0	1	1	1	0	1	1	16	/18	**88.9**
Metin Cubuk *et al*., 2000	1	1	1	1	1	1	1	0	UTD	UTD	UTD	1	1	UTD	UTD	0	0	9	/18	**50**
Muneta *et al*., 1994	1	1	1	1	1	1	1	0	UTD	UTD	UTD	1	1	1	UTD	0	0	10	/18	**55.6**
Pal *et al*., 2013c	1	1	1	1	2	1	1	1	1	1	UTD	1	1	1	1	1	1	17	/18	**94.4**
Pattyn *et al*., 2012a	1	1	1	1	2	1	1	1	1	1	1	1	1	1	1	1	0	17	/18	**94.4**
Pattyn *et al*., 2013c																				
Pinar, 1994	1	1	1	1	1	1	0	0	UTD	UTD	UTD	1	0	1	UTD	1	0	9	/18	**50**
Powers, 2000b	1	1	1	1	1	1	1	0	1	1	UTD	1	1	1	1	1	0	14	/18	**77.8**
Ribeiro *et al*., 2010	1	1	1	1	1	1	1	1	UTD	UTD	UTD	1	1	1	1	0	0	12	/18	**66.7**
Salsich & Perman, 2007	1	1	1	1	1	1	1	1	UTD	UTD	1	1	1	1	UTD	1	0	13	/18	**72.2**
Salsich & Perman, 2013	1	1	1	1	1	1	1	1	UTD	UTD	1	1	1	1	UTD	1	1	14	/18	**77.8**
Schoots *et al*., 2013	1	1	1	1	1	1	1	1	1	1	1	1	1	UTD	0	0	0	13	/18	**72.2**
Shultzer *et al*., 1986	1	1	1	1	1	1	0	0	UTD	UTD	UTD	0	1	UTD	UTD	0	0	7	/18	**38.9**
Souza *et al*., 2010	1	1	1	1	2	1	1	1	1	1	0	1	1	1	UTD	1	0	15	/18	**83.3**
Taskiran *et al*., 1998	1	1	1	1	1	1	1	0	UTD	UTD	UTD	1	1	1	UTD	1	0	11	/18	**61.1**
Teng *et al*., 2014	1	1	1	1	1	1	1	0	UTD	UTD	1	1	1	1	UTD	0	0	11	/18	**61.1**
Thuiller *et al*., 2013	1	1	1	1	1	1	1	1	1	1	UTD	1	1	1	0	0	1	14	/18	**77.8**
Tuncyurek *et al*., 2010	1	1	1	1	1	1	1	1	UTD	UTD	UTD	1	1	UTD	UTD	1	0	11	/18	**61.1**
Wilson *et al*., 2009	1	1	1	1	1	1	1	1	UTD	UTD	UTD	1	1	1	UTD	0	0	11	/18	**61.1**
Witzonzi & Goraj, 1999	1	1	1	1	1	1	1	0	UTD	UTD	UTD	1	1	UTD	UTD	1	0	10	/18	**55.6**
Studies scoring Yes	**40**	**40**	**40**	**40**	**50**	**37**	**37**	**25**	**17**	**17**	**7**	**38**	**38**	**31**	**18**	**24**	**7**			
Studies scoring Yes %	**100**	**100**	**100**	**100**	**62.3**	**92.5**	**92.5**	**62.5**	**42.5**	**42.5**	**17.5**	**95**	**95**	**77.5**	**45**	**60**	**17.5**			

UTD = Unable to detect; **Q1:** Is the hypothesis/aim/objective of the study clearly described?; **Q2:** Are the main outcomes to be measured clearly described in the Introduction or Methods section?; **Q3**: Are the characteristics of the patients included in the study clearly described?; **Q4**: Are the interventions of interest clearly described?; **Q5**: Are the distributions of principal confounders in each group to be compared clearly described?; **Q6**: Are the main findings of the study clearly described?; **Q7**: Does the study provide estimates of the random variability in the data for the main outcomes?; **Q8**: Have the actual probability values been reported (e.g., 0.035 rather than <0.05) for the main outcomes except where the probability value is less than 0.001: **Q9**: Were the subjects asked to participate in the study representative of the entire population from which they were recruited?; **Q10**: Were the subjects who were prepared to participate representative of the entire population from which they were recruited; **Q11**: Was an attempt to blind those measuring the main outcome?; **Q12**: If any of the results of the study were based on "data dredging" was this made clear?; **Q13**: Were the statistical tests used for the main outcomes appropriate?; **Q14**: Were the main outcome measures used accurate (valid and reliable)?; **Q15**: Were the case and controls recruited from the same population?; Q16: Was there adequate adjustment for confounding in the analyses from which the main findings were drawn?; **Q17**: Did the study have sufficient power to detect a clinically important effect?

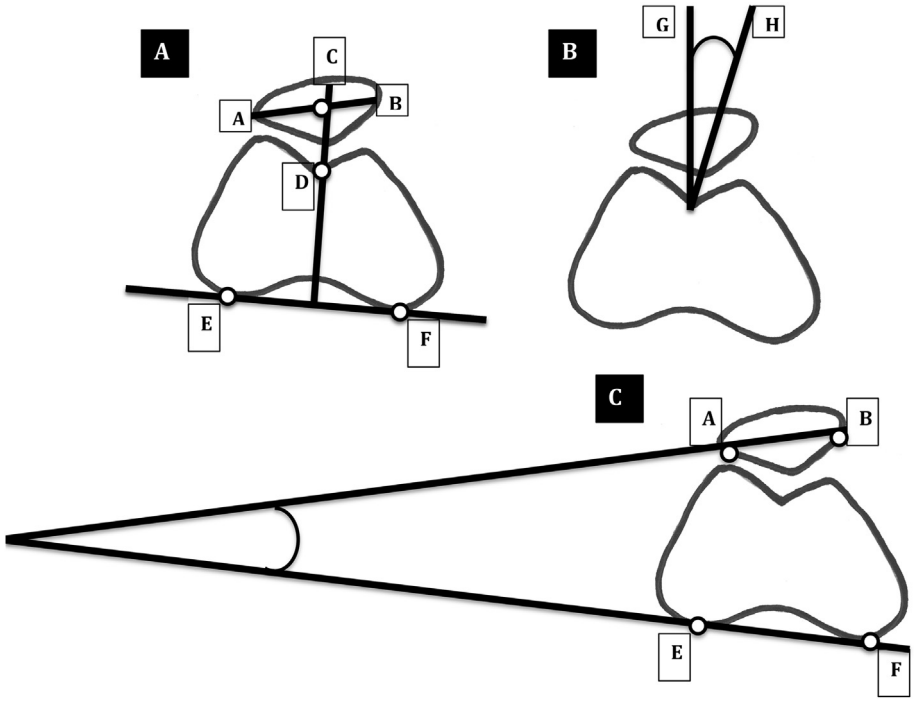

Fig. 2. Measurement of patella alignment. Line A to B forms the patella width. Line E to F forms a line along the most posterior femoral condyles. Point D is located at the deepest point of the trochlear groove. Point C is the bisecting point of the perpendicular line through the AB line. Line G bisects the sulcus angle to form a zero reference and line H is the projected from the apex of the sulcus angle through the most dorsal part of the patella. A) Bisect offset = (length of AC/length of BC) × 100%; B) Congruence angle = angle formed between G line and H line; C) Patella tilt = the angle formed by line between AB and EF[48].

whether their participants' knee was loaded or unloaded[63] or they adopted different measurement techniques for patella tilt angle[57]. Pooling was appropriate for congruence angle at 15° without load and congruence angle at 15° under load. Both features demonstrated a large SMD (1.24; 95% CI 0.37, 2.12; limited evidence)[57,58] and (1.40 95% CI: 0.04, 2.76; limited evidence)[57,58] (Fig. 3). For the data not amenable to pooling there is limited evidence to support a difference between PFP and a control group with regards to: congruence angle at 15° without load[58]; tibial tubercle rotation angle at 0° without load[59,60]; trochlear depth at 15° without load[57]. Conflicting evidence exists for patella tilt at 15° with load[57,58].

XR

XR features were assessed in five studies. Of these, three were judged as high quality[71,73,74] and two as moderate quality[60,72]. The following features were considered for meta-analysis: sulcus

Table IV
Results of the meta-analysis for all imaging feature amenable to pooling

Outcome or Subgroup	Studies	Participants	Statistical method	Effect estimate
1. MRI Patellofemoral contact area (mm^2)				
1.1 Patellofemoral Contact Area at 20° under load	2	71	Std. Mean Difference (IV, Fixed, 95% CI)	−0.53 [−1.01, −0.06]
2. MRI Patella tilt (°)				
2.1 Patella tilt at 0° under load	6	235	Std. Mean Difference (IV, Fixed, 95% CI)	0.63 [0.37, 0.90]
2.2 Patella tilt at 20° under load	4	143	Std. Mean Difference (IV, Fixed, 95% CI)	0.35 [0.02, 0.69]
2.3 Patella tilt at 30° without load	2	63	Std. Mean Difference (IV, Fixed, 95% CI)	0.25 [−0.24, 0.75]
2.3 Patella tilt at 45° under load	3	104	Std. Mean Difference (IV, Fixed, 95% CI)	0.14 [−0.25, 0.54]
2.4 Patella tilt at 0° under full weight bearing	2	66	Std. Mean Difference (IV, Fixed, 95% CI)	0.99 [0.47, 1.52]
3. MRI Bisect Offset (%)				
3.1 Bisect offset at 0° under load	6	235	Std. Mean Difference (IV, Random, 95% CI)	0.99 [0.49, 1.49]
3.2 Bisect offset at 20° under load	3	128	Std. Mean Difference (IV, Random, 95% CI)	0.73 [0.29, 1.17]
3.3 Bisect offset 40° under load	3	127	Std. Mean Difference (IV, Random, 95% CI)	0.61 [−0.09, 1.31]
3.4 Bisect offset at 45° under load	3	104	Std. Mean Difference (IV, Random, 95% CI)	0.39 [−0.13, 0.92]
3.5 Bisect offset at 60° under load	2	72	Std. Mean Difference (IV, Fixed, 95% CI)	0.50 [0.02, 0.98]
3.6 Bisect offset 0° under load	2	66	Std. Mean Difference (IV, Fixed, 95% CI)	1.91 [1.31, 2.52]
4. MRI T2 Relaxation times (ms)				
4.1 T2 Relaxation times at 0° without load	2	130	Std. Mean Difference (IV, Fixed, 95% CI)	−0.01 [−0.35, 0.34]
5. CT Congruence angle (°)				
5.1 Congruence angle at 15° under load	2	66	Std. Mean Difference (IV, Random, 95% CI)	1.40 [0.04, 2.76]
5.2 CT Congruence angle at 15° under load	2	66	Std. Mean Difference (IV, Random, 95% CI)	1.24 [0.37, 2.12]
6. MRI Sulcus angle (°)				
6.1 Sulcus angle at 0° under load	2	71	Std. Mean Difference (IV, Random, 95% CI)	0.44 [−0.17, 1.05]
6.2 Sulcus angle at 30° without load	2	63	Std. Mean Difference (IV, Random, 95% CI	0.43 [−0.48, 1.35]

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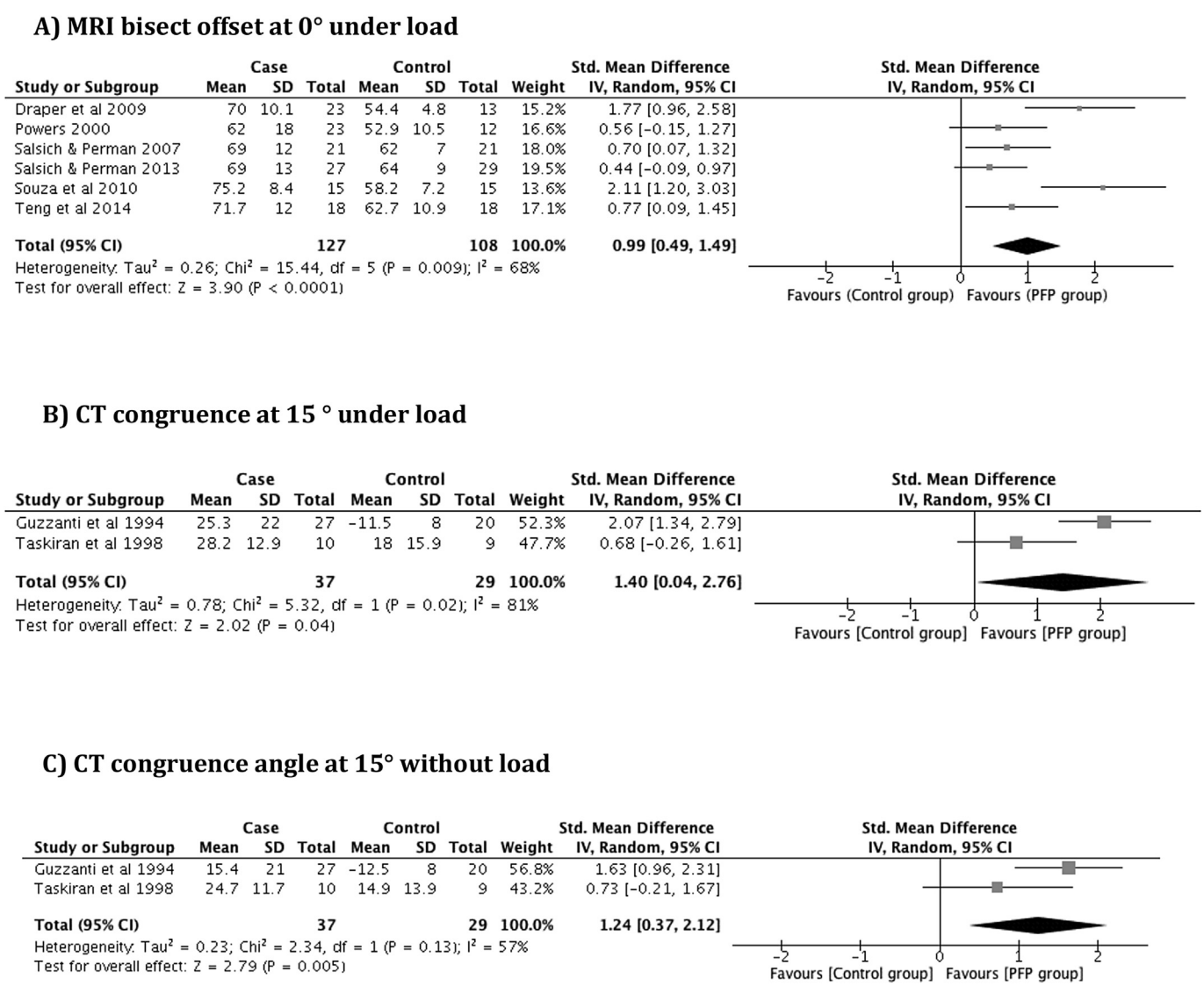

Fig. 3. Forest plots for: A) MRI bisect offset at 0° under load; B) CT congruence at 15° under load; C) CT congruence angle at 15° without load.

angle[71–73], congruence angle[71–73], Insall-Salvati index[72,73] and lateral patellofemoral angle[71,74]. It was not possible to pool data for any of these XR features however, due to variations in the knee flexion angle. For the data not amenable to pooling there was limited evidence to support a difference between PFP and a control group with regards to: congruence angle at 45° with load[72,74] but no evidence at 35°[71]. There was limited evidence to support sulcus angle at 45° without load[72,74] but no evidence to support it at 30°[73] and 35°[71]. There was conflicting evidence for Insall-Salvati index at 30° without load[60,72,73] and no evidence for lateral patellofemoral angle at 35°[71] and 45°[74] without load.

Sensitivity analysis

Two studies included in the meta-analysis[41,43] used a full weight-bearing procedure to load the PFJ during imaging. Analysing appropriate features under full weight bearing separately demonstrated a marked increase in the SMD (Fig. 4) of MRI patella bisect offset at 0° with load (1.91; 95% CI: 1.31, 2.52; limited evidence)[41,43] and MRI patella tilt at 0° with load (0.99; 95% CI: 0.47, 1.52; limited evidence)[41,43].

Discussion

The evidence from this review suggested that an increased MRI bisect offset at 0° knee flexion under load and CT-derived congruence angle at 15° knee flexion with and without load are both associated with PFP and there is a large SMD as determined from moderate and limited evidence respectively. A medium SMD was identified for the association between PFP and the following MRI features: patella tilt and patellofemoral contact area. Limited evidence existed to support the association of PFP with other features of MRI, US, CT and XR.

A previous comprehensive review by Lankhorst *et al.*[79] has provided insight into a broad range of factors associated with PFP (searched up to November 2010). We chose not to restrict inclusion by sample size to improve inclusivity[80] and together with inclusion of more recent studies, this resulted in over 70% of the current review studies being different from Lankhorst *et al.*[79]. Furthermore, by focusing only on imaging-detected features associated with pain, the present review controlled for variables such as imaging modality, knee flexion angle, and knee loading, known to influence the homogeneity of the imaging outcomes[81].

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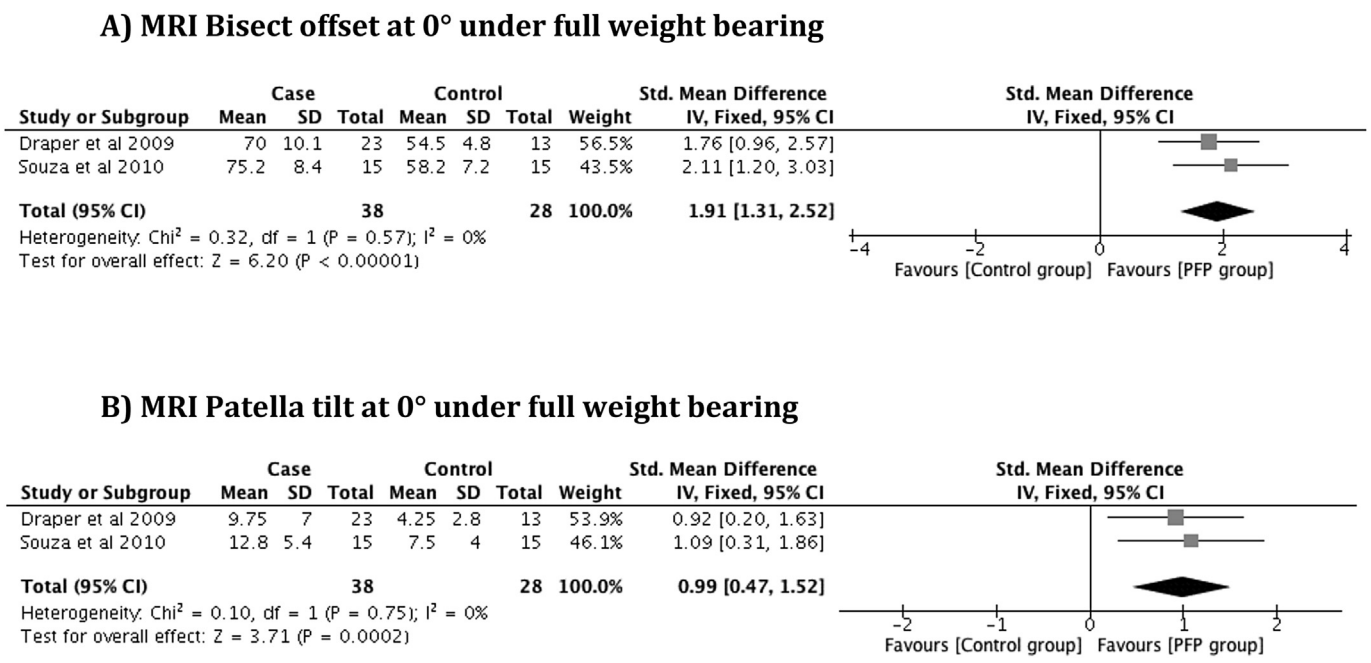

Fig. 4. Results of the sensitivity analyses for: A) MRI Bisect offset at 0° under full weight bearing; B) MRI patella tilt at 0° under full weight bearing.

Only MRI and CT features demonstrated sufficient homogeneity for appropriate meta-analysis. Bisect offset measured with MRI was most amenable to pooling across a variety of knee flexion angles demonstrating medium to large SMDs. This is notable as bisect offset has been shown to be the most significant feature in the progression of joint space narrowing over a five year period in adults with symptomatic knee pain aged 70–79 years[82]. Considerable clinical heterogeneity was present in the studies utilising XR and US. Studies using XR reported outcomes with subtle variations in knee flexion angle or assessment techniques that limited the pooling of data. The imaging features used in US were distinctly different and so offered no potential for pooling.

The present review considered loading of the knee as a dichotomous condition, as no consensus exists to the affect of the *quantity* of loading[83]. Our sensitivity analysis demonstrated an increase in SMD for both patella tilt and bisect offset when MR images were acquired under upright full weight bearing. This is in contrast to previous studies that have shown that bisect offset is more pronounced in the supine position when investigating people with PFP under both supine-loaded and upright full weight bearing conditions[76,84]. The reason for this disparity is unclear, however, it may be explained by the fact that the previous studies selected people with excessive patella lateralisation, whereas the studies included in the current review likely contained a range of patella alignments. Another possibility is that the control group in the current review demonstrated an average *reduction* in bisect offset under full weight bearing, which may also explain the increased SMD.

The concept of 'weight bearing' has been challenged by Harbaugh *et al.*[85] who suggest that quadriceps activity is the primary determinant of patella position in PFP rather than the axial loading. The full weight bearing studies in this review employed a 0.5T open, upright scanner and the field strength of 0.5 Tesla (T) may have affected image quality[86,87]. Full weight bearing conditions also have the potential to elicit pain during the procedure[88]. In PFP, pain is recognised as having an inhibitory affect on quadriceps[89]; altering quadriceps activity may influence the validity of the results by affecting patellar orientation[85].

This review identified a number of limitations in the literature based on participant selection. Firstly, a number of the included studies[30–36,41–43,45,46,52,53,60] used all female cohorts, and of these studies only a few selected a matched cohort. Controlling for gender, knee flexion angle and loading of the knee has been advocated because these factors have been reported to influence the PFJ mechanics and the comparisons made[81]. Furthermore, only half the studies clearly stated the recruitment source of participants e.g., hospital, military *etc*. Extrapolating results taken from a military or very physically active group and applying them to a more sedentary community dwelling population is likely to affect the external validity. Secondly, the quantification of pain in the PFP cohort was inconsistent. Over two thirds of the included studies selected participants based on reproducible pain with functional activities, however the number of provocative activities required for diagnosis and inclusion varied from one[49,53,59,64,73,74] to five[50,55,56]. The use of the VAS to quantify pain on provocation activities was used in six studies[30,31,42,43,47,51,53]. The duration of symptoms was also poorly reported, with fewer than a quarter of the included studies documenting the duration of PFP, and in these studies the data was presented differently (e.g., mean duration, range of duration). The duration of symptoms is important as this has been shown in PFP to be a predictor of poor long-term outcomes[5]. The effect of the duration of symptoms in relation to structural imaging findings is unknown. It is known however, that long term pain will lead to muscle inhibition[89] and thus there is a probability that a reduction quadriceps strength and activity could influence the PFJ structural features observed.

A number of limitations were identified in terms of the imaging assessment and outcomes. Fewer than a quarter of included studies clearly recorded who interpreted the images[37,38,44,47,50,51,53,67,71]. A person's level of experience interpreting imaging has been demonstrated to affect the accuracy of the analysis[90] and the level of confidence drawn from their findings. Furthermore, only a few studies documented whether the person analysing the images was blinded to group allocation. Blinding of allocation in this type of study design should be achievable[91] and lack of blinding raises the concern of confirmation bias[91]. The reliability of the imaging

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assessment was reported in fewer than half the included studies. Generally the ICCs showed a moderate to high reliability for the MRI variables: bisect offset, patella tilt angle, patellofemoral contact area, Insall-Salvati index and sulcus angle, supporting the use of these features in future studies.

The findings from a recent international expert consensus group highlight the need for sub-grouping of the PFP population[7]. The current review demonstrates a number of PFJ imaging features associated with PFP suggesting that these features should be considered as important components of future stratification. In addition, although most of the included studies employed a cross sectional analyses, two studies did employ an interventional pre-post study design[41,50]. These studies detected a significant change in patellofemoral contact area following strengthening exercise[50] and patellofemoral bisect offset and patella tilt following patella bracing[41]. As these imaging features have been shown to be modifiable it highlights the opportunity of using imaging features clinically as a treatment target.

Limitations of the current review

The nomenclature within the PFP literature is ambiguous, with the condition being referred to historically by a variety of other names[92]. In the present review, over 20% of the studies used terms differing from *patellofemoral pain* or *patellofemoral pain syndrome*. This makes study selection challenging with selection of the studies based on the description of the condition when more ambiguous terms are used. We attempted to minimise the potential bias in this process by using two reviewers to select studies and a third independent mediator. Secondly, the small sample sizes used in some of the included studies may influence the validity of the results. Meta-analyses was possible, however, for a number of imaging features thus increasing the overall sample size and improving statistical power[93]. Thirdly, the cross-sectional nature of the studies means the results from the current review cannot imply causality. To establish this, further research is warranted from prospective cohorts.

Conclusion

This systematic review with meta-analysis suggests that PFP is associated with MRI bisect offset and CT congruence angle analysed at 0° knee flexion and 15° knee flexion respectively; however, a degree of caution in interpretation of this data is advised due to the role of both features being derived from only moderate and limited evidence respectively. It is clear from this systematic review that future studies need to clearly document the specific population in which participants are recruited and to improve reporting of imaging-related issues. The inclusion of two interventional studies demonstrates that imaging features are potentially modifiable and future intervention strategies could be employed to target these features.

Contribution of authors

BD takes responsibility for the integrity of the work as a whole, from inception to the finished manuscript.

Conception & design: BD, AR, TS, PC.

Collection & Assembly of Data: BD, FP, TS.

Analysis &Interpretation of the data: BD, AR, FP, TS, PC.

Drafting & final approval of the manuscript: BD, AR, FP, TS, PC.

Conflicts of interest

No conflict of interest were declared.

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Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.joca.2015.09.004.

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