EXTENDED REPORT

Development of radiographic changes of osteoarthritis in the "Chingford knee" reflects progression of disease or non-standardised positioning of the joint rather than incident disease

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Objective: To ascertain the extent to which the "Chingford knee" (that is, contralateral knee of the middle aged, obese, female patient with unilateral knee osteoarthritis (OA)) is a high risk radiographically normal joint as opposed to a knee in which radiographic changes of OA would have been apparent in a more extensive radiographic examination.

Methods: Subjects were 180 obese women, aged 45–64 years, with unilateral knee OA, based on the standing anteroposterior (AP) view. Subjects underwent a series of radiographic knee examinations: semiflexed AP, supine lateral, and Hughston (patellofemoral (PF)) views. Bony changes of OA were graded by consensus of two readers. Medial tibiofemoral joint space width was measured by digital image analysis. Knee pain was assessed by the WOMAC OA Index after washout of all OA pain drugs.

Results: Despite the absence of evidence of knee OA in the standing AP radiograph, only 32 knees (18%) were radiographically normal in all other views. Ninety four knees (52%) exhibited TF knee OA in the semiflexed AP and/or lateral view. PF OA was seen in 121 knees (67%). Subjects with PF OA reported more severe knee pain than those without PF OA (mean WOMAC scores 9.9 v 8.3, $p < 0.05$).

Conclusion: The Chingford knee is not a radiographically normal joint. The high rate of incidence of OA reported previously for this knee (~50% within two years) may also reflect progression of existing OA or changes in radioanatomical positioning at follow up that showed evidence of stable disease that was present at baseline.

The goals of medical management of patients with osteoarthritis (OA) are symptomatic relief and preservation of function.^{1,2} However, the recent identification of potential disease modifying OA drugs (DMOADs) that may retard, if not halt, the breakdown of articular cartilage in OA^{3,4} has fostered interest in the characterisation of study populations at high risk for incident or progressive changes of OA for inclusion in clinical trials.

Unfortunately, because OA develops and progresses very slowly, primary or secondary prevention of OA is difficult to demonstrate. Epidemiological studies of knee OA have shown that incident and progressive radiographic changes occur at a rate of only 1–2% per year.⁵ Known risk factors for knee OA (for example, age, female sex, obesity) which if incorporated into the eligibility criteria for a DMOAD trial could shorten the time required to detect a significant DMOAD effect, increase the odds of developing radiographic changes of OA only two- to fivefold.⁵ It is, therefore, important that Spector *et al* have described subjects at extremely high risk for development of incident knee OA.⁶ In the Chingford Health Study, among women aged 45–64 who were in the upper tertile for body mass index (BMI) and had unilateral knee OA at baseline, within two years 47% developed incident changes of OA in the contralateral knee, in which radiographic evidence of OA was absent at baseline.

It is important to note that the radiographic outcome data in the Chingford Study were derived from the conventional weightbearing anteroposterior (AP) radiograph of both knees in full extension. More recently, it has been shown that reproducible positioning standards for the conventional standing AP view cannot be achieved, and often exaggerate, true radiographic changes of OA.⁸ Therefore, the extent to

which the frequency of "incident" radiographic changes of OA in the Chingford cohort reflects true incidence, as opposed to progressive changes or merely the presence of disease that was not apparent at baseline in a single non-standardised knee examination, is unknown. To evaluate the accuracy of the definition of the "Chingford knee" as a normal knee at high risk for imminent radiographic changes of OA, we identified a sample of women who fit the risk profile described by Spector *et al*⁶ and performed a series of radiographic examinations of the tibiofemoral (TF) and patellofemoral (PF) joints of the index (OA) and contralateral (non-OA) knee. This study provides a comprehensive evaluation of radiographic OA in the apparently disease-free contralateral knee and examines the significance of the radiographic findings with respect to knee pain.

METHODS

The procedures, radiation exposure, other research risks, and associated safeguards for this study were approved by the Radiation Safety Committee and the Institutional Review Board of Indiana University–Purdue University Indianapolis.

Subjects

Subjects in this study were 180 obese women, aged 45–64, who had unilateral knee OA, based on American College of

Abbreviations: AP, anteroposterior; BMI, body mass index; DMOADs, disease modifying osteoarthritis drugs; JSW, joint space width; K&L, Kellgren and Lawrence; OA, osteoarthritis; PF, patellofemoral; TF, tibiofemoral

Rheumatology criteria for the diagnosis of knee OA.⁹ The eligibility criterion for radiographic evidence of knee OA required Kellgren and Lawrence (K&L) grade 2 or 3 severity for one knee and grade 0 or 1 for the contralateral knee in a weightbearing AP view of both knees in full extension (single cassette).¹⁰ All subjects were in the upper tertile of the age, race, and sex appropriate norms for BMI established by the Second National Health and Nutrition Examination Survey.¹¹

Radiography

Each qualified subject underwent an additional series of radiographic examinations that included a standardised, fluoroscopically assisted AP view of each knee, obtained in the degree of flexion required to align the medial tibial plateau and central ray of the x ray beam (that is, 7–10°)¹²; a supine lateral view of each knee in 45° of flexion; and a Hughston view of both PF joints (subject prone, knees flexed to 55°; x ray beam angle adjusted to 45° relative to the tabletop).¹³

Measurement of medial tibiofemoral JSW

Minimum joint space width (JSW) in the medial TF compartment of the semiflexed AP view was measured using specialised edge detection software (xJSW) developed by Lynch *et al.*¹⁴ Input for the program is a digitised radiographic image of the TF joint (semiflexed AP view). Radiographs were converted to digitised images using a Lumiscan 75 laser film digitiser (Lumisys, Inc; Sunnyvale, CA), which can scan 14"×17" films at 2000×2500 pixels with a 100 µm focal spot. All JSW measurements were corrected for magnification, as reflected by the projected image of a magnification marker (6.35 mm chrome steel ball encased in methyl methacrylate) affixed with tape to the skin over the head of the fibula.

Measurement of bony features of knee OA

In addition to K&L grading of overall OA severity for the extended view of each knee, joint space narrowing and the severity of abnormalities of individual bony features of OA (that is, osteophytes, sclerosis, cysts) in the medial and lateral compartments of the TF joint (semiflexed AP) and PF joint (lateral and Hughston views) were graded separately, using standardised atlases.^{15–16} Each feature was rated on a scale of 0 (absent) to 3 (highly advanced), according to the consensus of two readers (CG, SAM) with adjudication, as needed, by a third reader (KDB). Adjudication of ratings of isolated individual radiographic features of OA was required in <1% of subjects.

Statistical analysis

Each knee was classified as exhibiting radiographic evidence of TF knee OA based on the presence or absence of definite osteophytes at the medial or lateral margin of the joint space in the semiflexed AP view (fig 1) or at the posterior margin of the tibia in the lateral view. Knees were classified as exhibiting PF OA if a definite (that is, grade 1 or larger) osteophyte was observed at the medial or lateral margins of the PF compartment in the Hughston view.¹⁵ In the lateral view, only grade 2 or 3 osteophytes at the superior and inferior poles of the posterior aspect of the patella were taken as evidence of PF OA (fig 2).¹⁶ Small (grade 1) osteophytes in the lateral view were not accepted as evidence of PF OA, nor were spurs on the anterior aspect of the patella, which were considered to reflect enthesopathy.

Contralateral knees were divided into four groups, based on radiographic evidence of OA: no OA, isolated PF OA, isolated TF OA, and concomitant PF and TF OA. As appropriate, χ^2 tests and two way analyses of variance were used to compare age, race, BMI, overall radiographic severity (K&L grade), minimum medial JSW, and WOMAC pain score

in subjects comprising the TF/PF OA subgroups. In addition, paired *t* tests were used to compare the JSW and WOMAC pain scores in the index and contralateral knees.

RESULTS

Table 1 shows the demographic and clinical characteristics of the subjects. Based on the standing AP view, 61% of the index knees exhibited grade 2 OA severity, by K&L criteria;¹⁰ the remainder were grade 3. The contralateral knees exhibited grade 0 and grade 1 OA severity in almost even proportions (52% and 48%, respectively). Mean JSW in the index knee (semiflexed AP view) was significantly smaller than that in the contralateral knee (3.7 mm *v* 4.0 mm, *p*<0.01). Subjects reported significantly greater pain in the index knee than in the contralateral knee (mean WOMAC pain score 11.3 *v* 9.4, *p*<0.0001).

Tibiofemoral osteophytes

Among the 180 contralateral knees, in which by definition a definite TF osteophyte was not seen in the standing AP view, only 98 (54%) were normal also in the semiflexed AP view (table 2); 82 contralateral knees (46%) exhibited definite marginal TF osteophytes that were not apparent when the knees were imaged in full extension (fig 1). Contralateral knees with grade 1 OA by K&L criteria, based on the standing AP view, were twice as likely to exhibit a marginal osteophyte in the semiflexed AP radiograph as those judged to be K&L grade 0. In addition, 31 contralateral knees (17%) were observed to have a definite osteophyte at the posterior tibia. In 12 of these knees the posterior tibial osteophyte was the only radiographic abnormality, thus increasing to 52% the overall percentage of contralateral knees with radiographic evidence of TF knee OA (table 2).

As a basis for comparison of radiographic findings in the contralateral knee, it is important to note that among the 180 index knees in which, by definition, definite TF osteophytes were present in the standing AP view, only 146 (81%) also showed marginal TF osteophytes in the semiflexed AP view (table 2). Lateral radiographs revealed posterior tibial osteophytes in 38 index knees (21%), but in only one case was a posterior TF osteophyte seen in an index knee in which marginal osteophytes were not seen in the AP view. Overall, only 82% of index knees were confirmed to have definite TF OA in the semiflexed AP or lateral views.

Patellofemoral osteophytes

The clinical significance of a grade 1 osteophyte at the superior or inferior pole of the posterior aspect of the patella (fig 2) is unknown. Therefore, before including such a finding in a definition of PF OA, we identified nine contralateral knees in which a grade 1 superior/inferior patellar osteophyte was the sole radiographic abnormality in any of the three radiographs of the PF or TF joints. Severity of knee pain in this subset of knees was not significantly different from that in 23 "pristine" contralateral knees, in which no abnormalities were found in any of the three radiographic views (mean WOMAC pain score 8.4 *v* 8.1, *p*=0.84). Therefore, only grade 2–3 patellar osteophytes seen in the lateral view were taken as radiographic evidence of PF knee OA.

As shown in table 2, definite osteophytes at the medial and/or lateral poles of the PF joint in the Hughston view were found in 67% of contralateral knees and 75% of index knees. In addition, lateral views revealed definite (grade 2–3) PF osteophytes in 12% of the contralateral knees and 24% of the index knees. Radiographic changes in the two PF views were largely overlapping. In all, 66% of contralateral knees and 79% of index knees were classified as having PF OA, based on evidence in either radiograph (table 2).

Figure 1 Contralateral knee in which no evidence of marginal osteophytes was apparent in the standing AP view (A). Note the large marginal osteophyte (arrow) and advanced joint space narrowing in the concurrent semiflexed AP view of the same knee (B).

Subchondral sclerosis and cysts

Readings of semiflexed AP and lateral radiographs of the contralateral knees yielded 14 knees (8%) with moderate (grade 2) subchondral sclerosis of the tibia. Ten of these 14 knees (71%) also exhibited definite TF osteophytes. In addition, three knees exhibited radiographic evidence of a subchondral cyst (two of which also had definite TF osteophytes).

Patellar subchondral sclerosis was seen in the Hughston or lateral view of 12 contralateral knees—11 of which (92%) also exhibited definite PF osteophytes. Four other knees had radiographic evidence of subchondral cysts (two grade 1, two grade 2). Osteophytes were found in the PF compartments of only two of these knees. Subchondral sclerosis and subchondral cysts did not coexist in any of the contralateral knees.

JSW and knee pain

Analyses of the effects of radiographic changes of OA on medial TF JSW and knee pain were based on the categorisation of 180 contralateral knees into four subgroups: 32 with

no radiographic evidence of knee OA, 54 with only PF OA, 27 with only TF OA, and 67 with both PF and TF OA (table 3). The subgroups did not differ in age, race, or BMI. Contralateral knees with definite TF osteophytes seen in the semiflexed AP or lateral view were significantly more likely than knees without TF OA to have exhibited grade 1 (doubtful) OA by K&L criteria in the standing AP view (67% v 28%, $p < 0.0001$).

Two way ANOVA showed no significant differences in JSW in the contralateral knee between the subgroups. However, ANOVA of WOMAC pain scores showed that subjects with radiographic evidence of PF OA in the contralateral knee (with or without TF OA) had significantly greater knee pain than those with no evidence of PF knee OA (mean WOMAC score 9.9 v 8.3, $p = 0.03$). Neither the effect of TF OA nor the interaction of PF and TF OA on WOMAC pain scores was significant.

Parallel analyses of JSW and knee pain in the index knee were not performed because of the greater prevalence of radiographic changes of OA in the index knees than in the contralateral knee, and the resulting inequality in the sizes of

Figure 2 Grade 1 osteophytosis (arrow) at the superior or inferior pole of the posterior aspect of the patella (A) was not associated with increased severity of pain in the contralateral knee, in comparison with that in subjects in whom the contralateral knee was radiographically normal in all views. In contrast, subjects in whom the contralateral knee exhibited grade 2 or more patellar osteophytosis (B, arrow) reported significantly greater knee pain than subjects who did not have PF OA.

Table 1 Characteristics of subjects

Number of subjects	180
Age (years), mean (SD)	55.3 (5.7)
Race, % white	83
Body mass index (BMI) (kg/m ²), mean (SD)	36.2 (6.1)
Overall severity of tibiofemoral OA, index knee*	
Kellgren and Lawrence grade 2 (%)	61
Kellgren and Lawrence grade 3 (%)	39
Overall severity of tibiofemoral OA, contralateral knee*	
Kellgren and Lawrence grade 0 (%)	52
Kellgren and Lawrence grade 1 (%)	48
Minimum medial tibiofemoral joint space width (mm)†	
Index knee, mean (SD)	3.7 (1.3)
Contralateral knee, mean (SD)	4.0 (0.9)
WOMAC pain score, range: 5–25	
Index knee, mean (SD)	11.3 (4.5)
Contralateral knee, mean (SD)	9.4 (4.3)
WOMAC function score, range 17–85, mean (SD)†	39.9 (13.7)

*Standing AP view; †semiflexed AP view.

the TF/PF OA subgroups: 10 with no radiographic evidence of knee OA, 23 with only PF OA only, 28 with only TF OA, and 119 with both PF and TF OA.

DISCUSSION

Idiopathic knee OA is a bilateral disease.⁷ It stands to reason, therefore, that in people with the cardinal risk factors for knee OA (female sex, middle age, obesity) to observe radiographic changes of OA in only one knee is to detect a temporary state that occurs before the development of bilateral knee OA. In the Chingford population study, Spector *et al* found that 47% of obese, middle aged women with unilateral knee OA at baseline exhibited bilateral knee OA two years later.⁶ However, designation of the contralateral knee in that study was based on the absence of radiographic changes of OA (specifically, definite marginal TF osteophytes) only in the conventional standing AP radiograph. As we have demonstrated previously, the lack of positioning standards for the standing AP examination frequently results

Table 3 Medial tibiofemoral joint space width (JSW) and knee pain in contralateral knees with and without radiographic evidence of tibiofemoral (TF) and/or patellofemoral (PF) osteoarthritis (OA)

	No OA (n = 32)	Only PF OA (n = 54)	Only TF OA (n = 27)	TF and PF OA (n = 67)
Minimum JSW (mm)*	4.0 (0.7)	4.1 (0.8)	3.8 (0.9)	4.0 (1.0)
WOMAC pain score†	8.2 (3.7)	9.5 (4.7)	8.4 (4.1)	10.3 (4.2)

Results are shown as mean (SD).

*Two way analysis of variance of JSW found no significant effects: PF OA (p=0.35), TF OA (p=0.16), and PF×TF OA interaction (p=0.75); †two way ANOVA of WOMAC pain scores found a significant effect only for PF OA: PF OA (p=0.03), TF OA (p=0.48), and PF×TF OA interaction (p=0.69).

in changes in the flexion and rotation of the knee in serial examinations.⁸ These unintended changes in joint positioning may alter the radiographic profile of marginal TF osteophytes in ways that can suggest the development, progression, regression, or even disappearance, of knee OA.

A knee that is truly at high risk for the development of OA offers a distinct advantage for the study of biomarkers of OA progression or of structure modifying drugs with as few subjects and/or in as short a time as possible. Furthermore, the risk factors for incident OA may differ from those for progression of established OA. It is important, therefore, to ascertain whether the so-called “Chingford knee” is, indeed, a high risk joint that is free of OA at baseline. Based on a thorough radiographic evaluation of subjects fitting the risk profile identified by Spector *et al*,⁶ we found definite TF knee OA that was not apparent in the conventional standing AP radiograph in 52% of contralateral knees. However, mean JSW in the medial compartment of knees exhibiting radiographic evidence of TF OA was not significantly different from that in knees in which no evidence of TF OA was apparent.

Table 2 Presence and severity of osteophytes in the tibiofemoral and patellofemoral compartments of index and contralateral knees

Location of osteophyte(s)	Radiographic view	x Ray severity*	No (%) of knees (n = 180)†	
			Contralateral	Index
Tibiofemoral compartment Medial/lateral margins	Semiflexed AP	0	98 (54)	34 (19)
		1	73 (41)	96 (53)
		2	8 (4)	47 (26)
		3	1 (1)	3 (2)
Posterior tibia	Lateral	0	149 (83)	142 (79)
		1	19 (11)	12 (7)
		2	5 (3)	17 (9)
		3	7 (4)	9 (5)
Any TF location	Either view	≥1	94 (52)	147 (82)
Patellofemoral compartment Medial/lateral margins	Hughston	0	62 (34)	45 (25)
		1	77 (43)	72 (40)
		2	35 (19)	57 (32)
		3	6 (3)	6 (3)
Superior/inferior poles	Lateral	0	68 (38)	48 (27)
		1	90 (50)	88 (49)
		2	22 (12)	42 (23)
		3	0 (0)	2 (1)
Any PF location	Either view	≥1‡	121 (67)	142 (79)
Any TF or PF location	Any view	≥1‡	148 (82)	170 (94)

*Most severe grade of OA severity, based on standardised pictorial atlases^{15 16}; †total of percentages may not add to 100% because of rounding off error; ‡in the absence of a definite osteophyte elsewhere in the PF joint, a grade 1 osteophyte on the superior or inferior pole of the posterior aspect of the patella¹⁶ was not accepted as evidence of definite OA. Spurs at the superior or inferior pole of the anterior patella were considered to reflect enthesopathy rather than osteophytosis.

In addition, radiographic evidence of PF knee OA was found in 67% of contralateral knees. The prevalence of PF OA in the present sample was higher than that reported in studies of other cohorts.^{18–22} This finding may be due, in part, to the high risk profile of our sample (middle aged, obese women with unilateral knee OA), as well as to our use of lateral and skyline radiographs to characterise PF OA—a more extensive series of radiographic examinations of the PF joint than in most previous studies.^{19–22} PF OA in the contralateral knee was unrelated to TF JSW. However, contralateral knees with radiographic evidence of PF OA were significantly more painful than those without PF OA. This finding is consistent with previous studies of symptomatic knee OA.^{18–20}

From these data we conclude that the risk profile described by Spector *et al*⁶ does not predict the imminent onset of knee OA. The percentage of contralateral knees in our study in which TF OA was not apparent in the conventional standing AP view—but was identified when knees were flexed and rotated under fluoroscopy into a standardised position according to the protocol for the semiflexed AP view¹²—was similar to the two year OA incidence rate for contralateral knees reported by Spector *et al*⁶ (46% and 47%, respectively). Furthermore, whereas incident OA in the Chingford study was more common among knees with grade 1 (doubtful) OA at baseline, grade 1 OA knees in the present study were significantly more likely than grade 0 knees to exhibit definite TF OA in concurrently obtained alternative radiographic views. Although the radiographic changes found in the Chingford study⁶ may, in some cases, have been evidence of incident OA, they may also have represented progression of established disease that was not identified in the baseline standing AP radiograph. More important, some of the changes observed by Spector *et al*⁶ may reflect neither the incidence nor the progression of knee OA, but the failure of the conventional weightbearing AP examination of the knee in full extension to standardise the flexion and rotation of the joint in serial radiographic examinations.

The fact that the Chingford knee frequently has existing OA at baseline does not necessarily diminish its value for studies of knee OA. A clinically defined risk profile may be more easily implemented in clinical trials than other test based approaches to identifying the high risk knee, such as bone scintigraphy,²³ bone marrow oedema²⁴ and surrogate biomarkers of articular cartilage degeneration in serum or urine.^{25–26} If the combination of risk factors represented in the Chingford profile identifies knees with a higher annual rate of radiographic change, whether incident or progressive OA, than knees that do not fit the profile, these risk factors will serve as useful eligibility criteria for clinical trials of DMOADs. It will be important, however, to ascertain in serial examinations the extent to which radiographic changes seen at follow up represent new or progressive disease, as opposed to pre-existing disease that was simply not apparent at baseline.

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REFERENCES

- Hochberg MC, Altman RD, Brandt KD, Clark BM, Dieppe PA, Griffin MR, *et al*. Guidelines for the medical management of osteoarthritis. Part II. Osteoarthritis of the knee. *Arthritis Rheum* 1995;**38**:1541–6.
- Altman RD, Hochberg MC, Moskowitz RW, Schnitzer TJ. Recommendations for the medical management of osteoarthritis of the hip and knee. *Arthritis Rheum* 2000;**43**:1905–15.
- Smith G Jr, Yu L Jr, Brandt K, Capello W. Oral administration of doxycycline reduces collagenase and gelatinase activities in extracts of human osteoarthritic cartilage. *J Rheumatol* 1998;**25**:532–5.
- Dougados M, Nguyen M, Berdahl L, Mazieres B, Vignon E, Lequesne M, for the ECHODIAH Investigators Study Group. Evaluation of the structure modifying effects of diacerhein in hip osteoarthritis. *Arthritis Rheum* 2001;**44**:2539–47.
- Felson DT. Epidemiology of osteoarthritis. In: Brandt KD, Doherty M, Lohmander LS, eds. *Osteoarthritis*. Oxford: Oxford University Press., 1998:13–22.
- Spector TD, Hart DJ, Doyle DV. Incidence and progression of osteoarthritis in women with unilateral knee disease in the general population: the effect of obesity. *Ann Rheum Dis* 1994;**53**:565–8.
- Davis MA, Ettinger WH, Neuhaus JM, Cho SA, Hauck WW. The association of knee injury and obesity with unilateral and bilateral osteoarthritis of the knee. *Am J Epidemiol* 1989;**130**:278–88.
- Mazzuca SA, Brandt KD, Dieppe PA, Doherty M, Katz BP, Lane KA. Effect of alignment of the medial tibial plateau and x ray beam on apparent progression of osteoarthritis in the standing anteroposterior knee radiograph. *Arthritis Rheum* 2001;**44**:1786–94.
- Altman R, Asche E, Bloch D, Bole G, Borenstein D, Brandt K, *et al*. Development of criteria for the classification and reporting of osteoarthritis: classification of osteoarthritis of the knee *Arthritis Rheum* 1986;**29**:1039–49.
- Kellgren JH, Lawrence JS. Radiographic assessment of osteoarthritis. *Ann Rheum Dis* 1956;**16**:494–502.
- DHSS. National Health and Nutrition Examination Survey II. Vital and health statistics arthropometric reference data and prevalence of overweight. 1987:21–2, (DHHS publication PHS 87–1688).
- Buckland-Wright C. Protocols for precise radio-anatomical positioning of the tibiofemoral and patellofemoral compartments of the knee. *Osteoarthritis Cart* 1995;**3**(suppl A):71–80.
- Carson WG Jr, James SL, Larson RL, Singer KM, Winternitz WW. Patellofemoral disorders: physical and radiographic evaluation. Part II: Radiographic examination *Clin Orthop* 1984;**185**:178–86.
- Lynch JA, Buckland-Wright JC, Macfarlane DG. Precision of joint space width measurement in knee osteoarthritis from digital analysis of high definition macroradiographs. *Osteoarthritis Cart* 1993;**1**:209–18.
- Altman RD, Hochberg M, Murphy WA Jr, Wolfe F, Lequesne M. Atlas of individual radiographic features in osteoarthritis. *Osteoarthritis Cart* 1995;**3**(suppl A):3–70.
- Burnett S, Hart DJ, Cooper C, Spector TD. A radiographic atlas of osteoarthritis. London: Springer, 1994.
- Bellamy N, Buchanan WW, Goldsmith CH, Campbell J, Stitt LW. Validation study of WOMAC: a health status instrument for measuring clinically important patient relevant outcomes to antirheumatic drug therapy in patients with osteoarthritis of the hip or knee. *J Rheumatol* 1988;**15**:1833–40.
- Ciuttini FM, Baker J, Hart DJ, Spector TD. Association of pain and radiological changes in different compartments and views of the knee joint. *Osteoarthritis Cart* 1996;**4**:143–7.
- Ciuttini FM, Spector TD, Baker J. Risk factors for osteoarthritis in the tibiofemoral and patellofemoral joints of the knee. *J Rheumatol* 1997;**24**:1164–7.
- Lanyon P, O'Reilly S, Jones A, Doherty M. Radiographic assessment of symptomatic knee osteoarthritis in the community: definitions and normal joint space. *Ann Rheum Dis* 1998;**57**:595–601.
- Elahi S, Felson DT, Engelman L, Sharma L. The association between varus-valgus alignment and patellofemoral osteoarthritis. *Arthritis Rheum* 2000;**43**:1874–80.
- Nagoosa Y, Lanyon P, Doherty M. Characterisation of the size and direction of osteophyte in knee osteoarthritis: a radiographic study. *Ann Rheum Dis* 2002;**61**:319–24.
- Dieppe P, Cusnahan J, Young P, Kirwan J. Prediction of the progression of joint space narrowing in osteoarthritis of the knee with bone scintigraphy. *Ann Rheum Dis* 1993;**52**:557–63.
- Link TM, Steinbach LS, Ghosh S, Ries M, Lu Y, Lane N, *et al*. Osteoarthritis: MR imaging findings in different stages of disease and correlation with clinical findings. *Radiology* 2003;**226**:373–81.
- Sharif M, Saxne L, Shepstone L, Kirwan JR, Elson CJ, Heingard D, *et al*. Relationship between serum cartilage oligomeric matrix protein levels and disease progression in osteoarthritis on the knee joint. *Br J Rheumatol* 1995;**34**:306–10.
- Sharif M, George E, Shepstone L, Knudson W, Thonar EJ-MA, Cusnahan J, *et al*. Serum hyaluronic acid level as a predictor of disease progression in osteoarthritis of the knee. *Arthritis Rheum* 1995;**38**:760–7.