EXTENDED REPORT

Risk factors for early radiographic changes of tibiofemoral osteoarthritis

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Objective: To evaluate the risk factors for early radiographic changes of knee osteoarthritis.

Methods: Subjects (n=114) with unilateral or bilateral grade 0–1 knee osteoarthritis underwent x ray examination of the knees (semiflexed anteroposterior view) and assessment with the Western Ontario and McMaster Universities (WOMAC) Osteoarthritis Index at baseline and 30 months later. Severity of joint space narrowing (JSN) and osteophytosis were graded in randomly ordered serial radiographs by two readers, blinded to the sequence of the films, using standard pictorial atlases.

Results: The odds of an initial appearance of radiographic features of knee osteoarthritis at month 30 were more than threefold greater in African Americans than in whites (osteophytosis: odds ratio (OR) 3.30, 95% confidence interval (CI) 1.04 to 10.54; JSN: OR 3.49, 95% CI 1.16 to 10.68). In addition, the appearance of osteophytosis was positively related to baseline stiffness (OR 1.91/2.1 points on the 2–10 WOMAC scale, 95% CI 1.29 to 2.82).

Conclusions: The distinction between incident and established, but early, radiographic knee osteoarthritis is difficult because of the limits to which all possible evidence of the disease can be ruled out in a conventional baseline knee radiograph. Nonetheless, our finding that African Americans were at greater risk of early osteophytosis and JSN than other subjects differs from the results of our previous analysis of risk factors for progressive knee osteoarthritis in the same subjects. The development of osteophytes also was associated with joint stiffness. Future investigations should focus on the systemic and local influences that these ostensible risk factors represent.

Osteoarthritis is the most common specific joint disease of humans. Moderate to severe osteoarthritis affects >22 million American adults between the ages of 25 and 74 years¹: >12% of the population in this age range.² Knee osteoarthritis is the most common cause of chronic disability in elderly people,^{3–5} and the most frequent indication for knee arthroplasty.⁶

Our understanding of the importance of accepted risk factors for the incidence and progression of radiographic tibiofemoral osteoarthritis (eg, age, sex, obesity and trauma^{7–11}) has been shaped by the historical reliance on the conventional standing anteroposterior knee radiograph,¹² on which ratings of the severity of radiographic changes of knee osteoarthritis by Kellgren and Lawrence (K&L) criteria¹³ are commonly based. The criterion for a diagnosis of radiographic knee osteoarthritis (ie, a change from grade 0 or 1 to grade 2 osteoarthritis by K&L criteria) requires the development of a definite marginal tibiofemoral osteophyte, whereas progression to more severe knee osteoarthritis (ie, from K&L grade 2 to grade 3 to grade 4) is generally based on the evidence of radiographic joint space narrowing (JSN)—the surrogate for thinning of articular cartilage. However, tibiofemoral osteophytes alone may not signify knee osteoarthritis; the results of a longitudinal radiographic study of adults in Sweden found that two thirds of knees with tibiofemoral or patellofemoral osteophytes at baseline did not exhibit further structural or clinical evidence of osteoarthritis in the subsequent 11–16 years.^{14–15} Moreover, as the standing anteroposterior radiograph is limited in its capacity to detect subtle changes in joint space width (JSW),¹⁶ the extent to which our current understanding of what constitutes early-stage versus late-stage radiographic knee osteoarthritis representing the natural history of the disease, rather than limitations in radiographic imaging of the joint, is

unknown. This may explain why observed risk factors for incident knee osteoarthritis (ie, osteophytosis) tend not to serve as useful risk factors for progressive knee osteoarthritis (JSN).^{17–18}

The conventional wisdom on the natural history of knee osteoarthritis has been challenged by the results of recent studies in which longitudinal changes in the radiographic features of the disease were monitored using the semiflexed anteroposterior view¹⁹—a protocol that uses fluoroscopy to standardise the radioanatomical positioning of the knee in serial examinations. The key to positioning with this protocol is flexion of the knee to superimpose (1 mm) the anterior and posterior margins of the medial tibial plateau—a reproducible radioanatomical marker of parallel alignment of the medial tibial plateau—and a central x ray beam that facilitates the precise measurement of JSW.^{19–22}

Mazzuca *et al*²³ have shown that approximately 50% of knees fitting the profile for a high risk of incident osteoarthritis in the Chingford Health Study²⁴ (ie, the contralateral knee of obese, middle-aged women with unilateral radiographic knee osteoarthritis in the standing anteroposterior view) showed definite osteophytes at baseline after standardised flexion and rotation of the knee under fluoroscopy or in the lateral view. Further evidence that the so-called “Chingford knee” is not a normal joint at high risk for incident osteoarthritis is provided by the markedly greater uptake of a bone-seeking radiopharmaceutical (technetium medronate) in knees fitting this risk profile than in the knees of normal controls.²⁵

Abbreviations: BMI, body mass index; GEE, generalised estimating equations; JSN, joint space narrowing; JSW, joint space width; K&L, Kellgren and Lawrence; RCT, randomised controlled trial; WOMAC, Western Ontario and McMaster Universities

The significance of JSN as the prime indicator of progressive, as opposed to incident, osteoarthritis has also been challenged by the results of a recent randomised controlled trial (RCT) of the structure-modifying effects of doxycycline, in which the Chingford risk profile was the basis for the radiographic eligibility of subjects. Brandt *et al*²⁶ found that the rate of JSN over 30 months in semiflexed anteroposterior views of the K&L grade 0 or 1 contralateral knee was as rapid as that in the index knee, which exhibited K&L grade 2 or 3 radiographic changes of osteoarthritis at baseline.

We have recently published an analysis of risk factors for the progression of established knee osteoarthritis in the semiflexed anteroposterior view among subjects from two cohorts: the placebo group of the doxycycline RCT, in which subjects were homogeneous with respect to age, sex, obesity and radiographic severity of knee osteoarthritis, and a concurrent observational study, in which subjects were more heterogeneous with respect to these characteristics.²⁷ This analysis showed that, after controlling for baseline severity, progression of both tibiofemoral osteophytosis and JSN were predicted not by age, sex or body mass index (BMI; (weight (kg)/height² (m²)), but by the presence of patellofemoral osteoarthritis at baseline. However, as this was an analysis of progressive osteoarthritis, knees that did not exhibit definite marginal tibiofemoral osteophytes in the baseline semiflexed anteroposterior view were excluded. Accordingly, we performed a similar analysis of “non-osteoarthritis knees” from these cohorts to ascertain the extent to which risk factors for radiographic features of early, if not truly incident, osteoarthritis are congruent with those for unquestionably progressive disease.

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 affiliated with Indiana University Purdue University Indianapolis, Indianapolis, Indiana, USA.

Subjects

Subjects in this analysis were drawn from the two research cohorts studied in our previous evaluation of risk factors of progression of knee osteoarthritis.²⁷ Cohort 1 comprised 253 men and women, ≥ 45 years of age, with mild to moderate knee osteoarthritis, based on radiographic evidence of a marginal tibiofemoral osteophyte in either the standing anteroposterior or semiflexed anteroposterior view and JSW ≥ 2 mm in the semiflexed anteroposterior view. Cohort 2 comprised 66 obese women, 45–64 years of age, with unilateral knee osteoarthritis in the standing anteroposterior radiograph, based on the K&L criteria,¹³ who were randomised to the placebo group of a concurrent RCT of structure modification with doxycycline.²⁶ Subjects in the second cohort were in the upper tertile of the age-appropriate, race-appropriate and sex-appropriate norms for BMI established by the Second National Health and Nutrition Examination Survey.²⁸ Both cohorts were recruited from the Greater Indianapolis Area and examined in a single radiology department by the same technologists. This analysis focused on a subset of these cohorts: 132 men and women, ≥ 45 years of age, in whom tibiofemoral osteoarthritis was absent in one or both knees, based on consensus ratings of the absence of marginal femoral and tibial osteophytes at baseline in the semiflexed anteroposterior view that was common to both studies.

Knee radiography

Each subject underwent a standardised series of radiographs at baseline, including a fluoroscopically assisted semiflexed

anteroposterior view of each knee,¹⁹ a supine lateral view of each knee and a bilateral Hughston view of each patellofemoral compartment. Positioning for the Hughston view required that the subject lie prone with knees flexed to 55°, with the central ray of the x ray beam at a 45° angle, relative to the tabletop.²⁹ A follow-up series of radiographs was obtained 30 months after baseline.

Analysis of radiographs

Minimum JSW in the medial tibiofemoral compartment at baseline was measured manually with digital calipers and was corrected for magnification, based on the projected diameter of a magnification marker (6.35 mm steel ball) that was affixed with tape to the skin over the lateral aspect of the head of the fibula. In addition, the severity of individual radiographic features of osteoarthritis (osteophytosis and JSN in the tibiofemoral and patellofemoral compartments) was rated independently by two readers (KDB and SM) who were blinded to the sequence of the radiographs and, in the case of cohort 2, to the treatment group. Ratings of severity (grades 0–3) were based on exemplars in standard pictorial atlases.^{30–31} Differences between the two readers were discussed until consensus was achieved; if consensus could not be reached, a musculoskeletal radiologist (KAB) was consulted and agreement was reached among the three examiners.

On the basis of the repeat ratings of a random sample of 24 semiflexed anteroposterior radiographs, estimates of reproducibility (κ) consensus ratings of the severity of medial and lateral JSN were 0.85 and 0.7, respectively. κ for osteophyte grade in each of the four tibiofemoral locations varied from 0.52 (medial tibia) to 0.68 (medial femur).

Overall grades of radiographic severity (grades 0–1, 2, 3 and 4) in the semiflexed anteroposterior view, similar to those defined by Kellgren and Lawrence¹³ in the standing anteroposterior radiograph, were assigned to each knee at baseline, according to the presence and severity of tibiofemoral osteophytosis and of JSN in consensus ratings based on the Osteoarthritis Research Society International atlas³⁰ (table 1). Patellofemoral osteoarthritis was judged to be present if a definite patellar or trochlear osteophyte $\geq$ grade 2 was seen in the lateral or Hughston view.^{30–31}

Clinical assessment

Knee pain, stiffness and functional limitation (disability) at baseline was measured with the Western Ontario and McMaster Universities (WOMAC) Osteoarthritis Index (five-point Likert version).³² WOMAC assessment occurred after a washout (five half lives) of all non-steroidal anti-inflammatory drugs and analgesics taken by the subject for knee pain or other reasons. Pain and stiffness were assessed separately in the left and right knees.

Statistical analysis

Osteophytosis was defined by the presence of one or more marginal tibiofemoral osteophytes in the 30-month radiograph. JSN was defined as an increase in the rating of severity of medial or lateral JSN between baseline and month 30.

Separate analyses were performed on each radiographic feature of tibiofemoral osteoarthritis: osteophytosis and JSN. To screen baseline variables as possible risk factors, logistic regression models with generalised estimating equations (GEE) were run separately for three domains: general clinical (ie, age, sex, race and BMI); osteoarthritis clinical (ie, duration of symptoms, duration of self-reported diagnosis and WOMAC Scores for pain, stiffness and function); and radiographic (medial tibiofemoral JSW (in mm), the presence of patellofemoral osteoarthritis in the ipsilateral knee and the presence of

Table 1 Comparison of Kellgren and Lawrence criteria for grading the severity of knee osteoarthritis in the standing anteroposterior radiograph and alternative criteria based on semi-quantitative ratings of the severity of osteophytosis and joint space narrowing in the semiflexed anteroposterior view

Grade	Kellgren and Lawrence criteria ¹³	Alternative criteria	
		Severity of osteophytosis*	Severity of JSN*
0	No features of OA	0	0
1	Minute osteophyte, doubtful significance	0	0
2	Definite osteophyte, unimpaired joint space	≥1	0
3	Definite osteophyte and moderate diminution of joint space	≥1	1 or 2
4	Definite osteophyte and joint space greatly narrowed, and sclerosis of subchondral bone	≥1	3

JSN, joint space narrowing; OA, osteoarthritis.

*Consensus ratings based on Osteoarthritis Research Society International atlas.²⁴

tibiofemoral or patellofemoral osteoarthritis in the contralateral knee). Screening within the domains identified the strongest risk factors among correlated variables. Use of GEE permitted adjustment of the results for the between-knees correlation for subjects with bilateral grade 0–1 osteoarthritis at baseline.

Variables found to have a marginal or stronger association ($p < 0.2$) with longitudinal changes of radiographic features of osteoarthritis were included as independent variables in a two-step multiple logistic regression model (also with GEE). The initial analysis entailed estimation of adjusted odds ratios (OR), 95% confidence intervals (CI) and p values for each variable that passed the preliminary screening for each domain. In the final model, backward selection removed variables with multivariate $p > 0.05$ until all remaining independent variables were significant. All ORs for continuous variables were expressed as the change in odds of increased severity of a radiographic feature of knee osteoarthritis (osteophytosis or JSN) for every standard deviation (SD) difference between subjects in the independent variable.

RESULTS

In all, 31 subjects showed no evidence of definite osteoarthritis in semiflexed anteroposterior radiographs of either knee (ie, they had bilateral grade 0–1 osteoarthritis), and 101 subjects had unilateral knee osteoarthritis, resulting in a total of 163 knees with grade 0–1 osteoarthritis at baseline. Patellofemoral osteoarthritis was present at baseline in 41% of grade 0–1 osteoarthritis knees.

Table 2 shows the demographic, clinical and radiographic characteristics of subjects. The 79 subjects from the longitudinal study (cohort 1) were significantly older than the 53

subjects from the placebo group of the Disease Modifying Osteoarthritis Drug Trial (cohort 2; 60.7 ν 53.7 years, respectively; $p < 0.001$ for each). Subjects from the doxycycline RCT were uniformly more obese than subjects in the longitudinal cohort (mean BMI 36.4 ν 30.2 kg/m², respectively; $p < 0.001$). The duration of symptoms of knee osteoarthritis was similar in the two cohorts (combined mean (SD) 5.2 (6.5) years). However, among subjects with a self-reported diagnosis of knee osteoarthritis made by a doctor (absence of radiographic evidence of osteoarthritis in the semiflexed anteroposterior view notwithstanding), the mean duration of diagnosis was significantly greater in the longitudinal cohort than in placebo subjects from the doxycycline RCT (2.4 ν 0.4 years; $p < 0.001$).

Follow-up (30-month) radiographs were obtained from 114 subjects (66 in cohort 1 and 48 in cohort 2) for an overall retention rate of 86%. The 18 subjects who failed to participate in the 30-month radiographic examination did not differ from those who completed the 30-month examination with respect to any baseline demographic, clinical or radiographic characteristics.

Those who completed the examination provided follow-up data on 141 knees that had grade 0–1 osteoarthritis at baseline. Osteophytosis at month 30 was observed in 55 (39%) knees and was more frequent in subjects from the placebo group of the RCT than in the longitudinal cohort (48% ν 31%, respectively; $p = 0.029$). JSN at month 30 was detected in 20% of knees and was 11-fold more likely to occur in the medial compartment than in the lateral compartment. Subjects in the two cohorts did not differ with respect to the frequency of JSN (23% and 17%, respectively; $p = 0.169$).

Table 2 Characteristics of subjects at baseline

	Cohort 1* (n=79)	Cohort 2† (n=53)	Combined (n=132)
Female sex, n (%)	63 (80)	53 (100)	116 (88)
Age, years	60.7 (11)§	53.7 (5.3)§	57.9 (9.8)
African American race, n (%)	12 (15)	11 (21)	23 (17)
BMI, kg/m ²	30.2 (7.6)§	36.4 (6.3)§	32.7 (7.7)
Duration of symptoms, years	5.4 (6.8)	5 (6)	5.2 (6.5)
Duration of self-reported diagnosis, years	2.4 (4)§	0.4 (0.9)§	1.6 (3.3)
Unilateral tibiofemoral OA, n (%)	65 (82)	36 (68)	101 (77)
WOMAC knee pain score, range 5–25	8.8 (4.1)	10.1 (4.2)	9.3 (4.1)
WOMAC knee stiffness score, range 2–10	4 (2)	4.5 (2)	4.2 (2)
WOMAC function score, range 17–85	35.9 (13.8)	37.7 (11.9)	36.6 (13.1)

BMI, body mass index; OA, osteoarthritis; WOMAC, Western Ontario and McMaster Universities.

*Community-based longitudinal cohort.

†Subjects from the placebo group of a randomised controlled trial of doxycycline in knee OA.

‡The knee with grade 0–1 OA at baseline. If grade 0–1 changes were present bilaterally, the knee with the greater value (ie, longer duration or greater severity of pain/stiffness) was used.

§ $p < 0.001$ for comparison between cohorts.

Table 3 Risk factors for osteophytosis

	Initial model*		Final model†	
	OR‡	95% CI	OR‡	95% CI
Age	0.70	0.46 to 1.07	—	—
Race (African American)	3.30	1.04 to 10.54	—	—
Duration of self-reported diagnosis	0.43	0.19 to 1	—	—
WOMAC pain score	1.46	0.79 to 2.7	—	—
WOMAC stiffness score	1.44	0.79 to 2.64	1.91	1.29 to 2.82
Ipsilateral patellofemoral OA	1.55	0.7 to 3.45	—	—

OA, osteoarthritis; WOMAC, Western Ontario and McMaster Universities.

*The initial model included all variables within three domains (general clinical, OA clinical and radiographic) associated with the dependent variable ($p \leq 0.2$).

†Backward selection of independent variables with $p > 0.05$ until all remaining predictors were significant ($p < 0.05$). There were no significant interactions.

‡OR for continuous independent variables are scaled to reflect the change in likelihood of progression for each SD increase in the independent variable.

Risk factors for osteophytosis

The screening analysis identified six possible risk factors for the development of new osteophytes in the grade 0–1 knee: age, race, duration of self-reported diagnosis of osteoarthritis, knee pain, knee stiffness and the presence of patellofemoral osteoarthritis in the ipsilateral knee.

In the initial multivariate model, only race and duration of diagnosis were significant (table 3). The odds of the appearance of one or more new osteophytes were more than threefold greater among African Americans than in the remainder of the sample, which was almost entirely white ($p = 0.044$). In addition, the duration of a self-reported diagnosis of knee osteoarthritis—even in the absence of radiographic evidence of osteoarthritis in the baseline semiflexed anteroposterior view—was inversely related to the appearance of new osteophytes in the contralateral knee; for every SD (5.2 years) difference between subjects with respect to duration of diagnosis, the odds of observing osteophytosis at month 30 in the subject with longer duration of osteoarthritis decreased 57% ($p = 0.049$). However, after backward elimination of non-significant predictors, particularly after removal of the WOMAC pain score from the model, the WOMAC knee stiffness score became the most prominent risk factor for osteophytosis: for each SD (2.1-point) difference between subjects in the baseline WOMAC stiffness scale, the odds that the subject with the higher stiffness score would exhibit osteophytosis nearly doubled ($p = 0.001$; table 3).

Risk factors for JSN

Preliminary screening identified three variables as potential risk factors for tibiofemoral JSN: duration of symptoms, the presence of osteoarthritis in the contralateral knee and race. In the initial analysis, the odds of JSN were 3.5-fold greater in African Americans than in whites ($p = 0.02$). After elimination of non-significant predictors in the final model, race remained the only significant risk factor for incident tibiofemoral JSN (table 4).

DISCUSSION

Standardised knee radiography has been lauded as an advance that may lead to new insights into disease progression and

structure modification in knee osteoarthritis.³³ The source of this optimism is accumulating evidence of the enhanced precision in measurement of tibiofemoral JSW and greater sensitivity to JSN permitted by standardised examination protocols, compared with that associated with the conventional standing anteroposterior view.^{19–22} These benefits derive from reproducible radioanatomical positioning of the joint³⁴ and negation of other extraneous influences—for example, longitudinal changes in knee pain—that may affect how the subject bears weight during the radiographic examination.³⁵

In a previous study of knees with established knee osteoarthritis at baseline in the fluoroscopically standardised semiflexed anteroposterior view, after controlling for baseline severity, we found that progression of tibiofemoral osteophytosis and JSN were both better predicted by the presence of ipsilateral patellofemoral osteoarthritis than by age, sex or BMI.²⁷ In this study of subjects from the same research cohorts, development of osteophytosis and JSN in knees in which these features of osteoarthritis were absent at baseline in the semiflexed anteroposterior view was related to race. The odds of developing osteophytes or JSN over 30 months were each more than threefold greater in African Americans than in other racial groups (mostly whites). However, given that African American women outnumbered African American men in our sample by a ratio of 9:1 (cf 4.5:1 among other whites), it is uncertain whether the observed risk associated with race in this study applies to men as much as to women.

This finding is consistent with those reported from the First National Health and Nutritional Examination Survey I³⁶ and from other studies of women's health,³⁷ in which knee osteoarthritis was more prevalent among African American women than white women—even after adjustment for age and weight. However, Jordan *et al*³⁸ were unable to confirm this discrepancy in a random sample of adults in Johnson County, North Carolina, USA. More recently, in a preliminary report of prevalence figures from participants aged ≥ 60 years in the National Health and Nutritional Examination Survey III, Hirsch *et al*³⁹ reported that non-Hispanic black men and women had a significantly higher prevalence of radiographic knee osteoarthritis than non-Hispanic white men and women.

Table 4 Risk factors for joint space narrowing

	Initial model*		Final model†	
	OR‡	95% CI	OR‡	95% CI
Duration of symptoms	0.68	0.37 to 1.25	—	—
Contralateral radiographic knee OA	2.26	0.66 to 7.70	—	—
Race (African American)	3.49	1.21 to 10.06	4.04	1.37 to 11.94

OA, osteoarthritis.

For footnotes, refer to table 3.

The greater rates of incident radiographic changes of knee osteoarthritis among African Americans, compared with whites, were not attributable to racial differences with respect to baseline JSW ($p = 0.47$) or the prevalence of osteoarthritis in the contralateral knee ($p = 0.71$). Alternatively, these racial differences may reflect the greater bone density observed in blacks than in non-blacks. High levels of bone density were associated with an increased risk of incident knee osteoarthritis, but not of progressive JSN in the Framingham cohort.⁴⁰ In our sample, the mean BMI of African Americans was marginally greater than that of other subjects (35.1 v 32.2 kg/m², respectively; $p = 0.101$). This is not to say that African Americans were more obese than other subjects; norms for BMI among different racial groups differ significantly.²⁸ However, African Americans also reported higher levels of knee stiffness and functional limitation than other subjects ($p < 0.01$). The association between race and stiffness may explain the failure of race to remain in the final model for the prediction of osteophytosis (table 3). Moreover, the inter-relatedness of race, functional limitation and stiffness may have confounded any predictive utility of BMI.

In addition, the greater muscle mass of blacks may be associated with a higher rate of development of traction osteophytes, which may be mistaken for the marginal osteophytes of osteoarthritis. We have previously shown that the phenotypic appearance of radiographic knee osteoarthritis is different in patients with diabetes than in those without diabetes, with the patients with diabetes exhibiting less osteophytosis.⁴¹ We speculated that the difference was due to less effect of insulin on new bone formation in osteoarthritis joints of patients with diabetes. Our study suggests a racial difference in the phenotype of radiographic knee osteoarthritis.

The high prevalence of obesity in our sample (mean BMI 32.7 kg/m²) may have precluded the variability required to allow evaluation of BMI as a risk factor for the progression of knee osteoarthritis. For this reason, the generalisability of results from our study to populations in which obesity is less prevalent may be limited.

The appearance of new osteophytes was related to the degree of joint stiffness reported by the patient at baseline. Before our previous analysis of these cohorts,²⁷ joint stiffness was a heretofore unrecognised risk factor for knee osteoarthritis. The cause of joint stiffness in osteoarthritis and whether the WOMAC stiffness questions are interpreted similarly by different ethnic groups are unclear. However, stiffness may have been due, at least partly, to synovitis or to the presence of chondrocytes that buttressed the joint and restricted mobility, but had not yet ossified sufficiently to be seen radiographically. Alternatively, as suggested by observations in people who had lower extremities amputated with rheumatoid arthritis⁴² who reported phantom limb stiffness, this sensation may have been due to central nervous system changes that affected sensory input.

The fact that subjects for this analysis came from two research cohorts, rather than from one cohort meeting a single set of eligibility criteria, may limit the generalisability of these results. However, subjects for both the longitudinal radiographic study and the doxycycline RCT were enrolled concurrently, using a combined recruitment effort. Volunteers who met the more selective eligibility criteria of the doxycycline RCT were enrolled in the prerandomisation run-in that we have described elsewhere.⁴³ Those who were not eligible for the RCT (and some of those who failed the pre-trial run-in) were asked to participate in the observational study. In light of these facts, inclusion of subjects from the placebo group of the RCT in the longitudinal study was not only permissible but also advisable. Failure to include these subjects would have resulted in a

sample in which subjects with multiple risk factors for knee osteoarthritis (ie, female sex, middle age and obesity) were under-represented. All the variables for which the two cohorts differed at baseline because of differing eligibility criteria (table 2) were evaluated as possible risk factors for incident radiographic changes of knee osteoarthritis.

In conclusion, race and the severity of joint stiffness seemed to be risk factors for early radiographic changes of tibiofemoral osteoarthritis in this study. Future investigations into risk factors of knee osteoarthritis should focus on the systemic and local influences that these ostensible risk factors represent.

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