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The natural history of emergent osteoarthritis of the knee in women

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Summary

Objective: We assessed the probability that mid-aged women with a Kellgren and Lawrence (K–L) score of 1 are likely to progress to a score of 2 or regress to a score of zero at a second time point, 2–3 years later.

Methods: Osteoarthritis (OA) measurements (weight-bearing X-rays and interviews) were undertaken in women from the Southeast Michigan population who were ≥ 40 years of age, and who participated in both the 1995 and 1998 measurements ($N=679$).

Results: Of the 17.1 % of women with a 1995 K–L score of 1 in their right knee, 37.1% had a K–L score of 1 in 1998 while 32.8 % had a score of ≥ 2 and 30.2% had a score of zero. For 26.0% of women, the score progressed by at least one unit over the 2.5 year period whereas scores for only 7.0% of women regressed in the same time period. Women who had a K–L score of 1 in the right knee in 1995 were 2.5 times more likely to have a K–L score of 1 in 1998 (95% CI=1.6–3.8); and were 2.2 times more likely to have a K–L score of 2 or greater (95% CI=1.4–3.5) in 1998 compared with other scores. These women were 74% less likely to have a score of zero in 1998 (95% CI=0.2–0.4). Further, other risk factors, specifically age and BMI were predictors of increasing K–L grade in 1998.

Conclusion: These findings suggest that a score of 1 is part of the advancement to emergent OAK; and suggest the following criteria to characterize individuals who are at an intervenable stage on the pathway toward OAK: age ≥ 40 , BMI ≥ 30 , and K–L score of ≥ 1 . From the perspective of both the individual and the examiner, these assessment characteristics are relatively simple to assess clinically. © 2002 Osteoarthritis Research Society International. Published by Elsevier Science Ltd. All rights reserved.

Key words: Osteoarthritis, Kellgren–Lawrence score, Progression, Epidemiology.

Introduction

Since the mid 1970s, much of the epidemiologic research to describe the natural history of radiographically-defined osteoarthritis (OA) and the outcomes of intervention strategies to ameliorate the associated symptoms has relied on a case definition using the standardized criteria and grading system depicted in the Kellgren–Lawrence (K–L) atlas¹. The scoring system ranges from 0 through 4 with scores 2–4 classified as representing osteoarthritis (Table I). The scoring system requires the X-ray reader to integrate the status of bone, joint space, and osteophyte development into a single summary measure.

The use of the K–L system has more recently been eclipsed and replaced by the evaluation of change in joint space narrowing as a marker of disease progression or response to therapy among those with established OA. However, the K–L system still has great utility in considering the early natural history of OA. The K–L scoring system, in the ranges between 0–2, is strongly based on the presentation of osteophytes while the upper ranges of 3 or 4 are weighted to address joint space narrowing and joint deformity. This infers that osteophyte formation may be the

most visible mark of early stages of clinical disease whereas joint space narrowing may be more useful as an index of severity or progression in established OA.

Newer therapeutic modalities and environmental interventions are being developed to address the structural damage associated with OA as opposed to the palliative relief of pain. It is useful to understand the earlier natural history of OA to assess the effectiveness of these agents prior to substantial deterioration in joint tissues. Within this context, there is a question whether those with a K–L grade of one, defined as having possible osteophytes, represents a clinically meaningful score. More importantly, if persons with this score might represent a sizeable high-risk population for the subsequent development of OA, this score may signify an efficacious, intervenable stage in the natural history of the disease process. This stage in the natural history would be particularly important in mid-aged populations where OA is newly emerging and the frequency of individuals in the population with a K–L grade of 1 may be relatively high.

There is precedent for this hypothesis. Previously, in the Baltimore Longitudinal Study of Aging², those with a K–L score of one were almost twice as likely to report ever having knee joint pain compared to those with a K–L grade of zero. The association with pain and radiographic OA increased with increasing K–L grade.

We examined the Kellgren and Lawrence scores and their relationship to risk factors associated with osteoarthritis at two points in time in the Southeast Michigan cohort population of African American and Caucasian

Received 27 March 2002; revision accepted 27 July 2002.

Support: NIAMS RO1–40888 (Sowers, PI)

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Table I
Kellgren and Lawrence Classification Scales for Osteoarthritis Outcome Measures

Radiographic outcomes for knee joints	Grade
Normal	0
Possible osteophytes; Doubtful narrowing of joint space	1
Definite osteophytes; Absent or questionable narrowing of joint space Moderate osteophytes;	2
Marked narrowing of joint space; Severe sclerosis; Possible deformity	3
Large osteophytes; Marked narrowing of joint space; Severe sclerosis; Definite deformity	4

*The Kellgren and Lawrence scale is the most widely used classification criteria for scoring the degree of OA in individual joints. Scoring is done on a 5-point scale, according to the Atlas of Standard Radiographs of Arthritis¹.

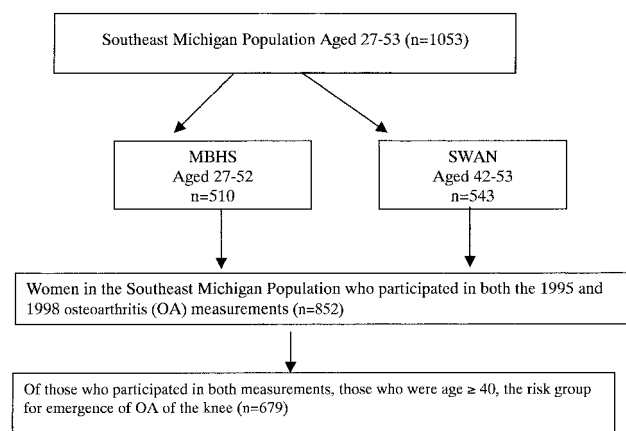


Fig. 1. Characterization of the Southeast Michigan Population Longitudinal Osteoarthritis Study Cohort.

women. We asked following questions. (1) What is the probability that mid-aged women with a K-L score of 1 are likely to progress to a score of 2 or regress to a score of 0 at a second time point 2–3 years later? (2) Does a Kellgren and Lawrence score of 1 represent a meaningful stage in the development of OA? (3) What are important risk factors that predict the K-L scores 2–3 years later?

Materials and methods

STUDY POPULATION

Populations used in this report include the Michigan Bone Health Study (MBHS) and the Study of Women's Health Across the Nation (SWAN-Michigan site), that together comprise the Southeast Michigan cohort. This report reflects the radiographic data from 679 women who participated in both the 1995 and 1998 osteoarthritis measurements and who were age >40, the risk group for emergence of OA of the knee (Fig. 1).

The Michigan Bone Health Study (MBHS) was organized in 1988 by one of the authors (MFS) to describe the natural history of peak bone mass and the factors contributing to that peak bone mass. The sample was derived from combining two sampling frames. The first frame was a list of pre-menopausal female offspring aged 24–44 years in 1992, who were identified from the family records of participants in the historical Tecumseh Community Health Study (TCHS) organized in 1959–1960. Eighty percent of eligible women were enrolled. The second frame was a community census in 1992 that identified additional women who had become residents since the initial family census in 1959–1960 and, of these, 90% were enrolled. The first X-ray examination for OA in the MBHS population was conducted in 1992/93. The second and third X-ray examinations for OA were conducted in 1995/96 and 1998/99, time frames parallel with the SWAN osteoarthritis site-specific study. Of the 664 women recruited into the MBHS study, 511 women had X-rays, 56 refused participation, three participated in study measurements but did not have X-rays taken, and 94 were not measured due to pregnancy, death, moving, or ill health. Of the 511 women with X-rays, one woman was eliminated from the OA cohort due to findings consistent with rheumatoid arthritis.

The SWAN study at Michigan is a population-based longitudinal study of African American and Caucasian women to understand health at the mid-life, including a study of OA. Enrollees were derived from a household census of two communities located within 20 miles of Detroit, Michigan. The initial census identified 24 283 households in the communities. SWAN personnel interviewed 2621 women between the ages of 40–55 (representing 65% of the eligible women). From this sample, there were 754 pre- and perimenopausal women aged 42–52 years eligible for the SWAN cohort study, and 72% of these women were enrolled ($N=543$). These enrollees met the age (42–52 years), menstrual status (menstrual bleeding within the previous 3 months and without the use of hormone replacement therapy), and ethnicity type and proportion specified by the Study protocol (African American and European American in a 2:1 ratio). A site-specific study of radiographically determined OA in pre- and perimenopausal women aged 42–52 years was implemented in this SWAN longitudinal population in 1996/97. OA measurements (X-rays and interviews) were undertaken in both the MBHS and SWAN populations under the same protocol³.

MEASUREMENTS

Radiographic OA

During the 1995/96 and 1998/99 examinations, antero-posterior (AP) radiographs were taken of the dominant hand and both knees bearing weight. At both time points, films were taken by one of three trained and experienced technicians using General Electric radiographic equipment (model X-GE MPX-80; General Electric Medical Systems, Milwaukee, WI) and Kodak film (X-DA with Kodak rare earth intensifying screens; Eastman Kodak, Rochester, NY). The source film distance was 40 inches, and standard radiographic techniques were used.

Both knee joints (with weight bearing) were evaluated. Scoring was based on the Kellgren–Lawrence (K–L) grading system shown in the Atlas of Standard Radiographs of Arthritis (19). Each joint was classified according

Table II
 Transitional probabilities indicating progression and regression of Kellgren and Lawrence (K-L) scores by knee from 1995 to 1998 in Southeast Michigan women aged ≥ 40 ($n=679$)

K-L score	1998 K-L=0 N (%)	1998 K-L=1 N (%)	1998 K-L ≥ 2 N (%)	Total N (%)
Right Knee				
1995 K-L=0	350 (51.6)	102 (15.0)	37 (5.5)	489 (72.0)
1995 K-L=1	35 (5.2)	43 (6.3)	38 (5.6)	116 (17.1)
1995 K-L ≥ 2	3 (0.4)	7 (1.0)	64 (9.4)	74 (10.9)
Total	388 (57.1)	152 (22.4)	139 (20.5)	679
Left Knee				
1995 K-L=0	369 (54.3)	92 (13.6)	30 (4.4)	491 (72.3)
1995 K-L=1	43 (6.3)	46 (6.8)	37 (5.5)	126 (18.6)
1995 K-L ≥ 2	2 (0.3)	6 (0.9)	54 (8.0)	62 (9.1)
Total	414 (61.0)	144 (21.2)	121 (17.8)	679

*% reflects % of total ($N=679$).

to a 5-point scale (0=normal, 1=doubtful OA, 2=minimal OA, 3=moderate OA, and 4=severe OA) based on the degree of osteophyte formation, joint space narrowing, sclerosis, and joint deformity. Apart from the K-L criteria, joints were classified as unable to evaluate, missing, or showing changes consistent with rheumatoid arthritis.

Standardization of joint grading and evaluation of the consistency of grading between evaluators followed a multi-step process. Each of the readers, although experienced, first reviewed the K-L grading criteria and evaluated films that were representative of all levels of OA. Then, 50 radiographs of knees from the current study were evaluated independently by each reader, and their results were compared.

After completing standardization procedures, two readers (DJ, MCH, or MFS) independently evaluated and classified each knee joint. The 1995/96 and 1998/99 readings were conducted within the timeframe shortly following completion of data collection for these two separate time periods, and at the 1995/96 readings, evaluators were blinded to the previous measurement findings. For each joint, the scores assigned by the two readers were compared. Joints without perfect correspondence were reread and, if necessary, subjected to consensus reading. In the 1995/96 readings there were 2028 knee joints with perfect concordance and 120 joints that required rereading and/or consensus evaluation; and in the 1998/99 readings there were 1645 knee joints with perfect concordance and 169 joints that required rereading and/or consensus evaluation. Kappa statistics indicated that agreement between the initial score and consensus score was almost evenly divided between the two readers. A group of preselected films, representative of all levels of OA, were also dispersed throughout the study films and used to ascertain drift in different days of reading. There was no evidence of drift.

OA was defined as the presence of at least one knee joint with a grade of 2 or higher. Women were defined as having knee OA if they had arthritis in either or both knees.

Arthritis Questionnaire

An arthritis questionnaire was administered to identify pain and clinical characteristics (yes/no), including current knee joint pain and previous knee injury. To determine whether or not a participant had current knee joint pain,

participants were asked if they had any joint pain in their knees during the last month. Participants were also asked if they had ever had a serious knee injury.

Other measures

Race/ethnicity was categorized as African American or Caucasian, based on self-report. Height (cm) and weight (kg) were measured using a stadiometer and balance beam scale, respectively. Body mass index (BMI) was calculated as weight (kg)/height (m^2). Smoking behavior was classified as current smoker, ever smoked, or never smoked.

DATA ANALYSIS

Univariate statistics were calculated for the continuous variables and frequency tables were developed for the categorical variables. Scores of both right and left knees in 1998 were described in relation to Kellgren and Lawrence scores in 1995 to evaluate the change over time.

Logistic regression analyses were used to determine the probability of the K-L classification in 1998 (possible responses were 0, 1, or ≥ 2) given a K-L score of 1 in 1995. The multinomial logit model was used to evaluate Kellgren and Lawrence score as a multinomial rather than binomial distribution. The Newton-Raphson algorithm was used to get the maximum likelihood estimates utilizing the CATMOD procedure in SAS⁵. Specifically, comparisons were made for K-L grade 1 vs 0 and K-L grade >2 vs 0.

Results

Kellgren and Lawrence scores by knee for those who participated in both the 1995 and 1998 assessments in Southeast Michigan are shown in Table II. In this population where OA is first emerging, most of the women (72%) had a K-L score of 0 in both knees and there was no K-L score greater than 3.

The transitional probabilities of K-L scores from 1995 to 1998 for each knee are also shown in Table II. Of the 17.1% of women with a 1995 K-L score of 1 in their right knee, 37.1% had a K-L score of 1 in 1998 while 32.8% had a score of 2 or greater and 30.2% had a score of 0. Similar

Table III
Odds ratios (OR) for 1998 Kellgren and Lawrence (K-L) score of the right knee based on 1995 K-L right knee scores in Southeast Michigan women \geq age 40 (N=679)

Kellgren and Lawrence score (K-L)	1998 K-L=0* OR (95% CI)	1998 K-L=1† OR (95% CI)	1998 K-L \geq 2‡ OR (95% CI)
1995 K-L=0	10.07 (6.71–15.12)	0.74 (0.50–1.09)	0.07 (0.05–0.11)
1995 K-L=1	0.26 (0.17–0.40)	2.45 (1.60–3.78)	2.23 (1.43–3.47)
1995 K-L \geq 2	0.02 (0.01–0.08)	0.33 (0.15–0.74)	45.23 (22.26–91.90)

*K-L=0 vs K-L=not 0.

†K-L=1 vs K-L=not 1.

‡K-L \geq 2 vs K-L<2.

transitional probabilities were found for the left knee over these two time periods. Additionally, these probabilities suggest that there was progression over the 2.5-year period. For 26.0% of women [(102+37+38)/679] the score progressed by at least one unit over the 2.5 year period whereas scores for only 7.0% of women [(35+3+7)/679] regressed in the same time period. For the left knee, there were 23.0% of women [(92+30+37)/679] with progression in K-L score by at least one unit over 2.5 years, and only 7.5% of women [(43+2+6)/679] with regression in the same time period.

Table III depicts the odds ratios for K-L scores in 1998 based on 1995 scores. Women who had a K-L score of 1 in the right knee in 1995 were 2.5 times more likely to have a K-L score of 1 or greater in 1998 (95% CI=1.6–3.8); and

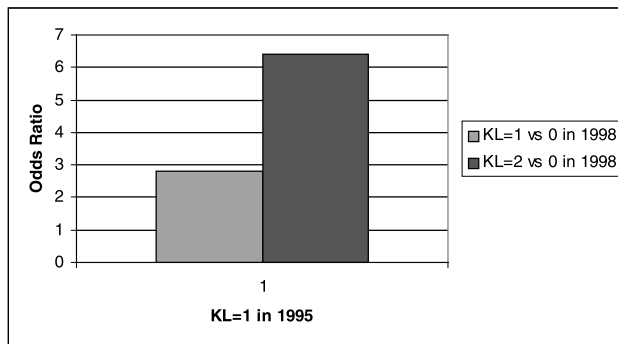


Fig. 2. For individuals with Kellgren and Lawrence (K-L) scores of 1 in 1995 there is an increased odds of being classified with K-L=1 (2.8) or K-L=2 (6.4) two and a half years later compared with K-L=0

were 2.2 times more likely to have a K-L score of 2 or greater (95% CI=1.4–3.5) in 1998 compared with other scores. These women were 74% less likely to have a score of 0 in 1998 (95% CI=0.2–0.4). Women with a K-L score of 2 or greater in 1995 were much more likely to have a K-L score of 2 or greater in 1998 (OR=45.2, 95% CI=22.3–91.9), and women with a K-L score of 0 in the right knee in 1995 were much more likely to stay at 0 in 1998 compared with the other categories (OR=10.1, 95% CI=6.7–15.1).

For individuals with a K-L score of 1 in 1995 there were increased odds of being classified as K-L=1 or K-L \geq 2 compared to K-L=0 in 1998 (Fig. 2). Those with a K-L score of 1 in 1995 were 2.8 times as likely to be classified as 1 in 1998 and 6.4 times as likely to be classified as 2 or greater in 1998 compared with a K-L score of 0.

If a K-L score of 1 is meaningful in advancement to emergent OA, then it is important to determine risk factor characteristics associated with that score of 1. As shown in Table IV, we evaluated whether a K-L score in 1995 was predictive of a K-L value greater than 0 (see model 1). The multinomial logit modeling for the K-L score in 1998 indicates that a previous K-L score of 1, BMI, and age are important predictors. There are increased odds of staying at a K-L classification of 1 or advancing to a classification of 2 or greater in 1998 for those who have attained a K-L grade of 1 in 1995. Further, other risk factors, specifically age and BMI were predictors of increasing K-L grade in 1998.

Discussion

There was an ordinal relationship among Kellgren and Lawrence scores from 1995 to 1998 in the Southeast

Table IV
Odds ratios (OR) for Kellgren and Lawrence (K-L) score in 1998 in Southeast Michigan women \geq 40 (N=679)

Variable	Model 1	Model 2	Model 3
	K-L=1 vs K-L=0 in 1998 Odds ratio (95% CI)	K-L \geq 2 vs K-L=0 in 1998 Odds ratio (95% CI)	K-L \geq 2 vs K-L=1 in 1998 Odds ratio (95% CI)
K-L=1 in 1995	2.80 (1.73–4.50)†	6.42 (3.65–11.23)†	2.29 (1.27–4.10)*
BMI (kg/m ²) (1995)	1.05 (1.02–1.08)†	1.14 (1.10–1.18)†	1.08 (1.04–1.12)†
Race (AA/Cauc)	1.42 (0.93–2.18)	1.00 (0.56–1.79)	0.70 (0.39–1.26)
Age (years)	1.13 (1.08–1.18)†	1.09 (1.03–1.17)*	0.97 (0.91–1.04)
Current pain (yes/no)	0.96 (0.59–1.59)	1.43 (0.78–2.58)	1.48 (0.81–2.72)
Smoker (vs never smoked)	0.73 (0.45–1.20)	0.79 (0.41–1.89)	1.08 (0.53–2.19)
Ex-smoker (vs never smoked)	1.12 (0.64–1.97)	0.74 (0.34–1.64)	0.66 (0.30–1.46)

* $P \leq 0.05$.

† $P \leq 0.001$.

Michigan population as indicated by the transition probabilities. Furthermore, those who had a Kellgren and Lawrence score of 1 in 1995 were more likely to have a score of 2 or greater in 1998 compared to those who had a Kellgren and Lawrence score of 0 in 1995. These findings suggest that a score of 1 is part of the advancement to emergent OAK. Higher body mass index was also an important factor contributing to subsequent classification with OAK in those who had a K-L score of one in the first measurement in the Southeast Michigan Population. There was an increased risk of changing from a classification of a K-L of 1 to a K-L of 2 or greater with each unit increase of BMI. If classification with a K-L grade of one accompanied by these risk factors is predictive of later OA development, then this stage of the process could represent an important time to intervene.

Pain continues to be the dominating symptom used for diagnosis of OAK clinically. The ACR clinical classification criteria for individuals with possible OAK, using a history and physical along with radiographic findings is based on pain in the knee accompanied by one of the following characteristics: age ≥ 50 , < 30 minutes of morning stiffness, crepitus on active motion and osteophytes⁶. These data suggest similar criteria to characterize individuals who are at an intervenable stage on the pathway toward OAK. These criteria include the following: age ≥ 40 , BMI ≥ 30 , and Kellgren and Lawrence score of 1 or greater. These characteristics represent an important potential location on a continuum toward the development of OAK. In addition, from the perspective of both the individual and the examiner, these characteristics are relatively simple to assess clinically.

This study offers a perspective on the development of OAK that cannot be currently addressed by other epidemiologic studies. First, this study has the unique advantage of following a younger population of women where baseline examination indicated they were truly at risk for OAK development in both knees. Other studies of OAK include older individuals and the emphasis is on defining progression in a population where disease is already well established. Additionally, this study assesses the development of OAK over two points with a relatively short time interval. This is a period of time when the early natural characteristics of OA are first developing and being expressed, and the data describe factors associated with these early stages of disease. This is clearly seen in examining the transition probabilities for advancement to higher K-L scores. These findings are important because, in this study, individuals are at a stage of the disease process where tissues have not been destroyed. Therefore, the focus of intervention at this stage would be tissue repair rather than rebuilding of tissue that has been severely compromised or destroyed.

Concerns with the Kellgren and Lawrence scale in recent years have been centered around possible misclassification due to the inability to distinguish joint space narrowing apart from osteophyte formation in OA progression. However, this report concerns the opposite end of the spectrum; that of distinguishing knee OA at earlier stages in younger populations. It is most likely that early in the OA process, the osteophyte is the most important determinant of K-L grade, and therefore the problem is not with the separation of individual features, as much as how the case definition of OA is determined. Although it would not necessarily be appropriate to group those with K-L grade 1 with those who have K-L grades of 2 and higher, these findings suggest that the present case definition of OA, which groups the score of 1s with the score of 0s may result in misclassifi-

cation or misinterpretation. This misclassification can lead to an inappropriate expectation about the potential efficacy of some interventions, including therapeutic interventions. For example, problems in the design of randomized clinical trials would include having a control group that does not comprise only those without disease. In addition, those who are classified as K-L=1 could actually benefit from an intervention that is responsive to structural elements in a way that those with a K-L of 3 or 4 may not benefit. These issues affect the efficacy of both trials and interventions.

In the Southeast Michigan Population, where change in K-L score was modeled over two points in time, 1998 classifications for most women either stayed at the 1995 classification level or moved to a higher level on the K-L scale. However, a proportion of women had a subsequent classification that was lower than their initial score on the K-L scale. Possible explanations for the observation of K-L scores moving from 1 to 0 include issues related to ineffectual measurement, as well as personal characteristics. It is unclear whether the shift could actually represent a true regression in osteophyte formation. In the process of developing OA, the time sequence of when articular cartilage is lost, subchondral bone changes occur, and new bone is formed is unclear. Further, in this study, we do not have enough women who have initiated hormone replacement therapy to determine if this is an important component.

In summary, a shift in perception is needed regarding the population at risk for OA. If women with the risk factors for early OAK were targeted for further follow-up or interventions aimed at prevention of OA, then it might be possible to decrease the number of individuals presenting with pain and functional limitations after the age of 50.

References

1. Kellgren JH, Lawrence JS. The Epidemiology of Chronic Rheumatism. Volume II. Atlas of Standard Radiographs of Arthritis. Philadelphia: F.A. Davis 1963.
2. Lethbridge-Cejku M, Scott WS Jr, Reichle R, Ettinger WH, Zonderman A, Costa P *et al.* Association of radiographic features of osteoarthritis of the knee with knee pain: data from the Baltimore Longitudinal Study of Aging. *Arthritis Care Res* 1995;8:182-8.
3. Sowers MF, Lachance L, Hochberg M, Jamadar D. Prevalence of radiographically defined osteoarthritis of the hand and knee in a population of pre- and perimenopausal women. *Osteoarthritis Cart* 2000; 8:69-77.
4. Sowers MF, Lachance L, Jamadar D, Hochberg M, Hollis B, Crutchfield M. *et al.* The associations of bone mineral density and bone turnover markers with osteoarthritis of the hand and knee in pre- and perimenopausal women. *Arthritis Rheum* 1999; 42:483-89.
5. Allison PD. Logistic Regression Using the SAS System: Theory and Application. SAS Institute, Inc., 1999.
6. Altman R, Asch 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. Diagnostic and Therapeutic Criteria Committee of the American Rheumatism Association. *Arthritis & Rheum.* 1986; 29:1039-49.

7. Spector TD, Hart DJ, Byrne J, Harris PA, Dacre JE, Doyle DV. Definition of osteoarthritis of the knee for epidemiological studies. *Ann Rheum Dis* 1993; 52:790–4.
8. Hart DJ, Spector TD. The classification and assessment of osteoarthritis. In: *Classification and assessment of rheumatic diseases: Part I*. Silman AJ, Symmons DPM. Eds. London: Bailliere Tindall, 1995. 407–32.
9. Altman RD, Fries JF, Bloch DA, Carstens U, Cooke TD, Genant H. *et al.* Radiographic assessment of progression in osteoarthritis. *Arthritis Rheum* 1987; 30:1214–25.
10. Hart DJ, Spector TD. Radiographic criteria for epidemiologic studies of osteoarthritis. *J Rheumatol (Suppl.)* 1995;43:46–8.
11. Spector TD, Hart DJ, Byrne J, Harris PA, Dacre JE, Doyle DV. Definition of osteoarthritis of the knee for epidemiological studies. *Ann Rheum Dis.* 1993;52: 790–4.
12. Menkes CJ. Radiographic criteria for classification of osteoarthritis. *J Rheumatol (Suppl.)* 1991;27:13–15.