

Epidemiology of the rheumatic diseases

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Emerging osteoarthritis studies suggest that certain occupations are associated with a high risk for development of hip and knee osteoarthritis, at least in men. The main activities identified are regular lifting for the hip and knee bending for the knee. Obesity is a well-known risk factor for the knee, and it has been suggested that this risk can be halved by losing weight. Studies of the natural history of knee osteoarthritis suggest that many individuals do not develop osteoarthritis, although precise prognostic indicators are lacking at present. No new etiologic information on rheumatoid arthritis has appeared recently, although hormonal and reproductive factors in women continue to be studied with variable results. Agreement is slowly being reached on how to define vertebral fractures for epidemiologic study, which should produce more consistent results. In a study from Rochester, Minnesota, US incidence rates were produced for clinically diagnosed vertebral fracture (117/100,000) that are similar to hip rates, although they occur at an earlier age. Continued study of risk factors continues to show them to be of little use in screening. In systemic lupus erythematosus, hair dyes have not been confirmed as a risk factor, although there may be a link with domestic pets. There are conflicting data on the roles of obesity and occupational factors in carpal-tunnel syndrome.

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This review concentrates on recent reports of epidemiologic studies that are either descriptive or etiologic. The studies covered are not exhaustive for all the rheumatic diseases, and readers are urged to consult the previous three years' (1990-1992) epidemiology review articles in *Current Opinion in Rheumatology* for a wider perspective.

Osteoarthritis

Basic epidemiologic data is at last beginning to emerge on this common disabling disease that has been relatively underresearched in the past. Much of the data is being generated from prospective population surveys, some of which (*ie*, Framingham, Baltimore) are well established. Although numerous studies have shown that 14% to 30% of adults over the age of 45 years have radiologically defined disease, little is known of the effects on disability. A recent review of the small number of studies in different populations estimated that 50% of adults with knee pain also experienced some loss of function [1]. Quam *et al.* [2], from the Mayo Clinic in Rochester, Minnesota, suggested that the rates of knee arthroplasty performed in the United States for knee osteoarthritis for end-stage disease are much lower than would be expected compared with rates of hip arthro-

plasty. Rates of replacement are out of proportion to the rates of disease, which are on average three times more common for the knee, and the two operations are now comparable in terms of outcome. In a similar review of the UK data on the two operations, a similar conclusion was reached [1]. Hadler [3] makes a case that we should be studying and treating knee pain rather than radiologic osteoarthritis.

Risk factors that could be modified to reduce disease have been reviewed by Hochberg [4]. Obesity consistently has been found to be the strongest risk factor for osteoarthritis of the knee. In the prospective Framingham study [5**], women who had lost an average of 5 kg in the 10 preceding years were found to have a 50% reduction in their odds of developing knee osteoarthritis (odds ratio, 0.46; 95% CI 0.24-0.86). Weight gain was associated with a nonsignificant increase in risk (Fig. 1). The same group [6*] has also reported that men with an occupational history of knee bending had an increased risk of knee osteoarthritis (odds ratio, 2.2; 95% CI 1.38-3.58). In women, no significant effect was seen, perhaps due to the difficulties in assessing occupational exposures in housewives.

Further evidence for an occupational relationship comes from Croft *et al.* [7], in a case-control study of 245 men with radiographically defined hip osteoarthritis.

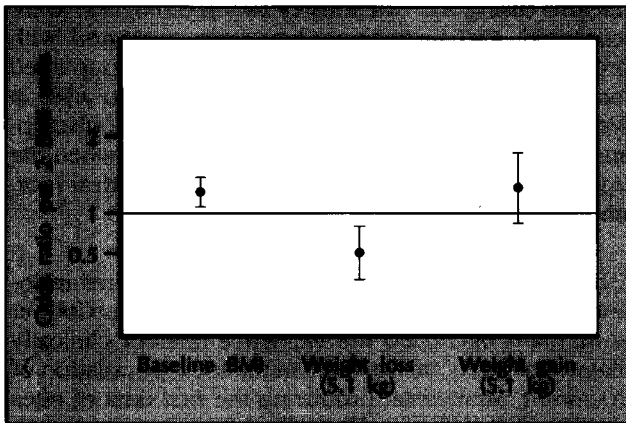


Fig. 1. Effect of weight loss and gain and risk of symptomatic knee osteoarthritis over a period of 10 years prior to examination. Odds ratio adjusted for age, baseline body mass index (BMI), cigarette smoking, knee injury, occupation, physical activity, and education. (Data from Felson *et al.* [5^{**}]; with permission.)

tis compared with 294 controls all aged 60 to 75 years. In patients with severe radiographic osteoarthritis, an odds ratio of 1.6 (95% CI 0.8–3.1) was found in farmers, and an odds ratio of 1.5 (95% CI 0.8–3.1) was found in laborers. These authors [8^{**}] also performed a cross-sectional study of 167 men farmers compared with a sedentary control cohort and found a relative risk of farming for more than 10 years of 9.3 (95% CI 1.9–44.5) (Fig. 2). Thus, in men at least, evidence is accumulating that osteoarthritis is an occupational and, therefore, potentially modifiable disease. Other risk factors include the influence of hysterectomy, which was examined using a retrospective cohort; this study confirmed an earlier case-control study, with increased odds ratios for symptomatic knee and carpometacarpal disease. The data were less impressive when radiologic criteria alone were used [9]. A cross-sectional study of the Baltimore male cohort did not find any significant association with hand osteoarthritis and bone mass, muscle mass, body composition, and muscle strength [10]. In an examination of the US National Health and Nutrition Examination Survey I data set, educational level was not found to be associated with radiologic knee osteoarthritis, although symptom reporting was significantly associated, particularly in those with fewer than 8 years of education [11].

The natural history of osteoarthritis is poorly understood, and few studies have addressed progression of clinical disease. In a follow-up study, 63 patients who were originally seen in a rheumatology clinic 11 years previously were successfully resurveyed [12^{*}]. Mean age was 69 years, and only 33% of the patients had radiographic progression with no increase in pain scores from baseline. The results of the three reported clinical follow-up studies [12^{*},13,14] are presented in Table 1. Apart from baseline knee pain, no obvious prognostic indicators were apparent in the small number

of patients in each group. In a similar study, a larger group of 142 patients from the Zootomeer population cohort with radiologic knee osteoarthritis were followed up over 12 years. Thirty-four percent of the patients were found to have osteoarthritis progression and cartilage loss [15^{*}]. A number of significant prognostic factors were identified, including body mass index, Heberden's nodes, and previous bow or knock knees. No associations were seen for previous knee injury, sex, uric acid levels, chondrocalcinosis, smoking, and occupation. Although there is undoubtedly considerable individual variation, it appears that overall, most radiologic disease does not progress. The future challenge is to correctly identify the subgroup of patients who are likely to have rapid progression.

Rheumatoid arthritis

Few new etiologic clues have come to light recently in rheumatoid arthritis. Bellamy *et al.* [16] surveyed 186 twin pairs with a self-reported diagnosis of rheumatoid arthritis in a study based on the Australian twin registry. Only one twin in each of 23 twin pairs was subsequently verified as having the disease, demonstrating the problems of self-report. The monozygotic concordance rates were only 21% in this small group.

Hormonal and reproductive factors continue to be studied. In a case-control study of 88 young women with recent-onset disease and 144 controls, a marked reduction in the risk of developing rheumatoid arthritis during pregnancy (odds ratio, 0.3) and a marked increase in the first 3 months postpartum (odds ratio, 5.3), which persisted for the first year, were reported [17^{*}]. A protective effect of estrogen-replacement therapy was not confirmed in a retrospective cohort study of 1075 women receiving estrogen-replacement therapy and 3251 controls [18]. No association was found between diabetes type I and rheumatoid arthritis in a study of 1460 patients with rheumatoid arthritis in

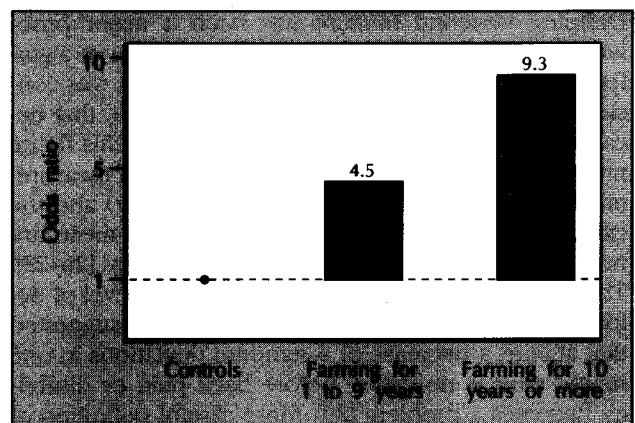


Fig. 2. Risk of osteoarthritis of the hip according to duration of farming. (Data from Croft *et al.* [8^{**}]; with permission.)

Table 1. Long-term outcome of osteoarthritis of the knee

Study	Time, y	Patients, n	Progression, %
Hernborg and Nilsson [13]	13	71	55
Massardo <i>et al.</i> [14]	8	31	61
Spector <i>et al.</i> [12*]	12	63	33
Schouten <i>et al.</i> [15*]	12	142	34

hospital databases in Finland [19]. The importance of rheumatoid factors as predictors of subsequent disease was confirmed in a Finnish follow-up study of 7217 individuals who underwent tests in 1978. Of the 20 persons who developed rheumatoid arthritis, 15 had positive sheep cell agglutination test titers of more than 1/20 [20]. MacGregor and Silman [21], in an accompanying editorial, discuss other relevant data [21]. The inverse relationship between schizophrenia and rheumatoid arthritis was again the subject of a review [22], and although no new data have emerged since a previous review of the subject [23], a number of possible mechanisms were proposed for this curious relationship.

Osteoporosis

Osteoporosis remains a health problem with a high public-health profile. A recent estimate of the impact of osteoporosis suggested that 54% of white women aged 50 years will sustain an osteoporosis-related fracture during their lifetimes [24]. Of these women, 7.8% more than expected were estimated to require nursing-home care for an average of 7.6 years due to fractures. Cummings [25*], in an excellent review of the major methodologic issues in osteoporosis, outlines the pros and cons of various study designs and flaws, particularly in self-report of fractures (mainly vertebral) and other exposures.

Defining vertebral fracture has been a major problem in epidemiologic research. Previously, a straightforward reduction in vertebral height of 20% was considered sufficient. It is now known, however, that because the dimensions of each vertebra vary, this figure must be adjusted for each individual vertebra; measurement of vertebral dimensions (morphometry) and the calculation of standard deviations from the mean are now used in determining level of deformity [26–28]. The problem remains, however, as to what level of deformity is considered a fracture. It has been suggested that at least a decrease of 4 standard deviations in one height ratio is necessary before back pain or disability becomes a problem [29]. More careful definition of vertebral fractures in population studies may alter our perceptions of prevalence. In a large study of 57,000 Finnish men and women, rates of thoracic vertebral

fracture (using the opinions of two radiologists) were measured, and surprisingly low rates compared with previous estimates were found [30]. In the group aged more than 45 years, rates varied from 0.2% to 2.9% in women to 0.7% to 2.8% in men. Many of the discrepancies among studies may only be resolved when the opinions of radiologists are replaced by identical morphometric methodology.

Estimates of the incidence of vertebral fractures in individuals with osteoporosis also vary widely. Cooper *et al.* [31**] examined the incidence rates of clinically diagnosed vertebral fractures in the local population of Rochester, Minnesota, producing the first data of rates for the United States. Three hundred forty-one residents were identified from medical records as having had a vertebral fracture between 1985 and 1989, with an age-adjusted rate of 117 per 100,000 person-years. The average age at fracture was 70.6 years, and the rates in men were half those of women, although fractures in men were more likely to be associated with severe trauma. Diagnosis was confirmed by morphometry, and 80% of the patients had deformities greater than 4 standard deviations. The authors suggest that up to 400,000 women are affected with osteoporosis annually in the United States. The overall rates were similar to those for hip fracture, although vertebral fractures occurred at an earlier age (Fig. 3).

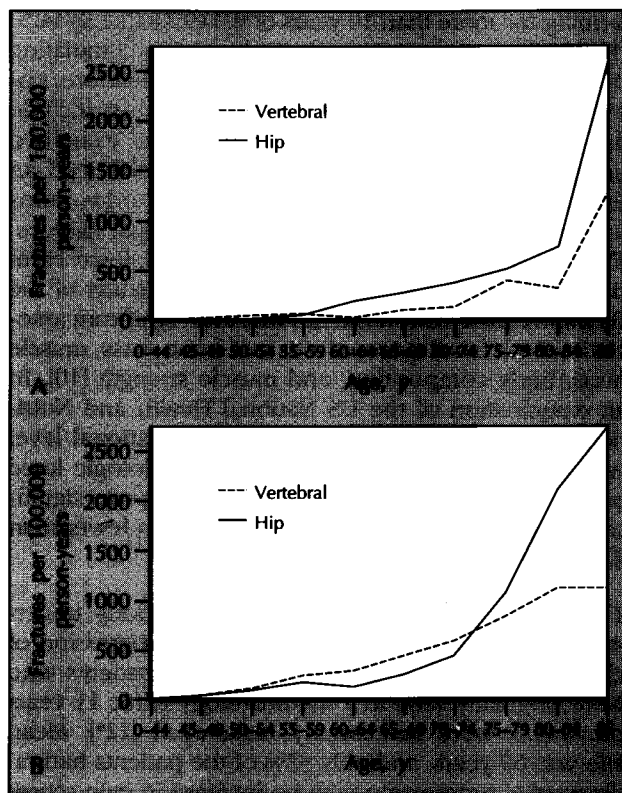


Fig. 3. Incidence by age group of vertebral fractures (1985 to 1989) and hip fractures (1978 to 1982) among men (*panel A*) and women (*panel B*) residents of Rochester, Minnesota. (From Cooper *et al.* [31**]; with permission.)

Methods of screening for osteoporosis are controversial. Law *et al.* [32**] found that although bone density measurements predicted fracture, they were not suitably sensitive or specific to be used on a widespread population basis. Risk-factor assessment continues to be promoted as a possible alternative to bone densitometry. Data, however, do not support this. Three recent studies have shown that although there are some significant associations between bone mass and risk factors, when used together they do not have sufficient sensitivity or specificity to be of predictive value [33–35]. Similar poor performance in predicting bone loss was also seen [34,35]. The variance of bone density explained by these risk factors is only 25% in most studies. Risk-factor assessment also compares poorly with vertebral fractures [36]. Thus risk-factor assessment cannot be used with any accuracy to screen for osteoporosis, and bone densitometry appears to be the best presently available method [37].

The information from bone densitometry has been shown to affect women's decisions about taking measures to prevent fracture. In a postal survey of 261 women in San Francisco, it was found that women with low results were more prepared to receive estrogen-replacement therapy and to take precautions to prevent falling [38]. A possible disadvantage, however, was that 24% of the women limited their activities to prevent fractures. The role of smoking in osteoporosis is still unclear; a study from the Framingham cohort found that smoking was not associated with hip fracture, although it did appear to counteract the protective benefits of estrogen-replacement therapy [39*]. Two studies of coffee drinking have failed to show any clear association of coffee drinking with fractures [40,41]. Results of twin studies suggest that up to 80% of variance in bone density is genetic [42]. A possible mechanism for this is the vitamin D receptor gene, which has various phenotypes and appears to account for the differences in bone density in dizygous twins as well as for the differences in circulating osteocalcin levels, which are markers of bone formation [43]. If this is the case, it is likely that individuals with various backgrounds will react differently to different exposures and risk factors.

Connective tissue diseases

New insights into the etiology of systemic lupus erythematosus are rare. An earlier report of the use of hair dyes as a risk factor for the disease was not confirmed in a case-control study [44]. A study from the United Kingdom, however, may revive some pet theories. In a small immunologic survey of 15 dogs owned by patients with lupus, significantly higher levels of double-stranded DNA and electrophoresis abnormalities were found compared with those in 10 healthy control dogs [45*]. Morbidity and mortality rates in patients with systemic lupus erythematosus were examined in several studies. Fifty-one deaths in 310 patients were observed

by Seleznick and Fries [46], who reported hypertension to be the most important risk factor. In another study, blacks were found to have the highest risk of renal disease, which appeared to be related to poor compliance rather than race [47*].

In a case-control study, women with scleroderma were found to have increased rates of reproductive problems before onset of disease compared with those of controls. Women with Raynaud's disease also appeared to suffer from reduced fertility or delay in conception [48].

Carpal-tunnel syndrome

Carpal-tunnel syndrome is considered by many authors to be an occupational disorder. In a survey of 1058 women grocery checkers, a prevalence of 12% was found, which was related to hours and years worked. The authors estimated that three of five cases of carpal-tunnel syndrome are caused by occupational activity [49]. However, in a follow-up study of 429 industrial workers seen between 1984 and 1989, a fourfold increase in nerve conduction defects was seen in obese workers. Once obesity and age had been accounted for, occupational exposure was no longer significant [50]. In an uncontrolled survey of 246 patients undergoing surgery for arthritis of the thumb base, a high prevalence of carpal-tunnel syndrome was found in 39%, suggesting that osteoarthritis may be a risk factor, although the results were not adjusted for obesity [51].

References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:

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A useful overview of current knowledge about risk factors and those that are likely to be modifiable as part of preventive programs.

Sixty-four women with recent-onset symptomatic disease were identified and compared with healthy women from a cohort of 796 women. Weight change over the previous 12 years was used as the exposure. A decrease of 2 units in body mass index (5.1 kg) produced an odds ratio of 0.46 (95% CI 0.24–0.86). Women who were obese at baseline also benefited. A nonsignificant increase in risk was seen in women who gained weight. Although women who lose

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