Osteoarthritis: New Insights

Part 1: The Disease and Its Risk Factors

Conference Chair: David T. Felson, MD, MPH; *Conference Organizer:* Reva C. Lawrence, MPH; *Discussants:* Paul A. Dieppe, MD; Rosemarie Hirsch, MD, MPH; Charles G. Helmick, MD; Joanne M. Jordan, MD, MPH; Raynard S. Kington, MD, PhD; Nancy E. Lane, MD; Michael C. Nevitt, PhD; Yuqing Zhang, DSc; MaryFran Sowers, PhD; Timothy McAlindon, MD, MPH; Tim D. Spector, MD, MSc; A. Robin Poole, PhD, DSc; Susan Z. Yanovski, MD; Gerard Ateshian, PhD; Leena Sharma, MD; Joseph A. Buckwalter, MD; and Kenneth D. Brandt, MD; and James F. Fries, MD

Osteoarthritis is the most common form of arthritis, affecting millions of people in the United States. It is a complex disease whose etiology bridges biomechanics and biochemistry. Evidence is growing for the role of systemic factors (such as genetics, dietary intake, estrogen use, and bone density) and of local biomechanical factors (such as muscle weakness, obesity, and joint laxity). These risk factors are particularly important in weight-bearing joints, and modifying them may present opportunities for prevention of osteoarthritis-related pain and disability. Major advances in management to reduce pain and disability are yielding a panoply of available treatments ranging from nutriceuticals to chondrocyte transplantation, new oral anti-inflammatory medications, and health education. This article is part 1 of a two-part summary of a National Institutes of Health conference. The conference brought together experts on osteoarthritis from diverse backgrounds and provided a multidisciplinary and comprehensive summary of recent advances in the prevention of osteoarthritis onset, progression, and disability. Part 1 focuses on a new understanding of what osteoarthritis is and on risk factors that predispose to disease occurrence. It concludes with a discussion of the impact of osteoarthritis on disability.

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For author affiliations and current addresses, see end of text.

Osteoarthritis: The Disease and Its Prevalence and Impact

Dr. David T. Felson (Boston University School of Medicine, Boston, Massachusetts), Ms. Reva C. Lawrence (National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health [NIH], Bethesda, Maryland), Dr. Paul A. Dieppe (University of Bristol, Bristol, United Kingdom), Dr. Rosemarie Hirsch (National Center for Health Statistics, Centers for Disease Control and Prevention [CDC], Hyattsville, Maryland), and Dr. Charles G. Helmick (National Center for Chronic Disease Prevention and Health Promotion, CDC, Atlanta, Georgia): For many years, osteoarthritis has been seen as a dull, commonplace disorder with few treatment options. That view is rapidly changing. Recent epidemiologic, clinical, and treatment studies have combined to produce a picture of a surprisingly complex disease whose pathophysiology bridges biomechanics and biochemistry and whose treatments range from surgery to nutriceuticals to patient education interventions. These understandings have already led to a shift in the approach to treatment.

This article is part 1 of a two-part summary of an NIH conference, "Stepping Away from OA: Prevention of Onset, Progression, and Disability of Osteoarthritis." The conference brought together experts in osteoarthritis from diverse backgrounds and provided a multidisciplinary and comprehensive summary of recent advances in the prevention of osteoarthritis onset, progression, and disability. For research questions and opportunities identified at the conference, see www.nih.gov/niams/reports/oa/oareport.htm (accessed on 25 May 2000).

Osteoarthritis is the most common form of arthritis. Among U.S. adults 30 years of age or older, symptomatic disease in the knee occurs in approximately 6% and symptomatic hip osteoarthritis in roughly 3% (1). Since osteoarthritis is a disease whose prevalence increases with age, it will become even more prevalent in the future as the bulging cohort of baby boomers grows older.

Because of its prevalence and the frequent disability that accompanies disease in the knee and hip, osteoarthritis accounts for more trouble with climbing stairs and walking than any other disease (2). Osteoarthritis is the most common reason for total hip and total knee replacement.

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Authors who wish to cite a section of the conference and specifically indicate its author may use this example for the form of the reference:

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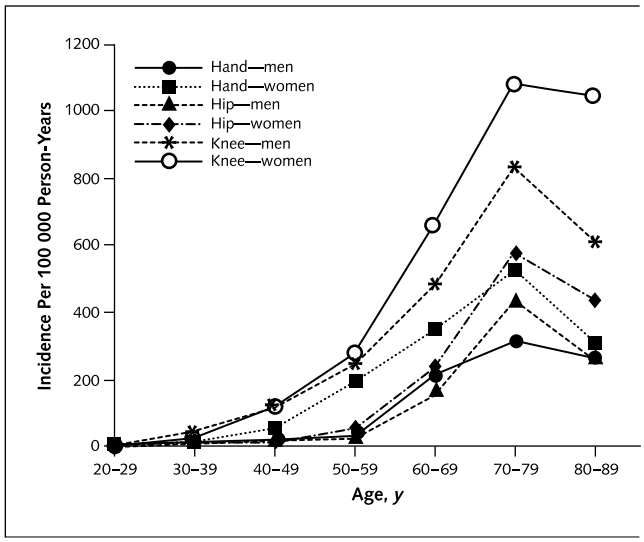
Figure 1. **Incidence of osteoarthritis of the hand, hip, and knee in members of the Fallon Community Health Plan, 1991–1992, by age and sex.**



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Because of the longevity of working careers and the substantial prevalence of osteoarthritis in middle-aged persons, osteoarthritis causes a considerable burden in lost time at work and early retirement (3). Recent estimates suggest that total costs for arthritis, including osteoarthritis, may exceed 2% of the gross domestic product (3).

Clear prevalence patterns emerge from most epidemiologic studies of osteoarthritis. Osteoarthritis increases with age, and sex-specific differences are evident (4–7). Before 50 years of age, the prevalence of osteoarthritis in most joints is higher in men than in women. After about age 50 years, women are more often affected with hand, foot, and knee osteoarthritis than men. In most studies, hip osteoarthritis is more frequent in men (4, 8). In a community-based survey, the incidence and prevalence of disease increased 2- to 10-fold from 30 to 65 years of age and increased further thereafter (9) (**Figure 1**).

Osteoarthritis can be defined by symptoms or pathology. The pathology of osteoarthritis involves the whole joint in a disease process that includes focal and progressive hyaline articular cartilage loss with concomitant changes in the bone underneath the cartilage, including development of marginal outgrowths, osteophytes, and increased thickness of the bony envelope (bony sclerosis). Soft-tissue structures in and around the joint are also affected. These structures include synovium, which may show modest inflammatory infiltrates; ligaments, which are often lax; and bridging muscle, which becomes weak. Many people with pathologic and radiographic evidence of osteoarthritis have no symptoms (10). From a clinical perspective, the most compelling definition of disease is one that combines the pathology of disease with pain that occurs with joint use. Unfortunately, the cause of pain in osteoarthritis is unknown (11).

It is unclear whether osteoarthritis is a single disease or many disorders with a similar final common pathway. The following points argue in favor of the idea that osteoarthritis is several distinct entities:

1. Osteoarthritis of the knee and hip may be associated with different risk factors, suggesting that we should regard them as unique diseases (12). It remains unclear whether osteoarthritis of other joints (such as interphalangeal joints or the spine) should also be regarded as separate entities.

2. "Generalized osteoarthritis" may be a distinct disease (13, 14) in which systemic (genetic) predisposition is more important than local (mechanical) factors (15).

3. One classification divides people with osteoarthritis into those in whom the cause is known (secondary) or those in whom the cause is unknown (primary) (16).

4. Osteoarthritis of the hip has been divided into hypertrophic and atrophic forms (17) on the basis of a person's tendency to develop large osteophytes; other joints may respond similarly to the presence of disease. Hypertrophic osteoarthritis may be associated with pyrophosphate crystal deposition and diffuse idiopathic skeletal hyperostosis, a disease of bony proliferation at ligament and tendon insertion sites; atrophic forms may be associated with the presence of basic calcium phosphate crystals and osteoporosis (18–20).

Severe joint injury may be sufficient to cause osteoarthritis; however, the disease is often the product of an interplay between systemic and local factors (21) (**Figure 2**). For example, a person may have an inherited predisposition to develop the disease but will develop it only where a biomechanical insult (such as a knee injury) has occurred.

We focus on osteoarthritis in the knees, hips, and, to a lesser extent, hands, since disease in these weight-bearing joints has great clinical impact. Although many of the same pathologic changes of disease occur in the back and neck, it is not clear whether clinical syndromes of back and neck pain are necessarily related to osteoarthritis.

Systemic Risk Factors for Osteoarthritis

Ethnicity

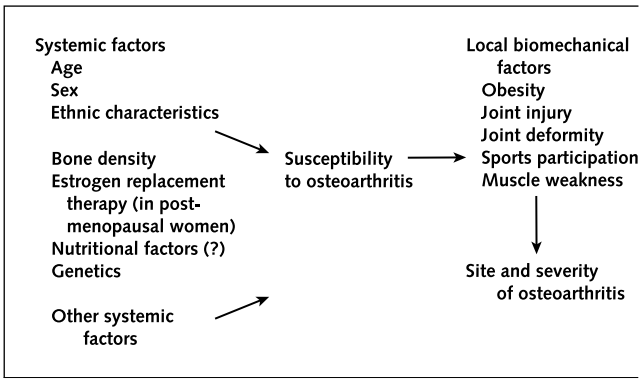
Dr. Joanne M. Jordan (University of North Carolina, Chapel Hill, North Carolina), Dr. Raynard S. Kington (National Center for Health Statistics, CDC, Hyattsville, Maryland), Dr. Nancy E. Lane (University of California at San Francisco, San Francisco, California), Dr. Michael C. Nevitt (University of California, San Francisco), Dr. Yuqing Zhang (Boston University School of Medicine), Dr. MaryFran Sowers (University of Michigan, Ann Arbor, Michigan), Dr. Timothy McAlindon (Boston University School of Medicine), Dr. Tim D. Spector (St. Thomas' Hospital, London, United Kingdom), and Dr. A. Robin Poole (McGill University, Montreal, Quebec, Canada): Ethnic differences in knee and hip osteoarthritis have been best studied in African-Americans and white persons, and evidence is conflicting. Results from one large national study, the National Health and Nutrition Examination Survey I, suggested higher rates of knee osteoarthritis in African-American women but not men. Another study from the rural South, the Johnston County Osteoarthritis Project, suggested no differences in disease prevalence (22, 23). The National Health and Nutrition Examination Survey I did not reveal ethnic differences in the prevalence of osteoarthritis of the hip (24), whereas in the Johnston County Osteoarthritis Project (25), African-American men were 35% more likely than white men to have hip osteoarthritis. African-Americans with knee or hip osteoarthritis have more severe radiographic features of disease and more frequent bilateral involvement and mobility impairment than do white persons (23, 26).

The relative contributions of biological, lifestyle, and socioeconomic factors to ethnic differences in osteoarthritis and disability are unclear. Although ethnic differences in such factors as body mass index might partially explain ethnic variation in radiographic osteoarthritis, ethnic differences in biomarkers of osteoarthritis suggest that biological and genetic factors may also play a role (27).

Hormonal Status and Bone Density

The high incidence of osteoarthritis in women just after menopause has suggested that estrogen deficiency plays a role in causing disease. Cohort studies have reported that women taking estrogen have a decreased prevalence (28) and incidence (29) of radiographic osteoarthritis. However, case–control studies evaluating current or past estrogen use in women with and those without symptomatic osteoarthritis (30, 31) have been inconsistent in their findings; as a result, the current evidence is at best suggestive of a protective effect of estrogen on osteoarthritis. Furthermore, any protective effect might be confounded by healthy habits of estrogen users, which might protect them from disease.

Figure 2. **Pathogenesis of osteoarthritis with putative risk factors.**



Modified with permission from Figure 1 of Dieppe P. The classification and diagnosis of osteoarthritis. In: Kuettner K, Goldberg V, eds. Osteoarthritic Disorders. Rosemont, IL: American Academy of Orthopaedic Surgeons; 1995:7.

Evidence suggests an inverse relationship between osteoarthritis and osteoporosis. The preponderance of cross-sectional studies demonstrate that high bone mineral density is associated with an increased prevalence of hip, hand, and knee osteoarthritis. For example, in the Study of Osteoporotic Fractures (32), women with radiographic hip osteoarthritis with osteophyte formation had an 8% to 12% increase in bone density compared with women without osteoarthritis ($P < 0.001$). Women with knee osteoarthritis also appear to have relatively high bone density (33).

The effect of bone density on the course of osteoarthritis and the impact of osteoarthritis on bone loss have only recently been probed. A longitudinal study of premenopausal and perimenopausal women found that women with knee osteoarthritis were less likely than those without radiographic disease to lose bone during 3 years of follow-up (34). In addition, levels of osteocalcin, a marker of bone turnover, were lower in women with knee and hand osteoarthritis than in women without the disease.

A report from the Framingham Study (35) suggests that although high bone mineral density increases the risk for knee osteoarthritis, it may actually protect against disease progression once disease is established. Furthermore,

Table 1. **Association of 25-Hydroxyvitamin D Level and Development or Progression of Radiographic Osteoarthritis Over 8 Years**

25-Hydroxyvitamin D Level	Odds Ratio (95% CI)		
	Development of Knee Osteoarthritis*	Progression of Knee Osteoarthritis*	Severe Narrowing of the Hip Joint Space†
Lowest third	0.9 (0.5–1.9)	2.9 (1.0–8.3)	3.3 (1.1–9.9)
Middle third	0.9 (0.5–1.8)	2.8 (1.0–7.9)	3.2 (1.1–9.7)
Highest third	1.0 (referent)	1.0 (referent)	1.0 (referent)

* Based on data for progressive and incident knee osteoarthritis on radiography from the Framingham Study (reference 45). No association was found for incident disease.
† Based on data from the Study of Osteoporotic Fractures Research Group (reference 46). A woman could have no or mild narrowing at baseline. A weaker association was found for other definitions of hip osteoarthritis.

bone loss in persons with established osteoarthritis of the knee may accelerate this risk for disease progression.

Women with high lifetime exposure to endogenous and exogenous estrogen have high bone mass, which, as noted above, appears to increase the risk for knee and hip osteoarthritis (32, 33). This indirect effect of estrogen could counteract the protective effect of estrogen on osteoarthritis suggested by some studies. On the other hand, for women with osteoarthritis, estrogen exposure could slow the subchondral bone changes and bone turnover that are associated with progression of knee and hip osteoarthritis. These arguments suggest complex and potentially conflicting roles of estrogen in osteoarthritis.

Nutritional Factors

Evidence indicates that continuous exposure to oxidants contributes to the development of many common age-related diseases, including osteoarthritis (36). Furthermore, chondrocytes are potent sources of reactive oxygen species, which may damage cartilage collagen and synovial fluid hyaluronate, the macromolecule that accounts for the viscosity of synovial fluid (37–40). Since micronutrient antioxidants provide defense against tissue injury, high dietary intake of these micronutrients could be postulated to protect against osteoarthritis.

In the longitudinal Framingham Knee OA Cohort Study (41), a threefold reduction in risk for progressive radiographic osteoarthritis was observed in persons in the middle and highest tertile of vitamin C intake compared with those whose intake was in the lowest tertile. Persons in the highest tertile of vitamin C intake also had reduced risk for knee pain during the course of the study (odds ratio for those with high intake of vitamin C vs. those with low intake, 0.3 [95% CI, 0.1 to 0.8]). Vitamin C intake did not seem to affect incident radiographic findings, and results for intake of β-carotene and vitamin E were inconsistent.

Normal bone metabolism is contingent on the presence of vitamin D (42, 43). Low tissue levels of vitamin D may impair the ability of bone to respond optimally to processes in osteoarthritis and predispose to progression. Vitamin D might also have direct effects on chondrocytes in osteoarthritic cartilage, which have been shown to redevelop vitamin D receptors (44).

The Framingham Study (45) reported that the risk for progression was increased threefold for persons in the middle and lower tertiles of both vitamin D intake (odds ratio for lowest vs. highest tertile, 4.0 [CI, 1.4 to 11.6]) and serum level (odds ratio, 2.9 [CI, 1.0 to 8.2]) (**Table 1**). On the other hand, vitamin D was not associated with risk for new-onset (incident) radiographic osteoarthritis. Further longitudinal evidence of the effect of vitamin D on osteoarthritis was recently provided by Lane and colleagues (46), who found that high levels of vitamin D protected against both incident and progressive hip osteoarthritis.

Genetics

Osteoarthritis in all its heterogeneous forms appears to be strongly genetically determined. Genetic factors account for at least 50% of cases of osteoarthritis in the hands and hips and a smaller percentage in the knees (15). Candidate genes for common forms of osteoarthritis include the vitamin D receptor gene (which influences bone density and is near the locus for type II collagen, the major form of collagen in hyaline articular cartilage), insulin-like growth factor I genes, cartilage oligomeric protein genes, and the HLA region. Three independent linkage studies of families and affected sibling pairs have suggested loci linked to disease in an area of chromosome 2q (47), and a recent study that included mostly women with hip osteoarthritis has

suggested linkage to an area on chromosome 11q (48). It is likely that most genes affecting osteoarthritis will affect disease occurrence in many joints, although there may be specific genes for specific sites, such as the hip.

Biochemical Markers of Cartilage or Bone Metabolism

In osteoporosis, the measurement of bone-derived collagen cross-links in urine has provided valuable insights into the development, progression, and treatment of disease. A similar approach is being used to develop synovial fluid, serum, and urine markers to study cartilage and bone turnover and synovial inflammation in osteoarthritis (49). Recent work in patients with osteoarthritis has demonstrated that candidate markers for cartilage turnover include molecules present especially during cartilage matrix synthesis and degradation, such as type II collagen degradation products and synthesis (c-propeptide) markers; cartilage oligomeric matrix protein; and two epitopes of aggrecan (a large macromolecule within cartilage): the 846 epitope (probably a synthetic marker) and keratan sulfate (49). In patients with accelerated disease progression, serum levels of cartilage oligomeric protein and hyaluronic acid are often elevated (49), which may reflect the frequent presence of synovitis in those with disease.

It is hoped that these biomarkers will help identify persons at high risk for disease occurrence and progression. They may also allow rapid and accurate assessment of the efficacy of treatment designed to control joint degeneration. By identifying and measuring molecular changes that the disease and its treatment produce, management of osteoarthritis should be improved.

Local Biomechanical Factors

Obesity

Dr. David T. Felson (Boston University School of Medicine), Dr. Susan Z. Yanovski (National Institute of Diabetes and Digestive and Kidney Diseases, NIH, Bethesda, Maryland), Dr. Gerard Ateshian (Columbia University, New York, New York), Dr. Leena Sharma (Northwestern University, Chicago, Illinois), Dr. Joseph A. Buckwalter (University of Iowa Hospitals, Iowa City, Iowa), and Dr. Kenneth D. Brandt (Indiana University School of Medicine, Indianapolis, Indiana): Persons who are overweight have a high prevalence of knee osteoarthritis. For many years, it was not clear whether being overweight preceded or was a consequence of osteoarthritis, given the immobility and disability the disease can produce. Recent studies (50, 51) have proved that being overweight antedates the development of disease. Furthermore, in persons with osteoarthritis, being overweight increases the risk for radiographic progression (52, 53). In most but not all studies, the increased risk for osteoarthritis of the knee among overweight persons is stronger in women than men (**Table 2**).

In persons who are overweight, weight loss can reduce the risk for osteoarthritis. In the Framingham Study, an observational study, women who lost an average of 11 lbs decreased their risk for knee osteoarthritis by 50% (54). The effect of weight loss on symptoms in persons with knee osteoarthritis has not been well studied. One small randomized trial of an appetite suppressant (55) showed that the amount of weight loss was strongly correlated with improvement in symptoms and signs of disease.

The relationship of increased body weight with hip osteoarthritis is weaker than its association with disease in the knee. Unilateral disease in the hip is not clearly associated with being overweight, whereas bilateral disease is.

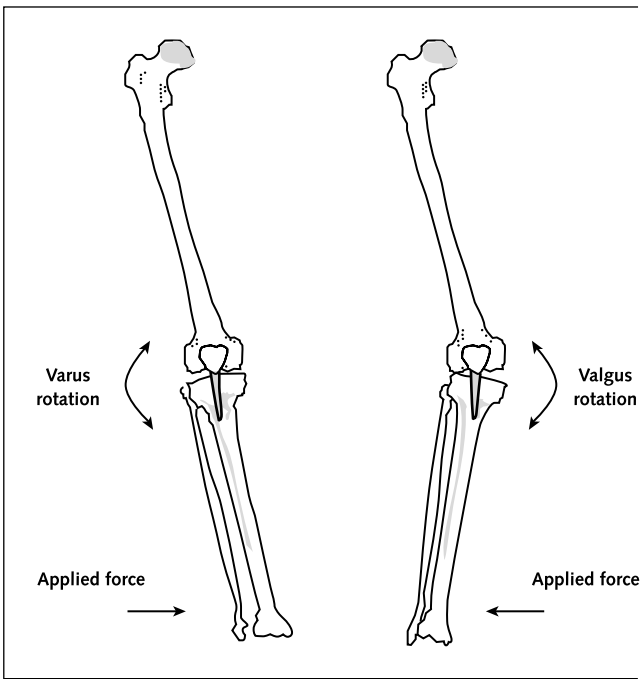
Overloading the knee and hip joints could lead to cartilage breakdown and failure of ligamentous and other structural support. For each 1-lb increase in weight, the overall force across the knee in a single-leg stance increases 2 to 3 lb. This load effect probably explains most of the increased risk for osteoarthritis of the knee and hip among overweight persons. A few (56, 57) but not most studies have reported an association of obesity with hand osteoarthritis, suggesting that a metabolic intermediary (such as diabetes or lipid abnormalities) may account in part for this potent relationship, but no such intermediary has been found.

Table 2. **Relationship of Weight and Incident Knee Osteoarthritis on Radiography in Male and Female Participants in the Framingham Osteoarthritis Study***

Risk Factor	Odds Ratio for Incident Knee Osteoarthritis (95% CI)†	
	Men	Women
Age (per 5-year stratum)	0.9 (0.5–1.6)	1.3 (0.9–1.7)
Body mass index (per 5-unit stratum)	1.0 (0.5–2.1)	1.8 (1.2–2.6)
Weight change (per 10-lb stratum)	0.9 (0.5–1.5)	1.6 (1.2–2.3)

* Data from reference 51. Twenty-four of 217 men and 69 of 381 women developed incident osteoarthritis.
† Adjusted simultaneously for age, body mass index, weight change, cigarette smoking, knee injury, chondrocalcinosis, prevalent hand osteoarthritis, and physical activity.

Figure 3. **Direction of force application and the resulting motion at the knee in the determination of varus–valgus laxity in the right lower extremity.**



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The effect of obesity on osteoarthritis is made more portentous because obesity is a serious and growing public health problem in the United States. According to NIH clinical guidelines (58), approximately 25% of women and 20% of men in the United States are obese, with a body mass index of 30 kg/m^2 or greater (59), a figure that has increased more than 50% in the past 10 to 15 years (58). The prevalence of obesity is even higher in some ethnic minority populations, particularly African-American, Hispanic, and Native American women. For example, more than 10% of African-American women 40 to 59 years of age have severe obesity (body mass index $\geq$ 40 kg/m^2).

Mechanical Environment of the Joint

Certain alterations in the mechanical environment of the joint adversely affect load distribution. The study of mechanical factors is complicated by the fact that they may be altered further by disease. Although longitudinal studies are under way, currently available information in knee osteoarthritis is based on cross-sectional studies.

Knee laxity is displacement or rotation of the tibia with respect to the femur. Frontal plane or varus–valgus laxity (**Figure 3**) increases with age and is greater in women than men (61). Furthermore, varus–valgus laxity is greater in the nonarthritic knees of patients with idiopathic disease than in the knees of controls, suggesting that a portion of the increased laxity of knee osteoarthritis precedes disease development and may predispose to disease (61). Sagittal plane or anterior–posterior laxity may be increased in persons with mild osteoarthritis (62, 63). Anterior–posterior laxity appears to decline with increasing severity of knee osteoarthritis (62, 63).

Proprioception is the conscious and unconscious perception of joint position and movement. Proprioception is critical to the maintenance of joint stability under dynamic conditions. Proprioceptive accuracy at the knee declines with age (64) and is especially limited in sedentary elderly persons (65). In the arthritic or nonarthritic knees of patients with osteoarthritis, proprioceptive accuracy was worse than that in age-matched controls, suggesting that this deficit precedes disease development (66).

Knee alignment is knee position in reference to the hip and ankle. Malalignment predicts worse surgical outcomes, but its role in the natural history of osteoarthritis has been minimally considered. The magnitude of the torque that adducts the knee during the stance phase of gait correlates with disease severity in knee osteoarthritis (67) and may predict the natural rate of disease progression.

Loading of Articular Cartilage

Normal articular cartilage has a unique load-support mechanism governed by its high water content and the stiffness and permeability of its collagen–proteoglycan matrix (68). Interstitial fluid pressurization during loading contributes more than 90% of the load support, shielding the collagen–proteoglycan matrix from excessive stresses and reducing friction at the articular surfaces (69–71). Pathologic changes in cartilage composition and molecular organization plus elevated water content alter the exquisite balance of biomechanical properties and joint loads, causing excessive cartilage deformation (72–76). In human cadaver studies of the thumb trapeziometacarpal joint, which is often affected by osteoarthritis, reductions in cartilage compressive stiffness were found to correlate linearly with increasing stages of disease, making change in stiffness one of the earliest manifestations of osteoarthritis. Cartilage erosion, a cardinal pathologic feature of osteoarthritis, does

not appear until cartilage has lost considerable stiffness (77). Furthermore, although stiffness of normal thumb joint cartilage is the same in men and women, it decreases faster with disease in women (77); this effect may be related to sex-based differences in articular stresses (78).

Acute Joint Injury and Joint Deformity

Joint dysplasias, fractures of articular surfaces, and tears of menisci and ligaments that increase joint instability precede the development of osteoarthritis in a high percentage of affected joints (79–82). The most extensively studied form of joint dysplasia, developmental dysplasia of the hip, consists of failure of the acetabulum in the pelvis to assume normal concavity. Studies of patients with this disorder have demonstrated a strong correlation between greater articular surface contact stress due to abnormal acetabular shape and development of hip joint degeneration (81, 82). These observations suggest that cumulative articular surface contact stress above a critical threshold causes joint degeneration and that decreasing joint contact stress in dysplastic joints could prevent or delay disease development.

In addition, experimental work has demonstrated that articular surface incongruities greater than 3 mm increase local contact stress (83, 84). Articular surface incongruities due to fractures in the cartilage surface have potential for remodeling and thereby decreasing the elevated contact stress (85, 86), but the variables that affect these processes have not been well defined. Although the relationships between acute joint trauma and development of post-traumatic osteoarthritis remain poorly understood, it is clear that articular surface fractures, joint dislocations, and ligament and meniscal ruptures increase the risk for later osteoarthritis (79, 80, 87). Apparent risk factors for post-traumatic osteoarthritis include high body mass, high level of activity, residual joint instability or malalignment, and persistent articular surface incongruity (79, 80).

Occupational Factors

Jobs in which workers do repetitious tasks, overworking the joints and fatiguing muscles that protect the joints, increase the risk for osteoarthritis in those joints. In a Virginia textile mill, female workers whose jobs required repeated pincer grip motions (pinching the thumb and index or middle finger together to hold something) had a much higher rate of osteoarthritis in the distal interphalangeal joints than did other female workers (88). Other studies have shown that workers whose jobs involve physical labor have high rates of knee osteoarthritis (89). Farmers have high rates of hip osteoarthritis (90). When specific job tasks were examined, jobs requiring kneeling or squatting along with heavy lifting were associated with especially high rates of both knee and hip osteoarthritis. Forces across the knee increase in the crouching or squatting position; lifting loads from such a position further increases loading. Turning while doing this provides additional torsional stress. Data from the Framingham Study suggest that such job activities cause anywhere from 15% to 30% of knee osteoarthritis in men (89). Other occupational activities, including climbing stairs, walking on uneven ground, standing, and sitting, have been inconsistently linked to osteoarthritis risk (90). Because so much of osteoarthritis in men is attributable to occupational activities, identification of the particular ergonomic activities that damage joints provides an opportunity to modify or prevent disease.

Sports Participation

Epidemiologic studies have demonstrated that participation in certain competitive sports increases the risk for osteoarthritis (79, 91, 92). Moderate regular running has low, if any, risk of leading to osteoarthritis (93–95). Sports activities that appear to increase the risk for osteoarthritis include those that demand high-intensity, acute, direct joint impact as a result of contact with other participants, playing surfaces, or equipment (79). Examples include injuries to the knees and necks of U.S. football players and the knees of soccer players. Repetitive joint impact and torsional loading (twisting) also appear to be associated with joint degeneration, as seen in the elbows of baseball pitchers and the knees of soccer players (79, 91). Efforts to decrease the risk for osteoarthritis in sports participants should include careful preparticipation evaluation of individual risk factors and counseling based on these evaluations; modification of rules to decrease direct player contact and high-intensity joint torsional and impact loading; use of equipment, including braces, pads, shoes, and playing surfaces that decrease joint impact loading; and training that improves joint dynamic stability. In addition, early diagnosis and effective treatment of joint injuries and ensuring complete rehabilitation after joint injury should decrease the risk for osteoarthritis among sports participants.

Table 3. **Quadriceps Weakness and Development of Knee Osteoarthritis***

Characteristic	Baseline Mean Peak Quadriceps Strength, *lb-ft*	Baseline Mean Peak Quadriceps Strength, per kg of Body Weight
Women		
No osteoarthritis at baseline or follow-up (n = 214)	36.9	0.57
Incident osteoarthritis at follow-up (n = 14)	33.4	0.47†
Men		
No osteoarthritis at baseline or follow-up (n = 224)	53.2	0.65
Incident osteoarthritis at follow-up (n = 18)	51.8	0.61

* Data from reference 94.
† $P = 0.053$ compared with no osteoarthritis at follow-up.

Muscle Weakness

It is well recognized that quadriceps muscle weakness is common in patients with osteoarthritis of the knee. Quadriceps muscle weakness in these patients has generally been ascribed to disuse atrophy, which is presumed to develop because the patient minimizes use of the painful limb. However, quadriceps weakness also exists in persons with knee osteoarthritis who have no history of joint pain and in whom quadriceps muscle mass is not diminished but is normal or even increased (because of obesity).

When the presence of knee osteoarthritis (based on radiographic changes with or without knee pain) as a function of sex, body weight, age, and lower-extremity strength was modeled, each 10–lb-ft increase in knee extensor strength was associated with a 20% reduction in the odds of prevalent radiographic disease and a 29% reduction in the odds of symptomatic knee osteoarthritis. A relatively small increase in strength (approximately 20% of the mean for men and 25% for women) was predicted to result in a 20% to 30% decrease in the odds of having osteoarthritis of the knee (96).

Furthermore, longitudinal studies suggest that quadriceps muscle weakness not only results from painful knee osteoarthritis but also is itself a risk factor for structural damage to the joint (97, 98). Among women with no radiographic evidence of knee osteoarthritis at initial examination who showed definite osteoarthritic changes on radiographs obtained 30 months later, baseline knee extensor strength was lower than that in women who did not have osteoarthritic changes ($P = 0.053$) (97) (**Table 3**), regardless of whether knee extensor was adjusted for body weight or for the amount of muscle mass in the lower extremity. However, this effect was not found for hamstring strength.

Osteoarthritis and Physical Disability

Dr. Leena Sharma (Northwestern University) and Dr. James F. Fries (Stanford University School of Medicine, Palo Alto, California): The impact of osteoarthritis on disability is substantial. For example, the risk for disability (defined as needing help walking or climbing stairs) attributable to osteoarthritis of the knee is as great as that attributable to cardiovascular disease and greater than that due to any other medical condition in elderly persons (99). In a study by Guccione and associates (100), the presence of radiographic knee osteoarthritis, even in the absence of symptoms, increased the risk for dependence on others in performing daily activities. The presence of coexistent chronic conditions further increases the likelihood of subsequent disability (101).

Current insights about disease and personal factors associated with a high risk for physical disability are based chiefly on cross-sectional studies. Factors linked to disability in patients with osteoarthritis include pain (96, 101–107); psychosocial factors, such as depressive symptoms (104, 105, 108–111); muscle weakness (60, 104–106, 112, 113); poor aerobic capacity (104); and, in some studies, radiographic disease severity (114). A better understanding of the causes of disability in osteoarthritis will facilitate the development of preventive strategies. The disease–disability relationship in osteoarthritis has been examined by using conventional radiography. Examination of specific anatomic and physiologic features of osteoarthritis, many of which are not revealed by radiography, may better elucidate the role of disease events in functional decline (114).

It is important to separate conceptually the disease process of osteoarthritis and the syndrome of musculoskeletal pain and disability; the two are only weakly correlated (111). Whereas osteoarthritis is associated with increasing age, obesity, injury, previous deformity, and ligamentous laxity, the broader clinical problem of musculoskeletal pain and disability is predicted by increasing age; osteoarthritis; obesity; lack of exercise; low personal self-efficacy; comorbid conditions caused by smoking, alcohol, and other risk factors; depression; low educational level; and poor socioeconomic status (115, 116). Many of these risk factors for musculoskeletal pain and disability can be altered.

Preventing or delaying the onset of osteoarthritis involves lifestyle changes that may prevent the broader clinical problems of musculoskeletal disability. If the average age at first chronic disability could be substantially postponed, morbidity could be compressed into a shorter period (116, 117). A consortium of federal and not-for-profit organizations has undertaken a large-scale effort, called the National Arthritis Action Plan: A Public Health Strategy, to focus on preventing arthritis and its associated disability (118). Reduction of total lifetime disability is among our leading health priorities in the United States (119, 120).

From Boston University School of Medicine, Boston, Massachusetts; National Institute of Arthritis and Musculoskeletal and Skin Diseases and National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, Maryland; MRC Health Services Research Collaboration, University of Bristol, Bristol, United Kingdom; Centers for Disease Control and Prevention, Atlanta, Georgia; University of North Carolina at Chapel Hill, Chapel Hill, North Carolina; University of California, San Francisco, San Francisco, and Stanford University School of Medicine, Palo Alto, California; University of Michigan, Ann Arbor, Michigan; St. Thomas' Hospital, London, United Kingdom; Shriners Hospital for Children and McGill University, Montreal, Quebec, Canada; Columbia University, New York, New York; Northwestern University, Chicago, Illinois; University of Iowa Hospitals, Iowa City, Iowa; and Indiana University School of Medicine, Indianapolis, Indiana.

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Requests for Single Reprints: Reva C. Lawrence, MPH, National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health, Building 45, Room 5AS-37G, Bethesda, MD 20892-6500.

Current Author Addresses: Drs. Felson and McAlindon: Boston University School of Medicine, 715 Albany Street, Room A203, Boston, MA 02118.

Ms. Lawrence: National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health, Building 45, Room 5AS-37G, Bethesda, MD 20892-6500.

Dr. Dieppe: MRC Health Services Research Collaboration, University of Bristol, Canynge Hall, Whiteladies Road, Bristol BS8 2PR, United Kingdom.

Dr. Hirsch: Division of Health Examination Statistics, National Center for Health Statistics, Centers for Disease Control and Prevention, 6525 Belcrest Road, Presidential Building, Room 900, Hyattsville, MD 20782.

Dr. Helmick: National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, 4770 Burford Highway, NE, MS K45, Atlanta, GA 30341.

Dr. Jordan: Thurston Arthritis Research Center, University of North Carolina, 3310 Thurston Building, CB 7330, Chapel Hill, NC 27599-7330.

Dr. Kington: Division of Health Examination Statistics, National Center for Health Statistics, Centers for Disease Control and Prevention, 6525 Belcrest Road, Presidential Building, Room 1000, Hyattsville, MD 20782.

Dr. Lane: Division of Rheumatology, University of California at San Francisco, 1001 Potrero Avenue, Building 30, Room 3300, San Francisco, CA 94110.

Dr. Nevitt: Department of Epidemiology and Biostatistics, University of California at San Francisco, 74 New Montgomery Street, Suite 600, San Francisco, CA 94105.

Dr. Zhang: Arthritis Center, Boston University School of Medicine, 80 East Concord Street, Room A203, Boston, MA 02115.

Dr. Sowers: University of Michigan, 109 S. Observatory, Ann Arbor, MI 48109-2029.

Dr. Spector: Twin Research and Genetic Epidemiology Unit, St. Thomas' Hospital, London SE1 7EH, United Kingdom.

Dr. Poole: Joint Diseases Laboratory, Shriners Hospitals for Children and Department of Surgery, McGill University, 1529 Cedar Avenue, Montreal, Quebec H3G1A6, Canada.

Dr. Yanovski: National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, 45 Center Drive, Room 6AN18B, Bethesda, MD 20892-6600.

Dr. Ateshian: Orthopedic Research Laboratories, Columbia University, Black Building 1412, 630 West 168th Street, New York, NY 10032.

Dr. Sharma: Northwestern University, 303 East Chicago Avenue, Ward Building 3-315, Chicago, IL 60611.

Dr. Buckwalter: Department of Orthopaedics, University of Iowa Hospitals, 200 Hawkins Drive, Room 01013JPP, Iowa City, IA 52242.

Dr. Brandt: Rheumatology Division, Indiana University School of Medicine, 541 Clinical Drive, Room 492, Indianapolis, IN 46202.

Dr. Fries: Stanford University School of Medicine, 1000 Welch Road, Suite 203, Palo Alto, CA 94304-5755.

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