

Epidemiology and burden of osteoarthritis

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Background: Osteoarthritis (OA) is a degenerative joint disease involving the cartilage and many of its surrounding tissues. Disease progression is usually slow but can ultimately lead to joint failure with pain and disability. OA of the hips and knees tends to cause the greatest burden to the population as pain and stiffness in these large weight-bearing joints often leads to significant disability requiring surgical intervention.

Sources of data: The article reviews the existing data on epidemiology of osteoarthritis and the burden of the disease.

Areas of agreement: Symptoms and radiographic changes are poorly correlated in OA. Established risk factors include obesity, local trauma and occupation. The burden of OA is physical, psychological and socioeconomic.

Areas of controversy: Available data does not allow definite conclusion regarding the roles of nutrition, smoking and sarcopenia as risk factors for developing OA.

Growing points: Variable methods of diagnosing osteoarthritis have significantly influenced the comparability of the available literature.

Areas timely for developing research: Further research is required to fully understand how OA affects an individual physically and psychologically, and to determine their healthcare need.

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Introduction

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Osteoarthritis (OA) is a common, debilitating disease which is associated with a large societal and economic burden, in addition to the physical and psychological sequelae it often manifests in the affected individual. OA has been characterized in various ways in the literature ranging from subjective assessments to clinical and radiographic definitions, often with low levels of concordance between them. This can have profound effects on the resultant epidemiology and risk factors identified. Several risk factors for OA have been firmly identified but there is still debate in

other areas. Whatever the cause, the significant burden of OA is not in question. The effect that this disease has on a given individual does however vary and the level of disability that develops has been found to depend on several factors. This review will discuss the issue of how best to define OA; its epidemiology in the hand, knee and hips joints; risk factors for its development and progression and the burden of disease along with factors that may modulate this.

Definition and classification

OA is a degenerative joint disease involving the cartilage and many of its surrounding tissues. In addition to damage and loss of articular cartilage, there is remodelling of subarticular bone, osteophyte formation, ligamentous laxity, weakening of periarticular muscles and, in some cases, synovial inflammation.¹ These changes may occur as a result of an imbalance in the equilibrium between the breakdown and repair of the joint tissue. Primary symptoms of OA include joint pain, stiffness and limitation of movement. Disease progression is usually slow but can ultimately lead to joint failure with pain and disability.

OA can be defined as radiological, clinical or subjective. There have been many attempts to accurately identify and grade radiographic disease in OA and it is most widely assessed in studies using the Kellgren and Lawrence (K&L) score. The overall grades of severity are determined from 0 to 4 and are related to the presumed sequential appearance of osteophytes, joint space loss, sclerosis and cysts.² The World Health Organization (WHO) adopted these criteria as the standard for epidemiological studies on OA. Cross-sectional imaging methods, such as magnetic resonance imaging (MRI), can visualize joint structures in more detail and continue to undergo evaluation to determine if they will provide a means by which the definition of OA can be refined.

Clinical OA is defined by features in the history and on examination. It invariably requires the presence of joint pain in addition to other features. Some of the most well recognized standards for the diagnosis of clinical OA are the American College of Rheumatology (ACR) criteria. These have been developed for the hip³, knee⁴ and hand.⁵ Subjective OA relies on the assessment of the patient as to whether or not the disease is present. Interestingly, individuals with early painful OA may be free from radiographic changes and, conversely, those with severe radiographic changes may be entirely asymptomatic. There is a correlation between the severity of radiographic disease and symptoms; however, the association is not strong.⁶

The explanation for this poor concordance may be first, that some of the structures within the joint imaged on radiographs do not have a nociceptive innervation and secondly, the experience of pain is more

complicated than purely a response to structural change, with other factors such as psychological aspects also playing a role. The diagnosis of symptomatic radiographic OA has been developed to take into consideration both structural change and joint pain or discomfort.

Epidemiology

OA may develop in any joint, but most commonly affects the knees, hips, hands, facet joints and feet. In 2005, it was estimated that over 26 million people in the USA had some form of OA.⁷ The prevalence of OA, however, varies greatly depending on the definition used, age, sex and geographical area studied. A radiographic case definition of OA results in the highest reported prevalence. The prevalence of radiographic osteoarthritis of the hand, hip and knee in the Dutch population is shown in Figure 1.⁸ The incidence of hand, hip and knee OA increases with age, and women have higher rates than men, especially after the age of 50 years. A levelling off or decline occurs at all joint sites around the age of 80 years. The age- and sex-standardized incidence rate from the Fallon Community Health Plan in Massachusetts (USA) was highest for knee OA 240/100 000 person-years, with intermediate rates for hand OA (100/100000 person-years) and lowest observed rates for hip OA (88/100000 person-years) (Fig. 2).⁹ Incidence rates found by the Dutch Institute for Public Health (RIVM) in 2000 were of a similar level. For hip OA, the reported prevalence was 0.9 and 1.6 per 1000 per year in men and women, respectively, and for knee OA

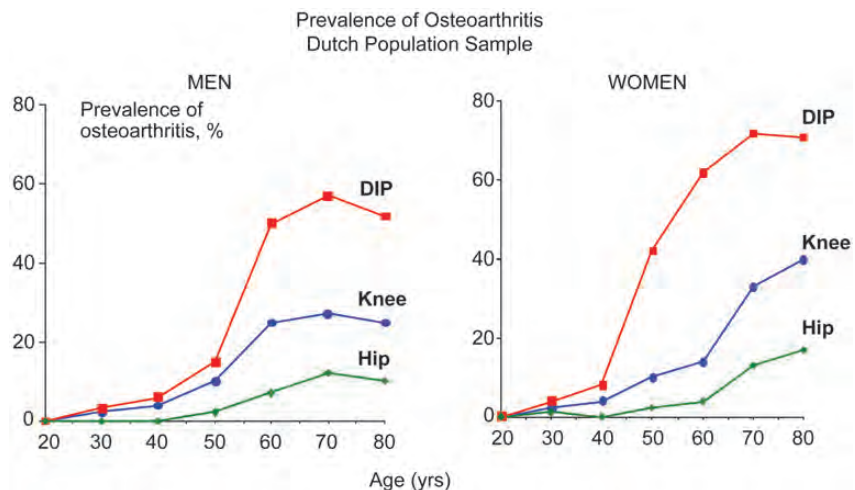


Fig. 1 Prevalence of radiographic osteoarthritis of the hand, hip and knee. (Reproduced from van Saase *et al.*⁸ with permission from BMJ Publishing Group Ltd).

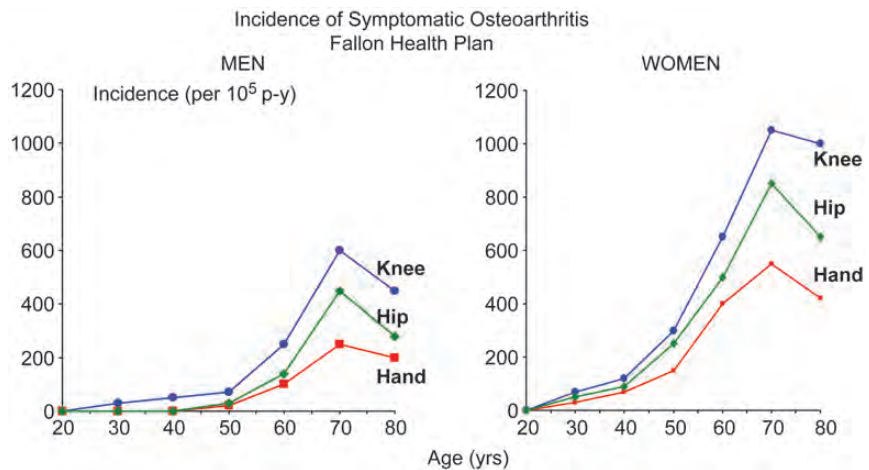


Fig. 2 Incidence of clinical osteoarthritis of the hand, knee and hip. (Reproduced from Oliveria *et al.*⁹ with permission from John Wiley and Sons).

the corresponding figures were 1.18 and 2.8 per 1000 per year in men and women, respectively.¹⁰

Hand OA

The prevalence of radiographic hand OA varies greatly and has been reported to range from 27 to over 80%.⁷ In a study from the Netherlands, 75% of women age 60–70 years had evidence of OA in the distal interphalangeal (DIP) joints, and 10–20% of subjects aged <40 years were reported to have OA radiological changes in their hands or feet.⁸ Data from the Framingham cohort demonstrated a prevalence of 13.2% in men and 26.2% in women aged 70 or more years with at least one hand joint with symptomatic osteoarthritis.¹¹ In a rural Turkish sample,¹² all males over the age of 65 years had at least one affected hand joint.

Symptomatic hand OA, as defined by the ACR criteria, is however far less common. Its prevalence was found to be 8% in the USA National Health and Nutrition Examination Survey (NHANES III) and 7% in the Framingham cohort. Rates increased among elderly subjects to 13 and 26% for men and women, respectively. A study from Teheran showed that the prevalence of hand OA in people aged 40–50 years was 2.2%, rising with age to 22.5% in people aged >70 years.¹³ As with many studies, including the Framingham cohort, differentiation by gender in this population showed that women were more frequently affected than men.¹³ Interestingly, data from China based on 13 surveys involving 29 621 adults demonstrated that symptomatic OA of the hand was rarely observed irrespective of age or gender.¹⁴

Knee OA

Knee involvement occurs less frequently than hand OA, although similarly it is more common in women, with female-to-male ratios varying between 1.5:1 and 4:1. Prevalence rates for knee OA, based on population studies in the USA, are comparable to those in Europe. These studies report that severe radiographic changes affect 1% of people aged 25–34 and this figure increases to nearly 50% in those 75 years and above. Among participants aged over 45 years in the Framingham Study, the prevalence of radiographic knee OA was 19.2% and, in those over 80 years, the figure rose to 43.7%. According to data produced by the Dutch Institute for Public Health, the prevalence of knee OA in those aged 55 and above was 15.6% in men and 30.5% in women.¹⁰ The prevalence of symptomatic knee OA is significantly lower: just 12.1% in NHANES III and 16.3% in participants aged 55–64 of Johnston County Osteoarthritis Project.¹⁵

Geographical variation in OA epidemiology also exists. Studies from China, which used similar methods and definitions to the Framingham Study, found that the prevalence of bilateral knee OA and lateral compartment disease were two to three times higher in Chinese cohorts compared with estimates from the Framingham OA study.¹⁶ Data on clinically diagnosed knee OA in the Community Oriented Program for Control of Rheumatic Disorders (COPCORD) studies in the Asian region showed that the prevalence within this area ranged from 1.4% in urban Filipinos to 19.3% in rural communities in Iran.¹⁷ Part of the reason for this difference could have been the physical and socio-economic environment. The COPCORD studies conducted in India, Bangladesh and Pakistan looked specifically into differences between rural and urban populations. In India the crude prevalence of clinically diagnosed knee OA was higher in the urban (5.5%) than those in the rural community (3.3%). After adjusting for age and sex distribution, the prevalence was higher in rural communities.¹⁷ Furthermore, in China, men aged 60 and above from a rural community demonstrated approximately double the prevalence of symptomatic knee OA when compared with their urban counterparts.¹⁶

Hip OA

Hip OA is less common than either hand or knee OA. The mean prevalence of primary radiographic hip OA in studies from Asia and Africa is 1.4 and 2.8%, respectively. These levels are much lower than those seen in Europe and North America, where the mean prevalence is 10.1 and 7.2%, respectively.¹⁸ In the Study of Osteoporotic Fractures, the

prevalence of radiographic hip OA was analysed, in women over the age of 65, using 11 different definitions. Excluding the definition of minimum joint space of <2.5 mm, the prevalence ranged from 1.8 to 9.4% depending on the definition used.¹⁹ This compares to a prevalence of symptomatic hip OA, from the analysis of the Johnston County group, of 5.9% in adults aged 45–54 to 17% in subjects aged 75 and above.²⁰

Risk factors

The risk of developing OA is determined by both systemic and local factors. Several systemic factors have been identified; these may act by increasing the susceptibility of joints to injury, by direct damage to joint tissues or by impairing the process of repair in damaged joint tissue. Local factors are most commonly biomechanical in nature and adversely affect the forces applied to the joint. A number of specific risk factors have been identified including obesity and metabolic disease, age, sex, ethnicity and race, genetics, nutrition, smoking, bone density and muscle function. The joint-specific effects of these factors have been summarized in Table 1 and some of them are discussed in greater detail below. Although several risk factors for the development of OA have been identified, far fewer have been associated with OA progression. It might be expected that factors that promote the onset of a disease might also hasten its progression; however, evidence for these relationships is often lacking. OA usually progresses slowly over many years. Figure 3 demonstrates radiographic knee OA progression over 15 years in persons with grade 0 and grade 1 K + L scores at baseline, observed in the Chingford women's study of OA and osteoporosis.

Table 1 Risk factors for development of osteoarthritis

| Risk factor | Hip OA | Knee OA | Hand OA |
|---------------------------|--------|---------|---------|
| Obesity | (+) | + | (+) |
| Age | + | + | + |
| Female sex | (+) | + | + |
| Ethnicity (vs. Caucasian) | | | |
| Chinese | – | + | – |
| Genotype | + | + | + |
| Bone mineral density | + | + | + |
| Smoking | | | |
| Muscle | | | |
| Grip strength | | | + |
| Quadriceps strength | | (–) | |

+, good evidence increases risk; (+), weak evidence increases risk; blank, inconsistent or no evidence of increased risk; (–), weak evidence of protective effect; –, good evidence of protective effect.

Obesity and metabolic disease

Obesity is one of the strongest and best-established risk factors of OA. The current literature suggests that, although both show associations in studies, the relationship between obesity (BMI >30) and hip OA is weaker than with knee OA (odds ratio (OR) 2.81; 95% confidence interval (CI): 1.32–5.96).²¹ Recent data suggest that OA is associated with the metabolic syndrome, suggesting a possible common pathogenic mechanism involving metabolic abnormalities and systemic inflammation. In a study using the NHANES III data, there was a 5.26-fold increased risk of metabolic syndrome in those individuals with OA at the age of 43.8 years (mean age of study population).²²

It is also likely that vascular disease may both initiate and hasten disease progression in OA. This could be due to venous occlusion, stasis or microemboli leading to episodic reduction in blood flow through small vessels within the subchondral bone. Subchondral ischaemia may subsequently reduce nutrient delivery and gas exchange to articular cartilage in addition to direct deleterious effects on the bone itself. Furthermore, individuals with osteoarthritis are at greater risk of physical inactivity and the use of analgesic medication, such as NSAIDs, that increases the risk of cardiovascular disease. This may further explain the association between these two conditions.

Studies have also suggested significant associations between OA and cardiovascular risk factors, such as hypertension and cholesterol

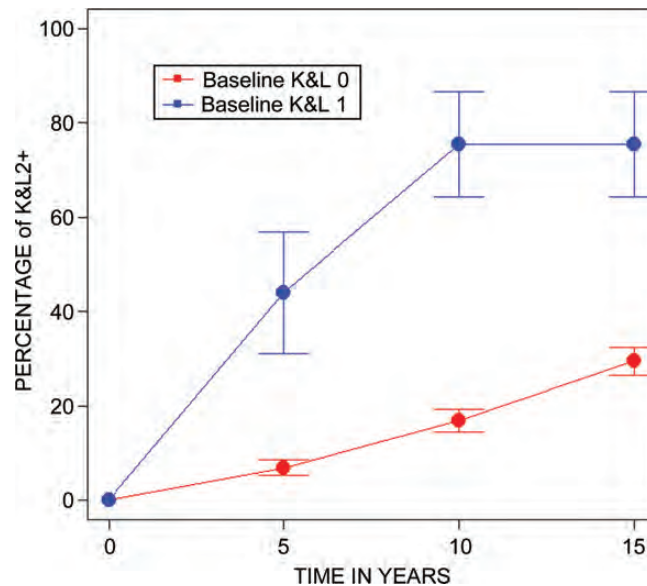


Fig. 3 Long-term progression of radiographic knee osteoarthritis. (Reproduced from Leyland *et al.*²³ with permission from John Wiley and Sons).

levels.²² However, clinical evidence of an association between diabetes and OA is inconsistent. Several studies did find an association between diabetes and OA²⁴ and fascinating hypotheses explaining this association have been suggested, including that high glucose concentration produces reactive oxygen species and advanced glycation end-products which induce cartilage degeneration and degradation. Other studies failed to confirm the association and further research is required.

Age

The prevalence and incidence of radiographic and symptomatic OA considerably increase with age.^{18,19} The relationship between age and the risk of OA is likely multifactorial, as a consequence of numerous individual factors; these include oxidative damage, thinning of cartilage, muscle weakening and a reduction in proprioception. Furthermore, basic cellular mechanisms that maintain tissue homeostasis decline with aging, leading to an inadequate response to stress or joint injury and resultant joint tissue destruction and loss.

Sex

The incidence of knee, hip and hand OA is higher in women than men and in women it increases dramatically around the time of menopause.²⁵ The latter finding has led investigators to hypothesize that hormonal factors may play a role in the development of OA, but the results of clinical and epidemiologic studies have not universally corroborated this.^{26–28} Some have shown a protective effect for oestrogen or hormone replacement therapy on radiographic knee and hip OA²⁶ or progression to joint replacement.²⁷ However, a recent systematic review of 16 studies found that there was no clear association between sex hormones and radiographic hand, knee or hip OA in women, although single analysis of the studies was not possible due to study heterogeneity.²⁸

Ethnicity and race

The prevalence of OA and patterns of joint involvement vary among different racial and ethnic groups. Both radiographic hip and hand OA were much less frequent among Chinese in the Beijing Osteoarthritis Study than in whites in the Framingham Study, but interestingly Chinese women had a higher prevalence of radiographic knee OA (prevalence ratio 1.45, 95% CI: 1.31–1.60) and symptomatic knee OA (prevalence ratio 1.43, 95% CI: 1.16–1.75), which may be explained by excessive knee loading from squatting.²⁹ Results from the Johnston

County Osteoarthritis Project have shown that the prevalence of radiographic hip OA in African American women was similar to that in white women, but that the prevalence was slightly higher in African American men than that in white men (21 and 17%, respectively).³⁰

Smoking

There have been conflicting reports on the role of smoking in OA. Some studies have reported a protective association between smoking and OA, but others in contrast, report that smoking may be associated with a greater risk both of cartilage loss and knee pain in OA. A recent meta-analysis of observational studies concluded that the protective effect of smoking in OA development (OR: 0.87; 95% CI: 0.80–0.94) observed is likely to be false.³¹ It may be caused by selection bias, as many studies have been conducted in a hospital setting where control subjects have smoking-related conditions, and subjects are recruited as part of studies that are not primarily designed to investigate smoking.³¹

Osteoporosis

Osteoporosis is, like OA, a common age-related skeletal disorder. While early results indicated the presence of reduced bone mineral density (BMD) might be protective against OA, further studies have been inconsistent with these findings. A systematic review and meta-analysis of the risk factors for the onset of osteoarthritis of the knee, defined by self-report or radiology, has shown in older adults that there is a consistent strong association between increased BMD and the onset of knee OA in the three studies that investigated this risk factor in women.³² Although a definite molecular basis and common pathophysiology has not been identified to explain the inverse relationship between OA and osteoporosis, a shared genetic component may explain why they seldom coexist.

Sarcopenia

Muscle weakness may be an important risk factor for knee OA. Men and women with pre-existing radiographic evidence of knee OA have been identified as having weaker quadriceps than those without OA, particularly when the joints are symptomatic.³³ It is likely that knee OA will in itself lead to quadriceps weakness due to disuse atrophy. It has been shown however that weakness can also be found around knees in the absence of pain or muscle atrophy. This may be due to arthrogenous inhibition of muscle contraction.³³ One consequence of

quadriceps weakness is that the knee becomes less stable during physical activity. It is hypothesized, therefore, that quadriceps exercises may offer some protective advantage to patients involved in activities that are known to be associated with a high risk of OA. Interestingly, studies that have investigated this issue have found either no effect³⁴ or, in those with biomechanical compromise, the converse effect with muscle strength hastening progression.³⁵

Greater muscle strength is not always protective as it corresponds to higher forces and thus increased joint loading during activity. It has been shown that higher grip strength in men is associated with a greater risk of developing incident radiographic OA in the proximal interphalangeal, metacarpophalangeal and the first carpometacarpal joints (highest tertile OR: 2.8, 95% CI: 1.1–7.4); the joints subjected to the largest forces during grip.³⁶

Local mechanical risk factors

A traumatic knee injury is one of the strongest risk factors for the development of knee OA. Acute injuries, including meniscal and cruciate tears, fractures and dislocations, can result in an increased risk of OA development and musculoskeletal symptoms. In addition to the direct damage of local tissues by the trauma, disruption of normal biomechanics and altered load distribution within the joint also contribute to the subsequent increased OA risk. This risk is greater still if the subject has OA in another joint.

Repetitive and excessive joint loading, that accompanies specific physical activities, increases the risk of developing OA in the involved joints. Workers whose jobs required repeated pincer grip have increased the risk of radiographic hand OA, particularly in the DIP joint.³⁷ Prolonged squatting and kneeling stresses the larger joints and is consequently associated with increased risk of moderate-to-severe radiographic knee OA.²⁹

There have been conflicting results in studies examining the relationship between sporting activities and subsequent OA. There is some evidence that elite long-distance runners are at high risk of developing knee and hip OA.³⁸ Other studies suggest that in the absence of joint injury, moderate recreational running and sports participation do not appear to increase the risk of developing radiographic hip or knee OA.³⁹

The mechanical alignment of the knee influences the distribution of load across the articular surfaces. In a normally aligned knee, 60–70% of weight-bearing load is transmitted through the medial compartment. Any shift in either a valgus or varus direction affects load distribution. Abnormal increases in compartmental loading are thought to increase stress on the articular cartilage, and other joint structures, subsequently

leading to degenerative change. A systematic review confirmed that knee malalignment is an independent risk factor for the progression of radiographic knee OA.⁴⁰

Burden of disease

OA of the hips and knees tends to cause the greatest burden to the population as pain and stiffness in these large weight-bearing joints often leads to significant disability requiring surgical intervention.⁹ Age- and sex-specific incidence rates of total knee arthroplasty are presented in Fig. 4.⁴¹ A considerable literature also exists relating OA, joint pain and physical function in older adults. In one such example, a prospective cohort study of 3907 people aged over 50 years and registered with three general practices in North Staffordshire was carried out. The main outcome measures were self-reported knee pain, general health and physical function as measured by the Short Form 36. The onset of knee pain was associated with a substantial and persistent reduction in physical function in these community-living older adults.⁴² OA in the ageing population most commonly affects the hand joints and, even though the symptoms are often less disabling than when the knee or hip joints are involved, it can still significantly interfere with hand function. This may have effects on an individual's ability to perform their normal activities of daily living.

The burden of OA not only includes physical problems but it also has detrimental psychological effects. Psychological distress is more frequently

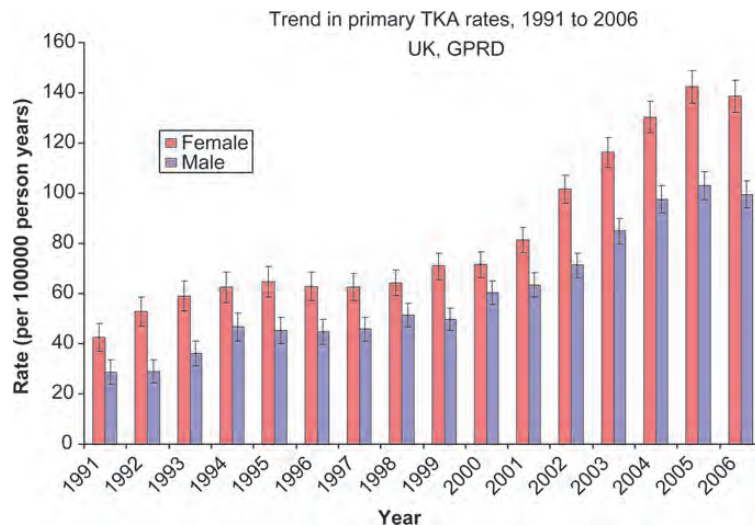


Fig. 4 Age- and sex-specific incidence rates of total knee arthroplasty. (Reproduced from Culliford *et al.*⁴¹ with permission and copyright © of the British Editorial Society of Bone and Joint Surgery)

experienced by patients with OA compared with patients with other chronic diseases such as diabetes.⁴³ OA patients on a waiting list for arthroplasty scored much lower on physical components of quality of life scores than both healthy controls and heart failure patients.⁴⁴

Predictors of disease burden

It is possible to predict to some extent which patients with OA are likely to be more disabled by the disease in the future. It has been found that, in knee OA, factors associated with poorer physical function, assessed by WOMAC and chair stands, after 3 years include age, BMI, knee pain intensity at baseline, joint laxity and proprioceptive inaccuracy.⁴⁵ Pain and quadriceps weakness have also been shown to be important; both were greater determinants of disability than radiographic change in a study of community-dwelling older adults. A subsequent study confirmed the importance of body habitus and knee strength and also found self-efficacy to be an important predictor. Together these findings suggest that those with dynapenic obesity—a combination of overweight/obesity and low muscle strength—might be at particular risk.

Riddle *et al.*⁴⁶ investigated the effect of psychological health on changes in pain and physical function in OA. They found that the most consistent psychological predictor of progressive worsening was baseline depressive symptoms. Although this was a statistically robust predictor of outcome, given that the changes were very small and highly dependent on baseline status, the results indicated that a considerable degree of persistent depressive symptoms would be required to have a meaningful effect on future outcome. Further psychological factors such as self-efficacy and social support also appear to be protective against a poor functional outcome. Healthcare utilization leads to the main societal burden of OA. However, there is little evidence available describing the factors which influence how much care an individual will access.

The effect of joint surgery on disease burden

Arthroplasty for the management of osteoarthritis of the hip and knee is increasing in frequency. Although there is a lack of consensus, the main indication amongst surgeons is the presence of severe daily pain with attendant X-ray evidence of loss of joint space.⁴⁷ Other treatments are available for the management of OA; however, they tend to have a smaller overall benefit. Although results following surgical intervention can vary, arthroplasty has been shown to improve pain, disability, function,⁴⁸ physical activity⁴⁹ and quality of life.^{50,51} When compared

with the overall number of people in the population as a whole with OA, the proportion that undergoes surgical intervention is relatively small. For that individual, however, it can have a meaningful effect on the burden of osteoarthritis.

Conclusion

OA is the commonest joint disease worldwide and mainly occurs in later life. It tends to be slowly progressive and can cause significant pain and disability. Symptoms and radiographic changes are poorly correlated and thus defining it for research purposes is challenging. Established risk factors include obesity, local trauma and occupation. These may explain some of the geographic variation seen. There is conflicting evidence regarding the roles of nutrition, smoking and sarcopenia. Interestingly, low BMD appears to be protective.

The burden of OA is physical, psychological and socioeconomic. It can be associated with significant disability, such as a reduction in mobility and activities of daily living. Psychological sequelae include distress, devalued self-worth and loneliness. Given the high frequency of OA in the population, its economic burden is large.

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