Editorial

Remember the Titanic: What We Know of Knee Osteoarthritis Is But the Tip of the Iceberg

Osteoarthritis (OA) is accepted as a major public health problem. As estimated by the World Health Organization, it is one of the major causes of impaired function that reduces quality of life worldwide[1]. It is not only widespread, but also has significant attributable morbidity. The magnitude of this problem is likely to rise due to the increasing life expectancy and the increasing rates of obesity now observed.

This disease already consumes a significant proportion of the health budget, as well as attracting many indirect costs related to caregivers, limited mobility, impaired function, and self-care ability[2]. It has been implicated as a major cause of admission to nursing homes. Planning effectively for the future will require estimates of disease prevalence and an understanding of factors affecting this.

In this issue, Dillon, *et al* provide us with the most current population based estimate of prevalence of knee OA[3]. However, we have few other recent representative prevalence data to compare this study to, despite these significant direct and indirect costs to society. Much of what we know is drawn from studies using limited methodology (clinical or radiographic criteria only), or from limited populations, or is old[4-6]. With our limited available data, it is not clear whether prevalence is changing, and whether this is in keeping with the predicted changing demographics of society. Will predictions based on an aging and increasingly obese society be accurate? How may the significant lifestyle changes over the latter half of the 20th century affect it? It is not clear that prevalence is comparable throughout countries seen as similar — the data do not exist. Indeed, prevalence differs across countries; for example, the recently described differences between the Beijing and Framingham cohorts[5,7].

Why are these data so scarce? To be representative, these studies must be large, and entail exposing many healthy subjects to radiation. The results of prevalence studies do not seem as exciting as those investigating new insight into pathogenesis of disease or efficacy of new therapy, so, although important, they are expensive and thus are difficult to fund. However, without these estimates, we are unable to plan for this appropriately; we require accurate estimates of disease prevalence.

The aim of the study by Dillon, *et al* was to describe the prevalence of radiographic, symptomatic knee OA and knee pain without OA using data from the National Health and Nutritional Examination Survey (NHANES III). NHANES III comprised a nationwide probability sample assembled to provide nationally representative data on the health and nutrition of inhabitants of the United States between 1990 and 1994. Participants underwent detailed standardized interviews, examinations, and investigations. This is the most recent, most comprehensive, and most representative community based population study examining this question using broad methodology.

As in all prevalence studies, a definition of disease is required to classify subjects according to the presence of disease and non-disease that minimizes misclassification. The study of OA has been troubled by the lack of an all-encompassing definition, which ideally includes symptoms and structural change. Knee OA is the result of the joint's limited repertoire in responding to a multitude of biologic and mechanical insults, initiated by widely varying stimuli. Once pathogenesis has been initiated, it involves all tissues of the joint, albeit to varying degrees. These pathological changes are loosely related to clinical evidence of disease that manifest as joint pain, swelling, loss of function, tenderness, limitation of range of movement, and inflammation without systemic effects.

It has been difficult to encapsulate this disease in one epidemiologic definition. The relationship between pathological change and symptom severity is not strong[8]. While the presence of increasingly severe pathological and radiographic change may be related to the presence of symptoms, symptom severity seems to bear little relationship to

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structural change of disease. It is unclear when pain, if present, is related to the disease process itself, or signifies only associated phenomena[9].

The most widely used current criteria were developed by the American College of Rheumatology[10]. Three diagnostic criteria were proposed, based on either a clinical basis or a radiologic basis, or using both clinical and radiographic criteria, to incorporate both the structural change and disease related symptoms. However, use of each set of criteria has potential problems, reflected in the balance between specificity and sensitivity, and cost of diagnosis (financial and to the participant). The authors of this study have provided data relating to radiographic change, symptoms, and the combination of both.

Achieving the criteria of radiographic OA requires the presence of the osteophyte. While this has been the most reliable way of differentiating the presence or absence of disease, not all with osteophytes will have or will develop clinically significant disease. The role of the osteophyte in disease pathogenesis is under scrutiny[11]. Osteophytes may occur throughout the joint, thus the number of radiographic views obtained affect the ability to detect disease, as will use of more sensitive imaging techniques (computer tomographic scans, magnetic resonance imaging)[12]. Thus use of single radiographs, as in this study, may underestimate disease prevalence.

While the use of clinical criteria may be especially attractive, and appear amenable to assessment using questionnaires or self-report, attempts to use these at the knee have been unsuccessful[13]. Clinical criteria have a high misclassification rate, possibly attributing pain due to other periarticular pathology to OA. Complicating this issue further, different epidemiologic studies have used different criteria for knee pain: it is not clear what signifies "significant pain." The use of varying definitions hinders comparison between studies. This study again used a conservative estimate of pain, a lifetime history of pain > 6 weeks, longer than that used for Framingham and the National Health and Nutrition Examination Survey (NHANES I). This again will tend to underestimate prevalence, compared to other studies.

Use of the combined clinical and radiographic criteria is an attempt to combine both dimensions of disease. However, the limitations of both other approaches may affect this as well.

This study also provides troubling data, although not unexpected: it is suggestive of an increase in prevalence of disease. Comparison of these data with those obtained in NHANES I (1971-75) suggests initially that the prevalence of radiographic knee OA may have risen significantly in the 20 years between the 2 studies[4], although there are concerns about the radiographic reporting in NHANES I. Comparison with the Framingham data (1983-85) suggests stable or increasing prevalence. However, due to differences in radiographic techniques, the Framingham study may have provided higher estimates of radiographic and symptomatic disease[5]. However, even these current data may not accurately reflect what is happening in OA at the moment, since they are already more than 10 years old and may not accurately reflect the aging of the population and the current obesity epidemic.

These data relate specifically to the US population. Other clinical and radiographic prevalence population based studies are limited. Data from the Beijing study suggest we cannot extrapolate results from one society to another[7]. The differences between populations that contribute to differences in prevalence are not clear: how do differences in genetics, lifestyle factors, occupational exposure, and anthropomorphic factors affect prevalence? How are we to generalize?

For a problem of this magnitude, where should resources be focused? While there is much research into factors affecting established disease, a small shift in reducing prevalence is surely likely to have significant downstream effects. Yet, perhaps largely due to methodological factors related to limitations of radiography as an insensitive measure of disease, studies are focused more on treatment than prevention. Large radiographic studies of incidence have been limited in their ability to identify modifiable risk factors of disease, due to the large numbers of study participants required to be exposed to radiography, and the significant duration of time needed.

The structural changes of OA occur over decades, and are present prior to radiographic change[14]. Structural changes in the articular joint are likely to occur in all joint tissues at varying rates. These early changes may be reliably imaged using MRI[8,14]. This technology thus enables us to study OA as a continuum, from the normal joint to the diseased one, rather than just as a disease that is present or absent. Changes may be identified over a short time period, using small numbers. This paradigm will allow us to identify modifiable factors that relate to structural change in a healthy population. By manipulating these factors we may be able to develop primary prevention strategies to reduce the effect of knee OA.

Dillon, *et al* present important data, at least for planning for provision of healthcare services. After a decade, it may be time to reconsider further similar studies to obtain more up to date data examining change in prevalence. However, these estimates underscore the urgency for identification of novel preventive measures, amenable to public health intervention.

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