Review

Factors that may mediate the relationship between physical activity and the risk for developing knee osteoarthritis

Donna M Urquhart[1], Cathy Soufan[1], Andrew J Teichtahl[1], Anita E Wluka[1,2], Fahad Hanna[1] and Flavia M Cicuttini[1]

[1]Department of Epidemiology and Preventive Medicine, Monash University, Alfred Hospital, Commercial Road, Melbourne 3004, Australia
[2]Baker Heart Research Institute, AMREP Centre, Commercial Road, Melbourne, 3004, Australia

Corresponding author: Donna Urquhart, Donna.Urquhart@med.monash.edu.au

Published: 4 February 2008
This article is online at http://arthritis-research.com/content/10/1/203

Arthritis Research & Therapy 2008, **10:**203 (doi:10.1186/ar2343)

Abstract

Studies investigating the effect of physical activity on risk for developing osteoarthritis at weight-bearing joints have reported conflicting results. We examine evidence to suggest that this may be due to the existence of subgroups of individuals who differ in their response to physical activity, as well as methodological issues associated with the assessment of knee joint structure and physical activity. Recommendations for future studies of physical activity and the development of knee osteoarthritis are discussed.

Introduction

It is widely accepted that participation in physical activity is associated with physical, psychological and social benefits [1]. Physical activity not only reduces the risk for cardiovascular disease [2] (a major cause of mortality in developed countries) but is also recommended for the management of obesity and the treatment of mental illness [3]. Globally, a vast number of large-scale public health campaigns is aimed at promoting physical activity. Exercise is also widely recommended by health care professionals in the prevention and management of chronic health conditions such as osteoarthritis (OA). However, our knowledge of the effect of physical activity on risk for developing OA is limited.

OA is the most common joint disorder affecting the elderly. In particular, radiographic knee OA affects at least 30% of people aged over 60 years [4] and is a major cause of functional disability [5]. With our population ageing, the prevalence of OA in the developed world is expected to increase and it is anticipated that OA will become the fourth leading cause of disability in the coming decades [6]. A population-wide initiative, such as promotion of physical activity, has the potential to contribute inadvertently to the growing burden of this disease.

Epidemiological studies that have investigated the effect of physical activity on the knee joint have reported conflicting findings. Although some studies have reported that physical activity is associated with risk for knee OA [7-9], other studies have shown that physical activity may have no effect [10,11] or may even protect the knee joint from degenerative changes [12,13]. These conflicting findings may be a result of individual variation in response to exercise and/or different methodology employed by studies to measure knee structure and physical activity.

We propose that there may be subgroups of individuals who differ in their response to physical activity within our community. Although some individuals may have specific characteristics that enable them to exercise without increasing their risk for knee OA, others may require these individual factors and/or their exercise programme to be modified before they can commence or continue to exercise safely. In this review, we examine the roles played by a number of parameters that may mediate the relationship between physical activity and knee OA. We focus on the role of physical activity in the risk for developing OA, and do not consider its effect on those individuals with established OA. We also suggest that the methodology used to assess knee joint structure and physical activity might have contributed to the conflicting results between studies of physical activity and knee joint health.

Methods

We conducted electronic searches of the Medline and EMBASE databases between 1980 and September 2007 to identify relevant studies for this review. The search involved the use of MeSH (medical subject headings) and 'free text' words, including physical activity, exercise and knee osteoarthritis, and was limited to studies relating to humans

BMI = body mass index; MRI = magnetic resonance imaging; OA = osteoarthritis.

and published in English. The reference lists of relevant articles were also screened to identify additional studies. We identified epidemiological studies that investigated the effects of age, sex, body mass index (BMI), knee injury and/or knee alignment on the relationship between physical activity and risk for developing radiological, symptomatic and physician diagnosed OA.

Results

Our Medline and EMBASE searches identified 193 and 601 potentially relevant papers, respectively. We identified 12 studies that met our inclusion criteria; nine of these examined the effect of age and/or sex (Table 1), four investigated BMI (Table 2) and four considered knee injury or alignment (Table 3). A variety of methods were used to examine knee OA. Seven studies [11,12,14-18] used radiographic methods; four [8,10,13,19] based their assessment on self-reported, physician diagnosed OA; three [11,19,20] examined self-reported symptoms; and a further two [15,16] involved a clinical assessment. All studies used a self-report measure to examine physical activity (Tables 1, 2 and 3).

Potential roles of mediating factors

Age

A number of studies have examined the influence of age on risk for developing knee OA in physically active individuals. Most of these investigations examined individuals in a specific stage of the lifespan, including early [20], middle [12] and later life stages [14]. Although individuals who reported being active at the age of 14 to 19 years or 20 to 24 years had no increased risk for OA as compared with inactive age-matched control individuals [20], a lower prevalence of OA was reported in middle-aged, physically active teachers (age range 48 to 60 years) as compared with control individuals [12]. In contrast, a cohort study of elderly individuals (age [mean ± standard deviation]: 70.1 ± 4.5 years) found heavy physical activity (including activities such as lifting objects >5 lb [>2.27 kg], gardening with heavy tools and strenuous sports) to be associated with risk for knee OA [14].

Although these studies provide insight into the effect of physical activity on risk for knee OA in specific age groups, they do not directly compare the risk for OA across individuals of different ages [8] (Table 1). A longitudinal study of 16,961 individuals (aged 20 to 87 years) conducted over 10 years [8] examined the risk for developing hip or knee OA in younger (20 to 49 years) and older individuals (≥50 years) with varying levels of activity. The results showed a positive association between high levels of physical activity (walking or jogging ≥20 miles per week) and the incidence of hip or knee OA in younger men but not in older men. It has been suggested that these findings may be the result of a greater incidence of injury in younger individuals.

Overall, these studies suggest that the effect of physical activity on knee joint health may differ across the lifespan. Moreover, the findings highlight the need for further longitudinal investigation to stratify the responses of physical activity to knee joint health for individuals of different ages.

Gender

Although several studies have reported sex to have no influence on risk for developing OA in physically active individuals [10,11], there is contrasting preliminary evidence to suggest that sex may play a significant role [8,13] (Table 1). A 10-year longitudinal study of 12,888 men and 4,073 women [8] identified a positive association between high levels of physical activity and risk for developing hip or knee OA among young men (<50 years) but not among young women. A nested case-control study of 1,827 men and 583 women [13] also identified sex-specific differences in physical activity and risk for hip and/or knee OA. Specifically, men exhibited a reduced risk for hip or knee OA if they performed moderate/high joint-stress activity (defined according to intensity, frequency and rate of joint injury, impact and torsional loading), whereas women had a reduced risk for OA regardless of the level of physical activity that they performed (low or moderate/high).

Several hypotheses have been proposed to explain why physically active males and females differ in their risk for developing OA. Cheng and coworkers [8] suggested that OA in men may be a result of injury and specific types or intensity of physical activity, whereas OA in women may be more strongly associated with systemic and metabolic components such as BMI, caffeine use and/or smoking. It is also possible that sex-specific differences in biomechanics and body composition may influence the effect of physical activity on joint health. Overall, these findings highlight the need to consider the role of sex when examining the relationship between physical activity and risk for knee OA.

Body mass index

Although obesity is a major risk factor for development of knee OA [21], it is unclear whether overweight individuals who exercise may further increase their risk for joint damage. It is possible that excess mass may, in the presence of activity, impart axial loads that stress joint structures beyond their physiological capabilities and cause accelerated joint degeneration. Several studies of physical activity and OA have investigated high BMI as a potential effect modifier (Table 2) [10,11,14,15]. A 12-year longitudinal study conducted by Hootman and colleagues [10] demonstrated that BMI did not modify the relationship between moderate physical activity and risk for self-reported, physician diagnosed knee OA. Similarly, Felson and coworkers [11] also identified no increased risk for radiographic knee OA in middle-aged and elderly persons who had a higher BMI and participated in recreational exercise. However, McAlindon and colleagues [14] found that obese, elderly individuals who participated in heavy physical activity (including lifting objects >5 lb [>2.27 kg], gardening with heavy tools, brisk cycling

Table 1

Studies examining the effect of age and sex on the relationship between physical activity and risk for developing knee OA

Author (year)	Study design/participants	Measure(s) of OA	Measure(s) of physical activity	Results: effect of age/sex
Studies investigating self-reported symptomatic OA				
Felson *et al.* (2007) [11]	9-year cohort study/1,279 participants from the Framingham Offspring cohort	Self-reported, symptomatic	Self-reported; frequency, type, intensity	No association between OA risk and the following in middle-aged and elderly individuals: walking (≥6 miles/week; OR 0.78, 95% CI 0.49 to 1.24); working up a sweat (≥3 times/week; OR 1.23, 95% CI 0.72 to 2.10); and activity level compared with peers (more active; OR 0.94, 95% CI 0.60 to 1.47) Sex analyses did not alter the results
Sutton *et al.* (2001) [20]	Retrospective case-control study/1,080 healthy participants	Self-reported, symptomatic	Self-reported; parameters not specified	Individuals who retrospectively reported being active in early life had no increased risk for knee OA compared with age-matched control individuals who reported a sedentary lifestyle (14 to 19 years: OR 1.2, 95% CI 0.8 to 1.9 [$P = 0.39$]; 20 to 24 years: OR 1.0, 95% CI 0.6 to 1.6 [$P = 1.0$]) Individuals who reported being highly active in early life (age 20 to 24 years) had an increased risk for knee OA (OR 1.60, 95% CI 0.94 to 2.73 [$P = 0.085$])
Studies investigating self-reported physician diagnosed OA				
Hootman *et al.* (2003) [10]	12.8-year cohort study/5,284 participants from the Cooper Clinic	Self-reported, physician diagnosed	Self-reported; joint stress physical activity score (intensity, frequency, duration and type)	Increasing levels of physical activity were not associated with an increased risk for hip/knee OA for both men (high level: OR 1.07, 95% CI 0.47 to 2.42) and women (high level: OR 1.31, 95% CI 0.92 to 1.87)
Rogers *et al.* (2002) [13]	2-year nested case-control study/415 cases and 1,995 control individuals from the Cooper Clinic	Self-reported, physician diagnosed	Self-reported; joint stress (based on activity type)	Physical activity involving low or moderate/high joint stress was associated with reduced risk for hip/knee OA in women (low: OR 0.58, 95% CI 0.34 to 0.99; moderate/high: OR 0.24, 95% CI 0.11 to 0.52) In contrast to low joint stress activity, moderate/high joint stress activity was associated with reduced risk for hip/knee OA in men (OR 0.62, 95% CI 0.43 to 0.89)
Cheng *et al.* (2000) [8]	10-year prospective, cohort study/16,961 patients from the Cooper Clinic	Self-reported, physician diagnosed	Self-reported; activity type, duration	High-level physical activity (running ≥20 miles per week) was significantly associated with hip/knee OA among younger men (OR 2.4, 95% CI 1.5 to 3.9) but not older men (OR 1.2, 95% CI 0.6 to 2.3) Nonsignificant findings were reported for younger women (HR 1.5, 95% CI 0.4 to 5.1) and older women (HR 1.4, 95% CI 0.4 to 4.6)
Radiographic studies investigating structural OA				
Felson *et al.* (2007) [11]	9-year cohort study/1,279 participants from the Framingham Offspring cohort	Radiographic, structural	Self-reported; frequency, type, intensity	No association between OA risk and the following in middle-aged and elderly individuals: walking (≥6 miles/week; OR 1.10, 95% CI 0.73 to 1.66); working up a sweat (≥3 times/week; OR 1.24, 95% CI 0.77 to 2.00); and activity level compared with peers (more active; OR 0.94, 95% CI 0.63 to 1.40) Sex analyses did not alter the results
McAlindon *et al.* (1999) [14]	8-year longitudinal cohort study/473 participants from the Framingham study cohort	Radiographic, structural	Self-reported: Framingham physical activity index; activity type, duration	The number of hours/day of heavy physical activity was associated with risk for knee OA (≥4 hours heavy activity/day compared with no heavy activity; OR 7.0, 95% CI 2.4 to 20 [$P = 0.0002$]) Heavy physical activity (≥4 hours/day) was associated with increased risk for OA in elderly men (OR 7.0, 95% CI 1.7 to 29) and women (OR 9.0, 95% CI 1.7 to 48)

Continued overleaf

Table 1 (continued)

Studies examining the effect of age and sex on the relationship between physical activity and risk for developing knee OA

Author (year)	Study design/participants	Measure(s) of OA	Measure(s) of physical activity	Results: effect of age/sex
Radiographic studies investigating structural OA				
Felson *et al.* (1997) [17]	8-year longitudinal study/ 598 participants from the Framingham Study cohort	Radiographic, structural	Framingham physical activity index; activity type	Habitual physical activity increased the risk for knee OA for participants in the highest quartile of physical activity compared with those in the lowest quartile (OR 3.3, 95% CI 1.4 to 7.5) A sex-specific effect was observed in an elderly cohort (men: OR 3.8, 95% CI 0.9 to 17.3; women: OR 3.1, 95% CI 1.1 to 8.6)
Hannan *et al.* (1993) [18]	Longitudinal cohort study (conducted over 19 years)/ 1,415 individuals from the Framingham study cohort	Radiographic, structural,	Self-reported: duration, frequency, type; physical capacity measures: FEV, pulse rate	Habitual physical activity did not increase the risk for knee OA in elderly men or women (highest quartile; men: OR 1.34, 95% CI 0.66 to 2.74; women: OR 1.09, 95% CI 0.63 to 1.90) In contrast to women, men in the highest quartile of habitual physical activity had significantly elevated rates of asymptomatic osteophytes (OR 2.14, 95% CI 1.01 to 4.54)
White *et al.* (1993) [12]	Case-control study/305 physical education teachers and age-matched control individuals	Radiographic, structural	Self-reported; frequency, duration	There was a significantly lower prevalence of knee OA in middle-aged physical education teachers compared with the control individuals in both 'younger' (48 to 54 years [$P < 0.001$]) and 'older' (55 to 60 years [$P < 0.001$]) age categories

CI, confidence interval; FEV, forced expiratory volume; HR, hazard ratio; OA, osteoarthritis; OR, odds ratio.

and other strenuous sports) were at greater risk for knee OA than those individuals in the lower tertile of BMI. Similarly, increased risk for knee OA was reported in former elite-level athletes with a higher BMI (at age 20 and 30 years) [15,22]. These findings suggest that individuals with a higher body mass may participate in moderate/recreational activity without increased risk for knee OA, but involvement in heavy physical activity increases their risk. Further longitudinal investigation that accurately examines the level of physical activity in obese individuals is required to confirm these preliminary results.

Body composition

Although the aforementioned studies tended to examine excess body mass in the context of knee OA, the measures employed (either weight [kg] or BMI [kg/m^2]) cannot differentiate between fat and fat-free mass. Toda and coworkers [23] recruited 22 patients with knee OA and a BMI greater than 26.4 kg/m^2 and implemented several interventions, including a 6-week walking programme. A decreasing percentage of body fat and increasing physical activity were shown to be more important than other indices of obesity, such as body weight, in producing symptomatic relief from OA. Such data suggest that physical activity leading to a reduction in body fat may prove beneficial to knee joint health in individuals with established knee OA.

Other studies that have examined the effect of body composition and knee joint structure have demonstrated that fat mass may be one of the determinants that mediate the association between excess body mass and joint abnormalities, such as the reduction in cartilage volume and the presence of cartilage defects [24-26]. Physical activity may therefore represent a management strategy to reduce total fat mass among obese individuals and subsequently improve their joint health. However, given that physically active, obese individuals (as indicated by BMI) may have relatively greater muscle mass than adipose tissue, future studies of physical activity and knee joint health would benefit from body composition analyses rather than crude adjustments for the BMI alone.

Muscle strength

The strength of the quadriceps is believed to be important in stabilizing the knee joint and protecting articular surfaces from high loads. In a prospective, longitudinal study of 342 elderly, community-based adults, quadriceps weakness was shown to be a risk factor for the development of knee OA [27]. An association between muscle mass and a reduction in the rate of cartilage loss has also been reported in a longitudinal investigation of 86 healthy men and women in midlife [24]. Moreover, a recent, randomized, attention-controlled trial of 221 older adults [28] identified a lower prevalence of radiographic progression of knee OA when a lower extremity strength training group was compared with a group of individuals who performed range of motion exercises over a 30-month period.

Table 2

Studies examining the effect of BMI on the relationship between physical activity and risk for developing knee OA

Author (year)	Study design/participants	Measure(s) of OA	Measure(s) of physical activity	Results: effect of BMI
Studies investigating self-reported symptomatic OA				
Felson *et al.* (2007) [11]	9-year longitudinal cohort study/1,279 participants from the Framingham Offspring cohort	Self-reported, symptomatic	Self-reported; frequency, type, intensity	Overall results are presented in Table 1 Among persons with BMI above the median, there was no relationship between the risk for knee OA and the following: walking (≥6 miles/week; OR 0.84, 95% CI 0.37 to 1.92); working up a sweat (≥3 times/week; OR 1.04, 95% CI 0.55 to 1.96); and activity level compared with peers (more active; OR 0.63, 95% CI 0.35 to 1.16)
Studies investigating self-reported physician diagnosed OA				
Hootman *et al.* (2003) [10]	12.8-year cohort study/ 5,284 participants from the Cooper Clinic	Self-reported, physician diagnosed	Self-reported; joint stress physical activity score (intensity, frequency, duration and type)	Increasing levels of the joint stress physical activity score were not associated with an increased risk for hip/knee OA for both men (high level; OR 1.07, 95% CI 0.47 to 2.42) and women (high level: OR 1.31, 95% CI 0.92 to 1.87) BMI did not modify the relationship between moderate physical activity and risk for knee OA for both men (OR 1.07, 95% CI 1.03 to 1.11) and women (OR 1.12, 95% CI 1.06 to 1.19)
Radiographic studies investigating structural OA				
Felson *et al.* (2007) [11]	9-year longitudinal cohort study/1,279 participants from the Framingham Offspring cohort	Radiographic, structural	Self-reported; frequency, type, intensity	Overall results presented in Table 1 Among persons with BMI above the median, there was no relationship between the risk of radiographic knee OA and the following: walking (≥6 miles/week; OR 0.95, 95% CI 0.55 to 1.62); working up a sweat (≥3 times/week; OR 1.22, 95% CI 0.67 to 2.21); and activity level compared with peers (more active; OR 0.82, 95% CI 0.48 to 1.40)
McAlindon *et al.* (1999) [14]	8-year longitudinal cohort study/473 participants from the Framingham Heart Study cohort	Radiographic, structural	Self-reported: Framingham physical activity index; activity type, duration	The number of hours per day of heavy physical activity was associated with risk for knee OA (≥4 hours heavy activity/day compared with no heavy activity; OR 7.0, 95% CI 2.4 to 20 [$P = 0.0002$]) Risk for OA was greatest among individuals in the upper tertile of BMI (≥3 hours/day of heavy physical activity; OR 13.0, 95% CI 3.3 to 51)
Kujala *et al.* (1995) [15]	Retrospective cohort study/117 male former top-level athletes	Radiographic, structural	Self-reported; parameters not-specified	Risk for knee OA was increased in athletes with a higher BMI at age 20 years (OR 1.76/unit increase, 95% CI 1.26 to 2.45)

BMI, body mass index; CI, confidence interval; OA, osteoarthritis; OR, odds ratio.

Table 3

Studies examining the effect of knee injury and/or alignment on the relationship between physical activity and risk for developing knee OA

Author (year)	Study design/participants	Measure(s) of OA	Measure(s) of physical activity	Results: effect of alignment/injury
Studies investigating self-reported symptomatic OA				
Sutton *et al.* (2001) [20]	Retrospective case-control study/1,080 healthy participants	Self-reported, symptomatic	Self-reported; parameters not specified	Past history of knee injury was associated with increased risk for knee OA (OR 8.0, 95% CI 2.0 to 32.0)
Kujala *et al.* (1999) [19]	11-year cohort study/269 runners and 188 control individuals	Self-reported, symptomatic	Self-reported; MET index (intensity, duration and frequency); level of breathlessness	Runners reported knee OA more often than control individuals (OR 1.79, 95% CI 1.10 to 3.54 [$P = 0.025$]) The age-adjusted OR for having had knee ligament or meniscus injury was 1.62 (95% CI 0.99 to 2.65 [$P = 0.055$]) in runners compared with control individuals
Studies investigating self-reported physician diagnosed OA				
Kujala *et al.* (1999) [19]	11-year cohort study/269 runners and 188 control individuals	Self-reported, physician diagnosed	Self-reported; MET index (intensity, duration and frequency); level of breathlessness	Runners reported knee OA more often than control individuals (OR 1.79, 95% CI 1.10 to 3.54 [$P = 0.025$]). The age-adjusted OR for having had knee ligament or meniscus injury was 1.62 (95% CI 0.99 to 2.65 [$P = 0.055$]) in runners compared with control individuals
Radiographic studies investigating structural OA				
Kujala *et al.* (1995) [15]	Retrospective cohort study/117 male former top-level athletes	Radiographic, structural; clinical	Self-reported; parameters not-specified	The risk of knee OA was increased in those with previous knee injuries (OR 4.73, 95% CI 1.32 to 17.0)
McDermott and Freyne (1983) [16]	Cross-sectional study/ 20 middle/long-distance runners	Radiographic, structural; clinical examination and arthroscopy	Self-reported; years of training/competition, training mileage	OA was reported in 6 of the 20 runners; athletes with degenerative changes had been running for a greater number of years ($P < 0.05$) Participants with degenerative changes had greater incidence of genu varum and had experienced more knee injuries ($P < 0.05$)

BMI, body mass index; CI, confidence interval; MET, metabolic equivalent; OA, osteoarthritis; OR, odds ratio.

These studies indicate the importance of muscle mass in protecting the structures of the knee joint and the need for longitudinal studies to account for this factor when exploring the influence of physical activity on knee OA. It may be that certain individuals will respond better to graduated strengthening programmes, rather than being encouraged to commence exercises that require significant baseline strength. However, it is also possible that individuals with a certain biomechanical profile, such as genu varum or ligamentous laxity, who increase their muscle strength may also inadvertently accelerate degenerative changes in the knee joint [29]. Thus, alignment may need to be considered to ensure that prescription of exercise is safe.

Previous injury

Injury to joint structures, such as the menisci or cruciate ligaments, is a known risk factor for development of knee OA [30]. Meniscal injuries are the most common injuries to the knee [31]. Although meniscal surgery is performed on almost 1.7 million people each year [32], this procedure has been reported to increase joint laxity and to lead to cartilage destruction and premature OA [33]. Similarly, injury to the anterior cruciate ligament (isolated or combined with meniscal or collateral ligament injury) has been shown to predate osteoarthritic changes in 60% to 90% of patients 10 to 20 years after injury [33].

Although some but not all epidemiological studies have included individuals with previous knee injuries and subsequently accounted for past history in regression models [7,13], it is possible that residual confounding remained because those exercising more vigorously were more likely to sustain an injury. It is well established that previous knee injury increases the risk for OA in physically active individuals. Several studies of physical activity and knee joint health have reported an association between risk for OA and previous knee injury (Table 3). Thus, a greater understanding of the types and intensities of exercise appropriate for individuals who have suffered a previous knee injury is required. In addition, more stringent study designs are required to better account for a past history of joint injury as a potential confounder among studies examining the relationship between physical activity and knee OA. However, it is considered optimal for people with a previous knee injury to be excluded from future study designs if the intention of a study is to examine the association between physical activity and primary knee OA.

Joint alignment

Static factors

Minor alterations in joint alignment can affect the normal load distribution imparted to the articular surfaces of a joint. Specifically, a 4% to 6% increase in varus alignment has been shown to increase loading in the medial compartment of the knee by up to 20% during single limb stance [34]. Moreover, both varus and valgus knee alignment have been shown to be associated with increased risks for joint space narrowing in the medial and lateral compartments, respectively, as well as the presence of osteophytes [35]. A recent longitudinal study including 1,501 participants [36] found that an increasing degree of varus alignment was associated with both development and progression of knee OA (when both tibiofemoral compartments were assessed together). Moreover, joint alignment has been shown to increase the risk for OA progression in individuals with knee OA [37].

However, there is a paucity of data on the effect of joint malalignment on risk for developing OA in physically active individuals. A study of 20 middle-distance and long-distance runners (mean age 39 years) who had been competing for at least 5 years and developed knee pain [16] revealed that genu varum was associated with degenerative changes of the knee (Table 3). To our knowledge, no other studies have directly investigated whether individuals who exercise in the presence of genu varum or valgum are at a greater risk for developing OA than individuals with neutral alignment. However, there is evidence to suggest that lateral wedge orthoses and knee braces may reduce the load on the medial compartment and improve the symptoms associated with OA [38]. In addition, a study of 300 community-based individuals with knee OA [39] examined the relationship between obesity and knee OA and found that joint alignment mediated the effect of obesity on knee OA. These studies not only highlight the effect of knee alignment on the development and progression of knee OA, but they also indicate that there is a need for future studies of physical activity and knee joint health to consider this potentially mediating factor.

Dynamic factors

As well as static knee alignment, dynamic biomechanical measures are likely to be important in mediating the role played by physical activity in development of knee OA. The peak external knee adductor moment during late stance, which is arguably the major determinant of medial tibiofemoral load during dynamic tasks such as walking, has proven to be associated with medial tibial bone size [40] and is of greater magnitude in people with knee OA [41,42]. Nevertheless, no study examining the role of physical activity in knee OA has accounted for knee adductor moment variability. Although the acquisition of these data requires adequate facilities for gait analysis, its potential role in mediating the relationship between physical activity and knee OA cannot be underestimated. It is our recommendation that future studies examining the influence of physical activity on the natural history of joint disease account for, or at least acknowledge, the differential impact that variations in biomechanical measures can have across the knee joint.

Issues related to measurement of joint structure

The use of different methods to measure the development of OA may also have contributed to inconsistency in results between studies of physical activity and knee joint health. Although some studies used radiographic measures of joint structure, including joint space width and/or the presence of osteophytes [7,11,14], others have based their assessment on individuals' self-reported symptoms [20] or self-reported presence of physician-diagnosed OA [8,13] (Table 1). In addition, two studies [16,19] performed clinical examinations of the knee joint.

There are methodological issues associated with each of these techniques, with self-reported data potentially influenced by poor recall, and the accuracy of physician diagnosed OA questionable. Moreover, indirect measurement of the joint space width as a surrogate for articular cartilage has proven to have inherent problems with respect to validity, reliability and sensitivity to change [43-45]. Thus, studies that have relied on radiographic measures of joint space may have missed an effect of physical activity on structural abnormalities, including cartilage defects and bony enlargement, which cannot be detected radiographically.

An over-reliance on the presence of osteophytes to diagnose knee OA may also have influenced the results of radiographic studies examining knee joint structure. The presence of osteophytes is required for diagnosing knee OA using the Kellgren and Lawrence grading system [46], and measurement of osteophytes is associated with greater reproducibility than that of joint space narrowing [47]. Even if osteophytes are more prevalent than joint space narrowing in physically active individuals, it is possible that this finding represents the effect of musculoskeletal traction forces produced by exercise, not direct cartilage damage to the knee joint [48].

Recently, a small number of studies have used magnetic resonance imaging (MRI) to assess the relationship between physical activity and knee joint structure. Although radiographs use ionizing radiation to provide a two-dimensional approximation of articular cartilage, MRI visualizes joint structures from a three-dimensional perspective without exposing the patient to radiation. MRI is recognized to be a valid, accurate and reproducible tool for measuring articular cartilage volume and cartilage defects [49].

A cross-sectional study of 176 community-based women [50] revealed that participation in vigorous activity (activity leading to sweating, shortness of breath, or an increased pulse rate) was associated with greater medial tibial cartilage volume. A longitudinal study of healthy, recreational long-distance runners [51] demonstrated no significant knee structural change at 6 to 8 weeks after a marathon. Moreover, there is accumulating evidence demonstrating that physical inactivity adversely affects cartilage development in children [52] and predisposes to rapid cartilage loss in adults [53]. Thus, MRI studies to date have consistently shown a beneficial effect of physical activity on knee joint cartilage [50-54].

In summary, although several techniques are available to measure knee joint structure in studies of physical activity, use of these techniques might have resulted in conflicting results in terms of the effect of physical activity on risk for OA. Radiographic assessment of both joint space narrowing and osteophytes is associated with issues of measurement and interpretation. We propose that a technique that is reliable and valid, examines different features of OA, and is sensitive to change in both healthy and OA populations must be consistently used in longitudinal investigations if the influence of physical activity, and of other potentially mediating factors, on knee joint health is to be clearly defined.

Issues related to measurement of physical activity

It has been suggested that use of self-report surveys to measure physical activity has contributed to inconsistency in findings between studies examining the relationship between physical activity and knee joint health. Although surveys are easy to implement in large cohorts and provide important physical activity data, they are associated with over-reporting of activity [55] and reduced accuracy for moderate intensity physical activity [56], poor recall over longer periods [55] and only moderate reproducibility [57]. An alternative, accelerometry, provides an objective and reliable measure of the frequency, duration and intensity of physical activity [58]. Although expensive and impractical for use in large cohorts, we propose that future longitudinal studies consider use of accelerometry in random samples of participants. This will allow investigators to confirm the accuracy of self-reported survey data, to ensure that those in different physical activity groups actually differ in their types and/or levels of activity, and to confirm that participants' physical activity patterns remain consistent over the course of the study.

Assessment of physical activity is further complicated by the different features of physical activity, including the type, intensity, frequency and duration, that can be examined. For instance, although Cheng and coworkers [8] assessed participants based on the distance they walked or jogged per week (for example, high activity was jogging or walking ≥20 miles/week), Rogers and colleagues [13] used a variety of self-reported activities to categorize participants into low/moderate or high joint stress groups. A small number of studies have performed subanalyses to investigate the effect of different aspects of physical activity on risk for OA. For instance, Hootman and coworkers [10] examined the association between hip/knee OA and training frequency, pace and total weekly mileage in a subgroup of participants, but they identified no association. It is clear that direct head-to-head comparisons of different dosages of physical activity, in particular those recommended by national health bodies, using reliable and valid measures are required.

Table 4

Summary of recommendations for future research studies examining the relationship between physical activity and the risk for developing knee OA

Recommendation	Details
1	There is evidence to indicate the importance of investigating the role of the following factors when examining the relationship between physical activity and knee joint health: age, sex, body mass index and body composition, muscle strength, varus-valgus alignment and external knee adductor moment, and injury history
2	The measurement tool employed to assess knee OA must be valid, reliable and sensitive to change among healthy and OA populations
3	Instruments for the measurement of physical activity must be reliable and valid, and able to assess accurately the type, frequency, intensity and duration of activity

OA, osteoarthritis.

Conclusion

In this review we examine possible reasons for the conflicting results arising from studies of physical activity and knee joint health, and we propose possible approaches that may be used in future investigations (Table 4). Novel methods that can be used to examine knee structure directly from health through to disease may overcome some of the problems associated with the use of radiography to examine knee joint structure. A more comprehensive examination of various knee structures and the implementation of objective and accurate assessments of physical activity may also enhance our understanding of the mechanism by which physical activity affects the knee joint.

Addressing these methodological issues will allow studies to explore the role of biophysical factors within an individual that may influence the effect of physical activity on risk for OA. There is evidence that factors such as age, sex, body mass and previous knee injury may influence knee joint health in physically active individuals. Rather than a uniform approach to the implementation of physical activity, we may find that certain types of exercise have different effects on different people and that individually tailored exercise programmes are needed to allow exercise to commence safely. In a society that is ageing and being encouraged to be physically active, such programmes may have the potential to reduce the growing burden of OA.

Competing interests

The authors desclare that they have no competing interests.

Acknowledgements

Donna Urquhart (284402), Anita Wluka (317840) and Fahad Hanna (418961) were supported by the NHMRC.

References

1. Bauman AE: **Updating the evidence that physical activity is good for health: an epidemiological review 2000-2003.** *J Sci Med Sport* 2004, **7:**6-19.
2. US Department of Health and Human Services, Centers for Disease Control and Prevention: *A report of the Surgeon General.* Atlanta, GA: Centers for Disease Control and Prevention; 1996.
3. Mathers E, Vos T, Stevenson C: *The Burden of Disease and Injury in Australia*. Canberra, Australia: Australian Institute of Health & Welfare; 1999.
4. Felson DT, Naimark A, Anderson J, Kazis L, Castelli W, Meenan RF: **The prevalence of knee osteoarthritis in the elderly. The Framingham Osteoarthritis Study.** *Arthritis Rheum* 1987, **30:** 914-918.
5. Gabriel SE: **Update on the epidemiology of the rheumatic diseases.** *Curr Opin Rheumatol* 1996, **8:**96-100.
6. World Health Organization: *World Health Report 2002. Reducing Risks, Promoting Healthy Life.* Geneva, Switzerland: World Health Organization; 2002.
7. Spector TD, Harris PA, Hart DJ, Cicuttini FM, Nandra D, Etherington J, Wolman RL, Doyle DV: **Risk of osteoarthritis associated with long-term weight-bearing sports: a radiologic survey of the hips and knees in female ex-athletes and population controls.** *Arthritis Rheum* 1996, **39:**988-995.
8. Cheng Y, Macera CA, Davis DR, Aiinsworth BE, Troped PJ, Blair SN: **Physical activity and self-reported, physician-diagnosed osteoarthritis: is physical activity a risk factor?** *J Clin Epidemiol* 2000, **53:**315-322.
9. Szoeke C, Dennerstein L, Guthrie J, Clark M, Cicuttini F: **The relationship between prospectively assessed body weight and physical activity and prevalence of radiological knee osteoarthritis in postmenopausal women.** *J Rheumatol* 2006, **33:**1835-1840.
10. Hootman JM, Macera CA, Helmick CG, Blair SN: **Influence of physical activity-related joint stress on the risk of self-reported hip/knee osteoarthritis: a new method to quantify physical activity.** *Prev Med* 2003, **36:**636-644.
11. Felson D, Niu J, Clancy M, Sack B, Aliabadi P, Zhang Y: **Effect of recreational physical activities on the development of knee osteoarthritis in older adults of different weights: The Framingham Study.** *Arthritis Rheum* 2007, **57:**6-12.
12. White JA, Wright V, Hudson AM: **Relationships between habitual physical activity and osteoarthrosis in ageing women.** *Public Health* 1993, **107:**459-470.
13. Rogers LQ, Macera CA, Hootman JM, Ainsworth BE, Blairi SN: **The association between joint stress from physical activity and self-reported osteoarthritis: an analysis of the Cooper Clinic data.** *Osteoarthritis Cartilage* 2002, **10:**617-622.
14. McAlindon TE, Wilson PW, Aliabadi P, Weissman B, Felson DT: **Level of physical activity and the risk of radiographic and symptomatic knee osteoarthritis in the elderly: the Framingham Study.** *Am J Med* 1999, **106:**151-157.
15. Kujala UM, Kettunen J, Paananen H, Aalto T, Battie MC, Impivaara O, Videman T, Sarna S: **Knee osteoarthritis in former runners, soccer players, weight lifters, and shooters.** *Arthritis Rheum* 1995, **38:**539-546.
16. McDermott M, Freyne P: **Osteoarthritis in runners with knee pain.** *Br J Sports Med* 1983, **17:**84-87.
17. Felson DT, Zhang Y, Hannan MT, Naimark A, Weissman B, Aliabadi P, Levy D: **Risk factors for incident radiographic knee osteoarthritis in the elderly: the Framingham Study.** *Arthritis Rheum* 1997, **40:**728-733.
18. Hannan MT, Felson DT, Anderson JJ, Naimark A: **Habitual physi-**

cal activity is not associated with knee osteoarthritis: the Framingham Study. *J Rheumatol* 1993, **20:**704-709.
19. Kujala UM, Sarna S, Kaprio J, Koskenvuo M, Karjalainen J: **Heart attacks and lower-limb function in master endurance athletes.** *Med Sci Sports Exerc* 1999, **31:**1041-1046.
20. Sutton AJ, Muir KR, Mockett S, Fentem P: **A case-control study to investigate the relation between low and moderate levels of physical activity and osteoarthritis of the knee using data collected as part of the Allied Dunbar National Fitness Survey.** *Ann Rheum Dis* 2001, **60:**756-764.
21. Felson DT, Anderson JJ, Naimark A, Walker AM, Meenan RF: **Obesity and knee osteoarthritis. The Framingham Study.** *Ann Intern Med* 1988, **109:**18-24.
22. Kujala UM, Kaprio J, Sarna S: **Osteoarthritis of weight bearing joints of lower limbs in former elite male athletes.** *BMJ* 1994, **308:**231-234.
23. Toda Y, Toda T, Takemura S, Wada T, Morimoto T, Ogawa R: **Change in body fat, but not body weight or metabolic correlates of obesity, is related to symptomatic relief of obese patients with knee osteoarthritis after a weight control program.** *J Rheumatol* 1998, **25:**2181-2186.
24. Cicuttini FM, Teichtahl AJ, Wluka AE, Davis SR, Strauss BJG, Ebeling PR: **The relationship between body composition and knee cartilage volume in healthy, middle-aged subjects.** *Arthritis Rheum* 2005, **52:**461-467.
25. Wang Y, Wluka AE, English DR, Teichtahl AT, Giles GG, O'Sullivan R, Cicuttini FM: **Body composition and knee cartilage properties in healthy, community-based adults.** *Ann Rheum Dis* 2007, 66:1244-1248.
26. Teichtahl AJ, Wang Y, Wluka AE, Cicuttini FM: **Obesity and knee osteoarthritis: new insights provided by body composition studies.** *Obesity* 2007:in press.
27. Slemenda C, Heilman DK, Brandt KD, Katz BP, Mazzuca SA, Braunstein EM, Byrd D: **Reduced quadriceps strength relative to body weight: a risk factor for knee osteoarthritis in women?** *Arthritis Rheum* 1998, **41:**1951-1959.
28. Mikesky AE, Mazzuca SA, Brandt KD, Perkins SM, Damush T, Lane KA: **Effects of strength training on the incidence and progression of knee osteoarthritis.** *Arthritis Rheum* 2006, **55:**690-699.
29. Sharma L, Dunlop DD, Cahue S, Song J, Hayes KW: **Quadriceps strength and osteoarthritis progression in malaligned and lax knees.** *Ann Intern Med* 2003, **138:**613-619.
30. Felson DT: **The epidemiology of knee osteoarthritis: results from the Framingham Osteoarthritis Study.** *Semin Arthritis Rheum* 1990, **20:**42-50.
31. Renström P, Johnson RJ: **Anatomy and biomechanics of the menisci.** *Clin Sports Med* 1990, **9:**523-538.
32. Rodkey WG: **Basic biology of the meniscus and response to injury.** *Instr Course Lect* 2000, **49:**189-193.
33. Saxon L, Finch C, Bass S: **Sports participation, sports injuries and osteoarthritis: implications for prevention.** *Sports Med* 1999, **28:**123-135.
34. Tetsworth K, Paley P: **Malalignment and degenerative arthropathy.** *Orthop Clin North Am* 1994, **25:**367-377.
35. Teichtahl AJ, Cicuttini FM, Janakiramanan N, Davis SR, Wluka AE: **Static knee alignment and its association with radiographic knee osteoarthritis.** *Osteoarthritis Cartilage* 2006, **14:**958-962.
36. Brouwer GM, van Tol AW, Bergink AP, Belo JN, Bernsen RM, Reijman M, Pols HA, Bierma-Zeinstra SM: **Association between valgus and varus alignment and the development and progression of radiographic osteoarthritis of the knee.** *Arthritis Rheum* 2007, **56:**1204-1211.
37. Sharma L, Song J, Felson DT, Cahue S, Shamiyeh E, Dunlop DD: **The role of knee alignment in disease progression and functional decline in knee osteoarthritis.** *JAMA*. 2001, **286:**188-195.
38. Krohn K: **Footwear alterations and bracing as treatments for knee osteoarthritis.** *Curr Opin Rheumatol* 2005, **17:**653-656.
39. Sharma L, Lou C, Cahue S, Dunlop DD: **The mechanism of the effect of obesity in knee osteoarthritis: the mediating role of malalignment.** *Arthritis Rheum* 2000, **43:**568-575.
40. Jackson BD, Teichtahl AJ, Morris ME, Wluka AE, Davis SR, Cicuttini FM: **The effect of the knee adduction moment on tibial cartilage volume and bone size in healthy women.** *Rheumatology* 2004, **43:**311-314.
41. Sharma L, Hurwitz DE, Thonar EJ, Sum JA, Lenz ME, Dunlop DD, Schnitzer TJ, Kirwan-Mellis G, Andriacchi TP: **Knee adduction moment, serum hyaluronan level, and disease severity in medial tibiofemoral osteoarthritis.** *Arthritis Rheum* 1998, **41:** 1233-1240.
42. Wluka AE, Stuckey S, Snaddon J, Cicuttini FM: **The determinants of change in tibial cartilage volume in osteoarthritic knees.** *Arthritis Rheum* 2002, **46:**2065-2072.
43. Salaffi F, Carotti M, Stancati A, Grassi W: **Radiographic assessment of osteoarthritis: analysis of disease progression.** *Aging Clin Exp Res* 2003, **15:**391-404.
44. Amin S, LaValley MP, Guermazi A, Grigoryan M, Hunter DJ, Clancy M, Niu J, Gale DR, Felson DT: **The relationship between cartilage loss on magnetic resonance imaging and radiographic progression in men and women with knee osteoarthritis.** *Arthritis Rheum* 2005, **52:**3152-3159.
45. Cicuttini FM, Hankin J, Jones G, Wluka AE: **Comparison of conventional standing knee radiographs and magnetic resonance imaging in assessing progression of tibiofemoral joint osteoarthritis.** *Osteoarthritis Cartilage* 2005, **13:**722-727.
46. Kellgren JH, Lawrence JS: **Radiological assessment of osteoarthrosis.** *Ann Rheum Dis* 1957, **16:**494-502.
47. Gunther KP, Sun Y: **Reliability of radiographic assessment in hip and knee osteoarthritis.** *Osteoarthritis Cartilage* 1999, **7:** 239-246.
48. van der Kraan PM, van den Berg WB: **Osteophytes: relevance and biology**. *Osteoarthritis Cartilage* 2007, **15:**237-244.
49. Eckstein F, Cicuttini F, Raynauld JP, Waterton JC, Peterfy C: **Magnetic resonance imaging (MRI) of articular cartilage in knee osteoarthritis (OA): morphological assessment.** *Osteoarthritis Cartilage* 2006, **14:**A46-A75.
50. Hanna F, Teichtahl AJ, Bell R, Davis SR, Wluka AE, O'Sullivan R, Cicuttini FM: **The cross-sectional relationship between fortnightly exercise and knee cartilage properties in healthy adult women in midlife.** *Menopause* 2006, **14:**1-5.
51. Krampla W, Mayrhofer R, Malcher J, Kristen KH, Urban M, Hruby W: **MR imaging of the knee in marathon runners before and after competition.** *Skeletal Radiology* 2001, **30:**72-76.
52. Jones G, Ding C, Glisson M, Hynes K, Ma D, Cicuttini F: **Knee articular cartilage development in children: a longitudinal study of the effect of sex, growth, body composition and physical activity.** *Pediatr Res* 2003, **54:**230-236.
53. Vanwanseele B, Eckstein F, Knecht H, Stussi E, Spaepen A: **Knee cartilage of spinal cord-injured patients displays progressive thinning in the absence of normal joint loading and movement.** *Arthritis Rheum* 2002, **46:**2073-2078.
54. Racunica TL, Teichtahl AJ, Wang Y, Wluka AE, English DR, Giles G, Sullivan R, Cicuttini FM: **The effect of physical activity on articular knee joint structures in community-based adults.** *Arth Care Res* 2007:in press.
55. Timperio A, Salmon J: *Physical Activity Monitoring and Evaluation Toolkit*. Melbourne, Australia: Centre for Physical Activity and Nutrition Research, Deakin University; 2003 [http://www.hbs.deakin.edu.au/healthsci]
56. Sallis JF, Conway TL, Prochaska JJ, McKenzie TL, Marshall SJ, Brown M: **The association of school environments with youth physical activity.** *Am J Public Health* 2001, **91:**618-620.
57. Masse LC, Ainsworth BE, Tortolero S, Levin S, Fulton JE, Henderson KA, Mayo K: **Measuring physical activity in midlife, older, and minority women: issues from an expert panel.** *J Womens Health* 1998, **7:**57-67.
58. Welk GJ, Schaben JA, Morrow JR: **Reliability of accelerometry-based activity monitors: a generalizability study.** *Med Sci Sports Exerc* 2004, **36:**1637-1645.