Is Physical Activity a Risk Factor for Primary Knee or Hip Replacement Due to Osteoarthritis? A Prospective Cohort Study

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ABSTRACT. ***Objective.*** To estimate prospectively any association between measures of physical activity and the risk of either primary knee or hip replacement due to osteoarthritis (OA).

Methods. Eligible subjects (n = 39,023) were selected from participants in a prospective cohort study recruited 1990-1994. Primary knee and hip replacement for OA during 2001-2005 was determined by linking the cohort records to the National Joint Replacement Registry. A total physical activity level was computed, incorporating both intensity and frequency for different forms of physical activity obtained by questionnaire at baseline attendance.

Results. There was a dose-response relationship between total physical activity level and the risk of primary knee replacement [hazards ratio (HR) 1.04, 95% CI 1.01–1.07 for an increase of 1 level in total physical activity]. Although vigorous activity frequency was associated with an increased risk of primary knee replacement (HR 1.42, 95% CI 1.08–1.86) for 1–2 times/week and HR 1.24 (95% CI 0.90–1.71) for ≥ 3 times/week), the p for trend was marginal (continuous HR 1.08, 95% CI 1.00–1.16, p = 0.05). The frequency of less vigorous activity or walking was not associated with the risk of primary knee replacement, nor was any measure of physical activity associated with the risk of primary hip replacement.

Conclusion. Increasing levels of total physical activity are positively associated with the risk of primary knee but not hip replacement due to OA. Physical activity might affect the knee and hip joints differently depending on the preexisting health status and anatomy of the joint, as well as the sort of physical activity performed. (First Release Oct 15 2010; J Rheumatol 2011;38:350–7; doi:10.3899/jrheum.091138)

Key Indexing Terms:
PHYSICAL ACTIVITY JOINT REPLACEMENT OSTEOARTHRITIS KNEE HIP

Regular, moderate physical activity is recommended for adults to improve general health and increase life expectancy but there is uncertainty whether it is beneficial or detrimental to the health of weight-bearing joints such as the knee and hip. Studies examining the relationship between physical activity and the incidence and progression of osteoarthritis (OA) have yielded inconsistent results[1,2,3,4,5,6,7,8,9,10,11,12]. These studies have used differ-

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The Melbourne Collaborative Cohort Study recruitment was funded by VicHealth and The Cancer Council of Victoria. This study was supported by a program grant from the National Health and Medical Research Council (NHMRC; 209057), capacity building grant (251533), and enabling grant (396414), and was further supported by infrastructure provided by The Cancer Council of Victoria. Dr. Wang and Dr. Wluka received NHMRC Public Health (Australia) Fellowships (NHMRC 465142 and 317840, respectively).

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Accepted for publication August 20, 2010.

ent indicators of OA, including radiographic findings[2,5,6,8], self-reported symptoms[9,10], or both[1,3,4,7,12]. Radiographic studies have used either composite scores[1,4,6,12] or individual characteristics such as joint space narrowing and osteophytes[2,4,5,6,8]. In most studies physical activity has not been measured prospectively, i.e., with past physical activity being recalled by the participants or measured after the onset of OA symptoms[3,7,8,11,12].

Total joint replacement may be considered a proxy outcome measure for severe, symptomatic endstage OA. The majority of case-control studies have implicated longterm exposure to sporting activity as a risk factor for joint replacement due to severe knee and hip OA[13,14,15], with only one study reporting a decreased risk of knee replacement due to OA associated with increasing cumulative hours of recreational physical activity[16]. Recall bias, inherent to case-control studies, in the assessment of physical activity might have limited the results and explain some of the discrepancies, in addition to the heterogeneity of study populations. Two previous prospective cohort studies found no significant association between recreational activity and the risk of hip replacement due to primary OA[17,18]. No longitudinal study has been performed to examine the relationship between physical activity and the risk of knee replacement.

The progression from symptomatic OA to a joint replacement is likely to be slow, occurring over a decade[19] and it is likely that many of the studies examining subjects undergoing joint replacement had selected individuals who were performing physical activity with joints that already had early OA. The intensity of physical activity might also be an important determinant of the risk of joint replacement[18]. The aim of this cohort study was to prospectively examine the associations between the frequency and intensity of physical activity and the risk of subsequent knee and hip replacement due to OA. The main hypothesis was that physical activity is positively associated with the risk of primary hip and knee replacement due to OA.

MATERIALS AND METHODS

Study cohort. The Melbourne Collaborative Cohort Study (MCCS) is a prospective cohort study of 41,528 people (17,049 men) aged between 27 and 75 years at baseline, 99.3% of whom were aged 40–69 years[20]. Participants were recruited via electoral rolls (registration to vote is compulsory for Australian adults), advertisements, and announcements in local media (e.g., television, radio, newspapers), between 1990 and 1994. The study protocol was approved by The Cancer Council Victoria's Human Research Ethics Committee. Followup was conducted by record linkage to electoral rolls, electronic telephone books, and the Victorian Cancer Registry and death records. To update lifestyle exposures, the cohort was followed up with a mailed questionnaire and (as necessary) by telephone from 1995 to 1998 (first followup) and by face to face interviews from 2003 to 2007 (second followup).

Anthropometric measurements. Height and weight were measured once at baseline attendance according to written protocols based on standard procedures[21]. Weight was measured to the nearest 0.1 kg using digital electronic scales and height was measured to the nearest 1 mm using a stadiometer. Body mass index (BMI) was calculated as weight in kilograms divided by the square of height in meters.

Physical activity and other questionnaire measures. At baseline, a structured interview was used to obtain information on a wide range of demographic variables and lifestyle exposures including date of birth, country of birth, smoking, alcohol consumption, physical activity, and highest level of education. Physical activity over the last 6 months was assessed by asking specific questions regarding the frequency of vigorous activity (exercise "making you sweat or feel out of breath, and includes such activities as swimming, tennis, netball, athletics and running"), less vigorous activity (exercise for recreation, sport or health and fitness purposes "which did not make you sweat or feel out of breath, and include such activities as bike riding, dancing, etc"), and walking. The reported frequency for each question was coded as follows: 0 (none), 1.5 (once or twice per week), and 4 (3 or more times per week). Walking and less vigorous activity frequencies were added together with twice the frequency of vigorous activity to compute a total physical activity level for each person (i.e., 2 × frequency of vigorous activity + 1 × frequency of less vigorous activity + 1 × frequency of walking; range 0–16, describing the amount of physical activity)[22]. Occupational physical activity was assessed by asking, "On average, in the course of your tasks at work, how much time are you involved in moderate to heavy physical exertion which makes your breath harder or puff and pant," where a participant can choose "None at all" or fill in the time (hours/minutes) per day/week.

At the first followup, physical functioning was assessed by asking 5 questions: Did health problems limit you in your everyday physical activity? Did pain interfere with your normal work? Has your physical health or emotional problems interfered with your normal social activities? Have you been bothered by emotional problems? Was it difficult doing your daily work because of your physical health or emotional problems? Self-description of health status was assessed by asking, "In general, how would you describe your health?", where a participant can choose from among the options poor, fair, good, very good, and excellent.

From 2003 onwards, 28,046 study participants (68% of the original MCCS participants) took part in the second followup. The participants were asked questions enquiring about their first joint replacement surgery: Have you ever had a knee replacement? When did you have your first knee replacement? Have you ever had a hip replacement? When did you have your first hip replacement?

Study participants. Of the 41,528 participants recruited, 2505 (6.0%) were excluded from analysis, because: they died or left Australia prior to January 1, 2001; at the MCCS second followup they had reported a primary joint replacement prior to January 1, 2001; or they had the first recorded procedure being a revision joint replacement as recorded in the Australian Orthopaedic Association National Joint Replacement Registry (AOA NJRR), leaving 39,023 participants eligible for analysis.

Identification of incident primary knee and hip joint replacement. All participants gave written consent allowing access to their medical records. Cases were identified from the AOA NJRR. AOA NJRR implementation commenced in 1999 and was introduced in a staged state-by-state approach that was completed nationally by mid-2002. Victorian data collection commenced in 2001. The AOA NJRR monitors the performance and outcome of both hip and knee replacement surgery in Australia. It has detailed information on the prostheses and surgical technique used and the clinical situation that it was used in, for both primary and revision joint replacement[23]. Although data collection for the AOA NJRR is voluntary, it receives full cooperation from all hospitals undertaking joint replacement surgery[23].

Identifying information for MCCS participants, including first name, last name, date of birth, and gender, was provided to the staff at the AOA NJRR in order to identify those who had had a primary or revision joint replacement between January 1, 2001, which is when the Registry commenced Victorian data collection, and December 31, 2005. The matching was performed using US Bureau of the Census Record Linkage Software. Exact matches were identified and probabilistic matches were reviewed.

The staff from the AOA NJRR forwarded this information to MCCS and it was then added to the MCCS database.

The study was approved by The Cancer Council Victoria's Human Research Ethics Committee and the Standing Committee on Ethics in Research Involving Humans of Monash University.

Statistical analysis. Cox proportional hazards regression models were used to estimate the hazard ratios (HR) for first recorded primary knee and hip replacement for OA associated with each physical activity measure with adjustment for confounding variables. Followup for primary knee and hip replacement (i.e., calculation of person-time) began at January 1, 2001, and ended at date of first primary knee or hip replacement for OA or date of censoring. Subjects were censored at either the date of first primary joint replacement performed for indications other than OA, the date of death, the date left Australia, or end of followup (i.e., December 31, 2005, the date that ascertainment of joint replacement by NJRR was complete), whichever came first.

A total physical activity level was computed, incorporating both intensity and frequency for different forms of physical activity. Total physical activity level was categorized as none (0), low (> 0–3), moderate (> 3–4), and high (> 4–16)[22]. All physical activity variables were analyzed as categorical, and as pseudo-continuous, assuming that, within each category, all subjects' physical activity exposure was at its median frequency.

Linear association between physical activity variables and the risk of knee and hip replacement was investigated by comparing models that included physical activity as a categorical variable and physical activity as a pseudo-continuous variable using the likelihood ratio test. These analyses were carried out prior to the analysis for linear trend. To control for the confounding of vigorous activity, we analyzed less vigorous activity and walking on those with no reported vigorous activity.

Age, sex, BMI, country of birth (Australia, United Kingdom, Italy, Greece), occupational physical activity (participation in moderate to heavy physical exertion at work: yes/no), and highest level of education (primary and some secondary, completed secondary, and degree/diploma) were included in all models. Other potential confounders such as alcohol consumption (g/day) and smoking (never, past, current) were included in all the definitive analyses if they changed the HR for any of the physical activity variables by at least 5%. To test whether associations between physical activity measures and joint replacement risk were modified by sex or obesity (BMI ≥ 30 kg/m^2), interactions between the latter 2 variables and physical activity measures were fitted and tested using the likelihood ratio test.

Tests based on Schoenfeld residuals and graphical methods using Kaplan-Meier curves showed no evidence that proportional hazard assumptions were violated for any of the physical activity measures. All statistical analyses were performed using Stata (Intercooled Stata 9.2 for Windows, StataCorp LP, College Station, TX, USA).

RESULTS

Over an average 4.8 (SD 0.7) years of followup per person, we identified 541 participants with incident primary knee replacements and 468 participants with incident primary hip replacements for OA. Descriptive statistics for the characteristics of the study participants are shown in Table 1. Participants who did high level physical activity were younger (61.7 vs 63.2 yrs), had lower BMI (25.9 vs 27.3 kg/m^2), and were less likely to be born in Italy and Greece (11.4% vs 30.0%), compared with those who did not. The incidence rate of knee and hip replacement by different levels of physical activity is presented in Table 2.

Participants exposed to the high level of physical activity (total physical activity level > 4) had an increased risk of primary knee replacement (HR 1.46, 95% CI 1.13–1.87) when compared with those who reported no physical activity. There was a significant positive dose-response relationship between the levels of total physical activity and risk of primary knee replacement (HR 1.04 for an increase of 1 activity/week, 95% CI 1.01–1.07). The frequency of vigorous activity was also associated with an increased risk of primary knee replacement: HR for 1–2 times/week 1.42 (95% CI 1.08–1.86) and HR for ≥ 3 times/week 1.24 (95% CI 0.90–1.71). However, only 64 (11.8%) and 43 (8.0%) of the 541 participants who underwent primary knee replacement performed vigorous activity at 1–2 times/week and ≥ 3 times/week, respectively. Our study may not have enough numbers to show the effect of the highest level of vigorous activity and the linear association. The continuous HR estimate per unit increase in vigorous activity frequency was 1.08 (95% CI 1.00–1.16) and the p for trend was marginal at 0.05. No associations were observed between the frequency of less vigorous activity or walking and the risk of primary knee replacement (Table 3), nor between the level of total physical activity, frequency of vigorous activity, less vigorous activity, or walking, and the risk of primary hip replacement (Table 4). Including self-description of health status and physical function limitation in the regression models did not alter the results (data not shown).

When sensitivity analyses were performed on participants for whom complete second MCCS followup data were available so that those who had a history of primary knee or hip replacement prior to January 1, 2001 could be excluded (Tables 3 and 4), there was a stronger effect of vigorous activity on the risk of knee replacement, and similar results for other physical activity variables. A significant positive dose-response relationship was observed between the frequency of vigorous activity and the risk of knee replacement (HR 1.11, 95% CI 1.02–1.21, p = 0.01).

There was no evidence that sex or obesity modified the associations between physical activity and risk of primary knee or hip replacement.

DISCUSSION

In this prospective cohort study, we found that increasing levels of total physical activity were associated with an increased risk of primary knee replacement due to OA. The effect appeared to be related to vigorous activity, since no significant association was observed for less vigorous activity or walking. No measure of physical activity was associated with the risk of primary hip replacement.

To our knowledge, this is the first prospective cohort study to examine the relationship between physical activity and the risk of primary knee replacement due to OA. Of the 2 previous case-control studies, one reported an increased risk associated with high levels of sports exposure (i.e., high total number of hours)[15], while the other reported a reduced risk related to increasing cumulative hours of recreational physical activity[16]. Both studies assessed lifetime exposure

Table 1. Characteristics of study participants. Values are reported as mean ± SD, or number (%).

Characteristic	Primary Knee Replacement, n = 541	Primary Hip Replacement, n = 468	No Primary Joint Replacement, n = 38,014
Age when entering MCCS, yrs	60.3 ± 6.8	59.7 ± 7.1	54.8 ± 8.6
Age when entering JR cohort, yrs	68.1 ± 6.9	67.3 ± 7.2	62.6 ± 8.8
Age at JR, yrs	70.7 ± 6.9	70.1 ± 7.2	
Women, n (%)	344 (63.6)	283 (60.5)	22699 (59.7)
Body mass index, kg/m^2	29.8 ± 5.1	27.5 ± 4.3	26.8 ± 4.4
Country of birth, n (%)			
Australia/United Kingdom	470 (86.9)	415 (88.7)	28751 (75.6)
Italy/Greece	71 (13.1)	53 (11.3)	9263 (24.4)
Education, n (%)			
Primary and some secondary	340 (63.1)	242 (51.9)	21529 (57.0)
Completed secondary and degree/diploma	199 (36.9)	224 (48.1)	16240 (43.0)
Participation in moderate to heavy physical exertion at work, n (%)	44 (8.1)	37 (7.9)	3763 (9.9)
Self-description of health status, n (%)			
Poor/Fair	99 (21.7)	66 (16.0)	5176 (16.1)
Good/Very good/Excellent	357 (78.3)	347 (84.0)	27034 (83.9)
Physical function limitation, n (%)	360 (80.0)	294 (71.4)	21626 (68.6)
Total physical activity level, n (%)			
None (0)	106 (19.6)	96 (20.6)	8435 (22.2)
Low (> 0–3)	107 (19.8)	75 (16.0)	7668 (20.2)
Moderate (> 3–4)	141 (26.0)	120 (25.7)	9793 (25.7)
High (> 4)	187 (34.6)	176 (37.7)	12115 (31.9)
Vigorous activity, n (%)			
None at all	434 (80.2)	363 (77.7)	29857 (78.6)
1–2 times/week	64 (11.8)	54 (11.6)	4308 (11.3)
≥ 3 times/week	43 (8.0)	50 (10.7)	3840 (10.1)
Less vigorous activity, n (%)*			
None at all	258 (59.4)	213 (58.7)	19430 (65.1)
1–2 times/week	84 (19.4)	73 (20.1)	5263 (17.6)
≥ 3 times/week	92 (21.2)	77 (21.2)	5162 (17.3)
Walking, n (%)			
None at all	183 (42.2)	157 (43.2)	12828 (43.0)
1–2 times/week	75 (17.3)	53 (14.6)	5704 (19.1)
≥ 3 times/week	176 (40.5)	153 (42.2)	11325 (37.9)

* For those who did not report any vigorous activity. MCCS: The Melbourne Collaborative Cohort Study; JR: joint replacement.

to different types of sports, without taking into account the intensity or frequency of physical activity. Moreover, the long periods of recall required might have reduced the accuracy of the estimated exposure and introduced bias. In our study we collected physical activity data in the decade prior to knee replacement. We further computed a total physical activity level incorporating both the intensity and the frequency of physical activity. An increased risk of primary knee replacement was found to be associated with an increased level of total physical activity and a higher frequency of vigorous activity, but not the frequency of less vigorous activity or walking, suggesting that the intensity of physical activity might be an important determinant of risk for primary knee replacement. Participants undergoing a primary knee replacement during followup are likely to have reduced their frequency of vigorous activity due to knee symptoms, which might partly explain why no clear dose-response relationship was observed for vigorous activity.

Consistent with 2 previous prospective cohort studies[17,18], we found no association between physical activity and the risk of hip replacement due to OA. The Nurses' Health Study estimated physical activity by averaging the hours per week of moderate or vigorous recreational physical activity for each followup period from 1990 to 1996 and found that recreational physical activity was not associated with the risk of self-reported hip replacement during the same period[17]. The Nurses' Health Study assessed physical activity during the same time period as the self-reported joint replacement. It is likely that the exposure to physical activity was influenced by the presence of late-stage OA in those who reported a joint replacement. Self-reported joint replacement and the indication for the procedure in that study might be unreliable and increase misclassification.

Table 2. Incidence rate of knee and hip replacement by levels of physical activity.

Activity	Incidence Rate*, Knee Replacement	Incidence Rate*, Hip Replacement	Person-yrs
Total physical activity level			
None (0)	2.5	2.3	42,000
Low (> 0–3)	2.8	2.0	38,000
Moderate (> 3–4)	2.9	2.5	48,000
High (> 4)	3.1	2.9	60,000
Vigorous activity**			
None at all	2.9	2.5	150,000
1–2 times/week	3.0	2.5	22,000
≥ 3 times/week	2.2	2.6	19,000
Less vigorous activity**†			
None at all	2.7	2.2	96,000
1–2 times/week	3.2	2.8	26,000
≥ 3 times/week	3.6	3.0	25,000
Walking**†			
None at all	2.9	2.5	63,000
1–2 times/week	2.7	1.9	28,000
≥ 3 times/week	3.2	2.7	56,000

* Incidence rate of primary knee or hip replacement (per 1000 person-years) within each physical activity category. ** Weekly frequency of physical activity undertaken for at least 20 minutes. † Excluding those reporting vigorous activity.

Table 3. Association between physical activity and risk of primary knee replacement.

	Total Population, n = 39,023		Sensitivity Analysis on Participants with Complete 2nd Followup Data, n = 27,323	
	Hazard Ratio (95% CI)†	p†	Hazard Ratio (95% CI)†	p†
Total physical activity level				
None (0)	1.00		1.00	
Low (> 0–3)	1.16 (0.88, 1.52)	0.28	1.17 (0.85, 1.62)	0.33
Moderate (> 3–4)	1.13 (0.87, 1.46)	0.35	1.08 (0.79, 1.47)	0.64
High (> 4)	1.46 (1.13, 1.87)	0.003	1.47 (1.09, 1.96)	0.01
Trend test	1.04 (1.01, 1.07)	0.003	1.04 (1.01, 1.08)	0.01
Vigorous activity*				
None at all	1.00		1.00	
1–2 times/week	1.42 (1.08, 1.86)	0.01	1.43 (1.06, 1.94)	0.02
≥ 3 times/week	1.24 (0.90, 1.71)	0.19	1.44 (1.02, 2.04)	0.04
Trend test	1.08 (1.00, 1.16)	0.05	1.11 (1.02, 1.21)	0.01
Less vigorous activity*††				
None at all	1.00		1.00	
1–2 times/week	1.09 (0.85, 1.40)	0.49	1.17 (0.88, 1.56)	0.28
≥ 3 times/week	1.19 (0.94, 1.52)	0.16	1.11 (0.83, 1.49)	0.49
Trend test	1.05 (0.98, 1.11)	0.15	1.03 (0.96, 1.11)	0.43
Walking*††				
None at all	1.00		1.00	
1–2 times/week	1.01 (0.77, 1.32)	0.95	0.95 (0.69, 1.31)	0.75
≥ 3 times/week	1.09 (0.89, 1.35)	0.41	1.04 (0.81, 1.33)	0.79
Trend test	1.02 (0.97, 1.08)	0.40	1.01 (0.95, 1.08)	0.75

† Adjusted for age, gender, body mass index, country of birth, occupational physical activity, and education level. * Weekly frequency of physical activity undertaken for at least 20 minutes. †† Analysis excluding those reporting vigorous activity.

The other previous cohort study, in a Norwegian population, assessed physical activity by enquiring about the level of exercise and physical exertion categorized as sedentary, moderate, intermediate, and intensive during leisure time for the previous one-year period of screening, and found no association between physical activity in leisure and hip replacement risk approximately 9 years later[18]. Our study assessed the weekly frequencies of different intensity of

Table 4. Association between physical activity and risk of primary hip replacement.

	Total Population, n = 39,023		Sensitivity Analysis on Participants with Complete 2nd Followup Data, n = 27,323	
	Hazard Ratio (95% CI)†	p†	Hazard Ratio (95% CI)†	p†
Total physical activity level				
None (0)	1.00		1.00	
Low (> 0–3)	0.76 (0.56, 1.03)	0.07	0.71 (0.50, 1.02)	0.07
Moderate (> 3–4)	0.89 (0.67, 1.16)	0.38	0.84 (0.61, 1.17)	0.30
High (> 4)	1.09 (0.84, 1.41)	0.52	1.13 (0.84, 1.52)	0.42
Trend test*	1.03 (1.00, 1.06)	0.09	NA	NA
Vigorous activity**				
None at all	1.00		1.00	
1–2 times/week	1.11 (0.83, 1.48)	0.49	1.19 (0.87, 1.63)	0.27
≥ 3 times/week	1.27 (0.94, 1.73)	0.12	1.32 (0.95, 1.86)	0.10
Trend test	1.06 (0.99, 1.14)	0.11	1.08 (0.99, 1.17)	0.07
Less vigorous activity**††				
None at all	1.00		1.00	
1–2 times/week	1.04 (0.80, 1.36)	0.76	1.04 (0.76, 1.42)	0.82
≥ 3 times/week	1.09 (0.83, 1.41)	0.55	1.10 (0.81, 1.50)	0.54
Trend test	1.02 (0.96, 1.09)	0.54	1.02 (0.95, 1.11)	0.54
Walking**††				
None at all	1.00		1.00	
1–2 times/week	0.75 (0.55, 1.03)	0.07	0.71 (0.49, 1.03)	0.07
≥ 3 times/week	0.97 (0.77, 1.21)	0.78	0.96 (0.74, 1.25)	0.77
Trend test*	1.00 (0.94, 1.06)	0.93	NA	NA

* No evidence of linear association found between total physical activity level or walking and the risk of hip replacement (likelihood ratio test, p = 0.05), thus no trend test results presented. † Adjusted for age, gender, body mass index, country of birth, occupational physical activity, and education level. ** Weekly frequency of physical activity undertaken for at least 20 minutes. †† Analysis excluding those reporting vigorous activity. NA: not applicable.

physical activity, i.e., vigorous activity, less vigorous activity, and walking, over 6 months and found they were not associated with the risk of hip replacement approximately 13 years later. Our findings suggest that physical activity has different effects on the risk of knee and hip replacement.

In the natural history of OA, the average time from symptoms to a joint replacement is approximately 16 years for the knee and 8 years for the hip[19]. With this in mind, it may be that in our cohort, we found physical activity mediated the risk of knee replacement among a subgroup of people who already had early knee OA. Therefore, physical activity may exert differential effects across the spectrum of disease, from a fully healthy joint to severe endstage OA. Although it has previously been shown that moderate/high joint stress is associated with a reduced risk of knee and hip OA[9], and that physical activity is beneficial for knee cartilage in children[24] and adults with no clinical knee OA[25], this might not be the case in the setting of early joint damage. There is evidence that knee cartilage with early degenerative change displays a lower level of deformation than the normal knee joint due to changes in the biomechanical properties of the affected tissue: the knee cartilage with early structural changes might be less resilient, leading to a reduced capacity to withstand loads imparted by similar physical activities[26,27]. Where physical activity imparts excessive forces across articular surfaces that have already been biomechanically abnormal, it could accelerate further joint damage and facilitate the progression of OA.

The adverse effect of physical activity was observed at the knee but not the hip joint. This discrepancy might be attributable to the different anatomical characteristics and function of the knee and hip. Congruity is particularly important for the hip joint as its anatomy, i.e., a ball that sits inside a deep socket, makes it one of the most stable joints in the body. In contrast, the knee joint lacks a stable bony configuration, and behaves more like a round ball on a flat surface, and the ability of knee joint to rotate makes it susceptible to injury associated with physical activity.

There are a number of potential limitations to our study. The measures of physical activity were taken at a single point in time, at baseline. Although we cannot comment on whether reported physical activity patterns were habitual, there is evidence that participation in high intensity physical activity remains stable over many years for an individual[28]. However, it is possible that a number of participants are likely to have changed their physical activity habits over the study period because of pain associated with progressive degenerative joint disease. The progression of OA is a slow process and sufficient exposure to vigorous activity to cause structural change is likely to have occurred before symptoms might have necessitated change in physical activity patterns. Another limitation is that the questionnaire did not differentiate between weight-bearing and non-weight-bearing physical activity, which might have different effects on the subsequent risk of joint replacement. In our questionnaire, swimming, a non-weight-bearing physical activity, which may not increase the risk of knee or hip replacement, has been included in vigorous activities. This may have underestimated the effect of physical activity on the risk of joint replacement.

Although total joint replacement is an efficacious procedure for the treatment of symptomatic endstage OA, the decision to proceed with surgery may be affected by socioeconomic factors, patient perception, preference, and willingness[29,30]. Inclusion of self-description of health status and physical function limitation in the regression analyses did not alter the results, nor did adjustment for country of birth and education level, which may have identified some differences in terms of socioeconomic status in the analysis. Further, there is no evidence that such factors affect the knee and hip replacement differently. We had no information on history of joint injury, which is associated with physical activity and a well known risk factor for OA[31,32,33]. The presence of joint injury is likely to have underestimated the relationship between physical activity and joint replacement risk since those with joint injury who also underwent a joint replacement during the study period are likely to have reduced their physical activity due to pain. Based on the MCCS questionnaire, the participants had to undertake moderate to heavy occupational activity in order to answer "yes" for that question. When we adjusted for this level of occupational activity, the observed associations between recreational physical activity and the risk of joint replacement persisted. However, we cannot exclude an effect of lower levels of occupational activity. Because we did not have detailed information on occupational workload such as heavy lifting, climbing, kneeling, or squatting, which has been associated with an increased risk of severe OA leading to total hip or knee replacement[18,34], we could not control for this in the analysis. Finally, we did not have complete and reliable information about knee and hip replacement prior to 2001. Although we excluded those participants with any self-reported knee and hip replacement prior to 2001, this information might be unreliable and is known for only 68% of the original cohort. As a result, some misclassification of joint replacement might have occurred, although it is most likely to have been nondifferential in relation to physical activity. This is supported by the sensitivity analyses, in which, when only those with complete second followup data were included, in order to exclude any participants that had a joint replacement prior to 2001, there was a stronger effect of vigorous activity on the risk of knee replacement, and similar results for other physical activity variables.

Increasing levels of total physical activity are positively associated with the risk of primary knee but not hip replacement due to OA. This association appears to be related to the frequency of vigorous activity. Physical activity might affect the knee and hip joints differently, depending on the preexisting health status and anatomy of the joint, as well as the kind of physical activity a joint is subject to. Further work is required to address these questions, since they have significant implications for the prevention and management of OA.

ACKNOWLEDGMENT

We thank the data manager, Lisa Ingerson, and statistician, Nicole Pratt, from the Australian Orthopaedic Association National Joint Replacement Registry, and Georgina Marr from The Cancer Council Victoria.

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