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Smoking, Body Weight, Physical Exercise, and Risk of Lower Limb Total Joint Replacement in a Population-Based Cohort of Men

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Objective. **To assess the associations of smoking, body weight, and physical activity with risk of undergoing total joint replacement (TJR) in a population-based cohort of men.**

Methods. **A cohort study of 11,388 men that integrated clinical data with hospital morbidity data and mortality records was undertaken. The risk of undergoing TJR was modeled on baseline weight, height, comorbidity, socioeconomic status, years of smoking, and exercise in 3 separate age groups, using Cox proportional hazards regressions and competing risk regressions (CRRs).**

Results. **Dose-response relationships between weight and risk of TJR and between smoking and risk of TJR were observed. Being overweight independently increased the risk of TJR, while smoking lowered the risk. The decreased risk among smokers was demonstrated in both Cox and CRR models and became apparent after 23 years of exposure. Men who were in the highest quartile (≥48 years of smoking) were 42–51% less likely to undergo TJR than men who had never smoked. Tests for trend in the log hazard ratios (HRs) across both smoking and weight quantiles yielded significant *P* values. Vigorous exercise increased the hazard of TJR; however, the association reached statistical significance only in the 70–74-year-old age group (adjusted HR 1.64 [95% confidence interval 1.19–2.24]). Adjusting for Deyo-Charlson Index or Elixhauser's comorbidity measures did not eliminate these associations.**

Conclusion. **Our findings indicate that being overweight and reporting vigorous physical activity increase the risk of TJR. This study is the first to demonstrate a strong inverse dose-response relationship between duration of smoking and risk of TJR. More research is needed to better understand the role of smoking in the pathogenesis of osteoarthritis.**

Total hip replacement (THR) and total knee replacement (TKR) are among the most common elective surgical procedures performed in developed countries (1–4). The most common indicator for total joint replacement (TJR) is severe osteoarthritis (OA) (5,6), and TJR is often considered an acceptable surrogate indicator of severe OA (7–9). Factors associated with OA (e.g., age, female sex, and obesity) are predictors of TJR (7,10).

In the aging population, OA is the most common form of arthritis (5), causing much disability and impairing quality of life (11). Independent risk factors for this disorder include older age (12), female sex (13), obesity (13–16), physical activity (12–14), and never having smoked (9,13,15). However, the reported association of some of these factors with an increased risk of OA or subsequent TJR has not been consistent. Being overweight shows the most consistent association with OA (9,13,15,16) and with TJR (7,8,14), while the results for physical activity and smoking have been the most inconsistent (7,9,12–15,17–26).

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Smoking has variously shown a negative association with OA (9,13,15,19,20,26) or TJR (21), a positive association with OA (22,23) or TJR (7), and no significant association with OA (12,17,24). Similarly, the association of physical activity with the risk of OA is unclear. An example of contradictory findings was observed in 2 studies of the population-based Framingham cohort. In the first publication on this topic, based on a subpopulation from the first cohort enrolled, patients in the highest quartile of physical activity had 3.3 times the odds of developing OA compared with those in the lowest quartile of physical activity (13). However, in a second publication, based on a subpopulation of the first cohort's children and their spouses, the association between physical activity and radiographic OA was weaker and did not reach statistical significance, with an adjusted odds ratio (OR) of 1.20 (95% confidence interval [95% CI] 0.65–2.21) (18).

Inconsistencies in the findings of those and other studies reflect sampling biases or nonrepresentative cases, a lack of or incomplete adjustment for comorbidities and other confounders, inconsistencies in definitions of disease, or inaccuracies in definitions of exposure (7,12,16,23). Some studies did not make an appropriate distinction between current and past smoking (16,23), while others disregarded the duration of smoking (7,12).

This study was undertaken to assess the predictors of undergoing a lower limb TJR in a large population-based cohort of elderly men, focusing on the modifiable factors of body weight, duration of smoking, and physical activity.

PATIENTS AND METHODS

Data sources and study population. The study population was drawn from the Health In Men Study (27,28), which arose from a randomized population-based trial of ultrasound screening for abdominal aortic aneurysm in men ages 65–83 living in Perth, Western Australia. A total of 41,000 men were identified via the electoral roll (voting is compulsory in Australia) and randomized into invited and control groups of equal size. Of the 19,352 men who were invited, 12,203 attended the baseline screening in 1996–1999. At baseline, the participants provided detailed health and other information, including a comprehensive history of smoking, whether they engaged in vigorous exercise (defined in the questionnaire as "exercise that makes you breathe harder, e.g., jogging, aerobics, tennis, football, squash, etc.") in a usual week (a yes/no question), and whether they engaged in nonvigorous exercise (defined as "exercise that does not make you breathe harder, e.g., slow walking or cycling, yoga, Tai Chi, etc.") in a usual week (a yes/no question). In addition, study nurses recorded weight, height, and waist and hip circumferences. Electronic record linkage was used to identify hospital admissions (hospital morbidity data) for TJR in the target population. All-cause mortality was ascertained through linkage to Western Australia Health Department mortality records. Followup for study end points started at baseline screening and ended in March 2007.

The hospital morbidity data system is a core part of the Western Australia Linked Data System (29) and includes demographic, diagnostic, and procedural information on all patients discharged from all public and private hospitals in Western Australia. The hospital morbidity data, which have been validated (30), can include up to 21 diagnoses and 11 procedure codes for each hospitalization in every hospital department. The validation analysis of the hospital morbidity data showed good to acceptable sensitivities and positive predictive values (PPVs) for major operations (e.g., sensitivity and PPV of 0.92 for TJR) and major morbidity (e.g., sensitivity of 0.90 and PPV of 0.78 for any cancer, sensitivity of 0.69 and PPV of 0.80 for past myocardial infarction, and sensitivity of 0.68 and PPV of 0.88 for diabetes mellitus) (30).

Definitions. The Deyo-Charlson Comorbidity Index (31) and Elixhauser's comorbidity measures (32), which were used to adjust for comorbidity, were based on all reported conditions in admissions that preceded baseline screening. The Deyo-Charlson Index was built using the original Charlson weights (33), and the corresponding International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) algorithms were used as delineated in the original report by Deyo et al (31). We further used an ICD-10-AM (Australian Modification) adaptation of the Deyo-Charlson Index as developed and validated using population-based hospital data from Australia (34). The coding algorithms defining Elixhauser's comorbidity measures were based on definitions by Quan et al (35).

The Socio Economic Index For Areas (SEIFA) (36) was used to define the participants' socioeconomic status. The SEIFA indicates relative social disadvantage of populations living in different geographic areas, with low scores reflecting disadvantage. Since most of the participants were recruited before 1999 (30), we used the 1996 census to calculate the index. At baseline screening, the participants provided their residential postcode, thus lowering the chances of misclassification of the SEIFA due to incorrect postcode. Presence of traumatic fracture of the lower limb on the day of surgery was also identified from the hospital morbidity data system. Body mass index (BMI) was defined as body weight in kilograms divided by height in meters squared. The ICD codes used to detect primary THR or TKR were checked by a professional clinical coder. (See Appendix 1, available on the *Arthritis & Rheumatism* web site at http://onlinelibrary.wiley.com/journal/10.1002/(ISSN)1529-0131.)

Statistical analysis. Men who had had a lower limb TJR before baseline screening were excluded from this analysis. The remaining eligible participants were followed up from baseline screening until they experienced their *first* TJR or died or were right censored at the end of followup (March 2007). Since the focus of the study was elective TJR, all patients who experienced a fracture of the lower limb (among those who had and those who did not have a TJR) were excluded from the analysis.

In 3 separate age groups (65–69 years, 70–74 years, and ≥75 years), we modeled time to TJR on weight, height,

Table 1. Baseline characteristics of the study population by TJR status after baseline screening*

Characteristic	Had TJR (n = 857)	Did not have TJR (n = 10,531)	*P*
Age, mean ± SD, (range) years	71.6 ± 4.2 (65–84)	72.0 ± 4.4 (65–84)	0.026
Deyo-Charlson Index, mean ± SD (range)	0.69 ± 1.2 (0–8)	0.89 ± 1.4 (0–11)	<0.001
BMI, mean ± SD (range) kg/m^2	28.1 ± 3.5 (19.3–41.0)	26.7 ± 3.7 (14.0–67.1)	<0.001
Vigorous exercise (during a usual week), %	27.4	25.3	0.175
Ever smoked, %	67.8	71.3	0.030
Years of smoking, mean ± SD (range)	21.8 ± 19.8 (0–70)	24.7 ± 20.6 (0–73)	<0.001
SES as measured by SEIFA distribution, %			
Lower tertile (low SES)	29.9	33.3	–
Middle tertile	32.1	33.0	–
Higher tertile (high SES)	38.0	33.7	0.024
Fracture of lower limb, %	4.4	4.2	0.802

* TJR = total joint replacement; BMI = body mass index; SES = socioeconomic status; SEIFA = Socio Economic Index For Areas.

socioeconomic status, Deyo-Charlson Comorbidity Index (or Elixhauser's comorbidity measures), vigorous or nonvigorous physical exercise, and years of smoking, using Cox proportional hazards regressions and competing risk regressions (CRRs) as defined by Fine and Gray (37). The latter analyses assessed the effect of predictors on the hazard of the subdistribution for TJR (the "subhazard") while accounting for the competing risk of death, since the study population was elderly and death represented a competing risk that reduced the number of individuals at risk of the event of interest, TJR (38,39). We also used the cumulative incidence function (39) to estimate the overall risks of TJR and of death in the study population.

Tests for trend in the log hazard ratios (HRs) across quantiles of duration of smoking and body weight were performed by introducing each of the ordered variables in the multivariable Cox models. The Cox proportional hazard assumptions were tested in each of the age groups using Schoenfeld residuals.

The crude attributable risk of dying among heavy smokers (≥48 years of smoking) was defined as incidence of death among the heavy smokers minus incidence of death among those who never smoked divided by the incidence of death among the heavy smokers (40). All analyses were performed using the Stata statistical program, version 11.

Ethical approval was obtained from the Human Research Ethics Committees of the Health Department of Western Australia and The University of Adelaide prior to commencement of the study. All analyses used deidentified data.

Table 2. Crude rate of TJR by age and body weight*

	Ages 65–69 years	Ages 70–74 years	Ages ≥75 years	Total
First quintile (n = 2,181)†	3.2	2.6	2.2	2.6
Second quintile (n = 2,240)	5.9	7.3	6.0	6.4
Third quintile (n = 2,186)	6.8	8.9	7.6	7.8
Fourth quintile (n = 2,118)	8.2	11.9	9.6	9.9
Fifth quintile (n = 2,177)‡	11.6	10.7	9.8	10.9
Total (n = 10,902)	7.5	8.3	6.4	7.5

* Values are the percentage of subjects (not accounting for censoring) who underwent total joint replacement (TJR). Subjects who had a lower limb fracture were excluded.
† Subjects in the first quintile had a body weight of ≤68.4 kg.
‡ Subjects in the fifth quintile had a body weight of ≥87.9 kg.

RESULTS

Of the total of 12,203 men (mean ± SD age 72.1 ± 4.4 years [range 65–84 years]) who participated in the baseline abdominal aortic aneurysm screening study, 815 men (6.7%) were excluded since they had already undergone a TJR prior to baseline screening, leaving a total of 11,388 participants for the current analysis. Of these remaining eligible participants, a total of 857 men (7.5%) had a TJR after screening. Of the participants who underwent TJR, 510 (59.5%) had a TKR and 347 (40.5%) had a THR. The baseline characteristics of these 857 men differed significantly from those of the participants who had never had a TJR. The former were

Table 3. Crude rate of TJR by age, BMI, and years of smoking*

	Ages 65–69 years	Ages 70–74 years	Ages ≥75 years
BMI <30 kg/m^2			
Never smoked	7.4	8.8	5.8
First tertile	7.6	7.5	6.6
Second tertile	6.5	8.1	6.7
Third tertile	4.6	6.2	3.8
BMI ≥30 kg/m^2			
Never smoked	15.2	10.2	13.5
First tertile	11.4	12.9	10.0
Second tertile	8.6	8.8	8.6
Third tertile	9.0	12.9	9.3

* Values are the percentage of subjects (not accounting for censoring) who underwent total joint replacement (TJR). Subjects who had a lower limb fracture were excluded. Subjects in the first tertile had smoked for 1–28 years, subjects in the second tertile had smoked for 29–43 years, and subjects in the third tertile had smoked for ≥44 years. BMI = body mass index.

Table 4. Crude and age-adjusted death rates by years of smoking*

	Ages 65–69 years	Ages 70–74 years	Ages ≥75 years	Crude total death rate	Age-standardized death rates†
Never smoked	64/1,281 (5.0)	111/1,119 (9.9)	191/896 (21.3)	366/3,296 (11.1)	11.3
First quartile	40/632 (6.3)	80/731 (10.9)	123/570 (21.6)	243/1,933 (12.6)	12.2
Second quartile	60/701 (8.6)	113/721 (15.7)	137/503 (27.2)	310/1,925 (16.1)	16.4
Third quartile	71/669 (10.6)	130/693 (18.8)	136/507 (26.8)	337/1,869 (18.0)	18.1
Fourth quartile	103/569 (18.1)	186/765 (24.3)	195/545 (35.8)	484/1,879 (25.8)	25.3

* Values are the number of deaths that preceded TJR/number of subjects (%). Subjects in the first quartile had smoked for 1–23 years, subjects in the second quartile had smoked for 24–36 years, subjects in the third quartile had smoked for 37–47 years, and subjects in the fourth quartile had smoked for ≥48 years.
† Adjusted for age by direct standardization method (using total population as the standard).

significantly younger, had less comorbidity (defined by the Deyo-Charlson Index), had a higher mean BMI, had a higher socioeconomic status, and smoked fewer years than those who did not undergo TJR after baseline (Table 1). A total of 486 men (with fracture of lower limb) were excluded, thus leaving 10,902 men for the study analysis.

To meet the proportionality assumptions of time-to-event models, the cohort was divided into 3 age groups based on the actual age distribution in the cohort (65–69 years, 70–74 years, and ≥75 years), and the subsequent analyses were performed separately on each of the age groups.

We stratified TJR by weight quintiles and found that within each age category, the crude proportion of men undergoing TJR increased with weight, while within quintiles of weight the proportion was relatively constant across age groups (Table 2). We further stratified TJR by years of smoking, age, and BMI and found an inverse association between duration of smoking and

Table 5. HRs for TJR by age group*

	Ages 65–69 years (n = 3,852)		Ages 70–74 years (n = 4,029)		Ages ≥75 years (n = 3,021)	
	HR (95% CI)	*P*	HR (95% CI)	*P*	HR (95% CI)	*P*
Deyo-Charlson Index†	0.69 (0.61–0.78)	0.000	0.77 (0.70–0.85)	0.000	0.67 (0.59–0.76)	0.000
SEIFA distribution						
Lower tertile (low SES)‡	1.00		1.00		1.00	
Middle tertile	0.94 (0.69–1.27)	0.696	1.19 (0.89–1.59)	0.244	1.01 (0.70–1.46)	0.952
Higher tertile (high SES)	1.00 (0.74–1.37)	0.951	1.50 (1.14–1.97)	0.004	0.81 (0.56–1.17)	0.269
Height, cm†	1.00 (0.98–1.02)	0.760	0.98 (0.97–1.00)	0.111	0.98 (0.96–1.00)	0.207
Weight, kg						
First quintile (≤68.4 kg)‡	1.00	–	1.00	–	1.00	–
Second quintile (68.5–74.8 kg)	1.69 (0.97–2.95)	0.061	2.98 (1.78–4.99)	0.000	2.98 (1.69–5.27)	0.000
Third quintile (74.9–80.6 kg)	2.23 (1.29–3.85)	0.004	4.65 (2.79–7.75)	0.000	3.34 (1.90–5.86)	0.000
Fourth quintile (80.7–87.8 kg)	2.68 (1.56–4.60)	0.000	5.09 (3.08–8.42)	0.000	4.53 (2.56–7.98)	0.000
Fifth quintile (≥87.9 kg)	3.17 (1.88–5.35)	0.000	4.36 (2.58–7.36)	0.000	4.09 (2.26–7.40)	0.000
Exercise						
None‡	1.00	–	1.00	–	1.00	–
Nonvigorous	1.33 (0.97–1.81)	0.078	1.04 (0.79–1.38)	0.763	1.27 (0.89–1.81)	0.191
Vigorous	1.29 (0.91–1.82)	0.145	1.64 (1.19–2.24)	0.002	1.29 (0.82–2.03)	0.261
Years of smoking						
Never smoked‡	1.00	–	1.00	–	1.00	–
First quartile (1–23 years)	1.06 (0.75–1.49)	0.756	0.88 (0.64–1.22)	0.453	0.89 (0.59–1.35)	0.587
Second quartile (24–36 years)	0.79 (0.56–1.11)	0.177	0.76 (0.54–1.07)	0.123	1.10 (0.72–1.69)	0.653
Third quartile (37–47 years)	0.52 (0.35–0.76)	0.001	0.65 (0.45–0.95)	0.024	1.11 (0.72–1.71)	0.637
Fourth quartile (≥48 years)	0.49 (0.32–0.74)	0.001	0.58 (0.41–0.82)	0.002	0.51 (0.30–0.85)	0.009

* Hazard ratios (HRs) were determined by a multivariable Cox proportional hazards model in each age group, which represents a multivariable analysis that assesses the association of each covariate with total joint replacement (TJR) while controlling for all other covariates listed in the table. The number (%) of subjects who underwent TJR was 290 (7.5) in the age group 65–69 years, 336 (8.3) in the age group 70–74 years, and 193 (6.4) in the age group ≥75 years. 95% CI = 95% confidence interval; SEIFA = Socio Economic Index For Areas; SES = socioeconomic status.
† Continuous variable.
‡ Reference group.

TJR (Table 3). To verify whether more deaths occurred among the smokers compared to those who had never smoked and whether this "selective mortality" (41) contributed to the inverse association of smoking and TJR, we assessed the crude and age-adjusted death rates as shown in Table 4. The crude mortality rate in each of the age groups increased as the years of smoking increased. In the younger men (ages 65–69 years), 72.4% of the crude mortality among the heavy smokers (≥48 years of smoking) was attributable to smoking. This attributable risk fell to 40.5% in the group who were ≥75 years old. The overall age-adjusted and crude mortality rates were similar, showing an increased risk of death as years of smoking increased (Table 4).

To investigate the etiologic associations of the study covariates with TJR, we calculated the cause-specific relative hazards (42) using multivariable Cox proportional hazards regressions (Table 5). After adjustment for other covariates in the models, being overweight was significantly associated with an increased hazard of TJR, showing a dose-response relationship across quintiles of the distribution of weight in all 3 age strata ($P < 0.001$). In the middle age group (ages 70–74 years), men weighing ≥87.9 kg were 4.4 times more likely to undergo TJR compared to men weighing ≤68.4 kg (HR 4.36 [95% CI 2.58–7.36]). Vigorous exercise reported at baseline increased the hazard of undergoing TJR, but this association was only statistically significant in the age group 70–74 years (HR 1.64 [95% CI 1.19–2.24]). Higher socioeconomic status was positively associated with TJR in the age group 70–74 years (HR 1.50 [95% CI 1.14–1.97]).

Smoking was inversely associated with TJR, showing a dose-response relationship across quartiles of the distribution of years of smoking in all 3 age strata ($P < 0.001$ in the age group 65–69 years, $P = 0.002$ in the age group 70–74 years, and $P = 0.05$ in the age group ≥75 years). Compared to men who had never smoked, men who had smoked 48 years or more were 42–51% less likely to undergo TJR (HR 0.49 [95% CI 0.32–0.74] in the age group 65–69 years, HR 0.58 [95% CI 0.41–0.82] in the age group 70–74 years, and HR 0.51 [95% CI 0.30–0.85] in the age group ≥75 years). Similar results were found after modeling time to TJR using CRR to account for the competing risk of death. However, the CRR modeling strengthened the significant associations of weight and of smoking with TJR (data not shown).

To control for potential confounding from other comorbidities not accounted for in the Deyo-Charlson Index, the CRR models were run using Elixhauser's method (instead of the Deyo-Charlson Index). This produced findings almost identical to those of the first models (data not shown).

To assess the association of weight with different joint replacements, we further modeled THR and TKR separately and found that the association of weight was stronger with TKR than with THR; however, the dose-response relationship across quintiles of the distribution of weight was maintained for both TKR and THR. Patients weighing ≥87.9 kg were 5.7 times more likely to have a TKR (adjusted HR 5.72 [95% CI 3.74–8.75]) and 2.7 times more likely to have a THR (adjusted HR 2.74 [95% CI 1.75–4.29]), compared with patients who weighed ≤68.4 kg. No statistically significant interactions were found between body weight and smoking or physical activity, nor between smoking and physical activity.

DISCUSSION

This study, involving a large population-based cohort of men, is the first to show an independent dose-response relationship of duration of smoking with reduction in the risk of undergoing subsequent TJR. Consistent with the findings of previous studies, we also demonstrated that being overweight (7,8,14) and engaging in vigorous exercise (14) each significantly increased the risk of TJR.

An association between smoking and a decreased risk of OA (9,13,15,19,20,26), or subsequent TJR (21), has been reported previously. One of the earliest reports came from the cross-sectional population-based first Health and Nutrition Examination Survey in the US (43), which showed an age-adjusted significant inverse association between number of cigarettes smoked per day and radiographic knee OA among both men and women. To test for confounding, researchers from the Framingham Study controlled for age, sex, BMI, physical activity, and past knee injury and found a similar negative association in 2 separate studies (13,15). In one, a prevalence analysis of 1,424 participants, the adjusted OR for knee OA was 0.74 among the smokers ($P < 0.05$) (15). The other study investigated the incidence of radiographic knee OA and showed that heavy smokers had a significantly lower risk of developing new knee OA among a cohort of 598 participants who initially did not have OA (OR 0.4 [95% CI 0.2–0.8]) (13).

A similar decrease in risk was reported in a large longitudinal study of a population-based cohort of construction workers (9). Subjects who had never smoked had an ~40% increased relative risk of undergoing hip replacement due to OA, while ex-smokers had an in-

creased risk of 20% compared with smokers (9). The findings of the present study confirmed the inverse association of smoking with risk of TJR. Smokers were more likely to die than those who had never smoked, but even accounting for this competing risk of death, men who smoked for more years were less likely to undergo TJR compared to those who had never smoked.

The mechanisms behind this decrease in risk are not clear. There is some evidence that smoking may directly reduce the severity of OA. An in vitro study showed a relationship between nicotine and stimulation of the anabolic activity of chondrocytes (cells found in joint cartilage) (44). This was supported by a population-based prospective cohort study that showed a positive dose-response relationship between pack-years of smoking and knee cartilage volume among healthy individuals (26).

The decrease in risk may have other explanations. In the present study, data on comorbid conditions were retrieved from the hospital morbidity data system, and since this data set was not originally formed for the purpose of health research, some comorbid conditions may have been underreported. If comorbidity were underestimated, the risk of TJR among those who had never smoked could have been overestimated (given that those who had ever smoked had more comorbidities than those who had never smoked). However, we have shown that the hospital morbidity data system is a valid tool to assess major health care outcomes (30). The validation analysis showed good to acceptable sensitivities and PPVs for serious conditions, such as major comorbidities and major surgical procedures. Another explanation is the possibility of confounding by factors not accounted for in this analysis or by selection biases prior to surgery. A survey that sought to find indications for THR or TKR as perceived by orthopedic surgeons showed that the decision against surgery was mainly affected by patient age, comorbidity, obesity, alcohol use, technical difficulties, and lack of motivation among the patients. Smoking was not indicated as a factor that would sway the decision against TKR or THR (45).

Body weight is one of the most investigated factors in the study of OA or TJR. In many studies, being overweight and measures of relative body mass have been associated with an increased risk of OA (9,13,15,16,46) and TJR (7,8,14), with some showing a stronger association in knee OA (16), suggesting a biomechanical component in the relationship between body weight and OA. However, more studies have shown a positive relationship between being overweight and OA at different body sites, including knee, hip (8,16), and non–weight-bearing joints such as small joints of the hands (47,48), suggesting a connection between OA and metabolically active adipose tissue.

In the present study, after controlling for physical activity, smoking, socioeconomic status, height, and comorbidities, we found a dose-response relationship between body weight and the risk of undergoing THR and TKR. However, the association of weight with TKR was stronger than that with THR.

Furthermore, we found that in the older age groups, the probability of undergoing TJR was similar in the 2 highest body weight quintiles. A possible explanation could be selection prior to surgery. Morbid obesity in these advanced ages may have swayed the decision against surgery (45), thus lowering the HR in the highest weight categories.

This study showed a positive association between vigorous exercise and TJR (14). This association could have been underestimated, since the participants were relatively old when asked about their weekly exercise habits and one would assume that old age might have naturally limited their physical activity. Nevertheless, these findings suggest that those who were physically active in their younger ages stayed active as they got older and that this activity was positively related to an increased risk of TJR.

This study has several strengths, including its longitudinal followup design, accurate clinical data on body weight, and inclusion of many years of past exposure to smoking. Moreover, the linkage of participants' records to the hospital morbidity data system allowed us to account for major comorbidities for each individual. However, the study has limitations. Although we considered TJR to be a surrogate indicator of severe OA, we did not directly ascertain OA status among study participants. The SEIFA ranked the socioeconomic status of the populations within areas rather than individuals themselves. Any area can include both relatively advantaged and disadvantaged people. Using the postcode may have introduced some misclassifications (49); however, since the postcode was provided by the participants, any misclassifications were minimized. Information on the physical activity of the participants was self-reported and not validated. The clinical data presented in the study were collected at baseline screening and, except for age, the study did not account for changes in patient characteristics (e.g., change in body weight or physical activity) that could have occurred over time. However, the time from baseline screening to TJR was not long (mean $\pm$ SD 4.6 $\pm$ 2.7 years), and one may assume that in this relatively elderly cohort, OA (a

degenerative disease that takes a long time to develop) was probably present at baseline, but this was not assessed in this study. Finally, this longitudinal study was observational, and a causal relationship between smoking and OA cannot necessarily be inferred.

This population-based cohort study has shown an increased risk of TJR with increased body weight and vigorous exercise, and an inverse association between smoking and risk of TJR. This is the first study to demonstrate a strong, inverse, dose-response relationship between duration of smoking and risk of TJR. More research is needed to better understand the role of smoking in the pathogenesis of OA, but also into the criteria that are used to determine whether patients should receive TJR. Notwithstanding the findings, this study reinforces the overwhelming excess risk of premature mortality associated with smoking.

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AUTHOR CONTRIBUTIONS

All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be published. Dr. Mnatzaganian had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study conception and design. Mnatzaganian, Ryan.

Acquisition of data. Norman.

Analysis and interpretation of data. Mnatzaganian, Ryan, Davidson, Hiller.

REFERENCES

1. Birrell F, Johnell O, Silman A. Projecting the need for hip replacement over the next three decades: influence of changing demography and threshold for surgery. Ann Rheum Dis 1999;58: 569–72.
2. Kim S. Changes in surgical loads and economic burden of hip and knee replacements in the US: 1997–2004. Arthritis Rheum 2008; 59:481–8.
3. Kurtz S, Ong K, Lau E, Mowat F, Halpern M. Projections of primary and revision hip and knee arthroplasty in the United States from 2005 to 2030. J Bone Joint Surg Am 2007;89:780–5.
4. Australian Institute of Health and Welfare. Australian hospital statistics 2005-05. Canberra: AIHW; 2006. URL: http://www.aihw.gov.au/publications/index.cfm/title/10305.
5. Felson DT, Lawrence RC, Dieppe PA, Hirsch R, Helmick CG, Jordan JM, et al. Osteoarthritis: new insights. Part 1: the disease and its risk factors. Ann Intern Med 2000;133:635–46.
6. Australian Orthopaedic Association National Joint Replacement Registry. Annual report. Adelaide: Australian Orthopaedic Association; 2008. URL: http://www.dmac.adelaide.edu.au/aoanjrr/publications.jsp?section=reports2008.
7. Karlson EW, Mandl LA, Aweh GN, Sangha O, Liang MH, Grodstein F. Total hip replacement due to osteoarthritis: the importance of age, obesity, and other modifiable risk factors. Am J Med 2003;114:93–8.
8. Wang Y, Simpson JA, Wluka AE, Teichtahl AJ, English DR, Giles GG, et al. Relationship between body adiposity measures and risk of primary knee and hip replacement for osteoarthritis: a prospective cohort study. Arthritis Res Ther 2009;11:R31.
9. Jarvholm B, Lewold S, Malchau H, Vingard E. Age, bodyweight, smoking habits and the risk of severe osteoarthritis in the hip and knee in men. Eur J Epidemiol 2005;20:537–42.
10. Harms S, Larson R, Sahmoun AE, Beal JR. Obesity increases the likelihood of total joint replacement surgery among younger adults. Int Orthop 2007;31:23–6.
11. World Health Organization. World Health Report 2002. Reducing risks, promoting healthy life. Geneva: WHO; 2002. URL: http://www.who.int/whr/2002/en/index.html.
12. Juhakoski R, Heliovaara M, Impivaara O, Kroger H, Knekt P, Lauren H, et al. Risk factors for the development of hip osteoarthritis: a population-based prospective study. Rheumatology (Oxford) 2009;48:83–7.
13. Felson DT, Zhang Y, Hannan MT, Naimark A, Weissman B, Aliabadi P, et al. Risk factors for incident radiographic knee osteoarthritis in the elderly: the Framingham Study. Arthritis Rheum 1997;40:728–33.
14. Flugsrud GB, Nordsletten L, Espehaug B, Havelin LI, Meyer HE. Risk factors for total hip replacement due to primary osteoarthritis: a cohort study in 50,034 persons. Arthritis Rheum 2002;46: 675–82.
15. Felson DT. The epidemiology of knee osteoarthritis: results from the Framingham Osteoarthritis Study. Semin Arthritis Rheum 1990;20:42–50.
16. Lohmander LS, Gerhardsson de Verdier M, Rollof J, Nilsson PM, Engstrom G. Incidence of severe knee and hip osteoarthritis in relation to different measures of body mass: a population-based prospective cohort study. Ann Rheum Dis 2009;68:490–6.
17. Wilder FV, Hall BJ, Barrett JP. Smoking and osteoarthritis: is there an association? The Clearwater Osteoarthritis Study. Osteoarthritis Cartilage 2003;11:29–35.
18. Felson DT, 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.
19. Cooper C, Inskip H, Croft P, Campbell L, Smith G, McLaren M, et al. Individual risk factors for hip osteoarthritis: obesity, hip injury, and physical activity. Am J Epidemiol 1998;147:516–22.
20. Sandmark H, Hogstedt C, Lewold S, Vingard E. Osteoarthrosis of the knee in men and women in association with overweight, smoking, and hormone therapy. Ann Rheum Dis 1999;58:151–5.
21. Wolfe F, Zwillich SH. The long-term outcomes of rheumatoid arthritis: a 23-year prospective, longitudinal study of total joint replacement and its predictors in 1,600 patients with rheumatoid arthritis. Arthritis Rheum 1998;41:1072–82.
22. Ding C, Cicuttini F, Blizzard L, Jones G. Smoking interacts with family history with regard to change in knee cartilage volume and cartilage defect development. Arthritis Rheum 2007;56:1521–8.
23. Martin SA, Haren MT, Taylor AW, Middleton SM, Wittert GA, for members of the Florey Adelaide Male Ageing Study (FAMAS). Chronic disease prevalence and associations in a cohort of Australian men: the Florey Adelaide Male Ageing Study (FAMAS). BMC Public Health 2008;8:261.

24. Hart DJ, Spector TD. Cigarette smoking and risk of osteoarthritis in women in the general population: the Chingford study. Ann Rheum Dis 1993;52:93–6.
25. Racunica TL, Teichtahl AJ, Wang Y, Wluka AE, English DR, Giles GG, et al. Effect of physical activity on articular knee joint structures in community-based adults. Arthritis Rheum 2007;57: 1261–8.
26. Racunica TL, Szramka M, Wluka AE, Wang Y, English DR, Giles GG, et al. A positive association of smoking and articular knee joint cartilage in healthy people. Osteoarthritis Cartilage 2007;15: 587–90.
27. Norman PE, Jamrozik K, Lawrence-Brown MM, Le MT, Spencer CA, Tuohy RJ, et al. Population based randomised controlled trial on impact of screening on mortality from abdominal aortic aneurysm [published erratum appears in BMJ 2005;330:596]. BMJ 2004;329:1259.
28. Norman PE, Flicker L, Almeida OP, Hankey GJ, Hyde Z, Jamrozik K. Cohort profile: the Health In Men Study (HIMS). Int J Epidemiol 2009;38:48–52.
29. Holman CD, Bass AJ, Rouse IL, Hobbs MS. Population-based linkage of health records in Western Australia: development of a health services research linked database. Aust N Z J Public Health 1999;23:453–9.
30. Mnatzaganian G, Ryan P, Norman PE, Hiller JE. Accuracy of the hospital morbidity data and performance of co-morbidity scores as predictors of mortality. J Clin Epidemiol. In press.
31. Deyo RA, Cherkin DC, Ciol MA. Adapting a clinical comorbidity index for use with ICD-9-CM administrative databases. J Clin Epidemiol 1992;45:613–9.
32. Elixhauser A, Steiner C, Harris DR, Coffey RM. Comorbidity measures for use with administrative data. Med Care 1998;36: 8–27.
33. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis 1987;40:373–83.
34. Sundararajan V, Henderson T, Perry C, Muggivan A, Quan H, Ghali WA. New ICD-10 version of the Charlson comorbidity index predicted in-hospital mortality. J Clin Epidemiol 2004;57:1288–94.
35. Quan H, Sundararajan V, Halfon P, Fong A, Burnand B, Luthi JC, et al. Coding algorithms for defining comorbidities in ICD-9-CM and ICD-10 administrative data. Med Care 2005;43:1130–9.
36. Australian Bureau of Statistics. SEIFA: Socio-Economic Indexes for Areas. URL: www.abs.gov.au/websitedbs/D3310114.nsf/home/Seifa_entry_page.
37. Fine JP, Gray RJ. A proportional hazards model for the subdistribution of a competing risk. J Am Stat Assoc 1999;94:496–509.
38. Berry SD, Ngo L, Samelson EJ, Kiel DP. Competing risk of death: an important consideration in studies of older adults. J Am Geriatr Soc 2010;58:783–7.
39. Fennema P, Lubsen J. Survival analysis in total joint replacement: an alternative method of accounting for the presence of competing risk. J Bone Joint Surg Br 2010;92:701–6.
40. Gordis L. Epidemiology. 2nd ed. Philadelphia: WB Saunders; 2000.
41. Morens DM, Grandinetti A, Davis JW, Ross GW, White LR, Reed D. Evidence against the operation of selective mortality in explaining the association between cigarette smoking and reduced occurrence of idiopathic Parkinson disease. Am J Epidemiol 1996; 144:400–4.
42. Lau B, Cole SR, Gange SJ. Competing risk regression models for epidemiologic data. Am J Epidemiol 2009;170:244–56.
43. Anderson JJ, Felson DT. Factors associated with osteoarthritis of the knee in the first national Health and Nutrition Examination Survey (HANES I). Evidence for an association with overweight, race, and physical demands of work. Am J Epidemiol 1988;128: 179–89.
44. Gullahorn L, Lippiello L, Karpman R. Smoking and osteoarthritis: differential effect of nicotine on human chondrocyte glycosaminoglycan and collagen synthesis. Osteoarthritis Cartilage 2005;13: 942–3.
45. Mancuso CA, Ranawat CS, Esdaile JM, Johanson NA, Charlson ME. Indications for total hip and total knee arthroplasties: results of orthopaedic surveys. J Arthroplasty 1996;11:34–46.
46. Sturmer T, Gunther KP, Brenner H. Obesity, overweight and patterns of osteoarthritis: the Ulm Osteoarthritis Study. J Clin Epidemiol 2000;53:307–13.
47. Davies MA, Neuhaus JM, Ettinger WH, Mueller WH. Body fat distribution. Am J Epidemiol 1990;4:701–7.
48. Pottie P, Presle N, Terlain B, Netter P, Mainard D, Berenbaum F. Obesity and osteoarthritis: more complex than predicted! Ann Rheum Dis 2006;65:1403–5.
49. Hyndman JC, Holman CD, Hockey RL, Donovan RJ, Corti B, Rivera J. Misclassification of social disadvantage based on geographical areas: comparison of postcode and collector's district analyses. Int J Epidemiol 1995;24:165–76.