

Risk Factors for Total Hip Replacement Due to Primary Osteoarthritis

A Cohort Study in 50,034 Persons

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Objective. To identify prospectively the possible risk factors for total hip replacement (THR) due to primary osteoarthritis in a large cohort.

Methods. Data from a cardiovascular screening were matched with 9 years of national data on THR. Mean age at the start of followup was 54.9 years, and the 50,034 participants were followed up for an average of 9 years. During followup, 672 persons had a first THR due to primary osteoarthritis.

Results. We found dose-response associations between body mass index (BMI), body weight, and the level of physical activity at work and THR for primary osteoarthritis. The highest versus the lowest quarter of BMI had a relative risk of 2.0 (95% confidence interval [95% CI] 1.4–2.9) among men and 3.0 (95% CI 2.1–4.1) among women. The highest versus the lowest quarter of body weight had a relative risk of 2.1 (95% CI 1.4–3.2) among men and 3.4 (95% CI 2.4–4.9) among women. Intensive versus sedentary physical activity at work had a relative risk of 2.1 (95% CI 1.5–3.0) among men and 2.1 (95% CI 1.3–3.3) among women. No association was found between physical activity in leisure and THR for primary osteoarthritis.

Conclusion. Intensive physical activity at work

and a high BMI each contribute significantly to the overall risk of undergoing THR due to primary osteoarthritis. Lowering the exposure to these risk factors may substantially reduce the need for hip replacement.

Osteoarthritis of the hip is a painful and disabling disease. It has been estimated that 12.1% of the United States population over the age of 25 have clinical signs and symptoms of this disease (1). Rheumatoid arthritis, Calvé-Legg-Perthes disease, congenital dysplasia of the hip, and previous hip fracture may all lead to osteoarthritis of the hip. In ~70% of patients undergoing total hip replacement, no underlying condition is identified (2), and the condition is termed primary osteoarthritis. The diagnosis is based on hip radiographs. The association between radiologic signs and clinical findings is weak (3); in the presence of diagnostic radiographs, treatment decisions rely on the patient's symptoms. For milder cases, conservative treatment alleviates symptoms. For severe cases, total hip replacement has been the treatment of choice since the 1960s, when Sir John Charnley developed modern hip arthroplasty (4). However, no treatment restores the normal joint cartilage (5,6). It is therefore important to identify modifiable risk factors.

In addition to age and sex (2), case-control studies have identified body mass index (body weight in kilograms divided by the square of body height in meters) (7), previous hip injury (8), sports activity (9–12), activity in work (13–15), and the presence of Heberden's nodes (8) as probable risk factors for primary osteoarthritis of the hip. A strong genetic contribution was found in a sibling study (16), and estrogen replacement treatment appears to be protective (17,18). Investigators have utilized several indicators of osteoar-

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Table 1. Questions regarding physical activity used in the cardiovascular screening*

Question	Type of activity	
	Work	Leisure
Question	“During the last year, have you had: (Mark YES for the best fitting description)”	“Exercise and physical exertion during leisure time. If your activity varies much, for example between summer and winter, then give an average. The question applies only to the last one-year period. (Mark YES for the best fitting description)”
Alternatives		
Sedentary	Mostly sedentary work? (e.g., office work, watchmaker, mounting of instruments)	Reading, watching television, or other sedentary activity?
Moderate	Work leading to much walking? (e.g., shop assistant, light industrial work, education)	Walking, bicycling, or moving around in other ways at least 4 hours a week? (including walking or cycling to place of work, walking on tours on Sundays, etc.)
Intermediate	Work leading to much walking and lifting? (e.g., postman, heavy industrial work, construction)	Participation in recreational athletics, heavy garden work, etc.? (note: duration of activity at least 4 hours a week)
Intensive	Heavy manual labor? (e.g., forestry work, heavy farm work, heavy construction work)	Participation in hard training or athletic competitions, regularly and several times a week?

* Participants were asked to pick one alternative to describe their activity at work, and one alternative to describe their activity during leisure.

thrititis of the hip, including findings on radiographs, self-reported symptoms, and total hip replacement. Investigators have mostly measured risk factors after the onset of osteoarthritis symptoms or recorded presymptomatic risk factors as recalled by the participants.

The aim of this study was to prospectively characterize risk factors for total hip replacement due to primary osteoarthritis in a large, unselected cohort. The main hypotheses were that body mass index and physical activity at work and during leisure are risk factors for primary osteoarthritis of the hip in both sexes.

PATIENTS AND METHODS

During the years 1977–1983, the National Health Screening Service conducted a cardiovascular screening in 3 Norwegian counties (19). In the county of Finnmark, all persons born between 1925 and 1942 were invited to participate, and the screening was performed during 1977–1978; in Sogn og Fjordane, all people born between 1926 and 1940 were invited and screened during 1980–1981; in Oppland, those born between 1927 and 1941 were invited and screened during 1981–1983. In all, 56,818 persons were invited, and 52,143 responded (91.8%). The participants received a questionnaire enclosed with the invitation, which included questions regarding physical activity during work and leisure (Table 1), and smoking habits. All participants (including those stating domestic work as their main occupation) were asked about physical activity at work. The answers reflect the degree of physical stress during the participants' daily, nonrecreational activity. The invited persons filled in the questionnaire at home and brought it to the screening. Screening nurses went through the questionnaire together with the participants to clarify misunderstandings. The nurses measured height, weight, and blood pressure in a standardized way.

The questions concerning physical activity were introduced in Sweden (20). Similar questions were used in the

World Health Organization's study Monitoring of Trends and Determinants in Cardiovascular Disease (21). Both questions have been validated against maximum oxygen uptake during exertion (22). The question concerning physical activity during work has been validated against a 7-day diary (23), and the question concerning leisure activity has been validated against maximum work capacity (24).

In 1987, the Norwegian Arthroplasty Register started a prospective registration of all total hip replacements and hip implant revisions done in Norwegian hospitals (2,25,26). The registration was initiated to facilitate identification of inferior implants by computing revision rates. For every total hip replacement (and hip implant revision), a form was completed to record previous hip surgery in either hip, the indication for surgery, the implants used, and other parameters related to the operation.

The cardiovascular screening register and the Norwegian Arthroplasty Register were matched using each person's national 11-digit personal identification code. We also included data from the Norwegian Registry of Vital Statistics on death and emigration. The study had a prospective design, and risk factors recorded at the cardiovascular screening were related to the occurrence of a first total hip replacement for primary osteoarthritis of the hip during followup. Followup started January 1, 1989, a time point at which the Norwegian Arthroplasty Register was considered efficient (2,26), and ended June 16, 1998. Of the invited persons, we excluded from the analysis those who did not attend the cardiovascular screening ($n = 4,675$); those who died or emigrated before the start of followup ($n = 1,912$), and those who, according to the Norwegian Arthroplasty Register, already had a total hip replacement at the start of followup ($n = 197$).

The analysis of the remaining 50,034 persons was performed as a survival study (Cox proportional hazards regression model) using the statistical software SPSS, version 9.0.1 (Chicago, IL). Relative risks were estimated with incidence rate ratios. The event was defined as the first total hip replacement for primary osteoarthritis recorded for an individual. Censoring occurred for total hip replacements performed for indications other than primary osteoarthritis of the

Table 2. Age-adjusted and multivariate-adjusted relative risks for total hip replacement due to primary osteoarthritis in a middle-age population attending a cardiovascular screening in 3 Norwegian counties

	No. of participants	Person-years	No. of events	Events per 10,000 person-years	Age-adjusted relative risk	Multivariate relative risk (95% CI)*
Body mass index, kg/m ²						
Men						
≤23.4	6,075	54,500	43	7.9	1.0	1.0
23.5–25.2	6,015	54,145	59	10.9	1.4	1.3 (0.9–1.9)
25.3–27.3	6,044	54,078	68	12.6	1.5	1.4 (1.0–2.1)
≥27.4	5,901	51,952	98	18.9	2.2	2.0 (1.4–2.9)
<i>P</i> (trend test)						0.0001
Women						
≤22.2	6,135	56,183	47	8.4	1.0	1.0
22.3–24.2	6,156	56,537	66	11.7	1.3	1.3 (0.9–1.8)
24.3–27.0	6,047	55,186	99	17.9	1.8	1.8 (1.3–2.6)
≥27.1	6,103	54,849	170	31.0	3.0	3.0 (2.1–4.1)
<i>P</i> (trend test)						<0.0001
Body weight, kg						
Men						
≤71.0	6,270	55,854	46	8.2	1.0	1.0
71.1–77.5	5,761	51,797	64	12.4	1.5	1.4 (1.0–2.1)
77.6–85.0	6,335	56,883	65	11.4	1.4	1.3 (0.9–2.0)
≥85.1	5,679	50,225	94	18.7	2.2	2.1 (1.4–3.2)
<i>P</i> (trend test)						0.0005
Women						
≤58.5	6,166	56,429	40	7.1	1.0	1.0
58.6–64.5	6,142	56,208	79	14.1	1.8	1.8 (1.3–2.7)
64.6–72.0	6,260	57,191	107	18.7	2.3	2.3 (1.6–3.3)
≥72.1	5,878	52,962	156	29.5	3.5	3.4 (2.4–4.9)
<i>P</i> (trend test)						<0.0001
Physical activity at work						
Men						
Sedentary	6,420	57,477	48	8.6	1.0	1.0
Moderate	6,290	56,035	68	12.1	1.4	1.5 (1.0–2.2)
Intermediate	5,972	53,293	65	12.2	1.5	1.7 (1.1–2.4)
Intensive	6,202	55,465	97	17.5	2.0	2.1 (1.5–3.0)
<i>P</i> (trend test)						<0.0001
Women						
Sedentary	3,423	31,166	42	13.5	1.0	1.0
Moderate	14,971	136,431	213	15.6	1.1	1.1 (0.8–1.6)
Intermediate	5,112	46,554	93	20.0	1.4	1.4 (0.9–2.0)
Intensive	1,368	12,494	43	34.4	2.3	2.1 (1.3–3.3)
<i>P</i> (trend test)						0.0003
Physical activity in leisure						
Men						
Sedentary	4,021	35,426	48	13.6	1.0	1.0
Moderate	12,891	114,714	138	12.0	0.9	0.9 (0.6–1.2)
Intermediate	7,549	68,226	89	13.0	1.0	0.9 (0.7–1.4)
Intensive	468	4,269	3	7.0	0.7	0.7 (0.2–2.3)
<i>P</i> (trend test)						0.80
Women						
Sedentary	4,334	39,079	73	18.7	1.0	1.0
Moderate	16,959	154,742	262	16.9	0.9	1.0 (0.7–1.2)
Intermediate	3,640	33,312	57	17.1	0.9	0.9 (0.6–1.2)
Intensive	53	501	0	0	–	–
<i>P</i> (trend test)						0.27

* Adjusted for age at screening, body height, body mass index (not for body weight), physical activity at work, physical activity in leisure, marital status, and smoking habits. 95% CI = 95% confidence interval.

hip ($n = 289$), for emigration ($n = 103$), for death ($n = 4,004$), or end of followup ($n = 44,966$). Survival time was computed as the number of years from the start of followup to the event or censoring. Age at screening was included in the model as a continuous variable. All of the other variables in the model

were categorical, except when performing trend tests (Table 2).

Physical activity at work and during leisure time were independently classified as sedentary, moderate, intermediate, or intensive (Table 1). Body height, weight, and body mass

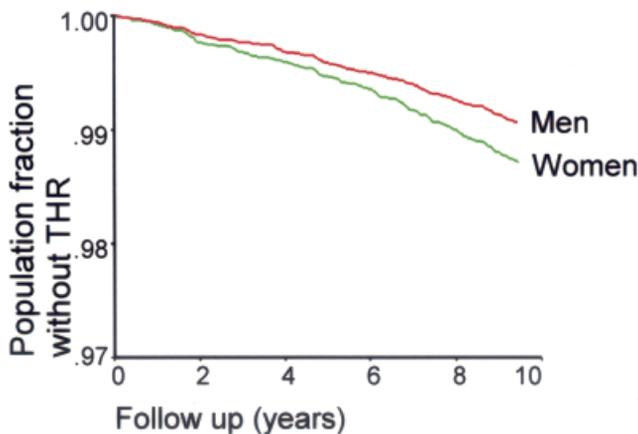


Figure 1. Survival curve by sex, for native hips undergoing first total hip replacement (THR) due to primary osteoarthritis in a middle-age population attending a cardiovascular screening in 3 Norwegian counties, adjusted for age at screening, body height, body mass index, physical activity at work, physical activity in leisure, marital status, and smoking habits.

index were categorized into sex-specific quarters. Smoking habits were classified as current smoker, former smoker, or never smoked. Marital status was classified as unmarried, married, widowed, divorced, or separated. Log-minus-log survival curves for each of the investigated risk factors confirmed the proportional hazards assumption of the Cox model (data not shown).

To estimate a theoretical benefit of prevention, we performed, for body mass index and physical activity at work, a Cox survival analysis comparing the quarter with least exposure with the other 3 quarters pooled together. We then computed the number needed to treat with the equation, $1/\{[\hat{S}(t)]h - S(t)\}$, in which $S(t)$ is the survival in the pooled upper 3 quarters and h is the hazard ratio of the pooled upper 3 quarters versus the lowest quarter (27). Dividing the number

of participants in the pooled 3 quarters by the number needed to treat, we found an estimate of the absolute number of preventable total hip replacements.

Approval for the study was obtained from the Norwegian Board of Health, the Data Inspectorate, and the Regional Committee on Ethics in Medical Research.

RESULTS

In the cardiovascular screening, 24,997 men and 25,037 women participated, and both sexes together had a median age at screening of 46.6 years (range 34–59 years). At the start of followup, the population had a median age of 54.9 years (range 46–67 years). A total of 451,268 observed person-years gave an average followup length of 9.0 years (range 0.1–9.5 years).

During followup, 672 participants underwent a first total hip replacement due to primary osteoarthritis. The risk for total hip replacement increased with higher age at screening (relative risk 1.76 per 5 years, 95% confidence interval 1.53–2.02). Women had a 34% higher risk for total hip replacement than did men (95% confidence interval 14–66%) (Figure 1). A total hip replacement was recorded for 392 (1.57%) of the included women and for 280 (1.12%) of the men.

Women in the highest body mass index quarter had ~3 times the risk of total hip replacement compared with those in the lowest quarter, while men in the highest quarter had double the risk compared with those in the lowest quarter (Figure 2 and Table 2). The association between body weight and total hip replacement was equally as strong as that identified for body mass index (Table 2). For men, there was a significantly reduced risk of total hip replacement for those with sedentary phys-

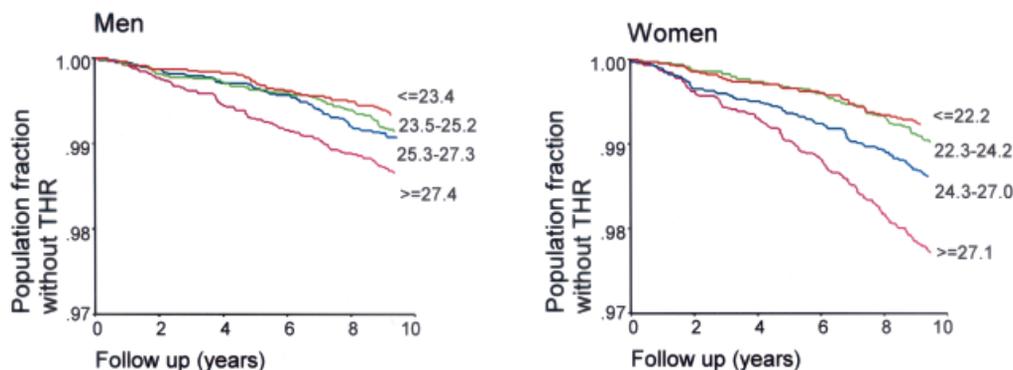


Figure 2. Survival curve by quartiles of body mass index (in kg/m^2), for native hips undergoing first total hip replacement (THR) due to primary osteoarthritis in a middle-age population attending a cardiovascular screening in 3 Norwegian counties, adjusted for age at screening, body height, physical activity at work, physical activity in leisure, marital status, and smoking habits.

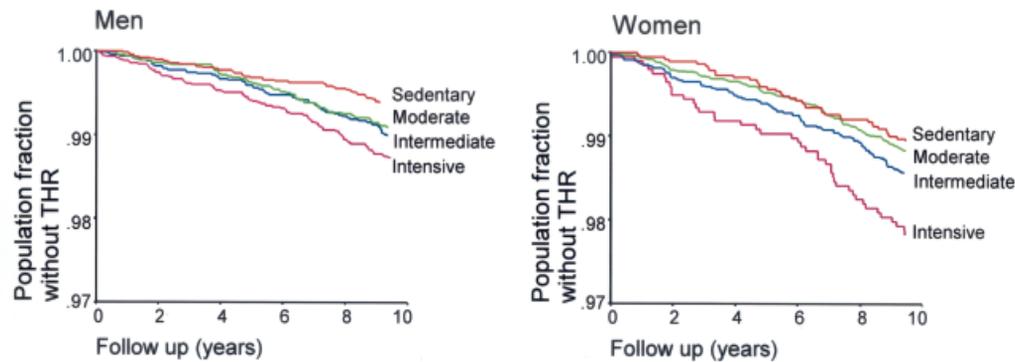


Figure 3. Survival curve by level of physical activity at work, for native hips undergoing first total hip replacement (THR) due to primary osteoarthritis in a middle-age population attending a cardiovascular screening in 3 Norwegian counties, adjusted for age at screening, body height, body mass index, physical activity in leisure, marital status, and smoking habits.

ical activity at work compared with all other levels of this risk factor. Among women, only those with intensive physical activity at work differed significantly in their risk for total hip replacement from those with sedentary physical activity, but as among the men, there appeared to be a dose-response association among all levels of activity (Figure 3 and Table 2). Both for men and for women, those with intensive physical activity at work had double the risk of total hip replacement compared with those with sedentary work. No association could be seen between body height or physical activity at leisure and the event.

We analyzed the combined effect of body mass index and physical activity at work on the risk for total hip replacement (Table 3). Women in the upper body mass index quarter with intensive physical activity at work had more than 4 and one-half times as high a risk

for total hip replacement as did women in the lowest body mass index quarter who had sedentary physical activity at work. The same comparison among men showed a relative risk of 2 and one-half times as high. The interaction term for the 2 risk factors was not significant.

We estimated the potential reduction in number of total hip replacements during followup, assuming either that all participants had sedentary physical activity at work or that all had a body mass index in the lowest quarter (Table 4). We estimated that as many as 234 of the total number of hip replacements performed during our followup might have been prevented if all participants had been exposed to the same risk as those in the lower quarter of both body mass index and physical activity at work, a reduction of 36% (95% confidence interval 5–55%).

Table 3. Relative risks (95% confidence interval) for total hip replacement due to primary osteoarthritis at different levels of body mass index and physical activity at work in a middle-age population attending a cardiovascular screening in 3 Norwegian counties, adjusted for age at screening, body height, physical activity in leisure, marital status, and smoking habits

Sex, body mass index (kg/m ²)	Physical activity at work			
	Sedentary	Moderate	Intermediate	Intensive
Men				
≤23.4	1.0	1.1 (0.5–2.7)	1.2 (0.5–2.8)	1.0 (0.4–2.4)
23.5–25.2	0.5 (0.2–1.5)	0.9 (0.4–2.1)	2.0 (0.9–4.3)	2.3 (1.1–4.9)
25.3–27.3	0.8 (0.3–1.9)	1.3 (0.6–2.9)	1.4 (0.6–3.1)	2.5 (1.2–5.2)
≥27.4	1.7 (0.8–3.6)	2.7 (1.3–0.6)	2.0 (1.0–4.3)	2.5 (1.2–5.1)
Women				
≤22.2	1.0	1.0 (0.4–2.3)	1.2 (0.4–3.1)	1.6 (0.4–6.4)
22.3–24.2	1.4 (0.5–3.7)	1.1 (0.5–2.6)	1.7 (0.7–4.2)	2.2 (0.7–6.6)
24.3–27.0	1.3 (0.5–3.5)	1.8 (0.8–3.9)	2.2 (0.9–5.0)	4.8 (1.9–11.8)
≥27.1	2.6 (1.0–6.6)	3.1 (1.4–6.8)	3.6 (1.6–8.1)	4.6 (1.1–11.2)

Table 4. Estimated reduction in number of total hip replacements for primary osteoarthritis of the hip in a middle-age population attending a cardiovascular screening in 3 Norwegian counties, if all persons had lowest-quarter body mass index or all had sedentary work

Risk factor, sex	Number of recorded events	Estimated reduction in number of events*	Estimated reduction, in percentage of recorded events (95% confidence interval)
Body mass index			
Men	268	67	25 (8–37)
Women	382	138	36 (23–46)
Physical activity at work			
Men	278	85	30 (15–42)
Women	391	53	14 (–9–30)

* If the risk in all levels of exposure was the same as the risk in the quarter/group with lowest exposure.

DISCUSSION

In this study, we found that body mass index and the level of physical activity at work are risk factors for later total hip replacement due to primary osteoarthritis, and we also found body weight to be a risk factor. We did not find that physical activity during leisure is a risk factor. The analysis controlled for sex, age at screening, body height, marital status, and smoking habits. Screening data did not include information on previous hip injury or hormone replacement therapy.

The standard indication for total hip replacement in Norway is pain at rest or during the night in spite of adequate conservative treatment. The incidence of total hip replacement for primary osteoarthritis in Norway is very similar to that in Sweden (28). The number of total hip replacements performed in Norway (population ~4.3 million) for all indications remained fairly constant at ~5,000 per year during our followup (29). The need for total hip replacement for all indications in England has been estimated at 2.2 per thousand in the population ages 35–85 years, and this represented 86% of all cases of severe hip disease. The incidence of surgery performed was 2.1 per thousand (3). The rate of total hip replacements for all indications in Norway during followup was 2.2 per thousand for the same age group (Espeshaug B: personal communication). We think that the participants in our study group who received a total hip replacement during followup represent the majority of all participants who had severely symptomatic primary osteoarthritis of the hip during the same period.

Almost all hospital care in Norway is publicly financed and free of charge for the patient. The public

sick leave pension system provides for the majority of patients who are temporarily or permanently away from work. Consequently, we do not think that socioeconomic factors represented a significant confounder.

The dose-response association between body mass index and the risk for total hip replacement was apparent over the whole range of exposure, and was not confined to extreme levels. Only 9.6% of the study population satisfied the World Health Organization criterion for obesity, with a body mass index >30 kg/m² (30). Some previous investigations are difficult to interpret due to concurrent measurement of body mass index and indicators of osteoarthritis (7,8,31,32) or nonspecific outcome measures (33–35). In 2 case-control studies of total hip replacement recipients (239 men ages 40–70 years and 203 women ages 50–70 years), Vingård et al demonstrated body mass index to be a risk factor for total hip replacement (18,36). Participants reported their recalled body mass index at ages 20, 30, 40, and 50 years, and for both sexes, body mass index at age 40 years was most predictive of later hip replacement. Based on data from the Third National Health and Nutrition Examination Survey, a strong association was found between body mass index and physician-diagnosed osteoarthritis in a cohort of 16,884 overweight and obese participants (37). To our knowledge, our study is the first to demonstrate the association between body mass index and total hip replacement due to primary osteoarthritis in an unselected cohort.

One recent case-control study found that women ages ≥65 years with a body weight of 60–70 kg had a higher risk of symptomatic osteoarthritis of the hip than did women with a body weight of <60 kg, but with a wide confidence interval (95% confidence interval 0.6–181.5) (7). We found that body weight increased the risk for total hip replacement in much the same way as body mass index. This was unexpected, since it might be speculated that a heavy person of high stature (and, consequently, middle-range body mass index) has bones and joints suited to carry his or her body weight. Contrary to this line of reasoning, we found that body weight alone is a strong predictor of risk for total hip replacement due to primary osteoarthritis, and that body height neither increases nor reduces this risk.

In a cohort study of 250,217 participants using occupational data from 3 censuses and hospitalization diagnoses from a nationwide register, male farmers, construction workers, and firefighters had an excess risk of hospitalization due to osteoarthritis of the hip. Among women, only mail carriers had excess risk (15). In a cross-sectional study of 7,217 participants ages ≥30

years, the risk for clinical osteoarthritis was found to be closely associated with lifetime “sum index of physical stress at work,” but the association was not shown for each sex separately (34). A case-control study of 611 patients ages 45–91 years on a waiting list for total hip replacement found a dose-response association between heavy lifting and the risk for osteoarthritis among men, but no association among women (13). The authors suggested low employment rates among the included women as a possible confounder. In a case-control study of 230 female recipients of total hip replacement ages 50–70 years, which assessed the combined effect of paid and unpaid nonrecreational physical activity, a dose-response association was found (38). In our cohort, we found the 2 sexes to have equivalent dose-response associations between nonrecreational physical activity and total hip replacement due to primary osteoarthritis. Combining heavy work and high body mass index further augmented the risk, particularly among women.

In our study, participants were asked to quantify physical activity during the 12 months preceding the screening. The strong association that we found may reflect a high correlation between life-long and middle-age physical activity at work. An alternative explanation might be that the hip is particularly vulnerable to physical activity at middle age, but this was not supported by the small risk for later total hip replacement that we found in persons with high levels of middle-age physical activity during leisure.

Case-control studies in male and female recipients of total hip replacement have indicated that high exposure to sports in general entails increased risk of total hip replacement due to primary osteoarthritis (12,39). Using varying indicators of hip osteoarthritis, some investigations have found (ex-)performers of specific sports to be at increased risk (8,9,11,40), while other investigators have not found such an increased risk (41,42). We did not find an association in our population between physical activity in leisure and later total hip replacement. This does not allow a general dismissal of the association between sports and osteoarthritis of the hip, since the questions used in our screening (assessing activity during the preceding 12 months) may be insensitive to lifetime exposure and to certain kinds of recreational physical activities.

Our estimates of the reduction in total hip replacements if all participants had a low body mass index and/or not more than sedentary physical activity at work probably represent a theoretical maximum for the effect of prevention. Still, they indicate that as much as one-third of the total hip replacements performed during our

followup might have been prevented. The need for preventive measures is further underscored by the increasing prevalence of excessive weight and obesity in Norway and other countries (30,43).

In our study, followup started 6–12 years after screening, and we had incomplete information about who had already undergone prosthetic hip surgery before the start of followup. The cohort was, however, so young at the start of followup that, based on data from the Norwegian Arthroplasty Register (Espehaug B: personal communication), only 5–10% of the amount of total hip replacements sustained by the cohort during their lifetime can be expected to have taken place before the start of followup. The number of persons erroneously classified as nonoperated at the start of followup was presumably insignificant compared with the number of truly nonoperated.

The prospective registration of risk factors and the large number of participants gives strength to the present study. It is further strengthened by the fact that all persons in the 3 geographic areas who had specified years of birth were invited, and by the very high level of participation (92%). The population's age at screening (34–59 years) indicates that the number of participants with osteoarthritic hip symptoms severe enough to have influenced anthropometrics and physical activity at the time of screening was probably low.

Our investigation used the clinically significant end point of total hip replacement. Thus, we describe the risk for an event that is of great importance both to the patient and to health care providers. The pathogenesis of primary osteoarthritis of the hip is poorly understood, and the diagnosis is one of exclusion. It therefore seems appropriate to focus on the most important clinical event for a patient with primary osteoarthritis of the hip, rather than study radiographic or mildly symptomatic osteoarthritis of the hip (44).

We have found dose-response relationships between body mass index, body weight, and the level of physical activity at work and later total hip replacement due to primary osteoarthritis in a large, unselected cohort of middle-age men and women. Our findings indicate that reducing exposure to these risk factors may substantially decrease the need for total hip replacements.

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