



LUND UNIVERSITY

Incidence of severe knee and hip osteoarthritis in relation to different measures of body mass. A population-based prospective cohort study.

Lohmander, Stefan; Gerhardsson, Maria; Rollof, Jan; Nilsson, Peter; Engström, Gunnar

Published in:
Annals of the Rheumatic Diseases

DOI:
[10.1136/ard.2008.089748](https://doi.org/10.1136/ard.2008.089748)

2009

[Link to publication](#)

Citation for published version (APA):
Lohmander, S., Gerhardsson, M., Rollof, J., Nilsson, P., & Engström, G. (2009). Incidence of severe knee and hip osteoarthritis in relation to different measures of body mass. A population-based prospective cohort study. *Annals of the Rheumatic Diseases*, 68(4), 490-496. <https://doi.org/10.1136/ard.2008.089748>

Total number of authors:
5

General rights

Unless other specific re-use rights are stated the following general rights apply:
Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal

Read more about Creative commons licenses: <https://creativecommons.org/licenses/>

Take down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

LUND UNIVERSITY

PO Box 117
221 00 Lund
+46 46-222 00 00



LUND UNIVERSITY
Faculty of Medicine

LUP

Lund University Publications
Institutional Repository of Lund University

This is an author produced version of a paper published in *Annals of the rheumatic diseases*. This paper has been peer-reviewed but does not include the final publisher proof-corrections or journal pagination.

Citation for the published paper:
Stefan Lohmander, Maria Gerhardsson,
Jan Rollof, Peter M Nilsson, Gunnar Engström.
"Incidence of severe knee and hip osteoarthritis in relation
to different measures of body mass.
A population-based prospective cohort study."
Annals of the rheumatic diseases, 2008, Issue: May 8.

<http://dx.doi.org/10.1136/ard.2008.089748>

Access to the published version may
require journal subscription.
Published with permission from: BMJ

Incidence of severe knee and hip osteoarthritis in relation to different measures of body mass

A population-based prospective cohort study

**L Stefan Lohmander¹, Maria Gerhardsson², Jan Rollof², Peter M Nilsson³,
Gunnar Engström⁴**

1 L Stefan Lohmander, MD, PhD, Department of Orthopedics, Clinical Sciences Lund, Lund University, Sweden

2 Maria Gerhardsson, PhD, Jan Rollof, MD, PhD, AstraZeneca R&D, Lund, Sweden

3 Peter M Nilsson, MD, PhD, Department of Clinical Sciences, Medicine, Lund University, University Hospital, Malmö, Sweden

4 Gunnar Engström, PhD, Epidemiology research group, Clinical Sciences Malmö, Lund University, and AstraZeneca R&D, Lund, Sweden

Corresponding author address:

Stefan Lohmander, Department of Orthopedics, Lund University Hospital, SE-22185 Lund, Sweden. Email stefan.lohmander@med.lu.se . Phone +4646171503, Fax +4646130732

Key words: Osteoarthritis, joint replacement, knee, hip, body mass index

Abstract

Objectives – To determine in a large prospective population-based cohort study relationships between different measures of body mass and incidence of severe knee and hip osteoarthritis (OA) defined as arthroplasty of knee or hip due to OA.

Materials and methods – Body mass index (BMI), waist circumference, waist-hip ratio (WHR), weight, and percentage of body fat (BF%) was measured at baseline in 11026 men and 16934 women, 45 to 73 years old, from the general population. Incidence of severe OA was defined as arthroplasty due to knee or hip OA monitored over 11 years of follow-up by linkage with the Swedish hospital discharge register.

Results – During follow-up, 471 individuals had knee OA and 551 had hip OA. After adjustment for age, sex, smoking and physical activity, the relative risks (RR) of knee OA (4th vs. 1st quartile) were 8.1 (95% CI 5.3-12.4) for BMI, 6.7 (4.5-9.9) for waist circumference, 6.5 (4.6-9.43) for weight, 3.6 (2.6-5.0) for BF% and 2.2 (1.7-3.0) for WHR. The corresponding RR for hip OA were 2.6 (2.0-3.4) for BMI, 3.0 (2.3-4.0) for weight, 2.5 (1.9-3.3) for waist, 1.3 (0.99-1.6) for WHR and 1.5 (1.2-2.0) for BF%.

Conclusions – All measures of overweight were significantly associated with incidence of knee OA leading to arthroplasty, with the strongest relative risk gradient observed for BMI. Even though incidence of hip OA showed smaller differences between normal weight and obesity, body mass was a significant risk factor also for hip OA leading to arthroplasty. Our results support a major link between overweight and biomechanics in increasing knee and hip OA risk in both men and women, but do not exclude a contributing role of metabolic factors associated with adipose tissue.

The relationship between overweight and obesity and increased risk of knee and hip osteoarthritis (OA) has been documented in several previous studies, in particular for the knee.[1-9] For the hip, the evidence is inconsistent, some studies finding an association, others not, with the association appearing stronger for case definitions based on symptoms than on radiological findings.[6, 8-23]

The increased OA risk associated with overweight and obesity is suggested to have a significant biomechanical component, but an additional role for metabolic factors associated with adipose tissue was suggested.[24] There are several different measures of overweight and obesity, e.g., BMI, waist circumference, waist to hip ratio and percentage of body fat. Even though these measures are positively related to each other, the correlations are sometimes quite low and the measures reflect different aspects of body mass and adipose tissue distribution and type. The latter aspect is of interest in light of the suggested connection between OA and metabolically active adipose tissue.[24] Few studies have explored whether the different measures of overweight differ in their relationships with knee or hip OA, and they have generally used OA as defined on plain radiographs for case identification,[3, 5, 11] or assessed cartilage volume by magnetic resonance imaging.[25] The relevance of radiographically defined OA in terms of symptomatic disease burden or health economics is uncertain. None of these studies have included both knee and hip OA.

The purpose of this large population-based, prospective cohort study was to compare the relationships between different measures of body mass and incidence of arthroplasty due to knee or hip OA in men and women, a measure of significant symptomatic and economic OA disease burden.

Methods

Study population

All men and women living in the city of Malmö in Sweden, who were born between 1923 and 1945 (men) or between 1923 and 1950 (women) were invited to participate in the Malmö Diet and Cancer (MDC) study. The subjects were invited by letters and advertisements in newspapers. Between March 1991 and September 1996, the respondents participated in a baseline examination with different clinical examinations at the screening center and filled in a self-administered questionnaire. The cohort consisted of 28449 subjects (11246 men and 17203 women) from the eligible population of about 74000 individuals. Characteristics of all participants and non-participants have been reported.[26] It was shown that the cohort was representative of the eligible population with respect to the prevalence of overweight, smoking, educational level, type of employment, and marital status.[26] However, the mortality rate was higher in non-participants. On January 1, 1991, the age of the participants was 54.9 (SD 7.6) years, and the non-participants 54.3 (7.8); 39.4 % of participants were men, and 43.6% of non-participants. Of the 28449 participants, 185 were excluded from the present study due to incomplete anthropometric or body fat data. Another 304 subjects who had been surgically treated due to knee or hip OA before the baseline examination were excluded. The research ethical committee at Lund University approved the MDC study (LU 51–90). Each participant signed a written informed consent.

Baseline examinations

Body weight, height, waist and hip circumferences were measured at the screening centre. The examinations were performed by two trained nurses. Standing height was measured with a fixed stadiometer calibrated in centimeters. Weight was measured to the nearest 0.1 kg using a balance beam scale with subjects wearing light clothing and no shoes. BMI was calculated as weight in kilograms divided by height squared in meters. Waist was measured as the circumference (in centimeters) between the lowest rib margin and iliac crest and hip circumference (in centimeters) as the largest circumference between waist and thighs. WHR was defined as the ratio of circumference of waist to hip. Weight at 20 years of age was assessed in the questionnaire. A total of 24166 subjects (86%) filled in this question. A bioelectrical impedance method (BIA) was used to measure body composition. The body fat percentage (BF%) was calculated using an algorithm according to procedures provided by the manufacturer (BIA 103, RJL systems, single-frequency analyzer, Detroit, USA).[27]

A self-administered questionnaire was used to assess medical history and lifestyle factors. Subjects were categorized into current smokers (i.e., those who smoked regularly or occasionally) or non-smokers (i.e., former smokers and never smokers). Information on physical activities in leisure time was explored through 18 questions covering a range of activities in the four seasons.[28, 29] The scores were divided into quartiles of physical activity when used in the analysis (29). Information about smoking or physical activity was missing for 505 (1.8%) of the subjects.

The subjects reported whether they had been treated for different medical problems, e.g., myocardial infarction, stroke, cancer, peripheral arterial disease, hypertension, diabetes, goiter, gastric ulcer, asthma or chronic obstructive pulmonary disease (COPD), inflammatory bowel disease, and renal stone. Subjects with history of any of these diseases were excluded in a separate analysis to examine the influence on the risk for arthroplasty.

Definition of knee and hip OA

The follow-up times were calculated separately for knee and hip. All participants were followed until the first OA surgery, emigration from Sweden, death or December 31, 2005, whichever came first. Information on knee and hip arthroplasty for OA and mortality were based on record linkage with the national Swedish Hospital Discharge Register and the Swedish Causes of Death Register. Subjects who moved out of Sweden were censored at the day of emigration.

Knee OA was defined as a first knee arthroplasty or high tibial osteotomy (procedures coded 8424, 8423, 8428, 8010, 8199 or NGB09, NGB19, NGB29, NGB39, NGB49, NGB99 and NGK59) in combination with a contemporaneous diagnosis of OA (715 or M17 according to ICD-9 and ICD-10, respectively). Only the first event was counted for patients with more than one knee arthroplasty.

Hip OA was defined as a first hip arthroplasty (procedures coded 8414, 8010, NFB09, NFB19, NFB29, NFB39, NFB49 and NFB99) in combination with a contemporaneous diagnosis of hip OA (715 or M16 according to ICD-9 and ICD-10, respectively). Patients with more than one hip arthroplasty were only counted once. Cases coded with a diagnosis of primary unilateral OA constituted 93% and 96% of all knees and hips included, respectively.

Statistics

Pearson's correlations were used to assess the covariation between the anthropometric measures. Kaplan-Meier curves were created to illustrate the crude incidence rates of knee and hip OA over time. Cox' proportional hazards model was used to assess incidence of surgery due to knee or hip OA, in relation to measures of body mass, with adjustments for confounding factors. Potential confounding factors were selected from those available based on a priori assumptions of risk factors for OA.[1, 7, 17] The fit of the proportional hazards model was confirmed by plotting incidence of OA over time for the different categories of risk factors. The anthropometric measures were divided into sex-specific quartiles before analysis. Age was entered as a continuous variable. Smoking was used as a dichotomous variable. Physical activity was categorized into quartiles in the regression analysis. All comparisons were two-sided and a 5% level of significance was used.

Results

Study cohort

The study population characteristics are presented in Table 1.

Table 1. Characteristics of the study population. Data presented as median (interquartile range) unless otherwise stated.

	Men	Women
N	11026	16934
Age, mean [SD] (range)	59.2 [7.0] (46-73)	57.4 [7.8] (45-73)
Smokers (%)	29	28
BMI (kg/m ²)	26.0 (23.9–28.3)	24.7 (22.5–27.0)
Waist (cm)	93 (87–100)	76 (70–83)
Weight (kg)	81 (74–89)	66 (60–74)
WHR	0.94 (0.90–0.98)	0.79 (0.76–0.83)
Body fat %	20 (17–24)	31 (28–34)
Height (cm)	176 (172-181)	164 (160-168)
Follow-up (years), mean [SD]	11.2 [2.6]	11.3 [2.2]
TKR for OA n, (rate per 1000 person years)	173 (1.4)	298 (1.6)
THR for OA n, (rate per 1000 person years)	186 (1.5)	365 (1.9)

Weight and BMI were highly correlated in both men and women. WHR showed moderate or low correlations with BMI, weight, and BF% (Table 2).

Table 2. Correlation coefficients between different measures of body mass in **men** (**bold**, upper right) and women (lower left).

	BMI	Weight	Waist	WHR	Body fat %	Height
BMI		0.86	0.70	0.34	0.58	-0.06
Weight	0.90		0.69	0.29	0.50	0.45
Waist	0.76	0.75		0.84	0.52	0.13
WHR	0.18	0.17	0.46		0.30	-0.02
Body fat %	0.83	0.73	0.66	0.15		-0.04
Height	-0.15	0.29	0.03	-0.02	-0.16	

N= 11026 men and 16934 women. All coefficients are significant $p < 0.05$.

Incidence of knee OA arthroplasty

A total of 27960 subjects were available for the analysis of incidence of OA. Of them, 421 were treated with knee arthroplasty or high tibial osteotomy ($n=50$) due to OA during the follow-up of 11.2 (0-14.8) years (median 11.3 (IQ range 10.2-12.8)). BMI, weight, waist, WHR and BF% were significantly related to knee OA in both sexes, with the strongest association between BMI and arthroplasty/osteotomy (Table 3). For example, the adjusted RR for men with BMI in the fourth quartile was 7.0 (3.3-14.8) and for women 8.7 (5.2-14.6).

When compared to subjects with $BMI < 25 \text{ kg/m}^2$, the RR for men with BMI 25-30 and $BMI > 30 \text{ kg/m}^2$ was 3.1 (2.0-4.9) and 4.4 (2.6-7.5), respectively, and for women 2.8 (2.0-3.9) and 6.9 (5.0-9.6), respectively (Fig. 1). In women, a dose-response gradient between BF% and RR for TKR was apparent, but less so for men (Fig. 1).

In men, there was no significant relationship between height and knee OA. In women, a non-linear relationship between height and knee OA was observed, with an increased incidence in the third quartile, while for men there was no such relationship (Fig. 1).

Table 3. Incidence of knee arthroplasty due to OA during a mean follow-up of 11 years, in relation to measures of overweight. Each quartile consists of approximately 2756 men and 4233 women. RR adjusted for age, sex, smoking, physical activity (in quartiles).

BMI	Q1	Q2	Q3	Q4
Median (kg/m ²) (men/women)	22.5/21.1	25.0/23.6	27.0/26.0	30.1/30.1
Knee OA n (per 1000 person years)	30 (0.38)	74 (0.93)	131 (1.7)	236 (3.1)
Adjusted RR (95% CI)	1.00	2.5 (1.6-4.0)	4.6 (2.9-7.1)	8.1 (5.3-12.4)
Weight	Q1	Q2	Q3	Q4
Median (kg) (men/women)	69/56	77/64	84/70	95/81
Knee OA n (per 1000 person years)	41 (0.50)	77 (1.0)	114 (1.4)	239 (3.1)
Adjusted RR (95% CI)	1.00	2.2 (1.4-3.2)	3.0 (2.0-4.4)	6.5 (4.6-9.3)
Waist	Q1	Q2	Q3	Q4
Median (cm) (men/women)	82/67	90/74	96/80	105/90
Knee OA n (per 1000 person years)	32 (0.40)	92 (1.1)	115 (1.5)	232 (3.0)
Adjusted RR (95% CI)	1.00	2.6 (1.7-4.1)	3.6 (2.4-5.5)	6.7 (4.5-9.9)
WHR	Q1	Q2	Q3	Q4
Median (men/women)	0.88/0.74	0.92/0.77	0.96/0.81	1.01/0.85
Knee OA n (per 1000 person years)	82 (1.0)	100 (1.3)	124 (1.6)	165 (2.2)
Adjusted RR (95% CI)	1.00	1.4 (1.01-1.9)	1.6 (1.2-2.2)	2.2 (1.7-3.0)
Body fat %	Q1	Q2	Q3	Q4
Median (%) (men/women)	15/25	19/29	22/32	26/37
Knee OA n (per 1000 person years)	51 (0.64)	84 (1.1)	139 (1.6)	197 (2.6)
Adjusted RR (95% CI)	1.00	1.8 (1.2-2.5)	2.2 (1.6-3.1)	3.6 (2.6-5.0)
Height	Q1	Q2	Q3	Q4
Median (cm) (men/women)	168/157	174/162	178/165	184/170
Knee OA n (per 1000 person years)	110 (1.5)	123 (1.5)	133 (1.8)	105 (1.3)
Adjusted RR (95% CI)	1.00	1.2 (0.9-1.5)	1.5 (1.2-2.0)	1.1 (0.8-1.5)

Incidence of hip OA arthroplasty

A total of 551 were treated with hip arthroplasty due to OA during the follow-up. BMI, weight and waist were significantly associated with hip OA (Table 4). These relationships were similar in men and women (Fig. 1). The gradient over the quartiles of BF% was weaker, but statistically significant. For WHR, the relationship with hip OA was non-significant both in men and women (Fig. 1).

When compared to subjects with BMI < 25 kg/m², the RR for men with BMI 25-30 and BMI > 30 kg/m² was 1.6 (1.1-2.3) and 3.3 (2.2-5.0), respectively, and for women 1.4 (1.1-1.8) and 2.1 (1.6-2.7), respectively.

In men, there was a non-linear relationship between height and hip OA (Fig. 1). In women, the RR of hip OA increased gradually over the quartiles of height.

Table 4. Incidence of hip arthroplasty due to OA during a mean follow-up of 11 years of follow-up, in relation to measures of overweight. Each quartile consists of approximately 2756 men and 4233 women. RR adjusted for age, sex, smoking and physical activity (in quartiles).

BMI	Q1	Q2	Q3	Q4
Hip OA n	70 (0.88)	119 (1.5)	161 (2.1)	201 (2.6)
(per 1000 person years)				
Adjusted RR (95% CI)	1.00	1.6 (1.2-2.1)	2.1 (1.6-2.8)	2.6 (2.0-3.4)
Weight	Q1	Q2	Q3	Q4
Hip OA n	74 (0.91)	117 (1.5)	149 (1.9)	211 (2.7)
(per 1000 person years)				
Adjusted RR (95% CI)	1.00	1.7 (1.3-2.3)	2.1 (1.6-2.8)	3.0 (2.3-4.0)
Waist	Q1	Q2	Q3	Q4
Hip OA n	73 (0.92)	119 (1.5)	151 (2.0)	208 (2.7)
(per 1000 person years)				
Adjusted RR (95% CI)	1.00	1.5 (1.1-2.0)	1.9 (1.4-2.6)	2.5 (1.9-3.3)
WHR	Q1	Q2	Q3	Q4
Hip OA n	128 (1.6)	127 (1.6)	141 (1.8)	155 (2.0)
(per 1000 person years)				
Adjusted RR (95% CI)	1.00	1.1 (0.8-1.4)	1.1 (0.9-1.4)	1.3 (1.0-1.6)
Body fat %	Q1	Q2	Q3	Q4
Hip OA n	98 (1.2)	104 (1.4)	169 (2.0)	180 (2.4)
(per 1000 person years)				
Adjusted RR (95% CI)	1.00	1.0 (0.8-1.4)	1.3 (1.0-1.7)	1.5 (1.2-2.0)
Height	Q1	Q2	Q3	Q4
Hip OA n	101 (1.4)	151 (1.9)	153 (2.0)	146 (1.7)
(per 1000 person years)				
Adjusted RR (95% CI)	1.00	1.6 (1.2-2.0)	1.8 (1.4-2.4)	1.7 (1.3-2.3)

Incidence of severe OA in relation to weight at age 20

Information about self-reported weight at age of 20 was available for 24008 subjects, 9341 men and 14667 women (Table 4). Weight at 20 years was significantly associated with knee OA after adjustments for age, sex, smoking and physical activity. However, this relationship was attenuated and non-significant after adjustment for BMI measured at the baseline examination at the median age of about 60. In contrast, both weight at 20 years and BMI at the examination were significant risk factors for hip OA, after mutual adjustments in the multivariate regression (Table 5).

Table 5. Incidence of severe knee and hip OA in relation to weight at age of 20. Each quartile includes approximately 2350 men and 3690 women. Analysis based on 9341 men (141 TKR and 145 THR) and 14667 women (240 knee and 314 hip replacements).

	Weight at 20 years			
	Q1	Q2	Q3	Q4
Median weight kg (men/women)	60/49	65/53	70/56	78/63
TKR for OA n (per 1000 person years)	85 (1.1)	51 (1.0)	108 (1.6)	137 (1.9)
RR * (95% CI)	1.00	0.80 (0.55-1.2)	1.3 (1.0-1.8)	1.6 (1.2-2.1)
RR ** (95% CI)	1.00	0.78 (0.54-1.1)	1.1 (0.84-1.5)	1.1 (0.82-1.4)
THR for OA n (per 1000 person years)	92 (1.2)	72 (1.4)	123 (1.8)	172 (2.4)
RR * (95% CI)	1.00	1.2 (0.90-1.7)	1.5 (1.1-1.9)	1.9 (1.5-2.5)
RR** (95% CI)	1.00	1.2 (0.88-1.6)	1.4 (1.0-1.8)	1.6 (1.3-2.1)

* RR adjusted for age, sex, smoking, physical activity

** RR adjusted for age, sex, smoking, physical activity and BMI at baseline examination (in quartiles)

Influence of co-morbidities on relationships between body mass and OA

To explore whether a healthy patient selection effect on arthroplasty or osteotomy decision could influence the relationships between body mass and OA, individuals with self-reported history of myocardial infarction, stroke, cancer, peripheral arterial disease, hypertension, diabetes, goiter, gastric ulcer, asthma or COPD, inflammatory bowel disease, and renal stone were excluded from the analyses. A total of 15287 subjects remained, 209 of them had arthroplasty or osteotomy for knee OA and 272 had arthroplasty for hip OA during the follow-up. In this group, the adjusted RR of knee OA for those with BMI in the top quartile was 14.9 (6.8-32.4). The adjusted RR for hip OA was 2.4 (1.6-3.5) for those with BMI in the top quartile.

Discussion

Previous studies have reported on risk of knee or hip OA in subjects with overweight or obesity. While the reported relationship between overweight measures and knee OA has been consistent, it has been inconsistent for the hip. To our knowledge no report has in the same population compared the incidence of severe knee and hip OA in men and women in relation to different measures of overweight, and used an outcome tightly linked to the disease burden of severe OA. The results from this large, prospective population-based cohort study show that BMI, weight and waist circumference were major risk factors for knee arthroplasty or osteotomy due to OA, with the highest RR for subjects with BMI in the top quartile (Figs. 1 and 2). BF% was associated with knee OA mainly in women and WHR showed substantially weaker associations with incidence of knee OA. All measures related to overweight showed weaker associations with incidence of severe hip OA than with severe knee OA. However, BMI, weight and waist were important risk factors also for OA of the hip leading to arthroplasty. These relationships held true for both men and women.

It was suggested that metabolic or inflammatory factors contribute to the relationships between obesity and knee OA.[24] Many studies have reported that e.g., BF% or WHR are more closely linked to inflammation and metabolic factors than BMI, particularly in women.[30] The fact that BMI was associated with much higher point estimates than were WHR or BF% suggest that mechanical factors associated with overweight are more strongly related to knee and hip OA than metabolic or inflammatory factors. However, all measures of overweight are very unspecific surrogate measures of inflammation and the present results do not exclude a role of systemic or local inflammatory and metabolic factors associated with adipose tissue as contributors to risk for knee or hip OA. It is here of interest to note the stronger relationship between BF% and severe knee and hip OA for women than for men (Fig. 1). The effect of BMI may be modified by other risk factors, such as sex, joint malalignment and joint injury.[22, 23, 31-34] If the influence of weight varies with other predisposing factors remains to be determined.

In the present study, we used a case definition of total arthroplasty or high tibial osteotomy of the knee or arthroplasty of the hip due to OA. Other studies that have explored the relationship between obesity and OA have used as case definitions these same criteria, or knee or hip arthroplasty without a confirmed diagnosis, OA diagnosed by variable radiographic criteria, OA defined by symptom criteria, or by self-reported diagnosis. The relationship between these different OA definitions is uncertain, and their relationship with obesity may not be the same, explaining some of the variability of the published results.[35] While the definition arthroplasty or osteotomy due to OA will only identify the tip of the iceberg of the very large OA population, it has the advantage of an unambiguous connection with disease burden of OA and being available in reliable national registries. Additional reasons for the variable results of previous studies include variations in study design, focus on different population subsets such as males or females, or occupation, duration of follow-up. Our finding that in the same population the association between BMI and severe hip OA was weaker than that between BMI and severe knee OA, suggests that some previous studies failing to show the association with hip OA may have been underpowered.

The national Swedish hospital discharge register was used for case-retrieval. This register has been active during the entire follow-up period, it covers all Swedish hospitals, has been validated against the national Swedish arthroplasty registers, and was estimated to include at least 95% of primary knee and hip arthroplasties.[36] Misclassification of diagnosis may represent a source of bias. Primary OA was the diagnosis for more than 85% of all primary knee arthroplasties and more than 75% of all primary hip arthroplasties in Sweden during the follow-up period. The proportion of diagnostic misclassification was estimated at about 5% for hip replacements.[36] We therefore suggest that the bias in the present study due to misclassification of contemporaneous OA is small, and likely nondifferential.

The decision to surgically treat a patient with OA is influenced by a number of factors, in addition to those related to severity of symptoms and radiographic signs.[37] Of particular relevance to this and other studies using arthroplasty is the possibility of a healthy patient selection bias in the decision to perform an arthroplasty. In our analyses we found that the strong relationships between overweight measures and arthroplasty for OA remained following exclusion of participants with self-reported significant co-morbidities at the baseline examination. This would argue against a healthy patient selection bias influencing our results.

The participant rate in MDC was approximately 41%, and it may be questioned whether the study cohort is representative of the source population. It was shown that BMI, prevalence of smoking, and sociodemographic status in the study cohort was similar to that of the source population, based on a mailed questionnaire to the source population in which the response rate was about 75%.[26] Similar to most cohort studies, the mortality rates were higher in non-participants than in participants.

The large size of the cohort and the prospective design are major strengths of the study. Subjects with knee or hip surgery for OA before the baseline examination were not included, excluding a major proportion of individuals with severe knee or hip OA already at baseline. A limitation is that we could not exclude all subjects with any baseline knee or hip pain for lack of complete baseline data on these symptoms. Therefore, the cases reported here may include some who had OA already at baseline. However, we monitored a proxy for severe symptomatic OA: incidence of knee or hip arthroplasty due to OA. Even though the prospective design minimized the risk of reverse causality, it is possible that pain in the knee or hip in some cases may have influenced health behavior already at the baseline examination.

Our results extend those of previous reports by comparing within the same large population based study risks for severe knee and hip OA in both men and women, using several different measures of overweight. We conclude that all measures of overweight were significantly associated with incidence of severe knee OA in men and women, and the strongest relative risk gradient was observed for BMI. Even though incidence of severe hip OA showed smaller differences between normal weight and obesity than for the knee, body mass was an important risk factor also for severe hip OA in men and women, consistent with some recent reports.[17, 20] There appeared to be a continuous dose response relationship between BMI and risk for arthroplasty for OA. A significant risk increase for both knee and hip OA, after adjustment for age, sex, smoking and physical activity, was apparent already for the second BMI quartile, corresponding to a median BMI of 25 for men and 23.6 for women.

Supported by:

AstraZeneca R&D, Swedish Research Council, Medical Faculty of Lund University, Region Skåne, Swedish Rheumatism Association and King Gustaf V 80th Birthday Fund.

Conflict of Interest statement:

MG, JR, GE are employees of AstraZeneca. LSL and PMN have no conflict of interest to report.

The Corresponding Author has the right to grant on behalf of all authors and does grant on behalf of all authors, an exclusive licence (or non-exclusive for government employees) on a worldwide basis to the BMJ Publishing Group Ltd and its Licensees to permit this article to be published in Annals of the Rheumatic Diseases editions and any other BMJ PGL products to exploit all subsidiary rights, as set out in our licence <http://ard.bmjournals.com/ifora/licence.pdf>.

Figure legends

Figure 1.

Adjusted relative risks for men and women for TKR or osteotomy for severe knee OA (top), or THR for severe hip OA (bottom). Error bars show 95% confidence intervals for relative risk estimates. Dotted line corresponds to RR=1.

Figure 2.

Kaplan-Meier survival analysis of knee and hip. Graphs show study population fractions without TKR or osteotomy for OA (A, top), and study population fraction without THR (B, bottom) for OA. For each panel, the four plots represent from top to bottom BMI quartiles 1 through 4, with a significant difference between each of the four curves in the upper and lower panels. The adjusted relative risks are given in Tables 3 and 4. Median BMI values for the quartiles are given in Table 3.

References

- 1 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.
- 2 Felson DT, Anderson JJ, Naimark A, Walker AM, Meenan RF. Obesity and knee osteoarthritis. The Framingham Study. *Ann Int Med* 1988;**109**:18-24.
- 3 Davis MA, Neuhaus JM, Ettinger WH, Mueller WH. Body fat distribution and osteoarthritis. *Am J Epidemiol* 1990;**132**:701-7.
- 4 Schouten JS, van den Ouweland FA, Valkenburg HA. A 12 year follow up study in the general population on prognostic factors of cartilage loss in osteoarthritis of the knee. *Ann Rheum Dis* 1992;**51**:932-7.
- 5 Hart DJ, Spector TD. The relationship of obesity, fat distribution and osteoarthritis in women in the general population: the Chingford Study. *J Rheumatol* 1993;**20**:331-5.
- 6 Felson DT, Chaisson CE. Understanding the relationship between body weight and osteoarthritis. *Bailliere's Clin Rheumatol* 1997;**11**:671-81.
- 7 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.
- 8 Gelber AC, Hochberg MC, Mead LA, Wang NY, Wigley FM, Klag MJ. Body mass index in young men and the risk of subsequent knee and hip osteoarthritis. *Am J Med* 1999;**107**:542-8.

- 9 Oliveria SA, Felson DT, Cirillo PA, Reed JI, Walker AM. Body weight, body mass index, and incident symptomatic osteoarthritis of the hand, hip, and knee. *Epidemiology* 1999;**10**:161-6.
- 10 van Saase JL, Vandenbroucke JP, van Romunde LK, Valkenburg HA. Osteoarthritis and obesity in the general population. A relationship calling for an explanation. *J Rheumatol* 1988;**15**:1152-8.
- 11 Hochberg MC, Lethbridge-Cejku M, Scott WW Jr, Reichle R, Plato CC, Tobin JD. The association of body weight, body fatness and body fat distribution with osteoarthritis of the knee: data from the Baltimore Longitudinal Study of Aging. *J Rheumatol* 1995;**22**:488-93.
- 12 Vingård E, Alfredsson L, Malchau H. Lifestyle factors and hip arthrosis. A case referent study of body mass index, smoking and hormone therapy in 503 Swedish women. *Acta Orthop Scand* 1997;**68**:216-20.
- 13 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.
- 14 Marks R, Allegrante JP. Body mass indices in patients with disabling hip osteoarthritis. *Arthritis Res* 2002;**4**:112-6.
- 15 Sturmer T, Gunther KP, Brenner H. Obesity, overweight and patterns of osteoarthritis: the Ulm Osteoarthritis Study. *J Clin Epidemiol* 2000;**53**:307-13.
- 16 Lieveense AM, Bierma-Zeinstra SM, Verhagen AP, van Baar ME, Verhaar JA, Koes BW. Influence of obesity on the development of osteoarthritis of the hip: a systematic review. *Rheumatology (Oxford, England)* 2002;**41**:1155-62.
- 17 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.
- 18 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.
- 19 Järvholm B, Lewold S, Malchau H, Vingård 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.
- 20 Flugsrud GB, Nordsletten L, Espehaug B, Havelin LI, Engeland A, Meyer HE. The impact of body mass index on later total hip arthroplasty for primary osteoarthritis: a cohort study in 1.2 million persons. *Arthritis Rheum* 2006;**54**:802-7.
- 21 Reijman M, Pols HA, Bergink AP, Hazes JM, Belo JN, Lieveense AM, et al. Body mass index associated with onset and progression of osteoarthritis of the knee but not of the hip: the Rotterdam Study. *Ann Rheum Dis* 2007;**66**:158-62.

- 22 Sharma L, Chang A. Overweight: advancing our understanding of its impact on the knee and the hip. *Ann Rheum Dis* 2007;**66**:141-2.
- 23 Franklin, J, Ingvarsson, T, Englund M, Lohmander, LS. Sex differences in the association between body mass index and total hip or knee joint replacement due to osteoarthritis. *Ann Rheum Dis* 2008 in press.
- 24 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.
- 25 Wang Y, Wluka AE, English DR, Teichtahl AJ, Giles GG, O'Sullivan R, et al. Body composition and knee cartilage properties in healthy, community-based adults. *Ann Rheum Dis* 2007;**66**:1244-8.
- 26 Manjer J, Carlsson S, Elmståhl S, Gullberg B, Janzon L, Lindström M, et al. The Malmö Diet and Cancer Study: Representativity, cancer incidence and mortality in participants and non-participants. *Eur J Cancer Prev* 2001;**10**:489–99.
- 27 Segal KR, Van Loan M, Fitzgerald PI, Hodgdon JA, Van Itallie TB. Lean body mass estimation by bioelectrical impedance analysis: a four-site cross-validation study. *Am J Clin Nutr* 1988;**47**:7-14.
- 28 Taylor HL, Jacobs DR, Jr. Schucker B, Knudsen J, Leon AS, Debacker G. A questionnaire for the assessment of leisure time physical activities. *J Chronic Dis* 1978;**31**:741–55.
- 29 Calling S, Hedblad B, Engström G, Berglund G, Janzon L. Effects of body fatness and physical activity on cardiovascular risk: risk prediction using the bioelectrical impedance method. *Scand J Publ Health* 2006;**34**:568-75.
- 30 Thorand B, Baumert J, Döring A, Herder C, Kolb H, Rathmann W, et al.; KORA Group. Sex differences in the relation of body composition to markers of inflammation. *Atherosclerosis* 2006;**184**:216-24.
- 31 Sharma L, Lou C, Cahue S, Dunlop DD. The mechanism of the effect of obesity in knee osteoarthritis: the mediating role of malalignment. *Arthritis Rheum* 2000;**43**:568-75.
- 32 Englund M, Lohmander LS. Risk factors for symptomatic knee osteoarthritis fifteen to twenty-two years after meniscectomy. *Arthritis Rheum* 2004;**50**:2811-9.
- 33 Felson DT, Goggins J, Niu J, Zhang Y, Hunter DJ. The effect of body weight on progression of knee osteoarthritis is dependent on alignment. *Arthritis Rheum* 2004;**50**:3904-9.
- 34 Spindler KP, Warren TA, Callison JC Jr, Secic M, Fleisch SB, Wright RW. Clinical outcome at a minimum of five years after reconstruction of the anterior cruciate ligament. *J Bone Joint Surg Am* 2005;**87**:1673-9.

35 Jacobsen S, Sonne-Holm S. Increased body mass index is a predisposition for treatment by total hip replacement. *Int Orthop* 2005;**29**:229-34.

36 Söderman P, Malchau H, Herberts P, Johnell O. Are the findings in the Swedish National Total Hip Arthroplasty Register valid? A comparison between the Swedish National Total Hip Arthroplasty Register, the National Discharge Register, and the National Death Register. *J Arthroplasty* 2000;**15**:884-9.

37 Hawker GA, Guan J, Croxford R, Coyte PC, Glazier RH, Harvey BJ, et al. A prospective population-based study of the predictors of undergoing total joint arthroplasty. *Arthritis Rheum* 2006;**54**:3212-20.

Figure 1

Adjusted Relative Risk of TKR or THR for OA by Quartiles

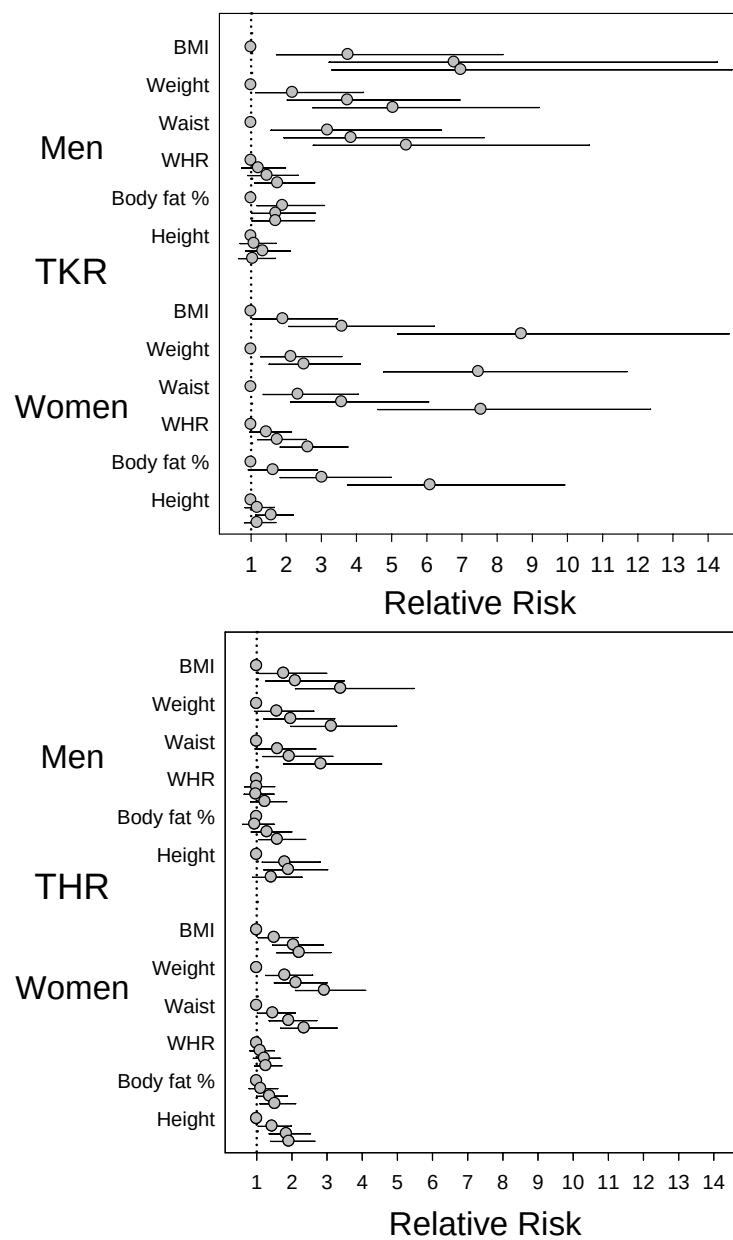
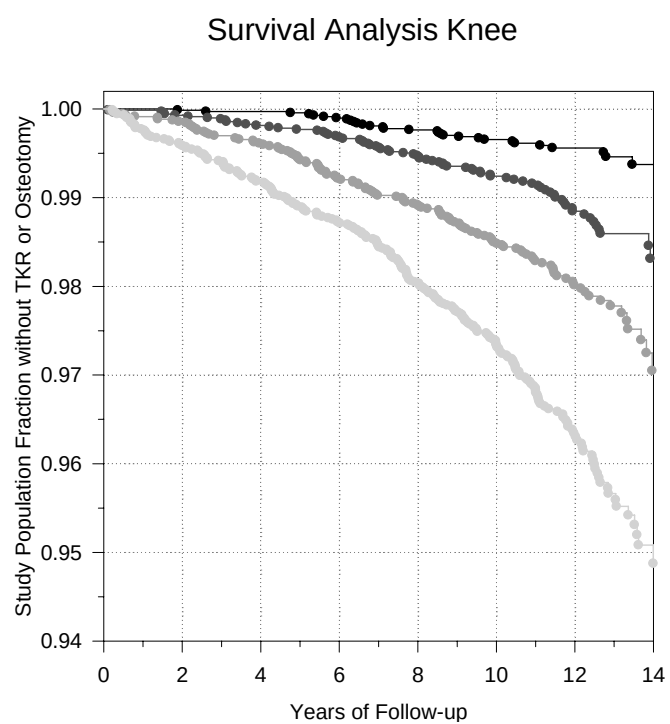


Figure 2

A



B

