# Relationship of height, weight and body mass index to the risk of hip and knee replacements in middle-aged women

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**Objectives.** To examine the effect of height, weight and body mass index (BMI) on the risk of hip and knee replacement in middle-aged women.

*Methods.* In a prospective cohort study 490 532 women aged 50–69 yrs who were recruited in the UK in 1996–2001 were followed over 2.9 yrs for incident primary hip and knee replacements.

**Results.** Height, weight and BMI were all associated with the risk of hip and knee replacement. Comparing the tallest group ( $\geq$ 170 cm) with the shortest (<155 cm) the relative risks were 1.90 (95%CI 1.55–2.32) for hip replacement and 1.55 (95%CI 1.19–2.00) for knee replacement. Comparing the heaviest group ( $\geq$ 75 kg) with the lightest (<60 kg) the relative risks of hip and knee replacement were 2.37 (95%CI 2.04–2.75) and 9.71 (95%CI 7.39–12.77), respectively. Comparing obese women (BMI  $\geq$  30 kg/m<sup>2</sup>) to women with a BMI < 22.5 kg/m<sup>2</sup>, the relative risks for hip and knee replacement were 2.47 (95%CI 2.11–2.89) and 10.51 (95%CI 7.85–14.08), respectively. These effects did not vary according to age, education, alcohol and tobacco consumption, or with use of hormonal therapies. Currently, an estimated 27% of hip replacements and 69% of knee replacements in middle-aged women in the UK are attributable to obesity.

**Conclusion.** In middle-aged women, the risk of having a hip or knee replacement increases with both increasing height and increasing BMI. From a clinical perspective, relatively small increases in average BMI among middle-aged women are likely to have a substantial impact on the already increasing rates of joint replacement in the UK.

KEY WORDS: Joint replacement, Obesity, Anthropometry, Prospective study, Million Women Study.

Rates of primary hip and knee joint replacement are rising in many developed countries and with the ageing of the population they are likely to continue to increase [1]. The main indication for both operations is severe osteoarthritis of the respective joint although rheumatoid arthritis, trauma and avascular necrosis account for a small percentage of replacements [2–4]. Many studies have examined risk factors for osteoarthritis of the hip and knee with case definitions depending upon radiological or clinical signs. Joint replacement is, however, a well-defined and clinically important endpoint with a significant cost to health systems [5], yet few studies have examined risk factors for this.

In England, hip and knee replacement rates are higher in women compared with men, and rise steeply after the age of 60 yrs [1]. Increasing body mass index (BMI) has consistently been associated with an increased risk of knee osteoarthritis [6-8] while the evidence has been less consistent for the relationship between BMI and hip osteoarthritis [8-10]. With respect to joint replacement, two prospective cohort studies have shown that BMI predicts total hip replacement for osteoarthritis [11, 12] and one study also found a relationship between adult height and hip replacement [13]. A case-control study found increasing BMI was associated with being on a waiting list for knee replacement, but we know of no studies that have looked at height and knee replacement. This is despite the fact that adult height correlates with joint dimensions and may reflect bone development [14, 15]. Therefore, we investigated the relationship between height, weight and BMI on the risk of primary hip and knee joint replacement in a prospective study of middle-aged women.

# Subjects and methods

# Study population

The Million Women Study is a population-based prospective cohort study that recruited 1.3 million women in the UK, mostly aged 50-64 yrs old, between 1996 and 2001. The study aims, methods and the characteristics of the study population have been described elsewhere [16]. Briefly, women were recruited through attendance at breast-screening clinics and were asked to complete a baseline questionnaire, which included questions on sociodemographic, lifestyle and anthropometric factors and medical history. In 1999-2004, women who entered the study were sent a follow-up questionnaire to update exposure information and ascertain certain incident morbidity. This included a question asking them, 'Have you had any major operations over the last 5 years?' If 'yes', the questionnaire asked participants to describe the operations and the dates on which they were performed. On the return of the questionnaire, if the respondents had written down an operation, this was manually coded by clinical coders and entered into the study database. A primary hip replacement code was assigned for any of the following operative descriptions, 'hip replacement', 'total hip replacement', 'THR', 'bilateral hip replacement'. A primary knee replacement code was assigned for the following descriptions, 'knee replacement', 'bilateral knee replacement'. Revision joint replacements were coded separately. A random sample of the database entries (1%) were checked against the participant questionnaire for accuracy. For a sample of the study population recruited in Scotland (n = 28524)self-reported primary hip and knee replacement was compared with hospital admission records and showed excellent agreement [kappa for agreement was 0.85 (95%CI 0.84-0.86) and 0.88 (95%CI 0.87-0.89) for hip and knee replacement, respectively]. We presumed that the accuracy of self-reporting would be similar between participants recruited in England and Scotland.

Participants who had returned a follow-up questionnaire and had their responses entered into a database by 31 December 2005 were eligible to be included in these analyses. All the participants provided written consent to be included in the study

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and the study protocol has been approved by the English National Health Service Eastern Multi-Centre Research Ethics Committee.

#### Analysis

Cases were defined as women who at follow-up reported a hip or knee replacement after recruitment. Women who reported more than one operation were counted once, in the respective analysis, taking the date of their first joint replacement since recruitment. As we were interested in operations that were performed for osteoarthritis and not resulting from fractures or inflammatory arthritis, we excluded women who reported fractures of the hip or knee (tibiofemoral region) within the 6 months preceding the date of their respective joint replacement and those who reported a history of rheumatoid arthritis or cancer (other than non-melanoma skin cancer) at entry to the study. This resulted overall in 5% (n=25251) of the original study population being excluded.

Relative risks for the relationship between height, weight and BMI on incident hip replacement or knee replacement were calculated using a Cox regression model. The time variable was defined as the time from recruitment to the first hip or knee replacement, respectively, or to the date that the follow-up questionnaire was completed, which ever was first. The relative risks were adjusted for potential and known risk factors; age (in 2-yr intervals), region of recruitment (10 regions, broadly representative of health authority areas, and hence a proxy for health service provision), socioeconomic status (in tertiles based on the deprivation index-a score based upon residential address that takes into account unemployment, overcrowding, car and home ownership [17]), and BMI and height, where appropriate. Further adjustment by other potential confounders including time since the menopause (pre/peri-menopausal, 0-4 yrs, 5-9 yrs and 10+ yrs), parity (nulliparous, parous), smoking status (never, ever), alcohol use (<1 unit per week, 1+ unit per week) and past medical history (self-reported heart disease, diabetes, asthma, thyroid disease and osteoporosis) was investigated.

Given that relative risks for height, weight and BMI were calculated for more than one category, and there is no natural baseline, variances and confidence intervals were estimated using 'floating absolute risks' [18]. Compared with conventional methods, this approach does not alter the relative risk estimates but reduces the variances attributed to them and permits comparisons between groups. Therefore, in the tables where multiple categories are compared, floating absolute risks with floated confidence intervals are quoted, however, when any two groups are directly compared in this report for example, comparing those with a BMI of  $30+ \text{ kg/m}^2$  to those with a BMI <22.5 kg/m<sup>2</sup>, conventional confidence intervals are given. This is generally the case in the text.

The proportion of joint replacements in England attributable to BMI were calculated using the relative risks estimated here and BMI (in females 50–69 yrs old) obtained from the Health Survey for England, 2003 [19]. We also examined the risk of height and BMI on hip and knee replacement in various subgroups to determine if the effects were modified by other factors and conducted a sensitivity analysis by excluding those who reported osteoarthritis at baseline to determine if this altered the effect of height and BMI. The STATA 9.2 statistical package was used for the analyses.

#### Results

A total of 490 532 women were eligible for the study with an average of 2.9 yrs of follow up per woman. There were 1917 women who reported a first incident hip replacement and 974 who reported a first incident knee replacement (giving rates of 1.4 and 0.7 per 1000 person-years, respectively for incident hip and

 $\mathsf{T}_{\mathsf{ABLE}}$  1. Annual incidence rates for joint replacement according to baseline characteristics

	Annualized incidence rate for hip replacement per 1000 women (n <sup>a</sup> )	Annualized incidence rate for knee replacement per 1000 women (n <sup>a</sup> )
Age at recruitment		
50–54 yrs	0.61 (384)	0.26 (164)
55–59 yrs	1.35 (557)	0.68 (282)
60–64 yrs	2.49 (845)	1.31 (445)
65–69 yrs	3.54 (131)	2.24 (83)
Socioeconomic status		
Highest	1.42 (679)	0.65 (312)
Average	1.35 (636)	0.67 (317)
Lowest	1.29 (595)	0.74 (342)
Smoking		
Never	1.33 (996)	0.72 (537)
Ever	1.38 (827)	0.62 (372)
Alcohol intake		
<1 unit/week	1.47 (631)	0.89 (383)
≥1 unit/week	1.30 (1286)	0.60 (591)
Parity		
Nulliparous	1.36 (223)	0.59 (96)
Parous	1.35 (1690)	0.70 (878)

<sup>a</sup>Numbers do not necessarily sum to the same total values due to missing values. Although most women were aged 50-64, a small number were aged 65-69 and they are included here.

knee replacement). Among these women, 34 reported both a first incident hip and a first incident knee replacement during the follow-up period.

Table 1 shows incidence rates for hip and knee replacement by baseline characteristics. Incidence rates for joint replacement increased with age but did not appear to be strongly affected by socioeconomic status, smoking, alcohol use or parity. Table 2 and Figs 1 and 2 show the relative risk of hip and knee replacement in relation to height, weight and BMI after controlling for age, region of recruitment and deprivation, and for BMI and height where appropriate. For each 5 cm increment in height (after controlling for BMI) the risk of both hip and knee joint replacement rose and the magnitude of the increase for both hip and knee joint replacement was similar. Comparing the tallest group of women ( $\geq$ 170 cm) to the shortest group (<155 cm), the relative risk of hip replacements the relative risk comparing the same groups was 1.55 (95%CI 1.19–2.00).

The risk of both hip and knee replacement increased with increases in both BMI and weight. For each 5kg increment in weight, the risk of hip and knee replacement was found to rise, although for equivalent comparisons, the effect of weight on knee replacement was substantially greater than its effect on hip replacement. Comparing the heaviest group of women (>75 kg)with the lightest group (<60 kg) the relative risk of hip replacement was 2.37 (95%CI 2.04-2.75) and for knee replacement the relative risk was 9.71 (95%CI 7.39-12.77). BMI had a significant effect on the relative risk of hip and knee replacement in all the BMI categories examined, and for a  $BMI \ge 25 \text{ kg/m}^2$ there was a marked difference comparing hip and knee replacement with relative risks for knee replacement rising almost exponentially (Fig. 2). Comparing obese women ( $\geq 30 \text{ kg/m}^2$ ) to those in the lowest BMI group ( $<22.5 \text{ kg/m}^2$ ) the relative risk of hip replacement rises to 2.47 (95%CI 2.12-2.89) whilst for knee replacement the equivalent comparison provides a risk estimate of 10.51 (95%CI 7.85-14.08). Given the similarities in the effect of weight and BMI on joint replacement and the relevance of BMI to current health research, we chose to concentrate on BMI in preference to weight in the remaining analyses.

When additional adjustment was made simultaneously by the potential confounders, time since menopause, smoking, alcohol use, parity or other illnesses reported at baseline, none of the calculated risks for height or BMI altered appreciably. For height,

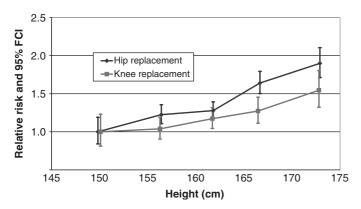
TABLE 2	Relative r	risk of	hip	and	knee	ioint	replacement	according	to	heiaht	weight	and BM	11

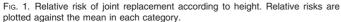
	Incident cases hip replacement/knee replacement <sup>a</sup>	Population with neither hip nor knee replacement <sup>a</sup>	Adjusted relative risk for hip replacement <sup>b</sup> (95% FCI <sup>c</sup> )	Adjusted relative risk for knee replacement <sup>b</sup> (95% FCI <sup>c</sup> )
Height (cm)				
<155	129/90	42 4 1 9	1.00 (0.84-1.19)	1.00 (0.81-1.23)
155-159	376/206	104 993	1.22 (1.11–1.36)	1.04 (0.91–1.19)
160–164	521/285	145 410	1.28 (1.17–1.39)	1.17 (1.04–1.32)
165–169	495/216	113 508	1.64 (1.50–1.79)	1.27 (1.11–1.45)
170+	368/163	75 254	1.90 (1.71–2.10)	1.55 (1.32–1.80)
P-value (trend)			<0.0001	< 0.0001
Weight (kg)				
<60	256/60	109778	1.00 (0.88-1.44)	1.00 (0.77-1.29)
60–64	281/95	98 405	1.19 (1.06–1.34)	1.89 (1.55–2.32)
65–69	295/94	78 341	1.51 (1.35–1.69)	2.38 (1.95–2.92)
70–74	338/148	69 102	1.92 (1.73–2.14)	4.27 (3.63–5.02)
75+	690/542	115810	2.37 (2.19–2.56)	9.71 (8.88–10.62)
P-value (trend)			<0.0001	< 0.0001
BMI (kg/m <sup>2</sup> )				
<22.5	254/51	101 408	1.00 (0.88–1.13)	1.00 (0.76-1.32)
22.5-24.9	441/113	130767	1.31 (1.19–1.44)	1.65 (1.37-1.98)
25.0-27.4	421/180	103 503	1.52 (1.38–1.67)	3.19 (2.75–3.69)
27.5-29.9	272/191	61 198	1.64 (1.46-1.85)	5.63 (4.88-6.48)
30+	452/395	70 402	2.47 (2.25–2.71)	10.51 (9.52–11.62)
P-value (trend)			< 0.0001	< 0.0001

<sup>a</sup>Numbers do not necessarily sum to the same total values due to missing values and cases with both an incident hip and incident knee replacement.

<sup>b</sup>All relative risks are adjusted for age, region of recruitment, deprivation index. Additionally, relative risks for height are adjusted for BMI and relative risks for weight are adjusted for height.

<sup>c</sup>FCI, Floating confidence interval.





the relative risk of hip replacement was 1.86 instead of 1.90 comparing the tallest with the shortest and the corresponding relative risk of knee replacement 1.57 instead of 1.55. For BMI comparing the highest with the lowest groups, the relative risk of hip replacement was 2.54 instead of 2.47 and the corresponding relative risk of knee replacement was 9.49 instead of 10.51.

We conducted a sensitivity analysis by restricting the population to women who had not reported having 'osteoarthritis' on the baseline questionnaire to determine if this would affect our risk estimates. Due to the reduced number of cases when the population was restricted, fewer categories of height and BMI were examined. Table 3 shows the relative risks for hip and knee replacement, respectively, by height and BMI first in the entire study population and secondly in women who did not report having osteoarthritis at baseline. The risk estimates obtained for each category of height and BMI were not significantly different (P > 0.01) in each analysis.

When the effect of height and BMI on hip and knee replacement was examined in subgroups, the estimates of effect were generally consistent and are illustrated in Figs 3 and 4. The effect of height and BMI when examined in dichotomous groups (<165 cm,  $\geq$ 165 cm and <25 kg/m<sup>2</sup>,  $\geq$ 25 kg/m<sup>2</sup>) on hip and knee replacements did not appear to differ according to potential

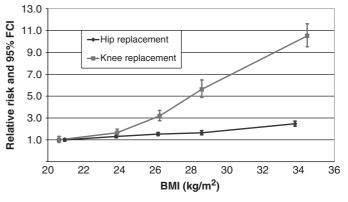


Fig. 2. Relative risk of joint replacement according to BMI. Relative risks are plotted against the mean in each category.

markers of service use such as use of hormonal therapies, age of school leaving or qualifications, nor did it differ according to other potential confounders (frequency of strenuous activity, parity, smoking, alcohol use). Within each set of subgroup comparisons, the overall global  $\chi^2$  was not significant (for height and hip and knee replacement, P=0.2 and 0.06, respectively and for BMI and hip and knee replacement, P=0.2 and 0.02, respectively), suggesting that other factors do not substantially modify the effect of height or BMI.

#### Discussion

Overall, our study has clearly demonstrated that in middle-aged women higher BMI results in an increased likelihood of hip and knee replacement, although the magnitude of risk is much greater for a knee replacement. We have also shown for the first time that after controlling for various socioeconomic and other factors, adult height in women is associated with a significantly increased risk of joint replacement and further investigation into the possible mechanisms for this association is warranted.

Studies that have used the outcome of osteoarthritis of the knee defined by radiographic and clinical evidence [6, 7, 20] and knee replacement for osteoarthritis [9, 21], have demonstrated

TABLE 3.	Sensitivity	analysis o	comparing	g relative	risks o	of hip an	d knee i	replacement
in entire	population	with thos	e who did	not repo	ort oste	eoarthriti	s at bas	eline

	All cases/cases who did not report osteoarthritis at baseline	Adjusted RR <sup>a</sup> among total population (95% FCI <sup>b</sup> )	Adjusted RR <sup>a</sup> among those who did not report osteoarthritis at baseline (95% FCI <sup>b</sup> )
Hip replacement			
Height (cm)			
<160	505/237	1.00 (0.92–1.09)	1.00 (0.88–1.14)
160–164	521/216	1.10 (1.01–1.20)	0.96 (0.84–1.10)
165+	863/382	1.50 (1.40–1.61)	1.40 (1.26–1.55)
BMI (kg/m <sup>2</sup> )			
<25	695/319	1.00 (0.93–1.08)	1.00 (0.90–1.12)
25-29.9	693/307	1.33 (1.24–1.43)	1.33 (1.19–1.48)
30+	452/186	2.10 (1.91–2.31)	2.07 (1.79–2.39)
Knee replacement			
Height (cm)			
<160	296/86	1.00 (0.89–1.12)	1.00 (0.81–1.24)
160–164	285/79	1.14 (1.02–1.28)	1.05 (0.85–1.31)
165+	379/120	1.34 (1.21–1.48)	1.38 (1.15–1.66)
BMI (kg/m <sup>2</sup> )			
<25	164/61	1.00 (0.86–1.17)	1.00 (0.78–1.29)
25-29.9	371/115	2.99 (2.70–3.31)	2.62 (2.18–3.14)
30+	395/100	7.65 (6.93-8.46)	5.83 (4.79–7.11)

<sup>a</sup>All relative risks are adjusted for age, region of recruitment, deprivation index. Additionally, relative risks for height are adjusted for BMI.

<sup>b</sup>FCI, Floating confidence interval.

an increasing risk of knee disease with increasing BMI. While evidence regarding the association between BMI and osteoarthritis of the hip is less well established [8], a recent large cohort study demonstrated that BMI measured on average 18 yrs previously, increases the risk of hip joint replacement for osteoarthritis in women by a factor of 2.3 (comparing those with BMI  $\geq$  32 kg/m<sup>2</sup> with a BMI 20.5–21.9 kg/m<sup>2</sup>) [13]. Despite differences in study populations and outcome definitions, our findings are in line with these other studies.

The size of our study population also allowed us to examine risks across a broad range of values. We demonstrated that higher BMI is associated with a significantly increased risk of both hip and knee joint replacement (the vast majority resulting from osteoarthritis) not only in those who are overweight and obese (BMI  $\geq 25 \text{ kg/m}^2$ ) but also in those who are considered within a healthy body size (BMI 20–25 kg/m<sup>2</sup>). Comparing women with a BMI of 22.5–24.9 kg/m<sup>2</sup> with those <22.5 kg/m<sup>2</sup> the risk is 31% greater for hip replacement and 65% greater for knee replacement. On a population level, these risks are not insubstantial and suggest that weight reduction in healthy sized women (BMI < 25 kg/m<sup>2</sup>) could be beneficial in reducing the risk of joint replacement.

It is generally thought that the association between BMI and hip or knee osteoarthritis is due to a mechanical load effect on these joints although biochemical intermediaries have also been suggested as a possible pathway [8]. Our results demonstrated a similarity in the effect of BMI and weight on the risk of joint replacement but a marked difference in their effects on the hip vs the knee joint. This suggests that mechanical loading is the predominant factor in the relationship between BMI and joint disease, as one would expect a biochemical intermediary to have a similar effect on both the hip and knee.

We are aware of only one study that has examined height in relation to hip replacement for osteoarthritis and none for knee. The other researchers found a significant positive association and increasing trend, with effect estimates for women similar to our results; however, they were unable to adjust for potential confounders [13]. Our study demonstrated that after controlling for age, region of recruitment, deprivation and BMI, the positive association with height extends to both hip and knee replacement, and that the risk estimate is similar for both joints. The fact that there is a significant trend in the association between height and both hip and knee replacement (P < 0.0001), and that the effect of height is consistent across the various subgroups examined including markers of education and health service use (Fig. 3), further emphasizes the likely biological plausibility of this association.

Bone development and subsequent adult height may be influenced by intrauterine or early childhood factors [14] and the positive association between height and the risk of hip and knee joint replacement that we observed is consistent with these hypotheses, that is, that factors influencing adult height (such as nutrition in early life), also influence bone development and mineralization, potentially pre-disposing the individual to osteoarthritis and subsequent joint replacement. However, like BMI, a mechanical explanation for this association is also plausible. With respect to the hip, adult height has been found to correlate with proximal femur dimensions including hip axis length, neck shaft angle and femoral head radius [15] and the greater surface area or variation in angle may contribute to different forces on the acetabular joint leading to more wear and tear. A cross-sectional study found that knee height in women was associated with radiographic evidence of knee osteoarthritis and knee pain, and that the association with pain was independent of radiographic changes [22]. The authors of this study suggested that greater force on the knee joint resulting from greater leg length may explain the observations. From a clinical perspective, height is not easily modifiable; however, it is possible that interventions that aim to reduce the force across the joint such as muscle strengthening may have a greater role in risk reduction for those who are taller.

A number of limitations to our study must be considered when interpreting our findings. Outcome and exposure information for this study was based on self-report and some misclassification is inevitable. However, we found that within this population self-reported hip and knee replacement agree closely with medical records. Validation studies of self-reported height and weight suggest that correlations between self-reported and measured anthropometric factors are excellent [23, 24]. Therefore, it is unlikely that our findings would be greatly influenced by the use of self-report. Certain physical activities, occupational activities, and knee and hip injuries have been linked to osteoarthritis of the respective joint [25, 26]. We were unable to examine the effect of these factors as they were not measured at recruitment. We also did not collect information on joint replacement at baseline, and therefore may not have excluded all past cases in our analyses. However, given the average age of study participants was 55 years at recruitment, and the small absolute numbers of joint replacements in those <50 yrs old [1], it is likely that these cases would contribute to an insignificant proportion of our cohort.

Evidence suggests that socioeconomic factors, overweight, as well as patient and doctor preferences may influence whether an individual has a joint replacement [2]. Two recent qualitative studies found that the patient or the treating doctors perceptions of need were barriers to joint replacement surgery [27, 28]. Weight has also been identified as a factor that may influence access [27, 29], and therefore when examining the outcome of joint replacement we must take into consideration these potential biases. While some of these factors are difficult to measure quantitatively, in our analyses we adjusted for deprivation score and region of recruitment to take into account socioeconomic factors and regional variations in surgical practice. We also examined the effects within subgroups that may be markers of access to medical services such as qualifications, age of school leaving, previous oral contraceptive use and hormone replacement therapy use as well as age and BMI. The consistency of the relative risks among all of the null groupings (Figs 3 and 4) suggests that our results are not likely to be greatly biased by these factors.

The outcome of hip and knee replacement was used to draw conclusions regarding possible mechanisms leading to

Knoo replacement

	lip replacem ases with he					Knee replace ases with he				
Subgroup <1	65 cm/≥165	cm	RR* (95% (		<	165 cm/≥165	cm	RR* (95%	CI)	
All women	1026/863	1.43 (1	.30-1.57)	📫		581/379	1.26 (	1.10-1.43)		
Oral contracept										
Never Ever	496/374 525/484		.16-1.52)			303/174 271/202		0.95-1.38)		
	323/464	1.51 (1	.34-1.72)		Γ	271/202	1.39 (	1.15-1.07)		-
HRT use Never	500/408	1 42 (1	.25-1.63)		_	263/163	1 23 (	1.01-1.50)		
Ever	522/448		.24-1.60)			314/214		1.08-1.54)	_	
Smoking										
Never	546/434	1.36 (1	.20-1.54)	-   📫		327/205	1.25 (	1.05-1.49)	- <b>-</b>	
Ever	425/392	1.53 (1	.33-1.76)	-	┣╴	209/155	1.34 (	1.09-1.65)		-
Alcohol										
<1 unit/week	347/274		.28-1.76)	1	F	242/134	,	0.95-1.45)		
≥1 unit/week	679/589	1.40 (1	.25-1.56)			339/245	1.32 (	1.11-1.55)		
Parity Nulliparous	104/115	1 54 (1	.18-2.02)		<b>—</b>	51/44	1 30 /	0.86-1.96)		
Parous	918/748		.29-1.56)		•	530/335		1.09-1.44)		
Strenuous exer	cise	,	,					,		
≤ once a week		1.43 (1	.27-1.60)	- i 📥		387/226	1.19 (	1.01-1.41)		
> once a weel	× 339/311	1.41 (1	.20-1.64)	-	-	175/140	1.36 (	1.09-1.71)	│-┾═╾	_
Age left school										
<16 yrs	538/346		.19-1.56)			349/171		0.95-1.38)		
≥16 yrs	487/516	1.46 (1	.28-1.65)		F	230/208	1.39 (	1.15-1.67)		-
Qualifications < A level	269/315	1 66 (1	41 1 05)			146/126	1.96 (	1 07 1 79)		
A level +	209/315 577/405		.41-1.95) .15-1.48)			325/183		1.07-1.73) 0.99-1.42)		_
BMI			, , ,					,,		
<25 kg/m <sup>2</sup>	321/374	1.44 (1	.24-1.67)	-   -	-	86/78	1.16 (	0.85-1.57)	_ <b></b>	
≥ <b>25 kg</b> /m²	679/466		.22-1.55)	-		474/292	,	1.07-1.44)	- <b> </b>	
Age										
<60 yrs	506/426		.19-1.54)			238/200		1.25-1.83)		⊢
≥60 yrs	520/437	1.49 (1	.31-1.70) ــــ		F	343/179	1.06 (	0.88-1.27) 	-	
				1.0	2.0				1.0	2.0

Fig. 3. Relative risk of heap and knee replacement according to height in various subgroups of women. \*Comparing women  $\geq$ 165 cm with those <165 cm. Relative risks are adjusted for age, region of recruitment, deprivation and BMI.

osteoarthritis of these joints. As joint replacement is one endpoint in the natural history of osteoarthritis of these joints, and given that our average time of follow up was relatively short (2.9 yrs) for a chronic disease process such as this, it is difficult to comment on whether the risk factors identified (height and BMI) contributed to instigating the disease process or to disease progression leading to joint replacement. For BMI but not height, it is conceivable that reverse causality may contribute to the effect witnessed. For instance, pain or stiffness from osteoarthritis affecting the joint may result in physical inactivity, and hence an increase in BMI. However, when we examined the effect of BMI within subgroups of strenuous physical activity reported at baseline there was no significant difference in the risk of joint replacement between women reporting strenuous exercise more than once a week than less often, suggesting any such effect would be small (Fig. 4). Similarly in the sensitivity analysis, while we found women not reporting osteoarthritis at baseline had marginally lower risks for knee replacement than those who had osteoarthritis at baseline, this was not significant (Table 3). Prospective studies with longer periods of follow-up have also demonstrated associations between BMI and knee osteoarthritis [6],

Hin ronlacement

and BMI and hip replacement [12], making reverse causality a less-plausible explanation.

Our study population involved women recruited through breast-screening clinics. In England and Scotland, all women aged 50–64 yrs who are registered with a general practitioner are invited to breast screening and those who attend are known to have a slightly higher socioeconomic status [30]. Study participants are, therefore, likely to have better access to joint replacement [1] and this needs to be considered when extrapolating our results to the general population.

Risk factors for hip and knee joint replacement are likely to reflect risk factors for severe osteoarthritis of these joints. From a public health perspective, with an ageing population, osteoarthritis is becoming an increasingly prevalent condition contributing to a significant burden of disease [31]. Hospital admission data for England show that in the year 2004/05, there were >43 000 admissions for primary hip replacements and >47 000 for primary knee replacements with the majority of these being performed in women >60 yrs old [32]. National survey data from 2003 suggest that 67% of women aged 50–69 yrs old in England have a BMI  $\ge 25 \text{ kg/m}^2$  [19]. Based on our relative risks we estimate that 27% (95%CI 22–32%) of hip replacements and

Knoo replacement

		15月1		Cases with I	DAAL		
ca Subgroup <25 k	ses with B g/m²/≥25 k		6 CI)	<25 kg/m²/≥25		RR* (95% C	1)
ll women	695/1145	1.55 (1.41-1.71)		164/766	4.34 (	3.66-5.14)	<b>↓</b>
Dral contraceptiv							
Never	287/562	1.71 (1.48-1.97)		66/398		4.01-6.79)	
Ever	405/578	1.45 (1.28-1.65)		97/360	3.75 (	3.00-4.70)	
IRT use							
Never	306/582	1.67 (1.45-1.92)		58/359		4.09-7.16)	
Ever	386/558	1.48 (1.30-1.68)		104/405	3.93 (	3.16-4.87)	
moking							
Never	364/594	1.60 (1.40-1.82)		- 86/428		3.82-6.07)	
Ever	297/495	1.51 (1.31-1.74)		► 72/281	3.52 (	2.71-4.57)	
lcohol							
<1 unit/week	196/410	1.60 (1.35-1.90)		48/320		3.76-6.91)	
≥1 unit/week	499/735	1.53 (1.36-1.71)		116/446	3.92 (	3.19-4.81)	
Parity							
Nulliparous	91/121	1.54 (1.17-2.03)		23/69		2.14-5.52)	
Parous	602/1022	1.56 (1.41-1.72)		141/697	4.48 (	3.73-5.37)	-
Strenuous exerci	se						
≤ once a week	387/763	1.55 (1.37-1.75)		- 78/513		3.95-6.36)	
> once a week	286/351	1.48 (1.27-1.74)		- 81/229	3.50 (	2.72-4.52)	- <b>-</b>
ge left school							
<16 yrs	279/577	1.58 (1.37-1.83)		- 77/422		3.26-5.31)	│ -♣-
≥16 yrs	415/568	1.58 (1.39-1.79)		- 87/342	4.49 (	3.55-5.69)	-
Qualifications							
< A level	240/335	1.54 (1.30-1.82)		50/216		3.43-6.36)	
A level +	330/625	1.64 (1.44-1.88)		- 81/411	4.31 (	3.39-5.47)	-
leight							
<165 cm	321/679	1.65 (1.44-1.89)		<b>6</b> /474	````	3.40-5.39)	<b>-</b> ♣-
≥165 cm	374/466	1.57 (1.37-1.80)		- 78/292	4.65 (	3.62-5.97)	
lge							
<60 yrs	340/570	1.76 (1.54-2.02)		82/342		3.40-5.51)	│ ——————
≥60 yrs	355/575	1.40 (1.23-1.60)	.   🖷	82/424	4.44 (	3.50-5.63)	
			1.0	2.0			1.0 3.0 5.0 7.0

Fig. 4. Relative risk of heap and knee replacement according to BMI in various subgroups of women. \*Comparing women  $\geq$ 25 kg/m<sup>2</sup> with those <25 kg/m<sup>2</sup>. Relative risks are adjusted for age, region of recruitment and deprivation.

69% (95% CI 64–73%) of knee replacements are attributable to overweight and obesity (i.e.  $BMI \ge 25 \text{ kg/m}^2$  [33]). With obesity increasing nationally and internationally, the need for joint replacements is likely to rise and effective strategies to address this are a public health necessity.

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