

# Body Mass Index- and Waist Circumference-Defined Obesity with the risk of Total Knee Arthroplasty for Osteoarthritis: A prospective cohort study

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## Research article

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# Abstract

**Background:** There is a discordance in classification of obesity when defined by body mass index (BMI) or waist circumference (WC). We aimed to examine whether categories of BMI- and WC-defined obesity are differentially associated with the risk of total knee arthroplasty for osteoarthritis.

**Methods:** 38,924 participants from the Melbourne Collaborative Cohort Study with BMI and WC measured at baseline (1990-1994) were included. Obesity status was defined as: not obese (non-obese BMI and non-obese WC); WC-defined obesity only (non-obese BMI and obese WC); BMI-defined obesity only (non-obese WC and obese BMI); and BMI- and WC-defined obesity. The incidence of total knee arthroplasty for osteoarthritis between January 2001 and December 2013 was determined by linking participant records to the National Joint Replacement Registry.

**Results:** Over  $11.5 \pm 3.1$  years follow-up, 1,875 participants underwent total knee arthroplasty for osteoarthritis. Participants with WC-defined obesity only (HR=1.79, 95%CI 1.51-2.53), BMI-defined obesity only (HR=2.39, 95%CI 2.02-2.84), and BMI- and WC-defined obesity (HR=3.14, 95%CI 2.82-3.49) had an increased risk of total knee arthroplasty compared with those who were not obese.

**Conclusions:** Individuals with either BMI- or WC-defined obesity should be targeted for prevention of knee osteoarthritis as both are significant predictors for severe osteoarthritis requiring a total knee arthroplasty.

## Background

Obesity is an important modifiable risk factor for knee osteoarthritis (OA)[1]. Although body mass index (BMI) is primarily used as a simple screening tool for obesity at the population level[2], it does not take into account the body fat distribution[3]. Waist circumference (WC) estimates central obesity and has been shown to be a better predictor for cardio-metabolic morbidity and premature mortality than BMI[3], particularly for people with low BMI[4] and for women[5]. Discordance between BMI and WC in classifying individuals as obese has been demonstrated in a number of studies. For example, an Australian study reported that approximately 40% of individuals with WC-defined obesity (WC  $\geq 102$  cm for men and  $\geq 88$  cm for women) were not obese with respect to BMI (BMI  $\geq 30$  kg/m<sup>2</sup>)[6]. This discordance was greater for Chinese adults with 75.7% who were obese with respect to WC not defined as obese based on BMI[7].

Previous studies have examined obesity as a risk factor for knee OA based on BMI or WC[1, 3, 8] but it is unknown whether the risk of knee OA differs in relation to different categories of BMI- and WC-defined obesity. Understanding this has implications for the prevention and treatment of knee OA. Thus we aimed to examine whether the risk of total knee arthroplasty due to OA differed by categories of BMI- and WC-defined obesity.

## Participants And Methods

### *Study participants*

The Melbourne Collaborative Cohort Study (MCCS) is a well-established cohort study that recruited 41,514 participants (17,045 men, 99.3% aged 40-69 years) during 1990-1994[9]. The study protocol was approved by the Cancer Council Victoria's Human Research Ethics Committee[9]. For the current study, 2,590 (6.2%) were excluded because they had either: died or left Australia or reported having an arthroplasty prior to 1 January 2001; or their first recorded procedure was a revision arthroplasty[9], leaving 38,924 participants available for analysis.

### ***Demographic data, anthropometric measurements and classification of obesity categories***

At baseline, demographic and lifestyle data, including date of birth, sex, country of birth, education, smoking and physical activity, were collected using standard questionnaires[9]. WC, height and weight were measured using standard procedures[9]. Obesity was defined by BMI  $\geq 30$  kg/m<sup>2</sup> or WC  $\geq 102$  cm for men and  $\geq 88$  cm for women[10]. Obesity status was classified based on combination of BMI-and WC-defined obesity: (i) not obese (non-obese BMI and non-obese WC, BMI<sup>N</sup>/WC<sup>N</sup>); (ii) WC-defined obesity only (non-obese BMI and obese WC, BMI<sup>N</sup>/WC<sup>O</sup>); (iii) BMI-defined obesity only (non-obese WC and obese BMI, BMI<sup>O</sup>/WC<sup>N</sup>); (iv) BMI- and WC-defined obesity (BMI<sup>O</sup>/WC<sup>O</sup>), where N = non-obese and O = obese.

### ***Incidence of total knee arthroplasty for OA***

The Australian Orthopaedic Association National Joint Replacement Registry (AOA NJRR) collects information on prostheses, patient demographics, type and reason for arthroplasty, with an almost complete data relating to arthroplasty (>99%) in Australia[11]. Linking the MCCS records to the AOA NJRR identified those who had a primary total knee arthroplasty performed between 1 January 2001 and 31 December 2013. Knee OA was defined as the first primary total knee arthroplasty with a contemporaneous diagnosis of OA, as recorded in the AOA NJRR. If one person had multiple arthroplasties, the first recorded procedure was considered the event. The linkage study was approved by the Human Research Ethics Committee of Cancer Council Victoria and Monash University.

### ***Statistical analysis***

Cox proportional hazard regression models were used to estimate the hazard ratio (HR) and 95% confidence interval (CI) for the incidence of total knee arthroplasty due to OA associated with obesity categories, with age as the time scale. Follow-up for arthroplasty (calculation of person-time) began 1 January 2001 and ended at the date of first knee arthroplasty for OA or date of censoring. Participants were censored at either the date of first knee arthroplasty for indications other than OA, the date of death, or end of follow-up, whichever came first. All analyses were adjusted for sex, education, smoking status, physical activity and country of birth. As men and women demonstrate different obesity category distributions and have different risks of knee arthroplasty, stratified analyses by gender were performed. Tests based on Cox regression methods showed no evidence that proportional hazard assumptions were violated for any analysis. All statistical analyses were performed using Stata 15.0 (StataCorp LP, College Station, TX, USA).

## Results

Of the whole population (n=38,884), 26.5% (n=10,311) had obesity defined as either BMI or WC. Of the 10,311 obese participants defined by either BMI or WC, 55.6% (n=5762) had both BMI- and WC-defined obesity, 22.9% (n=2363) had WC-defined obesity only, and 21.2% (n=2186) had BMI-defined obesity only.

A total of 1,875 participants underwent a total knee arthroplasty for OA over an average of 11.5±3.1 years follow-up. The characteristics of study participants according to knee arthroplasty are presented in Table 1. Those who had a total knee arthroplasty were older and more likely to be born in Australia/UK and had a higher BMI and WC than those without knee arthroplasty.

Table 2 shows the relationship between obesity categories and incidence of total knee arthroplasty for OA. After full adjustment, participants with WC-defined obesity only (HR 1.79, 95% CI 1.51-2.53), BMI-defined obesity only (HR 2.39, 95% CI 2.02-2.84), and BMI- and WC-defined obesity (HR 3.14, 95% CI 2.82-3.49) had an increased risk of knee arthroplasty for OA compared with those not obese. In the gender specific analysis, men with WC-defined obesity only (HR 1.92, 95% CI 1.45-2.55), BMI-defined obesity only (HR 2.23, 95% CI 1.68-2.94), and BMI- and WC-defined obesity (HR 2.71, 95% CI 2.24-3.28) and women with WC-defined obesity only (HR 1.72, 95% CI 1.39-2.14), BMI-defined obesity only (HR 2.52, 95% CI 2.03-3.13), and BMI- and WC-defined obesity (HR 3.31, 95% CI 2.91-3.78) had an increased risk of knee arthroplasty for OA compared with those not obese.

## Discussion

We found when obesity was defined by either BMI or WC alone, over 20% of obese persons were missed. However, any participant defined as obese (BMI only, WC only, or both BMI and WC) had an increased risk of total knee arthroplasty for OA compared with those defined as not obese. Those who had both BMI- and WC-defined obesity were at the greatest risk of total knee arthroplasty for OA.

In our study, over 40% of participants were classified as obese based on either BMI or WC, but not both. Using BMI alone to define obesity resulted in 7,948 participants, or 21.2% being defined as obese. Another 2,363 participants (6.1%) had WC-defined obesity associated with adverse outcomes, but were not defined as obese based on their BMI. We found that all categories of obesity (WC-defined obesity only, BMI-defined obesity only, or BMI- and WC-defined obesity) were associated with increased risk of total knee arthroplasty for OA. This is consistent with observations regarding other obesity-related chronic diseases such as cardiovascular disease[12] and type 2 diabetes[13]. Additionally, our study showed that, men and women with BMI- and WC-defined obesity had the greatest risk, which is more obvious for women. BMI mainly captures body weight related obesity whereas WC mostly reflects central obesity[12]. Having both BMI- and WC-defined obesity further increases the risk of total knee arthroplasty compared with having either BMI- or WC-defined obesity alone. This might be due to the interaction of biomechanical factors with metabolic and inflammatory factors to promote OA initiation and progression.

Those with elevated BMI or WC alone do not identify the same individuals as obese, and do not capture the whole obesity-related risk of knee OA. This is of particular importance for the aging population given the discrepancy between BMI and WC appears particularly in older age, when people tend to lose lean mass but continue to gain fat mass that is reflected by WC[6]. Recently, for the identification of individuals at risk of knee OA, BMI has been suggested as a sufficient measure of obesity[14] but our data show that individuals without BMI-defined obesity but with WC-defined obesity are also at increased risk of knee OA compared with those who are not obese. Our study supports the inclusion of both BMI and WC to identify and target those at risk of knee OA for the prevention and management of the disease.

The strengths of our study include its prospective design, large sample size, participants of varying age and countries of birth, and the validation and completeness of arthroplasty data from the AOA NJRR[11]. Our results need to be considered within the study's limitations. Arthroplasty is used as a proxy for severe symptomatic OA, however, there are other factors such as access to health care, patient and clinician factors that may influence the decision for arthroplasty[15]. However, the publicly-funded universal health system (Medicare) in Australia ensures that everyone has equal access to arthroplasty facilities. Additionally, our analyses have adjusted for age, sex, education, smoking status, physical activity and country of birth to attempt to control for these factors. Arthroplasty data were not available prior to 2001 and as a result, some misclassification of arthroplasty may have occurred. This is most likely to have been non-differential which might have attenuated the strength of our observed associations.

## **Conclusion**

Obesity should be assessed by both BMI and WC in order to identify those at risk of knee OA, as both measures are associated with an increased risk of severe knee OA and there is discordance between these measures at the individual level in defining obesity. Individuals with either BMI- or WC-defined obesity should be targeted for prevention and management of obesity in order to reduce the burden of severe knee OA.

## **Declarations**

### **Ethical Approval and Consent to participate**

The MCCA study protocol was approved by the Cancer Council Victoria's Human Research Ethics Committee. The linkage study was approved by the Human Research Ethics Committee of Cancer Council Victoria and Monash University. All participants provided written informed consent.

### **Consent for publication**

Not applicable

### **Availability of data and materials**

All data generated or analysed during this study are included in this published article [and its supplementary information files].

### **Competing interests**

The authors declare that they have no competing interests

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### **Authors' Contributions**

SMH and FC were involved in conception and design of the study. YW, GGG, SG and FMC were involved in the acquisition of data. YZL, YW and SMH were involved in statistical analysis and interpretation of the data. YZL, YW, FMC, GGG, SG, AEW and SMH were involved in the interpretation of the data. YZL and YW drafted the manuscript. All authors reviewed the manuscript with critical revision of the article for important intellectual content and approved the final manuscript. SMH took the responsibility for the integrity of the work as a whole, from inception to finished article. All authors had full access to all of the data in the study. SMH is the guarantor.

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## **Abbreviations**

BMI - body mass index

WC - waist circumference

HR – hazard ratio

OA- osteoarthritis

MCCS - Melbourne Collaborative Cohort Study

BMI<sup>N</sup>/WC<sup>N</sup> - non-obese BMI and non-obese WC

BMI<sup>N</sup>/WC<sup>O</sup> - non-obese BMI and obese WC

BMI<sup>O</sup>/WC<sup>N</sup> - non-obese WC and obese BMI

BMI<sup>O</sup>/WC<sup>O</sup> - BMI- and WC-defined obesity

## References

References were not provided by the author.

## Tables

**Table 1. Baseline characteristics of study participants**

	No knee arthroplasty N=37,049	Knee arthroplasty N=1,875	P value
Age, years	62.4 (8.9)	65.5 (7.5)	<0.001
Male, n (%)	14,463 (40.7)	667 (35.6)	<0.001
Country of birth, n (%)			<0.001
Australia and UK	27,698 (75.2)	1,019 (82.0)	
Italy and Greek	8,828 (24.8)	337 (18.0)	
Secondary education, degree/diploma, n (%)	7928 (22.5)	308 (16.5)	0.002
Moderate and high level of physical activity, n (%)	20,436 (57.5)	1114 (59.4)	0.10
Current/ex-smoker, n (%)	14,921 (42.0)	724 (38.6)	0.004
BMI, kg/m <sup>2</sup>	26.7 (4.4)	29.3 (4.9)	<0.001
Waist circumference, cm	85.0 (12.8)	90.0 (12.7)	<0.001
Obesity status, n (%)			<0.001
Non-obese BMI/non-obese WC (BMI <sup>N</sup> /WC <sup>N</sup> )	26,500 (74.6)	1,012 (54.0)	
Non-obese BMI/obese WC (BMI <sup>N</sup> /WC <sup>O</sup> )	2,105 (6.0)	155 (8.3)	
Obese BMI/non-obese WC (BMI <sup>O</sup> /WC <sup>N</sup> )	1,924 (5.4)	157 (8.4)	
Obese BMI/obese WC (BMI <sup>O</sup> /WC <sup>O</sup> )	4,977 (14.0)	551 (29.4)	

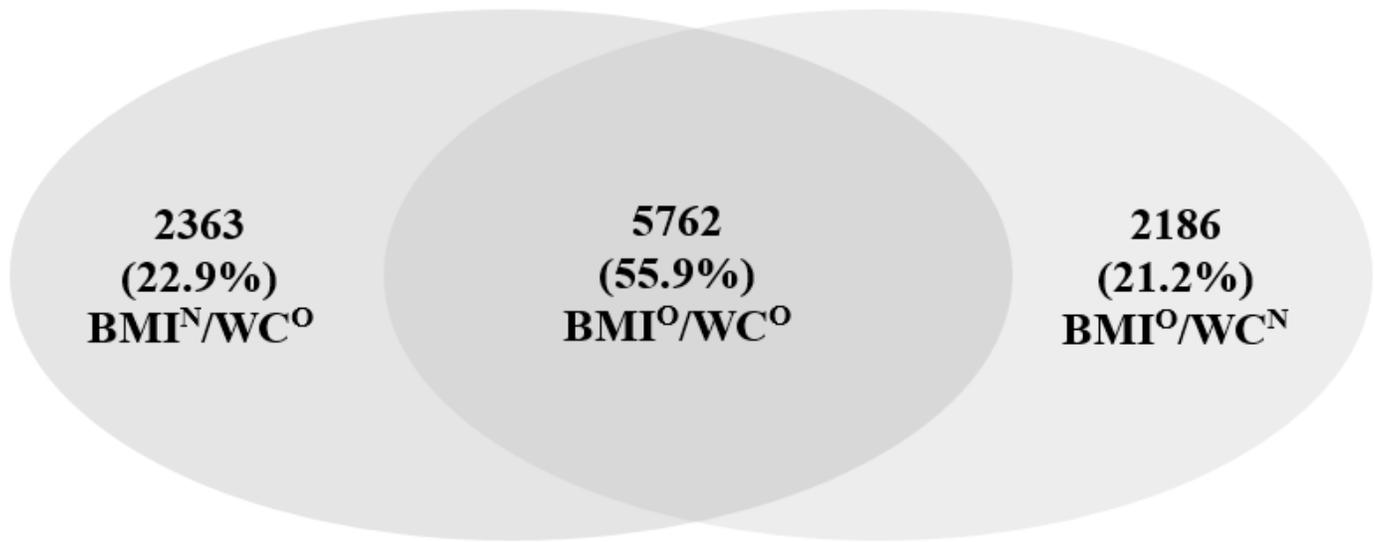
**Table 2. Relationship of body mass index- and waist circumference-defined obesity with incidence of total knee arthroplasty for osteoarthritis**

	Model 1 HR (95% CI)	Model 2 HR (95% CI)
<b>All</b>		
Non-obese BMI/non-obese WC (BMI <sup>N</sup> /WC <sup>N</sup> ), n=28,573	1 (reference)	1 (reference)
Non-obese BMI/obese WC (BMI <sup>N</sup> /WC <sup>O</sup> ), n=2,363	1.87 (1.53, 2.28)	<b>1.79 (1.51, 2.53)</b>
Obese BMI/non-obese WC (BMI <sup>O</sup> /WC <sup>N</sup> ), n=2,186	2.07 (1.67, 2.56)	<b>2.39 (2.02, 2.84)</b>
Obese BMI/obese WC (BMI <sup>O</sup> /WC <sup>O</sup> ), n=5,762	3.05 (2.68, 3.46)	<b>3.14 (2.82, 3.49)</b>
<b>Men*</b>		
Non-obese BMI/non-obese WC (BMI <sup>N</sup> /WC <sup>N</sup> ), n=11,867	1	1
Non-obese BMI/obese WC (BMI <sup>N</sup> /WC <sup>O</sup> ), n=861	1.81 (1.36, 2.40)	<b>1.92 (1.45, 2.55)</b>
Obese BMI/non-obese WC (BMI <sup>O</sup> /WC <sup>N</sup> ), n=967	1.75 (1.33, 2.31)	<b>2.23 (1.68, 2.94)</b>
Obese BMI/obese WC (BMI <sup>O</sup> /WC <sup>O</sup> ), n=1,940	2.35 (1.95, 2.84)	<b>2.71 (2.24, 3.28)</b>
<b>Women*</b>		
Non-obese BMI/non-obese WC (BMI <sup>N</sup> /WC <sup>N</sup> ), n=16,706	1	1
Non-obese BMI/obese WC (BMI <sup>N</sup> /WC <sup>O</sup> ), n=1,502	1.60 (1.29, 1.98)	<b>1.72 (1.39, 2.14)</b>
Obese BMI/non-obese WC (BMI <sup>O</sup> /WC <sup>N</sup> ), n=1,219	2.28 (1.84, 2.82)	<b>2.52 (2.03, 3.13)</b>
Obese BMI/obese WC (BMI <sup>O</sup> /WC <sup>O</sup> ), n=3,822	2.86 (2.52, 3.25)	<b>3.31 (2.91, 3.78)</b>

Model 1. adjusted for age and sex; \*adjusted for age only

Model 2: adjusted for sex, education, smoking status, physical activity and country of birth

## Figures



**Figure 1**

Distribution of body mass index- and waist circumference-defined obesity (BMIN/WCO, BMIO/WCN, BMIO/WCO) in obese participants identified by either body mass index or waist circumference (n=10,311)