# OBESITY IS RELATED TO INCIDENCE OF PATELLOFEMORAL OSTEOARTHRITIS: THE COHORT HIP AND KNEE (CHECK) STUDY


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**Running tile:** Obesity and incidence of PF OA

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**ABSTRACT**

**Objectives:** To determine the longitudinal association of baseline body mass index and change in body mass index over 8 years to incident patellofemoral osteoarthritis at the 8-year follow-up.

**Methods:** A sample of 528 women and men, aged 45-65 years, with knee complaints and without radiographic evidence of patellofemoral and tibiofemoral osteoarthritis at baseline, were selected from the Cohort Hip and Cohort Knee cohort. Incidence of patellofemoral osteoarthritis was defined as presence of radiographic patellofemoral osteoarthritis (with or without tibiofemoral osteoarthritis) at an 8-year follow-up. Baseline body mass index data were categorized into normal, overweight and obese weight categories. Logistic regression analyses, adjusted for age and sex, were conducted to determine the association of baseline body mass index and change in body mass index to patellofemoral osteoarthritis incidence 8 years later.

**Results:** Obesity was associated with greater odds of incident radiographic patellofemoral osteoarthritis (odds ratio: 1.8 [95% CI: 1.1, 3.1]) osteoarthritis 8 years later. There were no significant associations observed between body mass index change over 8 years and incidence of radiographic patellofemoral osteoarthritis in overweight and obese individuals.

**Conclusion:** Our study was the first to explore the longitudinal relation of BMI to incidence of radiographic patellofemoral osteoarthritis. Obesity is associated with increased odds of developing radiographic patellofemoral osteoarthritis 8 years later.

**KEYWORDS:** Knee osteoarthritis, body weight, obese, overweight

## INTRODUCTION

Knee osteoarthritis (OA) is associated with considerable pain and functional limitations [1]. The most frequent disease pattern is combined tibiofemoral joint (TF) OA and patellofemoral joint (PF) OA (44%), followed by isolated PF OA (25%), and isolated TF OA (1%) [2]. A recent systematic review highlights that PF disease is more prevalent than previously thought, with PF OA evident in one-half of the people with knee pain or radiographic OA [3]. Risk factors for PF OA likely differ from TF OA [4] and thus, it is important to understand risk factors associated with PF OA.

The PF joint plays an important role in knee function, during activities involving large ranges of knee flexion such as squatting and stair descent. The PF joint is subjected to loads ~2 to 3 times the bodyweight during high flexion activities [5]. Based on this, higher body mass would translate to higher loads borne by the PF compartment. Obesity is a well-known risk factor for development of TF OA [6] – excess body mass may alter biomechanical and biochemical factors [7, 8]. A recent systematic review synthesized body mass index (BMI) data (frequently used as a surrogate measure of body fat) reported in cross-sectional studies and revealed that individuals with PF OA have higher BMI compared to OA free controls [9]. However, it could not be determined whether obesity was related to development of PF OA. Cross-sectional studies have shown an association between obesity and radiographic PF OA. For example, McAlindon et al. [10] reported an association between higher BMI and radiographic PF OA in the Framingham cohort study and Ding et al. [11] reported negative association between BMI and patellar cartilage thickness and volume. Although it is assumed that obesity increases the risk of development of PF OA, no studies have investigated the longitudinal relation of obesity to radiographic PF OA.

We aimed to determine the relation of BMI to incidence of radiographic PF OA over 8 years and to determine the relation of change in BMI from baseline to 8-year follow-up to incidence of radiographic PF OA. We hypothesized that overweight and obese individuals at baseline and those who increase BMI over 8 years would have a greater risk of incident PF OA.

## METHODS

*Study population*

The Cohort Hip and Cohort Knee (CHECK) Study is a longitudinal, prospective, observational study of 1002 adults, aged 45 to 65 years, who had hip and/or knee complaints (pain or stiffness) and never visited a general

practitioner for their complaints before study entry. Full details of the study population have been previously published [12]. A sample of individuals who had no radiographic evidence of OA in either compartment in their index knee (i.e., side of worse knee pain) at baseline and underwent knee radiography at baseline and 8-year follow-up were included in the present study.

*Participant characteristics*

Body mass and body height measured at baseline and 8-year study visit were used to calculate BMI data for baseline and 8-year follow-up, respectively. The Western Ontario and McMaster Universities Index (WOMAC) data from baseline were included in the current study [13]. The WOMAC is divided into three subscales: pain (Score: 0-20), stiffness (Score: 0 to 8), and physical function (Score: 0-68) — with higher scores indicating worse pain, stiffness, physical function; respectively. Individuals rated their knee pain intensity on an 11-point numerical scale – the Numeric Pain Rating Scale (NPRS). A score of zero on the NPRS represents no pain at all and 10 worst pain imaginable.

*Radiographs acquisition and assessment*

Weight-bearing radiographs were acquired in posterior-anterior (PA) views in 7-10º knee flexion, lateral and skyline views in 30º knee flexion. The atlas of Altman [14] was used to assess joint space narrowing, femoral medial and lateral osteophytes, and tibial medial and lateral osteophytes using the PA views. The Kellgren and Lawrence (KL) criteria were used to grade the severity of TF OA on the PA radiographs [15]. Radiographic TF OA was defined as KL grade of ≥2. Lateral and skyline radiographs were used to assess the PF joint. Osteophytes were scored on the lateral views, and joint space narrowing and osteophytes were scored on the skyline views [16]. Radiographic PF OA was defined as osteophytes grade ≥2 on skyline or lateral radiographs, or joint space narrowing grade ≥2 and osteophytes grade ≥1 on skyline radiograph.

All radiographs were scored by five independent observers (intraclass correlation coefficient 0.62) [17]. Radiographic disease pattern was defined using previously published methods [18]. In the current study, participants who had no radiographic evidence of OA in PF (i.e., osteophytes grade <2 on both skyline and lateral radiographs or joint space narrowing grade <2 and osteophytes grade <1 on skyline radiograph) and TF compartments (KL<2) at baseline were included. PF OA incidence was defined as presence of radiographic PF OA (isolated or combined with TF OA) and TF OA incidence was defined as presence of radiographic TF OA

(isolated or combined with PF OA) at 8-year follow-up. If a participant received a radiographic disease score that was less than their previous score at any time point, then a senior reader re-read their radiographs in sequence (Baseline, 2-year, 5-year, and 8-year). We have also presented data on the relation between BMI and TF OA incident for completeness.

*Statistical analyses*

Baseline participants' characteristics were compared between individuals with and without knee OA at 8-year follow-up using independent t-test or chi-square test. Baseline BMI data were divided into normal (<25kg/m$^2$), overweight (≥25 and <30kg/m$^2$) and obese (≥30kg/m$^2$) categories. Logistic regression analyses were conducted to determine the relation of baseline BMI categories to incident PF OA and TF OA at an 8-year follow-up. Analyses were adjusted for age and sex. At the 8-year follow-up, percent change in BMI was calculated relative to baseline BMI for individuals who were categorized as overweight or obese at baseline. Logistic regression analyses were conducted to determine the relation of percent change in BMI to incidence of PF OA and TF OA. All analyses were adjusted for age, sex, and baseline BMI.

**RESULTS**

In the current study, 528 participants (79% females) without radiographic evidence of knee OA at baseline were included (Figure 1). At baseline, the mean age (±standard deviation) and BMI of the 528 participants were 55 (±5) years and 26.0 (±3.9) kg/m$^2$, respectively. The mean patient-reported pain and function scores were as follows: WOMAC pain 5(±3), stiffness 3(±2) and function 15(±11), and NPRS knee pain intensity 3(±2).

**FIGURE 1**

There were no statistically significant differences in age (p=0.150) or sex (p=0.594) between individuals with (age, 56±5years; females, 80%) and without (age, 55±5years; females, 78%) radiographic knee OA at 8 years follow-up — however, those with knee OA (26.6±4.1kg/m$^2$) were significantly heavier at baseline than those without knee OA (25.7±3.8kg/m$^2$) (p=0.013). Radiographic PF OA and TF OA were evident in 31.8% and 33.1% of individuals, respectively, at the 8-year follow-up. There were 51% without radiographic knee OA, 17% had isolated TF OA, 16% had isolated PF OA, and 16% had combined PF OA and TF OA.

Relative to individuals in the normal BMI range, obese individuals had approximately twice the odds of developing radiographic PF OA and TF OA 8 years later (Table 1).

**TABLE 1**

The percent change in BMI at 8-year follow-up in individuals who were overweight or obese at baseline ranged from -36% to 29% (mean ± standard deviation: 0.2 ± 7.8%). There were no significant associations observed between percent BMI change from baseline to 8-year follow-up and incident of PF OA and TF OA (Table 2).

**TABLE 2**

## DISCUSSION

This study was the first to explore the longitudinal relation of BMI to incident radiographic PF OA. Our findings suggest that obesity increases the risk of developing PF OA 8 years later. There were no significant associations observed between change in BMI from baseline to 8 years and incident of PF OA and TF OA 8 years later.

Obesity is a major risk factor for TF OA, and our study emphasizes that it is also associated with PF OA. Our findings showed that greater BMI at baseline significantly increases the risk of developing radiographic PF OA over-time, and our finding that obesity is related to development of TF OA agrees with previous research [6]. Those with radiographic OA at the 8-year follow-up were on average 0.9kg/m$^2$ heavier than those without radiographic OA at baseline. This indicates that, in individuals aged 45 to 65 years with knee pain, even slightly greater BMI at baseline could increase the risk of developing PF OA and/or TF OA.

We hypothesized that overweight or obese individuals with increased BMI at the 8-year follow-up relative to baseline would have increased odds of developing PF OA and TF OA. However, there were no associations observed between change in BMI and incidence of radiographic PF OA and TF OA. A possible explanation for this result may be that in the current study BMI change was based on two-time points (baseline and 8-year follow-up), which does not represent changes in BMI (e.g. fluctuations) over time. Our study showed no association between BMI change (gain or loss) over 8 years and incidence of radiographic PF OA. However, given that obesity

is linked with a spectrum of chronic diseases [19], maintaining a healthy body mass could have important implications for health outcomes.

Obesity may contribute to joint degeneration and OA development through mechanical stress —higher BMI has been associated with increased joint compressive forces [20]. Since obesity is also associated with OA in non-weight bearing joints [21], it is unlikely that mechanical stress is the sole means by which obesity contributes to development of OA. Obesity has been associated with elevated levels of a multitude of factors including cytokines (e.g. interleukins 1, and tumor necrosis factor-alpha) [22, 23] and adipokines (e.g. leptin, adiponectin) [24, 25]. Although the exact mechanism is not clear, it is thought that the altered profile of these factors may play a key role in cartilage degradation.

Weight gain has been associated with increased odds of progression of magnetic resonance imaging assessed PF OA structural features [26, 27]. Obesity is the strongest modified risk factors for knee OA, which can be targeted through interventions such as diet and exercise. Weight loss has been shown to reduce obesity-related inflammatory markers such as C-reactive protein, tumor necrosis factor-alpha, interleukins 6 and leptin [28, 29] and reduce joint compressive loading during walking in overweight or obese adults [30] — prolonged elevated joint compressive forces could result in cartilage degeneration [31]. In addition, weight loss has been shown significantly improve knee pain and function among overweight and obese individuals with knee OA [29].

A few limitations should be considered when interpreting the results of this study. Firstly, although BMI is widely used as a surrogate measure of body fat, its effectiveness is criticized because it measures body mass rather than body fat composition. For example, individuals with higher muscle mass could be incorrectly classified as overweight or obese. Future studies investigating the impact of body fat on PF OA disease may consider using tools that provide a more accurate estimation of body fat and muscle composition (e.g. Dual-energy X-ray Absorptiometry). Secondly, the analyses were limited to the relation of BMI to incident of radiographic PF OA and TF OA. We were unable to investigate the relation of BMI to progression of PF OA due to sample size restriction. Thirdly, BMI change was based on two-time points (baseline and 8-year follow-up) and does not consider the fluctuations in BMI over 8 years. Due to sample size restrictions, we could not develop trajectories of individuals based on their BMI over 8 years. However, we conducted sensitivity analyses by removing data from individuals whose BMI fluctuated ≥-/+5% at 2-year and/or 5-year study visits and the results were similar.

The relation of trajectories of body weight change over time to incidence and progression of PF OA is unknown and ought to be investigated. Lastly, we adjusted the analyses for age and sex. There are likely number of other factors (e.g. knee malalignment, occupation) that could increase the risk of incidence of PF and TF OA.

**CONCLUSION**

Obesity was associated with increased risk of developing radiographic PF OA and TF OA 8 years later among knees without OA

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**FIGURE CAPTION**

Figure 1: Flow chart of the included participants

**TABLES CAPTIONS**

Table 1. Relation of baseline body mass index categories to the incidence of patellofemoral and tibiofemoral osteoarthritis at 8-year follow-up (n = 528)

Table 2. Relation of percent body mass index change from baseline to 8-year follow-up to the incidence of patellofemoral and tibiofemoral osteoarthritis at 8-year follow-up (n = 316)

Figure 1:

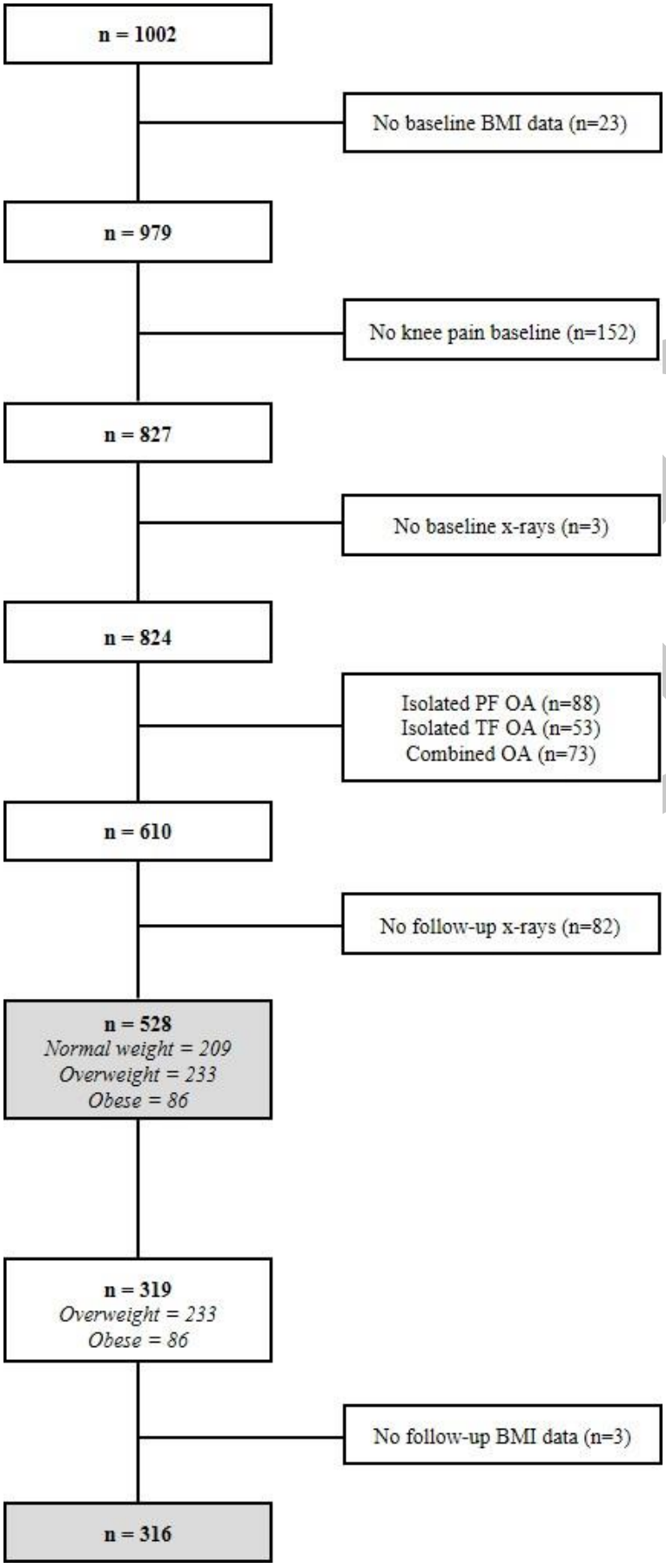
n = 1002
No baseline BMI data (n=23)
n = 979
No knee pain baseline (n=152)
n = 827
No baseline x-rays (n=3)
n = 824
Isolated PF OA (n=88)
Isolated TF OA (n=53)
Combined OA (n=73)
n = 610
No follow-up x-rays (n=82)
n = 528
Normal weight = 209
Overweight = 233
Obese = 86
n = 319
Overweight = 233
Obese = 86
No follow-up BMI data (n=3)
n = 316

**Table 1.** Relation of baseline body mass index categories to the incidence of patellofemoral and tibiofemoral osteoarthritis at 8-year follow-up (n =528)

| | Frequency of Outcome | Adjusted OR (95% CI)* |
|---|---|---|
| Radiographic PF OA | | |
| Normal | 57/209 (27%) | Reference |
| Overweight | 76/233 (32%) | 1.3 (0.8, 1.9) |
| Obese | 35/86 (41%) | **1.8 (1.1, 3.1)**† |
| Radiographic TF OA | | |
| Normal | 63/209 (30%) | Reference |
| Overweight | 73/233 (31%) | 1.1 (0.7, 1.6) |
| Obese | 39/86 (45%) | **1.9 (1.1, 3.3)**† |

Abbreviations: OR= Odds Ratios; CI: Confidence Interval; PF, patellofemoral; TF, tibiofemoral; OA, osteoarthritis *Adjusted for age and sex; †Statistically significant ($p<0.05$)

**Table 2.** Relation of percent body mass index change from baseline to 8-year follow-up to the incidence of patellofemoral and tibiofemoral osteoarthritis at 8-year follow-up (n = 316)

| | Frequency of Outcome | Adjusted OR (95% CI) |
|---|---|---|
| Radiographic PF OA | 111/316 (35.1%) | 1.00 (0.97 to 1.03) |
| Radiographic TF OA | 110/316 (34.8%) | 1.05 (0.98 to 1.12) |

Abbreviations: OR= Odds Ratios; CI: Confidence Interval; PF, patellofemoral; TF, tibiofemoral; OA, osteoarthritis Adjusted for age, sex and baseline body mass index