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Association Between Overweight and Obesity and Risk of Clinically Diagnosed Knee, Hip, and Hand Osteoarthritis

A Population-Based Cohort Study

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Objective. **Studies of previous cohorts have demonstrated an association between a status of overweight/obesity and the presence of knee and hand osteoarthritis (OA). However, no data on the effect of these factors on the OA burden are available. The aim of the present study was to analyze the effect of being overweight or obese on the incidence of routinely diagnosed knee, hip, and hand OA.**

Methods. **The study was conducted in a population-based cohort using primary care records from the Sistema d'Informació per al Desenvolupament de l'Investigació en Atenció Primària database (>5.5 million subjects, covering >80% of the population of Catalonia, Spain). Participants were subjects ages ≥40 years who were without a diagnosis of OA on January 1, 2006 and had available body mass index (BMI) data. All subjects were followed up from January 1, 2006 to December 31, 2010 or to the time of loss to follow-up or death. Measures included the World Health Organization categories of BMI (exposure), and incident clinical diagnoses of knee, hip, or hand OA according to International Classification of Diseases, Tenth Revision codes.**

Results. **In total, 1,764,061 subjects were observed for a median follow-up period of 4.45 years (interquartile range 4.19–4.98 years). Incidence rates (per 1,000 person-years at risk) of knee, hip, and hand OA were 3.7 (99% confidence interval [99% CI] 3.6–3.8),**

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1.7 (99% CI 1.7–1.8), and 2.6 (99% CI 2.5–2.7), respectively, among subjects in the normal weight category, and 19.5 (99% CI 19.1–19.9), 3.8 (99% CI 3.7–4.0), and 4.0 (99% CI 3.9–4.2), respectively, in those with a classification of grade II obesity. Compared to subjects with normal weight, being overweight or obese increased the risk of OA at all 3 joint sites, especially at the knee. A status of overweight, grade I obesity, and grade II obesity increased the risk of knee OA by a factor of 2-fold, 3.1-fold, and 4.7-fold, respectively.

Conclusion. **Being overweight or obese increases the risk of hand, hip, and knee OA, with the greatest risk in the knee, and this occurs on a dose-response gradient of increasing BMI.**

Obesity and osteoarthritis (OA) are 2 interconnected health care problems affecting a large proportion of the adult population worldwide. The increasing weight of the population will lead to nearly 1.3 billion adults being considered overweight and 573 million being classified as obese by 2030 (1). Moreover, the incidence of OA increases as the population ages (2), representing a leading cause of chronic pain and disability among older people (3).

There is extensive evidence supporting obesity as one of the major risk factors for knee OA (4–8), independent of the method of assessment used (9). To a lesser extent, there are reports describing an association of obesity with hand OA (8,10), whereas more conflicting results are found regarding an association with hip OA (6–8,11). Mechanical overload of the weight-bearing joint and the activation of metabolic factors contributing to joint damage have both been proposed as possible mechanisms to explain how weight increases the risk of knee or hand OA (12).

Nevertheless, the limited treatments for OA make prevention of modifiable risk factors, such as obesity, a key target for public health and medical interventions today. Consequently, the aim of this study was to analyze the effect of obesity on the incidence of symptomatic knee, hip, and hand OA, using a large population database.

PATIENTS AND METHODS

Study design and data source. We conducted a population-based cohort study using routinely collected data from the Sistema d'Informació per al Desenvolupament de l'Investigació en Atenció Primària (SIDIAP) database (details available at http://www.sidiap.org). The SIDIAP gathers clinical information from >5.5 million subjects (representing >80% of the population of Catalonia, Spain) as recorded by general practitioners (GPs) and primary care nurses during routine practice. The information gathered includes prescriptions, diagnostic events (based on International Classification of Diseases, Tenth Revision [ICD-10] codes), and routine clinical measurements such as body mass index (BMI), blood pressure, and spirometry results, among others, collected using structured spreadsheets. Subjects in this population are registered with 1 of the 3,414 GPs working in any of the 274 primary care practices run by the Catalan Institute of Health (known as the ICS in Catalan) (13). The Spanish (and, by extension, the Catalan) health care system provides universal health care coverage, and GPs are, as in the British National Health Service, gatekeepers to any of the other medical or allied health care professions, with the exception of accident and emergency room care.

Participants. Eligible participants were subjects at least 40 years of age at study entry who were without a history of diagnosed OA at the index joint, as noted in the primary care records as of January 1, 2006. In addition, participants were considered eligible if they had at least one measurement of BMI coded in the primary care computerized records (the SIDIAP database).

Study period. Participants were observed from study initiation (January 1, 2006) or from the date when they registered at any of the primary health care practices covered by the SIDIAP (whichever came last) to the earliest of the following: end of the study (December 31, 2010), transfer out of the catchment area, or death.

Variables. *Study exposure.* The BMI (in kg/m^2), coded by health care professionals during the study period, was the main study exposure. BMI values of <10 kg/m^2 or >60 kg/m^2 were assumed to be typing errors and were not used for the current analyses. When more than one measurement was available, the value closest to the index date (January 1, 2006) was used. Patients were classified as being normal weight, overweight, or obese according to the World Health Organization (WHO) definitions, as follows: normal weight (BMI below 25 kg/m^2), overweight (BMI ≥25 kg/m^2 and below 30 kg/m^2), grade I obesity (BMI ≥30 kg/m^2 and below 35 kg/m^2), and grade II obesity (BMI ≥35 kg/m^2).

Study outcomes. Incident clinical diagnoses of OA as registered by the GPs during the study period (January 1, 2006 to December 31, 2010) were identified using a previously validated list of ICD-10 codes, as follows: knee OA (M17, M17.0, M17.1, M17.2, M17.3, M17.4, M17.5, and M17.9), hip OA (M16, M16.0, M16.1, M16.2, M16.3, M16.4, M16.5, M16.6, M16.7, and M16.9), and hand OA (M15.1, M15.2, M18, M18.0–M18.5, and M18.9). OA coding within the SIDIAP database has been validated against self-reported OA in the Global Longitudinal Study of Osteoporosis in Women (GLOW) population-based cohort (14), as well as by reviewing free text and radiography reports collected in primary care records (2).

Statistical analysis. Age-specific (in 5-year groups) and sex-specific incidence rates with 99% confidence intervals (99% CIs) for each of the outcomes identified in the study period were estimated assuming a Poisson distribution. Cox regression modeling was used to compute age- and sex-adjusted hazard ratios (HRs) and 99% CIs for an incident clinical diagnosis of knee, hip, or hand OA according to BMI (continuous, per kg/m^2 increase) and BMI category (using normal weight as the referent group). Age-specific adjusted incidence rate ratios for a status of overweight, grade I obesity, and grade II obesity compared to normal weight were calculat-

Table 1. Baseline characteristics of the study subjects based on BMI category*

	BMI category			
	<25 kg/m^2	25 to <30 kg/m^2	30 to <35 kg/m^2	≥35 kg/m^2
Follow-up, median (IQR) years	5.99 (4.81–5.99)	5.99 (3.97–5.99)	5.99 (2.83–5.99)	5.99 (1.84–5.99)
Sex, no. (%)				
Female	271,175 (60.8)	350,771 (47.3)	218,236 (53.3)	115,151 (69.3)
Male	174,859 (39.2)	391,487 (52.7)	191,478 (46.7)	50,904 (30.6)
Age, mean ± SD years	60.7 ± 15.2	65.1 ± 13.9	66.1 ± 13.1	64.4 ± 12.9
Clinical characteristic, no. (%)				
Ischemic heart disease	2,258 (0.5)	7,664 (1.0)	6,168 (1.5)	2,648 (1.6)
Cerebrovascular disease	1,735 (0.4)	4,667 (0.6)	3,379 (0.8)	1,339 (0.8)
COPD	2,865 (0.6)	7,812 (1.0)	6,346 (1.5)	2,933 (1.8)
Diabetes mellitus	5,137 (1.15)	20,798 (2.8)	19,541 (4.8)	11,847 (7.1)
Hypertension	16,804 (3.8)	63,659 (8.6)	58,850 (14.4)	32,645 (19.7)

* BMI = body mass index; IQR = interquartile range; COPD = chronic obstructive pulmonary disease.

ed using Poisson regression. All statistical analyses were carried out using Stata SE software for Mac (version 12.0; StataCorp).

Ethics approval. Scientific approval was obtained from the SIDIAP Scientific Committee, and ethics approval was granted by the relevant board (El Comité Ético de Investigación Clínica del IDIAP Jordi Gol; certificate number P14/153). Patient consent was not required, as only anonymized retrospective data were used for this study, and no patient or GP contact was required.

RESULTS

Baseline characteristics. A total of 1,764,061 (54.0%) of 3,266,826 potentially eligible subjects registered in the SIDIAP database had available data on BMI, and therefore these subjects were included in the study. Compared to the source population, the included participants (i.e., with BMI data available) were slightly older (64.1 years versus 62.4 years) and more likely to be women (54.2% versus 51.8%).

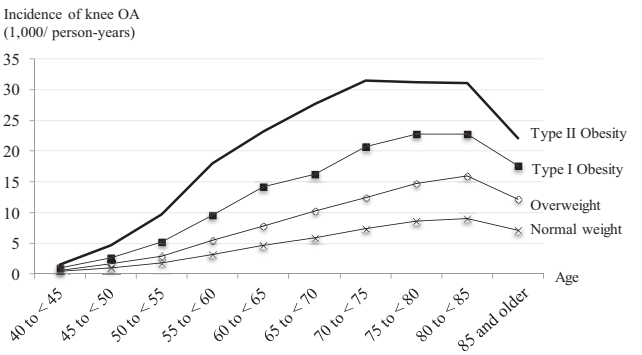

Figure 1. Incidence of knee osteoarthritis (OA) per age group according to each range of body mass index (BMI) per 1,000/person-years at risk. BMI categories are based on the World Health Organization definitions: normal weight <25 kg/m^2, overweight 25 kg/m^2 to <30 kg/m^2, grade I obesity 30 kg/m^2 to <35 kg/m^2, and grade II obesity ≥35 kg/m^2.

Eligible subjects were categorized into the following BMI categories: 446,034 subjects (25.3%) classified as normal weight, 742,258 subjects (42.1%) classified as overweight, 409,714 subjects (23.2%) classified with grade I obesity, and 166,055 (9.4%) classified with grade II obesity. Baseline characteristics of the subjects according to their BMI category are shown in Table 1.

Incidence rates of knee, hip, and hand OA in the study population. Participants were observed for a median of 4.45 years (interquartile range [IQR] 4.19–4.98 years). Incidence rates of knee, hip, and hand OA according to each BMI category and age group are shown in Figures 1, 2, and 3. During the follow-up period, 83,469 incident cases of knee OA were identified, with a crude incidence rate of 9.1 (99% CI 9.0–9.2) per 1,000 person-years at risk, while 27,701 incident cases of hip OA were identified, with a crude incidence rate of 2.9 (99% CI 2.8–2.9) per 1,000 person-years at risk, and 30,909 incident cases of hand OA were identified, with a crude incidence rate of 3.2 (99% CI 3.2–3.3) per 1,000 person-years at risk. Crude incidence rates of knee, hip, and hand OA overall and for each BMI category are presented in Table 2.

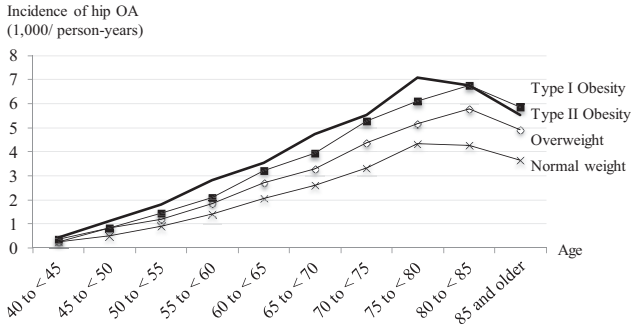

Figure 2. Incidence of hip osteoarthritis (OA) per age group according to each range of body mass index (BMI) per 1,000/person-years at risk. BMI categories are based on the World Health Organization definitions (see Figure 1).

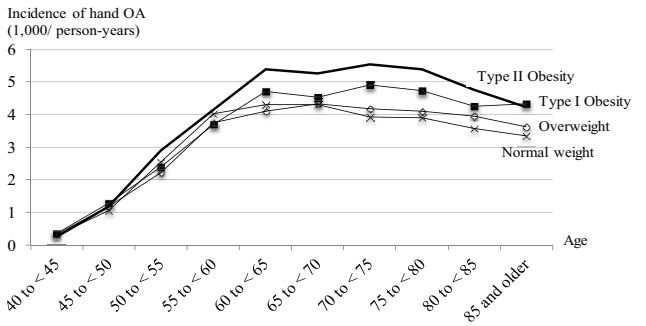

Figure 3. Incidence of hand osteoarthritis (OA) per age group according to each range of body mass index (BMI) per 1,000/person-years at risk. BMI categories are based on the World Health Organization definitions (see Figure 1).

The incidence rates of knee and hip OA increased in subjects beginning at the age of 40 years, with the sharpest increases seen in knee OA and hip OA at ages 55–60 years and 70–75 years, respectively (Figures 1 and 2).

Association between BMI and knee, hip, and hand OA. The incidence of knee, hip, and hand OA increased in parallel with increasing BMI (Figures 1–3), with the greatest increase seen in those diagnosed as having knee OA. The adjusted HRs for the effect of BMI on OA at the 3 joint sites is shown in Table 3. In the fitted survival model, age increased the risk of OA to a similar extent at all 3 sites (knee, hip, and hand), whereas female sex mostly increased the risk of hand OA.

After categorization into the WHO-recommended BMI groups, and compared to those with normal weight (BMI <25 kg/m^2), subjects classified as being overweight had an excess risk of OA, especially at the knee. This excess risk continued increasing as the BMI increased, being more pronounced for knee OA in subjects with grade II obesity (BMI ≥ 35 kg/m^2); these subjects were 4.7-fold more frequently diagnosed as having knee OA compared to subjects with normal weight (BMI <25 kg/m^2).

The observed associations between BMI classifications of overweight/obesity and the risk of knee and hip OA were present in the participants throughout all age groups (ages ≥ 40 years) (Figures 1 and 2). However, for knee OA, the excess risk of OA associated with obesity varied at different ages, whereas this association was more constant (unmodified by age) for the risk of hip OA (Figure 4).

Table 2. Incidence of diagnosed knee, hip, and hand OA in the study population*

	No. of subjects with incident OA	Crude IR (99% CI)
Knee OA		
Overall	83,469	9.1 (9.0–9.2)
BMI category		
Normal weight	8,785	3.7 (3.6–3.8)
Overweight	31,415	8.0 (7.9–8.2)
Grade I obesity	27,777	13.5 (13.2–13.7)
Grade II obesity	15,492	19.5 (19.1–19.9)
Hip OA		
Overall	27,701	2.9 (2.8–2.9)
BMI category		
Normal weight	4,250	1.7 (1.7–1.8)
Overweight	11,846	2.9 (2.8–3.0)
Grade I obesity	8,141	3.6 (3.5–3.7)
Grade II obesity	3,464	3.8 (3.7–4.0)
Hand OA		
Overall	30,909	3.2 (3.2–3.3)
BMI category		
Normal weight	6,302	2.6 (2.5–2.7)
Overweight	12,856	3.2 (3.1–3.3)
Grade I obesity	8,141	3.7 (3.6–3.8)
Grade II obesity	3,610	4.0 (3.9–4.2)

* Values are the incidence rates (IRs) with 99% confidence intervals (99% CIs) of osteoarthritis (OA) per 1,000 person-years. Body mass index (BMI) categories are based on World Health Organization definitions: normal weight <25 kg/m^2, overweight (25 kg/m^2 to <30 kg/m^2), grade I obesity (30 kg/m^2 to <35 kg/m^2), and grade II obesity (≥ 35 kg/m^2).

Table 3. Adjusted hazard ratios for the effects of BMI on incidence of any OA and joint site–specific OA*

	Any OA	Knee OA	Hip OA	Hand OA
Age (per year)	1.04 (1.04–1.05)	1.04 (1.04–1.04)	1.05 (1.05–1.05)	1.03 (1.02–1.03)
Female sex	1.75 (1.75–1.78)	1.53 (1.51–1.56)	1.20 (1.16–1.23)	2.56 (2.5–2.63)
BMI				
Overall	1.05 (1.05–1.06)	1.09 (1.08–1.09)	1.04 (1.04–1.04)	1.02 (1.01–1.02)
<25 kg/m^2	Referent	Referent	Referent	Referent
25 to <30 kg/m^2	1.49 (1.46–1.51)	2.00 (1.94–2.06)	1.46 (1.39–1.52)	1.22 (1.17–1.27)
30 to <35 kg/m^2	1.96 (1.93–2.00)	3.19 (3.09–3.30)	1.75 (1.66–1.83)	1.30 (1.25–1.36)
≥ 35 kg/m^2	2.51 (2.45–2.56)	4.72 (4.56–4.89)	1.93 (1.82–2.05)	1.31 (1.24–1.38)

*Results are the adjusted hazard ratios (99% confidence intervals) for an incident clinical diagnosis of knee, hip, or hand osteoarthritis (OA) according to age, sex, and body mass index (BMI) (expressed as continuous [per kg/m^2 increase] and based on World Health Organization category, using normal weight [<25 kg/m^2] as the referent group). All values were significant at $P < 0.001$.

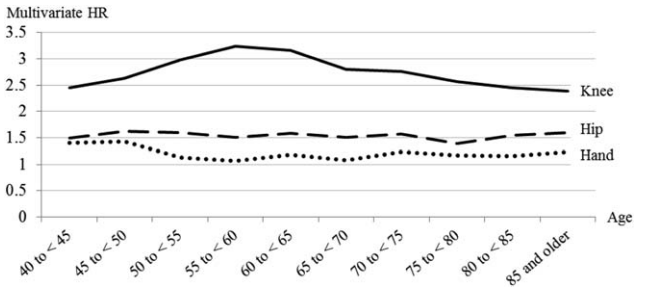

Figure 4. Multivariate hazard ratios (HRs) per age group for the effect of a body mass index (BMI) of ≥35 kg/m^2 (obesity) compared to a BMI of <25 kg/m^2 (normal weight) on the incidence of knee, hip, and hand osteoarthritis.

DISCUSSION

The principal findings of our study confirm that incident OA was found mostly in the knee, compared to the other joint sites, in our population, reaching a maximum incidence rate of 19.5 per 1,000 person-years in subjects with grade II obesity compared to 3.7 per 1,000 person-years in subjects with normal weight. Obesity seemed to increase the risk of OA in all 3 joint sites, including the hip, but the greatest increase was reported for the knee. The effect of obesity on the knees was more pronounced at younger ages, which could be useful for public health messaging.

We found a positive association between a status of overweight/obesity and the risk of developing OA at the knee, hip, and hand. The excess risk found was greater in subjects with grade II obesity, who were 4.7 times more likely to develop knee OA compared to subjects with normal weight.

The main strength of this study is the large sample size of our population, which allowed us to easily extrapolate our results using a clinically relevant outcome. Moreover, to our knowledge, this is the first study to analyze the impact of obesity on OA using routinely collected data from primary care. However, this study must also be interpreted in light of certain limitations. The main outcome was based on symptomatic OA, and no information was collected regarding radiographic OA. However, there is strong evidence to indicate that obesity is associated with radiographic OA (7), which suggests that our results would remain unchanged. Moreover, the SIDIAP database does not contain information on the side of the joint affected (e.g., left or right side of the knee).

Furthermore, nearly 46% of the subjects had missing information on their BMI. These missing BMI values could be a source of bias. However, registration of the BMI in Spain is part of the recommended health check program (the Programa de Actividades Preventivas y de Promoción de la Salud) required by the government in order to give funding to primary health care (15), and therefore it is not always linked to a population with a higher preponderance of disease, but rather could be linked to a population of individuals who may more frequently use primary health care resources. We compared the distribution of the BMI in our study population with that in another large national study carried out in Spain, in which the trends in the BMI were analyzed in >11,000 subjects (16). In that study, similar percentages of obesity were reported between 2008 and 2010 (16), which reinforces the representativeness of our population. Conversely, we analyzed the incidence rates of knee, hip, and hand OA in those subjects with missing BMI data, and found a lower incidence rate of OA in this population (unadjusted incidence rates 2.98 per 1,000 person-years for knee OA, 1.03 per 1,000 person-years for hip OA, and 1.33 per 1,000 person-years for hand OA), although we do not think that this invalidates the association between BMI and OA at the different joint sites found in this study, but may limit its representativeness.

Another limitation to be considered is the lack of information on subjects classified as overweight during the study period. The information on BMI relied on the data available from the SIDIAP database, and given that periodic BMI registering is quite uncommon, we were not able to account for this. Despite previous validation of the data collected in the SIDIAP database (13), and due to the retrospective nature of this study, the possibility of misclassification and registration biases should be considered.

Finally, we did not collect information on occupation, physical activity, or previous injuries, which could have influenced our results. Previous studies have shown an increased risk of OA associated with manual labor occupations (17), while physical activity has been found to have an unclear association with OA (6).

Being overweight or obese has been previously identified as a risk factor for development of OA. In particular, this association has been reported in subjects diagnosed as having knee OA (4–8) or hand OA (10), with more inconsistent results for hip OA (6–8,11). Our results confirm these previous findings for knee and hand OA and extend what has been previously published regarding hip OA (11). Compared to the subjects with normal weight, our population classified as overweight or grade II obese had a 46% and 93% excess risk of hip OA, respectively. Some previous studies did not find an association between BMI and hip OA (6–8), which could be attributable to the low number of subjects with hip OA included (compared to the 27,701 cases included in our population), the fact that OA was self-reported (6,7) (compared to our data on diagnoses routinely collected by primary

health care professionals), or the selection of a rather healthy and younger population (6–8), leading to an underestimation of this association.

Among the studies that did analyze the association between obesity and OA through a life-course approach (18–22), the periods of early and middle adulthood (18,19,21,22) and up to the age of 60 years (19,21,22) were identified as periods in life during which there was an excess risk of OA for obese and overweight subjects. Furthermore, another previous study based on data from the National Health Interview Survey in the US (23) found that the incidence of knee OA peaked in those subjects ages 55–64 years and was higher among obese subjects. Our results are consistent with these findings. Compared to subjects with normal weight, those with obesity (grades I and II) had an excess risk of OA that varied with age, especially at the knee.

Obesity is a modifiable risk factor, and correctly identifying a population of subjects who may be at higher risk of developing OA, such as the one identified by our study, could help shape prevention strategies aimed at reducing the symptoms or even the future progression of OA. Despite the fact that interventions aimed at reducing the clinical outcomes of OA have been proven to be effective (24,25), changes in lifestyles and habits are not easy to implement. By identifying the age at which obesity would more seriously influence the risk of OA, health care providers could focus prevention strategies on a narrower target population (i.e., middle adulthood).

The mechanism through which obesity increases the risk of OA has not yet been fully elucidated and falls outside the scope of this study. Whether the peak excess risk observed in middle adulthood for knee and hand OA reflects the pathogenic pathways involved in the appearance of OA at the different sites (for example, due to an increase in metabolic disorders, such as diabetes, or due to menopause [26,27]) should be investigated in future research.

In conclusion, our findings show that being overweight or obese increases the risk of hand, hip, and especially knee OA. Moreover, this increase in OA risk occurs on a dose-response gradient of increasing BMI. Health care providers should implement prevention tools, particularly focused on the age groups discussed herein, in order to reduce the risk of developing OA at these 3 joint sites.

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AUTHOR CONTRIBUTIONS

All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be published. Dr. Prieto-Alhambra had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study conception and design. Reyes, Leyland, Peat, Cooper, Arden, Prieto-Alhambra.

Acquisition of data. Reyes, Prieto-Alhambra.

Analysis and interpretation of data. Reyes, Leyland, Peat, Cooper, Arden, Prieto-Alhambra.

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