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Original article

The contribution of age and obesity to the number of painful joint sites in individuals reporting osteoarthritis: a population-based study

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Abstract

Objective. To investigate the association of OA risk factors with number of painful joint sites in a representative population sample.

Methods. Analysis of the 2009 Survey on Living with Chronic Diseases in Canada – Arthritis Component ($n = 1614$) for respondents reporting symptomatic OA. Variables: painful joints sites (hands, wrists, elbows, shoulders, hips, knees, ankles, feet, back, neck), joint symptom duration, sociodemographic characteristics, smoking, comorbidities and BMI. Zero-truncated negative binomial regressions were used to investigate the association between number of painful joint sites and the variables. Generalizability of findings was assessed by a similar analysis in a clinical hip/knee OA sample.

Results. The sample comprised 73% women and 56% were aged <65 years. The mean number of painful joint sites was 3.8: 84% reported pain at ≥2 sites, and 45% at ≥4 sites. Age, BMI, education and smoking were not associated with the number of joint sites. Significant associations were found with being female [rate ratio (RR) = 1.23, 95% CI 1.09, 1.39], having more comorbidities (RR = 1.11, 95% CI 1.07, 1.15) and longer symptom duration (RR = 1.16, 95% CI 1.09, 1.24), although the increase in joint sites with duration was small. Similar regression results were found with the clinical OA sample.

Conclusion. The lack of an association of age and BMI (obesity) with number of painful joint sites in OA raises questions about the role of these risk factors and our understanding of OA as a multi-joint disease. Filling this knowledge gap is critical to making progress with defining OA phenotypes and identifying potential aetiological mechanisms.

Key words: osteoarthritis, age, sex, BMI, obesity, joints, generalized osteoarthritis, GOA, MJOA

CLINICAL SCIENCE

Rheumatology key messages

- In a representative OA population, 84% had pain at ≥2 joint sites (sample mean = 3.8 sites).
- There was no association between the number of painful joint sites and age or BMI.
- The increase in number of joint sites over time while significant was minimal.

Introduction

OA is one of the most frequently reported chronic physical health conditions, characterized by pain and stiffness in the joints, and a major cause of disability [1–3]. Medical care use data suggests upwards of 10% of the population has symptomatic OA [4, 5]. Most research on OA, both clinical and epidemiological, focuses on a single joint site regardless of whether other sites are affected. The knee is overwhelmingly the most studied joint, followed by the hip and hand [6]. OA in other joints, including the spine, has received very little attention.

Multiple joint OA (MJOA) is often referred to as generalized OA (GOA), a term first proposed by Kellgren and Moore [7]. A recent systematic review of literature published from 1952 to 2017 found only 30 eligible studies that included a clear definition of MJOA and found little

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consensus between study definitions [8]. Hand joints were included in the definition of MJOA in all but two of the 27 studies that included specific joints in their definition, and all but four specified the knee. Other joints were less consistently included. As can be inferred by the small number of papers meeting criteria for this review, MJOA is not well characterized either clinically or epidemiologically.

Despite general recognition that OA can affect multiple joints, relatively few studies have reported on the frequency of MJOA in representative population-based samples. A study of adults aged ≥50 years surveyed with a joints homunculus indicated that more than half had joint pain consistent with OA, of whom 70% reported pain at two or more joint sites (out of seven) [9]. Similarly, a community survey showed 39% of the population aged >55 years reported joint pain, of whom 80% reported pain in two or more joints out of eight sites [10]. European clinical studies of patients with OA have shown that >50% of patients had OA at multiple joint sites [11, 12]. Finally, analysis of data from the Osteoarthritis Initiative (OAI) and Multicenter Osteoarthritis Study (MOST) population-based cohort studies of knee OA showed that 79.6% of those with bilateral knee pain, and 63.8% of those with unilateral knee pain had pain in other joints [13]. While generally neglected, the impact of having MJOA is considerable. No matter how it is defined or what outcomes are considered, clinical and community studies that have investigated the impact of having multiple joint *vs* single joint OA consistently show a more negative impact for MJOA with greater disability and reduced quality of life [8, 10, 14–17].

It is surprising, particularly given the high prevalence and impact of MJOA, that there have been few previous studies of the risk factors for having pain at multiple joint sites. A Canadian survey of a representative sample of people with self-reported OA, including sites of painful joints, provided us with the opportunity to study this. Age, sex, education (as an indicator of socioeconomic status), smoking and BMI are established risk factors for OA [1–3]. These are also risk factors for many chronic conditions that are associated with OA [18]. Our assumption was that risk factors for OA generally and at individual joint sites would also be risk factors for a greater number of painful joints in OA.

In particular, we hypothesized that increasing age and higher BMI would be associated with a higher number of painful joints sites in OA. Separate epidemiological studies of knee OA, hip OA and hand OA have consistently reported that the prevalence of these conditions increases with age [19, 20]. Given this, it seems likely that the probability of having OA in two or more of these joints should also increase with age. Overweight and obesity are well-established risk factors for OA, particularly the knee [21–23], but also to a lesser extent for the hip and hand [24–26]. Indeed, the association of obesity with OA at the hand, a non-weight-bearing joint, has contributed to the developing body of literature suggesting that OA might have a metabolic component [27–29]. In addition to a mechanical contribution to knee OA [21, 30, 31], a postulated mechanism for the role of obesity in OA is that adipokines released by adipose tissue act as systemic inflammatory mediators that cause a low-grade inflammatory state involving damage to joints and other tissues [32]. If this is a mechanism associated with obesity and OA, one might speculate that the inflammatory processes would affect all joints and that MJOA should be more frequent in overweight or obese individuals. Therefore, the purpose of this study was to investigate the association of OA risk factors, including age and obesity (BMI), with the number of sites of symptomatic joint pain in a representative sample of the population with self-reported OA.

Methods

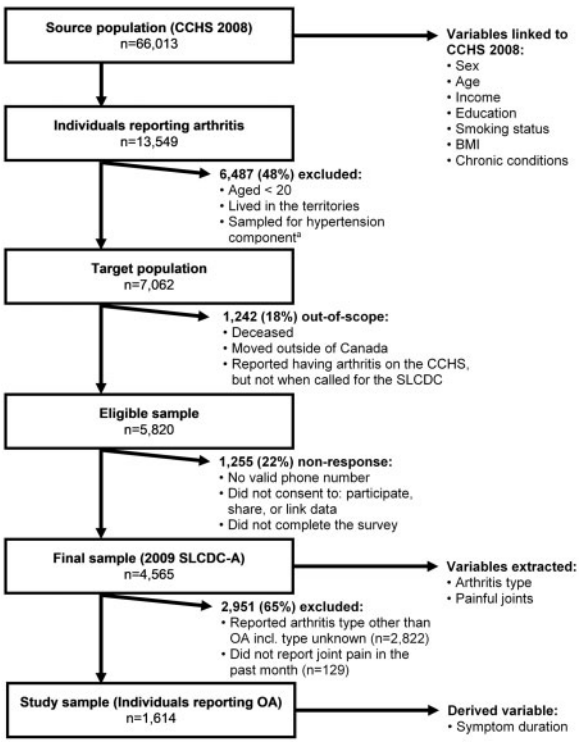
Study design and setting

Data were obtained from the 2009 Survey on Living with Chronic Diseases in Canada –Arthritis Component (SLCDC-A). The purpose of this survey was to provide information on the impact of arthritis on individuals and their families, and to assess clinical and self-management strategies. This survey was conducted by Statistics Canada in collaboration with the Public Health Agency of Canada (PHAC) as an extension to the 2008 Canadian Community Health Survey (CCHS) [33]. The CCHS is an annual cross-sectional survey to collect data on the health of the population. The CCHS uses a complex cluster design to generate a nationally representative sample of the household population, estimated to cover ∼98% of the Canadian population. Details of the methodology of the 2008 CCHS are provided elsewhere [34]. The sample for the arthritis component of the 2009 SLCDC-A was drawn from respondents aged ≥20 years responding affirmatively to an arthritis question in the 2008 CCHS. The question asked 'Do you have arthritis, excluding fibromyalgia?' as part of a series of questions about long-term health conditions diagnosed by a health professional that had lasted or were expected to last for 6 months or longer. Figure 1 outlines the sampling strategy for the SLCDC-A. Trained personnel administered the survey via structured telephone interviews (English and French) in February and March of 2009. A total of 4565 respondents with arthritis consented to participate and to share their linked data with partnering organizations (PHAC, Health Canada and provincial governments): 78.4% participation rate. Figure 1 also indicates how the sample for the current study was selected. Respondents to the SLCDC-A who confirmed that they had arthritis were asked what kind of arthritis they had: our analyses were restricted to respondents reporting having OA and no other kind of arthritis. Questions were then asked about whether they had ever experienced joint symptoms of pain, aching or stiffness related to their arthritis and at what age they first started experiencing these symptoms. Joint symptom

duration was calculated as the difference between the age at which participants reported they first experienced joint symptoms and their age at the time of the survey, and was grouped into year quartiles (0–5, 6–10, 11–19 and 20+ years) for descriptive analyses. Respondents were further asked to indicate which joints had been painful in the past month. The joints were right and left shoulder, elbow, wrist, hand/fingers/thumb, hip, knee, ankle, foot/toes, neck, back and other. Individual joints were grouped into sites (i.e. one or both knees) for a total of 11 sites including the neck and back. Analyses were limited to respondents with OA who reported pain in the past month in at least one specified joint site for a final sample size of 1614. The SLCDC-A was linked to the more comprehensive data set of the CCHS, enabling us to include key variables in our analyses as indicated in Fig. 1.

Age was categorized as 20–44, 45–54, 55–64, 65–74 and 75+ years. We calculated BMI [weight (kg)/height (m^2)] using self-reported height and weight, excluding pregnant women. For descriptive analyses, BMI was categorized as under/normal weight ($\leq$24.9 kg/m^2), overweight (25–29.9 kg/m^2) and obese ($\geq$30 kg/m^2). The highest level of education achieved was dichotomized as less than secondary school and completed secondary school or more. Smoking status was dichotomized as current or former smoker and never smoker. Respondents were asked to indicate the presence of health professional diagnosed long-term health conditions as indicated above. The conditions included were high blood pressure, mood disorder, diabetes, migraine, cancer, lung disease (asthma, chronic obstructive pulmonary disease), heart disease, stomach illness (ulcers, bowel disorder) and stroke. For descriptive analyses, the number of comorbidities was grouped as 1, 2 and 3+.

Fig. 1 Flow chart of the sample selection from the CCHS 2008 for the SLCDC-A 2009



[a]The 2009 SLCDC included two questionnaires: one questionnaire for arthritis and one questionnaire for hypertension. To reduce response burden, every respondent sampled could receive only one questionnaire even if they reported both chronic conditions in the CCHS 2008. The sample allocation by questionnaire was done proportionally to the size of the number of 2008 CCHS respondent for each condition and weighting adjustments were made to account for individuals with arthritis and hypertension not selected for the arthritis questionnaire.

Statistical analysis

Descriptive statistics were generated for the population overall and by grouping of painful joint sites (1, 2–3 and 4+ sites). Differences between groups were assessed using Chi-squared tests. Zero-truncated negative binomial regression models were used to evaluate the adjusted associations between number of painful joint sites and study variables, allowing the calculation of rate ratios (RRs) for a continuous count of number of painful joint sites, starting with one [35]. A consolidated set of weights provided by Statistics Canada that took into account sampling and response issues for the parent CCHS as well as the SLCDC-A were used to derive descriptive estimates representative of the population in Canada, with bootstrapping to estimate statistical significance taking into account potential clustering in the sample.

This study is based on analyses of previously de-identified data collected by Statistics Canada and accessed through their Research Data Centre (Toronto). The data were made available for this study through a formally reviewed research proposal to Statistics Canada, and in view of this our Institutional Review Board waived the requirement for institutional ethics approval.

Supplementary analyses

As MJOA has been variously defined in the literature as being $\geq$2 or $\geq$3 joint sites [8], we carried out sensitivity analyses using ordinal logistic regression with categories of joint count site grouping the number of painful joint sites as 1, 2–3 and 4+, and 1–2, 3–4 and 5+. We further replicated our analyses excluding cases with only one joint site to eliminate the possibility that our findings had been affected by trauma-related single-joint OA [36].

To establish generalizability of our findings to clinical populations, we carried out a parallel analysis using data from 843 patients scheduled for primary knee or hip joint replacement surgery for OA who completed a questionnaire within the 3-week period prior to their scheduled surgery [37]. Variables parallel to those in the

SLCDC-A were extracted from the data set: age, sex, highest level of education, BMI (based on measured height and weight), smoking status and a comorbidity count derived from the sum of yes responses to a list of 20 health conditions similar to those in the SLCDC-A. The number of painful joint sites was ascertained from a homunculus diagram asking which joints (neck, back, right and left shoulder, elbow, wrist, hand, hip, knee, ankle and foot) were 'painful, stiff or swollen on most days of the past month'. Unfortunately, no information was available for duration of joint symptoms. Further details of this study are given in the Supplementary materials, available at *Rheumatology* online.

Results

Table 1 shows the distribution of characteristics of the sample. The majority of people reporting OA were women, over half were <65 years (56%), and two-thirds were overweight or obese. A fifth reported painful joint symptoms for ≤5 years, and three-quarters had at least one other chronic condition. Only 16% of respondents with OA reported pain at only one joint site, while 84% reported pain at two or more sites, and 45% at four or more sites. The reported painful joint sites in descending order of frequency were the knee (62.0%), hand (52.1%), back (51.6%), hip (43.7%), shoulder (38.1%), neck (34.1%), foot (27.2%), wrist (26.1%), ankle (23.2%) and elbow (17.3%).

Table 1 Characteristics of the sample: reported OA in the 2009 SLCDC-A

	Distribution (%)
Sex	
Male	27.2
Female	72.8
Age	
20–44	7.3
45–54	19.7
55–64	29.0
65–74	25.0
75+	19.0
Education	
<Secondary school	22.0
Secondary school or more	78.0
Smoking status	
Never smoker	31.3
Current/former smoker	68.7
BMI	
Normal/underweight	33.3
Overweight	39.3
Obese	27.4
Comorbidities	
0	25.6
1	34.4
2	23.3
3+	16.7
Symptom duration, years	
0–5	22.5
6–10	24.1
11–19	26.1
20+	27.3
Number of painful joint sites	
1	15.9
2–3	39.0
4+	45.1

Table 2 provides the distribution of painful joint site count categories and mean number of painful sites by sample characteristics. Women reported more painful joint sites than men. There were no clear trends in the number of painful joint sites by age, nor in the distribution of joint sites by education, smoking status or BMI. The proportion of respondents with 4+ joint sites increased with comorbidity count and symptom duration. The overall mean number of painful joint sites in the sample was 3.8. While mean painful joint site counts varied somewhat across characteristics of the sample, all were within a limited range of 3.1–4.5.

Results from the zero-truncated negative binomial regression model are presented in Table 3. Age, education, smoking status and BMI were not associated with the number of painful joint sites. Being female was significantly associated with a higher number of painful joint sites, as was having more comorbidities and a longer symptom duration. However, as can been seen from Fig. 2, which shows the mean number of painful joint sites by age and symptom duration, there was only a slight increase in the number of painful joint sites with increasing duration. The mean number of painful sites increased by only 1.4 from a mean of 3.1 sites for the shortest symptom duration category (0–5 years) to 4.5 for the longest symptom duration category (20+ years). The number of painful joint sites did not show any consistent increase with age within each duration category.

The overall findings from our sensitivity analyses using the SLCDC-A sample were unchanged from the main findings. The findings from our parallel analyses in the clinical sample scheduled for joint replacement surgery were also consistent with our main findings (Table 4): neither age nor BMI was associated with the number of painful joint sites. Further information, including the characteristics of the sample (Supplementary Table S1, available at *Rheumatology* online) and the characteristics of the sample by number of painful joint sites and mean painful joint site count (Supplementary Table S2, available at *Rheumatology* online) is given in the supplementary material.

Discussion

This population-based study of individuals with OA with information on the number of painful joint sites showed the vast majority of participants (84%) had two or more painful joint sites, with nearly half having four or more. The frequency and distribution of painful joint sites was similar to that of the limited number of clinical studies that have looked at this in patients with OA [12, 15, 38, 39] and in population studies of arthritis [10, 40].

TABLE 2 Distribution and mean of painful joint sites: 2009 SLCDC-A OA sample

	Distribution of painful joint sites category (%)			*P*-value[a]	Mean painful joint site count (∓95% CI)
	1	2–3	4+		
Overall	15.9	39.0	45.1		3.8 (0.2)
Sex					
Male	21.6	39.1	39.3	0.044	3.2 (0.3)
Female	13.8	38.9	47.3		4.0 (0.2)
Age					
20–44	24.6	36.2	39.2	0.038	3.6 (0.9)
45–54	15.9	49.1	35.0		3.4 (0.4)
55–64	12.5	41.5	45.9		3.7 (0.3)
65–74	14.9	31.4	53.8		4.2 (0.4)
75+	19.2	35.8	45.0		3.8 (0.4)
Education					
<Secondary school	13.2	36.7	50.1	0.351	4.2 (0.5)
Secondary school or more	16.9	39.3	43.8		3.7 (0.2)
Smoking status					
Never smoker	15.7	38.6	45.7	0.975	3.8 (0.4)
Current/former smoker	16.1	39.2	44.7		3.8 (0.2)
BMI					
Normal/underweight	18.8	40.4	40.8	0.420	3.6 (0.3)
Overweight	15.6	36.6	47.8		3.9 (0.3)
Obese	12.5	40.2	47.3		3.8 (0.4)
Comorbidities					
0	23.2	44.4	32.4	<0.001	3.1 (0.3)
1	19.0	39.2	41.8		3.5 (0.3)
2	11.0	31.2	57.8		4.4 (0.5)
3+	5.4	41.2	53.4		4.3 (0.5)
Symptom duration, years					
0–5	24.4	42.7	32.8	<0.001	3.1 (0.4)
6–10	14.7	47.8	37.6		3.5 (0.3)
11–19	13.7	40.1	46.2		3.8 (0.3)
20+	12.2	27.1	60.8		4.5 (0.4)

[a] Chi-squared test assessing significance of relationship between categories of number of painful joint sites and sample characteristics.

Contrary to our hypotheses, neither age nor BMI were associated with the number of joint sites reported as painful.

The increase with age of the prevalence of OA [1–3, 5] has led to suggestions that at least some phenotypes of OA are related to cellular and other processes of ageing of the musculoskeletal system [31, 41, 42]. If OA is associated with cellular processes of ageing, one might expect these processes should affect all joints, so it is surprising that we did not find a greater number of painful joint sites at older ages. Data from a population-based survey of a primary care population asking about the number of painful joint sites (up to seven) showed no indication of a higher number with age [9], with similar findings from a community survey for the population aged ≥45 years [40]. A potential explanation of the null finding is that OA can onset at any age, so that at any given age there is a range of durations of symptoms. It might, thus, be expected that the relationship between the number of joint sites should be one with duration rather than age. In our regression analyses we found that a longer duration of joint symptoms was associated with a higher number of painful joint sites in the multivariable analysis (Table 3). While this might be interpreted as being consistent with ageing processes, the magnitude of the RR from this analysis (RR = 1.16) gives a somewhat misleading impression. As can been seen from Fig. 2, there is only a very modest increase of just over one extra site between durations of 0–5 and 20+ years across quartiles of duration. Moreover, the number of joint sites affected within each duration category was similar for each age group. Cushnaghan *et al.* [12] also found only a weak correlation ($r = 0.29$) for symptom duration with increasing age. One provoking interpretation of these findings is that the onset of OA, regardless of age, can be at several joint sites with only a modest increase in number of joint sites over time. A potential implication is that OA does not inevitably progress with the involvement of more painful joints over time, although this would need to be confirmed with longitudinal data.

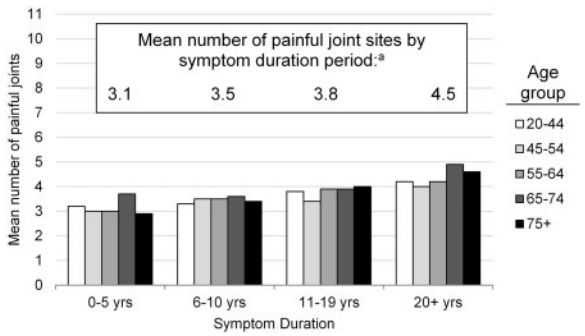
The lack of association of BMI with the number of painful joint sites was also an unexpected finding. Few studies have considered the relationship of BMI and

Table 3 Multivariable zero-truncated negative binomial regression for number of painful joint sites: 2009 SLCDC-A OA sample

Variable	RR (95% CI)	*P*-value
Age (ref: 20–44)		
45–54	0.91 (0.67, 1.24)	0.551
55–64	0.95 (0.72, 1.26)	0.734
65–74	1.01 (0.77, 1.34)	0.933
75+	0.98 (0.73, 1.32)	0.898
Sex (ref: Male)		
Female	**1.23 (1.09, 1.39)**	**0.001**
Education (ref: ≥ Secondary school)		
<Secondary school	1.13 (1.00, 1.27)	0.058
Smoking status (ref: Never smoker)		
Current/former smoker	0.98 (0.87, 1.11)	0.775
BMI	1.00 (0.99, 1.01)	0.549
Comorbidities	**1.11 (1.07, 1.15)**	**<0.001**
Symptom duration (years)	**1.16 (1.09, 1.24)**	**<0.001**

Statistically significant ($P < 0.05$) *P*-values are indicated in bold.

Fig. 2 Mean painful joint sites by age and symptom duration: 2009 SLCDC-A OA sample ($n = 1614$)



[a]Based on 95% CIs (given in Table 1) there is a significant difference in the mean number of painful joint sites for the longest duration (20+ years) with each other duration period. There is no difference between the adjacent categories 0–5 and 6–10 years, and 6–10 and 11–19 years, but the difference in mean count between 0–5 and 11–19 years is significant.

multiple joint involvement in OA. Hoogeboom *et al.* [43] found no difference in mean BMI in patients with hip or knee OA with and without pain in other joints. There is growing interest in a possible systemic component to OA, and in this context Bruyere *et al.* [31] suggested that multi-site OA is a feature of OA comorbid with inflammation or metabolic syndrome. That obesity does not appear to be associated with the number of painful joint sites does not fit with this nor with those speculations about metabolic or other mechanisms for OA that are grounded in the association with overweight and obesity, particularly in the hands, a non-weight-bearing joint [28, 29, 32]. As the knee is one of the most frequently affected joints and the joint that is most strongly associated with BMI [23] we further examined how knee pain was distributed by number of joint sites. We found respondents with knee pain at all levels of painful joint site count. We therefore suggest the lack of association of the number of joint sites with BMI is likely a reflection of the effect of the distribution of painful knees. The role of obesity in multi-joint OA clearly requires further exploration.

Table 4 Multivariable zero-truncated negative binomial regression for number of painful joint sites: clinical hip/knee OA sample

Variable	RR (95% CI)	*P*-value
Age (ref: 38–54)		
55–64	1.12 (0.90, 1.38)	0.304
65–74	1.05 (0.85, 1.31)	0.632
75+	0.99 (0.76, 1.29)	0.951
Sex (ref: Male)		
Female	**1.48 (1.29, 1.71)**	**<0.001**
Education (ref: ≥ Secondary school)		
<Secondary school	1.05 (0.91, 1.22)	0.471
Smoking status (ref: Never smoker)		
Current/former smoker	**1.17 (1.02, 1.34)**	**0.022**
BMI	1.00 (0.99, 1.01)	0.861
Comorbidities	**1.15 (1.08, 1.22)**	**<0.001**

Statistically significant ($P < 0.05$) *P*-values are indicated in bold.

Consistent with other studies, women were more likely to have pain at multiple joint sites than men [8]. The number of painful joint sites was associated with having two or more comorbidities, independently of age. As noted above, current theories of OA suggest a role for low-grade inflammation. Chronic inflammation is implicated in the progression of many chronic diseases including heart disease, diabetes, bowel disease and asthma [44]. The association of number of joint sites with the number of comorbidities could thus be a reflection of overall inflammatory load or other systemic processes. This finding needs further investigation, along with the lack of association with obesity.

Major strengths of this study are that it utilized data from a nationally representative survey on arthritis that meant we were able to focus on number of painful joints sites in respondents reporting OA. However, it is also necessary to bear in mind several limitations. The cross-sectional nature of the data means we were limited to looking at associations. We have no information on the site of back pain, whether lumbar or thoracic, nor on the specific joint sites for pain in the foot and hand. As with most population-based surveys, OA diagnosis was self-reported. While self-report may introduce misclassification, self-report of arthritis in population-based studies has been found to be adequate for surveillance purposes including for OA [45–47]. Moreover, a review of

the effect of OA definition on prevalence showed similar estimates for self-reported and symptomatic OA definitions [48]. There is also uncertainty about whether all the painful joint sites are attributable to OA as there may be other pathologies affecting the soft-tissues such as tendonitis or bursitis. A study of older women (96% had OA) showed that while 80% also had soft-tissue pathology most (85%) had OA at multiple sites [49]. We therefore presume that a high proportion of the painful joint sites in our studies are likely associated with OA. Our replication study in a clinical population with confirmed severe hip or knee OA similarly found no association between number of painful joint sites and increasing age or BMI, supporting the generalizability of our findings.

The findings from this study raise new questions about the role of age and BMI (obesity) in the development of multi-joint OA, especially as this and other studies show that most people with OA have multiple joint sites involved. Studies of OA that focus on only one primary joint site may be misleading in that they do not adequately represent the totality of OA. Neglect of the possibility of multiple joint involvement in studies of OA could potentially lead to the false attribution of particular risk factors or adverse outcomes to the joint under study, giving rise to potentially misleading conclusions. Understanding OA as a multi-joint disease is critical to making progress with defining disease phenotypes and identifying potential etiological mechanisms as well as the provision of care. Multiple joint site involvement may make compliance with management strategies such as exercise difficult. Furthermore, the involvement of joint sites other than a primary joint may also contribute to limiting the success of otherwise successful procedures such as total joint replacement surgery [50]. Further research is needed to elucidate the frequency and characteristics of multi-joint OA, with implications for understanding phenotypes, and the development of prevention and treatment strategies.

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Supplementary data

Supplementary data are available at *Rheumatology* online.

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