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Risk Factor Profiles for Individuals With Diagnosed OA and With Symptoms Indicative of OA: Findings From the Canadian Longitudinal Study on Aging

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Objective. The vast majority of published estimates of osteoarthritis (OA) burden are based on an OA diagnosis. These data are limited, as individuals often do not visit a physician until their symptoms are moderate to severe. This study compared individuals with an OA diagnosis to those with OA joint symptoms but without a diagnosis considering a number of sociodemographic and health characteristics. A further distinction was made between individuals with symptoms in one joint site and those with symptoms in multiple joint sites.

Methods. Data are from 23 186 respondents aged 45 to 85 years from the first cycle of the Canadian Longitudinal Study on Aging. A multinomial logistic regression model examined the relationship between sociodemographic- and health-related characteristics and OA status (diagnosed OA, joint symptoms without OA, no OA or joint symptoms). In addition, logistic regression models assessed the relationship between OA status and usually experiencing pain and having some degree of functional limitation.

Results. Twenty-one percent of respondents reported a diagnosis of OA, and 25% reported symptoms typical of OA but without an OA diagnosis. Other than being slightly younger, the characteristic profile of individuals with symptoms in two or more joint sites was indistinguishable from that of those with diagnosed OA.

Conclusion. It may be warranted to consider OA-like multiple joint symptoms when deriving estimates of OA-attributed population health and cost burden.

INTRODUCTION

Osteoarthritis (OA) is among the leading contributors to pain and disability globally (1,2). It is also a key driver of health care utilization and lost productivity. A systematic review estimated the cost of OA to be between 0.25% and 0.50% of the Gross Domestic Product in industrialized nations (3). With the aging of the population, the clinical and economic burden of OA is expected to increase substantially (4–6).

From a health and policy planning perspective, understanding the number of individuals who have OA or may be at an elevated risk for OA is essential. The majority of published estimates of OA burden are based on an OA diagnosis whether determined from administrative health data or population-based health surveys that specifically ask about "doctor-diagnosed"

OA (1,7). By their very nature, these data are limited by their dependence on individuals visiting a physician. Individuals with arthritis often do not visit a physician until symptoms are moderate to severe (8–10); therefore, those with disease with milder symptoms may not be captured in administrative health or survey data. The consequence is that individuals without diagnosed OA but with OA joint symptoms and the resulting negative life and health impacts are missed. For assessing health and economic burden and for planning, these individuals matter as they also can contribute to costs through use of over-the-counter medications, aids, assistive devices, and lost productivity. Furthermore, OA joint symptoms, such as pain and disability, may act as barriers to the uptake of broader clinical and public health recommendations for individuals to be physically active and to maintain mobility.

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Although some studies have reported on the overall prevalence of arthritis-like joint symptoms without an arthritis diagnosis in the population (11–13), there has been limited study of these individuals. In this study, we take advantage of data from a large population-based longitudinal study that elicited information on both OA diagnosis and joint symptoms indicative of OA. Our objectives were to compare individuals with an OA diagnosis to those with OA joint symptoms but without a diagnosis considering a number of sociodemographic and health characteristics, and additionally to assess the extent to which having OA and joint symptoms are associated with overall pain and functional limitations. Additionally, we subdivided individuals with joint symptoms into those with symptoms in one joint site and those with symptoms in multiple joint sites. This is an important distinction as it has been reported that there may be underlying and/or health outcome differences between individuals with and without multiple symptomatic joint involvement (14,15).

MATERIALS AND METHODS

Data are from the Canadian Longitudinal Study on Aging (CLSA) (16). The CLSA is a study that collects medical, psychological, and sociodemographic information from men and women aged 45 to 85 years (at baseline) residing in Canada. The CLSA began in 2011 and will follow respondents for 20 years or until death. The first cycle of data (collected between 2013 and 2015) from the comprehensive sample was the basis for the present study, and analysis was restricted to those with complete data on study variables (n = 23186). The comprehensive sample of the CLSA included a representative sample of respondents who resided within 25 to 50 km of one of the following 11 major centers across Canada: Vancouver, Victoria, Surrey, Calgary, Winnipeg, Hamilton, Ottawa, Montreal, Sherbrooke, Halifax, and St. John's.

Respondents were asked whether a doctor had ever told them they have OA in the knee, in the hip, or in the hand. Those responding in the affirmative to any of these were categorized as having OA. Respondents were asked about the presence of typical OA symptoms over the previous 4 weeks in the knees: knee pain on most days, knee pain while climbing stairs or walking down slopes, and swelling in the knee. Respondents were also asked about typical OA symptoms over the previous 4 weeks in the hips: pain in the groin or upper inner thigh on most days, and pain in the groin or upper inner thigh when climbing stairs or walking down slopes. Finally, respondents were also asked about typical OA symptoms over the previous 4 weeks in the hands: enlargement of small joints close to the fingernails, pain on most days in the small joints close to the fingernails, enlargement in the base of the thumbs, and pain on most days in the base of the thumbs. Those providing a positive response to any of the joint symptom questions but who provided a negative response to the OA diagnosis questions were categorized as having joint symptoms indicative of OA (labeled "possible OA"). For greater granularity, the possible OA group was subdivided into two groups based on the extent of joint symptoms. From the totality of these questions, all respondents were placed into one of four mutually exclusive categories: diagnosed OA, possible OA in one joint site (possible OA1), possible OA in more than one joint site (possible OA2), and no OA or joint symptoms (Nn).

A number of sociodemographic and health-related characteristics were included in the study. For analysis, age was categorized as 45 to 54, 55 to 64, 65 to 74, and 75 to 85 years. Body mass index (BMI) was calculated using measured height and weight and operationalized as "normal" (BMI below 25), "overweight" (BMI between 25 and 29.99), and "obese" (BMI of 30 or more). Education level was dichotomized as "post-secondary" and "high school or less," and a four-level annual household income variable was derived (in Canadian dollars: $50000 or less, $50000 to $99999, $100000 to $149999, and $150000 or more). Respondents were asked about the presence of co-occurring conditions (cancer, cardiovascular, neurological, gastrointestinal, respiratory, ocular, mental, and endocrine). The number of positive responses was summed, and the number of co-occurring conditions was categorized as 0, 1 to 2, and 3 or more (17).

Respondents were asked generally if they usually experienced pain or discomfort (yes/no). Functional limitations were assessed by asking respondents whether they could perform the following 14 Activities of Daily Living (ADLs) without help: dressing, feeding, taking care of one's appearance, walking, getting out of bed, bathing, using the telephone, traveling, shopping, preparing meals, doing housework, taking medicine, handling money, and getting to the bathroom on time. Individuals were categorized (yes/no) as needing help if they were unable to perform at least one of these activities without help.

Descriptive statistics were calculated for the overall sample and by OA status (ie, diagnosed OA, possible OA1, possible OA2, and Nn). A multinomial logistic regression model examined the relationship between sociodemographic and health-related characteristics and OA status (model outcome: diagnosed OA/possible OA1/possible OA2/Nn [referent group]). Two subsequent logistic regression models assessed the relationship between OA status and usually experiencing pain (outcome: yes/no) and having some

degree of functional limitation (outcome: yes/no). These two models were adjusted for the sociodemographic and health characteristics.

Sampling weights provided by the CLSA were used to produce descriptive statistics. All analyses were performed in SAS version 9.4.

RESULTS

Characteristics of the sample, overall and by OA status, are presented in Table 1. Just over 21% of respondents reported a diagnosis of OA, and 21% and 4.5% were categorized as having possible OA1 and possible OA2, respectively. Compared with the possible OA1 group, the possible OA2 group was more likely to be female and older, to have a lower household income, to be obese, to have three or more co-occurring conditions, and to be more likely to report usually experiencing pain and having difficulty with at least one ADL. There was minimal difference between the diagnosed OA and possible OA2 groups, other than the diagnosed OA group being somewhat older. A description of the frequency of typical OA symptoms at each joint site by group is provided in Table S1.

Results from the single multinomial logistic regression analysis examining adjusted associations between sociodemographic and health characteristics and OA status are presented in Table 2 (four-category outcome: ref = Nn). The same set of factors associated with a significantly higher likelihood of reporting diagnosed OA were also associated with a significantly higher likelihood of both possible OA designations. These factors were older age, female sex, being overweight or obese, having a greater number of co-occurring conditions, and lower household income. Other than for increasing age, where associations were greatest for diagnosed OA, the magnitudes of associations were statistically similar between those with diagnosed OA and those with possible OA2 (Table S2). Comparatively, magnitudes of associations were lower for possible OA1.

Results from the logistic regression models examining usual pain and functional limitations and their association with OA status are presented in Table 3. Adjusted for age, sex, BMI, number of co-occurring conditions, level of education and household income, individuals in the diagnosed OA group and possible OA2 group were equally likely to report experiencing pain and functional limitations compared with the Nn group (odds ratio for usual

Table 1. Characteristics of respondents from the Canadian Longitudinal Study on Aging: comprehensive sample, overall, and by OA status[a]

	Overall	Diagnosed OA	Possible OA2	Possible OA1	Nn
Characteristics			(%)		
Sample size	23 186	5865	1157	4921	11 243
% of sample	100	21.2	4.5	21.0	53.3
Sex					
Female	49.0	59.8	65.0	51.5	42.3
Age (y)					
45-54	44.6	24.3	37.7	43.8	53.6
55-64	30.7	34.5	32.5	32.6	28.4
65-74	15.9	25.4	20.1	14.9	12.2
75-85	8.7	15.8	9.7	8.7	5.8
Household income					
$150 000+	22.8	16.1	18.1	20.2	26.9
$100 000-$149 999	23.5	19.4	18.8	24.8	25.1
$50 000-$99 999	34.1	38.5	37.9	34.6	31.8
<$50 000	19.6	25.0	25.2	20.4	16.2
Education					
Postsecondary	81.3	78.2	77.8	80.7	83.1
Body mass index					
Normal	33.1	26.1	28.1	30.8	37.2
Overweight	40.3	37.2	37.6	42.0	41.2
Obese	26.6	36.7	34.3	27.2	21.6
Co-occurring conditions					
0	22.2	11.5	10.8	20.7	27.9
1-2	50.5	43.5	42.5	51.9	53.4
3+	27.3	45.0	46.7	27.4	18.7
Usual pain					
Yes	34.4	55.5	55.2	37.2	23.1
Difficulty with ≥1 ADL					
Yes	12.9	23.1	19.3	12.0	8.6

Abbreviation: ADL, Activities of Daily Living; Nn, no osteoarthritis and no symptoms; OA, osteoarthritis; Possible OA1, no OA diagnosis but symptoms in one joint site; Possible OA2, no OA diagnosis but symptoms in two or more joint sites.
[a]All proportions were calculated using sampling weights provided by the Canadian Longitudinal Study on Aging.

Table 2. Results from multinomial logistic regression model (four-category outcome: OA, OA2, OA1, Nn)

	Model Outcome Categories		
	Diagnosed OA vs. Nn	Possible OA2 vs. Nn	Possible OA1 vs. Nn
Model Variables	Odds Ratios (95% CI)		
Age (vs. 45-54)			
55-64	2.45 (2.22-2.70)	1.46 (1.24-1.72)	1.39 (1.28-1.51)
65-74	3.69 (3.31-4.10)	1.72 (1.43-2.07)	1.41 (1.27-1.56)
75-85	4.66 (4.13-5.27)	1.77 (1.42-2.19)	1.69 (1.50-1.90)
Sex (female vs. male)	2.27 (2.11-2.43)	2.64 (2.31-3.01)	1.58 (1.47-1.69)
BMI (vs. normal)			
Overweight	1.31 (1.21-1.42)	1.39 (1.19-1.62)	1.24 (1.14-1.34)
Obese	2.22 (2.03-2.42)	2.02 (1.73-2.37)	1.42 (1.30-1.56)
Comorbidities (vs. none)			
1-2	1.49 (1.34-1.66)	1.54 (1.24-1.91)	1.20 (1.09-1.32)
3+	2.88 (2.58-3.21)	3.17 (2.56-3.93)	1.55 (1.40-1.71)
Education (high school or less vs. postsecondary)	0.96 (0.88-1.04)	1.08 (0.93-1.25)	1.05 (0.96-1.21)
Income (vs. $150 000+)			
$100 000-$149 999	1.08 (0.96-1.21)	1.15 (0.93-1.43)	1.10 (0.99-1.22)
$50 000-$99 999	1.19 (1.07-1.32)	1.29 (1.06-1.57)	1.12 (1.01-1.24)
<$50 000	1.20 (1.07-1.34)	1.38 (1.11-1.70)	1.17 (1.04-1.31)

Abbreviation: BMI, body mass index; CI, confidence interval; Nn, no osteoarthritis and no symptoms; OA, osteoarthritis; Possible OA1, no OA diagnosis but symptoms in one joint site; Possible OA2, no OA diagnosis but symptoms in two or more joint sites.

pain, diagnosed OA vs. possible OA2: 1.07 [0.94, 1.23]; odds ratio for needing help with one or more ADL, diagnosed OA vs. possible OA2: 1.13 [0.96, 1.33]). The possible OA1 group was

Table 3. Results from the two logistic regression analyses

	Outcome: Usually Experience Pain vs. Not	Outcome: Needing Help with ≥1 ADL vs. Not
Model Variables	Odds ratios (95% CI)	
OA status (ref = Nn)		
Possible OA1	1.76 (1.63-1.90)	1.05 (0.94-1.17)
Possible OA2	3.07 (2.70-3.50)	1.25 (1.06-1.47)
Diagnosed OA	3.30 (3.07-3.56)	1.41 (1.28-1.55)
Age		
Age in years	0.98 (0.97-0.98)	1.03 (1.03-1.04)
Sex (ref = male)		
Female	1.04 (0.97-1.10)	2.19 (2.01-2.38)
BMI (ref = normal)		
Overweight	1.13 (1.05-1.21)	1.13 (1.02-1.25)
Obese	1.48 (1.37-1.60)	1.73 (1.57-1.92)
Co-occurring conditions (continuous)		
Number of conditions	1.31 (1.29-1.34)	1.31 (1.28-1.34)
Education (ref = postsecondary)		
High school or less	1.13 (1.05-1.21)	1.11 (1.01-1.22)
Household income (ref = ≥$150 000)		
$100 000-$149 999	1.19 (1.08-1.31)	1.27 (1.09-1.48)
$50 000-$99 999	1.32 (1.21-1.44)	1.43 (1.25-1.65)
<$50 000	1.77 (1.61-1.96)	1.92 (1.66-2.22)

Abbreviation: ADL, Activities of Daily Living; BMI, body mass index; Nn, no osteoarthritis and no symptoms; OA, osteoarthritis; Possible OA1, no OA diagnosis but symptoms in one joint site; Possible OA2, no OA diagnosis but symptoms in two or more joint sites.

also more likely to report usually experiencing pain but comparatively to a lesser degree.

DISCUSSION

In this large population-based study, we found that one quarter of respondents reported symptoms indicative of OA but without an OA diagnosis. Unlike most previous work in this area, a distinction was made between individuals with symptoms in a single joint site versus those with symptoms in multiple joint sites, and we report strong similarities in the personal characteristics and outcomes between those with symptoms in multiple sites (but without an OA diagnosis) and those reporting an OA diagnosis.

The prevalence estimates of joint symptoms without a diagnosis that we report are consistent with those reported by others. In a population-based US sample aged 45 years or older, Feinglass et al reported a "possible arthritis" (ie, having arthritis-like joint symptoms but without diagnosed arthritis) prevalence of 22% (11), as was found in a Canadian-based study (12). Busija et al reported a joint symptom (pain, aching, stiffness, or swelling in or around a joint excluding the back or neck) prevalence of 24% from a population-based Australian sample (13). Together, these findings suggest that individuals with joint symptoms but without an OA/arthritis diagnosis represent a significant segment of the population.

Compared to those with neither an OA diagnosis nor joint symptoms, we found that older age, female sex, obesity, and a greater number of comorbid conditions were associated with a greater likelihood of having diagnosed OA and having possible OA. Other than comorbid conditions, these are known risk factors for OA (18), and the literature reports that individuals with OA are

at an increased risk of having co-occurring conditions, adjusting for age and sex (19,20). The associations of sex, obesity, and co-occurring conditions with having an OA diagnosis and having multiple symptomatic joints were strikingly similar and statistically indistinguishable. The only observed difference was the older age of those with a diagnosis. Although the same factors were also associated with an increased likelihood of reporting single joint symptoms, the magnitudes of associations were significantly lower compared with those for diagnosed OA.

Joint symptoms are associated with adverse consequences that include disability, poor self-rated physical and mental health, and increased health service use, not unlike the case for OA specifically (11–15). Previous research has found that individuals with either diagnosed arthritis or joint symptoms generally are more likely to report difficulty with ADLs (11,13). Our research builds on these findings in that, by distinguishing between those with single versus multiple joint symptoms, we identified similar likelihoods of reporting overall pain and difficulties with ADL between the diagnosed OA group and those reporting multiple symptoms, adjusted for the characteristics noted above. Considered together, our findings suggest the possibility that the multiple symptomatic joint group may represent an as-of-yet undiagnosed and younger cohort of individuals with OA. If this is the case, it means that in excess of half a million individuals with OA disease are being missed in Canada alone within the 45- to 85-year age range when OA estimates are based exclusively on a doctor diagnosis. These numbers suggest that prudent health planning, policy making, and population-level epidemiological work should consider this large group, which from a population burden and needs assessment perspective is often neglected. The widening of the "definition" of OA may raise initial concerns relating to the implications of overdiagnosis, for example. However, it must be considered that "overdiagnosis" in this case would apply to individuals who report having symptoms in multiple joints. Currently, OA treatment is targeted at symptom management; there are no disease-modifying drugs. OA symptom management strategies, including self-management and pharmacological treatment, are not dependent on a diagnosis. Whether these individuals are given an OA label or not, they have joint symptoms for which management strategies can be effective. Targeted messaging within this context to individuals with joint symptoms (diagnosis or not) seems advantageous from an individual and societal perspective.

Several limitations need to be considered when interpreting the findings of the study. Only the knee, hip, and hand joints were considered, both for the OA diagnosis and joint symptoms. Although these are the joint sites most frequently affected by OA (21,22), the exclusion of other joint sites means that the prevalence of diagnosed OA and possible OA presented here are underestimates. As other joint sites were not considered, our "possible OA" and study referent group may have included individuals with OA and OA-like symptoms, respectively. Although this would minimize discrimination between the groups, we nevertheless found gra-

dients of association across groups, increasing from those with single joint symptoms to multijoint symptoms and OA diagnosis. As 94% of the sample identified as "white," ethnicity could not be assessed. The study was also cross-sectional in design, limiting our ability to make causal inferences. Future work with longitudinal CLSA data will make it possible to examine what proportion of individuals with "possible OA" go on to report an OA diagnosis. Finally, data were self-reported and are therefore subject to potential recall and reporting biases. However, self-reported arthritis data have been found to be adequate for assessing burden in the population (23,24).

Strengths of this study include the use of a large population-based sample and the inclusion of data on diagnosed OA specifically, unlike the previously cited studies based on a general "arthritis" diagnosis, and inclusion of data on joint symptoms indicative of OA. Moreover, with respect to the latter, respondents were asked about specific joint symptoms, including activity, rather than on symptoms generally. This increased specificity may have captured joint symptoms that otherwise would have been missed or not recalled. Unlike previous work in this area, we made a distinction between individuals with single versus multijoint symptoms to gain further insight and specificity. Our study extends the work by Thomas et al (21) in that the single- and multiple-joint symptom groups, among those without a diagnosis (the group often not considered in health planning), were compared to those with a diagnosis (the group typically and exclusively considered in health planning). The similarity we report between the diagnosed group and those with multiple joint symptoms but without a diagnosis provides a basis for a reasonable argument that health and policy planners and epidemiological researchers should consider this latter group for population OA burden and needs assessments.

In summary, a quarter of the population had joint symptoms typical of OA but did not report an OA diagnosis. For those with multiple joint symptoms, representing one in four of this group, their characteristic profile and outcome profile were indistinguishable from those with an OA diagnosis, other than being younger. From a health and policy planning perspective, our results suggest that the dichotomy between doctor-diagnosed disease versus not may be too restrictive and that an underlying continuum of amount of joint pain or number of joints with typical OA symptoms may be a more rational basis for policy and planning.

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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. Perruccio had full access to the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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REFERENCES

1. Cross M, Smith E, Hoy D, Nolte S, Ackerman I, Fransen M, et al. The global burden of hip and knee osteoarthritis: estimates from the Global Burden of Disease 2010 study. Ann Rheum Dis 2014;73:1323–30.

2. Litwic A, Edwards MH, Dennison EM, Cooper C. Epidemiology and burden of osteoarthritis. Br Med Bull 2013;105:185–99.

3. Puig-Junoy J, Ruiz Zamora A. Socio-economic costs of osteoarthritis: a systematic review of cost-of-illness studies. Semin Arthritis Rheum 2015;44:531–41.

4. Turkiewicz A, Petersson IF, Björk J, Hawker G, Dahlberg LE, Lohmander LS, et al. Current and future impact of osteoarthritis on health care: a population-based study with projections to year 2032. Osteoarthritis Cartilage 2014;22:1826–32.

5. Ackerman IN, Pratt C, Gorelik A, Liew D. Projected burden of osteoarthritis and rheumatoid arthritis in Australia: a population-level analysis. Arthritis Care Res (Hoboken) 2018;70:877–83.

6. Badley EM, Goulart CM, Millstone DB, Perruccio AV. An update on arthritis in Canada – national and provincial data regarding the past, present, and future. J Rheumatol 2019;46:579–86.

7. Glyn-Jones S, Palmer AJ, Agricola R, Price AJ, Vincent TL, Weinans H, et al. Osteoarthritis. Lancet 2015;386:376–87.

8. Mølbaek K, Hørslev-Petersen K, Primdahl J. Diagnostic delay in rheumatoid arthritis: a qualitative study of symptom interpretation before the first visit to the doctor. Musculoskeletal Care 2016;14:26–36.

9. Raciborski F, Klak A, Kwiatkowska B, Batko B, Sochocka-Bykowska M, Zoń-Giebel A, et al. Diagnostic delays in rheumatic diseases with associated arthritis. Reumatologia 2017;55:169–76.

10. Bolen J, Helmick CG, Sacks JJ, Gizlice Z, Potter C. Should people who have joint symptoms, but no diagnosis of arthritis from a doctor, be included in surveillance efforts? [comparative study]. Arthritis Care Res 2011;63:150–4.

11. Feinglass J, Nelson C, Lawther T, Chang RW. Chronic joint symptoms and prior arthritis diagnosis in community surveys: implications for arthritis prevalence estimates. Public Health Rep 2003;118:230–9.

12. Canizares M, Badley EM. Comparison of health-related outcomes for arthritis, chronic joint symptoms, and sporadic joint symptoms: a population-based study. Arthritis Care Res (Hoboken) 2012;64:1708–14.

13. Busija L, Buchbinder R, Osborne RH. Quantifying the impact of transient joint symptoms, chronic joint symptoms, and arthritis: a population-based approach. Arthritis Rheum 2009;61:1312–21.

14. Perruccio AV, Chandran V, Power JD, Kapoor M, Mahomed NN, Gandhi R. Systemic inflammation and painful joint burden in osteoarthritis: a matter of sex? [research support]. Osteoarthritis Cartilage 2017;25:53–9.

15. Perruccio AV, Mahomed NN, Chandran V, Gandhi R. Plasma adipokine levels and their association with overall burden of painful joints among individuals with hip and knee osteoarthritis. J Rheumatol 2014;41:334–7.

16. Raina PS, Wolfson C, Kirkland SA, Griffith LE, Oremus M, Patterson C, et al. The Canadian Longitudinal Study on Aging (CLSA). Can J Aging 2009;28:221–9.

17. Badley EM, Millstone DB, Perruccio AV. Back pain and co-occurring conditions: findings from a nationally representative sample. Spine (Phila Pa 1976) 2018;43:E935–41.

18. Silverwood V, Blagojevic-Bucknall M, Jinks C, Jordan JL, Protheroe J, Jordan KP. Current evidence on risk factors for knee osteoarthritis in older adults: a systematic review and meta-analysis. Osteoarthritis Cartilage 2015;23:507–15.

19. Schieir O, Tosevski C, Glazier RH, Hogg-Johnson S, Badley EM. Incident myocardial infarction associated with major types of arthritis in the general population: a systematic review and meta-analysis. Ann Rheumatic Dis 2017;76:1396–404.

20. Kadam U, Jordan K, Croft P. Clinical comorbidity in patients with osteoarthritis: a case-control study of general practice consulters in England and Wales. Ann Rheum Dis 2004;63:408–14.

21. Thomas E, Peat G, Croft P. Defining and mapping the person with osteoarthritis for population studies and public health. Rheumatology (Oxford) 2014;53:338–45.

22. Allen KD, Golightly YM. State of the evidence. Curr Opin Rheumatol 2015;27:276–83.

23. Ratzlaff C, Koehoorn M, Cibere J, Kopec J. Clinical validation of an Internet-based questionnaire for ascertaining hip and knee osteoarthritis. Osteoarthritis Cartilage 2012;20:1568–73.

24. March LM, Schwarz JM, Carfrae BH, Bagge E. Clinical validation of self-reported osteoarthritis. Osteoarthritis Cartilage 1998;6:87–93.