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Current and future impact of osteoarthritis on health care: a population-based study with projections to year 2032.

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Link to publication

Current and future impact of osteoarthritis on health care: a population-based study with projections to year 2032

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Running headline: OA impact on healthcare with projection

Abstract

Objective: To estimate the current and future (to year 2032) impact of osteoarthritis health care seeking.

Method: Population-based study with prospectively ascertained data from the Skåne Healthcare Register, Sweden, encompassing more than 15 million person-years of primary and specialist outpatient care and hospitalizations. We studied all Skåne region residents aged ≥45 by the end of 2012 (n=531,254) and determined the prevalence of doctor-diagnosed osteoarthritis defined as the proportion of the prevalent population that had received a diagnosis of osteoarthritis of the knee, hip, hand, or other locations except the spine between 1999 and 2012. We projected consultation prevalence of osteoarthritis until year 2032 using Statistics Sweden's projected age and sex structure and prevalence of overweight and obesity.

Results: In 2012 the proportion of population aged ≥45 with any doctor-diagnosed osteoarthritis was 26.6% (95% CI: 26.5-26.8) (men 22.4%, women 30.5%). The most common locations were knee (13.8%), hip (5.8%) and hand (3.1%). Of the prevalent cases 26.8% had osteoarthritis in multiple joints. By the year 2032, the proportion of the population aged ≥45 with doctor-diagnosed osteoarthritis is estimated to increase from 26.6% to 29.5% (any location), from 13.8% to 15.7% for the knee and 5.8% to 6.9% for the hip.

Conclusion: In 2032, at least an additional 26 000 individuals per 1 million population aged ≥45 years are estimated to have consulted a physician for osteoarthritis in a peripheral joint compared to 2012. These findings underscore the need to address modifiable risk factors and develop new effective osteoarthritis treatments.

Keywords: osteoarthritis, knee osteoarthritis, epidemiology

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Introduction

Osteoarthritis (OA) is a leading cause of pain and functional impairment in working age adults and the elderly.(1-3) Number of years lived with disability due to knee and hip OA alone increased by 64% between 1990 and 2010 and OA is currently ranked 11th in the world on the list of leading causes of years lived with disability.(4) Between 1999 and 2007/2008 the number of total knee replacements due to OA in the United States (US) and Scandinavia more than doubled. (5-7)

However, patients who receive total joint replacement constitute only a minority of all OA patients. While the 20th century prevalence and incidence of symptomatic or radiographic OA has been extensively studied, the impact of OA on health care use has been much less studied. (1, 6, 8-10) Further, disease occurrence in OA is not in a steady state due to aging of the population and the major risk factor for OA which is increased body mass index. For instance, there is evidence that obesity increases the risk for knee OA, but an increase in risk of hip and hand OA has been reported as well.(11-14) Thus, as the prevalence of obesity in most societies is projected to increase, it is expected that OA prevalence will increase as well.(15, 16) The prevalence of self-reported doctor diagnosed arthritis in US adults has been projected to increase from 22% in 2003 to 25% by 2030.(17) Presently there is a substantial lack of valid information on the future prevalence of OA leading to health care seeking. Expected changes in disease occurrence require changes in planning and resource prioritization. Hence, we posed two important questions: What proportions of the population consult due to OA at various joint sites? What proportions can be expected to consult a physician in the future?

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Methods

Data sources

The Skåne region with 1.26 million inhabitants (by December 31, 2012) is located in southern Sweden, and contains both rural and urban areas. Primary and specialist level healthcare is provided by public and private payers through the same tax-based financing system. The patient's co-pay is similar irrespective of whether the care is provided by a public or private healthcare provider and it is common that patients seek care from, or are referred to, both types of providers.

A personal identification number is assigned to all Swedish residents and provides information on age and sex. Swedish law requires that all healthcare contacts are registered by the personal identification number, serving as the basis for reimbursement to the healthcare provider. The Skåne Healthcare Register (SHR) contains information about every healthcare contact made in the region and includes data on healthcare provider, the profession (physician, physical therapist etc.), type of contact (e.g. primary/specialist care, in- or out-patient visit, clinic etc.) and contact date. Furthermore, the register contains the publicly practicing physicians' diagnostic codes according to the International Classification of Diseases (ICD) 10 system. These codes are assigned by the doctors themselves and are retrieved from the electronic medical records to the register. The diagnostic codes assigned by privately practicing physicians are not forwarded to the register (while other details of the visit are).

The Swedish population register contains information about vital events such as births, deaths, and changes in residential address for all inhabitants in Sweden through the personal identification number. The register is continuously updated by the Swedish Tax Agency. Statistics Sweden (SCB) provided us with individual information on income, which we linked by the personal identification number. SCB also provided age and sex specific longitudinal data on the prevalence of overweight and obesity and the population projection for Sweden until year 2032.

The study was approved by the Lund University Ethics Committee.

Multiple imputation of missing diagnoses

Of all *persons* who had at least one health care visit to a physician during the study period, 96% had at least one ICD-10 code registered. Of all physician health care *visits* 29.5% were made in the private care and had no diagnostic code registered, as the codes from private care are not yet forwarded to the SHR (while other details of the visits are). We considered these codes to be missing at random and adjusted for this.(18) Further, 15% of all physician health care *visits* had no diagnostic code registered in the public health care system. A majority of those visits were made in primary care before the year 2004, as the registration of diagnostic codes was less reinforced before 2004. We used multiple imputation to adjust for missing diagnostic codes in both private and public healthcare as detailed in web appendix A.(19)

Current point prevalence of doctor-diagnosed OA

First, as a measure of the current impact on health care, we estimated the 2012 point prevalence of doctor-diagnosed OA, defined as the proportion of the population that, using

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data from 1999 onward, had been diagnosed with OA at least once and were still alive, aged 45+ years and residing in the region as of December 31, 2012.

Hence, we retrieved data from all clinic visits with a physician at a primary care unit or with a specialist (or a physician under specialty training) at an internal medicine, rheumatology, orthopedics, rehabilitation, surgery (including hand surgery and oral and maxillofacial surgery) or emergency medicine clinic made between 1999 and 2012 for all Skåne region residents aged 45 years or older in 2012. Subjects who received a diagnosis of OA in any joint (excluding the spine) at least once during this time period were defined as having 'any OA'. Subjects were classified as having OA of the knee, hip, hand or other joints, respectively, according to the ICD-10 diagnosis received (Table 1). In the prevalence calculation each person was counted only once. A person with OA in more than one location (knee, hip, hand or other) contributed to the prevalence of OA in every location where diagnosed. We then calculated the prevalence of doctor-diagnosed OA by December 31, 2012 by individual linkage with the population register to exclude all subjects who had died or relocated from the region.

Validation of knee OA diagnosis in the register (positive predictive value)

To validate if the SHR diagnosis of knee OA was correct we used the population based Malmö Osteoarthritis (MOA) study carried out between 2007 and 2008.(20-23) We obtained the positive predictive values of the knee OA diagnosis in the register as specified in the appendix B.

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Projected prevalence of OA to 2032

We used the age and sex specific 2012 prevalence estimates of doctor-diagnosed knee OA, hip OA, hand OA or 'any OA' to predict the prevalence until 2032. First we used the sex and age specific (in age categories: 45-49, 50-59, 60-69, 70-79, 80+ years) population projection provided by Statistics Sweden and sex and age specific prevalence estimates to project the future prevalence of OA due to changes in the age and sex structure of the population. Further, we used the observed sex and age specific prevalence of overweight and obesity in Sweden measured by Statistics Sweden in 1988, 2008 and 2010 (3 measurements) to assess the impact of obesity on the future prevalence of OA. We assumed that the linear increase observed between 1988 and 2010 would continue until 2032. We used previously published results from meta-analyses and assumed that an increase in BMI of 5 units (which represents moving one "full step" from the normal weight category to overweight, or from overweight to obese) increases the risk for incident OA by 1.35 for the knee (1.22 for men and 1.38 for women) and 1.11 for hip and hand (for both men and women).(24, 25) As 50% of all 2012 prevalent OA cases had knee OA, we assumed the risk for 'any OA' equal to the mean of those for knee and hip. The calculations were made using the following formula linking the prevalence proportions and incidence rates: (number of prevalent OA) *(1/disease duration) =incidence*(number of people in population-number of prevalent OA), where we assumed that the disease duration is equal to the life expectancy at the mean age of subjects with OA in our cohort.(14)(Table 2) The years of life expectancy for those aged 65 in the year 2012 were retrieved from Statistics Sweden publications. The estimates of the prevalence of overweight, obesity and the years of life expectancy as well as the exact formulas used to derive projections are available in web appendix C.

To assess sensitivity of the projections with respect to assumptions on BMI increase and its impact on risk of OA we modified the risk rates for incident OA to be equal with their lower or upper confidence limits, i.e. 1.23 (lower limit) or 1.54 (upper limit) for knee OA in women, 1.19 or 1.25 for knee OA in men and 1.07 or 1.16 for hip and hand OA.(24, 25) Second, we modified the projected prevalence of overweight and obesity and assumed that the increase would be 10% lower or 10% higher than the one observed between 1988 and 2010.

Statistical analysis

We used a logit regression model to obtain the prevalence estimates with confidence intervals. In a sensitivity analysis, we repeated the analyses using an expanded definition for OA, which incorporated a diagnosis of pain in joint (ICD-10 code: M25.5, no location specified) at age 55 years or older.(10) All presented prevalence numbers were based on the imputed data. Analyses were performed using R (R Core Team) and STATA 13.

Results

Current point prevalence of doctor-diagnosed OA

The current proportion of the population aged ≥45 (n=531,254, 52% women) that had any doctor-diagnosed OA between 1999 and 2012 was 26.6% (95% confidence interval [CI]: 26.5, 26.8). The prevalence in men was 22.4% (95% CI: 22.2, 22.6) and in women 30.5% (95% CI: 30.3, 30.7). The most common location was the knee joint with the prevalence of 13.8% (95% CI: 14.7, 13.9) followed by other joints, 12.4% (95% CI: 12.3, 12.5), hip, 5.8%

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(95% CI: 5.7, 5.9) and hand, 3.11% (95% CI: 3.06, 3.16) (Figure 1). The prevalence typically increased with increasing age and was higher in women. (Table 3).

Of all OA cases, 26.8% had been diagnosed with OA in more than one location. Knee OA and OA of other joints was the most common combination (10.9%). (Figure 1) Of all hand OA cases 53.6% had been diagnosed with OA in at least one other location.

When we expanded our OA definition to include a diagnostic code for 'joint pain' (location not specified) in those aged 55 years or older, the 2012 prevalence of OA in the population ≥45 was estimated to be 42.3% (36.4% in men and 47.7% in women).

Validation of knee OA diagnosis in the register (positive predictive values)

The probability of an ICD-10 code M17 diagnosis (knee OA) in the SHR to be in a MOA study subject fulfilling either the American Colleague of Rheumatology (ACR) clinical & radiographic criteria (with respect to the side) or having radiographic knee OA equivalent to Kellgren/Lawrence grade ≥2 was 88%.

Projected prevalence of OA to 2032

Taking into account only the projected changes in the sex-age structure of the population the prevalence of 'any OA', knee OA and hip OA, respectively, is expected to increase from 26.6% to 29.0%, from 13.8% to 15.2% and from 5.8% to 6.8%, respectively over the next two decades. When accounting additionally for the increase in the estimated prevalence of overweight and obesity the prevalence of 'any' OA, knee and hip OA may increase from

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26.6% to 29.5%, from 13.8% to 15.7% for the knee and 5.8% to 6.9% for the hip, respectively. The pattern was similar for men and women (Figure 2) This corresponds to the relative increase of 10%, 12% and 18%, respectively. Thus, by 2032 there may be over 26 000 more doctor diagnosed OA prevalent cases per 1 000 000 population aged 45 or older as compared to 2012. The grey areas in the Figure 2 show the impact of different assumptions on the increase in prevalence of overweight and obesity and its impact on the risk of OA as specified in the sensitivity analyses.

Discussion

We examined the current impact of OA on the health care system by determining the proportion of the population with doctor diagnosed OA using 14 years of comprehensive Swedish health register data. Currently, one in four adults aged ≥45 has doctor-diagnosed OA in at least one joint, excluding the spine, and more than one in eight had doctor-diagnosed OA of the knee. We also made projections over the next two decades. These projections indicate that almost 30% of adults aged ≥45 in 2032 are expected to have consulted for OA by 2032 and half of those for knee OA.

In our report the prevalence of OA in any location excluding spine in adults aged ≥45 that had led to healthcare consultation was 26.6%, higher than the prevalence in 2001 reported from Canada.(26) The prevalence of self-reported doctor-diagnosed OA in a Norwegian survey of 44-76 year-olds was 10.7% for knee and 8.7% for hip.(27) Our estimates (10.9% and 3.6%) in the corresponding age group are lower for the hip but may be explained by 43% nonresponse in the Norwegian survey that was not adjusted for, or recall bias. Prevalence of symptomatic OA (combining radiographic evidence and pain in the symptomatic joint in epidemiologic

studies) in those aged ≥45 varies between studies from 6.7% to 15.9% in the knee and 1.6% to 9.2% in the hip.(1, 8, 9, 28) Our estimates of clinically relevant OA of 13.8% in the knee and 5.8% in the hip are in the middle of this range. The prevalence of symptomatic hip OA in Johnston County OA Project was 9.2% and our estimate of 5.8% can be expected as not all symptomatic patients seek care.(9)

As many as one in four of the prevalent OA cases were diagnosed with the disease at multiple joint sites. In a study of symptomatic limb joint OA patients attending a rheumatologist in Bristol, United Kingdom, where both clinical symptoms and radiographic changes in the symptomatic joint were required for the diagnosis, 50% of the study sample was diagnosed with the disease in multiple joints.(29) However, substantially more severe OA cases are to be expected at a rheumatology clinic than in health care in general. The associations found in the literature between knee OA or hip OA and hand OA are classically based on radiographic definition of the disease, but has been shown even for clinically diagnosed OA.(30, 31) In our study, 26% of patients with doctor-diagnosed hand OA were diagnosed with OA of knee and 11% with OA of the hip. The OA cases with multiple sites involved might require more healthcare resources than others which warrant more research to understand the implications of their disease.

We projected a relative increase on 10% over two decades (by year 2032) in the occurrence of 'any OA' that leads to health care consultation taking into account the future age and sex structure of the population as well as the prevalence of overweight and obesity. This increase is higher that the projected increase of self-reported doctor diagnosed arthritis from 29.6% in 2010 to 31.7% of the US population aged ≥20 when only change in age structure was accounted for.(32) Our estimates are lower than those of other researchers in US and Canada

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who reported projections of the prevalence of self-reported arthritis with relative increase that ranged from 16 % to 50% within two decades in population aged 15 or older.(17, 33) In a 2011 national report from Canada the projected increase in the prevalence of OA in any location by the year 2030 compared to 2010 was 75% for the whole population.(34) Those results reflect to a high extent the expected shift in the population structure of USA and Canada with a higher share of older adults. This shift didn't affect our results to the same extent as we used the age group 45 or older, a group typically affected by OA. Comparisons with other countries are challenging also due to different current and projected age and sex structures. Furthermore, our projection didn't take into account the potential for increased awareness of OA in the society which would increase the propensity to consult health care. The current high prevalence of obesity and its expected increase in the populations over the world is another important factor that will affect the future prevalence of OA, especially of the knee.(35) Our results indicate though that the highest relative increase is to be expected in the hip OA. This is due to the greatest population growth in those aged 70 or older, where the hip OA is highly prevalent.

As a measure of impact on health care, we estimated the location-specific as well as the overall occurrence of doctor-diagnosed OA based on 14 years of data in a register with validated ICD-10 codes covering a well-defined population. This approach enables direct interpretation in terms of healthcare utilization. Naturally, myriad factors impact consultation patterns beyond the actual occurrence of disease. The capacity of health care systems may change, the policies and national campaigns focusing on different aspects of health may influence patients' willingness to consult or receive a treatment. Easier access to healthcare for persons with OA, through e.g. care programs such as 'Better management of OA' in Sweden or Affordable Care Act in US, may result in an increase of number of persons

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consulting for OA but also contribute to alleviating the consequences of the increasing prevalence of OA. As the number of effective drugs for the treatment of OA is limited, and no widely accepted disease modifying intervention exists, there appear to be no reasons for the burden of OA on health care to plateau (or decline) within the next two decades. The expected increase in OA occurrence poses a growing threat to public health as also proven by historical data.(4) OA accounts for a substantial number of healthcare visits in populations with access to medical care and caused 6.8% of all disability adjusted life years in 2010, an increase from 2% reported in 2004.(10, 36) Between 1991 and 2010 the number of knee replacement surgeries increased by 162% for those aged 65 or older in the US, a 673% increase in rates is projected by 2030.(37, 38)

Importantly, our aim was *not* to estimate the occurrence of OA disease in general but only the occurrence of OA that directly impacts the health care system in terms of visits to a physician. That is undoubtedly an underestimation of the "true" prevalence of the disease as about 40% of symptomatic knee OA patients identified in the Malmö OA study hadn't consulted a physician due to knee OA or knee pain or didn't receive those diagnoses during the 3 years preceding the study examination (unpublished data). Primary care physicians may have difficulties with clinical examination of musculoskeletal disorders that could bias our estimates.(39) However, specialist care is relatively easily accessed in Sweden (even without referral from a primary care physician) and we used data over a 14-year period. In the Skåne region the formal guidelines for the diagnosis of OA were implemented first in 2012. The diagnoses registered between 1999 and 2011 were based on the physicians' clinical judgment. However, the validity of rheumatic diagnoses in the SHR has been shown to be high.(40, 41) In the present study, we performed an extensive validation for knee OA against a number of OA criteria. The positive predictive value of knee OA diagnosis in SHR was 88% and is

higher than for example in the Massachusetts health maintenance organization for OA in any location.(42)

Our projections took into account the future age and sex structure of the population and the future prevalence of overweight and obesity. There are other factors, such as the incidence of knee injuries or willingness to consult that will impact the future prevalence of doctor-diagnosed OA. The uncertainty of the population projections, the assumed increase in the prevalence of overweight and obesity and risk for developing OA at different joints sites all contribute to the uncertainty of the projection. We assumed that the linear increase in the prevalence of overweight and obesity observed between 1988 and 2010 would continue in the next 20 years, which might not hold true, e.g., if effective prevention programs will be implemented. We assumed the same mortality in persons with and without OA which could bias our estimates upwards if patients with OA will experience significantly higher mortality than the general population. The 2012 net immigration in the Skåne region was 0.07% of the population aged 45 or older and thus we expect that migration would have a negligible effect of the projected estimates when accounting for an increase in BMI. As we have studied the population aged 45 or older, we were not able to assess the potential increase in prevalence in younger patients.

Our results show that in 2012 almost one in seven adults aged ≥45 in Southern Sweden had doctor-diagnosed OA of the knee. As the 2012 prevalence of persons with knee prosthesis aged ≥45 in Sweden was 2.3%, it implies that 17% of prevalent doctor-diagnosed knee OA cases have undergone knee replacement surgery (unpublished data). By 2032, over 26 000 new OA cases per 1 000 000 population aged 45 or older will have consulted healthcare. To a large extent it will be the primary care physicians who will face the increased workload but a

crisis in supply of total joint replacement surgery is also anticipated.(43, 44) This will put a considerable stress on the health care system. In most western European countries the age of retirement is increasing and therefore, the future work force will include an increasing number of individuals suffering from OA. Prioritization of research on population health strategies to reduce OA, including weight loss and knee injury prevention, and, for those affected by OA, the development of effective therapies is needed. Further research on the burden of OA on health care is needed to evaluate the accuracy of these projections, especially since many previous predictions of both the incidence of surgery in OA and the prevalence of arthritis have been far outgrown by reality.(33)

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Author contributions

Conception and design: ME, AT

Analysis and interpretation of the data: all authors

Drafting the article: ME, AT

Critical revision of the article for important intellectual content and approval of the final version: all authors

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Competing interests

Authors declare no competing interests.

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Figure 1. The 2012 site distribution of osteoarthritis that burdens health care and its overlap in adults aged ≥45. Numbers are percentages of all cases with osteoarthritis. Other - includes osteoarthritis of joints other than knee, hip and hand such as shoulder, elbow, ankle and foot, jaw and polyarthrosis (excluding Bouchard's and Heberden's nodes as those are included in the hand). Other combinations – includes all combinations of knee, hand, hip and other, not already listed in a pie. Spine is not included.

Knee OA (51.9% of all OA)

- 21% -knee & other
- 5% -knee & hip & other
- 7% -knee & hip
- 6% -other combinations
- 61% -knee only

Hip OA (21.7% of all OA)

- 48% -hip only
- 16% -hip & other
- 6% -other combinations
- 12% -knee & hip & other
- 18% -knee & hip

Hand OA (11.7% of all OA)

- 46% -hand only
- 21% -hand & other
- 11% -other combinations
- 10% -knee & hand & other
- 11% -knee & hand

Other OA (46.4% of all OA)

- 8% -hip & other
- 5% -knee & hip & other
- 23% -knee & other
- 9% -other combinations
- 55% -other only

Figure 2. The 2012 prevalence and the projection for years 2013-2032 of osteoarthritis that burdens health care. The projection is based on the predicted changes in age-structure of the Swedish population, predicted increase in the age and sex specific prevalence of overweight

and obesity in Sweden and differential effects of increased body mass index on different joint sites.
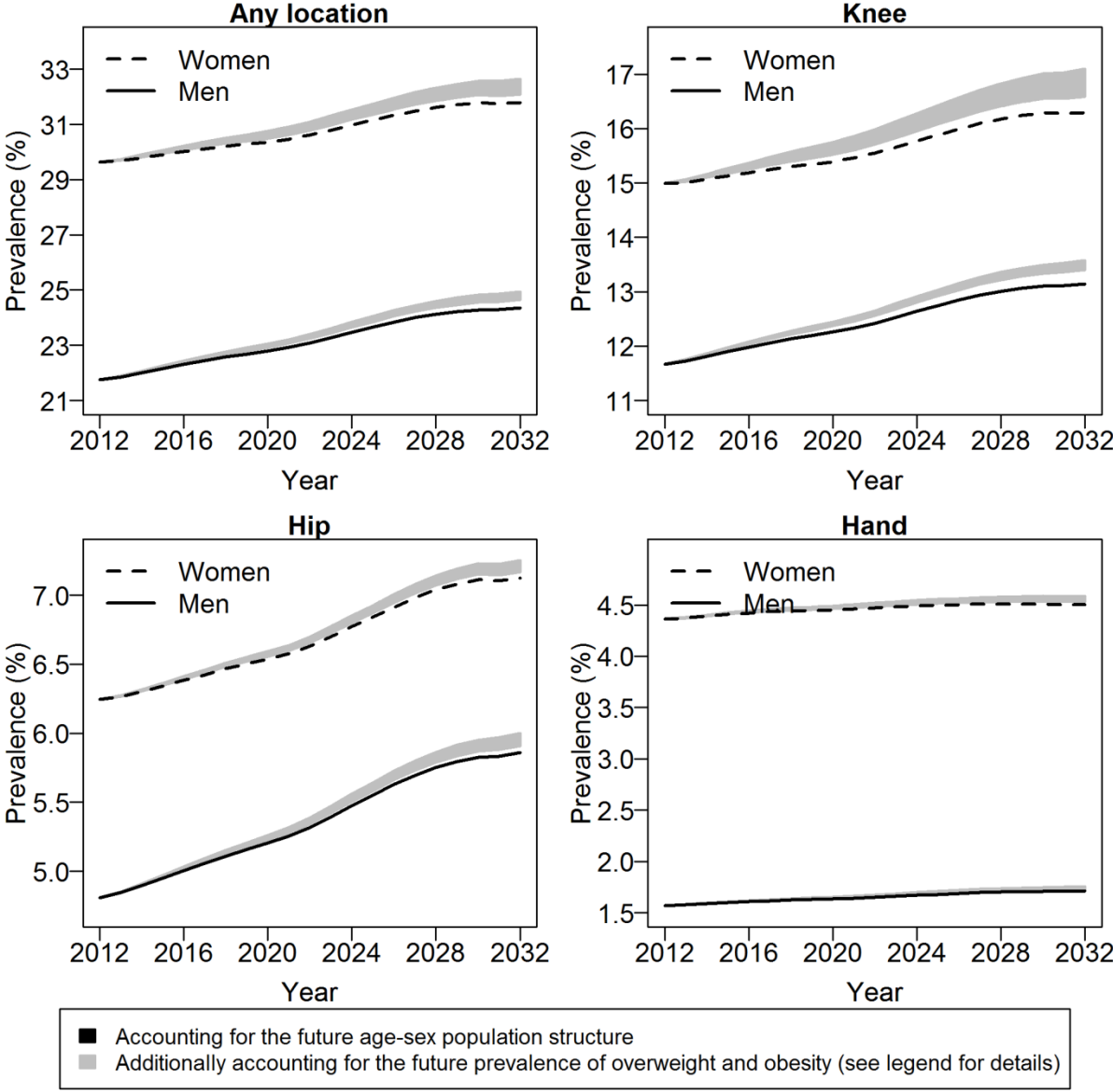
*The lower boundary of the grey area shows the projected prevalence when assuming the impact of body mass index on the incidence of osteoarthritis equal to the lower confidence level and the increase in the prevalence of overweight and obesity 10% lower than that observed in Sweden between 1988 and 2010. Accordingly, the upper bound of the grey area show the projected prevalence assuming the impact of body mass index equal to its upper

confidence level and the increase in the prevalence of overweight and obesity 10% higher

than that observed in Sweden between 1988 and 2010.

Table 1. International Classification of Diseases (ICD) 10 system of osteoarthritis.

Location	ICD 10 code	Diagnosis
Knee	M17	Gonarthrosis [arthrosis of knee]
Hip	M16	Coxarthrosis [arthrosis of hip]
Hand/wrist	M18	Arthrosis of first carpometacarpal joint
	M15.1	Heberden's nodes (with arthropathy)
	M15.2	Bouchard's nodes (with arthropathy)
	M19.0D	Primary arthrosis of other joints , site: wrist/hand
	M19.1D	Post-traumatic arthrosis of other joints, site: wrist/hand
	M19.2D	Other secondary arthrosis, site: forearm
Other	M15 (other than M15.1, M15.2)	Polyarthrosis (exluding Heberden's/Bouchard's nodes)
	M19 (other than M19.0D, M19.1D, M19.2D)	Other arthrosis (exluding arthrosis in hand/wrist)
Any	M25.5*	Pain in joint

*The code for pain in joint was used only in the sensitivity analysis

Table 2. The mean age of osteoarthritis (OA) subjects in the Skåne Healthcare Register, by sex and OA location.

	Knee OA	Hip OA	Hand OA	Any OA
Women	68.1	72.0	65.6	70.0
Men	66.5	70.9	67.2	67.6

Table 3. The 2012 population prevalence (%) and 95% confidence intervals (in brackets) of osteoarthritis (OA) that burdens health care, by age, sex and joint site. Other OA- includes osteoarthritis of joints other than knee, hip and hand such as shoulder, elbow, ankle and foot, jaw and polyarthrosis (excluding Bouchard's and Heberden's nodes as those are included in the hand). Spine is not included.

		Age (years)					
		45 – 54	55 – 64	65 – 74	75 – 84	85+	45+
Knee OA	All	4.1 (3.9-4.2)	10.3 (10.1-10.5)	17.5 (17.3-17.8)	25.9 (25.4-26.3)	30.8 (30.2-31.4)	13.8 (13.7-13.9)
	Men	4.0 (3.8-4.1)	9.2 (9.0-9.5)	16.1 (15.7-16.4)	23.4 (22.8-24.0)	27.4 (26.4-28.6)	12.0 (11.9-12.2)
	Women	4.1 (4.0-4.3)	11.3 (11.0-11.6)	19.0 (18.6-19.3)	27.8 (27.2-28.4)	32.4 (31.7-33.1)	15.5 (15.3-15.6)
Hip OA	All	0.8 (0.8-0.9)	2.3 (2.3-2.4)	7.0 (6.9-7.2)	14.8 (14.5-15.1)	17.9 (17.5-18.4)	5.8 (5.7-5.9)
	Men	0.8 (0.7-0.9)	2.3 (2.2-2.4)	6.5 (6.3-6.7)	13.5 (13.1-14.0)	17.5 (16.7-18.3)	5.0 (4.9-5.1)
	Women	0.8 (0.7-0.9)	2.4 (2.3-2.5)	7.5 (7.3-7.8)	15.7 (15.3-16.1)	18.2 (17.6-12.5)	6.5 (6.3-6.7)
Hand OA	All	0.9 (0.9-1.0)	3.1 (3.0-3.1)	4.7 (4.6-4.8)	4.6 (4.4-4.7)	3.5 (3.3-3.7)	3.1 (3.1-3.2)

	Men	0.4 (0.4-0.5)	1.4 (1.3-1.5)	2.5 (2.3-2.6)	2.8 (2.6-3.0)	2.4 (2.1-2.7)	1.6 (1.6-1.7)
	Women	1.4 (1.3-1.5)	4.7 (4.5-4.8)	6.9 (6.7-7.1)	5.9 (5.7-6.2)	4.0 (3.7-4.3)	4.5 (4.4-4.6)
	All	3.4 (3.3-3.5)	9.9 (9.8-10.1)	16.4 (16.2-16.6)	22.0 (21.6-22.4)	25.0 (24.3-25.7)	12.4 (12.3-12.5)
Other OA	Men	2.9 (2.8-3.1)	7.7 (7.5-7.9)	13.1 (12.8-13.4)	18.0 (17.4-18.5)	21.0 (19.8-22.2)	9.6 (9.4-9.7)
	Women	3.9 (3.7-4.0)	12.2 (11.9-12.4)	19.6 (19.2-20.0)	25.1 (24.5-25.6)	26.9 (26.2-27.7)	14.9 (14.8-15.1)
	All	8.2 (8.0-8.4)	21.1 (20.9-21.4)	34.8 (34.5-35.1)	47.5 (47.0-47.9)	53.1 (52.4-53.7)	26.6 (26.5-26.8)
Any OA	Men	7.4 (7.2-7.6)	17.6 (17.4-18.0)	30.3 (29.8-30.8)	42.7 (42.0-43.3)	48.8 (47.6-50.1)	22.4 (22.2-22.6)
	Women	9.0 (8.8-9.2)	24.6 (24.3-25.0)	39.1 (38.6-39.6)	51.2 (50.6-51.8)	55.2 (54.5-55.9)	30.5 (30.3-30.7)

Multiple imputation of missing diagnostic codes in the Skåne Healthcare Register

Manuscript: Current and future impact of osteoarthritis on health care: population-based study with projection to year 2030.

A Turkiewicz, IF Petersson, J Björk, G Hawker, LE Dahlberg, LS Lohmander, M Englund

For each health care visit there was either an osteoarthritis (OA) diagnosis set (knee, hip, or hand OA or OA in other location) or a non-OA diagnosis set, or the diagnosis was missing. We created four dummy variables with missing values, one for every OA location. We used the multivariate normal model for clustered data as implemented in the statistical software R, package *pan*, to create 10 imputed datasets.(1) The model was first run with 1000 iterations and imputations were made taking 200 iterations in between. The model converged for all estimated parameters and the convergence behavior was assessed with time-series and autocorrelation function plots. Imputation was stratified on age (45-54, 55-64, 65-74, 75-84 and over 85 years of age) because of distinct prevalence age patterns for different OA locations. The fixed effects covariates included in the imputation model were associated with both the outcome and missingness and were as follows: sex, age at December 31, 2011 and their interaction, clinic and its interaction with sex, area of residence, an indicator for having visited a physiotherapist during the study period, the year of visit, an indicator for in- or outpatient care, a logarithm of the total number of doctor visits during the study period and the individual disposable income in the year 2010. (Table) The patient was included as a random effect to account for the correlation between visits made by the same person. Data on all covariates were available for all patients and visits except for income which was missing for 3% of the study population. Persons with missing information on income were excluded

from the imputation and prevalence estimation. We assumed missing at random mechanism given the observed data.(2) To avoid bias that could occur when imputing the dichotomous variables with the multivariate normal model those variables where rounded using cut-off points determined by simulation separately for each age strata and location.(3) We aggregated the imputed data on person level. Each person having at least one visit with a missing ICD-10 code was considered missing in the prevalence estimation.

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Table. Associations of fully observed prognostic variables with a missing ICD-10 code at the health care visit. Skåne Healthcare Register, public outpatient care 1999-2011; OR – odds ratio; 95% CI – 95% confidence intervals; SEK – Swedish crown.

Variable		OR	95% CI	
Age (years)		0.9999	0.9997	1.0001
Sex		1.029	1.024	1.034
Area of residence (urban vs. rural)		1.059	1.053	1.164
Having consulted the physiotherapist (yes vs. no)		0.912	0.907	0.018
Income (1000 SEK)		1.003	1.001	1.006
Total number of doctor visits		1.061	1.047	1.077
Year of visit	1999	1		
	2000	0.929	0.919	0.938
	2001	0.526	0.520	0.531
	2002	0.446	0.441	0.451
	2003	0.346	0.342	0.349
	2004	0.0436	0.0431	0.0441
	2005	0.0342	0.0338	0.0346
	2006	0.0223	0.0220	0.0226
	2007	0.0161	0.0159	0.0164
	2008	0.0122	0.0120	0.0124
	2009	0.0205	0.0203	0.0208
	2010	0.0257	0.0254	0.0260
	2011	0.0458	0.0453	0.0463
Clinic	Primary care	1		
	Emergency	0.133	0.132	0.134
	Internal medicine	0.0644	0.0637	0.0651
	Orthopedics	0.0513	0.0507	0.0519
	Other	0.104	0.102	0.105

Validation of knee OA diagnosis in the register (positive predictive value)

Manuscript: Current and future impact of osteoarthritis on health care: population-based study with projection to year 2030.

A Turkiewicz, IF Petersson, J Björk, G Hawker, LE Dahlberg, LS Lohmander, M Englund

To validate if the SHR diagnosis of knee OA was correct (positive predictive value) we used the population based Malmö Osteoarthritis (MOA) study carried out between 2007 and 2008. (1-4) A self-reported questionnaire about knee pain was sent to 10,000 subjects aged 56-84 from the population-based Malmö Diet and Cancer cohort in Southern Sweden. The response rate was 77.4%. Those reporting knee pain in the last 12 months with duration of at least 4 weeks were classified as having frequent knee pain. A random subset of 1300 MOA subjects with frequent knee pain (56% of all with frequent knee pain) and 650 of MOA subjects without (9% of all without) were invited to a clinical examination including knee radiography and an interview. Of those, 1527 (78.3% of all invited) attended the clinical visit. Both knees were radiographed in weight-bearing and semi-flexion. A musculoskeletal radiologist assessed all radiographs according to the atlas from Osteoarthritis Research Society International.(5) We classified the knee as having radiographic OA if one or more of the following criteria were fulfilled in either the medial, lateral or patellofemoral compartment: joint space narrowing grade 2 or worse, the sum of marginal osteophyte grades in the same compartment 2 or worse, joint space narrowing grade 1 and osteophyte grade 1 in the same compartment (approximating Kellgren & Lawrence grade 2 or worse).(6) We classified a patient as fulfilling criteria for clinical & radiographic OA according to American College of Rheumatology (ACR) criteria if having knee pain and osteophyte grade 1 or worse (as all

participants of the MOA study were older than 50). We used two different knee pain questions: "Have you ever had pain in one or both knees for most days of the same month?" with no information on side, or "Have you had pain in left, right or both knees during the last 12 months" with information on side. For the second question we required osteophytes to be present in the symptomatic knee. MOA subjects who had a history of knee replacement or osteotomy were considered to fulfill both the radiographic criterion and the ACR clinical & radiographic OA criteria. We calculated the percentage of subjects with valid (according to MOA examination) knee OA diagnosis (positive predictive value) in SHR data between 1999 and the medical examination (2007 or 2008) in the MOA study on 1495 subjects that had at least one health care visit during this time. We used weighting to account for different sampling probabilities for subjects with and without knee pain.

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Data and formulas used for projection of the prevalence of osteoarthritis (OA)

Manuscript: Current and future impact of osteoarthritis on health care: population-based study with projection to year 2032.

A Turkiewicz, IF Petersson, J Björk, G Hawker, LE Dahlberg, LS Lohmander, M Englund

Table 1. The prevalence of overweight and obesity in Sweden in 1988 and 2010 (provided by Statistics Sweden, (1))

Age group	Sex	Prevalence of overweight 1988 (%)	Prevalence of obesity 1988 (%)	Prevalence of overweight 2010 (%)	Prevalence of obesity 2010 (%)
45-49	Men	37.5	7.1	49.7	12.2
45-49	Women	21.0	5.2	32.4	11.2
50-59	Men	44.0	6.9	50.3	16.0
50-59	Women	31.2	9.0	36.1	13.1
60-69	Men	46.8	8.9	48.7	15.2
60-69	Women	36.0	11.4	37.6	13.0
70-79	Men	38.5	6.7	46.3	13.9
70-79	Women	34.9	7.9	37.7	15.9
80+	Men	32.1	6.7	39.6	6.3
80+	Women	29.5	4.4	31.7	8.2

Table 2. The risk for incident knee osteoarthritis (OA) with an increase in body mass index of 5 units (kg/m^2). (2, 3)

RR (95% CI*)		OA location			
		Knee OA (2)	Hip OA (3)	Hand OA*	Any OA †
Sex	Women	1.38 (1.23-1.54)	1.11 (1.07-1.16)	1.11 (1.07-1.16)	1.24 (1.15-1.35)
	Men	1.22 (1.19-1.25)	1.11 (1.07-1.16)	1.11 (1.07-1.16)	1.16 (1.13-1.21)

CI- confidence intervals

*Assumed to be the same as for the hip

†Assumed to be equal to the mean of risks for the knee OA and other OA, as the knee OA subjects constitute 50% of all OA subjects

Table 3. The 2012 life expectancy at the age of 65 as published by Statistics Sweden (1)

	Life expectancy (years)
Women	21.02
Men	18.42

Table 4. The mean age of osteoarthritis (OA) subjects in the Skåne Healthcare Register, by sex and OA location.

	Knee OA	Hip OA	Hand OA	Any OA
Women	68.1	72.0	65.6	70.0
Men	66.5	70.9	67.2	67.6

Equation 1: For a population in steady state (i.e. with stable incidence rate and stable disease duration) the prevalence and incidence of a disease can be linked through following formula:

$$P * \frac{1}{D} = I * (N - P)$$

Where P is the number of persons with a disease, N is the number of persons in population, I is the incidence rate of the disease and D is the disease duration.(4)

Equation 2: The formula for the incidence rate in a population with a particular prevalence of overweight and obesity:

$$I_{total} = P_{normal} * I_{normal} + P_{over} * \alpha * I_{normal} + P_{obese} * \alpha * \alpha * I_{normal}$$

Where I_{total} is the incidence rate in population, P_{normal} is the prevalence of normal weight (here defined as *body mass index* (BMI)≤25), P_{over} is the prevalence of overweight (here defined as BMI between 25 and 30), P_{obese} is the prevalence of obesity (here defined as BMI>30); I_{normal} is the incidence rate in normal weight, α is the relative increase in incidence rate due to the 5 unit increase in the BMI. We assume that this increase represents on average the transition from normal weight to overweight or from overweight to obesity (see Table 2 in this appendix to see values of α that were used in the study).

Estimation of the incidence of Osteoarthritis.

The 2012 observed incidence of osteoarthritis (OA) was calculated using multiply imputed SHR data for all residents in Skåne any time between 1999 and 2012 (using the same model as described in the Supplementary Appendix B). All those having received a diagnosis of OA during the year 2012 and not having received a diagnosis of OA during 1999-2011 were considered to be incident cases of OA. The Skåne population at the Dec 31st 2011 was used as denominator for incidence calculation. The 2012 prevalence estimates derived using the formula in equation 1 and the 2012 prevalence estimated directly from the data were consistent for knee, hip, hand and any OA.

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