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Lifetime risk of knee and hip replacement following a GP diagnosis of osteoarthritis: a real-world cohort study

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SUMMARY

Objective: The aim of this study was to estimate lifetime risk of knee and hip replacement following a GP diagnosis of osteoarthritis and assess how this risk varies with patient characteristics.
Methods: Routinely collected data from Catalonia, Spain, covering 2006 to 2015, were used. Study participants had a newly recorded GP diagnosis of knee or hip osteoarthritis. Parametric survival models were specified for risk of knee/hip replacement and death following diagnosis. Survival models were combined using a Markov model and lifetime risk estimated for the average patient profile. The effects of age at diagnosis, sex, comorbidities, socioeconomic status, body mass index (BMI), and smoking on risk were assessed.
Results: 48,311 individuals diagnosed with knee osteoarthritis were included, of whom 2,561 underwent knee replacement. 15,105 individuals diagnosed with hip osteoarthritis were included, of whom 1,247 underwent hip replacement. The average participant's lifetime risk for knee replacement was 30% (95% CI: 25–36%) and for hip replacement was 14% (10–19%). Notable patient characteristics influencing lifetime risk were age at diagnosis for knee and hip replacement, sex for hip replacement, and BMI for knee replacement. BMI increasing from 25 to 35 was associated with lifetime risk of knee replacement increasing from 24% (20–28%) to 32% (26–37%) for otherwise average patients.
Conclusion: Knee and hip replacement are not inevitable after an osteoarthritis diagnosis, with average lifetime risks of less than a third and a sixth, respectively. Patient characteristics, most notably BMI, influence lifetime risks.

Introduction

Osteoarthritis is a clinical syndrome of failure of the joint characterised by joint pain, functional limitation, and reduced quality of life[1]. The hip and knee are the principal large joints affected by osteoarthritis. Following diagnosis of knee or hip osteoarthritis, patient care is primarily managed in primary care. A broad range of non-pharmacological and pharmacological interventions are available as initial treatments after diagnosis[2]. However, if patients develop persistent pain and functional impairment, they may be offered a knee or hip replacement.[3,4]

One of the barriers to implementing recommended osteoarthritis management after diagnosis is inaccurate beliefs about the disease process and progression among health professionals and patients[5]. There is general negativity around the condition, with a prevailing belief that the development of osteoarthritis is an unavoidable consequence of aging and that further deterioration is inevitable[6]. This pessimism may lead to apathy or avoidance when managing people with osteoarthritis[7], which may explain the limited adherence to treatment guidelines.[8]

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Findings from previous research, however, have indicated that structural deterioration is not a predictable consequence of aging[1]. Further progression of osteoarthritis also does not appear to be inevitable. In two community-based studies, for example, 39% of knees with radiographic knee osteoarthritis had not worsened after 15 years[9] while 35% of hips with radiographic hip osteoarthritis had not progressed after 8 years[10]. Individuals with osteoarthritis experience different symptom trajectories. In one study, disability progressively worsened over time for only 24% of patients. The remaining patients were stable, had short-term fluctuations, or steadily improved over time.[11]

Better understanding of prognosis has been identified as a particular area of unmet need in patients with osteoarthritis[12], and patients desire clear and understandable information[13]. The lifetime risks of knee and hip replacement would satisfy these requirements and give patients and healthcare providers a better idea of an individual's future healthcare needs. Understanding the effect of modifiable and non-modifiable patient characteristics on lifetime risk can help instigate self-management and patient-driven treatments following diagnosis.

In this study, we estimated the lifetime risks of knee and hip replacement following a GP diagnosis of knee and hip osteoarthritis, respectively. We then assessed the effect of patient characteristics on lifetime risk.

Methods

Setting

This analysis was based on actual practice data from patients from Catalonia, Spain. Individual-level primary care data were extracted from the *Sistema d'Informació pel Desenvolupament de la Investigació a l'Atenció Primària* (SIDIAP). SIDIAP (www.sidiap.org) is a database containing patient records of 80% of the Catalan population and is highly representative of the population in terms of geographical, age, and sex distributions[14]. It has been used extensively for research[15]. About 30% of the contributing practices are also linked to the regional *Conjunt Mínim Bàsic de Dades* (CMBD), a database containing details of admissions to every hospital of Catalonia. The linked records gave us a total source population of 1.7 million active subjects for the period 1 January 2006 to 31 December 2015.

Study participants

Individuals were eligible for inclusion into the study if they had an incident diagnosis of knee or hip osteoarthritis. Diagnostic coding in SIDIAP is based on ICD-10 codes. The recording of knee and hip osteoarthritis have previously been validated, with a sensitivity of 94% and specificity of 71% when compared to self-reported physician diagnosed osteoarthritis[16]. A further validation using free text records review confirmed the quality of osteoarthritis diagnosis in SIDIAP[17]. Individuals were excluded if they were younger than 50 at their date of diagnosis, had less than 1year of observation time prior to their diagnosis, had a prior diagnosis of inflammatory arthritis, or had a knee or hip replacement recorded before or on their date of diagnosis. The identification of knee and hip replacement is summarised in the outcomes section below.

Participant characteristics at diagnosis

Participant characteristics at diagnosis were extracted from the primary care records. Age and sex were extracted. Participants' comorbidities were summarised using the Charlson score, with possible scores of 0, 1, 2, or 3+, and a higher score indicating a higher degree of comorbidity[18]. All observation time prior to the index diagnosis of osteoarthritis were used to identify generate this score. Socioeconomic status was summarised using MEDEA, a census-based indicator that has a distinct category for those living in rural areas[19]. MEDEA has previously been used to assess the effect of socioeconomic status on the risk of hand, hip, and knee osteoarthritis in Catalonia[20]. Participants were grouped by MEDEA quintile (first indicating least deprived and fifth most deprived), or as living in a rural area.

We extracted the most recent record of body mass index (BMI) and smoking status (non-smoker, ex-smoker, or current smoker) before the osteoarthritis diagnosis and kept only those recorded within a year of diagnosis. For the purposes of summarising the observed outcomes, continuous variables were categorised. BMI was categorised following the World Health Organisation categories: normal or underweight (BMI <25), overweight (≥ 25 and < 30), obese class I (≥ 30 and < 35), obese class II (≥ 35 and < 40), and obese class III (≥ 40). Age was categorised by splitting the data into quartiles (with first indicating the youngest and fourth the oldest).

Outcomes

Instances of total knee and hip replacement (ICD-9 procedure codes 8154 and 8151) were identified using linked hospital records, with the database used collecting details of admissions to every public and private hospital of Catalonia[21]. All knee and hip replacements were included in the analysis, and so procedures were not necessarily attributable to the prior osteoarthritis diagnosis. Deaths were identified based on recorded date of death in SIDIAP. In the absence of a knee or hip replacement or death during the study period, subjects were censored at the date of exit from a GP practice linked to SIDIAP (e.g., due to moving out of Catalonia or changing practice within Catalonia to one not linked to SIDIAP) or the end of the study (31 December 2015).

Statistical methods

Comparison of cumulative incidence of knee/hip replacement

Observed knee and hip replacement over 9 years following diagnosis of knee or hip osteoarthritis were summarised by their cumulative incidence. Cumulative incidence allows the incidence of an event to be estimated while taking competing risk into account[22]. We summarised cumulative incidence for the study populations as a whole and compared cumulative incidence stratified by participant characteristics of interest (age, sex, Charlson score, MEDEA quintile or living rurally, BMI, and smoking status).

Estimating parametric survival models for risks of knee/hip replacement and mortality

Parametric survival models were estimated for cause-specific risks of knee/ hip replacement and death following diagnosis of knee or hip osteoarthritis, respectively. Such models require an assumption of the underlying distribution of the events of interest. Alternative distributions were compared and chosen on the basis of their fit to the observed data and the plausibility of extrapolation[23]. Further details on the choice of distributions is provided in Appendix Section 3, with the chosen distributions shown in Appendix Fig. A2-A4.

Univariable and multivariable survival models were estimated for each of the participant characteristics of interest. Non-linearity in continuous variables was incorporated through the use of polynomials, if their inclusion improved fit relative to specifying a linear relationship. Fit was assessed by comparing Akaike information criteria (AIC). Non-proportionality in hazards was assessed using a visual inspection of a log-log plot and by testing the weighted residuals[24]. As there was evidence of non-proportionality in age for risks of knee and hip replacement, the models were estimated separately for each of the age groups, with age included as an explanatory variable within each of the stratified models.[25]

Missing data in MEDEA, BMI, and smoking status was addressed using multiple imputation, with 50 imputed datasets generated. Both explanatory variables and outcomes were used as predictors for missing data, with predictive mean matching used for BMI and multinomial logit models used for MEDEA and smoking status. Hazard ratios and corresponding 95% confidence intervals (CIs) were calculated using Rubin's rules. Estimates from models based on complete case data were also provided for comparison.

Estimating lifetime risk

To estimate lifetime risk, parametric survival models for knee replacement and death or hip replacement and death were combined using a state-based cohort Markov model. For lifetime risk of knee replacement, a cohort of individuals began as being diagnosed with knee osteoarthritis and then they remained in the diagnosis state or progressed to either the knee replacement or death state as time progressed in yearly cycles. An equivalent structure was used for lifetime risk of hip replacement following a diagnosis of hip osteoarthritis.

Transition probabilities for knee and hip replacement were based exclusively on the parametric survival models estimated for these events. These models were extrapolated beyond the 9 years of observed data to participants' total remaining lifetime. Transition probabilities for death were based on the relevant parametric models for the first 9 years of the model, after which they were assumed to revert to estimates based on age- and sex-specific lifetables for Spain[26]. Estimated hazard ratios were similar across multiply imputed datasets and so to reduce computational time, lifetime risks were estimated using the survival models estimated on the first imputed dataset. Parameter uncertainty was incorporated using 1,000 bootstrapped models.

The models were first run for cohorts of individuals with average characteristics (median for continuous variables and mode for categorical ones) for those diagnosed with knee replacement and hip replacement, separately. The partial effect of explanatory factors on lifetime risk was assessed by re-running the models with participant profiles varying in the explanatory factor of interest, while holding other characteristics constant at their average. For the partial effect of continuous variables, a smoothed line was fitted across the lifetime risk estimates for the different simulated values of the variable.

Results

Study participants

48,311 and 15,105 individuals were included in the knee and hip osteoarthritis cohorts, respectively. A study inclusion flow chart is provided in Appendix Fig. A1. The characteristics of these individuals are summarised in Table I. The median prior observation time over which prior diagnoses and events could be observed was 5 years (with an interquartile range of 3–8 years). A comparison of those with and without missing data in socioeconomic status (MEDEA), BMI, or smoking status is given in Appendix Table A1, and combinations of missing data are summarised in Appendix Figs. A2 and A3. Individuals with missing data were generally younger and had fewer comorbidities than those with complete data. A comparison of observed and imputed values for BMI, the one continuous variable that was imputed, are also summarised in Appendix Figs. A4 and A5.

Observed risks of knee/hip replacement and mortality

Cumulative incidence of knee and hip replacement in the 9-year period following primary care diagnosis was 9.4% and 11.6% respectively. Cumulative incidences stratified by participant characteristics of interest are summarised in Table II. Those patients in the oldest age quartile had a substantially lower cumulative incidence of both knee and hip replacement than younger patients, males had a substantially higher cumulative incidence of hip replacement than females, and cumulative incidence of knee replacement was greater for those with a higher BMI. The hazard ratios estimated for explanatory factors in each of the cause-specific survival models for knee replacement and death or hip replacement and death are detailed in Appendix Tables A2 and A3. Estimates for models based on complete case data were similar, Appendix Tables A4 and A5.

Average lifetime risks of knee and hip replacement

At diagnosis, the average participant with knee osteoarthritis was a non-smoking 69-year-old woman in the fourth MEDEA quintile, with a Charlson score of 0 and a BMI of 30. At diagnosis, the average participant with hip osteoarthritis was a non-smoking 70-year-old woman living rurally, with a Charlson score of 0 and a BMI of 29. For participants with these characteristics at diagnosis, the parametric models indicated that the risks of knee and hip replacement peaked in the second year after diagnosis, then fell over time (Fig. 1). After accounting for the competing risk of mortality, these translated into a lifetime risk of knee replacement following a diagnosis of knee osteoarthritis of 30% (95% CI: 25–36%) and a lifetime risk of hip replacement following a diagnosis of hip osteoarthritis of 14% (10–19%).

Participant characteristics and lifetime risks of knee/hip replacement

Lifetime risk of knee and hip replacement following a diagnosis of knee or hip osteoarthritis generally fell as age at diagnosis increased (Fig. 2). Younger women generally had a slightly higher lifetime risk of knee replacement than younger men. For example, a 60-year-old woman had a 37% (27–50%) lifetime risk of knee replacement, while a 60-year-old man had a 30% (22–46%) risk. However, men had a substantially higher lifetime risk of hip replacement than women at younger ages. An average 60-year-old man, for example, had a 30% (25–36%) lifetime risk of hip replacement after a diagnosis of hip osteoarthritis, while a 60-year-old woman had a 17% (12–24%) lifetime risk.

A higher BMI was associated with a substantially higher lifetime risk of knee replacement, but relatively little difference in lifetime risk of hip replacement (see Fig. 3 for the partial effect of BMI on transition probabilities, and Fig. 4 for the partial effect on lifetime risks). Holding other explanatory variables fixed at their average, lifetime risk of knee replacement after a diagnosis of knee osteoarthritis was 24% (20–28%) for a BMI of 25 which increased to 32% (26–37%) for a BMI of 35. Meanwhile, the lifetime risk of hip replacement after a diagnosis of hip osteoarthritis was 12% (9–17%) for a BMI of 25% and 15% (11–19%) for a BMI of 35. Differences in comorbidities, smoking status, and socioeconomic status and rurality had relatively little effect on lifetime risk of knee or hip replacement (Appendix Figures A9-A11).

Discussion

This is to our knowledge the first study to assess the lifetime risks of knee or hip replacement for a patient diagnosed with knee or hip osteoarthritis in a primary care setting. Despite the

Table I
Participant characteristics at the time of a knee or hip osteoarthritis diagnosis

	Knee osteoarthritis cohort	Hip osteoarthritis cohort
N	48,311	15,105
Age at diagnosis (median [IQR])	69 [62, 77]	70 [62, 78]
Age at diagnosis group* (%)		
1st (youngest)	11,436 (23.7)	3,503 (23.2)
2nd	11,212 (23.2)	3,666 (24.3)
3rd	13,034 (27.0)	3,944 (26.1)
4th (oldest)	12,629 (26.1)	3,992 (26.4)
Gender: male (%)	16,076 (33.3)	6,024 (39.9)
Charlson score (%)		
0	25,967 (53.7)	7,634 (50.5)
1	12,258 (25.4)	3,779 (25.0)
2	5,840 (12.1)	1,982 (13.1)
3+	4,246 (8.8)	1,710 (11.3)
BMI (median [IQR])	30.4 [27.5, 33.9]	29.1 [26.5, 32.3]
BMI group (%)		
Normal or underweight (<25)	2,401 (5.0)	1,170 (7.7)
Overweight (≥25 and < 30)	9,550 (19.8)	3,444 (22.8)
Obese class I (≥30 and < 35)	8,770 (18.2)	2,372 (15.7)
Obese class II (≥35 and < 40)	3,538 (7.3)	788 (5.2)
Obese class III (≥40)	1,437 (3.0)	2,10 (1.4)
Missing	22,615 (46.8)	7,121 (47.1)
MEDEA quintile or rural (%)		
1st (least deprived)	4,708 (9.7)	1,726 (11.4)
2nd	6,971 (14.4)	2,326 (15.4)
3rd	8,676 (18.0)	2,666 (17.6)
4th	9,472 (19.6)	2,736 (18.1)
5th (most deprived)	7,298 (15.1)	2,010 (13.3)
Rural	9,244 (19.1)	2,938 (19.5)
Missing	1,942 (4.0)	703 (4.7)
Smoking status (%)		
Non-smoker	32,128 (66.5)	9,328 (61.8)
Ex-smoker	6,307 (13.1)	2,334 (15.5)
Current smoker	4,140 (8.6)	1,656 (11.0)
Missing	5,736 (11.9)	1,787 (11.8)

* Age groups based on quartiles for knee osteoarthritis cohort: 50 to 62, 62 to 69, 69 to 77, 77 to 105, and quartiles for hip osteoarthritis: 50 to 62, 62 to 70, 70 to 78, 78 to 103. MEDEA is a measure of socioeconomic status developed for Catalonia (Spain), with those living in rural areas having a distinct category. BMI: body mass index; IQR: interquartile range.

prevailing belief that further deterioration is inevitable following diagnosis, we find that the lifetime risks of knee and hip replacement are less than one-third and less than one-sixth following a diagnosis of knee osteoarthritis and hip osteoarthritis, respectively. The risk of undergoing a knee or hip replacement peaks in the second year after diagnosis, then steadily falls.

Older participants generally had lower lifetime risks of both knee and hip replacement than younger participants. Young women had a lower lifetime risk of hip replacement than young men. The lifetime risk of knee replacement increased as BMI increased.

Study findings in context

We found that joint replacement was not inevitable following a GP diagnosis of osteoarthritis. This finding is consistent with previous research into the structural and symptomatic progression of osteoarthritis[9–11]. As would be expected, our estimates for lifetime risks of joint replacement following diagnosis of osteoarthritis were higher than the lifetime risks previously estimated for the general population[27–29]. One previous study combined prevalence and progression estimates from the literature to estimate that a 25-year old with no history of knee injury would have a 6% lifetime risk of knee replacement[30]. This latter study estimated that 13.5% of the cohort would develop osteoarthritis, implying a 45% lifetime risk of knee replacement for those diagnosed. Although above the estimate for average lifetime risk found in our study, it is not dramatically so.

Risk of knee and hip replacement appears to be highest in the second year for those at average age at time of osteoarthritis diagnosis. This implies that there is a sizeable proportion of patients whom referral to surgery is made shortly following diagnosis. This may be explained to some degree by rapid progression of osteoarthritis for some patients[1]. It is likely though to be in large part because of a proportion of patients being diagnosed at a late-stage in the disease process, at which point knee or hip replacement was already merited.

We identified participant characteristics associated with differences in lifetime risk. These differences could be due to variation in need, disease progression, time at risk (i.e., risk of mortality), or access to care.

Age at diagnosis had a substantial effect on lifetime risks of knee and hip replacement. With mortality as a competing risk, younger age at diagnosis was associated with a longer time at risk due to greater life expectancy. All else being equal, lifetime risks of knee and hip replacement can be expected to be higher for younger patients. Age also appeared to influence cause-specific risks of knee and hip replacement, with those older at diagnosis generally having a reduced risk. This finding is consistent with previous research that found those over 82 to have less than half the risk of knee and hip replacement than younger patients, even after controlling for severity of osteoarthritis symptoms[31]. Indeed, individuals aged over 85 have previously been found to receive less knee and hip replacement relative to need than younger patients[32], which is may be due to a perception of a perceived worse risk-benefit trade-off for surgery in the elderly.

Table II
Cumulative incidence of knee or hip replacement at 9 years follow-up

	Knee OA		Hip OA	
	KR/PY	9-year cumulative incidence (% (95% CI))	HR/PY	9-year cumulative incidence (% (95% CI))
Total	2561/209508	9.4% (8.9–9.9%)	1247/60723	11.6% (10.9–12.3%)
Age at diagnosis group* (%)				
1st (youngest)	452/54625	7.7% (6.9–8.8%)	359/14779	15.0% (13.3–16.9%)
2nd	730/49643	13.0% (11.5–14.7%)	329/15124	13.0% (11.5–14.7%)
3rd	1002/56855	12.3% (11.4–13.2%)	371/16491	12.8% (11.5–14.4%)
4th (oldest)	377/48386	4.4% (3.7–5.2%)	188/14328	5.9% (5.0–6.8%)
Gender				
Male	790/69000	8.4% (7.6–9.2%)	609/37361	14.5% (13.3–15.7%)
Female	1771/140508	9.9% (9.2–10.6%)	638/23362	9.7% (8.8–10.7%)
Charlson				
0	1416/120475	9.7% (8.9–10.5%)	718/32869	13.2% (12.1–14.3%)
1	702/52364	9.4% (8.6–10.3%)	300/14917	10.8% (9.6–12.3%)
2	284/22691	9.5% (7.8–11.6%)	149/7450	10.6% (8.8–12.8%)
3+	159/13978	6.3% (5.2–7.5%)	80/5487	6.0% (4.8–7.5%)
BMI group (%)				
Normal or underweight (<25)	62/9556	6.3% (3.0–13.5%)	67/4361	7.8% (6.1–10.0%)
Overweight (≥25 and < 30)	424/39791	8.5% (7.3–9.8%)	254/13534	11.1% (9.6–12.8%)
Obese class I (≥30 and < 35)	543/37410	10.5% (9.5–11.7%)	205/9630	12.6% (10.7–14.8%)
Obese class II (≥35 and < 40)	278/15260	13.9% (11.9–16.3%)	82/3074	13.7% (11.0–17.1%)
Obese class III (≥40)	97/6015	14.3% (10.9–18.8%)	15/886	10.1% (6.0–16.9%)
Missing	1157/101476	8.6% (7.9–9.4%)	624/29238	11.9% (10.9–13.0%)
MEDEA quintile or rural (%)				
1st (least deprived)	218/20180	7.4% (6.4–8.5%)	146/6946	11.7% (9.9–13.9%)
2nd	367/30180	10.0% (8.5–11.7%)	210/9095	12.7% (11.0–14.7%)
3rd	478/37924	10.3% (8.8–12.0%)	204/10565	10.4% (9.0–12.2%)
4th	606/41932	11.7% (10.3–13.3%)	246/11088	13.2% (11.5–15.3%)
5th (most deprived)	448/31745	11.0% (9.7–12.3%)	189/8,634	14.1% (11.8–16.9%)
Rural	377/39555	6.7% (5.8–7.6%)	213/11587	9.8% (8.4–11.4%)
Missing	67/7992	4.6% (3.6–5.9%)	39/2807	6.5% (4.7–8.9%)
Smoking status				
Non-smoker	1729/133845	9.7% (8.9–10.5%)	697/36458	10.4% (9.5–11.3%)
Ex-smoker	285/23815	9.4% (7.4–11.9%)	208/8,150	13.1% (11.4–15.1%)
Current smoker	179/17950	7.4% (6.3–8.8%)	167/6393	16.2% (13.4–19.5%)
Missing	368/33897	8.9% (8.0–10.0%)	175/9721	11.5% (9.9–13.3%)

Cumulative incidence of total knee or hip replacement 9 years after a diagnosis of knee or hip osteoarthritis.
* Age groups based on quartiles for knee osteoarthritis cohort: 50 to 62, 62 to 69, 69 to 77, 77 to 105, and quartiles for hip osteoarthritis cohort: 50 to 62, 62 to 70, 70 to 78, 78 to 103. MEDEA is a measure of socioeconomic status developed for Catalonia (Spain), with those living in rural areas having a distinct category. BMI: body mass index; CI: confidence interval; HR: hip replacement; KR: knee replacement; OA: osteoarthritis; PY: person years.

Being a woman has consistently been linked with an increased risk of developing osteoarthritis[10], as reflected in our study cohorts with both being majority women. However, our findings suggest that once diagnosed, young men have a substantially higher lifetime risk of hip replacement than young women. Previous research has found that the effect of sex on risk of surgery is mediated by willingness to undergo surgery[31], which may be due to differences in perceptions of the risks and benefits of knee and hip replacement and general preferences for surgery[33]. Gender bias has also been observed, with physicians more likely to recommend knee replacement to a male patient than an otherwise equivalent female patient.[34]

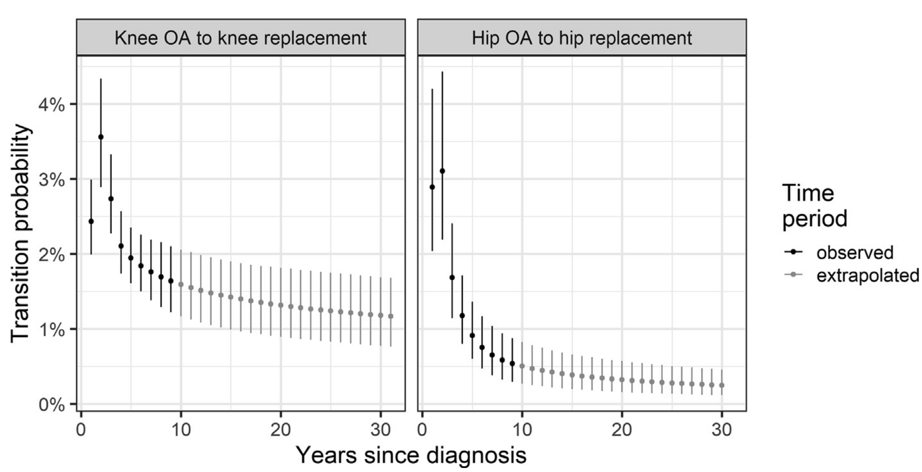

Fig. 1. Annual transition probabilities of knee and hip replacement following a diagnosis of knee and hip osteoarthritis for average patient profiles. Point estimates with 95% confidence intervals (CIs). OA: osteoarthritis.

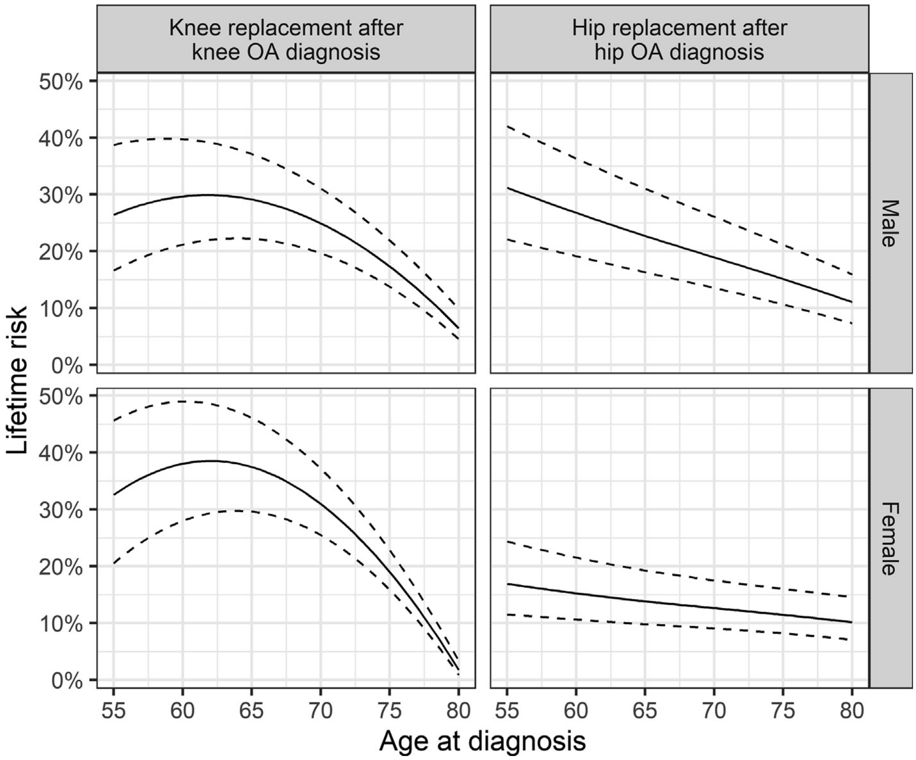

Fig. 2. Partial effect of age and sex on lifetime risks of knee and hip replacement after diagnosis of knee and hip osteoarthritis. Point estimates with 95% CIs. OA: osteoarthritis.

Higher BMI was associated in this study with a substantially increased lifetime risk of knee replacement following an osteoarthritis diagnosis. Higher BMI has previously been associated with an increased risk of developing knee osteoarthritis[35], greater structural and clinical progression[36–38], and an increased risk of undergoing knee replacement among the general population[39]. Higher BMI has also previously been shown to be associated with an increased risk of knee replacement over 6 years after a GP diagnosis of osteoarthritis using data from SIDIAP[40]. In contrast, higher BMI at time of diagnosis of hip osteoarthritis appeared to have little effect on the risk of hip replacement following that diagnosis. This discordance has previously been found in a large population-based cohort study, and may be explained by differences in biomechanical effects.[41]

Strengths and limitations of this study

This study was based on a large, representative sample from routinely collected data, with lifetime risks of knee and hip replacement estimated from time of GP diagnosis of knee or hip osteoarthritis. The routinely collected data used, however, only covered a window of time and so historical diagnoses and procedures may have been missed, leading to a possible underestimation of comorbidities and a failure to exclude some patients, for example those who had a diagnosis of inflammatory arthritis prior to their observation time. In addition, further research into the generalisability of our findings would be useful. Previous research has shown that risks of joint replacement for the general

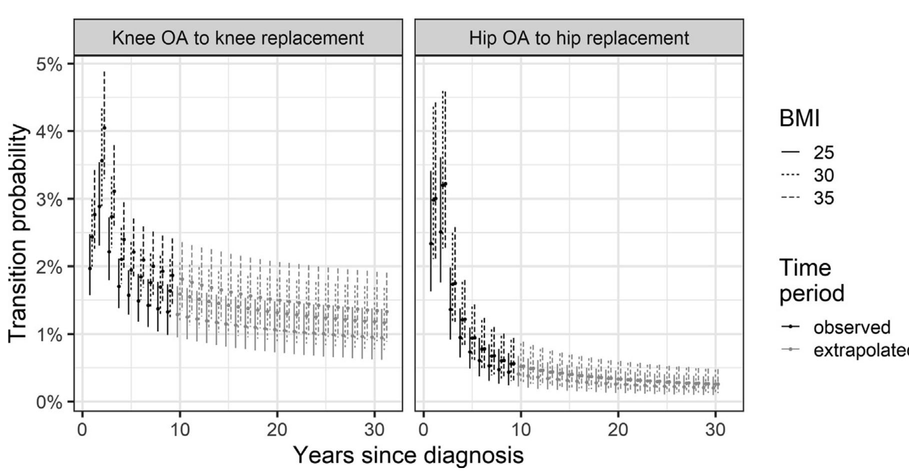

Fig. 3. Partial effect of body mass index (BMI) on annual transition probabilities of knee and hip replacement following a diagnosis of knee and hip osteoarthritis. Point estimates with 95% CIs. OA: osteoarthritis.

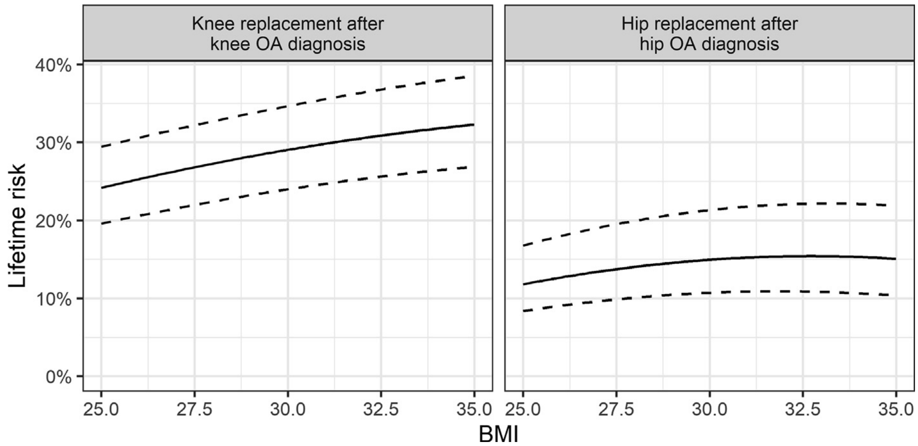

Fig. 4. Partial effect of BMI on lifetime risks of knee and hip replacement after diagnosis of knee and hip osteoarthritis. BMI: BMI; OA: osteoarthritis.

population vary across countries[27,28], and this will likely also be the case for risks for those diagnosed with osteoarthritis.

The use of parametric survival models with flexible distributions allowed us to estimate lifetime risk, which is an understandable, and possibly the most pertinent, description of risk. By using parametric models instead of lifetable methods, we were able to thoroughly analyse the effect of patient characteristics on the risk of knee or hip replacement and mortality. However, this approach required extrapolation well beyond the end of study follow-up, particularly for younger patients. This extrapolation necessarily had a high degree of uncertainty, as reflected in the wide CIs around estimates for younger patients.

When analysing the relationship between patient characteristics and lifetime risks of knee and hip replacement, we were limited to those factors available in routinely collected data. A wide range of other factors are likely to influence lifetime risk, such as willingness to undergo knee or hip replacement and disease severity[31,42]. In addition, this analysis was limited to risk of first knee or hip replacement following a diagnosis of osteoarthritis with no data available on laterality at diagnosis or at knee or hip replacement. If data on laterality were available for future research, analyses incorporating this information could provide a more detailed assessment of prognosis.

Conclusion

Knee and hip replacement are not inevitable following a GP diagnosis of knee or hip osteoarthritis. Those with knee osteoarthritis have a lifetime risk of less than a third for knee replacement, and those with hip osteoarthritis have a lifetime risk of less than a sixth for hip replacement. These findings provide a clear indication of prognosis for doctors and patients, which should help to inform treatment choices after diagnosis.

Risk of knee and hip replacement generally peaked in the second year following diagnosis in this study. This is likely because of a late diagnosis for a proportion of the study participants, with diagnosis made at a point where knee or hip replacement was already merited. This finding underscores the importance of timely diagnosis, following which non-operative treatments can be pursued.

Lifetime risks of knee and hip replacement vary depending on patient characteristics at diagnosis. In particular, higher BMI is associated with an increased risk of knee replacement. Effective weight loss interventions provided at the time of a knee osteoarthritis diagnosis would therefore likely lead to substantial health benefits for patients and cost savings for the health system.

Contributors

EB, DWM, RPV, and DPA made substantial contributions to the conception and design of the study. EB, DWM, GH, RPV, and DPA made substantial contributions to the interpretation of the data for the work. EB, RPV, and DPA undertook the statistical analysis. EB, RPV, and DPA drafted the manuscript, with GH and DWM revising it for important intellectual content. All authors read and approved the final manuscript.

Conflict of interest

All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: DPA reports grants from Amgen, Servier and UCB Biopharma, and non-financial support from Amgen, all outside the submitted work. RPV reports consultancy fees from Kyowa Kirin, UCB, and Mereo, all outside the submitted work. DWM reports grants and personal fees from Zimmer Biomet. In addition, DWM has various patents related to Unicompartmental Knee Replacement (Zimmer Biomet) with royalties paid, all outside the submitted work.

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Ethical approval

Approval for all observational research using SIDIAP data is obtained from a local ethics committee (Clinical Research Ethics Committee of the IDIAP Jordi Gol).

Data sharing

Data were provided under a licence that does not permit sharing. Data are obtainable from the SIDIAP subject to a full application.

Transparency

The senior and corresponding authors (DPA and RPV) affirm that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained.

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Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.joca.2019.06.004.

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