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Healthcare utilisation and mortality in people with osteoarthritis in the UK- findings from a national primary care database

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Abstract

Background: Burden of osteoarthritis (OA) in the UK primary care has not been investigated thoroughly.

Aim: To estimate the healthcare use and mortality in people with OA (overall and joint specific)

Design and setting: A matched cohort study of adults with an incident diagnosis of OA in primary care were selected for the study using the UK national Clinical Practice Research Datalink (CPRD) electronic records.

Methods: Healthcare utilisation was measured as the annual average number of primary care consultations and hospitalisations after the index date for any cause and all-cause mortality data in 221,807 OA and an equal number of controls (no OA diagnosis) matched to cases by age (+/-2 years), sex, practice, and year of registration. The associations between OA and healthcare utilisation and all-cause mortality were estimated using multinomial logistic regression and Cox regression respectively, adjusting for covariates.

Results: The mean age of the study population was 61 years and 58% were women. In the OA group the median number of primary care consultations per year after the index date was 10.92 compared to 9.59 in non-OA controls ($p = 0.001$). OA was associated with an increased risk of GP consultation and hospitalisation. The adjusted hazard ratio for all-cause mortality was 1.89 (95% CI 1.85-1.93) for any OA, 2.09 (2.01-2.19) for knee OA, 2.08 (1.95-2.21) for hip OA and 1.80 (1.58-2.06) for wrist/hand OA compared to respective non-OA controls.

Conclusion: People with OA had increased rates of GP consultation, hospitalisation, and all-cause mortality which varied across joint sites.

How this fits in

- Nearly 10% of the people attending primary care in the UK have osteoarthritis (OA) but the health care utilisation pattern in the health system is not well known.
- We found people with osteoarthritis had increased primary care consultations, hospitalisation and all-cause mortality compared to similar age and sex matched controls.
- The burden was high for people diagnosed with hip, knee, and ankle/foot OA.

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Introduction

Osteoarthritis (OA) is the most common chronic joint condition, affecting different sites and presenting with pain, functional impairment, and reduced quality of life (1,2). In recent decades, one in ten people attending UK primary care consulted for OA (3). Globally, years of life with disability (YLDs) for hip and knee OA increased by 6.6 million over the period 1990 to 2010 (10.5 million in 1990 to 17.1 million in 2010) (4).

The rising prevalence of chronic conditions, such as OA, increases the burden on the health system, especially in primary care settings where most of these conditions are managed. OA incurs a large expenditure in primary care and is a financial burden to health systems worldwide (5,6). In addition to clinical need, health care utilisation in primary care depends on a wide range of factors such as socioeconomic and demographic factors, accessibility, and availability (7). There are various methods used to measure healthcare utilisation from a health system perspective. Two commonly used indicators are the number of hospital visits and the number of inpatient admissions per person (8). Previous studies have shown increased health care visits by people with knee OA compared to controls (9,10) although data for healthcare utilisation for joint-specific OA are currently lacking.

Another measure of disease burden is the risk of mortality. Traditionally, OA has been considered a low priority among chronic conditions because of a minimal risk of mortality despite it being highly prevalent and a significant cause of morbidity in older people (11). The evidence of an association between all-cause mortality and OA is inconclusive (12). Studies have shown significant associations with cause-specific cardiovascular disease (CVD) and all-cause mortality (13,14)

In the context of multiple chronic conditions, it is not well understood whether the health utilisation pattern increases after the first diagnosis of OA. It is also important to study the outcomes for different types of OA based on the joint involved, as different joint involvement can have different physiological and pathological explanations and result in different outcomes for those affected. Information on healthcare utilisation and mortality would provide a clearer picture of health resources used and can guide prioritisation in primary care. Therefore, the current study examined all-cause mortality, general practice (GP) consultations, and inpatient

admissions in people with OA and matched controls using a large primary care database in the UK.

Methods

We undertook a matched retrospective cohort study in the Clinical Practice Research Datalink (CPRD GOLD) which is UK's large prospective primary care electronic medical record database (15). The study involved analyses of anonymised patient level data of ~17.5 million individuals from 736 general practices as of 31st December 2017, generalisable to the wider UK population (16). It was approved by the Independent Scientific Advisory Committee for Medicines and Healthcare Products Regulatory Agency (MHRA) Database Research (protocol 19_030R).

Case definition of OA

We used Read codes, which are a standard clinical coding system used in UK general practice, to identify people with a diagnosis of incident OA between 1st January 1997 and 31st December 2017. For this study, the date of the first recorded physician diagnosis for hip, knee, ankle/foot, wrist/hand, or site recorded as 'unspecified' OA was used as the index date and the start date of follow-up. Other inclusion criteria were: 1) aged 20 years or more at the index date; 2) having active registration for at least 36 months with an up-to-standard (UTS) practice (determined by CPRD database standards) prior to the index date. Details of the selection of OA population is given in Supplementary file page 1.

Selection of controls

Controls were people registered for at least 36 months with UTS practices and with no record of diagnosed OA, OA related joint pain or total joint replacement during the study period. One control per OA case matched by year of birth (within +/- 2 years), sex, year of first registration and practice was selected and assigned with the same index date as their matched case.

Outcomes

Average number of annual primary care consultations:

The definition of "consultation" includes a consultation with a general practitioner, practice nurse or any other primary care healthcare practitioner for any purposes which has been recorded in the CPRD GOLD database. The average was calculated by dividing the total number of GP

consultations recorded per person from the index date until the last record available for the person or the 31st of December 2017, if earlier by the number of years followed up. For example, if a person had a total of 15 years of follow-up, and had 120 consultations recorded during that period, then the average annual number of consultations for that person was eight consultations per year (120/15).

Average number of annual inpatient admission/hospitalisations: Information on inpatient admissions was available for 432,572 people (97.5% of total study population) obtained from hospital episode statistics (HES) linkage data. The total number of hospitalisations during follow-up, irrespective of cause, was divided by the years of follow-up to estimate average inpatient admissions per year for each person

All-cause mortality: All-cause mortality data were obtained from office of national statistics (ONS) linkage data. The recorded date of death was used in the analysis to estimate the mortality rate in the OA group compared to that in the non-OA group.

Covariates

Information available at the index date including age, sex, smoking status, alcohol use, and body mass index (BMI) was used in the analysis. BMI (Kg/m^2) was categorised as underweight (<18.5), normal (18.5-24.9), overweight (25.0-29.9), obese (≥ 30.0), and missing (20). Smoking status was categorised as ex-smoker, current smoker, non-smoker, and missing. Alcohol use was grouped into non-user, ex-user, current user 1-9 units/week, current user ≥ 10 units/week, current user (unknown quantity), and missing.

We also assessed the status of 49 chronic conditions at the index date in both groups, and the Elixhauser comorbidity index (ECI) at baseline was calculated to estimate the burden of comorbidities(17). Each comorbidity was categorised as either present or not at the index date. Details of the selection of chronic conditions and list of conditions are given in Supplementary file page 1 and Table 1, respectively.

Statistical analysis

The outcomes were compared between the OA and the matched control group. Descriptive statistics of each outcome were reported as either mean (standard deviation (SD)) or median (inter quartile range (IQR)) as per distribution. Normal distribution of outcomes was checked

using histograms and the Shapiro-Wilk test. Primary care consultations were grouped into four equal groups using quartiles, i.e., 25% participants per group. Hospitalisations were grouped into four unequal groups as about 60% of participants had zero hospitalisations, the four groups were formed as 'no hospitalisations (zero)' and three other groups using terciles (Table 2).

Associations between consultation/hospitalisation groups and OA (yes/no) were analysed using the multinomial logistic regression model and reported as ratios (OR) and 95% confidence intervals (CI). In the adjusted model, covariates included age, sex, smoking, alcohol, BMI, number of chronic conditions, and ECI at the index date. The ordinal logistic regression model was used to calculate the OR (95%CI) per quartile and p values for trend.

The follow-up period for all-cause mortality was from the index date until the earliest date of death, transfer out of practice, or end of the study (31st Dec 2017). The Kaplan-Meier method was used to display the cumulative probability of all-cause mortality. Hazard ratios (HRs) and 95% CI were calculated using a Cox regression model adjusting for age, gender, BMI, smoking, alcohol use, count of chronic conditions, and ECI at the index date. The proportional hazard assumption was examined with Schoenfeld residual tests. In a sensitivity analysis we estimated all-cause mortality risk in people with OA (n=22,333) and age (± 2), sex, registration year and practice matched controls (n=22,333) without any of the 49 Specified chronic conditions at baseline using the same approach as that for the full cohort.

The statistical analyses were performed using STATA statistical software V.15 (STATA corp, Texas) and R software V3.5.

Results

A total of 221,807 OA cases and 221,807 age, sex, registration year and practice matched non-OA controls were included in the analysis. Mean age of the study population was 61 years (SD 13.2 years) and 58% were women. Among people with OA, 71.5% had at least record of unspecified OA and 24.7% had knee OA either alone or with other OA. The median number of chronic conditions in people with OA at the index date was 2 (IQR 1-4) compared to 1 (IQR 0-3) in non-OA controls ($p < 0.05$).

Primary care consultations

The median number of average annual primary care consultations after the index date was higher in the OA group compared to controls with medians of 10.91 (IQR 4.7-21.9) and 9.43 (IQR 3.64-20.35) ($p < 0.05$), respectively. Within the OA group, the median number of annual primary care consultations was 12.4 (IQR 5.6-24.3) for hip OA, 12.1 (5.3-23.9) for knee OA and 11.6 (5.1-23.6) for ankle/foot OA.

The median number of annual consultations increased with increasing age in both sexes. (Supplementary Figure 1) The OR for average annual consultations increased gradually from 1 for quartile 1 (referent) to 1.16 (95%CI 1.15-1.19) for quartile 2, 1.24 (95%CI 1.22-1.26) for quartile 3 and 1.27 (95%CI 1.25-1.29) for quartile 4 (p for trend =0.001) in the adjusted model. (Figure 1 a) The association of the primary care consultations with quartile 4 in people with hip OA was 49% (OR 1.49; 95% CI 1.44-1.55) more compared to quartile 1. The association was 42% higher for ankle/foot OA (OR 1.42; 95% CI 1.31-1.54), and 38% more for knee OA (OR 1.38; 95% CI 1.34-1.42). (Figure 1 b-e)

Hospitalisations

65% of people in OA group and 70% in the non-OA group had zero hospitalisations after the index date during follow-up. (Table 2) The median number of hospitalisations per year increased with increasing age in both sexes and was higher in people with OA compared to non-OA controls. (Supplementary Figure 2) After the index date, people with OA had a greater risk of hospital admissions than people without OA and the OR increased from 1 for zero hospitalisations (referent) to 0.98 (0.96-1.00) for tertile 1, 1.24 (95% CI 1.22-1.27) for tertile 2, and 1.46 (95% CI 1.43-1.48) for tertile 3, respectively in adjusted model. (Figure 2a) The association of unspecified, hip and knee OA in the highest hospitalisation group was 44% (OR 1.44; 95% CI 1.41-1.47), 27% (OR 1.27; 95% CI 1.23-1.33), and 25% (OR 1.25; 95% CI 1.21-1.29) compared to zero hospitalisations group, respectively. (Figure 2)

All-cause mortality

Of those with OA, 20,617 (9.3%) died during the study follow-up period, compared with 13,087 (5.9%) in the non-OA group. Median duration of follow-up in people with OA was 6.03 years [IQR 2.89-10.13] compared to 7.90 years [IQR 4.13 -12.13] in the control group. The crude all-cause mortality rate was nearly two times higher in the OA group (13.52 per 1000 person-years compared to 7.14 per 1000 person-years in the non-OA group). The adjusted HR comparing the

OA group with the non-OA group was 1.89 (95% CI 1.85-1.93). (Table 3) Knee (HR 2.09: 95%CI 2.01-2.19) and hip (HR 2.08: 95% CI 1.95-2.21) had higher risk of mortality followed by for wrist/hand (HR 1.80: 95% CI 1.58-2.06). Proportional hazard assumptions were satisfied. The cumulative probability of death increased with follow up time and more in people with OA. (Figure 3) Joint specific cumulative probability of mortality is provided as supplementary Figure 4 (A-D).

Sensitivity analysis

In the restricted matched cohorts without any of the 49 comorbidities at the index date, the mortality rate among people with OA was 6.26 per 1000 person-years compared to 2.99 in non-OA controls. The HR for all-cause mortality in OA was 2.15 (95% CI 2.00-2.43) after adjustment for other covariates. (Supplementary Table 2) The cumulative probability of death was higher in people with OA. (Supplementary Figure 3)

Discussion

Summary

This study has demonstrated: (1) people with OA had an increased number of GP consultations and hospitalisations; (2) people with OA had twice the mortality rate compared with people without OA; (3) the associations varied slightly between joint sites and were independent from age, sex, BMI, and comorbidities.

Comparing with the existing literature

The reasons for the increased consultation rate per year in the OA group is multifactorial. Musculoskeletal (MSK) problems were the second highest for consultations reason after respiratory problems in UK primary care (18). It is most likely to result from the joint pain or incident comorbidities (19,20). For OA frequent visit is to confirm the diagnosis through further clinical examinations such as radiographs, and/or are solely for management of pain and disability due to OA (19). Bedson et al found no difference in the median number of consultations for comorbidities between knee pain consulters and knee pain non-consulters (19). We adjusted for the number of chronic conditions at the index date and still found an association with higher consultation in people with OA. Often people living with more chronic conditions

are prescribed with multiple medications, thus demanding more visits for medication review in GPs. Surprisingly, we found the annual average primary care consultations after the index date increased in people with ankle/foot OA, one of the least researched sites for OA contrary to as reported in knee OA (9,21). The increased consultations overall support the high burden of osteoarthritis using primary care services could be for OA or other factors such as medications, which merits more detailed investigation and comparison with other chronic conditions.

Average annual hospitalisations were higher in people with OA, similar to that reported in the USA (21) and UK (22). The number and burden of other chronic conditions in those with OA have been suggested as the cause of increased hospitalisations (23). However, our model adjusted for the ECI index and count of chronic conditions at baseline, suggesting the excess hospitalisations could be due to the new comorbidities developed after the diagnosis of OA. Increased risks of falls and injury (24) and the requirement for joint replacement, especially of the knee (25,26) could be the reasons for such hospitalisation rates. Another important associated factor could be adverse events such as gastrointestinal bleeding (27) and CVD from use of analgesics such as NSAIDs in OA(28). The association of unspecified OA sites with increased annual average hospitalisations after the index date is difficult to explain in the absence of a clear definition of unspecified OA. The non-significant association with wrist/hand OA indirectly suggests less secondary health care resource use.

The evidence for an association of all-cause mortality with OA is inconclusive (14,29). We found people with OA had excess all-cause mortality rate compared with non-OA controls, similar to that previously reported in the Somerset and Avon Survey of Health study (13). Reasons for these discordant findings may be from the methodological differences, including the definition of OA, age range, study design, and length of follow-up. Several reasons, apart from comorbidities, may help explain the higher mortality in people with OA, for example, obesity, pain, and disability or functional limitations (13). Another explanation could be risk of CVD from chronic subclinical inflammation (30) or the use of analgesics such as NSAIDs (31). In this study, comorbidity counts and the severity of comorbidities at the index date along with BMI at the index date were adjusted for in the model, but they did not explain the increased mortality rate. In the sensitivity analysis people did not have any comorbidities at the index date, the increased mortality rate could be due to the subsequent higher comorbidity incidence in the OA

group after the index date rather than pre-existing comorbidities at the time of OA diagnosis. Even though cause-specific mortality was not part of the current research, further studies to explore the causes and pattern of mortality appear warranted.

Strengths and limitations

Major strength of the study is the inclusion of 49 comorbidities, longer follow-up, and adjusting for the number and severity of other chronic conditions in analysis of outcomes. Several limitations to this study are: 1) ascertainment biases due to misdiagnosis, miscoding, and delayed recording in the GP database, 2) many people had unspecified OA, which weakens the findings regarding site-specific OA, 3) only all-cause mortality was estimated, whereas cause-specific mortality might provide further insights about specific causal pathways to the excess deaths in people with OA, and 4) underreporting of OA in primary care because of the ‘joint replacement’ in secondary care (32). The hospital admissions and primary care visits were calculated irrespective of any specific reason, which could have been influenced by the diagnosis of other conditions. People who visited more frequently may have had more chance of being diagnosed with multiple chronic conditions. However, both the number and severity of the chronic conditions at the index date were adjusted for. Differences in lifestyle and health behaviour patterns and medication use were not considered, which might have confounded the associations with OA.

Implications for Research and/or practice

People with OA have significant increased annual primary care consultations, hospitalisation and doubled all-cause mortality rate in the UK. It would be interesting to find out the exact factors associated, to reduce the burden on the health services. They also provide essential information to estimate additional costs incurred in individuals with OA and the cost-effectiveness of a specific intervention. The increasing burden of OA healthcare utilisation in the primary care should be noticed and the reasons should be identified to design effective strategy to reduce the burden.

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Contributor and guarantor information: SS, WZ, CC and MD conceived and designed the study. SS and WZ acquired the data. SS performed the analysis and CC, AS and WZ supervised the statistical analysis. SS, AS, CM, CC, WZ, CFK, and MD interpreted the results. SS and WZ drafted the manuscript. All authors contributed to the critical revision of the manuscript for important intellectual content. WZ, CC and MD supervised the study. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

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Conflict of interest: The authors declare that they have no conflict of interest.

Data sharing statement: We used anonymised data on individual patients on which the analysis, results, and conclusions reported in the paper are based. The CPRD data is not distributed under licence. However, the relevant data can be obtained directly from the agency (<https://www.cprd.com/>). The codes developed for the analysis can be available upon a valid request.

Figure legend

Figure 1. Adjusted risk association with annual average primary care consultations in people with OA compared to non-OA

Figure 2. Association with annual average number of hospitalizations per year in the OA and non-OA groups

Figure 3. Cumulative probabilities of all-cause mortality in the OA and non-OA groups after index date

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Table 1 Characteristics of incident OA patients and matched controls at index date

	Incident OA (n=221,807) n (%)	Controls (n=221,807) n (%)	Unadjusted Odds Ratio [#] (95%CI)
Mean age, Total (SD)	61.05(13.17)	60.88(13.31)	
Mean age, Men (SD)	60.71(12.85)	60.54(12.97)	
Mean age, Women (SD)	61.30(13.40)	61.12(13.55)	
Age (years)			
<40	12266(5.53)	13018(5.87)	NA
40-49	30809(13.89)	31673(14.28)	NA
50-59	60287(27.18)	59606(26.87)	NA
60-69	60442(27.25)	59294(27.02)	NA
70-79	40879(18.43)	40418(18.22)	NA
80-89	15926(7.18)	15815(7.13)	NA
≥90	1198(0.54)	1353(0.61)	NA
Gender			
Men	93895(42.33)	93895(42.33)	NA
Women	127912(57.67)	127912(57.67)	NA
BMI (kg/m²)			
Mean BMI (SD)	28.28(5.62)	26.62(4.98)	
<18.5 (Underweight)	3020 (1.36)	4738 (2.14)	0.85 (0.82-0.90) *
18.5- 24.9 (Normal)	63531 (28.64)	85534 (38.56)	Reference
25.0-29.9 (Overweight)	82683 (37.28)	82190 (37.05)	1.35 (1.33-1.37) *
≥30 (Obese)	72442 (32.66)	46898 (21.14)	2.08 (2.04-2.11) *
Missing	131 (0.06)	2447 (1.10)	0.07 (0.06-0.09) *
Alcohol consumption (units/week)			
Never	44084 (19.87)	40889 (18.43)	Reference
Ex-drinker	6040 (2.72)	5311 (2.39)	1.05 (1.01-1.08) *
Current 1-9	77549 (34.96)	79502 (35.84)	0.89 (0.88-0.91) *
Current ≥10	43148 (19.45)	42753 (19.27)	0.93 (0.91-0.95) *
Current Unknown	50860 (22.93)	50922 (22.96)	0.92 (0.91-0.94) *
Missing	126 (0.06)	2430 (1.10)	0.05 (0.04-0.06) *
Smoking Status			
Never smoked	117498 (52.97)	122551 (55.25)	Reference
Ex-smoker	41683 (18.79)	39646 (17.87)	1.15 (1.14-1.17) *
Current smoker	62545 (28.20)	57208 (25.79)	1.10 (1.08-1.12) *
Missing	81 (0.04)	2402 (1.08)	0.03 (0.02-0.04) *
Joints involved			
Hip	25091 (11.31)		
Knee	54841 (24.72)		
Wrist/Hand	13255 (5.97)		
Ankle/Foot	5311 (2.39)		
Unspecified	158620 (71.51)		
ECI at index (Mean, SD)	62.74 (3.45)	62.51 (3.10)	
Number of chronic conditions at index (Mean, SD)	2.51 (2.14)	1.92 (1.89)	
Number of chronic conditions at index (Median, IQR)	2 (1,4)	1(0,3)	

[#]Matched by gender, age, practice, and index date; *p value < 0.05; NA- not applicable; BMI- body mass index; CI- confidence interval; ECI- Elixhauser Comorbidity index; OR- Odds ratio; SD- standard deviation.

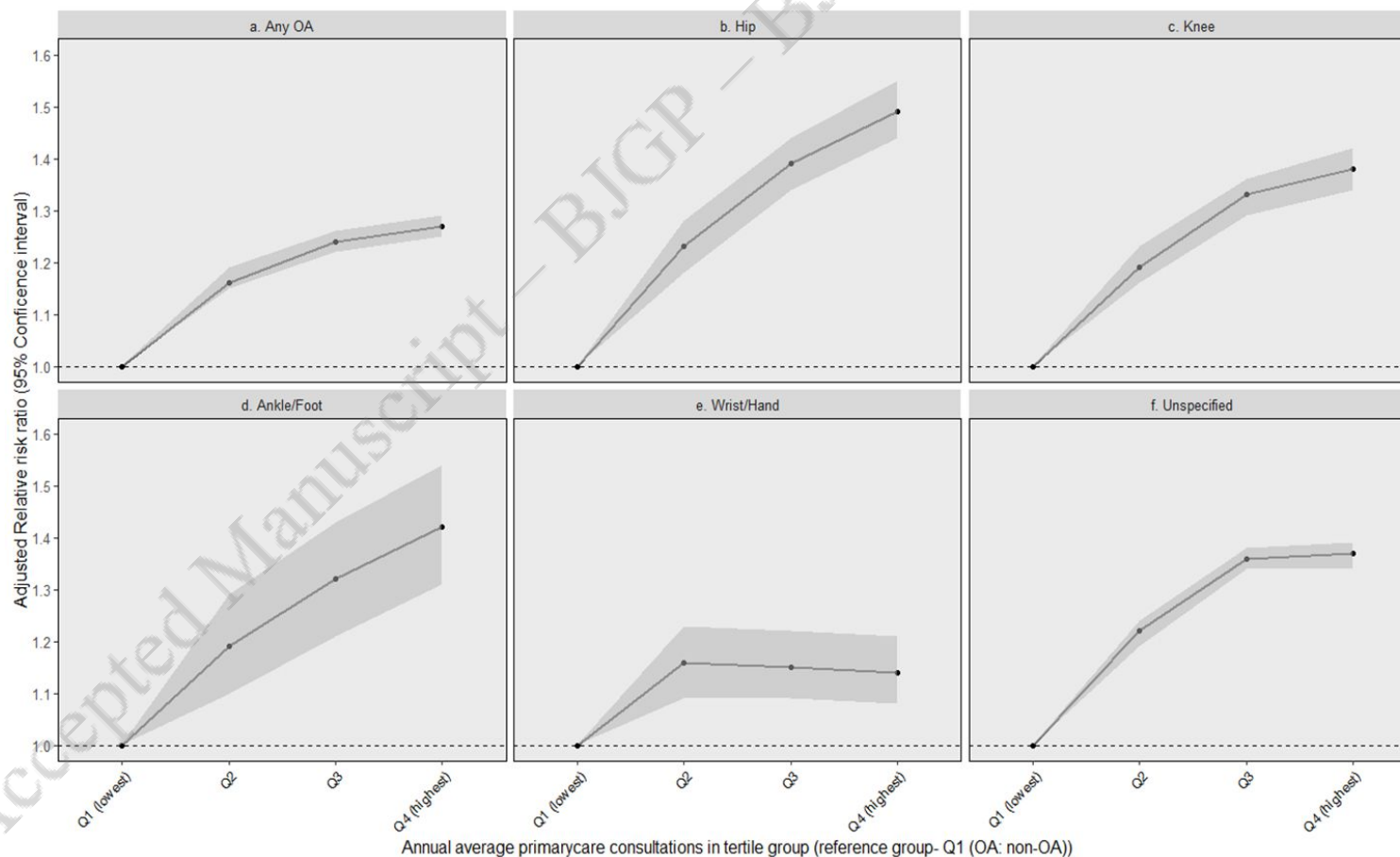
Table-2 Summary for the average number of primary care consultations and hospitalizations per year in the OA and non-OA groups

	Primary care consultations per year after index date		Inpatient admissions/hospitalizations per year after index date	
	Median [IQR]	Mean [SD]	Median [IQR]	Mean [SD]
OA (n=221,807)	10.91 [4.66-21.96]	16.86 [20.04]	0 [0-0.19]	0.25 [1.70]
Non-OA (n=221,807)	9.43 [3.64-20.35]	16.13 [21.22]	0 [0-0.09]	0.18 [1.09]
Knee (n=54841)	12.15 [5.34-23.93]	18.45 [21.98]	0 [0-0.20]	0.25 [1.38]
Hip (n=25091)	12.38 [5.59-24.31]	18.72 [21.97]	0 [0-0.22]	0.25 [1.58]
Ankle/Foot (n=5311)	11.66 [5.11-23.56]	18.12 [22.16]	0 [0-0.17]	0.23 [0.67]
Wrist/Hand (n= 13255)	10.46 [4.46-20.86]	16.28 [20.18]	0 [0-0.14]	0.19 [0.68]
Unspecified (n=158620)	11.55 [5.02-22.79]	17.48 [20.40]	0 [0-0.19]	0.27 [1.93]

IQR- Inter quartile range; OA-Osteoarthritis; SD- Standard deviation

An expanded version of the table can be seen at eTable3

Figure 1. Adjusted* risk association with average annual primary care consultations in people with OA compared to non-OA

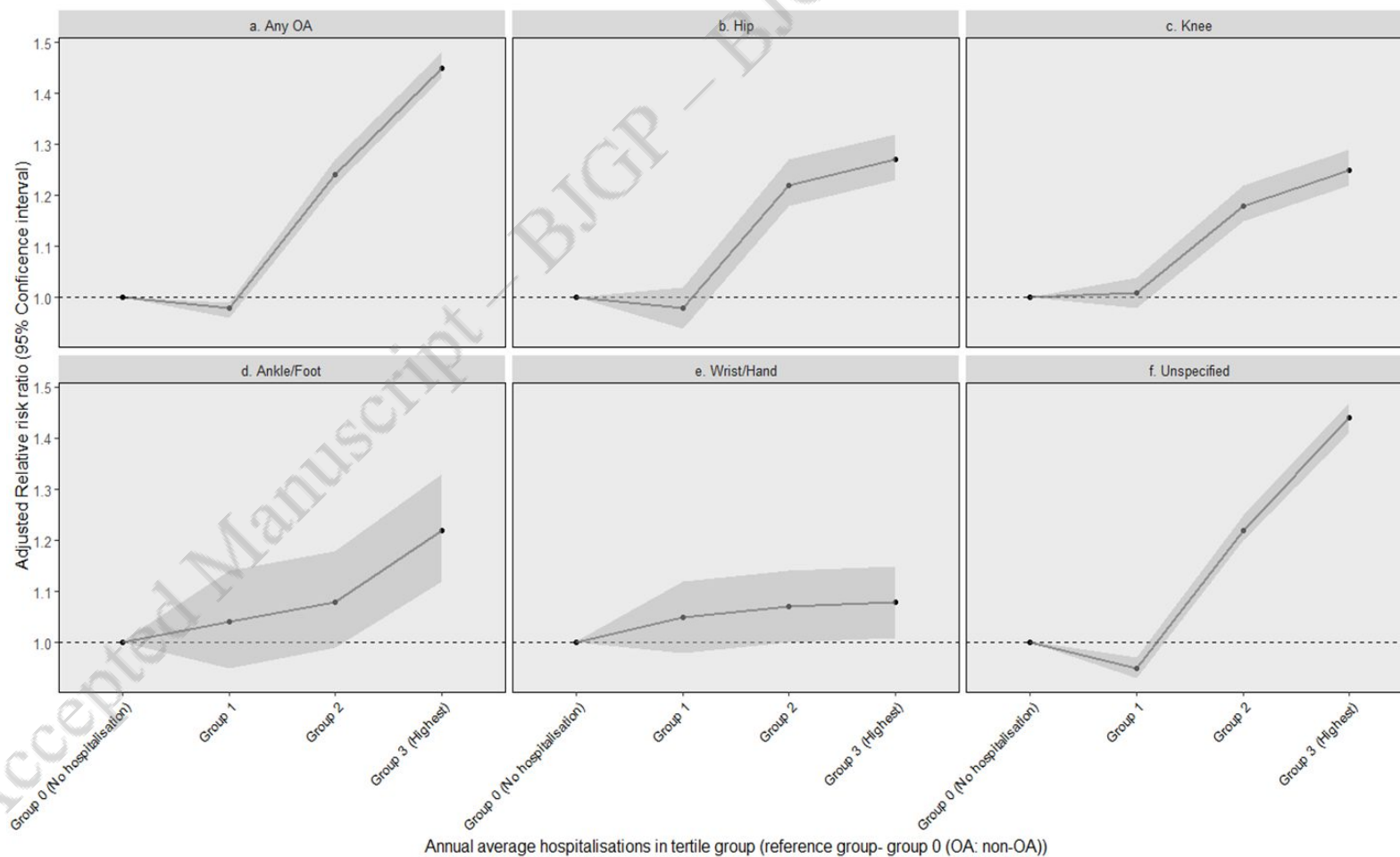


* Adjusted for age, sex, smoking, alcohol, BMI, ECI and number of comorbidities at baseline using multinomial regression model; *P-value <0.05

OA- Osteoarthritis. Detailed information can be found in the supplementary Table 4.

Median and IQR value of average annual primary care consultations in each group: Q1-1.84 [0.89-2.95]; Q2- 6.84 [5.43-8.41]; Q3- 14.61 [12.21-17.50]; Q4- 33.66 [26.17-48.08]

Figure 2. Adjusted* risk association with annual average number of hospitalizations per year in the OA and non-OA groups



* Adjusted for age, sex, smoking, alcohol, BMI, ECI and number of chronic conditions at baseline; *P-value <0.05

aOR-Adjusted odds ratio; CI- Confidence interval; OA- Osteoarthritis. Detailed information can be found in Supplementary Table 5

Median and IQR value of annual average hospitalisations in each group

Q1- 0.11 [0.06-0.15]; Q2- 0.32 [0.26-0.42]; Q3- 0.97 [0.70-1.59]

Table-3. Association with all-cause mortality in the OA and non-OA groups

	N (Total)	Number of deaths	Mortality rate per 1000 person-years (95% CI)	Unadjusted hazard ratio (95% CI)	Adjusted* hazard ratio (95% CI)
Non-OA controls	221807	13087	7.14 (7.02, 7.27)	Reference	Reference
OA cases (any site)	221807	20617	13.52 (13.34, 13.70)	2.02 (1.98, 2.06) *	1.89 (1.85, 1.93) *
Site of OA:					
Non-Knee controls	59351	3637	7.94 (7.68, 8.20)	Reference	Reference
Knee	53982	5038	14.70 (14.30, 15.11)	1.98 (1.90, 2.06) *	2.09 (2.01, 2.19) *
Non-Hip controls	27521	1783	8.38 (8.00, 8.78)	Reference	Reference
Hip	24701	2503	15.90 (15.29, 16.54)	2.03 (1.91, 2.16) *	2.08 (1.95, 2.21) *
Non- Ankle/Foot controls	5874	252	5.34 (4.72, 6.04)	Reference	Reference
Ankle/Foot	5231	355	9.89 (8.91, 10.98)	1.95 (1.66, 2.28) *	2.00 (1.70, 2.36) *
Non- Wrist/Hand controls	9570	361	4.99 (4.50, 5.53)	Reference	Reference
Wrist/Hand	9729	605	9.68 (8.94, 10.48)	2.03 (1.79, 2.32) *	1.80 (1.58, 2.06) *
Non- Unspecified controls	161568	10055	7.43 (7.28, 7.57)	Reference	Reference
Unspecified	155540	14981	14.27 (14.05, 14.50)	2.05 (2.00, 2.10) *	1.80 (1.75, 1.84) *

* Adjusted for age, sex, smoking, alcohol, BMI, ECI and number of comorbidities at baseline; *P-value <0.05

CI- Confidence interval; OA- Osteoarthritis

Figure 3. Cumulative probabilities of all-cause mortality in the OA and non-OA groups after index date

