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Original article

Osteoarthritis and risk of hospitalization for ambulatory care-sensitive conditions: a general population-based cohort study

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Abstract

Objective. To determine the association between OA and risk of hospitalization for ambulatory care-sensitive conditions (HACSCs).

Methods. We included all individuals aged 40–85 years who resided in Skåne, Sweden on 31 December 2005 with at least one healthcare consultation during 1998–2005 ($n = 515\,256$). We identified those with a main diagnosis of OA between 1 January 1998 and 31 December 2016. People were followed from 1 January 2006 until an HACSC, death, relocation outside Skåne, or 31 December 2016 (whichever occurred first). OA status was treated as a time-varying covariate (those diagnosed before 1 January 2006 considered as exposed for whole study period). We assessed relative [hazard ratios (HRs) using Cox proportional hazard model] and absolute (hazard difference using additive hazard model) effects of OA on HACSCs adjusted for potential confounders.

Results. Crude incidence rates of HACSCs were 239 (95% CI: 235, 242) and 151 (150, 152) per 10 000 person-years among OA and non-OA persons, respectively. The OA persons had an increased risk of HACSCs [HR (95% CI) 1.11 (1.09, 1.13)] and its subcategories of medical conditions except chronic obstructive pulmonary disease [HR (95% CI) 0.86 (0.81, 0.90)]. There were 20 (95% CI: 16, 24) more HACSCs per 10 000 person-years in OA compared with non-OA persons. While HRs for knee and hip OA were generally comparable, only knee OA was associated with increased risk of hospitalization for diabetes.

Conclusion. OA is associated with an increased risk of HACSCs, highlighting the urgent need to improve outpatient care for OA patients.

Key words: avoidable hospitalization, ambulatory care-sensitive conditions, osteoarthritis, register-based study

CLINICAL SCIENCE

Rheumatology key messages

- OA is associated with an 11% increased risk of a hospitalization for ACSCs.
- Only knee OA was associated with an increased risk of hospitalization for diabetes.
- Our findings highlight the urgent need to improve outpatient care for OA patients.

Introduction

OA is the most common form of arthritis, representing a major cause of pain, disability and deteriorated quality of life [1, 2]. According to the Global Burden of Diseases Study 2015, OA was ranked as the 16th leading cause of total years with disability among 315 diseases in Sweden [3]. In southern Sweden, about one in four people aged 45 years and older had a doctor-diagnosed OA in 2012 [4]. OA is also among the diseases with the highest rate of comorbidity [5] with around two in three OA patients having one or more other comorbidity [6–8]. Moreover, the risk of comorbidity is significantly higher in patients with OA compared with those without OA [6, 9, 10] with a pooled prevalence ratio of 1.2 for any comorbidity in studies matched for age and sex [6].

The consequences of OA (e.g. pain, disability, comorbidity) translate into substantial increase in healthcare utilization including hospitalization among these patients [11–14]. Previous studies suggested that OA patients were more likely to be hospitalized and incurred higher hospitalization costs compared with people without OA

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[11, 15, 16]. OA was reported to be associated with 70 additional hospitalizations per 100 patients annually in US [17]. Given that hospitalizations are a main driver of total expenditure attributable to OA [13, 18], reducing hospitalizations among OA patients should be a critical component of any effort to decrease the high and rising burden of OA.

A considerable proportion of hospital admissions could potentially be avoided through effective outpatient care [known as 'ambulatory care-sensitive conditions (ACSCs)' or 'potentially avoidable hospitalizations'] [19]. The concept of ACSC is internationally used as a measure of health system performance and the quality of primary care [20]. It includes chronic and acute conditions 'for which timely and effective outpatient care can help to reduce the risks of hospitalization by either preventing the onset of an illness or condition, controlling an acute episodic illness or condition, or managing a chronic disease or condition' [19]. Examples of such conditions are diabetes, heart failure, diarrhoea and bleeding gastric ulcer.

Higher incidence and prevalence of some specific ACSCs such as heart failure and diabetes in individuals with OA than those without OA is well-documented [6, 7, 21, 22]. In addition, several studies also reported an increased risk of hospital admission for a specific ACSC due to OA and OA-related walking disability [23–26]. However, to our best knowledge, no previous study has examined the association between OA and hospitalization for the ACSCs as a whole and across its subdiagnoses. To address this great knowledge gap, we used a comprehensive longitudinal register-based data from the southernmost region of Sweden to assess the risk of hospitalization for ACSCs in people with OA. Such insights provide great opportunities for informed decision making and resource prioritization, improve the primary OA management, enhance patients' quality of life, as well as ultimately reducing the total healthcare spending associated with OA.

Methods

Study design and data sources

This is an observational longitudinal register-based cohort study using the data from the Swedish Population Register (SPR), the Skåne Healthcare Register (SHR) and the Longitudinal Integration Database for Health Insurance and Labour Market Studies (LISA by Swedish acronym). The SHR is a regional legislative administrative healthcare database covering all healthcare consultations (public and private) in the Skåne region from 1998 onwards. The LISA database contains annual individual level data on socioeconomic measures such as education, income and immigration status since 1990. These registers were linked using the personal identification number assigned to all residents in Sweden.

Study population

From the SPR, we identified all individuals aged 40–85 years resided in Skåne on 31 December 2005 and have been living there since 1 January 1998 ($n = 523\,926$). To minimize potential confounding due to propensity to seek care, we excluded 8670 individuals with no healthcare consultation recorded in the SHR during 1998–2005.

Exposure

Using International Classification of Disease, 10th revision (ICD-10) codes registered in the SHR, we identified persons who had been diagnosed with OA at peripheral joints (ICD-10 codes M15–M19)– *the exposure of interest*—as main diagnosis within primary or secondary care between 1 January 1998 and 31 December 2016. The OA was treated as a time-varying exposure with time from start of follow-up to the date of an OA diagnosis being treated as unexposed. Persons with an OA diagnosis prior to start of follow-up were treated as exposed for the whole study period. In our subgroup analyses, we also studied knee (ICD-10 code M17) and hip OA (ICD-10 code M16), which are the two most commonly affected joints.

Outcomes and follow-up

We used the definition of ACSCs developed by the Swedish National Board of Health and Welfare and Swedish Association of Local Authorities and Regions [27] to identify hospital admissions for ACSCs based on ICD-10 codes in the SHR (Supplementary Table S1, available at *Rheumatology* online). This list includes seven chronic conditions (anaemia; angina; asthma; chronic obstructive pulmonary disease (COPD); diabetes; heart failure; and hypertension) and six acute conditions (bleeding gastric ulcer; diarrhoea; ear, nose and throat infection; epileptic seizures; inflammatory diseases of female pelvic organs; and pyelitis). We studied the risk of any ACSC, any chronic ACSC, any acute ACSC, as well as the five most common conditions (angina; COPD; diabetes; heart failure; and pyelitis).

Each participant was followed from 1 January 2006 until the outcome of interest, death, relocation outside Skåne or 31 December 2016 (whichever occurred first).

Statistical analysis

We used Cox proportional hazards model to compute the relative effect [hazard ratio (HR)] of OA on time to hospitalization for ACSCs. We assessed the proportional hazards assumption (i.e. constant HR over time) using plots of Schoenfeld residuals and it was fulfilled for our exposure of interest (i.e. OA status). In cases where the assumption was not fulfilled for other covariates, we used a stratified Cox model. To assess absolute effect of OA, we used an additive hazard model, which is a flexible (at least as flexible as Cox model) semiparametric model for survival outcomes [28–30]. In the additive hazard model, the hazard is modelled as a linear

function of the explanatory variables plus an unspecified baseline hazard [29, 30]. One can interpret the effect estimate obtained from the model as the number of additional hospitalizations for ACSCs attributable to OA per unit of time (e.g. per 10 000 person-years). We confirmed the time-invariant effect of OA using the Kolmogorov–Smirnov test and plotting the cumulative coefficients and hence applied the additive hazard model with constant hazard difference for OA [29]. We allowed the effect of other covariates with time-variant hazard to change over time.

In both Cox and additive hazard models, we used time-on-study (i.e. follow-up time) as the time scale. All models were adjusted for participants' sex, age group (40–54, 55–64, 65–74 and 75–85 years), level of education (0–9 years, 10–12 years, 13 years and more, and missing), nativity (born in Sweden *vs* abroad) and marital status (not married, previously married and married) at the year 2005 as well as tertiles of average of household individualized disposable income, prior hospitalization for ACSCs (yes or no) and Charlson comorbidity index (0, 1, ≥2) [31] during 1998–2005.

In subgroup analysis, we performed our analyses separately in men and women. In two further subgroup analyses, we excluded those with an OA diagnosis or with a hospitalization for ACSC, prior to the start of follow-up (i.e. during 1998–2005). In a sensitivity analysis, we replaced Charlson comorbidity index with Elixhauser comorbidity index (0, 1, ≥2) [31]. Analyses were performed using STATA 15 (Stata Corporation, College Station, TX, USA) and R version 4.0.2 (package 'timereg').

Results

After exclusion of 34 persons with missing information on marital status or place of birth, a total of 515 222 individuals were included in the study (we included 4246 with missing information on education attainment as a subcategory in the analyses). Of these, 40 709 persons had an OA diagnosis prior to the start of follow-up and 75 820 were diagnosed with OA during follow-up. At baseline, individuals with OA were older and more often women than those without OA (Table 1). Moreover, the proportions of low education attainment, being married, born in Sweden, and having at least one comorbidity was greater in people with OA than those without. The proportion of persons with a hospitalization for ACSCs during 1998–2005 was comparable between two groups.

We observed 16 368 and 61 444 hospitalizations for ACSCs in those with and without OA, respectively, during the follow-up. The crude incidence rates were (95% CI) 239 (235, 242) and 151 (150, 152) per 10 000 person-years among OA and non-OA persons, respectively (Table 2). After adjustment for covariates, persons with OA had 11% higher hazard of hospitalization for

Table 1 Baseline characteristics of participants at baseline (1 January 2006)

	No OA	OA		
		Any site	Knee	Hip
N	398 693	116 529	61 378	31 154
Age at entry (years), mean (s.d.)	58.5 (9.4)	62.4 (11.4)	62.5 (11.4)	65.8 (10.8)
Women, %	49.6	60.9	59.0	58.3
Level of education, %				
0–9 years of education	31.2	34.6	35.7	38.1
10–12 years of education	42.1	42.6	42.2	39.8
≥13 years of education	25.8	22.1	21.3	21.5
Missing	0.9	0.7	0.8	0.6
Marital status at entry, %				
Never married	16.7	10.1	9.6	9.4
Previously married	25.9	29.0	28.8	30.9
Married	57.4	60.9	61.6	59.7
Born in Sweden, %	85.9	87.7	87.6	89.9
Income tertiles,[a] %				
Lowest tertile	34.4	29.9	30.6	29.2
Middle tertile	32.9	34.6	34.5	34.5
Highest tertile	32.7	35.5	34.9	36.3
Charlson comorbidity index,[a] %				
0	74.2	70.7	70.7	66.9
1	11.8	14.6	14.7	15.8
≥2	14.0	14.7	14.6	17.3
Hospitalization for ACSCs,[a] %	7.3	7.2	7.3	8.4

[a]Based on data from 1 January 1998 to 31 December 2005. ACSCs: ambulatory care-sensitive conditions.

TABLE 2 Number, rates, hazard ratios and hazard differences of hospitalization for ambulatory care-sensitive conditions by OA status

	Number of hospitalizations		Crude incidence rate per 10 000 person years (95% CI)		Hazard ratio (95% CI)[a]	No. of extra hospitalizations per 10 000 person-years (95% CI)[b]
	With OA	Without OA	With OA	Without OA		
Any ACSCs	16 368	61 444	238.6 (234.9, 242.2)	151.1 (149.9, 152.3)	1.11 (1.09, 1.13)	19.6 (15.7, 23.6)
Any chronic ACSCs	11 705	44 093	165.6 (162.6, 168.6)	106.7 (105.7, 107.7)	1.11 (1.08, 1.13)	11.9 (8.6, 15.1)
Angina	3504	13 535	47.4 (45.8, 49.0)	32.0 (31.4, 32.5)	1.26 (1.21, 1.30)	8.3 (6.6, 10.0)
COPD	1757	7264	23.2 (22.2, 24.3)	17.0 (16.6, 17.4)	0.86 (0.81, 0.90)	−4.0 (−5.2, −2.8)
Diabetes	3030	12 432	40.5 (39.0, 41.9)	29.2 (28.7, 29.7)	1.05 (1.00, 1.09)	0.5 (−1.1, 2.1)
Heart failure	4876	14 470	65.1 (63.3, 66.9)	33.9 (33.4, 34.5)	1.15 (1.11, 1.19)	7.1 (5.1, 9.0)
Any acute ACSCs	7076	23 709	96.1 (93.9, 98.4)	56.1 (55.4, 56.8)	1.13 (1.10, 1.16)	10.5 (8.1, 12.9)
Pyelitis	4572	13 414	61.1 (59.4, 62.9)	31.5 (30.9, 32.0)	1.16 (1.12, 1.20)	8.1 (6.3, 10.0)

[a]Obtained from Cox proportional hazard model adjusted for age, sex, education, income, marital status, nativity, Charlson comorbidity index and prior hospitalization for ACSCs. [b]Obtained from additive hazard model adjusted for age, sex, education, income, marital status, nativity, Charlson comorbidity index and prior hospitalization for ACSCs. ACSCs: ambulatory care-sensitive conditions; COPD: chronic obstructive pulmonary disease.

any ACSC than persons without OA (adjusted HR 1.11, 95% CI: 1.09, 1.13). In absolute terms, this translated into 19.6 (95% CI: 15.7, 23.6) more hospitalizations for ACSCs per 10 000 person-years in those with OA. The adjusted HRs for acute and chronic ACSCs were comparable (1.11 *vs* 1.13). Compared with persons without OA, those with OA were at increased hazard for all types of ACSCs except COPD where OA diagnosis was associated with 14% lower risk of hospitalization for COPD (adjusted HR 0.86, 95% CI: 0.81, 0.90). Among ACSCs, the greatest adjusted HR was estimated for angina (adjusted HR 1.26, 95% CI: 1.21, 1.30).

Assessing the risk of hospitalization for ACSCs in knee and hip OA revealed that while the HRs were generally comparable, only knee OA was associated with increased risk of hospitalization for diabetes (Fig. 1). Moreover, although both hip and knee OA were associated with decreased risk of COPD, the decreased risk was greater in knee OA. In absolute terms, knee and hip OA were associated with 26.1 (95% CI: 20.6, 31.6) and 30.4 (95% CI: 22.1, 38.7) more hospitalizations for any ACSC per 10 000 person-years (Supplementary Table S2, available at *Rheumatology* online). While the number of additional hospitalizations attributable to knee OA were slightly larger for chronic than acute ACSCs (15.7 *vs* 13.7 per 10 000 person-years), the opposite was seen for hip OA (16.8 *vs* 18.1 per 10 000 person-years).

Limiting the OA sample to the incident cases (i.e. those diagnosed with OA during follow-up) decreased the magnitude of the relative and absolute hazards, but the directions of the associations were generally the same as the main analysis (Table 3). Moreover, while in the main analysis, the absolute hazard for chronic ACSCs was slightly larger than acute ACSCs (11.9 *vs* 10.5 per 10 000 person-years), in the incident cases the estimates for chronic ACSCs were substantially smaller than acute ACSCs (1.8 *vs* 8.3 per 10 000 person years). In subgroup analysis excluding those with hospitalization for ACSCs prior to the start of follow-up, the estimates were almost identical to the main analysis (Supplementary Table S3, available at *Rheumatology* online). While the directions of associations between OA and hospitalization for ACSCs were generally comparable between men and women, there were some differences in term of the effect size. For instance, while among men both knee and hip OA were associated with decreased risk of hospitalization for COPD (Supplementary Fig. S1, available at *Rheumatology* online), this was case only for knee OA among women (Supplementary Fig. S2, available at *Rheumatology* online). Moreover, while among women additional hospitalizations attributable to OA for acute ACSCs was equal or larger than chronic ACSCs, among men the hospitalizations for chronic ACSCs were greater than acute ACSCs (Supplementary Table S2, available at *Rheumatology* online). Replacing Charlson with Elixhauser comorbidity index in the sensitivity analysis resulted in slight attenuation in estimated HRs with no influence on our conclusions (Supplementary Fig. S3,

available at *Rheumatology* online). The only exception was the associations with hospitalization for diabetes where 95% CI for knee OA included 1 (HR 1.04, 95% CI: 0.99, 1.10) and hip OA was associated with a decreased hazard (HR 0.93, 95% CI: 0.87, 1.00).

Discussion

In this large population-based cohort study, for the first time, we investigated the risk of hospitalizations for ACSCs due to OA. Our results showed that the crude incidence rate of hospitalization for any ACSCs was about 1.6-fold higher in persons with OA than those without OA. After adjustment for potential confounders, OA was associated with an 11% increased risk of hospitalization for any ACSCs, corresponding to about 20 additional hospitalizations for ACSCs per 10 000 person-years. Our subgroups analyses revealed some variations in the size and direction of our estimates by OA site, type of ACSCs, and participants' sex. For instance, there was an increased risk of hospitalization for diabetes in knee OA but not hip OA. Moreover, OA was associated with an increased risk of all types of ACSCs but COPD.

Because, to our best knowledge, this is the first investigation of the association between OA and hospitalization for ACSCs, there is no previous study with which to compare our findings. However, consistent with our findings, a previous study suggested an increased risk of hospitalization for ASCSs in persons with rheumatoid arthritis (RA) compared with age- and sex-matched controls without RA [32]. In addition, the observed increased risk of hospitalization for specific ACSCs (e.g. diabetes and heart failure) in our study is consistent with prior research [23–26]. For instance, Rahman *et al.* [24] found that OA is associated with a higher risk of hospital admission for heart failure with an adjusted relative risk of 1.15 (95% CI: 1.04, 1.28) which is similar to HR (1.15) estimated in our study. We also previously found a comparable HR (1.2) for association between OA and heart failure mortality in the Skåne region [33].

We speculate that the increased risk of hospitalization for ACSCs in our study might partially be explained by higher comorbidity rates in OA [6]. The high rate of coexistence of OA and other chronic conditions might possibly be a consequence of shared risk factors (e.g. ageing, obesity, smoking, physical inactivity) and common inflammatory and molecular pathways [21, 34]. Furthermore, OA is associated with pain and mobility limitations that might raise the risk of comorbidity including diabetes and cardiovascular diseases [22, 23, 25, 35]. Comorbidity increases the complexity of the

Fig. 1 Risk of hospitalization for ambulatory care-sensitive conditions associated with knee and hip OA

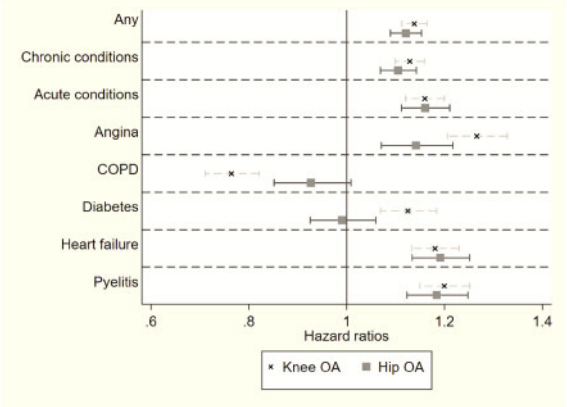

Table 3 Number, rates, hazard ratios and hazard differences of hospitalization for ambulatory care-sensitive conditions among incident OA cases

	Number of hospitalizations	Crude incidence rate per 10 000 person-years (95% CI)	Hazard ratio (95% CI)[a]	No. of extra hospitalizations per 10 000 person-years (95% CI)[b]
Any ACSCs	6471	188.5 (184.0, 193.2)	1.07 (1.04, 1.09)	7.9 (3.1, 12.8)
Any chronic ACSCs	4427	125.2 (121.5, 128.9)	1.05 (1.02, 1.08)	1.8 (−2.1, 5.7)
Angina	1357	36.8 (34.9,38.8)	1.20 (1.13, 1.27)	4.7 (2.6, 6.7)
COPD	712	18.9 (17.5, 20.3)	0.85 (0.78, 0.92)	−3.9 (−5.4, −2.4)
Diabetes	1086	29.1 (27.4, 30.8)	0.99 (0.92, 1.05)	−1.9 (−3.8, −0.1)
Heart failure	1833	49.0 (46.8, 51.3)	1.05 (1.00, 1.11)	2.5 (0.1, 4.8)
Any acute ACSCs	3072	83.7 (80.8, 86.7)	1.10 (1.06, 1.14)	8.3 (5.2, 11.4)
Pyelitis	1978	53.0 (50.8, 55.4)	1.09 (1.03, 1.14)	5.6 (3.2, 8.1)

[a]Obtained from Cox proportional hazard model adjusted for age, sex, education, income, marital status, nativity, Charlson comorbidity index and prior hospitalization for ACSCs. [b]Obtained from additive hazard model adjusted for age, sex, education, income, marital status, nativity, Charlson comorbidity index and prior hospitalization for ACSCs. ACSCs: ambulatory care-sensitive conditions; COPD: chronic obstructive pulmonary disease.

disease management for patients and healthcare providers leading to more disability, lower quality of healthcare, reduced continuity of care, increased exposure to medication and poor adherence to treatment [6, 36, 37]. It should be noted that while we adjusted for baseline comorbidity in our study, potential differences between persons with and without OA in the trajectory of comorbidity during follow-up should not be overlooked. Moreover, while Charlson and Elixhauser comorbidity indices include a long list of comorbidities, there might be other underlying diseases and comorbidity that are not captured by these indices. In addition to comorbidity, the management of OA might also increase the risk of hospitalization for ACSCs. For example, paracetamol and NSAIDs are widely used in OA management and recent evidence suggest that these are associated with increased risks of several ACSCs including heart diseases, diarrhoea and gastrointestinal diseases (e.g. peptic ulcer) [38–41]. While further research is required to explore the underlying reasons for increased risk of hospitalization for ACSCs among persons with OA, our findings call for a better management of these patients at outpatient care including access to multidisciplinary team, self-management support and tailored, person-centered care [42].

OA was associated with increased risk of hospitalization for all types of ACSCs but COPD. Previous research on the association between OA and COPD is limited and generally inconclusive [6, 43, 44]. Moreover, Mendy *et al.* [45] reported a decreased risk of mortality due to chronic lower respiratory disease for self-reported OA (HR 0.85) and an increased risk for radiographic knee OA (HR 1.21), albeit in both cases the 95% CI included one suggesting inconclusive findings. In addition, our previous study [33] suggested a lower hazard of mortality from respiratory diseases (including COPD) for knee and hip OA (with wide CIs for hip OA) which is consistent with findings from this study. Further research is warranted to identify mechanisms underlying the inverse association between OA and risk of hospitalization for COPD. Moreover, our subgroup analysis revealed that increased risk of hospitalization for diabetes was evident only for knee OA but not for hip OA. This is consistent with a recent meta-analysis that reported an increased risk of diabetes in patients with knee OA but not for hip OA [46]. This difference might likely be largely explained by stronger association between obesity and knee OA as compared with hip OA, and thus metabolic factors associated with obesity [47, 48].

The use of register-based data, which in its original format is continuously and prospectively ascertained, with limited selection and no recall bias from a large population-based sample with long follow-up are the main strengths of this study. Moreover, we reported both relative and absolute hazard differences that provide more insightful knowledge for policy-making. However, several limitations of the current study should be pointed out. High BMI is a common risk factor for OA and several ACSCs, but no data on BMI was available in the registers. Lack of adjustment for BMI and other risk factors, particularly health-risk behaviours such as smoking and alcohol consumption, may have inflated our estimates. We used diagnostic codes assigned by doctors as source to identify people with OA which might suffer from coding errors and misclassification, even though a previous study reported a high positive predictive value (88%) of knee OA diagnosis in the SHR [4]. Moreover, persons with OA who didn't seek healthcare or those who have solely visited private caregivers are not captured in our data (diagnosis codes within private care are not transferred to the SHR). We also lack data on the severity of OA and severity of comorbidities. Our study has been conducted in Sweden, which has universal access to healthcare that limits the generalizability of our findings to many other countries. In addition, we used the list of ACSCs developed by Swedish authorities, which limits cross-study comparability. Given these limitations and the observational design of our study, any casual inference from our findings should be avoided.

Conclusion

In this large population-based longitudinal study, we found that OA is associated with an increased risk of hospitalization for ACSCs, even though there were some heterogeneities in the association by OA site, type of ACSC and participants' sex. Further research is needed to explore underlying mechanisms linking OA to hospitalization for ACSCs. Our findings highlight the urgent need to improve outpatient care for OA patients including monitoring of comorbidities and self-management support.

Acknowledgements

A.K. and M.E. conceived the study. A.K. designed the study, performed the statistical analysis and drafted the manuscript. M.E. participated in acquisition of data and revising the manuscript critically for important intellectual content. Both authors contributed to the interpretation of the results and approved the final manuscript for submission. This study received ethical approval from the Lund University Ethical Review Committee (Dnr 2011–432 and 2014–276).

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Data availability statement

No data are available. The data supporting the findings of this study are available within the article and its Supplementary Information files or upon reasonable request.

Supplementary data

Supplementary data are available at *Rheumatology* online.

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