

# Gout and Hospital Admission for Ambulatory Care–Sensitive Conditions: Risks and Trajectories

Ali Kiadaliri<sup>1</sup> , Tuhina Neogi<sup>2</sup> , and Martin Englund<sup>3</sup> 

**ABSTRACT.** *Objective.* To investigate the risks and trajectories of hospital admission for ambulatory care–sensitive conditions (ACSCs) in gout.

*Methods.* Among individuals aged 35 years to 85 years residing in Skåne, Sweden, in 2005, those with no doctor-diagnosed gout during 1998 to 2005 ( $n = 576,659$ ) were followed from January 1, 2006, until a hospital admission for an ACSC, death, relocation outside Skåne, or December 31, 2016. Treating a new gout diagnosis (International Classification of Diseases, 10th revision, code M10) as a time-varying exposure, we used Cox proportional and additive hazard models to estimate the effects of gout on hospital admissions for ACSCs. We investigated the trajectory of hospital admissions for ACSCs from 3 years before to 3 years after gout diagnosis using generalized estimating equations and group-based trajectory modeling in an age- and sex-matched cohort study.

*Results.* Gout was associated with a 41% increased rate of hospital admission for ACSCs (hazard ratio 1.41, 95% CI 1.35–1.47), corresponding to 121 (95% CI 104–138) more hospital admissions for ACSCs per 10,000 person-years compared with those without gout. Our trajectory analysis showed that higher rates of hospital admission for ACSCs among persons with gout were observed from 3 years before to 3 years after diagnosis, with the highest prevalence rate ratio (2.22, 95% CI 1.92–2.53) at the 3-month period after diagnosis. We identified 3 classes with distinct trajectories of hospital admissions for ACSCs among patients with gout: almost none (88.5%), low-rising (9.7%), and moderate-sharply rising (1.8%). The Charlson Comorbidity Index was the most important predictor of trajectory class membership.

*Conclusion.* Increased risk of hospital admissions for ACSCs in gout highlights the need for better management of the disease through outpatient care, especially among foreign-born, older patients with comorbidities.

*Key Indexing Terms:* ambulatory care, gout, heterogeneity, hospitalization, longitudinal study, population registers

Gout is the most common form of inflammatory arthritis experienced by 0.7% to 1.7% of people aged  $\geq 18$  years in Sweden.<sup>1,2</sup> Uncontrolled gout can cause pain, joint deformity, impaired quality of life, and disability. There have been increasing trends in the incidence of the prevalence of gout in many countries, possibly as a result of changes in lifestyle and of an aging population with increased multimorbidity.<sup>3</sup> For instance, the

age-standardized hospitalization rate for gout almost doubled between 1998–2000 and 2013–2015 in Sweden.<sup>4</sup> Moreover, the number of years lived with disability attributable to gout rose by 25% between 1990 and 2015 in Sweden.<sup>5</sup>

Gout is also associated with the cooccurrence of multiple conditions, particularly metabolic, cardiovascular (CV), and renal diseases.<sup>6–8</sup> For instance, the prevalence of diabetes, obesity, hypertension, and renal disease was approximately 1.5 times to 2.6 times higher among people with gout than sex- and age-matched controls without gout in Sweden.<sup>6</sup> The importance of these coexisting conditions in the management of gout has been acknowledged in current clinical guidelines and recommendations.<sup>9,10</sup> The presence of these coexisting conditions has been suggested as a driver of substantial healthcare use including hospitalization in people with gout.<sup>3,11</sup> The presence of comorbidity can complicate the management of gout and might potentially lead to fragmented care including suboptimal care and nonadherence to treatment, which is common among persons with gout.<sup>12,13</sup> Both comorbidities and suboptimal care can, in turn, contribute to increased inpatient care, including preventable hospital admissions and readmissions.<sup>14–17</sup> For instance, Sharma et al<sup>14</sup> reported that 89% of hospital admissions with a primary diagnosis of gout were preventable (defining preventable admission as an admission with the primary admitting

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<sup>1</sup>A. Kiadaliri, PhD, Clinical Epidemiology Unit, Department of Clinical Sciences Lund, Orthopaedics, and Centre for Economic Demography, Lund University, Lund, Sweden; <sup>2</sup>T. Neogi, MD, PhD, Section of Rheumatology, Boston University School of Medicine, Boston, Massachusetts, USA;

<sup>3</sup>M. Englund, MD, PhD, Clinical Epidemiology Unit, Department of Clinical Sciences Lund, Orthopaedics, Lund University, Lund, Sweden.

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Address correspondence to Dr. A. Kiadaliri, Skåne University Hospital, Clinical Epidemiology Unit, Remissgatan 4, SE-221 85 Lund, Sweden. Email: ali.kiadaliri@med.lu.se.

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diagnosis as mono- or polyarthritis subsequently diagnosed as gout on hospitalization) in their sample.

However, a more commonly used measure of preventable hospitalization is hospital admission for ambulatory care-sensitive conditions (ACSCs).<sup>18</sup> The concept of ACSCs is based on the idea that for some chronic and acute conditions, “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.”<sup>18</sup> Hospitalizations for ACSCs are associated with increased healthcare expenditures and reflect ineffectiveness of primary healthcare,<sup>19</sup> and hence, have important policy implications. Despite high burden of comorbidity in gout, particularly ACSCs such as diabetes, hypertension, and chronic obstructive pulmonary disease (COPD),<sup>6,7</sup> there is limited evidence on hospital admissions for ACSCs among persons with gout. In particular, the evidence on the longitudinal pattern (trajectory) of hospital admissions for ACSCs and its variability is scarce. This study aims to address this knowledge gap by exploring the risks and trajectories of hospital admissions for ACSCs among persons with gout using individual-level, longitudinal, register-based data from Sweden.

## METHODS

**Study design and data sources.** This is an observational, longitudinal, register-based (matched) cohort study conducted in Skåne, the southernmost region of Sweden, with approximately 1.4 million inhabitants (13% of the Sweden population). We used data from the Swedish Population Register (SPR), the Skåne Healthcare Register (SHR), and the Longitudinal Integration Database for Health Insurance and Labour Market Studies (abbreviated to LISA by Swedish acronym). The SHR is a regional legislative administrative healthcare database covering all healthcare consultations (public and private) in the region from 1998 onwards. The LISA database contains annual individual-level data on socioeconomic measures such as education, income, and immigration status from 1990 onwards. These registers were linked using the unique personal identification number, which was replaced with an arbitrary code by the Swedish authorities to ensure the anonymity of the subjects. This study received ethical approval from the Lund University ethical review committee (Dnr 2011-432 and 2014-276). The need for individual informed consent was waived by the ethics committee. The study was advertised in the major newspapers, where a possibility to opt out was offered. This is a principle used in Sweden for population-wide studies using nonidentifiable register data.

**Study population and exposure.** From the SPR, we identified people aged 35 to 85 years who resided in Skåne on December 31, 2005, and who have been living in the region since January 1, 1998 (N = 590,797). We excluded 9945 individuals with no healthcare consultation recorded in the SHR during 1998 to 2005 in order to minimize potential confounding as a result of propensity to seek care. In addition, since we were interested in gout incidence, we excluded 4152 individuals with a principal diagnosis of gout (International Classification of Diseases, 10th revision [ICD-10], code M10) in the SHR from 1998 to 2005. We then identified those with a new principal diagnosis of gout (ICD-10 code M10)—the exposure of interest—within primary or secondary care between January 1, 2006, and December 31, 2016 (n = 16,043). A previous study reported the validity of this case definition against the use of allopurinol in the SHR.<sup>2</sup> Moreover, comorbidity and socioeconomic patterns for this case definition were comparable to more stringent case definitions in Sweden.<sup>2,6</sup> We treated gout

as a time-varying exposure, meaning that people were treated as unexposed up to the date of gout diagnosis.

To investigate the trajectory of hospital admissions for ACSCs from 3 years before to 3 years after gout diagnosis, we matched persons with their first gout diagnosis during 2006 to 2013 (n = 10,115) by age and sex with up to 4 persons without gout (n = 40,454).

**Hospital admission for ACSCs.** To identify hospital admissions for ACSCs, we adopted the definition of avoidable hospitalization developed by the Swedish National Board of Health and Welfare and Swedish Association of Local Authorities and Regions (Supplementary Table S1, available with the online version of this article).<sup>20</sup> A total of 7 chronic conditions (anemia, angina, asthma, COPD, diabetes, heart failure, and hypertension) and 6 acute conditions (bleeding gastric ulcer; diarrhea; ear, nose, and throat infections; epileptic seizures; inflammatory diseases of female pelvic organs; and pyelitis) are included in this definition.

**Statistical analysis.** We applied the Cox proportional hazards model and additive hazard model (using R *timereg* Package; [www.jstatsoft.org/v38/i02](http://www.jstatsoft.org/v38/i02)) to assess the relative and absolute effects of gout on the risks of hospital admission for ACSCs. Using time-on-study (ie, follow-up time) as the time scale in both the Cox and additive hazard models, we followed each participant from January 1, 2006, until the outcome of interest, death, or relocation outside Skåne, or December 31, 2016 (whichever occurred first). The proportional hazards assumption for Cox regression was assessed using plots of Schoenfeld residuals and the stratified Cox model was used whenever the assumption was not fulfilled for a covariate. We used the Kolmogorov-Smirnov test and plotted the cumulative coefficients to confirm the time-invariant effect of gout, and hence, applied the additive hazard model with constant hazard difference for gout.<sup>21</sup> The effects of other covariates with time-variant hazard were allowed to change over time. The absolute hazard obtained from the additive hazard model can be interpreted as the number of additional hospital admissions for ACSCs attributable to gout per unit of time. We investigated the risks of all ACSCs, chronic ACSCs, acute ACSCs, as well as 5 single conditions (angina, COPD, diabetes, heart failure, and pyelitis). These analyses were also repeated for males, females, and those with no history of hospital admission for ACSCs from 1998 to 2005.

For trajectory analysis, we divided our data into 3-month periods (12 periods prior to and 12 periods after a gout diagnosis). Persons without gout were assigned the same diagnosis date as their gout-matched subject. We then examined if a person had a hospital admission for an ACSC in each period (yes or no). To account for the dependencies of observations for each individual, we applied generalized estimating equations (GEE).<sup>22</sup> We used modified Poisson regression (ie, GEE with Poisson distribution and log link function) with robust standard errors to compute prevalence rate ratios (PRRs) and 95% CIs comparing people with gout to those without.<sup>23</sup> We applied an unstructured covariance matrix based on the quasi-likelihood under independence model criterion selection criterion.<sup>24</sup> We used inverse probability weighting to account for dropout during the follow-up (using the Stata “*xtrecipw*” command).<sup>25</sup> Using these data, we applied semiparametric, group-based trajectory modeling (GBTM) to identify (potential) variability in the trajectory of hospital admission for ACSCs among people with gout.<sup>26</sup> This was done using the Stata “*traj*” command.<sup>27</sup> GBTM is a data-driven approach dividing the sample under study into classes assuming individuals within each class follow exactly the same trajectory over time.<sup>26</sup> Since hospital admission for ACSCs was a binary outcome, we used logistic distribution in our estimation. The final model was selected based on a combination of the Bayesian information criterion (lower value indicates better fit), average posterior probability of class membership (> 0.7 for each class), the odds of correct classification (> 5 for each class), class size (≥ 1% of participants in the smallest class), and relative entropy (values closer to 1 reflect better fit).<sup>26,28</sup> We also considered model parsimony and interpretability in selecting the final model.<sup>28</sup> After estimating the final model, we used the

posterior probability to assign each individual to the class with the highest probability. We then used class membership as an outcome and explored its associations with baseline characteristics using multinomial logistic regression. We used polytomous discrimination index (PDI, using R package: mcca; <https://cran.r-project.org/web/packages/mcca/index.html>), and the McFadden pseudo- $R^2$  to assess the predictive ability of baseline characteristics.<sup>29,30</sup> For an outcome with  $k$  categories, PDI calculates the probability that a subject from a randomly chosen category is correctly identified within a set of  $k$  subjects (1 from each  $k$  category) with random performance reflected by  $1/k$ . To explore the relative importance of each predictor in predicting class membership, we computed the contribution of each predictor to the change in the McFadden pseudo- $R^2$  across all possible subset models using dominance analysis (Stata “domin” command).<sup>31</sup>

We adjusted for the following covariates in our statistical analyses (all measured at baseline; ie, prior to a gout diagnosis): sex, age, level of education, nativity (born in Sweden vs abroad), marital status, household individualized disposable income, prior hospitalization for ACSCs (yes or no), obesity (ICD-10 code E66), diabetes (ICD-10 codes E10-E14), chronic pulmonary disease (ICD-10 codes I278-I279, J40-J47, J60-J67, J684, J701, and J703), renal disease (I120, I131, N032-N037, N052-N057, N18-N19, N250, Z490-Z492, Z940, and Z992), and Charlson Comorbidity Index (CCI; 0, 1,  $\geq 2$ ). The last 7 covariates were measured using the data from the period 1998 to 2005. The comorbidities were identified using the doctor-diagnosed codes in the SHR. Inclusion of the specific comorbidities, in addition to the CCI, was done in order to reach a better adjustment for difference in comorbidity burden between people with and without gout.

Table 1. Baseline characteristics of study participants.

	Reference		Gout	
	All	Matched Analysis	All	Matched Analysis
N	560,616	40,454	16,043	10,115
Age at baseline, yrs, mean (SD)	56.6 (13.6)	64.2 (12.6)	63.3 (12.4)	64.2 (12.6)
Female	296,079 (52.8)	12,012 (29.7)	4837 (30.2)	3003 (29.7)
Level of education, yrs				
0-9	163,611 (29.2)	15,203 (37.6)	6475 (40.3)	4232 (41.8)
10-12	245,392 (43.8)	16,236 (40.1)	6565 (40.9)	4057 (40.1)
$\geq 13$	147,355 (26.3)	8629 (21.3)	2880 (18.0)	1737 (17.2)
Missing	4258 (0.8)	386 (1.0)	123 (0.8)	89 (0.9)
Marital status at entry				
Never married	103,489 (18.5)	5426 (13.4)	1842 (11.5)	1105 (10.9)
Previously married	138,358 (24.7)	10,491 (25.9)	4207 (26.2)	2778 (27.5)
Married	318,769 (56.9)	24,537 (60.7)	9994 (62.3)	6232 (61.6)
Born outside Sweden	77,081 (13.8)	5141 (12.7)	1811 (11.3)	1188 (11.7)
Income tertile <sup>a</sup>				
Lowest	187,700 (33.5)	12,091 (29.9)	4654 (29.0)	3137 (31.0)
Middle	186,560 (33.3)	13,650 (33.7)	5502 (34.3)	3513 (34.7)
Highest	186,356 (33.2)	14,713 (36.4)	5887 (36.7)	3465 (34.3)
CCI <sup>a</sup> , mean (SD)	0.5 (1.2)	0.6 (1.2)	0.9 (1.4)	1.0 (1.5)
CCI <sup>a</sup>				
0	426,879 (76.1)	27,832 (68.8)	9717 (60.6)	5699 (56.3)
1	64,382 (11.5)	5790 (14.3)	2834 (17.7)	1879 (18.6)
$\geq 2$	69,355 (12.4)	6832 (16.9)	3492 (21.7)	2537 (25.1)
Hospital admission for ACSC <sup>a</sup>	35,486 (6.3)	3564 (8.8)	2221 (13.8)	1644 (16.3)
Obesity <sup>a</sup>	10,283 (1.8)	627 (1.6)	683 (4.3)	458 (4.5)
Diabetes <sup>a</sup>	33,147 (5.9)	3269 (8.1)	1769 (11.0)	1243 (12.3)
Chronic pulmonary disease <sup>a</sup>	32,219 (5.8)	2371 (5.9)	1342 (8.4)	959 (9.5)
Renal disease <sup>a</sup>	3065 (0.6)	250 (0.6)	302 (1.9)	258 (2.6)

Values are n (%) unless otherwise indicated. <sup>a</sup> Based on data from January 1, 1998, to December 31, 2005. ACSC: ambulatory care–sensitive condition; CCI: Charlson Comorbidity Index.

## RESULTS

After excluding 41 persons with missing information on marital status and/or place of birth, a total of 576,659 individuals with no gout diagnosis during 1998 to 2005 were included in the study. Of these, 2.8% had a principal gout diagnosis during 2006 to 2016. Compared with the reference cohort, those with gout were older and included more men (Table 1). Moreover, the proportion of persons with  $\geq 2$  comorbidities and hospital admission for ACSCs during 1998 to 2005 were approximately 2 times to 2.5 times higher than those without gout.

*Risk of hospital admission for ACSCs.* During follow-up, there were approximately 382 (95% CI 366-399) and 142 (95% CI 141-143) hospital admissions for ACSCs per 10,000 person-years (PY) in persons with and without gout, respectively (Table 2). The adjusted hazard ratio (HR) was 1.41 (95% CI 1.35-1.47) which corresponds to 121 (95% CI 104-138) extra hospital admissions for ACSCs per 10,000 PY among people with gout compared with those without. Among individual ACSCs, adjusted HRs ranged from 1.20 (95% CI 1.06-1.36) for COPD to 1.83 (95% CI 1.71-1.96) for heart failure. The magnitudes of HRs were generally comparable for males and females (Supplementary Table S2, available with the online version of this article). Excluding those with a hospital admission for ACSCs during 1998 to 2005 did not alter our findings.

Table 2. Number, rates, HRs, and hazard differences of hospitalization for ACSCs by gout status.

	No. of Hospital Admissions		Crude Incidence Rate Per 10,000 PY (95% CI)		HR (95% CI) <sup>a</sup>	No. of Extra Hospital Admissions Per 10,000 PY (95% CI) <sup>b</sup>
	With Gout	Without Gout	With Gout	Without Gout		
Any ACSC	2002	76,267	382 (366-399)	142 (141-143)	1.41 (1.35-1.47)	121 (104-138)
Any chronic ACSC	1561	53,953	284 (271-299)	99 (98-100)	1.49 (1.41-1.56)	97 (83-111)
Angina	437	16,503	71 (65-78)	30 (29-30)	1.36 (1.23-1.50)	18 (11-25)
COPD	264	8654	41 (36-46)	15 (15-16)	1.20 (1.06-1.36)	9 (4-14)
Diabetes	515	14,869	82 (75-89)	27 (26-27)	1.51 (1.38-1.65)	25 (18-32)
Heart failure	926	17,925	151 (141-161)	32 (31-32)	1.83 (1.71-1.96)	77 (68-87)
Any acute ACSC	944	30,429	152 (143-162)	55 (54-55)	1.32 (1.23-1.41)	47 (38-57)
Pyelitis	648	17,376	102 (94-110)	31 (31-32)	1.33 (1.22-1.44)	36 (28-44)

<sup>a</sup> Estimated using Cox proportional hazard model adjusted for age, sex, education, income, marital status, nativity, obesity, diabetes, chronic pulmonary disease, renal disease, CCI, and prior hospitalization for ACSCs. <sup>b</sup> The number of extra hospitalizations for ACSCs per 10,000 PY and estimated using an additive hazard model adjusted for age, sex, education, income, marital status, nativity, obesity, diabetes, chronic pulmonary disease, renal disease, CCI, and prior hospitalization for ACSCs. ACSC: ambulatory care-sensitive condition; CCI: Charlson Comorbidity Index; COPD: chronic obstructive pulmonary disease; HR: hazard ratio; PY: person-year.

**Mean trajectory.** The prevalence of hospital admissions for ACSCs was at least 1.5 times higher in persons with gout than their sex- and age-matched controls from 3 years before to 3 years after diagnosis, with the highest PRR (2.22, 95% CI 1.92-2.53) at the 3-month period immediately after diagnosis (Figure 1). A similar pattern was seen for chronic conditions. For acute conditions, while PRR was generally > 1, there was high uncertainty

with a wide 95% CI spanning 1 (the only exceptions were the immediate 3-month periods before and after the diagnosis date). **Variability in trajectory among people with gout.** Our GBTM suggested that the final model consisted of 3 classes, with 1 class with only intercept term, 1 with intercept and linear terms, and 1 with intercept, linear, and quadratic terms (Supplementary Table S3, available with the online version of this article). The

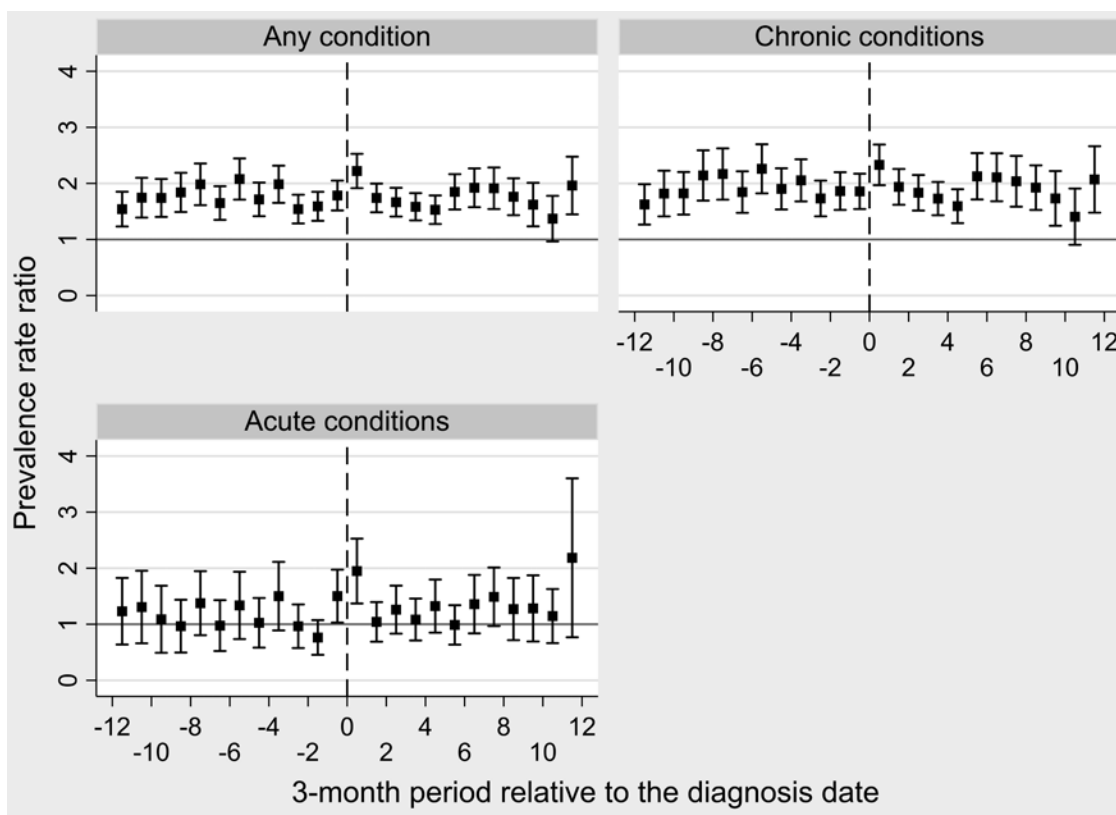


Figure 1. Prevalence rate ratio (95% CIs) for hospital admission for ambulatory care-sensitive conditions among patients with gout compared with age- and sex-matched controls without gout.

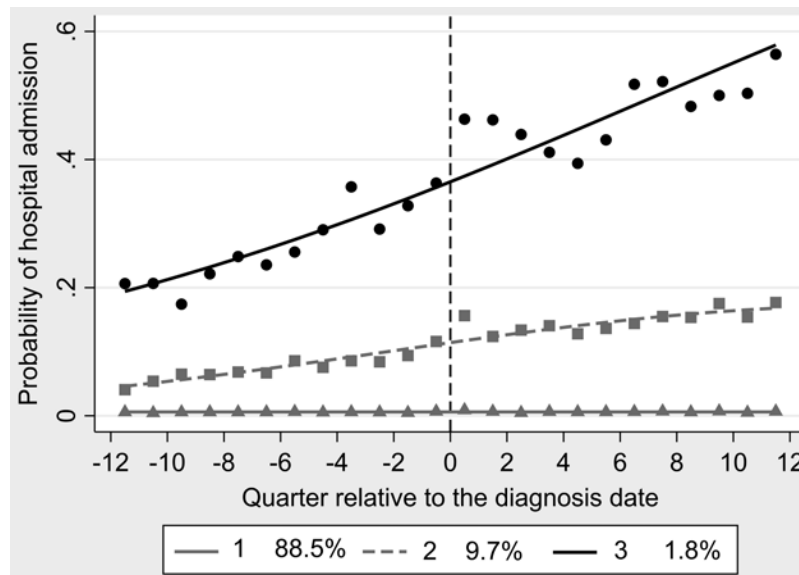


Figure 2. Distinct trajectory classes of hospital admission for ambulatory care-sensitive conditions among patients with gout starting from 3 years prior to 3 years after diagnosis (observed: symbols, estimated: solid line). Class 1: almost none; class 2: low-rising; class 3: moderate-sharply rising).

largest trajectory class included 8951 (88.5%) of patients with gout with almost no hospital admission for ACSCs (mean 0.02 admissions/yr) from 3 years prior to and 3 years after gout diagnosis (Figure 2). Trajectory class 2 (9.7% of patients with gout) was characterized by low initial probability of hospital admission for ACSCs which increased over the study period (mean 0.47 admissions/yr). The smallest trajectory class (1.8%) included those patients with a moderate probability of hospital admission for ACSCs at the start of follow-up which sharply rose over time (mean 1.2 admissions/yr). Patients in trajectory class 1 were, on average, younger, had higher education and income, were born in Sweden, had lower comorbidity, and had lower previous history of hospital admission for ACSCs (Table 3).

The results of multinomial logistic regression (Table 4) suggested that being male, of older age, born outside Sweden, having a higher comorbidity index, having a history of obesity, diabetes, and chronic pulmonary disease, as well as previous hospital admission for ACSCs were associated with higher odds of membership in trajectory classes 2 (low-rising) or 3 (moderate-sharply rising) relative to trajectory class 1 (almost none). The baseline covariates, however, had a moderate predictive ability in predicting the trajectory class membership with a PDI of 0.59 (95% CI 0.58-0.60) and a McFadden pseudo- $R^2$  of 0.21. Dominance analysis indicated that CCI followed by previous hospital admission for ACSCs, age, and history of diabetes diagnosis at baseline had the greatest relative importance in predicting trajectory class membership (Supplementary Figure S1, available with the online version of this article).

## DISCUSSION

We assessed, for the first time to our knowledge, the risk and trajectory of hospital admission for ACSCs among patients

with gout in a large population-based cohort study. We found that after adjustment for potential confounders, gout was associated with a 41% elevated rate of hospital admission for any ACSC. In absolute terms, there were 121 more admissions for ACSCs per 10,000 PY among persons with gout than those without. Moreover, compared with sex- and age-matched controls, the increased risk of hospital admission for ACSCs were seen from 3 years before to 3 years after gout diagnosis, with the greatest risk observed around the date of diagnosis. We also identified 3 distinct trajectories of hospital admission for ACSCs among patients with gout: almost none, low-rising, and moderate-sharply rising. Older age, being an immigrant, having higher comorbidity burden, and previous hospital admission for ACSCs were associated with lower odds of membership in the "almost none" trajectory class.

Previous studies have reported high proportions of avoidable hospital admission among those admitted with a primary diagnosis of gout.<sup>14,17</sup> Consistent with these, we also found a high prevalence of avoidable hospital admissions among patients with gout compared with the reference population free of gout, even though previous studies only included hospitalized patients with gout and applied a different definition of avoidable hospital admission, which make the cross-study comparison difficult. Moreover, elevated risks of hospital admission for a single ACSC among patients with gout have been documented.<sup>32-34</sup> For instance, Colantonio et al<sup>32</sup> reported a HR of 1.97 (95% CI 1.22-3.19) for heart failure hospital admission, which is comparable to the 1.83 (95% CI 1.71-1.96) reported in this study. In addition, our findings are in line with elevated risks of hospital admission for ACSCs reported for rheumatoid arthritis<sup>35</sup> and osteoarthritis (OA).<sup>36</sup> More importantly, in our previous study in the Skåne region, we found that OA was associated with an

Table 3. Description of the latent trajectory classes of hospital admission for ACSCs among patients with gout.

	Class 1 (Almost None)	Class 2 (Low-Rising)	Class 3 (Moderate-Sharply Rising)
N	8951	977	187
No. of 3-month periods with a hospitalization for any ACSC, mean/median	0.1/0	2.8/2	7.2/7
Females, %	29.2	34.4	27.3
Age at baseline, yrs, mean (SD)	63.1 (12.7)	72.3 (9.2)	72.3 (8.9)
Age at baseline, yrs, %			
35-49	16.8	2.3	2.7
50-64	35.0	18.1	15.5
65-74	26.3	31.9	34.2
75-85	21.9	47.7	47.6
Level of education, yrs, %			
0-9	40.4	53.4	52.4
10-12	40.9	33.7	34.2
≥ 13	18.0	11.2	9.1
Missing	0.7	1.7	4.3
Marital status, %			
Never married	11.3	9.0	5.9
Previously married	26.6	33.8	34.2
Married	62.1	57.2	59.9
Born outside Sweden, %	11.3	13.8	20.3
Income tertile <sup>a</sup> , %			
Lowest	29.9	39.7	39.6
Middle	34.4	37.3	38.0
Highest	35.7	23.0	22.4
CCI <sup>a</sup> , mean (SD)/median	0.8 (1.3)/0	2.3 (2.0)/2	3.7 (2.5)/3
CCI <sup>a</sup> , %			
0	61.2	21.1	8.6
1	18.3	21.9	12.3
≥ 2	20.5	57.0	79.1
Hospitalization for ACSC <sup>a</sup> , %	12.1	44.5	66.8
Obesity <sup>a</sup>	4.1	8.2	8.0
Diabetes <sup>a</sup>	9.2	32.5	54.6
Chronic pulmonary disease <sup>a</sup>	7.7	21.2	31.6
Renal disease <sup>a</sup>	2.0	5.8	9.6

<sup>a</sup> Based on data from January 1, 1998, to December 31, 2005. ACSC: ambulatory care-sensitive condition; CCI: Charlson Comorbidity Index.

11% higher rate of hospital admissions for ACSCs, which was substantially lower than the 41% higher rate estimated for gout in this study.<sup>36</sup>

We speculate that the observed associations between gout and hospital admission for ACSCs might be attributable to chronic inflammation caused by gout,<sup>37</sup> which is associated with increased risks of several ACSCs including CV diseases,<sup>38</sup> epilepsy,<sup>39</sup> and type 2 diabetes.<sup>40</sup> Limitations in patients' physical functioning caused by gout might be another potential explanation of the increased risks in our present study.<sup>41</sup> Nonsteroidal antiinflammatory drugs used in gout treatment have also been associated with increased risks of several ACSCs.<sup>42,43</sup> Moreover, the observed associations might, at least partially, be a consequence of unmeasured confounding such as hyperuricemia,<sup>44</sup> obesity,<sup>45</sup> and alcohol consumption.<sup>46</sup> It also should be noted that despite adjustment for CCI in our analyses, the possible contribution of other comorbidities not captured by the index

should not be overlooked. Higher risks of hospital admission for ACSCs from 3 years before diagnosis in our trajectory analysis might be a result of a lag between gout presence and its diagnosis.<sup>6</sup> In addition, the observed spike in PRR in the quarter of diagnosis is consistent with patterns in healthcare use in persons with gout and might be possibly explained by increased disease activity leading to other health problems and higher healthcare needs.<sup>47</sup> However, we cannot rule out that such a spike might be partially a result of increased monitoring and/or higher propensity for hospital admission among newly diagnosed patients with gout. Regardless of the mechanisms underlying the association between gout and hospital admission for ACSCs, the elevated risk of these avoidable hospital admissions possibly reflects suboptimal management of gout and its comorbidities in the outpatient care setting (eg, rheumatology clinics), medication noncompliance, and poor adherence to treatment guidelines as suggested in previous studies.<sup>48,49</sup> Indeed, a previous systematic

Table 4. ORs and 95% CIs for trajectory class membership.

	Class 3 (Moderate-Sharply Rising) vs Class 1 (Almost None)	Class 2 (Low-Rising) vs Class 1 (Almost None)
Sex (female = 1)	0.59 (0.41-0.86)	0.86 (0.73-1.02)
Age at baseline	1.04 (1.02-1.06)	1.06 (1.05-1.07)
Level of education, yrs		
0-9	Ref	Ref
10-12	0.98 (0.69-1.39)	0.96 (0.82-1.13)
≥ 13	0.70 (0.40-1.23)	0.88 (0.69-1.12)
Missing	2.84 (1.11-7.28)	1.28 (0.68-2.42)
Marital status		
Never married	Ref	Ref
Previously married	1.15 (0.57-2.32)	0.75 (0.56-0.99)
Married	1.01 (0.52-1.95)	0.69 (0.53-0.90)
Born outside Sweden	1.68 (1.09-2.60)	1.26 (1.01-1.57)
Income tertile <sup>a</sup>		
Lowest	Ref	Ref
Middle	1.00 (0.69-1.44)	0.97 (0.82-1.16)
Highest	0.84 (0.54-1.30)	0.76 (0.62-0.93)
Charlson Comorbidity Index <sup>a</sup>	1.49 (1.36-1.64)	1.22 (1.15-1.29)
Hospitalization for ACSC <sup>a</sup> (yes = 1)	4.32 (3.05-6.11)	2.68 (2.28-3.16)
Obesity <sup>a</sup>	1.28 (0.70-2.34)	1.87 (1.40-2.50)
Diabetes <sup>a</sup>	2.74 (1.88-4.00)	1.99 (1.62-2.43)
Chronic pulmonary disease <sup>a</sup>	2.09 (1.44-3.02)	1.74 (1.42-2.13)
Renal disease <sup>a</sup>	0.75 (0.40-1.40)	0.94 (0.65-1.37)

<sup>a</sup> Based on data from January 1, 1998 to December 31, 2005. ACSC: ambulatory care-sensitive condition; OR: odds ratio.

review reported that lower adherence to treatment is associated with higher hospitalization costs in gout.<sup>3</sup>

We identified 3 subgroups with a distinct trajectory of hospital admission for ACSCs from 3 years prior to 3 years after gout diagnosis. While the majority (88.5%) of patients with gout had almost no experience of hospital admissions for ACSCs, approximately 2% of patients experienced a moderate-sharply rising trajectory. A higher number of comorbidities, previous hospital admission for ACSCs, older age, and birth outside of Sweden were associated with higher odds of membership in the latter than former subgroup. Moreover, comorbidity had a greater relative importance than other covariates in predicting trajectory class membership. Previous studies also identified comorbidity as an important predictor of hospital readmission and healthcare costs in gout.<sup>3,11,16</sup> Moreover, higher hospital admission for ACSCs among foreign-born patients with gout is consistent with the patterns in the general population, where the rates of hospital admission for ACSCs are higher among immigrants and ethnic minorities.<sup>50</sup> These results highlight the importance of comorbidity management among patients with gout, especially older, foreign-born patients. Moreover, the moderate predictive accuracy of patients' sociodemographic and clinical characteristics in identifying the trajectory class membership calls for further research.

This study is not without limitations. Data from administrative sources are prone to misclassification and coding errors. More importantly, since these registries were established mainly for healthcare planning and reimbursement purposes, there is a

lack of data on several confounders such as hyperuricemia, BMI, serum urate levels, dietary patterns, and health-risk behaviors. In addition, we lack data on the severity of gout and comorbidities. These imply that the observed associations in this study might be explained by unmeasured confounding. Nonetheless, it should be noted that adjustment for comorbidities is expected to reduce the bias resulting from these unmeasured factors. Using the data from the Skåne region and the list of ACSCs developed by Swedish authorities might limit the generalizability of our findings as well as cross-country comparisons. It also should be noted that hospital admission for ACSCs is only an (incomplete) surrogate for the quality of and access to ambulatory care. Moreover, register data used in this study did not allow us to determine the extent to which the admission for ACSCs were actually avoidable. One should also note that trajectory classes identified in this study should be treated as an approximation of a more complex underlying reality, not as "real entities."<sup>26</sup>

The results of this population-based, longitudinal study suggest that gout is associated with an elevated risk of hospital admission for ACSCs and these higher risks were evident from 3 years prior to a gout diagnosis. Moreover, there were variabilities in the trajectories of hospital admissions for ACSCs among people with gout, highlighting the need for a person-centered approach to its management. Our findings call for improvement in gout management in the outpatient setting, especially comorbidity management among older, foreign-born patients.

## ONLINE SUPPLEMENT

Supplementary material accompanies the online version of this article.

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