

Supplements

Covariates

Covariates included patient characteristics (age, gender, body mass index [BMI]), lifestyle factors (smoking status and alcohol consumption), comorbidities and drug treatment. Only GP records occurring within the 5-year period before initial diagnosis of gout were used to evaluate comorbidities and drug treatment. Comorbidities were grouped into 17 diagnostic categories (myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, dementia, chronic pulmonary disease, rheumatologic disease, peptic ulcer disease, mild liver disease, moderate or severe liver disease, diabetes mellitus [DM], DM with chronic complications, renal diseases, any malignancy [including leukaemia and lymphoma], metastatic solid tumour and human immunodeficiency virus [HIV] infection) for calculation of the Charlson comorbidity index[52, 53] and other comorbidities (alcohol abuse, anaemia, cardiac arrhythmias, depression, drug abuse, hip fracture, hypertension, hypothyroidism, multiple sclerosis, neurological diseases, psoriasis, psychosis, urolithiasis and valvular heart disease). The definitions of these conditions were also based on physician diagnoses recorded as READ codes. Medications evaluated include aspirin, anticoagulants, anticonvulsants, lipid lowering agents (statin, fibrate and other), antihypertensives (angiotensin converting enzyme inhibitor/angiotensin-receptor antagonist, beta blockers, calcium channel blockers, diuretics and other), nitrates, other cardiovascular medications, insulin, other hypoglycaemic agents, anti-inflammatory agents (non-steroid anti-inflammatory drugs [NSAIDs], colchicine, corticosteroids), bisphosphonate and vitamin D.

Propensity score adjustment analysis

Similar results were obtained to our main analysis when we used propensity score adjustment for all included patients in both the one-year and three-year landmark analysis. In the one-

year landmark analysis, allopurinol was associated with an unadjusted hazard ratio (95% confidence interval) of 1.49 (1.32–1.67) and a propensity score adjusted hazard ratio (95% confidence interval) of 1.02 (0.95–1.09) for all-cause mortality. In the three-year analysis, the unadjusted and propensity score-adjusted hazard ratios (95% confidence interval) were 1.35 (1.26–1.44) and 1.05 (0.93–1.20), respectively.

Supplementary table 1. Performance of CPRD recorded death

GPRD	Death registration		Total	PPV	NPV
	recorded	Not recorded			
Recorded	195,047	14,107	209,154	93.3%	
Not recorded	2,092	3,311,355	3,313,447		99.9%
Total	197,139	3,325,462	3,522,601		
Sensitivity	98.94%	99.6%			

Footnote: PPV, positive predictive value; NPV, negative predictive value.

Supplementary Table 2. Characteristics of cohort at cohort entry (initial diagnosis of gout).

Values are numbers (percentage) unless stated otherwise.

	Entire cohort (n=23,332)	One-year Landmark cohort			Three-year landmark cohort		
		Included patients (n=21,947)	Excluded patients (n = 1,385)	P value	Included patients (n=19,549)	Excluded patients (n=3,783)	P value
Age (years)							
Median (interquartile range)	62 (50–73)	62 (49–73)	73 (60–82)	<0.001	61 (49–71)	72 (58–81)	<0.001
Gender							
Men	17,197 (73.71)	16,276 (74.16)	921 (66.50)	<0.001	14,628 (74.83)	2,569 (67.91)	<0.001
Women	6,135 (26.29)	5,671 (25.84)	464 (33.50)		4,921 (25.17)	1,214 (32.09)	
BMI (kg/m²)							
<18.5	162 (0.69)	146 (0.67)	16 (1.16)	<0.001	123 (0.63)	39 (1.03)	<0.001
18.5 – 24.9	4,975 (21.32)	4,678 (21.31)	297 (21.44)		4,142 (21.19)	833 (22.02)	
25.0 – 29.9	8,910 (38.19)	8,536 (38.89)	374 (27.00)		7,846 (40.14)	1,064 (28.13)	
≥30	6,119 (26.23)	5,889 (26.83)	230 (16.61)		5,466 (27.96)	653 (17.26)	
Unknown	3,166 (13.57)	2,698 (12.29)	468 (33.79)		1,972 (10.09)	1,194 (31.56)	
Smoking							
Non-smoker	2,688 (11.52)	2,523 (11.50)	165 (11.91)	0.80	2,307 (11.80)	381 (10.07)	0.03
Current smoker	1,910 (8.19)	1,804 (8.22)	106 (7.65)		1,588 (8.12)	322 (8.51)	
Ex-smoker	13,889 (59.53)	13,059 (59.50)	830 (59.93)		11,543 (59.05)	2,346 (62.01)	
Unknown	4,845 (20.77)	4,561 (20.78)	284 (20.51)		4,111 (21.03)	734 (19.40)	
Alcohol consumption (units/week)							
Never/ Ex-drinker	2,525 (10.82)	2,299 (10.48)	226 (16.32)	0.07	1,992 (10.19)	533 (14.09)	0.35
Current 1-9	8,957 (38.39)	8,421 (38.37)	536 (38.70)		7,461 (38.17)	1,496 (39.55)	
Current ≥10	5,496 (23.56)	5,281 (24.06)	215 (15.52)		4,799 (24.55)	697 (18.42)	
Unknown	6,354 (27.23)	5,946 (27.09)	408 (29.46)		5,297 (27.10)	1,057 (27.94)	
Charlson comorbidity index							
0	16,211 (69.48)	15,575 (70.97)	636 (45.92)	<0.001	14,365 (73.48)	1,846 (48.80)	<0.001
1-2	5,916 (25.36)	5,384 (24.53)	532 (38.41)		4,476 (22.90)	1,440 (38.07)	
3-4	1,141 (4.89)	947 (4.31)	194 (14.01)		687 (3.51)	454 (12.00)	
≥4	64 (0.27)	41 (0.19)	23 (1.66)		21 (0.11)	43 (1.14)	
Medications							
Aspirin	4,188 (17.95)	3,750 (17.09)	438 (31.62)	<0.001	3,047 (15.59)	1,141 (30.16)	<0.001
Statin	105 (4.52)	986 (4.49)	69 (4.98)	0.40	883 (4.52)	172 (4.55)	0.94
Diuretics	8,878 (38.05)	8,023 (36.56)	855 (61.73)	<0.001	6,687 (34.21)	2,191 (57.92)	<0.001
Insulin	122 (0.52)	103 (0.47)	19 (1.37)	<0.001	84 (0.43)	38 (1.00)	<0.001
NSAID	17,024 (72.96)	16,045 (73.11)	979 (70.69)	0.50	14,324 (73.27)	2,700 (71.37)	0.02

Supplementary Table 3. Comparison of patients exposed to or unexposed to allopurinol within three year from initial diagnosis of gout before and after matching. Values are numbers (percentage) unless described otherwise.

	Exposure groups before matching			Exposure groups after matching		
	Allopurinol users (n=3,540)	Allopurinol nonusers (n = 16,009)	P value	Allopurinol users (n = 3,519)	Allopurinol nonusers (n = 3,519)	P value
Age (years)						
Median (interquartile range)	64 (52–73)	60 (48–71)	<0.001	64 (52–73)	63 (51–73)	0.69
Gender						
Men	2,530 (71.90)	12,085 (75.49)	<0.001	2,530 (71.90)	2,542 (72.24)	0.75
Women	989 (28.10)	3,924 (24.51)		989 (28.10)	977 (27.76)	
BMI (kg/m2)						
<18.5	14 (0.40)	109 (0.68)	0.009	14 (0.40)	16 (0.5)	0.93
18.5 – 24.9	633 (17.99)	3,508 (21.91)		633 (17.99)	642 (18.24)	
25.0 – 29.9	1,357 (38.56)	6,482 (40.49)		1,357 (38.56)	1,351 (38.39)	
≥30	1,205 (34.24)	4,248 (26.54)		1,205 (34.24)	1,202 (34.16)	
Unknown	310 (8.81)	1,662 (10.38)		310 (8.81)	308 (8.78)	
Smoking						
Non-smoker	427 (12.13)	1,877 (11.72)	0.006	427 (12.13)	426 (12.11)	0.93
Current smoker	273 (7.716)	1,312 (8.21)		273 (7.716)	290 (8.24)	
Ex-smoker	2,136 (60.70)	9,392 (58.62)		2,136 (60.70)	2,117 (60.16)	
Unknown	683 (19.41)	3,426 (21.40)		683 (19.41)	686 (19.49)	
Alcohol consumption (units/week)						
Never/ Ex-drinker	419 (11.91)	1,567 (9.79)	0.004	419 (11.91)	425 (12.08)	0.79
Current 1-9	1,391 (39.53)	6,058 (37.84)		1,391 (39.53)	1,369 (38.90)	
Current ≥10	820 (23.30)	3,979 (24.85)		820 (23.30)	846 (24.04)	
Unknown	889 (25.26)	4,405 (27.52)		889 (25.26)	879 (24.98)	
Charlson comorbidity index						
0	2,330 (66.82)	12,035 (75.18)	<0.001	2,329 (66.18)	2,341 (66.52)	0.75
1-2	1,017 (28.73)	3,459 (21.61)		1,008 (28.64)	999 (28.39)	
3-4	187 (5.28)	500 (3.12)		176 (5.00)	174 (4.49)	
≥4	6 (0.17)	15 (0.09)		6 (0.17)	5 (0.14)	
Medications						
Aspirin	799 (22.57)	2,248 (14.04)	<0.001	785 (22.31)	796 (22.62)	0.75
Statin	263 (7.43)	620 (3.87)	<0.001	255 (7.25)	248 (7.05)	0.75
Diuretics	1,778 (50.23)	4,909 (30.66)	<0.001	1,757 (49.93)	1,778 (50.53)	0.62
Insulin	18 (0.51)	66 (0.41)	0.43	18 (0.51)	14 (0.40)	0.48
NSAID	2,560 (72.32)	11,764 (73.48)	0.16	2,544 (72.29)	2,549 (72.44)	0.89

Figures

Figure 1. Diagram of one-year and three-year landmark analysis (a) decomposition of study population. (b) details of timeline.

Figure 2. Kaplan-Meier survival plot for all-cause mortality in (a) one-year and (b) three-year landmark analysis. Blue line represents allopurinol users and green line represent nonusers.