

## Supplemental Material

### Supplemental Material TOC:

- Definition of confounders and other measured covariates
- Early- and moderate-stage CKD
- ICD-10 codes identifying CKD
- Supplemental Table 1
- Supplemental Table 2
- Supplemental Figure 1

#### Definition of Confounders and Other Measured Covariates

The covariates were based on Read codes recorded in CPRD any time prior to index date. In addition, hypertension and obesity were also based on the following recorded values:

- Hypertension: blood pressure  $\geq 140/90$  mm Hg
- Obesity: body mass index  $\geq 30$  kg/m<sup>2</sup>

Early- and moderate-stage CKD were defined in the following ways:

- Early-stage CKD: if a diagnosis code for stage 1 or 2 CKD was present or eGFR was  $\geq 60$  ml/min/1.73m<sup>2</sup> during the 12 months before index date
- Moderate-stage CKD: if there was a diagnosis code for stage 3 or 4 CKD or eGFR was 15-59 ml/min/1.73m<sup>2</sup> during the 12 months before index date

For patients with  $\geq 1$  serum creatinine measurement recorded during the 12 months before index date, the closest measurement to index date was used to estimate eGFR and classify patients according to GFR category.

ICD-10 codes identifying CKD used in determination of death associated with CKD:

- E10.2, E11.2, E13.2, E14.2, I12.0, I13.0, I13.1, I13.2, I13.9, N17.0, N17.1, N17.2, N17.8, N17.9, N18.0, N18.5, N19.X, N99.0, O08.4, O90.4

**Supplemental Table 1.** Demographic and clinical characteristics of patients with and without gout – final study population

	Study Population	Patients With Gout	Patients Without Gout
	(N=623,861)	(n=68,897)	(n=554,964)
<b>Demographic characteristics:</b>			
Age at index date (yr)			
Median (IQR)	60 (48-71)	62 (50-73)	59 (48-70)
Sex (%) <sup>a</sup>			
Male	76.8	76.7	77.1
Female	23.2	23.3	22.9
<b>Townsend score of social deprivation (%)<sup>a</sup></b>			
1 (most affluent)	24.4	24.7	24.4
2	24.4	24.88	24.4
3	21.2	21.7	21.2
4	18.5	18.1	18.5
5 (least affluent)	11.5	10.7	11.5
<b>Comorbid conditions, No. (%):</b>			
Diabetes mellitus	51,148 (8.2)	7661 (11.1)	43 487 (7.8)
Chronic obstructive pulmonary disease	24,702 (4.0)	3580 (5.2)	21,122 (3.8)
Hypertension	175,240 (28.1)	31,967 (46.4)	143,273 (25.8)
Hyperlipidemia	63,902 (10.2)	10,899 (15.8)	53,003 (9.6)
Obesity	25,485 (4.1)	5550 (8.1)	19,935 (3.6)
<b>Cardiovascular Conditions</b>			
Myocardial infarction	26,874 (4.3)	4991 (7.2)	21,883 (3.9)
Angina	41,554 (6.7)	7665 (11.1)	33,889 (6.1)
Heart failure	17,850 (2.9)	5264 (7.6)	12,586 (2.3)
Ischemic heart disease	64,023 (10.3)	11,682 (17.0)	52,341 (9.4)
Peripheral vascular disease	19,094 (3.1)	3179 (4.6)	15,915 (2.9)
Stroke	18,752 (3.0)	2807 (4.1)	15,945 (2.9)
Transient ischemic attack	14,106 (2.3)	2360 (3.4)	11,746 (2.1)

History of CKD			
Stage 1 CKD <sup>b</sup>	38,776 (6.2)	5725 (8.3)	33,051 (6.0)
Stage 2 CKD <sup>b</sup>	117,295 (18.8)	17,435 (25.3)	99,860 (18.0)
Stage 3 CKD <sup>b</sup>	67,238 (10.8)	16,026 (23.3)	51,212 (9.2)
Stage 4 CKD <sup>b</sup>	6969 (1.1)	2891 (4.2)	4078 (0.7)
Other Renal Diagnosis			
General renal disease	7944 (1.3)	2594 (3.8)	5350 (1.0)
Nephrolithiasis	8781 (1.4)	1349 (2.0)	7432 (1.3)
Acute kidney injury	720 (0.1)	200 (0.3)	520 (0.1)
Prostatic hypertrophy	21,436 (3.4)	2946 (4.3)	18,490 (3.3)
Other Diagnosis			
Liver failure/disease	5398 (0.9)	866 (1.3)	4532 (0.8)
Peptic ulcer disease	93,133 (14.9)	12,855 (18.7)	80,278 (14.5)
Rheumatological disease	132,302 (21.2)	21,049 (30.6)	111,253 (20.1)
Depression	91,379 (14.7)	10,459 (15.2)	80,920 (14.6)
Dementia	5661 (0.9)	286 (0.4)	5375 (1.0)
Charlson Comorbidity Index at index date, No. (%)			
0	141,266 (22.6)	12,539 (18.2)	128,727 (23.2)
1	133,780 (21.4)	12,972 (18.8)	120,808 (21.8)
2	119,633 (19.2)	12,105 (17.6)	107,528 (19.4)
3	96,017 (15.4)	10,413 (15.1)	85,604 (15.4)
4	63,780 (10.2)	7900 (11.5)	55,880 (10.1)
5	34,620 (5.6)	5344 (7.8)	29,276 (5.3)
≥6	34,765 (5.6)	7624 (11.1)	27,141 (4.9)
Lifestyle traits:			
Smoking status, No. (%)			
Current smoker	136,753 (24.6)	11,343 (17.5)	125,410 (25.6)
Former smoker	169,717 (30.6)	24,625 (38.0)	145,092 (29.6)
Never smoker	248,725 (44.8)	28,842 (44.5)	219,883 (44.8)
Unknown status	68,666 (N/A)	4087 (N/A)	64,579 (N/A)
Drug and alcohol use, No. (%)			
History of alcohol use	16,133 (2.6)	2591 (3.8)	13,542 (2.4)
History of drug addiction	4805 (0.8)	374 (0.5)	4431 (0.8)
Therapy information:			

Drugs related to gout treatment, No. (%)			
ULT	9290 (1.5)	9290 (13.5)	0 (0.0)
Allopurinol	9239 (1.5)	9239 (13.4)	0 (0.0)
Febuxostat	0 (0.0)	0 (0.0)	0 (0.0)
Probenecid	147 (0.0)	147 (0.2)	0 (0.0)
Benzbromarone	0 (0.0)	0 (0.0)	0 (0.0)
Sulfinpyrazone	38 (0.0)	38 (0.1)	0 (0.0)
Nonsteroidal anti-inflammatory drug	308,955 (49.5)	50,350 (73.1)	258,605 (46.6)
Colchicine	4418 (0.7)	3762 (5.5)	656 (0.1)
Oral corticosteroid	65,274 (10.5)	10,397 (15.1)	54,877 (9.9)
Interleukin 1 receptor antagonist	0 (0.0)	0 (0.0)	0 (0.0)
Drugs related to kidney function, No. (%)			
Renin angiotensin therapy	129,420 (20.8)	25,508 (37.0)	103,912 (18.7)
Angiotensin receptor blocker	33,121 (5.3)	6887 (10.0)	26,234 (4.7)
Angiotensin converting enzyme inhibitor	118,828 (19.1)	23,728 (34.4)	95,100 (17.1)
Beta blocker	133,651 (21.4)	24,847 (36.1)	108,804 (19.6)
Thiazide diuretic	116,671 (18.7)	22,889 (33.2)	93,782 (16.9)
Other diuretic	78,112 (12.5)	17,826 (25.9)	60,286 (10.9)
Other drugs, No. (%)			
Statin	118,180 (18.9)	19,551 (28.4)	98,629 (17.8)
Aspirin	122,176 (19.6)	20,123 (29.2)	102,053 (18.4)
Warfarin	25,352 (4.1)	6107 (8.9)	19,245 (3.5)

Abbreviations: CKD, chronic kidney disease; IQR, interquartile range; N/A, not applicable; ULT, urate lowering therapy.

Note. The study population includes both the gout and nongout cohorts. 28,435 patients were included in both cohorts (as matched nongout patients who subsequently developed gout became gout patients); information is provided on both exposures according to the different index dates.

<sup>a</sup> For the patients included in both cohorts, sex and Townsend score are reported once as they do not vary between being a nongout and a gout patient.

<sup>b</sup> Early-stage CKD defined as either a Read code for stage 1 or 2 CKD or an eGFR in the 12 months prior to study index date  $\geq 60$  ml/min (calculated using Chronic Kidney Disease Epidemiology Collaborative equation). Moderate-stage CKD defined as either a Read code for stage 3 or 4 CKD or an eGFR in the 12 months prior to study index date between 30 and 59 ml/min.

Note. Patients with stage 5 CKD were excluded from the study.

**Supplemental Table 2.** Demographic and clinical characteristics of patients with and without gout – original cohort prior to exclusions for no linked HES or ONS data available

	Study Population	Patients With Gout	Patients Without Gout
	(N=1,012,471)	(n=112,009)	(n=900,462)
<b>Demographic characteristics:</b>			
Age at index date (yr)			
Median (IQR)	59 (48-70)	62 (50-73)	59 (48-70)
Sex (%) <sup>a</sup>			
Male	76.6	76.5	76.9
Female	23.4	23.5	23.1
Townsend score of social deprivation (%) <sup>a</sup>			
1 (most affluent)	24.4	24.7	24.4
2	24.4	24.8	24.4
3	21.2	21.7	21.2
4	18.5	18.1	18.5
5 (least affluent)	11.5	10.7	11.5
<b>Comorbid conditions, No. (%):</b>			
Diabetes mellitus	82,724 (8.2)	12,396 (11.1)	70,328 (7.8)
Chronic obstructive pulmonary disease	40,486 (4.0)	5790 (5.2)	34,696 (3.9)
Hypertension	283,854 (28.0)	52,156 (46.6)	231,698 (25.7)
Hyperlipidemia	105,748 (10.4)	18,248 (16.3)	87,500 (9.7)
Obesity	44,288 (4.4)	9520 (8.5)	34,768 (3.9)
<b>Cardiovascular Conditions</b>			
Myocardial infarction	44,320 (4.4)	8286 (7.4)	36,034 (4.0)
Angina	68,399 (6.8)	12,649 (11.3)	55,750 (6.2)
Heart failure	29,266 (2.9)	8733 (7.8)	20,533 (2.3)
Ischemic heart disease	106,041 (10.5)	19,408 (17.3)	86,633 (9.6)
Peripheral vascular disease	31,696 (3.1)	5320 (4.8)	26,376 (2.9)
Stroke	30,851 (3.1)	4759 (4.3)	26,092 (2.9)
Transient ischemic attack	23,099 (2.3)	3900 (3.5)	19,199 (2.1)
<b>History of CKD</b>			
Stage 1 CKD <sup>b</sup>	62,790 (6.2)	9293 (8.3)	53,497 (5.9)
Stage 2 CKD <sup>b</sup>	182,089 (18.0)	27,197 (24.3)	154,892 (17.2)
Stage 3 CKD <sup>b</sup>	104,438 (10.3)	25,030 (22.4)	79,408 (8.8)

Stage 4 CKD <sup>b</sup>	10,969 (1.1)	4607 (4.1)	6362 (0.7)
Other Renal Diagnosis			
General renal disease	13,033 (1.3)	4288 (3.8)	8745 (1.0)
Nephrolithiasis	14,734 (1.5)	2329 (2.1)	12,405 (1.4)
Acute kidney injury	1246 (0.1)	354 (0.3)	892 (0.1)
Prostatic hypertrophy	32,984 (3.3)	4477 (4.0)	28,507 (3.2)
Other Diagnosis			
Liver failure/disease	8866 (0.9)	1386 (1.2)	7480 (0.8)
Peptic ulcer disease	157,453 (15.6)	21,695 (19.4)	135,758 (15.1)
Rheumatological disease	216,103 (21.3)	34,463 (30.8)	181,640 (20.2)
Depression	147,567 (14.6)	17,004 (15.2)	130,563 (14.5)
Dementia	9111 (0.9)	493 (0.4)	8618 (1.0)
Charlson Comorbidity Index at index date, No. (%)			
0	231,893 (22.9)	20,748 (18.5)	211,145 (23.5)
1	218,334 (21.6)	21,083 (18.8)	197,251 (21.9)
2	193,110 (19.1)	19,627 (17.5)	173,483 (19.3)
3	154,830 (15.3)	16,755 (15.0)	138,075 (15.3)
4	102,337 (10.1)	12,687 (11.3)	89,650 (10.0)
5	55,792 (5.5)	8691 (7.8)	47,101 (5.2)
≥6	56,175 (5.6)	12,418 (11.1)	43,757 (4.9)
Lifestyle traits:			
Smoking status, No. (%)			
Current smoker	224,284 (25.0)	18,578 (17.7)	205,706 (26.0)
Former smoker	269,868 (30.1)	39,385 (37.5)	230,483 (29.1)
Never smoker	402,961 (44.9)	47,030 (44.8)	355,931 (44.9)
Unknown status	115,358 (N/A)	7016 (N/A)	108,342 (N/A)
Drug and alcohol use, No. (%)			
History of alcohol use	29,289 (2.9)	4606 (4.1)	24,683 (2.7)
History of drug addiction	7912 (0.8)	623 (0.6)	7289 (0.8)
Therapy information:			
Drugs related to gout treatment, No. (%)			
ULT	15,213 (1.5)	15,213 (13.6)	0 (0.0)
Allopurinol	15,119 (1.5)	15,119 (13.5)	0 (0.0)
Febuxostat	0 (0.0)	0 (0.0)	0 (0.0)

Probenecid	249 (0.02)	249 (0.2)	0 (0.0)
Benzbromarone	0 (0.0)	0 (0.0)	0 (0.0)
Sulfipyrazone	55 (<0.01)	55 (0.1)	0 (0.0)
Nonsteroidal anti-inflammatory drug	507,352 (50.1)	82,332 (73.5)	425,020 (47.2)
Colchicine	7139 (0.7)	6041 (5.4)	1098 (0.1)
Oral corticosteroid	104,158 (10.3)	16,644 (14.9)	87,514 (9.7)
Interleukin 1 receptor antagonist	0 (0.0)	0 (0.0)	0 (0.0)
Drugs related to kidney function, No. (%)			
Renin angiotensin therapy	209,858 (20.7)	41,603 (37.1)	168,255 (18.7)
Angiotensin receptor blocker	53,710 (5.3)	11,215 (10.0)	42,495 (4.7)
Angiotensin converting enzyme inhibitor	192,293 (19.0)	38,614 (34.5)	153,679 (17.1)
Beta blocker	218,824 (21.6)	40,465 (36.1)	178,359 (19.8)
Thiazide diuretic	189,661 (18.7)	37,584 (33.6)	152,077 (16.9)
Other diuretic	128,155 (12.7)	29,398 (26.3)	98,757 (11.0)
Other drugs, No. (%)			
Statin	193,929 (19.2)	32,275 (28.8)	161,654 (18.0)
Aspirin	201,562 (19.9)	33,078 (29.5)	168,484 (18.7)
Warfarin	41,394 (4.1)	10,042 (9.0)	31,352 (3.5)

Abbreviations: CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; HES, Hospital Episode Statistics; IQR, interquartile range; N/A, not applicable; ONS, Office for National Statistics; ULT, urate lowering therapy.

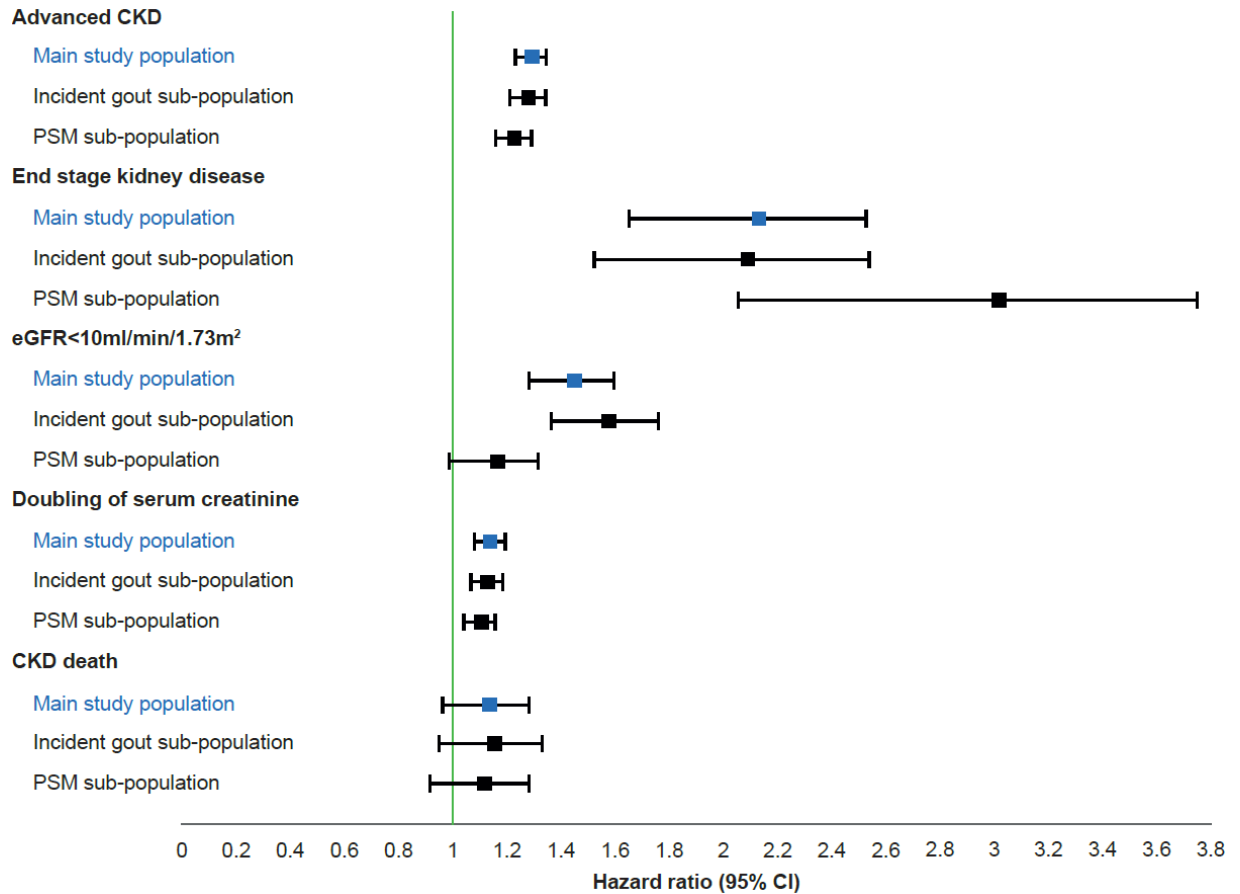
Note. The study population includes both the gout and nongout cohorts. 45,531 patients were included in both cohorts (as matched nongout patients who subsequently developed gout became gout patients); information is provided on both exposures according to the different index dates.

<sup>a</sup> For the patients included in both cohorts, sex and Townsend score are reported once as they do not vary between being a nongout and a gout patient.

<sup>b</sup> Early-stage CKD defined as either a Read code for stage 1 or 2 CKD or an eGFR in the 12 months prior to study index date  $\geq 60$  ml/min (calculated using Chronic Kidney Disease Epidemiology Collaborative equation). Moderate-stage CKD defined as either a Read code for stage 3 or 4 CKD or an eGFR in the 12 months prior to study index date between 30 and 59 ml/min.

Note. Patients with stage 5 CKD were excluded from the study.

**Supplemental Figure 1. Sensitivity analyses illustrating association between gout and advanced chronic kidney disease and its four components, according to study population; main study population, incident gout and propensity score matched patients.**



CKD, chronic kidney disease; PSM, propensity score matched; eGFR, estimated glomerular filtration rate; 95% CI, 95% confidence interval.