

Supplemental Online Content

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This supplemental material has been provided by the authors to give readers additional information about their work.

eMethods

UK Biobank Study Population

The UK Biobank (UKB) resource is a prospective cohort of more than 500,000 residents of the United Kingdom (UK) aged 40 to 69 years at the time of enrollment (years 2006 to 2010) when participants provided blood samples and attended a baseline visit where data on baseline characteristics were obtained through a touchscreen questionnaire, in-person interview, and measurements.

Assessment of Race in UKB

Ethnic group was self-reported by participants when completing the touchscreen questionnaire, who were asked to select from one of the following categories: Asian, Black, White, Mixed (e.g., White and Black African, White and Asian), and Other. Although the term ‘ethnic group’ is used in place of ‘race’ in the UK,¹ ‘race’ is used to avoid confusion with the distinct US categories of Hispanic and non-Hispanic ethnicity.

Assessment of Covariates in UKB

At the baseline visit, information was obtained through a touchscreen questionnaire and in-person interview on sociodemographics, diet and lifestyle factors, and medical conditions and medications taken on a regular basis (including diuretics and urate-lowering therapy); anthropometrics, including height and weight, were also obtained by assessment center staff using calibrated instruments.² Body mass index was computed by dividing the weight in kilograms by the square of the height in meters. Coffee consumption was computed from responses on the number of cups consumed per day, and categorised as 0, 1-2, 3-5, or > 5. Alcoholic beverage consumption was computed from responses to questions on the frequency of alcoholic beverage consumption, with six categories ranging from Never to Special Occasions Only, 1-3 Times per Month, Once or Twice per Week, Three or Four Times per Week, and Daily. Red meat, fish, and poultry intake were computed from responses to questions on weekly consumption of beef, lamb, pork, processed meats, poultry, and oily and non-oily fish, ranging from Never to ≥ 1 serving per day. Smoking status was categorised as Current, Former, or Never. Cardiovascular disease and type 2 diabetes status were based upon self-reported diagnoses at baseline. Prevalent hypertension was defined according to self-reported diagnosis at baseline, or primary care or hospitalisation diagnosis recorded before baseline. As with urate, creatinine was measured from each participant’s baseline blood sample using an enzymatic assay on a Beckman Coulter AU5800 platform.³ Serum creatinine levels were used to determine glomerular filtration rate (eGFR)⁴ and chronic kidney disease (CKD) status, defined as eGFR <60 mL/min.

eReferences.

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eTable 1: Baseline Characteristics of the UK Biobank Participants with and without Linked Primary Care Data Available

	Primary Care Data Available	Primary Care Data Not Available
N	228,939	273,551
Females, N (%)	125,258 (54.7%)	148,117 (54.1%)
Males, N (%)	103,681 (45.3%)	125,433 (45.9%)
Age, mean (SD)	56.5 (8.07)	56.5 (8.12)
Race, N (%)		
Asian	5292 (2.3%)	6164 (2.3%)
Black	2502 (1.1%)	5559 (2.0%)
White	217,217 (94.9%)	255,463 (93.4%)
Multiple*	1169 (0.5%)	1789 (0.7%)
Other**	1680 (0.7%)	2878 (1.1%)
Serum urate (mg/dL), mean (SD)	5.19 (1.35)	5.20 (1.35)
BMI, mean (SD)	27.5 (4.82)	27.4 (4.79)
Alcohol consumption		
Daily, N (%)	44,975 (19.6%)	56,793 (20.8%)
Never, N (%)	18,782 (8.2%)	21,857 (8.0%)
Smoking status, N (%)		
Never	125,419 (54.8%)	148,987 (54.5%)
Former	78,609 (34.3%)	94,441 (34.5%)
Current	24,011 (10.5%)	28,966 (10.6%)
Coffee intake, cups/day, N (%)		
0	50,828 (22.2%)	60,377 (22.1%)
1-2	87,417 (38.2%)	106,718 (39.0%)
3-5	58,795 (25.7%)	69,075 (25.3%)
>5	14,508 (6.3%)	16,193 (5.9%)
Red meat intake (servings/week) mean (SD)	3.52 (2.39)	3.53 (2.41)
Poultry intake (servings/week) mean (SD)	1.91 (1.31)	1.92 (1.33)
Fish intake (servings/week) mean (SD)	2.24 (1.69)	2.23 (1.72)
Diuretic use, N (%)	16,305 (7.1%)	18,829 (6.9%)
Urate lowering therapy use, N (%)	2646 (1.2%)	3024 (1.1%)
Hypertension, N (%)	28,779 (12.6%)	22,830 (8.3%)
Cardiovascular disease, N (%)	11,715 (5.1%)	13,106 (4.8%)
Diabetes, N (%)	11,942 (5.2%)	14,457 (5.3%)
Chronic kidney disease stage ≥ 3 , N (%)	3420 (1.5%)	3934 (1.4%)

Serum urate levels were measured from blood samples taken at the baseline assessment, at the same time that data were collected on height and weight and self-reported dietary intake, lifestyle factors, and current medication use. N, number; SD, standard deviation.

*Self-selected by participants, with further response options including ‘White and Black Caribbean’, ‘White and Black African’, ‘White and Asian’, and ‘Any other mixed background’; **Self-selected by participants, no further response options available. ***Glomerular filtration rate < 60 mL/min.

eTable 2. Diagnostic Codes for Gout Encounters and Procedures in Primary Care Medical Records

Diagnoses of Gout Flare	
Read Code	Term
N023300	Gouty arthritis of the forearm
N023z00	Gouty arthritis NOS
N023200	Gouty arthritis of the upper arm
N023.00	Gouty arthritis
N023800	Gouty arthritis of toe
N023y00	Gouty arthritis of other specified site
N023400	Gouty arthritis of the hand
N023x00	Gouty arthritis of multiple sites
C346.00	Acute exacerbation of gout
N023700	Gouty arthritis of the ankle and foot
N023600	Gouty arthritis of the lower leg
N023100	Gouty arthritis of the shoulder region
N023000	Gouty arthritis of unspecified site
ICD-10 Code	Term
M10	Gout

Diagnoses of Gout	
Read Code	Term
34..00	Gout
N023.00	Gouty arthritis
1443	H/O: gout
C34y200	Gouty tophi of other sites
C34y500	Gouty tophi of hand
C340.00	Gouty arthropathy
C342.00	Idiopathic gout
N023z00	Gouty arthritis NOS
6691	Initial gout assessment
669..00	Gout monitoring
2D52.00	O/E - auricle of ear - tophi
C345.00	Gout due to impairment of renal function
C34z.00	Gout NOS
C34yz00	Other specified gouty manifestation NOS
C34y.00	Other specified gouty manifestation
6693	Joints gout affected
6695	Date gout treatment started
6699	Gout treatment changed
6692	Follow-up gout assessment

Diagnoses of Gout (continued)

N023700	Gouty arthritis of the ankle and foot
C34y000	Gouty tophi of ear
669A.00	Date gout treatment stopped
C344.00	Drug-induced gout
N023300	Gouty arthritis of the forearm
N023600	Gouty arthritis of the lower leg
C34y300	Gouty iritis
N023400	Gouty arthritis of the hand
6698	Gout drug side effects
669Z.00	Gout monitoring NOS
C341.00	Gouty nephropathy
G557300	Gouty tophi of heart
N023x00	Gouty arthritis of multiple sites
6697	Gout associated problems
C34y400	Gouty neuritis
N023y00	Gouty arthritis of other specified site
C341z00	Gouty nephropathy NOS
6696	Date of last gout attack
N023100	Gouty arthritis of the shoulder region
N023800	Gouty arthritis of toe
C34y100	Gouty tophi of heart
Nyu1700	[X]Other secondary gout
N023200	Gouty arthritis of the upper arm
C346.	00 Acute exacerbation of gout
C343.	00 Lead-induced gout
N0230	00 Gouty arthritis of unspecified site
C3410	00 Gout nephropathy unspecified

Gout-Related Procedures

Read Code	Term
7K6U4	Aspiration of joint NEC
7K6Z0	Aspiration of joint
7K6Z8	Aspiration of fluid from knee joint
XM13x	Joint -diag.aspiration
XM16K	Therapeutic aspiration - joint
Xa1t3	Aspiration of elbow joint
Xa1t5	Aspiration of knee joint
Xa84w	Aspiration of joint
4B...	Synovial fluid examination

Gout-Related Procedures (continued)

XE26K	Joint fluid sample
X76zq	Synovial fluid observation
X76zs	Synovial fluid composition
X76zt	Stringing of synovial fluid
XC0T3	Synovial fluid cells
XC0T4	Synovial fluid inclusion
XC0tz	Particulate matter in synovial fluid
XE26L	Synovial fluid: bloodstained
XE276	Synovial fluid for organism
XE29u	Synovial fluid source
XM1Wl	Synovial fluid - C/S
XaXOZ	Synovial fluid mucin clot test
XaXkc	Synovial fluid sample sent to laboratory
569H.	Magnetic resonance imaging of shoulder
569L.	Magnetic resonance imaging of knee
569Q.	Magnetic resonance imaging of femur
569R.	MRI of upper limb
569S.	MRI of lower limb
7P0A9	MRI of ankle
X70oy	MRI of upper limb
X70oz	MRI of shoulder
X70p0	MRI of upper arm
X70p1	MRI of elbow
X70p2	MRI of forearm
X70p3	MRI of wrist
X70p4	MRI of hand
X70p5	MRI of lower limb
X70p6	MRI of hip
X70p7	MRI of thigh
X70p8	MRI of knee
X70p9	MRI of lower leg
X70pA	MRI of ankle
X70pB	MRI of foot
XaMdR	MRI of femur
5287.	Elbow X-ray
5289.	Wrist X-ray
529..	Hand X-ray
52A7.	Plain X-ray knee

Gout-Related Procedures (continued)

52A8.	Patella X-ray
52AA.	Ankle X-ray
52AB.	Stress X-ray knee
52AC.	Stress X-ray ankle joint
52B..	Foot X-ray
X70eB	Wrist X-ray skyline views
X70eC	Metacarpal X-ray
X70eE	Fingers X-ray
X70eF	Thumb X-ray
X70eK	Metatarsal X-ray
X70eL	Plain X-ray tarsus
X70eM	Hindfoot X-ray
X70eN	Hallux X-ray
X70eO	Toe X-ray
XE1RF	Scaphoid X-ray
XE2rY	Carpal bones X-ray
XM1ZI	Forefoot X-ray

eTable 3. Rate and Rate Ratio (RR) for Recurrent Gout Flares According to Serum Urate Level and Follow-Up Time from Baseline, Reference <5 mg/dL

	No of Gout Patients	Follow-up, Person years (PY)	No of Flares	Flares per 1000 PY	Unadjusted RR (95% CI)	Adjusted* RR (95% CI)	Extended Adjusted** RR (95% CI)
1 Year							
<5 mg/dL	522	522	4	7.7	1.0 (ref)	1.0 (ref)	1.0 (ref)
5 to 6 mg	535	535	6	11.2	1.46 (0.41 to 5.25)	1.35 (0.38 to 4.84)	1.31 (0.36 to 4.72)
6 to 7	781	780	43	55.2	7.19 (2.55 to 20.29)	6.09 (2.15 to 17.30)	5.47 (1.90 to 15.81)
7 to 8	872	870	109	125.3	16.33 (5.95 to 44.86)	13.72 (4.96 to 37.96)	11.44 (4.02 to 32.53)
8 to 9	609	609	77	126.4	16.49 (5.95 to 45.70)	14.04 (5.03 to 39.20)	11.50 (3.99 to 33.10)
9 to 10	212	212	41	193.8	25.26 (8.82 to 72.36)	22.44 (7.79 to 64.66)	19.67 (6.59 to 58.74)
≥10 mg/dL	82	82	25	306.7	40.29 (13.30 to 122.01)	34.57 (11.37 to 105.14)	31.69 (9.96 to 100.80)
Per mg/dL	3613	3608	305	84.5	1.67 (1.54 to 1.82)	1.66 (1.52 to 1.80)	1.63 (1.48 to 1.80)
Per SD	3613	3608	305	84.5	2.31 (2.01 to 2.65)	2.27 (1.98 to 2.62)	2.22 (1.89 to 2.61)
2 Years							
<5 mg/dL	522	1043	10	9.6	1.0 (ref)	1.0 (ref)	1.0 (ref)
5 to 6	535	1068	12	11.2	1.17 (0.50 to 2.75)	1.09 (0.46 to 2.56)	1.08 (0.46 to 2.55)
6 to 7	781	1554	79	50.8	5.30 (2.71 to 10.37)	4.60 (2.33 to 9.05)	4.26 (2.13 to 8.52)
7 to 8	872	1735	184	106.0	11.05 (5.77 to 21.18)	9.56 (4.96 to 18.44)	8.43 (4.27 to 16.66)
8 to 9	609	1217	155	127.3	13.27 (6.89 to 25.58)	11.62 (5.99 to 22.52)	10.13 (5.08 to 20.17)
9 to 10	212	421	81	192.3	20.02 (10.08 to 39.77)	18.21 (9.13 to 36.35)	16.43 (7.98 to 33.83)
≥10 mg/dL	82	162	44	272.4	28.63 (13.59 to 60.29)	25.19 (11.91 to 53.28)	24.18 (11.02 to 53.07)
Per mg/dL	3613	7200	565	78.5	1.68 (1.58 to 1.80)	1.67 (1.57 to 1.79)	1.65 (1.53 to 1.78)
Per SD	3613	7200	565	78.5	2.34 (2.10 to 2.60)	2.31 (2.08 to 2.57)	2.26 (2.00 to 2.55)

	No of Gout Patients	Follow-up, Person years (PY)	No of Flares	Flares per 1000 PY	Unadjusted RR (95% CI)	Adjusted* RR (95% CI)	Extended Adjusted** RR (95% CI)
5 Years							
<5 mg/dL	522	2583	27	10.5	1.0 (ref)	1.0 (ref)	1.0 (ref)
5 to 6	535	2647	31	11.7	1.12 (0.66 to 1.92)	1.03 (0.60 to 1.77)	1.03 (0.60 to 1.77)
6 to 7	781	3845	170	44.2	4.22 (2.75 to 6.48)	3.64 (2.36 to 5.61)	3.34 (2.14 to 5.21)
7 to 8	872	4299	407	94.7	9.05 (6.00 to 13.66)	7.80 (5.14 to 11.84)	6.85 (4.43 to 10.59)
8 to 9	609	3023	369	122.0	11.71 (7.72 to 17.74)	10.18 (6.68 to 15.52)	8.85 (5.69 to 13.77)
9 to 10	212	1041	172	165.2	15.79 (10.07 to 24.77)	14.10 (8.95 to 22.21)	12.48 (7.74 to 20.12)
≥10 mg/dL	82	397	76	191.4	18.48 (10.95 to 31.19)	16.06 (9.48 to 27.20)	15.32 (8.81 to 26.63)
Per mg/dL	3613	17,836	1252	70.2	1.69 (1.61 to 1.78)	1.67 (1.59 to 1.76)	1.63 (1.54 to 1.73)
Per SD	3613	17,836	1252	70.2	2.35 (2.17 to 2.55)	2.30 (2.12 to 2.50)	2.23 (2.03 to 2.44)
10 Years							
<5 mg/dL	522	4374	42	9.6	1.0 (ref)	1.0 (ref)	1.0 (ref)
5 to 6	535	4459	52	11.7	1.21 (0.79 to 1.86)	1.12 (0.73 to 1.72)	1.12 (0.73 to 1.73)
6 to 7	781	6458	259	40.1	4.16 (2.93 to 5.90)	3.59 (2.52 to 5.12)	3.37 (2.34 to 4.85)
7 to 8	872	7260	595	82.0	8.52 (6.09 to 11.93)	7.37 (5.23 to 10.38)	6.62 (4.62 to 9.48)
8 to 9	609	5106	517	101.3	10.59 (7.53 to 14.91)	9.22 (6.51 to 13.05)	8.30 (5.75 to 11.97)
9 to 10	212	1756	220	125.3	12.94 (8.87 to 18.89)	11.50 (7.84 to 16.85)	10.47 (6.99 to 15.67)
≥10 mg/dL	82	663	88	132.8	14.02 (8.90 to 22.11)	12.15 (7.67 to 19.22)	12.04 (7.44 to 19.48)
Per mg/dL	3613	30,076	1773	59.0	1.64 (1.57 to 1.71)	1.61 (1.54 to 1.68)	1.58 (1.50 to 1.66)
Per SD	3613	30,076	1773	59.0	2.23 (2.08 to 2.40)	2.18 (2.02 to 2.34)	2.11 (1.95 to 2.28)

No, number; PY, person years; SD, standard deviation; 95% CI, 95% confidence interval.

* Adjusted for age, sex, and race

**Adjusted for variables included in the primary model (age, sex, and race) plus body mass index (continuous), smoking status, alcohol intake, coffee intake, red meat, fish, and poultry intake, diuretic and urate-lowering therapy use, and prevalent diabetes, cardiovascular disease, hypertension, and chronic kidney disease.

eTable 4. Rate and Rate Ratio (RR) for Recurrent Gout Flares According to Serum Urate Level from Baseline Over 10 Years' Follow-Up, Reference <6 mg/dL, Generated Using Poisson Regression Models with Robust Variance

	No of Gout Patients	Follow-up, Person years (PY)	No of Flares	Flares per 1000 PY	Unadjusted RR (95% CI)	Adjusted* RR (95% CI)	Extended Adjusted** RR (95% CI)
<6 mg/dL	1057	8833	94	10.6	1.0 (ref)	1.0 (ref)	1.0 (ref)
6 to 7	781	6458	259	40.1	3.77 (2.81 to 5.05)	3.41 (2.53 to 4.58)	3.18 (2.34 to 4.31)
7 to 8	872	7260	595	82.0	7.70 (5.90 to 10.05)	6.93 (5.27 to 9.10)	6.17 (4.63 to 8.22)
8 to 9	609	5106	517	101.3	9.51 (7.27 to 12.46)	8.59 (6.53 to 11.30)	7.63 (5.70 to 10.22)
9 to 10	212	1756	220	125.3	11.77 (8.81 to 15.73)	10.93 (8.17 to 14.62)	9.74 (7.15 to 13.28)
≥10 mg/dL	82	663	88	132.8	12.47 (8.17 to 19.06)	11.40 (7.47 to 17.39)	10.91 (7.02 to 16.96)
Per mg/dL	3613	30,076	1773	59.0	1.50 (1.44 to 1.56)	1.49 (1.43 to 1.55)	1.48 (1.41 to 1.55)
Per SD	3613	30,076	1773	59.0	1.94 (1.81 to 2.07)	1.91 (1.79 to 2.04)	1.90 (1.76 to 2.05)

No, number; PY, person years; SD, standard deviation; 95% CI, 95% confidence interval.

* Adjusted for age, sex, and race

**Adjusted for variables included in the primary model (age, sex, and race) plus body mass index (continuous), smoking status, alcohol intake, coffee intake, red meat, fish, and poultry intake, diuretic and urate-lowering therapy use, and prevalent diabetes, cardiovascular disease, hypertension, and chronic kidney disease.

eTable 5. Rate and Rate Ratios (RR) for Recurrent Gout Flares Requiring Hospitalization

	No of Gout Patients	Follow-up, Person years (PY)	No of Flares	Flares per 1000 PY	Unadjusted RR (95% CI)	Adjusted* RR (95% CI)
<5 mg/dL	522	5537	0	0	-	-
5 to 6	535	5661	2	0.35	-	-
6 to 7	781	8214	8	0.97	-	-
7 to 8	872	9226	17	1.8	-	-
8 to 9	609	6450	14	2.2	-	-
9 to 10	212	2229	15	6.7	-	-
≥10 mg/dL	82	825	8	9.7	-	-
Per mg/dL	3613	38,142	64	1.7	1.89 (1.59 to 2.25)	1.87 (1.57 to 2.23)
Per SD	3613	38,142	64	1.7	2.83 (2.14 to 3.75)	2.77 (2.08 to 3.69)

Rate ratios not reported by serum urate category since no events occurred in the reference category (i.e., <5 mg/dL).

No, number; PY, person years; SD, standard deviation; 95% CI, 95% confidence interval.

* Adjusted for age, sex, and race