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Joint Association of Serum Urate and Healthy Diet with Chronic Obstructive Pulmonary Disease Incidence: Results from the UK Biobank Study

Method

Assessment of genetic risk score

Genetic background is thought to account for approximately 40% of the variation in susceptibility to COPD [1, 2]. Therefore, in our sensitivity analysis, we categorized the genetic risk into three groups. Detailed information on the genetic data of the UK Biobank study is available elsewhere [3]. Briefly, the custom Affymetrix UK Biobank Axiom array was used to genotype samples of study participants from the UK Biobank. Genotype data were phased using SHAPEIT3, and IMPUTE3 was used to impute to a merged reference panel of the UK10K and 1000 Genomes phase 3 [4]. To evaluate the genetic predisposition for COPD, a genetic risk score (GRS) for COPD was created. After LD clumping ($r^2 < 0.2$, 1000 kb), we selected 279 independent single nucleotide polymorphisms (SNPs) from a previously published genome-wide association analysis [5] (Table S2). A weighted-GRS was calculated based on the amount of risk alleles of each SNP, coding as 0, 1, or 2, then multiplied by the relative effect size (β coefficient) obtained from the previously published genome-wide association analysis [5], summed, and then *z*-standardized to create a COPD-GRS for all individuals. The COPD-GRS was oriented, so that a higher COPD-GRS was associated with lower lung function. GRS was categorized into high (tertile 3), middle (tertile 2), and low (tertile 1). The distribution of COPD-GRS was normal and is presented in Fig. S2.

Assessment of Mediterranean diet score (MDS)

The MDS is a composite scoring system that incorporates both food-based and nutrient-based elements to evaluate adherence to a Mediterranean-style diet. In this investigation, a nine-item index, previously described and adapted, was employed [6, 7]. Food and nutrient consumption were assessed based on nine specific components, including vegetables, legumes, fruits and nuts, cereals, fish and seafood, the ratio of monounsaturated fats to saturated fats, dairy products, meat and meat products, and alcohol. Cut-off points for the score of each component were determined using sex-specific median intakes. Participants surpassing the median intake for vegetables, legumes, fruits and nuts, cereals, fish and seafood, and the monounsaturated to saturated fats ratio received a score of 1. Conversely, participants falling below the median intake for dairy products and meat and meat products were also assigned a score of 1. For alcohol, a score of 1 denoted low to moderate intake, equivalent to consuming alcohol once or twice daily. A score of 0 was assigned for either no

alcohol intake or an intake exceeding twice daily. The overall MDS score ranged from 0 to 9, with higher scores indicative of greater adherence to the Mediterranean diet.

Reference:

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7. Livingstone, K.M., et al., Diet quality indices, genetic risk and risk of cardiovascular disease and mortality: a longitudinal analysis of 77 004 UK Biobank participants. BMJ Open, 2021. 11(4): p. e045362.

Table legends:

Table S1. Healthy diet components.

Table S2. Single nucleotide polymorphisms (SNPs) used to build the genetic risk score for COPD.

Table S3. Participants baseline characteristics according to COPD status (n = 155,403).

Table S4. Association between hyperuricemia and risk of COPD (n = 155,403).

Table S5. Hazards ratios (HRs) and 95% confidence interval (CIs) of COPD by joint effect of SU levels and diet score after excluding COPD occurred within first 3 years of follow up (n = 154,990).

Table S6. Association between genetic risk and the risk of COPD (n = 153,620).

Table S7. Hazards ratios (HRs) and 95% confidence interval (CIs) of COPD by joint effect of SU levels and diet score in subgroup analyses.

Table S8. Hazards ratios (HRs) and 95% confidence interval (CIs) of COPD by joint exposures of SU levels and diet score: results from competing risk regression model (n = 155,403).

Table S9. Association between weighted diet score and risk of COPD (n = 155,403).

Table S10. Hazards ratios (HRs) and 95% confidence interval (CIs) of COPD by joint exposures of SU levels and weighted diet score (n = 155,403).

Table S11. Hazards ratios (HRs) and 95% confidence interval (CIs) of COPD by joint effect of SU levels and diet score additionally adjusted for baseline estimated glomerular filtration rate.

Table S12. Association between SU levels and risk of COPD after excluding baseline FEV1/FVC<0.7 (n = 132,192).

Table S13. Hazards ratios (HRs) and 95% confidence interval (CIs) of COPD by joint effect of SU levels and diet score after excluding participants diagnosed with diabetes, hypertension, and kidney disease at baseline (n = 118,185).

Table S14. Associations between Mediterranean diet score (MDS) and risk of COPD (n = 155,403).

Table S15. The associations of joint exposures of SU levels and MDS with the risk of COPD (n = 155,403).

Figure legends:

Fig. S1 Flowchart for the selection of the analyzed study sample.

Fig. S2 Distribution of COPD-GRS.

Table S1. Healthy diet components.

Diet factors	Field IDs	Description	Score	
			0	1
Vegetables	1289, 1299	Cooked vegetable and salad /raw vegetable	<3 servings/day	≥3 servings/day
Fruits	1309, 1319	Fresh fruit and dried fruit	<3 servings/day	≥3 servings/day
Fish	1329, 1339	Oily fish and non-oily fish	<2 servings/week	≥2 servings/week
Processed meats	1349	Processed meat	>1 servings/week	≤1 servings/week
Unprocessed red meat	1369, 1379, 1389, 1359	Beef, lamb or mutton, and pork intake	>1.5 servings/week;	≤1.5 servings/week
Whole grains		Brown bread, wholemeal and wholegrain bread, bran and oat cereal	<3 servings/day	≥3 servings/day
Refined grains	1369, 1379, 1389, 1359	White and other type of bread, biscuit cereal, muesli and other type of cereal	>1.5 servings/week;	≤1.5 servings/week

Table S2. Single nucleotide polymorphisms (SNPs) used to build the genetic risk score for COPD.

SNP	Chr	BP	A1	A2	FreqRisk	Beta	SE	P
rs9661802	1	6678864	A	C	0.6649	0.0247	0.0025	5.56E-23
rs12737805	1	22612690	A	G	0.7787	0.0022	0.0029	4.50E-01
rs9438626	1	26775367	C	G	0.21	0.0067	0.0029	2.03E-02
rs12096239	1	26796922	C	G	0.253	-0.0099	0.0027	2.68E-04
rs1416685	1	51243374	C	G	0.4053	0.0202	0.0024	5.62E-17
rs72673461	1	60966772	T	G	0.9507	0.0508	0.0055	3.12E-20
rs9661687	1	78387270	T	C	0.8633	-0.0271	0.0035	6.11E-15
rs10874851	1	92106637	A	C	0.4776	-0.0139	0.0024	5.07E-09
rs9970286	1	111737398	A	G	0.3291	0.0236	0.0025	1.92E-20
rs11205354	1	150249101	A	C	0.444	0.0112	0.0024	3.46E-06
rs141942982	1	155137395	T	G	0.1066	-0.0362	0.0039	9.57E-21
rs4651005	1	178719306	T	C	0.3214	0.0048	0.0025	6.13E-02
rs2146098	1	186090370	A	G	0.6452	0.0164	0.0025	4.15E-11
rs17531405	1	186113852	C	G	0.1804	0.028	0.0031	2.80E-19
rs10919604	1	198898157	A	G	0.6028	0.0198	0.0024	4.48E-16
rs4309038	1	201884647	C	G	0.4346	0.0153	0.0024	2.13E-10
rs2799098	1	218521609	A	G	0.8201	-0.0285	0.0031	5.00E-20
rs75128958	1	219483218	A	G	0.0774	-0.0445	0.0045	2.33E-23
rs17009288	1	221204299	A	C	0.7061	0.0072	0.0026	6.08E-03
rs2544536	2	15906854	T	C	0.4881	-0.0239	0.0024	4.15E-24
rs6751968	2	18570024	A	C	0.1787	0.0065	0.0031	3.51E-02
rs13430465	2	18702313	T	C	0.0803	0.0079	0.0044	7.10E-02
rs13009582	2	24018480	A	G	0.4505	0.0022	0.0024	3.49E-01
rs732990	2	26842146	C	G	0.4431	0.0122	0.0024	2.84E-07
rs4952564	2	42243850	A	G	0.681	0.001	0.0025	7.01E-01
rs12470864	2	102926362	A	G	0.3854	-0.0203	0.0024	1.04E-16
rs1406225	2	145797829	T	G	0.2836	-0.0197	0.0026	8.73E-14
rs7424771	2	161276378	A	G	0.4468	-0.0097	0.0024	5.34E-05
rs2304340	2	179260382	A	G	0.4084	0.0007	0.0024	7.74E-01
rs2084448	2	187530520	T	C	0.7063	0.0197	0.0026	4.65E-14

rs1249096	2	199723365	A	G	0.5634	-0.0026	0.0024	2.76E-01
rs985256	2	201208692	A	C	0.2185	0.0179	0.0029	5.86E-10
rs12997625	2	202970250	T	C	0.5284	0.0065	0.0024	6.20E-03
rs6435952	2	217614730	A	T	0.1505	0.0258	0.0033	1.06E-14
rs4294980	2	218604356	A	G	0.7894	0.0031	0.0029	2.95E-01
rs4674407	2	220382700	T	C	0.4969	0.0096	0.0024	6.80E-05
rs6431620	2	239604970	T	G	0.7887	0.0086	0.0029	3.31E-03
rs6437219	2	241844033	T	C	0.5217	-0.0108	0.0025	2.01E-05
rs6733504	2	242495953	A	G	0.5464	-0.0032	0.0024	1.84E-01
rs2974389	3	13787641	A	G	0.4265	0.0037	0.0024	1.18E-01
rs73048404	3	25179533	T	G	0.8529	-0.0044	0.0033	1.86E-01
rs35480566	3	71583177	A	G	0.56	0.0002	0.0024	9.22E-01
rs586936	3	73862616	A	G	0.4022	-0.018	0.0025	2.11E-13
rs1610265	3	99420192	T	C	0.0769	0.0074	0.0045	9.74E-02
rs1799807	3	165548529	T	C	0.9809	0.0598	0.0088	8.59E-12
rs6780171	3	185503456	A	T	0.3129	-0.0106	0.0026	3.65E-05
rs12331869	4	56012149	A	G	0.1789	-0.0076	0.0031	1.41E-02
rs62316310	4	75676529	A	G	0.2603	0.0272	0.0027	2.24E-23
rs11098196	4	79403952	T	G	0.5083	-0.0196	0.0024	2.42E-16
rs13109426	4	145330628	A	G	0.5918	0.0093	0.0024	1.32E-04
rs13116999	4	145442364	A	G	0.5379	0.0535	0.0024	6.63E-111
rs11739847	5	609661	A	G	0.1992	-0.0179	0.003	1.40E-09
rs4866846	5	43976162	A	G	0.1499	0.012	0.0033	3.22E-04
rs10059661	5	121410529	C	G	0.8263	-0.0308	0.0032	1.78E-22
rs17163397	5	128767384	A	G	0.8764	-0.0307	0.0036	3.30E-17
rs1800888	5	148206885	T	C	0.0147	-0.1081	0.01	2.41E-27
rs10059996	5	170901463	T	G	0.3548	-0.0352	0.0026	1.53E-42
rs79898473	5	179598771	T	C	0.671	-0.0308	0.0026	2.31E-33
rs12198986	6	7720059	A	G	0.478	-0.0005	0.0024	8.22E-01
rs9689096	6	34188892	A	C	0.9374	-0.0085	0.005	8.52E-02
rs9357446	6	44447598	A	G	0.5169	0.0011	0.0024	6.38E-01
rs12202314	6	45530471	T	C	0.6753	-0.0209	0.0025	2.17E-16
rs9472541	6	45622748	A	T	0.2853	0.0068	0.0026	1.01E-02

rs2894837	6	56336406	A	G	0.6398	0.0147	0.0025	3.78E-09
rs2627237	6	134339265	A	G	0.5893	0.0037	0.0024	1.29E-01
rs1102077	6	140271357	A	C	0.7574	0.0168	0.0028	2.02E-09
rs9385988	6	142560957	A	G	0.7232	-0.0315	0.0027	2.43E-32
rs4721457	7	15872324	T	C	0.8494	0.0244	0.0033	1.73E-13
rs559233	7	26848830	T	C	0.4857	0.0105	0.0024	1.19E-05
rs62454414	7	27182329	T	G	0.8668	-0.0046	0.0035	1.85E-01
rs1513272	7	28200097	T	C	0.4996	0.005	0.0024	3.29E-02
rs17232687	7	46448518	T	C	0.4956	-0.0036	0.0024	1.35E-01
rs12707691	7	84569510	C	G	0.6642	-0.011	0.0025	1.54E-05
rs193686	7	116431427	T	C	0.6834	-0.0178	0.0026	4.07E-12
rs330939	8	9018590	T	G	0.6216	0.0232	0.0025	4.46E-21
rs4128298	8	11823332	T	C	0.7176	-0.0199	0.0026	4.97E-14
rs7465401	8	70367248	T	C	0.7263	-0.0175	0.0027	6.84E-11
rs7838717	8	145504343	T	C	0.3631	0.0008	0.0025	7.60E-01
rs7041139	9	18013733	T	C	0.3221	-0.008	0.0025	1.54E-03
rs72743974	9	98878881	A	G	0.8328	-0.0232	0.0032	3.98E-13
rs57649467	9	101632854	A	G	0.3885	0.0178	0.0025	5.39E-13
rs967497	9	131943843	A	G	0.3102	0.0101	0.0026	9.14E-05
rs1274475	10	34480582	A	G	0.3922	0.0168	0.0025	8.30E-12
rs60820984	10	75639578	T	C	0.1867	-0.0233	0.0031	4.32E-14
rs11191841	10	105639611	T	C	0.4914	-0.0092	0.0024	1.14E-04
rs10836366	11	35308988	T	C	0.7486	0.0191	0.0027	2.33E-12
rs56196860	12	2908330	A	C	0.0312	0.0063	0.007	3.65E-01
rs12811814	12	4243749	T	C	0.4576	0.0061	0.0024	1.14E-02
rs10841302	12	19808912	C	G	0.5464	0.0167	0.0024	2.29E-12
rs1244869	12	65075332	T	G	0.632	0.0153	0.0025	6.16E-10
rs11176001	12	66409367	A	C	0.1309	-0.0151	0.0035	2.04E-05
rs972936	12	102824921	T	C	0.2625	0.003	0.0027	2.65E-01
rs2701110	12	114669870	A	C	0.1664	0.0189	0.0032	4.53E-09
rs9533803	13	44820608	T	C	0.2134	-0.0261	0.0029	2.92E-19
rs2812208	13	50707087	C	G	0.0212	0.0048	0.0083	5.58E-01
rs803765	13	71647588	A	C	0.3452	0.0079	0.0025	1.56E-03

rs4885681	13	80467235	T	C	0.7248	0.0055	0.0027	4.05E-02
rs11620380	13	99665512	A	C	0.1046	-0.027	0.0039	4.61E-12
rs9634470	13	109918493	T	C	0.7347	-0.0208	0.0027	2.73E-14
rs1951121	14	23429729	T	G	0.6011	0.0189	0.0024	7.55E-15
rs74053129	14	54346010	A	G	0.0959	0.0392	0.004	2.15E-22
rs10141786	14	74817418	A	G	0.4017	-0.0041	0.0024	9.61E-02
rs34245505	15	40397191	C	G	0.805	-0.0218	0.003	6.83E-13
rs2304645	15	40716253	C	G	0.5179	-0.0005	0.0024	8.40E-01
rs4924525	15	41255396	A	C	0.5221	0.0047	0.0024	4.66E-02
rs79234094	15	49409527	A	G	0.2624	0.0268	0.0027	3.18E-23
rs35251997	15	49706145	A	T	0.931	-0.0506	0.0047	2.82E-27
rs62012772	15	63866877	T	C	0.8222	-0.0288	0.0031	2.42E-20
rs7176074	15	73833600	T	G	0.0509	0.0339	0.0055	6.60E-10
rs3751837	16	3583173	T	C	0.2202	0.0108	0.0029	1.66E-04
rs56104880	16	4361138	T	C	0.6948	0.0205	0.0026	5.29E-15
rs11074547	16	10136889	T	G	0.7378	0.0059	0.0027	2.73E-02
rs76219171	16	50188929	A	G	0.0601	0.0089	0.0051	7.95E-02
rs35420030	16	53935407	T	C	0.9466	-0.045	0.0053	3.08E-17
rs12918140	16	86403821	C	G	0.1146	-0.027	0.0038	6.72E-13
rs6539952	16	86579223	A	C	0.2615	-0.0159	0.0027	6.84E-09
rs8082036	17	3882613	C	G	0.5123	0.0238	0.0024	7.31E-24
rs4796334	17	6469793	A	G	0.5025	-0.0068	0.0024	4.03E-03
rs1215	17	7163350	A	G	0.8567	-0.006	0.0034	7.95E-02
rs4968200	17	7448457	C	G	0.1421	-0.0127	0.0034	1.81E-04
rs34351630	17	16030520	T	C	0.4654	0.0001	0.0024	9.55E-01
rs12945803	17	46552229	T	C	0.7822	-0.0021	0.0029	4.71E-01
rs28519449	17	54195453	T	C	0.4043	0.0017	0.0024	4.82E-01
rs8068952	17	59286644	C	G	0.7839	-0.0285	0.0029	1.21E-22
rs77672322	17	62497964	T	C	0.0264	0.0279	0.0077	3.06E-04
rs11653958	17	62686730	A	G	0.7425	0.0197	0.0028	9.17E-13
rs996865	17	69371318	T	C	0.0753	-0.0475	0.0046	1.82E-25
rs59606152	17	79952944	T	C	0.1115	-0.0175	0.004	1.10E-05
rs8089099	18	10078071	A	G	0.2746	0.0235	0.0027	1.52E-18

rs1985511	18	19816712	A	T	0.4503	0.0165	0.0024	5.60E-12
rs303752	18	21074255	A	G	0.409	-0.0011	0.0024	6.57E-01
rs1668091	18	22290711	T	C	0.681	0.0015	0.0025	5.44E-01
rs9807668	18	42827898	T	C	0.0946	0.0252	0.0041	4.93E-10
rs2202572	18	53566471	A	C	0.3289	0.0005	0.0025	8.37E-01
rs11085744	19	10819967	T	C	0.5595	-0.0098	0.0024	4.01E-05
rs2967516	19	36881643	A	G	0.709	0.0092	0.0026	4.18E-04
rs6032942	20	10745545	C	G	0.2325	0.0227	0.0028	5.19E-16
rs12627254	21	35368402	T	G	0.1279	0.0357	0.0035	6.85E-24
rs113111175	22	50867711	T	C	0.1219	0.0102	0.0037	5.72E-03
rs9435733	1	17308254	T	C	0.4817	0.0389	0.0024	5.95E-61
rs755249	1	39995074	T	C	0.2328	-0.0239	0.0028	9.82E-18
rs1192415	1	92077097	A	G	0.8122	0.044	0.003	2.28E-47
rs11165787	1	92381483	A	G	0.6878	0.0245	0.0026	1.63E-21
rs35043843	1	118911295	T	G	0.7562	0.0039	0.0028	1.63E-01
rs878471	1	150547747	A	G	0.5797	0.0063	0.0024	9.02E-03
rs2816992	1	200069216	A	G	0.5879	0.0042	0.0024	7.98E-02
rs1008833	1	204426295	A	G	0.8541	-0.0129	0.0034	1.27E-04
rs556648	1	215120596	A	G	0.2166	-0.0018	0.0029	5.36E-01
rs6604614	1	218631452	C	G	0.7152	-0.0085	0.0026	1.25E-03
rs28613267	1	218855029	C	G	0.5112	0.0062	0.0024	9.94E-03
rs1338227	1	219853742	T	G	0.5774	0.0245	0.0024	3.92E-24
rs12757436	1	221631938	A	G	0.3349	-0.0079	0.0025	1.64E-03
rs2355237	1	239857524	A	G	0.5124	0.0278	0.0024	1.77E-31
rs55884799	2	18287623	T	C	0.8271	-0.0415	0.0031	4.02E-40
rs3791679	2	56096892	A	G	0.7714	-0.0231	0.0028	3.02E-16
rs62168891	2	135672187	T	C	0.4032	0.0023	0.0024	3.48E-01
rs72902177	2	157016257	T	C	0.1346	-0.0332	0.0035	2.20E-21
rs2571445	2	218683154	A	G	0.3971	-0.0199	0.0024	3.08E-16
rs62201738	2	229502197	A	C	0.9218	-0.0743	0.0044	9.45E-63
rs6710301	2	239441308	A	C	0.1492	0.0223	0.0033	2.71E-11
rs4308141	2	239881309	C	G	0.8011	-0.0484	0.003	3.58E-59
rs1529672	3	25520582	A	C	0.1736	0.0423	0.0031	1.73E-41

rs17666332	3	29469675	T	G	0.7235	0.0267	0.0027	9.22E-24
rs12715478	3	55152319	A	G	0.5941	0.025	0.0024	1.35E-24
rs6445932	3	57879611	T	G	0.7519	-0.0248	0.0028	2.38E-19
rs4132748	3	67455803	T	C	0.3068	-0.0044	0.0026	9.11E-02
rs12497779	3	98822050	T	G	0.2334	0.0003	0.0028	9.19E-01
rs2999090	3	127931340	A	G	0.881	-0.0433	0.0037	6.76E-32
rs12634907	3	158226886	A	G	0.6558	-0.0051	0.0025	4.29E-02
rs879394	3	168709843	T	G	0.2348	-0.0298	0.0028	4.71E-26
rs78101726	3	169295436	A	G	0.8459	0.0182	0.0033	3.65E-08
rs62289340	4	7879027	T	C	0.4358	0.0167	0.0024	2.36E-12
rs2609279	4	89855495	T	C	0.2145	0.0537	0.0029	2.08E-76
rs2869966	4	89869078	T	C	0.4065	-0.0415	0.0024	5.78E-66
rs6533183	4	106133184	T	C	0.6545	-0.0297	0.0025	2.60E-32
rs11722225	4	106766430	T	C	0.9335	-0.0478	0.0048	1.68E-23
rs34712979	4	106819053	A	G	0.2561	-0.0682	0.0028	4.18E-134
rs13141641	4	145506456	T	C	0.601	-0.0704	0.0024	3.65E-184
rs2353940	4	145740898	T	C	0.7462	0.0246	0.0028	5.01E-19
rs268717	5	33352738	T	C	0.9074	-0.0004	0.0041	9.18E-01
rs6859730	5	44367221	A	T	0.3275	-0.004	0.0025	1.10E-01
rs12522114	5	52187038	A	C	0.265	-0.0367	0.0027	1.47E-41
rs2441026	5	53444498	T	C	0.4625	0.003	0.0024	2.11E-01
rs425102	5	77396400	T	G	0.7597	-0.0075	0.0028	7.13E-03
rs987068	5	95025146	C	G	0.6889	-0.0296	0.0026	1.46E-30
rs3843503	5	131466629	A	T	0.4482	0.0118	0.0024	1.28E-06
rs7733410	5	147856522	A	G	0.4407	0.0505	0.0024	1.56E-96
rs11952673	5	148652302	T	G	0.3989	-0.0125	0.0025	3.35E-07
rs11134766	5	156908317	T	C	0.0635	-0.0628	0.0049	8.04E-38
rs11134789	5	156944199	A	C	0.3412	-0.0408	0.0025	3.06E-59
rs1294417	6	6741932	T	C	0.4577	-0.0311	0.0024	3.93E-39
rs2076295	6	7563232	T	G	0.5497	-0.0234	0.0024	6.95E-23
rs10498672	6	7797840	C	G	0.8227	-0.0034	0.0031	2.70E-01
rs13198081	6	22017543	C	G	0.3532	0.0297	0.0025	3.07E-33
rs7752448	6	28301099	A	G	0.8746	0.0288	0.0036	7.31E-16

rs2070600	6	32151443	T	C	0.0629	0.1452	0.0049	3.00E-189
rs9274247	6	32631295	A	G	0.3212	-0.0469	0.003	9.79E-57
rs13206405	6	73663814	A	C	0.2015	0.0344	0.003	4.67E-31
rs2798641	6	109268050	T	C	0.1829	-0.045	0.0031	3.89E-48
rs6918725	6	126990392	T	G	0.4813	0.0097	0.0024	5.19E-05
rs17280293	6	142688969	A	G	0.973	-0.1803	0.0074	2.34E-131
rs7753012	6	142745883	T	G	0.6949	-0.0712	0.0026	4.71E-165
rs4318980	7	7256490	A	G	0.4147	-0.0172	0.0024	9.08E-13
rs4721442	7	15506007	T	G	0.8339	-0.0048	0.0032	1.32E-01
rs2261360	7	99692993	T	G	0.2322	0.0219	0.0028	8.74E-15
rs12698403	7	156127246	A	G	0.4418	-0.0236	0.0024	1.48E-22
rs771662	9	1568941	T	C	0.3493	-0.0024	0.0025	3.39E-01
rs1570203	9	4120648	A	G	0.5296	0.0246	0.0024	5.78E-25
rs1107677	9	23587027	T	C	0.4845	0.0219	0.0024	3.88E-20
rs28446321	9	98266855	A	T	0.0907	-0.0523	0.0042	4.72E-36
rs1491106	9	109483517	T	G	0.3764	0.0245	0.0025	2.81E-23
rs10983184	9	119234058	T	C	0.6404	0.0273	0.0025	9.05E-28
rs7024579	9	139100413	T	C	0.3154	0.008	0.0026	1.99E-03
rs4073153	9	139259349	A	G	0.5613	-0.0013	0.0024	6.07E-01
rs7090277	10	12278021	A	T	0.5165	0.0409	0.0024	3.97E-67
rs7914842	10	30268770	A	G	0.5787	0.0134	0.0024	2.70E-08
rs7082066	10	64998971	A	G	0.1848	0.0087	0.0031	4.40E-03
rs10998018	10	69962954	A	G	0.4965	-0.0025	0.0024	2.94E-01
rs7098573	10	75580014	A	G	0.7177	-0.0173	0.0027	6.12E-11
rs1259605	10	77119039	T	C	0.7515	0.0009	0.0028	7.49E-01
rs2637254	10	78312002	A	G	0.5108	-0.0188	0.0024	3.02E-15
rs721917	10	81706324	A	G	0.5811	0.0193	0.0024	1.65E-15
rs4279944	10	124297637	T	C	0.1514	0.0218	0.0034	2.18E-10
rs17596617	11	43690717	T	C	0.3172	0.0002	0.0025	9.48E-01
rs10838435	11	45244903	C	G	0.1439	0.0096	0.0034	4.45E-03
rs71490394	11	62370155	A	G	0.3671	0.0108	0.0025	1.26E-05
rs2027761	11	73036179	T	C	0.113	0.0369	0.0038	1.31E-22
rs11234768	11	86448839	T	C	0.8458	0.0303	0.0033	5.07E-20

rs541601	11	126009500	T	C	0.1829	-0.0241	0.0031	5.29E-15
rs7977418	12	28588242	T	C	0.5415	-0.0045	0.0024	5.67E-02
rs1689510	12	56396768	C	G	0.3373	-0.0145	0.0025	8.36E-09
rs11172113	12	57527283	T	C	0.5889	-0.0227	0.0024	7.04E-21
rs12825748	12	65793153	C	G	0.3087	0.0039	0.0026	1.34E-01
rs56390486	12	85719906	A	G	0.2905	0.0051	0.0026	5.10E-02
rs9788269	12	94194890	A	G	0.7324	0.0016	0.0027	5.53E-01
rs113745635	12	95554771	T	C	0.2163	-0.0275	0.0029	2.36E-21
rs7970544	12	96242109	T	G	0.1869	0.0439	0.0031	1.45E-46
rs10850377	12	115201436	A	G	0.3408	0.0098	0.0025	1.07E-04
rs35505	12	115501127	A	G	0.6861	-0.0013	0.0026	6.11E-01
rs35107139	14	54419106	A	C	0.5962	0.0315	0.0025	3.40E-36
rs1756281	14	84338431	A	G	0.6987	0.0237	0.0026	1.38E-19
rs11160037	14	92512143	A	G	0.6206	-0.0079	0.0025	1.36E-03
rs11621587	14	93098339	C	G	0.1821	0.0023	0.0031	4.56E-01
rs2012453	15	41840238	A	G	0.4107	0.0239	0.0024	4.26E-23
rs56383987	15	41953211	T	C	0.0549	-0.0364	0.0053	7.08E-12
rs12917612	15	67491274	A	C	0.2295	0.0141	0.0028	5.82E-07
rs1441358	15	71612514	T	G	0.6642	0.0642	0.0025	4.12E-145
rs62015883	15	71803450	T	C	0.1784	-0.031	0.0031	1.22E-23
rs1896797	15	84274591	A	G	0.4904	0.0292	0.0024	2.48E-34
rs78442819	16	10740982	C	G	0.1997	-0.0355	0.0031	2.25E-31
rs12446589	16	28870962	A	G	0.3998	-0.0059	0.0024	1.38E-02
rs11648508	16	58063513	T	G	0.6832	0.0332	0.0026	9.86E-39
rs8047194	16	69891510	T	G	0.4961	-0.0028	0.0024	2.38E-01
rs11858992	16	75411445	A	C	0.4037	0.038	0.0024	4.83E-55
rs2345443	16	78225633	A	G	0.3114	0.011	0.0026	2.11E-05
rs2244592	17	28072327	A	G	0.4526	-0.0323	0.0024	4.60E-42
rs62070648	17	29210595	A	G	0.27	-0.0027	0.0027	3.05E-01
rs35246838	17	36915540	T	C	0.8681	0.0386	0.0036	1.41E-27
rs8069451	17	37504933	T	C	0.7494	0.0008	0.0027	7.69E-01
rs79412431	17	43940021	A	G	0.2161	-0.0108	0.0029	2.44E-04
rs6501431	17	68976415	T	C	0.7843	-0.0111	0.0029	1.32E-04

rs6501455	17	69201811	A	G	0.5015	0.0206	0.0024	5.68E-18
rs9892893	17	73525670	T	G	0.2606	0.0124	0.0027	6.58E-06
rs513953	18	8801351	A	G	0.2542	-0.0255	0.0027	7.42E-21
rs11082051	18	20234336	A	G	0.5298	0.006	0.0024	1.10E-02
rs9947743	18	20708321	A	G	0.7867	-0.006	0.0029	4.01E-02
rs12607758	18	51022606	T	C	0.5932	-0.0078	0.0024	1.24E-03
rs9636166	19	31829613	A	C	0.8739	0.0355	0.0036	3.66E-23
rs34093919	19	41117300	A	G	0.0128	0.1535	0.0106	1.69E-47
rs2145272	20	6626218	A	G	0.6376	-0.0087	0.0025	4.11E-04
rs2236180	20	25282608	T	C	0.815	0.016	0.003	1.41E-07
rs4413223	20	30858967	A	G	0.1722	-0.0232	0.0031	1.30E-13
rs143384	20	34025756	A	G	0.5964	-0.0095	0.0024	9.19E-05
rs12481092	20	45486817	T	C	0.2723	-0.0022	0.0027	4.21E-01
rs4809221	20	62372706	A	G	0.6753	0.0006	0.0026	8.04E-01
rs62213732	21	35675966	T	C	0.6317	0.0246	0.0025	9.34E-24
rs1978968	22	18448113	T	C	0.2367	0.0223	0.0028	1.25E-15
rs9610955	22	20790723	C	G	0.1972	-0.0269	0.003	2.69E-19
rs2283847	22	28181399	T	C	0.5569	-0.0219	0.0024	3.621E-19

Chr, Chromosome; BP, position (GRCh37); FreqRisk, allele frequency of risk allele; Beta, effect estimate; SE, standard error.

Table S3. Participants baseline characteristics according to COPD status (n = 155,403).

Characteristics	COPD status	
	No	Yes
NO.	152,485	2,918
Demographics		
Age (years)	55.3 (7.9) [1]	60.4 (6.4)
Sex (male, %)	44.4 [2]	52.6
Education (≥ College graduate, %)	44.0	25.6
Townsend Deprivation Index	-1.6 (2.8)	-0.9 (3.1)
Household income (≥ £31,000, %)	56.6	32.4
Ethnicity (white, %)	90.8	92.7
Lifestyle factors		
Smoking status		
Never	58.7	23.4
Previous	33.9	49.8
Current	7.4	26.8
Alcohol drinker status		
Never	3.1	3.0
Previous	2.8	4.9
Current	94.0	92.1
Alcoholic beverages (g/d)	154.2 (128.2)	196.8 (177.4)
Seafood intake (≥1 servings/d, %)	0.4	0.5
Animal organs intake (≥1 servings/d, %)	1.2	1.6
Total energy intake (kcal/d)	2116.5 (648.6)	2142.7 (690.2)
Regular physical activity (≥ 500 MET-min/week)	72.9	66.7
Diet score		
0	0.7	1.2
1	4.0	5.8
2	11.8	16.6

3	22.4	23.6
4	28.0	26.0
5	22.7	18.1
6	9.5	7.8
7	1.0	0.9
Diet score ≥ 4	61.1	52.8
Clinical and laboratory measures		
Urate (umol/L)	303.1 (78.2)	323.8 (82.6)
FEV_1 (L)	2.8 (0.76)	2.2 (0.7)
FVC (L)	3.7 (1.0)	3.2 (0.9)
FEV_1/FVC	0.7 (0.0)	0.7 (0.0)
Height (cm)	169.2 (9.1)	169.5 (9.1)
Body mass index (kg/m^2)	26.7 (4.5)	27.9 (5.3)
Waist circumference (cm)	88.4 (13.0)	93.8 (14.3)
Creatinine (umol/L)	71.7 (15.9)	73.3 (25.6)
Metabolic syndrome (yes, %)	22.0	35.1
Asthma (yes, %)	2.0	10.4
Systemic inflammation Index	21.4 (10.4)	23.3 (12.5)
Family diseases history		
Cardiovascular disease (yes, %)	55.0	60.1
Hypertension (yes, %)	49.5	42.7
Diabetes (yes, %)	20.8	20.2
Personal diseases history		
Kidney disease (yes, %)	1.6	2.0
Hypertension (yes, %)	21.3	35.2
Diabetes (yes, %)	3.3	7.6
Medication history		
Antihypertensive drugs (yes, %)	8.0	17.3
Lipid-lowering drugs (yes, %)	7.1	15.2
Hypoglycemic drugs (yes, %)	0.4	1.0
Urate-affecting drugs (yes, %)	0.8	1.8

[1] Mean (standard deviation) (all such values).

[2] Percentage (all such values).

Table S4. Association between hyperuricemia and risk of COPD (n = 155,403).

	Serum urate levels		*P* value [1]
	Normal	Hyperuricemia	
Number of participants	138,388	17,015	
Number of incident COPD	2,446	472	
Person-years	1,256,168	153,801	
Model 1 [2]	Reference	**1.53 (1.38, 1.68)**	**<0.0001**
Model 2 [4]	Reference	**1.25 (1.13, 1.38)**	**<0.0001**
Model 3 [5]	Reference	**1.14 (1.02, 1.26)**	**0.01**
Model 4 [6]	Reference	**1.11 (1.00, 1.24)**	**0.03**

Abbreviations: SU, serum urate; SD, standard deviation; COPD, chronic obstructive pulmonary disease.

[1] Analysis by Cox proportional hazards regression models.

[2] Crude model.

[3] Hazard ratios (95% confidence interval) (all such values).

[4] Adjusted for age, sex, and BMI.

[5] Additionally adjusted for height, household income, education levels, physical activity, Townsend deprivation index, physical activity, baseline metabolic syndrome, family history of diseases (hypertension, cardiovascular disease, and diabetes), and baseline FEV1/FVC ratio.

[6] Additionally adjusted for smoking status, drinking status, diet score, baseline asthma, SII, ethnicity, creatinine, seafood and animal organs intake, alcoholic beverages, medication history (including antihypertensive drugs, lipid-lowering drugs, hypoglycemic drugs, allopurinol, and diuretics), and personal history of diseases (hypertension, diabetes, and kidney disease).

Table S5. Hazards ratios (HRs) and 95% confidence interval (CIs) of COPD by joint effect of SU levels and diet score after excluding COPD occurred within first 3 years of follow up (n = 154,990).

Joint effect		Number of participants	Number of incident COPD	Model 1 [1]	Model 2 [2]	Model 3 [3]	Model 4 [4]
Serum urate levels	Diet score						
Hyperuricemia	<4	7,991	209	Reference	Reference	Reference	Reference
Hyperuricemia	≥4	8,958	197	**0.80 (0.66, 0.97)** [5]	**0.72 (0.59, 0.88)**	0.84 (0.69, 1.03)	0.83 (0.68, 1.01)
Normal	<4	52,452	968	**0.71 (0.61, 0.83)**	**0.84 (0.72, 0.97)**	0.93 (0.80, 1.09)	0.90 (0.77, 1.06)
Normal	≥4	85,589	1,131	**0.50 (0.43, 0.58)**	**0.56 (0.48, 0.66)**	**0.70 (0.60, 0.82)**	**0.74 (0.63, 0.86)**

Abbreviations: SU, serum urate; COPD, chronic obstructive pulmonary disease.

[1] Crude model.

[2] Adjusted for age, sex, and BMI.

[3] Additionally adjusted for height, household income, education levels, physical activity, Townsend deprivation index, baseline metabolic syndrome, family history of diseases (hypertension, cardiovascular disease, and diabetes), and baseline FEV1/FVC ratio.

[4] Additionally adjusted for smoking status, alcohol consumption, baseline asthma, SII, ethnicity, creatinine, seafood and animal organs intake, alcoholic beverages, medication history (including antihypertensive drugs, lipid-lowering drugs, hypoglycemic drugs, allopurinol, and diuretics), and personal history of diseases (hypertension, diabetes, and kidney disease).

[5] Hazard ratios (95% confidence interval) (all such values).

Table S6. Association between genetic risk and the risk of COPD (n = 153,620).

	Genetic risk			*P* for trend [1]
	Low (tertile 1)	Middle (tertile 2)	High (tertile 3)	
Number of participants	51,155	51,155	51,310	
Number of incident COPD	840	955	1,091	
Person-years	464,667	464,522	465,405	
Model 1 [2]	Reference	**1.14 (1.04, 1.25)** [3]	**1.30 (1.19, 1.42)**	**<0.0001**
Model 2 [4]	Reference	**1.13 (1.03, 1.24)**	**1.3 (1.18, 1.42)**	**<0.0001**
Model 3 [5]	Reference	**1.14 (1.03, 1.25)**	**1.31 (1.19, 1.43)**	**<0.0001**
Model 4 [6]	Reference	**1.12 (1.02, 1.23)**	**1.27 (1.16, 1.39)**	**<0.0001**

Abbreviation: COPD, chronic obstructive pulmonary disease.

[1] Analysis by Cox proportional hazards regression models.

[2] Crude model.

[3] Hazard ratios (95% confidence interval) (all such values).

[4] Adjusted for age, sex, and BMI.

[5] Additionally adjusted for height, household income, education levels, physical activity, Townsend deprivation index, physical activity, baseline metabolic syndrome, and family history of diseases (hypertension, cardiovascular disease, and diabetes).

[6] Additionally adjusted for smoking status, drinking status, diet score, baseline asthma, SII, ethnicity, creatinine, seafood and animal organs intake, alcoholic beverages, medication history (including antihypertensive drugs, lipid-lowering drugs, hypoglycemic drugs, allopurinol, and

diuretics), and personal history of diseases (hypertension, diabetes, and kidney disease), first 10 genetic principal components, and genotype measurement batch.

Table S7. Hazards ratios (HRs) and 95% confidence interval (CIs) of COPD by joint effect of SU levels and diet score in subgroup analyses.

Subgroups	Joint effect		Number of participants	Number of incident COPD	Model 1 [1]	Model 2 [2]	Model 3 [3]	Model 4 [4]
	Serum urate levels	Diet score						
Men								
	Hyperuricemia	<4	5,819	174	Reference	Reference	Reference	Reference
	Hyperuricemia	≥4	4,939	126	0.82 (0.65, 1.03)	**0.73 (0.58, 0.92)**	0.86 (0.68, 1.08)	0.84 (0.66, 1.06)
	Normal	<4	27,878	697	0.85 (0.72, 1.00)	0.88 (0.74, 1.04)	1.01 (0.85, 1.19)	1.00 (0.84, 1.19)
	Normal	≥4	30,668	539	**0.58 (0.49, 0.69)**	**0.56 (0.47, 0.67)**	**0.72 (0.61, 0.86)**	**0.78 (0.65, 0.93)**
Women								
	Hyperuricemia	<4	2,206	69	Reference	Reference	Reference	Reference
	Hyperuricemia	≥4	4,051	103	0.74 (0.54, 1.00)	**0.68 (0.50, 0.92)**	0.79 (0.58, 1.08)	0.82 (0.60, 1.11)
	Normal	<4	24,741	438	**0.54 (0.42, 0.70)**	**0.74 (0.57, 0.96)**	0.80 (0.62, 1.03)	0.79 (0.61, 1.03)
	Normal	≥4	55,101	772	**0.42 (0.33, 0.54)**	**0.52 (0.40, 0.67)**	**0.63 (0.49, 0.81)**	**0.69 (0.53, 0.89)**
Age<60								
	Hyperuricemia	<4	4,900	78	Reference	Reference	Reference	Reference
	Hyperuricemia	≥4	4,684	60	0.77 (0.55, 1.09)	0.72 (0.51, 1.02)	0.85 (0.60, 1.19)	0.80 (0.57, 1.12)
	Normal	<4	35,273	431	**0.77 (0.60, 0.98)**	0.87 (0.68, 1.12)	1.00 (0.78, 1.28)	0.95 (0.74, 1.22)

	Normal	≥4	52,998	447	**0.52 (0.41, 0.66)**	**0.57 (0.44, 0.73)**	**0.74 (0.57, 0.95)**	0.77 (0.60, 1.00)
Age≥60								
	Hyperuricemia	<4	3,125	165	Reference	Reference	Reference	Reference
	Hyperuricemia	≥4	4,306	169	**0.71 (0.57, 0.88)**	**0.73 (0.59, 0.91)**	0.86 (0.69, 1.07)	0.87 (0.70, 1.08)
	Normal	<4	17,346	704	**0.77 (0.65, 0.91)**	**0.81 (0.69, 0.97)**	0.91 (0.76, 1.08)	0.91 (0.76, 1.08)
	Normal	≥4	32,771	864	**0.50 (0.42, 0.59)**	**0.55 (0.46, 0.65)**	**0.69 (0.58, 0.82)**	**0.74 (0.62, 0.88)**
BMI<25								
	Hyperuricemia	<4	786	25	Reference	Reference	Reference	Reference
	Hyperuricemia	≥4	1,160	30	0.76 (0.44, 1.29)	0.72 (0.42, 1.22)	1.01 (0.59, 1.73)	1.09 (0.63, 1.86)
	Normal	<4	19,149	377	**0.63 (0.42, 0.95)**	0.85 (0.56, 1.28)	0.95 (0.63, 1.43)	0.82 (0.54, 1.26)
	Normal	≥4	38,708	477	**0.39 (0.26, 0.59)**	**0.49 (0.32, 0.74)**	**0.63 (0.41, 0.94)**	0.67 (0.44, 1.02)
BMI≥25								
	Hyperuricemia	<4	7,239	218	Reference	Reference	Reference	Reference
	Hyperuricemia	≥4	7,830	199	**0.81 (0.67, 0.98)**	**0.73 (0.60, 0.88)**	0.83 (0.68, 1.01)	**0.81 (0.67, 0.99)**
	Normal	<4	33,470	758	**0.76 (0.65, 0.89)**	**0.82 (0.70, 0.95)**	0.92 (0.79, 1.07)	0.93 (0.80, 1.09)
	Normal	≥4	47,061	834	**0.58 (0.50, 0.68)**	**0.59 (0.50, 0.68)**	**0.73 (0.63, 0.86)**	**0.77 (0.66, 0.90)**
Low genetic risk								
	Hyperuricemia	<4	2,670	77	Reference	Reference	Reference	Reference
	Hyperuricemia	≥4	2,979	83	0.89 (0.65, 1.21)	0.81 (0.59, 1.11)	0.88 (0.64, 1.20)	0.83 (0.61, 1.14)
	Normal	<4	17,303	313	**0.62 (0.48, 0.80)**	**0.73 (0.57, 0.94)**	0.81 (0.63, 1.05)	**0.77 (0.59, 0.99)**

Normal	≥4	28,203	367	**0.44 (0.34, 0.56)**	**0.50 (0.39, 0.64)**	**0.59 (0.46, 0.77)**	**0.61 (0.47, 0.79)**
Middle genetic risk							
Hyperuricemia	<4	2,616	74	Reference	Reference	Reference	Reference
Hyperuricemia	≥4	2,972	63	0.74 (0.52, 1.03)	**0.65 (0.47, 0.92)**	**0.71 (0.50, 0.99)**	0.75 (0.53, 1.06)
Normal	<4	17,392	384	0.79 (0.61, 1.01)	0.92 (0.71, 1.18)	0.99 (0.77, 1.28)	0.96 (0.74, 1.24)
Normal	≥4	28,175	434	**0.54 (0.42, 0.70)**	**0.60 (0.46, 0.77)**	**0.70 (0.54, 0.90)**	**0.75 (0.58, 0.98)**
High genetic risk							
Hyperuricemia	<4	2,663	88	Reference	Reference	Reference	Reference
Hyperuricemia	≥4	2,947	81	0.80 (0.59, 1.09)	**0.73 (0.54, 0.99)**	0.83 (0.61, 1.13)	0.83 (0.61, 1.13)
Normal	<4	17,307	427	**0.76 (0.60, 0.96)**	0.90 (0.71, 1.14)	1.04 (0.82, 1.31)	1.03 (0.81, 1.32)
Normal	≥4	28,393	495	**0.52 (0.42, 0.66)**	**0.59 (0.47, 0.75)**	**0.74 (0.58, 0.94)**	0.78 (0.61, 1.00)
Never smoking							
Hyperuricemia	<4	3,980	38	Reference	Reference	Reference	Reference
Hyperuricemia	≥4	4,662	59	1.28 (0.85, 1.93)	1.10 (0.73, 1.66)	1.20 (0.80, 1.81)	1.16 (0.77, 1.76)
Normal	<4	30,197	204	0.72 (0.51, 1.02)	0.82 (0.58, 1.16)	0.87 (0.61, 1.23)	0.89 (0.62, 1.28)
Normal	≥4	51,391	382	0.78 (0.55, 1.09)	0.82 (0.58, 1.15)	0.92 (0.65, 1.29)	0.93 (0.65, 1.32)
Previous smoker							
Hyperuricemia	<4	3,326	150	Reference	Reference	Reference	Reference
Hyperuricemia	≥4	3,820	146	**0.78 (0.62, 0.98)**	**0.74 (0.58, 0.93)**	0.84 (0.67, 1.06)	0.83 (0.66, 1.04)
Normal	<4	16,894	512	**0.66 (0.55, 0.79)**	**0.77 (0.64, 0.92)**	0.90 (0.75, 1.08)	0.91 (0.75, 1.10)

Normal	≥4	29,143	644	**0.47 (0.4, 0.57)**	**0.56 (0.46, 0.67)**	**0.69 (0.57, 0.83)**	**0.69 (0.57, 0.83)**
Current smoker							
Hyperuricemia	<4	719	55	Reference	Reference	Reference	Reference
Hyperuricemia	≥4	508	24	0.63 (0.39, 1.02)	**0.55 (0.34, 0.89)**	**0.54 (0.33, 0.87)**	**0.50 (0.31, 0.82)**
Normal	<4	5,528	419	1.05 (0.79, 1.40)	1.11 (0.83, 1.48)	1.02 (0.76, 1.36)	1.02 (0.76, 1.37)
Normal	≥4	5,235	285	0.75 (0.56, 1.00)	**0.72 (0.54, 0.98)**	0.80 (0.59, 1.08)	0.80 (0.59, 1.08)

Abbreviations: SU, serum urate; COPD, chronic obstructive pulmonary disease.

[1] Crude model.

[2] Adjusted for age, sex, and BMI.

[3] Additionally adjusted for height, household income, education levels, physical activity, Townsend deprivation index, baseline metabolic syndrome, family history of diseases (hypertension, cardiovascular disease, and diabetes), and baseline FEV1/FVC ratio.

[4] Additionally adjusted for smoking status, alcohol consumption, baseline asthma, SII, ethnicity, creatinine, seafood and animal organs intake, alcoholic beverages, medication history (including antihypertensive drugs, lipid-lowering drugs, hypoglycemic drugs, allopurinol, and diuretics), and personal history of diseases (hypertension, diabetes, and kidney disease).

[5] Hazard ratios (95% confidence interval) (all such values).

Table S8. Hazards ratios (HRs) and 95% confidence interval (CIs) of COPD by joint exposures of SU levels and diet score: results from competing risk regression model (n = 155,403).

Joint effect		Number of participants	Number of incident COPD	Model 1 [1]	Model 2 [2]	Model 3 [3]	Model 4 [4]
Serum urate levels	Diet score						
Hyperuricemia	<4	8,025	243	Reference	Reference	Reference	Reference
Hyperuricemia	≥4	8,990	229	**0.82 (0.68, 0.98)** [5]	**0.74 (0.62, 0.89)**	0.87 (0.72, 1.04)	0.86 (0.71, 1.03)
Normal	<4	52,619	1,135	**0.73 (0.63, 0.83)**	**0.85 (0.74, 0.98)**	**0.95 (0.82, 1.10)**	0.92 (0.80, 1.07)
Normal	≥4	85,769	1,311	**0.51 (0.44, 0.58)**	**0.56 (0.49, 0.65)**	**0.71 (0.61, 0.82)**	**0.75 (0.64, 0.87)**

Abbreviations: SU, serum urate; COPD, chronic obstructive pulmonary disease.

[1] Crude model.

[2] Adjusted for age, sex, and BMI.

[3] Additionally adjusted for height, household income, education levels, physical activity, Townsend deprivation index, baseline metabolic syndrome, family history of diseases (hypertension, cardiovascular disease, and diabetes), and baseline FEV1/FVC ratio.

[4] Additionally adjusted for smoking status, alcohol consumption, baseline asthma, SII, ethnicity, creatinine, seafood and animal organs intake, alcoholic beverages, medication history (including antihypertensive drugs, lipid-lowering drugs, hypoglycemic drugs, allopurinol, and diuretics), and personal history of diseases (hypertension, diabetes, and kidney disease).

[5] Hazard ratios (95% confidence interval) (all such values).

Table S9. Association between weighted diet score and risk of COPD (n = 155,403).

	Tertiles of weighted lifestyle score			*P* for trend [1]
	Tertile 1	Tertile 2	Tertile 3	
Weighted lifestyle score: median	24.7	51.4	73.3	
Number of participants	52,803	57,262	45,338	
Number of incident COPD	2,975	2,198	1,176	
Person-years	297,500	219,800	117,600	
Model 1 [2]	Reference	**0.72 (0.66, 0.78)** [3]	**0.57 (0.52, 0.63)**	**<0.0001**
Model 2 [4]	Reference	**0.68 (0.62, 0.74)**	**0.54 (0.49, 0.60)**	**<0.0001**
Model 3 [5]	Reference	**0.76 (0.70, 0.82)**	**0.63 (0.57, 0.70)**	**<0.0001**
Model 4 [6]	Reference	**0.82 (0.75, 0.89)**	**0.70 (0.64, 0.78)**	**<0.0001**

Abbreviation: COPD, chronic obstructive pulmonary disease.

[1] Analysis by Cox proportional hazards regression models.

[2] Crude model.

[3] Hazard ratios (95% confidence interval) (all such values).

[4] Adjusted for age, sex, and BMI.

[5] Additionally adjusted for height, household income, education levels, physical activity, Townsend deprivation index, physical activity, baseline metabolic syndrome, family history of diseases (hypertension, cardiovascular disease, and diabetes), and baseline FEV1/FVC ratio.

[6] Additionally adjusted for smoking status, alcohol consumption, baseline asthma, SII, ethnicity, creatinine, seafood and animal organs intake, alcoholic beverages, medication history (including antihypertensive drugs, lipid-lowering drugs, hypoglycemic drugs, allopurinol, and diuretics), personal history of diseases (hypertension, diabetes, and kidney disease), total energy intake, and serum urate.

Table S10. Hazards ratios (HRs) and 95% confidence interval (CIs) of COPD by joint exposures of SU levels and weighted diet score (n = 155,403).

Joint effect		Number of participants	Number of incident COPD	Model 1 [1]	Model 2 [2]	Model 3 [3]	Model 4 [4]
Serum urate levels	Weighted diet score						
Hyperuricemia	Tertile 1	7,290	224	Reference	Reference	Reference	Reference
Hyperuricemia	Tertile 2	6,059	166	**0.86 (0.70, 1.05)** [5]	**0.79 (0.65, 0.97)**	0.94 (0.77, 1.15)	0.88 (0.72, 1.07)
Hyperuricemia	Tertile 3	3,666	82	**0.71 (0.55, 0.91)**	**0.64 (0.49, 0.82)**	**0.76 (0.59, 0.98)**	**0.77 (0.59, 0.99)**
Normal	Tertile 1	45,513	1,043	**0.76 (0.66, 0.88)**	0.90 (0.78, 1.04)	1.01 (0.88, 1.18)	0.95 (0.82, 1.11)
Normal	Tertile 2	51,203	845	**0.54 (0.46, 0.62)**	**0.60 (0.51, 0.69)**	**0.74 (0.64, 0.86)**	**0.78 (0.66, 0.91)**
Normal	Tertile 3	41,672	558	**0.43 (0.37, 0.50)**	**0.48 (0.41, 0.56)**	**0.62 (0.53, 0.73)**	**0.66 (0.56, 0.78)**

Abbreviations: SU, serum urate; COPD, chronic obstructive pulmonary disease.

[1] Crude model.

[2] Adjusted for age, sex, and BMI.

[3] Additionally adjusted for height, household income, education levels, physical activity, Townsend deprivation index, baseline metabolic syndrome, family history of diseases (hypertension, cardiovascular disease, and diabetes), and baseline FEV1/FVC ratio.

[4] Additionally adjusted for smoking status, alcohol consumption, baseline asthma, SII, ethnicity, creatinine, seafood and animal organs intake, alcoholic beverages, medication history (including antihypertensive drugs, lipid-lowering drugs, hypoglycemic drugs, allopurinol, and diuretics), and personal history of diseases (hypertension, diabetes, and kidney disease).

[5] Hazard ratios (95% confidence interval) (all such values).

Table S11. Hazards ratios (HRs) and 95% confidence interval (CIs) of COPD by joint effect of SU levels and diet score additionally adjusted for baseline estimated glomerular filtration rate.

Joint effect		Number of participants	Number of incident COPD	Model 1 [1]	Model 2 [2]	Model 3 [3]	Model 4 [4]
Serum urate levels	Diet score						
Hyperuricemia	<4	8,025	243	Reference	Reference	Reference	Reference
Hyperuricemia	≥4	8,990	229	**0.80 (0.67, 0.96)** [5]	**0.73 (0.61, 0.87)**	0.85 (0.71, 1.02)	0.84 (0.70, 1.01)
Normal	<4	52,619	1,135	**0.72 (0.62, 0.82)**	**0.84 (0.73, 0.97)**	0.94 (0.82, 1.08)	0.90 (0.78, 1.04)
Normal	≥4	85,769	1,311	**0.50 (0.44, 0.57)**	**0.56 (0.49, 0.64)**	**0.70 (0.61, 0.81)**	**0.73 (0.63, 0.84)**

Abbreviations: SU, serum urate; COPD, chronic obstructive pulmonary disease.

[1] Crude model.

[2] Adjusted for age, sex, and BMI.

[3] Additionally adjusted for height, household income, education levels, physical activity, Townsend deprivation index, baseline metabolic syndrome, family history of diseases (hypertension, cardiovascular disease, and diabetes), and baseline FEV1/FVC ratio.

[4] Additionally adjusted for smoking status, alcohol consumption, baseline asthma, SII, ethnicity, creatinine, seafood and animal organs intake, alcoholic beverages, medication history (including antihypertensive drugs, lipid-lowering drugs, hypoglycemic drugs, allopurinol, and diuretics), personal history of diseases (hypertension, diabetes, and kidney disease), and baseline estimated glomerular filtration rate.

[5] Hazard ratios (95% confidence interval) (all such values).

Table S12. Association between SU levels and risk of COPD after excluding baseline FEV1/FVC<0.7 (n = 132,192).

	Uric acid levels				
	Level 1	Level 2	Level 3	Level 4 (hyperuricemia)	*P* for trend [1]
Number of participants	38,965	39,221	39,579	14,427	
Number of incident COPD	315	369	511	250	
Person-years	355,372	356,893	359,334	130,854	
Model 1 [2]	Reference	**1.17 (1.01, 1.36)** [3]	**1.61 (1.39, 1.85)**	**2.10 (1.78, 2.48)**	**<0.0001**
Model 2 [4]	Reference	**1.04 (0.90, 1.21)**	**1.28 (1.11, 1.48)**	**1.52 (1.28, 1.80)**	**<0.0001**
Model 3 [5]	Reference	**1.04 (0.89, 1.21)**	**1.25 (1.08, 1.45)**	**1.34 (1.13, 1.60)**	**<0.0001**
Model 4 [6]	Reference	**1.08 (0.93, 1.26)**	**1.30 (1.12, 1.51)**	**1.32 (1.10, 1.59)**	**0.0001**

Abbreviations: SD, standard deviation; COPD, chronic obstructive pulmonary disease.

[1] Analysis by Cox proportional hazards regression models.

[2] Crude model.

[3] Hazard ratios (95% confidence interval) (all such values).

[4] Adjusted for age, sex, and BMI.

[5] Additionally adjusted for height, household income, education levels, physical activity, Townsend deprivation index, physical activity, baseline metabolic syndrome, family history of diseases (hypertension, cardiovascular disease, and diabetes), and baseline FEV1/FVC ratio.

[6] Additionally adjusted for smoking status, drinking status, diet score, baseline asthma, SII, ethnicity, creatinine, seafood and animal organs intake, alcoholic beverages, medication history (including antihypertensive drugs, lipid-lowering drugs, hypoglycemic drugs, allopurinol, and diuretics), and personal history of diseases (hypertension, diabetes, and kidney disease).

Table S13. Hazards ratios (HRs) and 95% confidence interval (CIs) of COPD by joint effect of SU levels and diet score after excluding participants diagnosed with diabetes, hypertension, and kidney disease at baseline (n = 118,185).

Joint effect		Number of participants	Number of incident COPD	Model 1 [1]	Model 2 [2]	Model 3 [3]	Model 4 [4]
Serum urate levels	Diet score						
Hyperuricemia	<4	4,638	97	Reference	Reference	Reference	Reference
Hyperuricemia	≥4	4,984	95	0.86 (0.64, 1.14) [5]	0.77 (0.58, 1.02)	0.91 (0.68, 1.21)	0.89 (0.66, 1.18)
Normal	<4	41,023	736	0.84 (0.68, 1.04)	0.97 (0.78, 1.21)	1.04 (0.83, 1.29)	0.90 (0.72, 1.12)
Normal	≥4	67,540	861	**0.59 (0.48, 0.73)**	**0.65 (0.52, 0.81)**	**0.76 (0.61, 0.95)**	**0.74 (0.59, 0.92)**

Abbreviations: SU, serum urate; COPD, chronic obstructive pulmonary disease.

[1] Crude model.

[2] Adjusted for age, sex, and BMI.

[3] Additionally adjusted for height, household income, education levels, physical activity, Townsend deprivation index, baseline metabolic syndrome, family history of diseases (hypertension, cardiovascular disease, and diabetes), and baseline FEV1/FVC ratio.

[4] Additionally adjusted for smoking status, alcohol consumption, baseline asthma, SII, ethnicity, creatinine, seafood and animal organs intake, alcoholic beverages, and medication history (including antihypertensive drugs, lipid-lowering drugs, hypoglycemic drugs, allopurinol, and diuretics).

[5] Hazard ratios (95% confidence interval) (all such values).

Table S14. Associations between Mediterranean diet score (MDS) and risk of COPD (n = 155,403).

	Number of participants	Number of incident COPD	Model 1 [1]	Model 2 [2]	Model 3 [3]	Model 4 [4]
MDS						
0-3	28,864	780	Reference	Reference	Reference	Reference
≥3-5	63,881	1,270	**0.72 (0.66, 0.78)** [5]	**0.69 (0.63, 0.75)**	**0.76 (0.69, 0.83)**	**0.83 (0.76, 0.91)**
≥5	62,658	868	**0.49 (0.45, 0.54)**	**0.46 (0.42, 0.51)**	**0.58 (0.52, 0.64)**	**0.67 (0.60, 0.74)**
Diet factors						
Vegetables						
<median	77,886	1,537	Reference	Reference	Reference	Reference
≥median	77,517	1,381	**0.90 (0.84, 0.97)**	**0.80 (0.74, 0.86)**	**0.87 (0.81, 0.93)**	**0.90 (0.83, 0.97)**
Legumes						
<median	105,273	2,022	Reference	Reference	Reference	Reference
≥median	50,130	896	**0.91 (0.84, 0.99)**	0.93 (0.86, 1.00)	0.96 (0.89, 1.04)	0.98 (0.91, 1.07)
Fruit and nuts						
<median	78,075	1,664	Reference	Reference	Reference	Reference
≥median	77,328	1,254	**0.74 (0.69, 0.80)**	**0.67 (0.62, 0.72)**	**0.75 (0.69, 0.81)**	**0.84 (0.78, 0.91)**
Cereals						

<median	78,467	1,748	Reference	Reference	Reference	Reference
≥median	76,936	1,170	**0.67 (0.62, 0.72)**	**0.70 (0.65, 0.75)**	**0.77 (0.72, 0.83)**	**0.83 (0.76, 0.89)**
Fish and seafood						
<median	90,376	1,881	Reference	Reference	Reference	Reference
≥median	65,027	1,037	**0.75 (0.69, 0.80)**	**0.71 (0.66, 0.77)**	**0.81 (0.75, 0.87)**	**0.83 (0.77, 0.90)**
Monounsaturated/ saturated fats ratio						
<median	77,721	1,545	Reference	Reference	Reference	Reference
≥median	77,682	1,373	**0.90 (0.84, 0.97)**	0.97 (0.91, 1.05)	0.95 (0.88, 1.02)	0.94 (0.87, 1.01)
Dairy products						
≥median	92,374	1,851	Reference	Reference	Reference	Reference
<median	63,029	1,067	**0.83 (0.77, 0.89)**	**0.83 (0.77, 0.89)**	**0.87 (0.81, 0.94)**	**0.88 (0.81, 0.95)**
Meat and meat products						
≥median	79,232	1,589	Reference	Reference	Reference	Reference
<median	76,171	1,329	**0.87 (0.81, 0.94)**	**0.91 (0.84, 0.98)**	**0.91 (0.84, 0.98)**	0.95 (0.88, 1.03)
Alcohol						
Never drink or over 2 drinks/day	82,828	1,790	Reference	Reference	Reference	Reference
No more than 2 drinks/day	72,575	1,128	**0.70 (0.65, 0.75)**	**0.68 (0.63, 0.73)**	**0.78 (0.72, 0.84)**	**0.84 (0.78, 0.91)**

Abbreviations: COPD, chronic obstructive pulmonary disease.

[1] Crude model.

[2] Adjusted for age, sex, and BMI.

[3] Additionally adjusted for height, household income, education levels, physical activity, Townsend deprivation index, baseline metabolic syndrome, family history of diseases (hypertension, cardiovascular disease, and diabetes), and baseline FEV1/FVC ratio.

[4] Additionally adjusted for smoking status, alcohol consumption, baseline asthma, SII, ethnicity, creatinine, medication history (including antihypertensive drugs, lipid-lowering drugs, hypoglycemic drugs, allopurinol, and diuretics), personal history of diseases (hypertension, diabetes, and kidney disease), total energy intake, and serum urate.

[5] Hazard ratios (95% confidence interval) (all such values).

Table S15. The associations of joint exposures of SU levels and MDS with the risk of COPD (n = 155,403).

Joint effect		Number of participants	Number of incident COPD	Model 1 [1]	Model 2 [2]	Model 3 [3]	Model 4 [4]
Serum urate levels	MDS						
Hyperuricemia	0-3	7,290	248	Reference	Reference	Reference	Reference
Hyperuricemia	≥3-5	6,700	161	**0.68 (0.56, 0.83)** [5]	**0.64 (0.52, 0.78)**	**0.73 (0.60, 0.89)**	**0.73 (0.60, 0.89)**
Hyperuricemia	≥5	3,025	63	**0.58 (0.44, 0.76)**	**0.54 (0.41, 0.71)**	**0.66 (0.50, 0.88)**	**0.70 (0.53, 0.93)**
Normal	0-3	51,708	1,193	**0.68 (0.60, 0.79)**	**0.81 (0.71, 0.94)**	0.90 (0.78, 1.03)	0.88 (0.77, 1.02)
Normal	≥3-5	56,554	887	**0.46 (0.40, 0.53)**	**0.53 (0.46, 0.61)**	**0.65 (0.56, 0.75)**	**0.70 (0.60, 0.81)**
Normal	≥5	30,126	366	**0.35 (0.30, 0.41)**	**0.39 (0.33, 0.46)**	**0.53 (0.45, 0.63)**	**0.61 (0.52, 0.73)**

Abbreviations: SU, serum urate; COPD, chronic obstructive pulmonary disease.

[1] Crude model.

[2] Adjusted for age, sex, and BMI.

[3] Additionally adjusted for height, household income, education levels, physical activity, Townsend deprivation index, baseline metabolic syndrome, family history of diseases (hypertension, cardiovascular disease, and diabetes), and baseline FEV1/FVC ratio.

[4] Additionally adjusted for smoking status, alcohol consumption, baseline asthma, SII, ethnicity, creatinine, medication history (including antihypertensive drugs, lipid-lowering drugs, hypoglycemic drugs, allopurinol, and diuretics), and personal history of diseases (hypertension, diabetes, and kidney disease).

[5] Hazard ratios (95% confidence interval) (all such values).

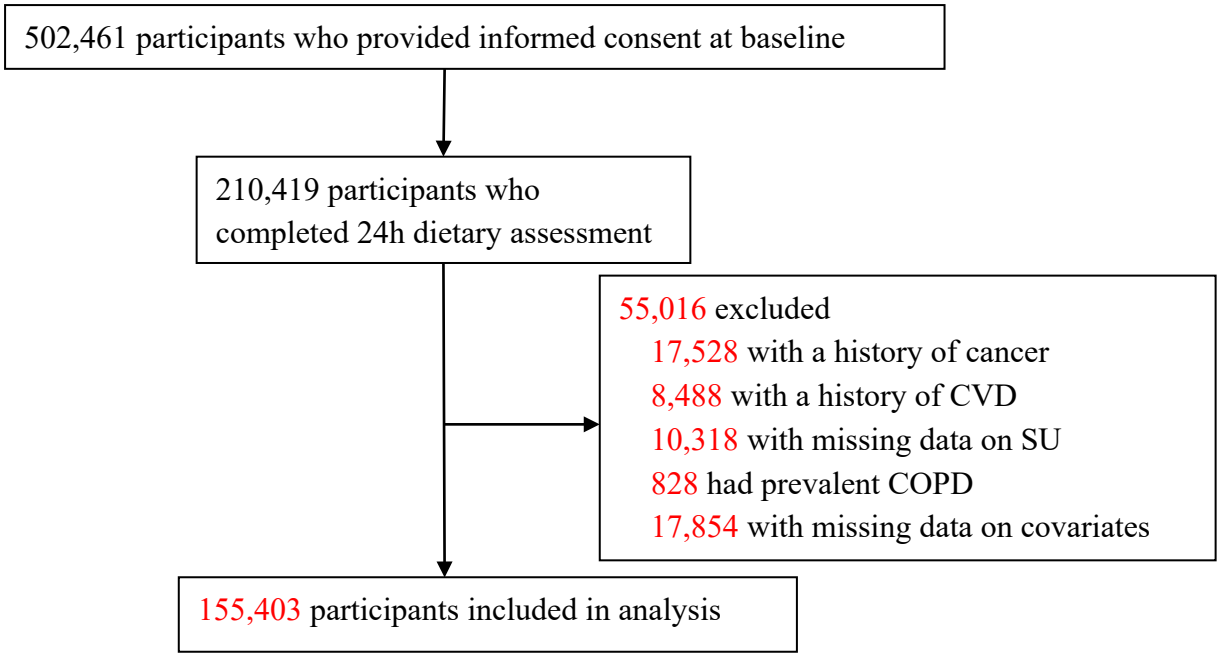

Fig. S1 Flowchart for the selection of the analyzed study sample

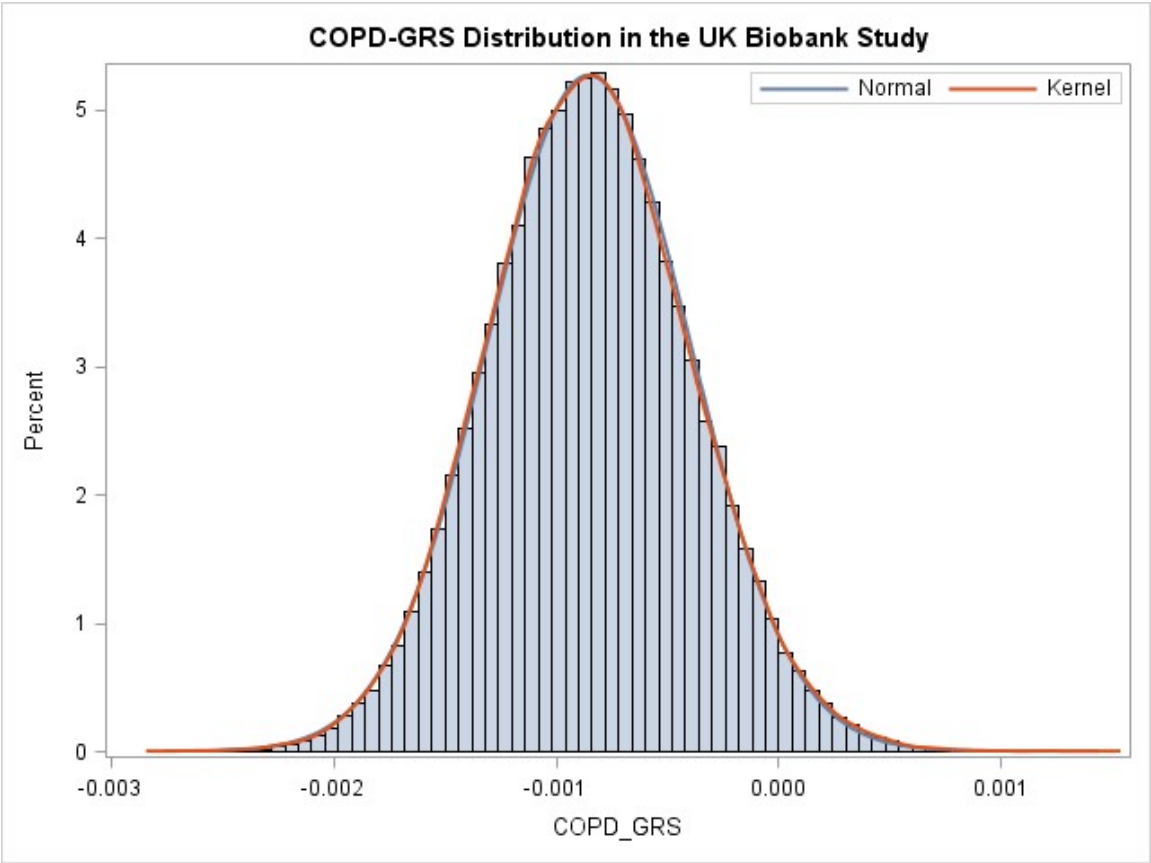

Fig. S2 Distribution of COPD-GRS