Electronic Supplementary Material (ESI) for Food & Function.

Sugar types, genetic predictors of gut microbe, and the risk of chronic kidney disease: a prospective cohort study

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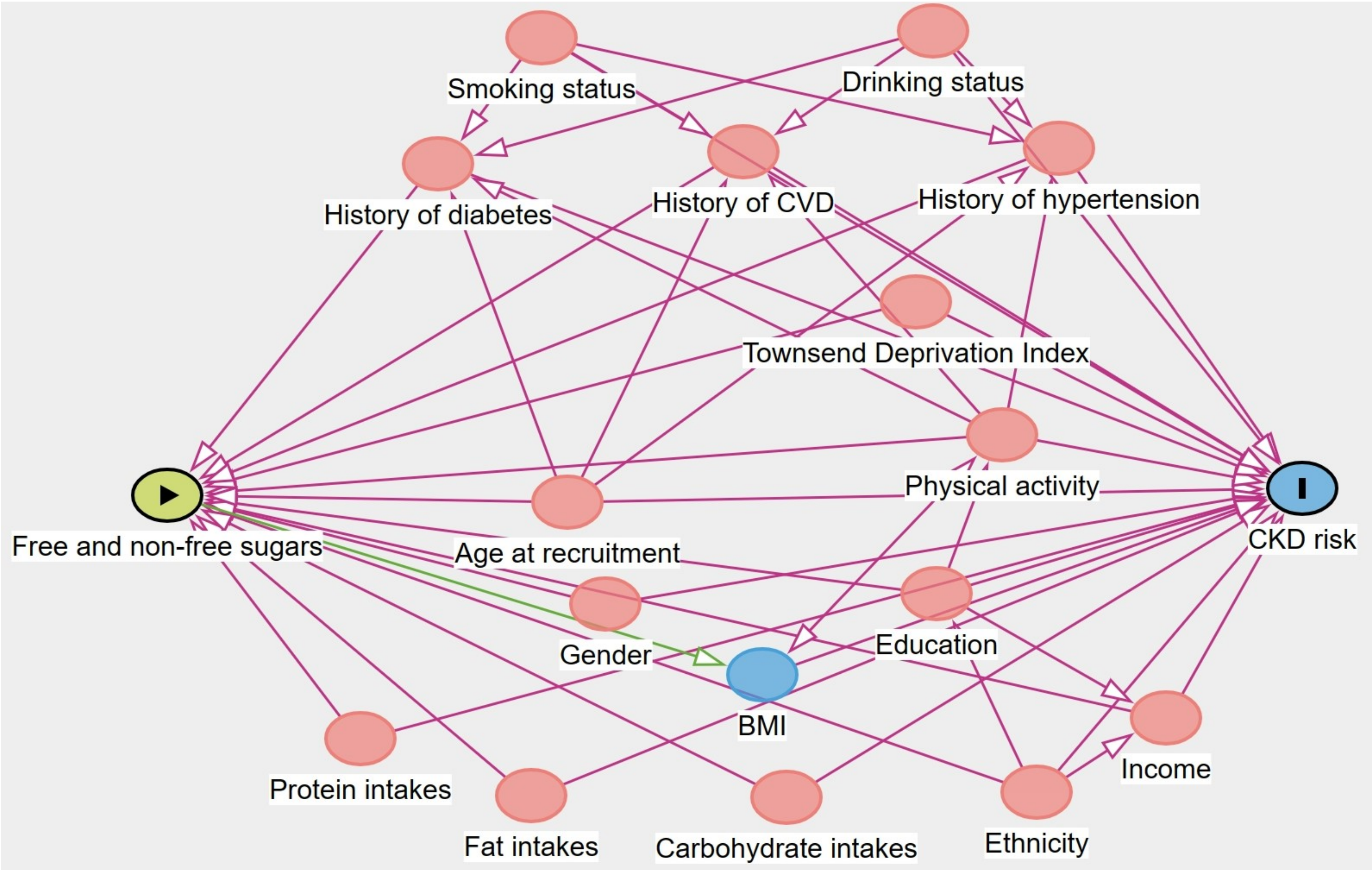
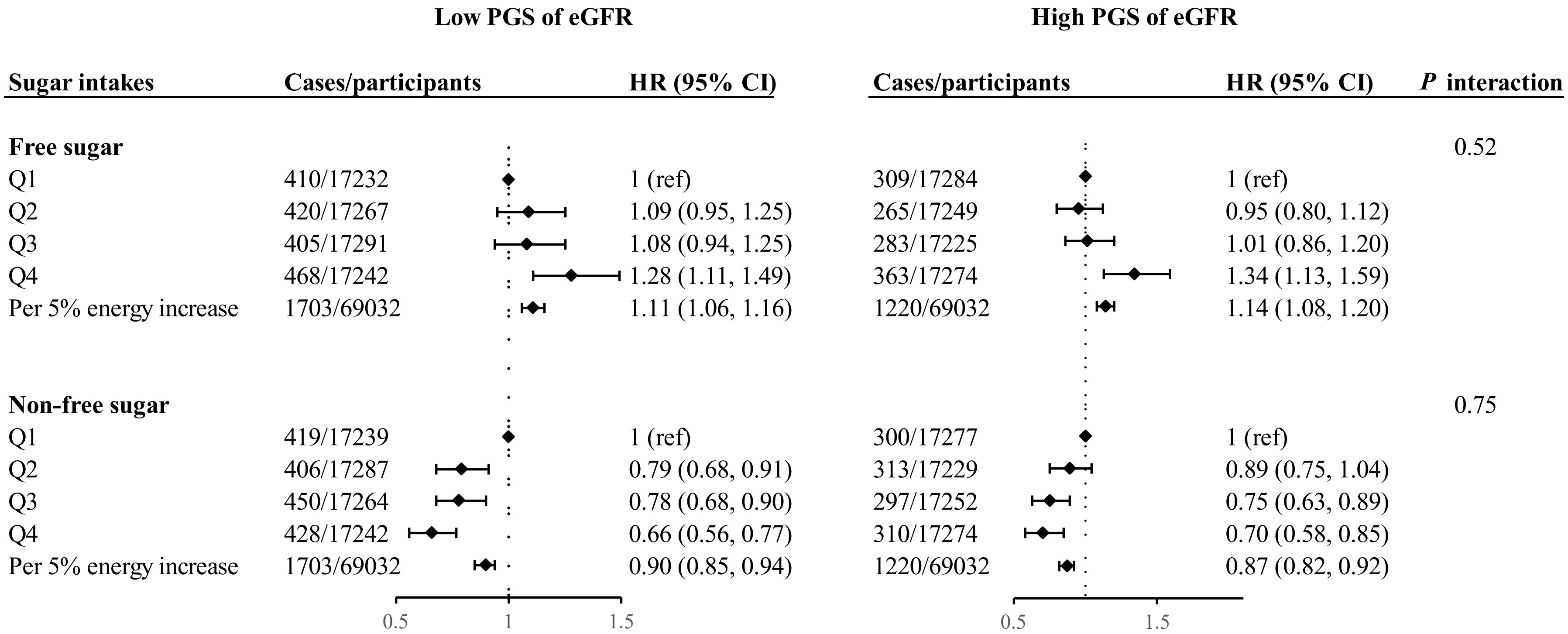

Smoking status
Drinking status
History of diabetes
History of CVD
History of hypertension
Townsend Deprivation Index
Physical activity
Free and non-free sugars
Age at recruitment
CKD risk
Gender
Education
BMI
Income
Protein intakes
Fat intakes
Carbohydrate intakes
Ethnicity

Supplementary Figure S1. Directed acyclic graph for the associations of free and non-free sugar intakes with the risk of CKD. BMI, body mass index; CKD, chronic kidney disease; CVD, cardiovascular diseases. Red circles represent ancestors of the exposure and outcome, blue circles represent ancestors of the outcome, and green circles represent ancestors of exposure.



Sugar intakes	Low PGS of eGFR: Cases/participants	Low PGS of eGFR: HR (95% CI)	High PGS of eGFR: Cases/participants	High PGS of eGFR: HR (95% CI)	*P* interaction
Free sugar					0.52
Q1	410/17232	1 (ref)	309/17284	1 (ref)	
Q2	420/17267	1.09 (0.95, 1.25)	265/17249	0.95 (0.80, 1.12)	
Q3	405/17291	1.08 (0.94, 1.25)	283/17225	1.01 (0.86, 1.20)	
Q4	468/17242	1.28 (1.11, 1.49)	363/17274	1.34 (1.13, 1.59)	
Per 5% energy increase	1703/69032	1.11 (1.06, 1.16)	1220/69032	1.14 (1.08, 1.20)	
Non-free sugar					0.75
Q1	419/17239	1 (ref)	300/17277	1 (ref)	
Q2	406/17287	0.79 (0.68, 0.91)	313/17229	0.89 (0.75, 1.04)	
Q3	450/17264	0.78 (0.68, 0.90)	297/17252	0.75 (0.63, 0.89)	
Q4	428/17242	0.66 (0.56, 0.77)	310/17274	0.70 (0.58, 0.85)	
Per 5% energy increase	1703/69032	0.90 (0.85, 0.94)	1220/69032	0.87 (0.82, 0.92)	

Supplementary Figure S2. Associations (HRs and 95% CIs) between free sugar intake, non-free sugar intake, and incident CKD by genetically predicted eGFR. CIs, confidence intervals; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; HRs, hazard ratios; PGS, polygenic score; Q, quintile; ref, reference group. The model was adjusted for age at recruitment (years), sex (men, women), ethnicity (White, Asian, Black, Mixed), education (college or university degree, high school, below), average total household income before tax (<£18,000, £18,000–£51,999, >£52,000), Townsend Deprivation Index (continuous), physical activity (MET-min/week), intakes of carbohydrate, protein, and fat (percentage of energy intake), history of hypertension, cardiovascular disease, diabetes (yes, no), the first 10 genetic principal components, and genotyping batch. A high polygenic score for eGFR indicates a higher genetic predisposition to elevated eGFR levels, with a low polygenic score indicating a lower genetic predisposition.

Subgroup analyses	Cases/No. of participants		Free sugar intake HR (95% CI)	P for interaction	Non-free sugar intake HR (95% CI)	P for interaction
Gender				0.12		0.30
Men	1695/67509	Quartile 4 vs. Quartile 1	1.22 (1.05, 1.41)		0.71 (0.60, 0.84)	
		Per 5% energy increase	1.09 (1.05, 1.15)		0.88 (0.84, 0.93)	
Women	1228/70555	Quartile 4 vs. Quartile 1	1.46 (1.23, 1.73)		0.64 (0.53, 0.78)	
		Per 5% energy increase	1.17 (1.11, 1.23)		0.89 (0.84, 0.94)	
Age				0.62		0.34
≤ 60 years	1066/94598	Quartile 4 vs. Quartile 1	1.19 (0.99, 1.42)		0.87 (0.71, 1.06)	
		Per 5% energy increase	1.10 (1.04, 1.16)		0.97 (0.91, 1.02)	
> 60 years	1857/43466	Quartile 4 vs. Quartile 1	1.34 (1.17, 1.54)		0.70 (0.60, 0.82)	
		Per 5% energy increase	1.12 (1.07, 1.17)		0.89 (0.85, 0.93)	
BMI				0.54		0.04
< 25kg/m^2	655/52569	Quartile 4 vs. Quartile 1	1.42 (1.12, 1.80)		0.59 (0.46, 0.77)	
		Per 5% energy increase	1.20 (1.12, 1.29)		0.89 (0.82, 0.96)	
≥ 25kg/m^2	2268/85495	Quartile 4 vs. Quartile 1	1.27 (1.12, 1.44)		0.73 (0.63, 0.83)	
		Per 5% energy increase	1.10 (1.06, 1.14)		0.89 (0.86, 0.93)	
Physical activity				0.78		0.26
Below the median	1421/64317	Quartile 4 vs. Quartile 1	1.37 (1.17, 1.61)		0.74 (0.62, 0.88)	
		Per 5% energy increase	1.14 (1.09, 1.20)		0.90 (0.85, 0.95)	
Above the median	1502/73747	Quartile 4 vs. Quartile 1	1.26 (1.08, 1.47)		0.63 (0.53, 0.75)	
		Per 5% energy increase	1.11 (1.06, 1.16)		0.88 (0.83, 0.92)	
Diabetes				0.73		0.29
(+)	457/6532	Quartile 4 vs. Quartile 1	1.35 (1.02, 1.79)		0.65 (0.48, 0.89)	
		Per 5% energy increase	1.12 (1.03, 1.22)		0.87 (0.79, 0.96)	
(-)	2466/131532	Quartile 4 vs. Quartile 1	1.31 (1.16, 1.48)		0.68 (0.60, 0.78)	
		Per 5% energy increase	1.13 (1.09, 1.17)		0.89 (0.85, 0.93)	
Hypertension				0.44		0.43
(+)	2111/68715	Quartile 4 vs. Quartile 1	1.33 (1.16, 1.51)		0.65 (0.56, 0.75)	
		Per 5% energy increase	1.12 (1.07, 1.16)		0.87 (0.83, 0.91)	
(-)	812/69349	Quartile 4 vs. Quartile 1	1.31 (1.06, 1.62)		0.76 (0.60, 0.95)	
		Per 5% energy increase	1.15 (1.08, 1.23)		0.92 (0.85, 0.98)	
Total protein intake				0.90		0.02
≤ 0.8g/kg/day	836/28646	Quartile 4 vs. Quartile 1	1.26 (1.04, 1.54)		0.75 (0.61, 0.94)	
		Per 5% energy increase	1.09 (1.04, 1.15)		0.91 (0.86, 0.97)	
> 0.8g/kg/day	2087/109418	Quartile 4 vs. Quartile 1	1.37 (1.20, 1.57)		0.64 (0.55, 0.75)	
		Per 5% energy increase	1.15 (1.10, 1.20)		0.86 (0.82, 0.91)	

Supplementary Figure S3. Subgroup analyses for the associations (HRs and 95% CIs) of free and non-free sugar intake with incident

CKD in 138,064 participants. BMI, body mass index; CIs, confidence intervals; HRs, hazard ratios. HRs were calculated from cause-specific competing risk models adjusted for age at recruitment (years), sex (men, women), ethnicity (White, Asian, Black, Mixed), education (college or university degree, high school, below), average total household income before tax (<£18,000, £18,000–£51,999, >£52,000), Townsend Deprivation Index (continuous), physical activity (MET-min/week), intakes of carbohydrate, protein, and fat (percentage of energy intake), history of hypertension, and cardiovascular disease, diabetes (yes, no).

Supplementary Table S1. Characteristics of the 19 SNPs associated with gut microbiome abundance.

SNP ID	Chr	EA	OA	Beta	EAF	Phylum
rs10769159	11	G	C	-0.06403	0.56	Firmicutes
rs10805326	4	G	A	0.077515	0.34	Firmicutes
rs11098863	4	T	A	-0.0966	0.53	Actinobacteria
rs11110281	12	T	C	-0.13404	0.06	Firmicutes
rs12320842	12	C	G	0.094833	0.15	Firmicutes
rs12781711	10	C	T	-0.06561	0.30	Firmicutes
rs17159861	7	C	T	0.096223	0.11	Firmicutes
rs182549	2	C	T	0.116333	0.49	Actinobacteria
rs4428215	3	G	A	0.12561	0.25	Proteobacteria
rs602075	9	A	G	0.168974	0.23	Firmicutes
rs61841503	10	G	A	0.092427	0.13	Firmicutes
rs67476743	19	T	G	0.132164	0.26	Firmicutes
rs7221249	17	A	G	0.083986	0.51	Firmicutes
rs7322849	13	T	C	0.11126	0.13	Actinobacteria
rs736744	9	C	T	0.117882	0.49	Proteobacteria
rs75754569	3	C	G	0.181434	0.10	Firmicutes
rs8009993	14	G	C	-0.13594	0.11	Firmicutes
rs830151	19	G	A	0.194561	0.11	Firmicutes
rs9864379	3	T	C	-0.16052	0.11	Cyanobacteria

SNP: single nucleotide polymorphism. Chr: chromosome. EA: effective allele, OA: other allele, EAF: effective allele frequency.

Supplementary Table S2. SNPs used for creating the eGFR-PGS in the UK Biobank Study.

SNP	Effect Allele	Chr	Effect	Locus
rs61830291	a	1	-0.0036	LINC01352
rs2490391	a	1	-0.0024	SDCCAG8
rs12061708	a	1	-0.0026	KLHDC7A
rs2749153	a	1	-0.0033	ZNF436-AS1
rs688540	a	1	-0.0030	FOXD2
rs3845534	a	1	-0.0019	LOC100422212
rs1011731	a	1	-0.0019	DNM3
rs78444298	a	1	-0.0105	EDEM3
rs78329830	a	1	-0.0054	PLA2G4A
rs1887252	c	1	-0.0019	LINC01362
rs7543734	c	1	0.0031	BCAR3
rs74748843	t	1	-0.0048	CASZ1
rs659437	t	1	-0.0027	AKR1A1
rs10159261	t	1	-0.0034	AGMAT
rs267738	t	1	-0.0048	CERS2
rs17413465	a	1	0.0025	MIR4422HG
rs11211257	a	1	0.0027	PIK3R3
rs1757915	a	1	0.0021	LINC01755
rs11166440	a	1	0.0020	CDC14A
rs10857788	a	1	0.0030	SYPL2
rs4971100	a	1	0.0020	TRIM46
rs3850625	a	1	0.0046	CACNA1S
rs2808454	a	1	0.0019	PFKFB2
rs12736457	c	1	0.0054	PPM1J
rs75625374	c	1	0.0045	CD34
rs7536433	t	1	0.0021	AK5
rs679843	t	1	0.0021	MGC27382
rs3118119	t	1	0.0030	LOC105371433

rs4656220	t	1	0.0020	PRRX1
rs3795503	t	1	0.0020	KIAA1614
rs7535253	t	1	0.0021	PTPN14
rs2577134	t	1	0.0020	RNU5F-1
rs417237	t	1	0.0018	OBSCN
rs1047891	a	2	-0.0065	CPS1
rs17050272	a	2	-0.0022	LINC01101
rs2971880	a	2	-0.0024	SPTBN1
rs60980181	a	2	-0.0027	CALCRL
rs4664475	t	2	-0.0020	NEB
rs35472707	t	2	-0.0073	LRP2
rs2301343	t	2	-0.0023	SLC8A1
rs35284526	a	2	0.0029	NFE2L2
rs4491726	a	2	0.0032	RDH14
rs6546869	a	2	0.0059	ALMS1P1
rs11694902	a	2	0.0041	TFCP2L1
rs7425436	a	2	0.0024	ORC4
rs35669853	a	2	0.0024	MIR5702
rs10197255	a	2	0.0018	LINC01812
rs10865189	c	2	0.0024	ZFP36L2
rs187355703	c	2	0.0100	HOXD8
rs780093	t	2	0.0044	GCKR
rs11123169	t	2	0.0025	PSD4
rs1548945	t	2	0.0036	TNP1
rs1050816	t	2	0.0026	SPEG
rs13003198	t	2	0.0018	SAG
rs807624	t	2	0.0032	DDX1
rs4666821	t	2	0.0020	PDE1A
rs3791221	a	2	0.0022	SH3YL1

rs6779998	a	3	-0.0017	TGFBR2
rs4625	a	3	-0.0023	DAG1
rs9828976	c	3	-0.0024	SLC35G2
rs56065557	c	3	-0.0029	SENP2
rs6778731	t	3	-0.0017	WNT7A
rs3774726	t	3	-0.0021	ATXN7
rs2289746	t	3	-0.0019	CBLB
rs35320690	t	3	-0.0025	MSL2
rs11919484	t	3	-0.0026	KNG1
rs2581820	a	3	0.0021	SFMBT1
rs9868185	a	3	0.0026	SLC15A2
rs1397764	a	3	0.0043	TFDP2
rs9823161	a	3	0.0022	LINC02028
rs11914389	t	3	0.0030	ACVR2B
rs7651407	t	3	0.0025	PLXNB1
rs10934754	t	3	0.0020	ALDH1L1-AS2
rs7624084	t	3	0.0017	ZBTB38
rs76272256	t	3	0.0024	MECOM
rs795009	t	3	0.0020	SYN2
rs3775932	a	4	-0.0018	WDR1
rs16874073	t	4	-0.0045	PPARGC1A
rs4864890	t	4	-0.0023	DCUN1D4
rs12509595	t	4	-0.0035	FGF5
rs75501914	a	4	0.0039	HGFAC
rs71606723	a	4	0.0025	UGT8
rs223471	c	4	0.0028	LOC102723704
rs55929207	c	4	0.0019	ETNPPL
rs28817415	t	4	-0.0073	SHROOM3
rs12163971	a	5	-0.0029	AFF4

rs13159523	a	5	-0.0024	TPPP
rs13157326	a	5	-0.0027	RAI14
rs2010352	a	5	-0.0018	AK6
rs1362800	t	5	-0.0049	DAB2
rs3812036	t	5	-0.0065	SLC34A1
rs72759880	t	5	-0.0056	PIK3R1
rs3797537	a	5	0.0019	DMGDH
rs12520984	c	5	0.0019	FST
rs12777	c	5	0.0050	SLC22A4
rs11746506	t	5	0.0017	MRPS30
rs11743174	t	5	0.0019	ABLIM3
rs495237	t	5	0.0027	LINC00603
rs79760705	t	5	0.0056	ARL15
rs881858	a	6	-0.0054	LINC01512
rs72912510	a	6	-0.0024	RRAGD
rs9375818	a	6	-0.0031	ARG1
rs3822939	a	6	-0.0025	EYA4
rs12207180	a	6	-0.0085	SLC22A2
rs12212034	t	6	-0.0018	PKHD1
rs6458868	t	6	-0.0020	GSTA2
rs3925003	t	6	-0.0018	HMGCLL1
rs13200335	a	6	0.0024	TFEB
rs11755724	a	6	0.0027	RREB1
rs1857859	a	6	0.0019	SIM1
rs1268168	a	6	0.0024	FOXO3
rs9397738	a	6	0.0027	SCAF8
rs77915916	a	6	0.0046	CRIP3
rs7740107	a	6	0.0027	L3MBTL3
rs3765502	t	6	0.0024	DCDC2

rs144100226	t	6	0.0059	HMGA1
rs720989	t	6	0.0021	SUPT3H
rs35154268	a	7	-0.0022	SND1
rs6968554	a	7	-0.0019	AHR
rs62491533	t	7	-0.0027	UBE2H
rs10254101	t	7	-0.0068	PRKAG2
rs62435145	t	7	-0.0060	UNCX
rs3750081	t	7	-0.0022	KBTBD2
rs801193	t	7	-0.0020	GS1-124K5.11
rs6973656	a	7	0.0035	TMEM60
rs700753	c	7	0.0031	LOC730338
rs55773927	t	7	0.0019	VKORC1L1
rs41301394	t	7	0.0023	POR
rs3757387	t	7	0.0030	IRF5
rs12671694	t	7	0.0025	SHH
rs868822	t	7	0.0029	LINC01006
rs11783418	a	8	-0.0020	XKR6
rs10102889	c	8	-0.0036	NRG1
rs2976178	c	8	-0.0025	WWP1
rs2980423	t	8	-0.0023	PRAG1
rs35353426	t	8	-0.0026	LOC157273
rs10098664	t	8	-0.0021	BLK
rs34861762	t	8	-0.0043	STC1
rs1533059	a	8	0.0025	MFHAS1
rs7832708	t	8	0.0022	MSRA
rs2954017	t	8	0.0024	TRIB1
rs12377027	a	9	-0.0026	MLLT3
rs13287724	a	9	-0.0030	B4GALT1-AS1
rs1321917	c	9	-0.0023	ASTN2

rs544169	a	9	0.0022	UBAP2
rs2039424	a	9	0.0044	PIP5K1B
rs7024579	t	9	0.0023	QSOX2
rs2068888	a	10	-0.0024	CYP26A1
rs4918943	a	10	-0.0022	SORBS1
rs12240572	a	10	-0.0032	DNAJC9-AS1
rs7095954	a	10	-0.0018	TSPAN14
rs816850	c	10	-0.0020	KCNMA1
rs1536225	t	10	-0.0021	PDCD11
rs7072591	a	10	0.0019	PARD3-AS1
rs10821905	a	10	0.0037	A1CF
rs1055256	a	10	0.0025	EEF1AKMT2
rs80282103	a	10	0.0078	LARP4B
rs6481598	c	10	0.0024	SVIL
rs8474	c	10	0.0020	PARG
rs7475348	t	10	0.0031	MYPN
rs9420446	t	10	0.0023	FAM35A
rs10821944	t	10	0.0020	ARID5B
rs284859	t	10	0.0026	WBP1L
rs1541937	a	11	-0.0029	OR52H1
rs1783827	a	11	-0.0020	MIR130A
rs3892895	a	11	-0.0023	TPCN2
rs963837	t	11	-0.0057	DCDC1
rs6484504	t	11	-0.0026	DNAJC24
rs2727040	t	11	-0.0026	TRIM49B
rs948493	t	11	-0.0033	MIR1234
rs11237450	a	11	0.0032	GAB2
rs63934	a	11	0.0041	KCNQ1
rs6589750	a	11	0.0020	USP2-AS1

rs11564722	t	11	0.0033	INS-IGF2
rs61897431	t	11	0.0029	SLC39A13
rs7127946	t	11	0.0023	OR4B1
rs1813937	t	11	0.0022	LOC646813
rs10790452	t	11	0.0020	SORL1
rs10846157	a	12	-0.0034	RERG
rs11062167	a	12	-0.0039	SLC6A13
rs632887	a	12	0.0032	TSPAN9
rs117113238	a	12	0.0039	BCL2L14
rs2634675	a	12	0.0025	ZNF641
rs1275609	a	12	0.0024	PHLDA1
rs4238020	t	12	0.0029	C12orf4
rs12313306	t	12	0.0029	R3HDM2
rs41284816	t	13	-0.0078	DLEU2
rs500830	t	13	0.0029	DACH1
rs61993680	a	14	-0.0019	SLC25A29
rs72683923	t	14	-0.0074	L2HGDH
rs6574652	t	14	-0.0017	STON2
rs17184313	t	14	-0.0029	RIN3
rs1028455	a	14	0.0020	SPATA7
rs690428	a	15	-0.0039	WDR72
rs1994887	a	15	-0.0020	CGNL1
rs351237	a	15	-0.0018	STRA6
rs4886696	a	15	-0.0032	SIN3A
rs6492982	t	15	-0.0033	INO80
rs11071738	t	15	-0.0025	APH1B
rs11071939	t	15	-0.0039	SMAD3
rs1145077	t	15	-0.0085	GATM
rs59646751	t	15	-0.0023	IGF1R

rs4886755	a	15	0.0041	NRG4
rs17507300	a	15	0.0024	BTBD1
rs7169629	c	15	0.0018	WDR73
rs12913015	t	15	0.0027	C15orf54
rs956006	t	15	0.0019	MGC15885
rs2472297	t	15	0.0039	CYP1A1
rs166906	t	15	0.0033	SCAPER
rs9932625	a	16	-0.0030	LINC01571
rs28581385	a	16	-0.0028	LINC01229
rs154656	a	16	-0.0030	CHMP1A
rs1635404	t	16	-0.0025	TRAP1
rs193538	t	16	-0.0020	ABCC1
rs7185391	t	16	-0.0027	SLC7A6
rs62053077	t	16	-0.0021	MARVELD3
rs7203398	a	16	0.0025	CHD9
rs77924615	a	16	0.0098	PDILT
rs62050038	a	16	0.0028	WWP2
rs438339	t	16	0.0035	RPL3L
rs1858800	t	16	0.0020	ZFHX3
rs883541	a	17	-0.0022	PRKAR1A
rs2411192	a	17	-0.0024	MYO19
rs8866	c	17	-0.0018	PITPNC1
rs2349648	t	17	-0.0017	MPRIP
rs4794813	a	17	0.0055	CDK12
rs35662455	c	17	0.0030	TEX14
rs9903801	c	17	0.0047	BCAS3
rs9891340	t	17	0.0024	SMCR2
rs2440165	t	17	0.0040	SLC47A1
rs9895661	t	17	0.0069	BCAS3

rs28735420	t	17	0.0039	MAP2K4
rs227731	t	17	0.0018	C17orf67
rs16942751	a	18	-0.0029	AQP4
rs1719934	a	18	0.0026	EPB41L3
rs8096658	c	18	0.0050	NFATC1
rs4940525	t	18	0.0025	LINC01544
rs34647824	a	19	-0.0021	RRAS
rs78241494	t	19	-0.0030	ZNF585A
rs281380	t	19	-0.0021	MAMSTR
rs2974751	a	19	0.0018	CALR
rs8101667	t	19	0.0044	CEP89
rs7251730	t	19	0.0024	ZNF260
rs113445505	t	19	0.0037	ZNF781
rs6087579	a	20	-0.0028	ITCH
rs4408777	a	20	-0.0021	RGS19
rs2235826	a	20	-0.0030	PCK1
rs1041606	t	20	-0.0021	MACROD2
rs17216707	t	20	-0.0051	CYP24A1
rs1509117	a	20	0.0024	PLCB1
rs72629024	c	20	0.0035	PPDPF
rs62187537	t	20	0.0039	FKBP1ASDCBP2
rs1407040	t	20	0.0018	GNAS
rs35636653	t	20	0.0022	OSBPL2
rs2273684	t	20	0.0032	GSS
rs2823139	a	21	-0.0026	NRIP1
rs2834317	a	21	-0.0035	LOC101928126
rs2244237	t	21	0.0027	CLDN14
rs80576	a	22	-0.0028	APOL3
rs4820324	c	22	-0.0023	MAFF

rs131263	t	22	0.0024	ZMAT5
rs112880707	t	22	0.0052	MKL1
rs738527	t	22	0.0032	A4GALT

Abbreviations: Chr, chromosome; eGFR, estimated glomerular filtration rate; PGS, polygenic score; SNP, single nucleotide polymorphism.

Supplementary Table S3. Associations (HRs and 95% CIs) between genetic risk of gut microbial abundance and incident CKD in 138,064 participants*.

PGS of gut microbe	Cases/participants	Model 1	Model 2	Model 3
		HR (95% CI)	HR (95% CI)	HR (95% CI)
Per standard deviation increase	-	1.03 (0.99, 1.07)	1.03 (0.99, 1.07)	1.03 (0.99, 1.07)
Low genetically predicted gut microbial abundance[a]	1409/69032	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)
High genetically predicted gut microbial abundance[b]	1514/69032	1.02 (0.94, 1.09)	1.02 (0.94, 1.09)	1.02 (0.95, 1.09)

*HR and 95% CI were calculated using the cause-specific competing risk model.

Model 1: age at recruitment (years), sex (men, women), ethnicity (White, Asian, Black, Mixed), first 10 genetic principal components, genotyping batch.

Model 2: Model 1 + education (college or university degree, high school, below), average total household income before tax (<£18,000, £18,000–£51,999, >£52,000), Townsend Deprivation Index (continuous), physical activity (MET-min/week), intakes of carbohydrate, protein, and fat (percentage of energy intake), healthy dietary components (intake of fiber, vegetable, fruit, whole grain, and poultry; g/day), geographic location (England area or non-England area), and antibiotic usage as child or teenager (yes, no).

Model 3: Model 2 + history of hypertension, cardiovascular disease, diabetes (yes, no).

[a] Low genetically predicted gut microbial abundance (below the median of gut microbe PGS).

[b] High genetically predicted gut microbial abundance (above the median of gut microbe PGS).

Abbreviations: CIs, confidence intervals; CKD, chronic kidney disease; HRs, hazard ratios; PGS, polygenic score.

Supplementary Table S4. Associations (HRs and 95% CIs) between genetic risk of eGFR and incident CKD in 138,064 participants*.

PGS of eGFR	Cases/participants	Model 1	Model 2	Model 3
		HR (95% CI)	HR (95% CI)	HR (95% CI)
Per standard deviation increase	-	0.82 (0.79, 0.85)	0.82 (0.79, 0.85)	0.81 (0.78, 0.84)
Low genetically predicted eGFR[a]	1703/69032	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)
High genetically predicted eGFR[b]	1220/69032	0.71 (0.66, 0.76)	0.71 (0.66, 0.76)	0.70 (0.65, 0.76)

*HR and 95% CI were calculated using the cause-specific competing risk model.

Model 1: age at recruitment (years), sex (men, women), ethnicity (White, Asian, Black, Mixed), first 10 genetic principal components, and genotyping batch.

Model 2: Model 1 + education (college or university degree, high school, below), average total household income before tax (<£18,000, £18,000–£51,999, >£52,000), Townsend Deprivation Index (continuous), physical activity (MET-min/week), intakes of carbohydrate, protein, and fat (percentage of energy intake).

Model 3: Model 2 + history of hypertension, cardiovascular disease, diabetes (yes, no).

[a] Low genetically predicted eGFR (below the median of eGFR PGS).

[b] High genetically predicted eGFR (above the median of eGFR PGS).

Abbreviations: CIs, confidence intervals; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; HRs, hazard ratios; PGS, polygenic score.

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Supplementary Table S5. The associations (HRs and 95% CIs) between free sugar intake, non-free sugar intake, and incident CKD in sensitivity analyses restricting to participants who conducted two or more dietary assessments (n = 85,410).

Sugar intakes	**Model 1**	**Model 2**	**Model 3**
	HR (95% CI)	**HR (95% CI)**	**HR (95% CI)**
Free sugar intake (% energy intake)			
Quartile			
< 8.21%	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)
≥8.21% and <11.11%	0.99 (0.87, 1.14)	1.01 (0.88, 1.16)	1.09 (0.95, 1.25)
≥11.11% and <14.47%	0.92 (0.80, 1.06)	0.94 (0.82, 1.09)	1.03 (0.90, 1.19)
≥14.47%	1.23 (1.08, 1.40)	1.22 (1.05, 1.41)	1.34 (1.16, 1.55)
P-trend [a]	<0.01	<0.01	<0.001
Continuous (per 5% energy increase)	1.10 (1.05, 1.15)	1.08 (1.03, 1.14)	1.12 (1.06, 1.17)
Non-free sugar intake (% energy intake)			
Quartile			
<8.94%	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)
≥8.94% and <12.12%	0.96 (0.84, 1.10)	0.93 (0.81, 1.06)	0.93 (0.81, 1.07)
≥12.12% and <15.98%	0.90 (0.79, 1.04)	0.84 (0.73, 0.97)	0.85 (0.73, 0.98)
≥15.98%	0.89 (0.77, 1.03)	0.77 (0.65, 0.90)	0.77 (0.66, 0.91)
P-trend [a]	0.08	<0.001	<0.001
Continuous (per 5% energy increase)	0.96 (0.92, 1.00)	0.88 (0.83, 0.93)	0.88 (0.84, 0.93)

*HRs and 95% CIs were calculated with the use of the cause-specific competing risk model.

Model 1: age at recruitment (years), sex (men, women), and ethnicity (White, Asian, Black, Mixed).

Model 2: Model 1 + education (college or university degree, high school, below), average total household income before tax (<£18,000, £18,000–£51,999, >£52,000), Townsend Deprivation Index (continuous), physical activity (MET-min/week), intakes of carbohydrate, protein, and fat (percentage of energy intake).

Model 3: Model 2 + history of hypertension, cardiovascular disease, diabetes (yes, no).

[a] Test for trend based on variables containing the median value for each quartile.

Abbreviations: CIs, confidence intervals; CKD, chronic kidney disease; HRs, hazard ratios.

Supplementary Table S6. The associations (HRs and 95% CIs) between free sugar intake, non-free sugar intake, and incident CKD in sensitivity analyses restricting to participants with ≥ two years of follow-up (n = 137,342).

Sugar intakes	**Model 1**	**Model 2**	**Model 3**
	HR (95% CI)	**HR (95% CI)**	**HR (95% CI)**
Free sugar intake (% energy intake)			
Quartile			
<7.89%	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)
≥7.89% and <11.08%	0.94 (0.84, 1.04)	0.97 (0.87, 1.08)	1.03 (0.92, 1.15)
≥11.08% and <14.76%	0.92 (0.83, 1.03)	0.95 (0.85, 1.07)	1.04 (0.93, 1.16)
≥14.76%	1.17 (1.05, 1.29)	1.18 (1.05, 1.32)	1.29 (1.15, 1.44)
P-trend [a]	<0.01	<0.01	<0.0001
Continuous (per 5% energy increase)	1.08 (1.05, 1.12)	1.09 (1.05, 1.13)	1.12 (1.08, 1.16)
Non-free sugar intake (% energy intake)			
Quartile			
<8.58%	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)
≥8.58% and <12.06%	0.88 (0.79, 0.98)	0.83 (0.75, 0.93)	0.85 (0.76, 0.95)
≥12.06% and <16.26%	0.84 (0.75, 0.93)	0.76 (0.67, 0.85)	0.77 (0.69, 0.87)
≥16.26%	0.82 (0.73, 0.91)	0.69 (0.61, 0.78)	0.70 (0.62, 0.80)
P-trend [a]	<0.001	<0.0001	<0.0001
Continuous (per 5% energy increase)	0.94 (0.91, 0.97)	0.89 (0.85, 0.92)	0.89 (0.86, 0.93)

*HRs and 95% CIs were calculated with the use of the cause-specific competing risk model.

Model 1: age at recruitment (years), sex (men, women), and ethnicity (White, Asian, Black, Mixed).

Model 2: Model 1 + education (college or university degree, high school, below), average total household income before tax (<£18,000, £18,000–£51,999, >£52,000), Townsend Deprivation Index (continuous), physical activity (MET-min/week), intakes of carbohydrate, protein, and fat (percentage of energy intake).

Model 3: Model 2 + history of hypertension, cardiovascular disease, diabetes (yes, no).

[a] Test for trend based on variables containing the median value for each quartile.

Abbreviations: CIs, confidence intervals; CKD, chronic kidney disease; HRs, hazard ratios.

Supplementary Table S7. The associations (HRs and 95% CIs) between free sugar intake and non-free sugar intake in grams and incident CKD in 138,064 participants.

Sugar intakes	Model 1	Model 2	Model 3
	HR (95% CI)	HR (95% CI)	HR (95% CI)
Free sugar intake (g/day)			
Quartile			
<36.36 g/day	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)
≥36.36 g/day and <55.01 g/day	0.95 (0.86, 1.05)	0.98 (0.88, 1.09)	1.03 (0.92, 1.14)
≥55.01 g/day and <78.54 g/day	0.89 (0.80, 0.99)	0.92 (0.82, 1.03)	1.00 (0.90, 1.12)
≥78.54 g/day	1.13 (1.02, 1.25)	1.14 (1.02, 1.27)	1.26 (1.12, 1.41)
P-trend [a]	0.01	0.01	<0.0001
Continuous (per 5g increase)	1.01 (1.01, 1.02)	1.01 (1.01, 1.02)	1.02 (1.01, 1.02)
Non-free sugar intake (g/day)			
Quartile			
<42.53 g/day	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)
≥42.53 g/day and <59.89 g/day	0.87 (0.79, 0.96)	0.86 (0.78, 0.95)	0.88 (0.79, 0.97)
≥59.89 g/day and <80.17 g/day	0.76 (0.69, 0.85)	0.75 (0.67, 0.83)	0.77 (0.69, 0.85)
≥80.17 g/day	0.74 (0.67, 0.82)	0.70 (0.62, 0.78)	0.72 (0.64, 0.80)
P-trend [a]	0.001	<0.0001	<0.0001
Continuous (per 5g increase)	0.99 (0.98, 0.99)	0.98 (0.97, 0.99)	0.98 (0.98, 0.99)

*HRs and 95% CIs were calculated with the use of the cause-specific competing risk model.

Model 1: age at recruitment (years), sex (men, women), and ethnicity (White, Asian, Black, Mixed).

Model 2: Model 1 + education (college or university degree, high school, below), average total household income before tax (<£18,000, £18,000–£51,999, >£52,000), Townsend Deprivation Index (continuous), physical activity (MET-min/week), intakes of carbohydrate, protein, and fat (percentage of energy intake).

Model 3: Model 2 + history of hypertension, cardiovascular disease, diabetes (yes, no).

[a] Test for trend based on variables containing the median value for each quartile.

Abbreviations: CIs, confidence intervals; CKD, chronic kidney disease; HRs, hazard ratios.

Supplementary Table S8. Associations (HRs and 95% CIs) between free and non-free sugar intakes to carbohydrates intakes ratio, and incident CKD in 138,064 participants.

Sugar intakes	Model 1	Model 2	Model 3
	HR (95% CI)	**HR (95% CI)**	**HR (95% CI)**
Free sugars to carbohydrates ratio			
Quartile			
<16.26%	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)
≥16.26% and <22.50%	0.98 (0.89, 1.09)	1.02 (0.91, 1.13)	1.08 (0.97, 1.20)
≥22.50% and <29.47%	1.03 (0.93, 1.15)	1.08 (0.97, 1.20)	1.17 (1.05, 1.30)
≥29.47%	1.15 (1.04, 1.28)	1.19 (1.07, 1.33)	1.30 (1.17, 1.45)
P-trend [a]	<0.01	<0.001	<0.0001
Continuous (per 5% increase)	1.03 (1.01, 1.05)	1.04 (1.02, 1.06)	1.05 (1.03, 1.07)
Non-free sugars to carbohydrates ratio			
Quartile			
<18.08%	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)
≥18.08% and <24.35%	0.87 (0.79, 0.97)	0.88 (0.80, 0.98)	0.89 (0.80, 0.99)
≥24.35% and <31.65%	0.80 (0.72, 0.88)	0.80 (0.72, 0.89)	0.81 (0.73, 0.90)
≥31.65%	0.75 (0.67, 0.84)	0.74 (0.66, 0.83)	0.75 (0.67, 0.84)
P-trend [a]	<0.001	<0.0001	<0.0001
Continuous (per 5% increase)	0.94 (0.93, 0.96)	0.94 (0.92, 0.96)	0.94 (0.92, 0.96)

*HRs and 95% CIs were calculated with the use of the cause-specific competing risk model.

Model 1: age at recruitment (years), sex (men, women), and ethnicity (White, Asian, Black, Mixed).

Model 2: Model 1 + education (college or university degree, high school, below), average total household income before tax (<£18,000, £18,000–£51,999, >£52,000), Townsend Deprivation Index (continuous), physical activity (MET-min/week), intakes of carbohydrate, protein, and fat (percentage of energy intake).

Model 3: Model 2 + history of hypertension, cardiovascular disease, diabetes (yes, no).

[a] Test for trend based on variables containing the median value for each quartile. *Abbreviations:* CIs, confidence intervals; CKD, chronic kidney disease; HRs, hazard ratios.

Supplementary Table S9. Associations (HRs and 95% CIs) between free sugar intake, non-free sugar intake, and incident CKD using the sub-distribution competing risk model in 138,064 participants.

Sugar intakes	Model 1	Model 2	Model 3
	HR (95% CI)	HR (95% CI)	HR (95% CI)
Free sugar intake (% energy intake)			
Quartile			
<7.89%	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)
≥7.89% and <11.08%	0.94 (0.85, 1.04)	0.97 (0.88, 1.08)	1.04 (0.93, 1.16)
≥11.08% and <14.77%	0.93 (0.84, 1.03)	0.97 (0.87, 1.08)	1.06 (0.95, 1.18)
≥14.77%	1.18 (1.06, 1.30)	1.20 (1.08, 1.34)	1.31 (1.17, 1.46)
P-trend[a]	<0.001	<0.001	<0.0001
Continuous (per 5% energy increase)	1.07 (1.03, 1.10)	1.10 (1.06, 1.14)	1.12 (1.08, 1.16)
Non-free sugar intake (% energy intake)			
Quartile			
<8.58%	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)
≥8.58% and <12.05%	0.86 (0.78, 0.96)	0.82 (0.74, 0.91)	0.83 (0.75, 0.93)
≥12.05% and <16.25%	0.84 (0.75, 0.93)	0.75 (0.68, 0.84)	0.77 (0.69, 0.86)
≥16.25%	0.80 (0.72, 0.89)	0.67 (0.59, 0.76)	0.68 (0.60, 0.77)
P-trend[a]	<0.0001	<0.0001	<0.0001
Continuous (per 5% energy increase)	1.00 (0.97, 1.03)	0.88 (0.85, 0.92)	0.89 (0.85, 0.92)

*HR and 95% CI were calculated with the use of the sub-distribution competing risk model (Fine and Gray's model).

Model 1: age at recruitment (years), sex (men, women), and ethnicity (White, Asian, Black, Mixed).

Model 2: Model 1 + education (college or university degree, high school, below), average total household income before tax (<£18,000, £18,000–£51,999, >£52,000), Townsend Deprivation Index (continuous), physical activity (MET-min/week), intakes of carbohydrate, protein, and fat (percentage of energy intake).

Model 3: Model 2 + history of hypertension, cardiovascular disease, diabetes (yes, no).

[a] Test for trend based on variables containing the median value for each quartile.

Abbreviations: CIs, confidence intervals; CKD, chronic kidney disease; HRs, hazard ratios.

Supplementary Table S10. Associations (HRs and 95% CIs) between free sugar intake, non-free sugar intake, and incident CKD with further adjustments of cardiometabolic biomarkers or eGFR.

Model 1 (N = 131,340)		**Model 2 (N = 131,396)**	
Sugar intakes	**HR (95% CI)**	**Sugar intakes**	**HR (95% CI)**
Free sugar intake (% energy intake)		**Free sugar intake (% energy intake)**	
Quartile		**Quartile**	
<7.89%	1.00 (Ref)	<7.89%	1.00 (Ref)
≥7.89% and <11.08%	1.02 (0.92, 1.14)	≥7.89% and <11.08%	0.99 (0.88, 1.10)
≥11.08% and <14.77%	1.04 (0.93, 1.16)	≥11.08% and <14.77%	0.99 (0.89, 1.11)
≥14.77%	1.28 (1.14, 1.44)	≥14.77%	1.18 (1.05, 1.32)
P-trend [a]	<0.0001	P-trend [a]	<0.01
Continuous (per 5% energy increase)	1.11 (1.07, 1.15)	**Continuous (per 5% energy increase)**	1.08 (1.04, 1.12)
Non-free sugar intake (% energy intake)		**Non-free sugar intake (% energy intake)**	
Quartile		**Quartile**	
<8.58%	1.00 (Ref)	<8.58%	1.00 (Ref)
≥8.58% and <12.05%	0.83 (0.74, 0.93)	≥8.58% and <12.05%	0.87 (0.78, 0.97)
≥12.05% and <16.25%	0.78 (0.70, 0.88)	≥12.05% and <16.25%	0.85 (0.75, 0.95)
≥16.25%	0.69 (0.61, 0.79)	≥16.25%	0.78 (0.69, 0.89)
P-trend [a]	<0.0001	P-trend [a]	<0.001
Continuous (per 5% energy increase)	0.89 (0.86, 0.93)	**Continuous (per 5% energy increase)**	0.92 (0.89, 0.96)

*HRs and 95% CIs were calculated with the use of the cause-specific competing risk model.

Participants with missing value on cardiometabolic biomarkers (triglycerides, LDL-c, hs-CRP) or eGFR was excluded.

Model 1: age at recruitment (years), sex (men, women), and ethnicity (White, Asian, Black, Mixed), education (college or university degree, high school, below), average total household income before tax (<£18,000, £18,000–£51,999, >£52,000), Townsend Deprivation Index (continuous), physical activity (MET-min/week), intakes of carbohydrate, protein, and fat (percentage of energy intake), history of hypertension, cardiovascular disease, diabetes (yes, no), and cardiometabolic biomarkers (triglycerides, LDL-c, hs-CRP).

Model 2: age at recruitment (years), sex (men, women), and ethnicity (White, Asian, Black, Mixed), education (college or university degree, high school, below), average total household income before tax (<£18,000, £18,000–£51,999, >£52,000), Townsend Deprivation Index (continuous), physical activity (MET-min/week), intakes of carbohydrate, protein, and fat (percentage of energy intake), history of hypertension, cardiovascular disease, diabetes (yes, no), and eGFR).

[a] Test for trend based on variables containing the median value for each quartile. excluding non-free sugar.

Abbreviations: CIs, confidence intervals; CKD, chronic kidney disease; HRs, hazard ratios; eGFR, estimated glomerular filtration rate; LDL-C, low-density lipoprotein cholesterol; hs-CRP, high-sensitive C-reactive protein.