

Genetic evidence for different adiposity phenotypes and their opposing influence on ectopic fat and risk of cardiometabolic disease

Susan Martin^{1*}, Madeleine Cule^{2*}, Nicolas Basty³, Jessica Tyrrell¹, Robin N. Beaumont¹, Andrew R Wood¹, Timothy M. Frayling¹, Elena Sorokin², Brandon Witcher³, Yi Liu², Jimmy D. Bell³, E. Louise Thomas^{3*}, Hanieh Yaghootkar^{1,3*}

*These authors contributed equally

1. Genetics of Complex Traits, University of Exeter Medical School, University of Exeter, RILD Level 3, Royal Devon & Exeter Hospital, Barrack Road, Exeter, UK.
2. Calico Life Sciences LLC, South San Francisco, California, USA.
3. Research Centre for Optimal Health, School of Life Sciences, University of Westminster, London, UK.

Corresponding author:

Dr Hanieh Yaghootkar, RILD Building, Royal Devon and Exeter NHS trust, Barrack Road, Exeter, EX2 5DW, Telephone (+44) 1392 408207, Email: h.yaghootkar@exeter.ac.uk

Table S1. Summary characteristics of participating studies. N: sample size; SD: standard deviation.

	Statistics	Unit	UK Biobank	FinnGen	Published GWAS	Published GWAS Reference
Age	N	years	451,099	176,899	NA	NA
	mean (SD)		57.32 (8.02)	NA	NA	NA
Sex	males / females	NA	206,251/244,848	NA	NA	NA
Body fat percentage	N (males / females)	%	442,278	NA	100,716 (52,416/48,956)	PMID: 26833246
	mean (SD)		31.39 (8.52)		Not available	
BMI	N (males / females)	kg/m ²	448,621	NA	681,275	PMID: 30124842
	mean (SD)		27.37 (4.76)		Not available	
HDL-cholesterol	N (males / females)	mmol/ L	392,965	NA	188,577	PMID: 24097068
	mean (SD)		1.45 (0.38)		Not available	
Sex hormone-binding globulin	N (males / females)	nmol/L	389,354	NA	21,791 (12,401/9,390)	PMID: 22829776
	mean (SD)		51.98 (27.77)		Not available	
Triglycerides	N (males / females)	mmol/ L	429,011	NA	188,577	PMID: 24097068
	mean (SD)		1.75 (1.02)		Not available	
Aspartate transaminase	N (males / females)	U/L	427,778	NA	61,089	PMID: 22001757
	mean (SD)		26.21 (10.61)		Not available	
Alanine transaminase	N (males / females)	U/L	429,203	NA	61,089	PMID: 22001757
	mean (SD)		23.54 (14.14)		Not available	
C-reactive protein	N (males / females)	mg/L	428,430	NA	204,402	PMID: 30388399
	mean (SD)		2.59 (4.37)		Not available	
Visceral adipose tissue	N (males / females)	L	32,859	NA	18,332 (8738/9594)	PMID: 27918534
	mean (SD)		3.92 (2.3)		Not available	

Subcutaneous adipose tissue	N (males / females)	L	32,859	NA	18,247 (8685/9562)	PMID: 27918534
	mean (SD)		8.16 (4.1)		Not available	
VATSAT ratio	N (males / females)		32,859	NA	18,191 (8374/9823)	PMID: 27918534
	mean (SD)				Not available	
Liver fat	N	%	32,655	NA	NA	NA
	mean (SD)		5.06 (5)			
Pancreas fat	N	%	24,673	NA	NA	NA
	mean (SD)		10.41 (7.9)			
Liver volume	N	L	32,859	NA	NA	NA
	mean (SD)		1.38 (0.3)			
Pancreas volume	N	L	31,758	NA	NA	NA
	mean (SD)		0.06 (0.018)			
Pericardial adipose tissue	N (males / females)		NA	NA	12,204 (5842/6362)	PMID: 27918534
	mean (SD)				Not available	
Type 2 diabetes	N cases / N controls	NA	14,371/428,017	23,338/148,190	74,124/824,006	PMID: 30297969
Heart disease	N cases / N controls	NA	43,054/407,969	25,366/151,533	60,801/123,504	PMID: 26343387
Hypertension	N cases / N controls	NA	101,426/349,599	43,576/97,214	NA	NA
Stroke	N cases / N controls	NA	11,926/439,096	14,171/133,027	40,585/406,111	PMID: 29531354
Fatty liver disease	N cases / N controls	NA	5225/445,800	NA	NA	NA
Non-alcoholic fatter liver disease	N cases / N controls	NA	NA	651/176,248	NA	NA
Polycystic ovary syndrome	N cases / N controls	NA	738/244,064	462/96,172	10,074/103,164	PMID: 30566500

Table S2. The summary of 254 genetic variants associated with both adiposity and a composite metabolic biomarker. EA: effect allele; EAF: effect allele frequency; P: p-value; BFP: body fat percentage; HDL: HDL-cholesterol; SHBG: sex-hormone binding globulin; ALT: alanine transaminase; AST: aspartate transaminase.

RSID	Chr:Position	EA	EAF	Nearest gene	Cluster	meta CCA P	BFP beta	BFP P	HDL beta	HDL P	SHBG beta	SHBG P	Triglycerides beta	Triglycerides P	ALT beta	ALT P	AST beta	AST P
rs11642015	16:53802494	T	0.40	[FTO]	UFA	2E-157	0.041	7E-165	-0.014	4E-16	-0.018	3E-20	0.003	0.13	0.018	8E-20	0.010	7E-7
rs13107325	4:103188709	T	0.07	[SLC39A8]	UFA	5E-32	0.031	3E-28	-0.078	5E-118	-0.004	0.19	0.029	2E-14	0.022	8E-10	0.058	3E-54
rs143684747	2:633053	AC	0.83	NA	UFA	4E-24	0.029	3E-49	-0.009	2E-5	-0.013	2E-7	0.005	0.01	0.009	0.001	0.009	6E-4
rs539515	1:177889025	C	0.21	FAM5B---[]-SEC16B	UFA	1E-35	0.028	9E-54	-0.007	0.002	0.002	0.49	3E-4	0.97	0.008	5E-4	0.010	2E-4
rs6567160	18:57829135	C	0.23	PMAIP1---[]---MC4R	UFA	1E-35	0.026	5E-48	-0.023	5E-25	-0.020	2E-19	0.013	4E-8	0.004	0.08	0.007	0.002
6:34650934_CGT_C	6:34650934	C	0.14	[C6orf106]	UFA	1E-30	0.026	2E-33	-0.027	4E-28	0.013	8E-6	4E-4	1.00	0.002	0.51	0.019	3E-11
5:87969925_CGG_C	5:87969925	C	0.14	TMEM161B---[]--MEF2C	UFA	4E-10	0.025	3E-30	-0.010	6E-4	-0.011	1E-4	0.007	0.02	0.009	0.003	0.001	0.68

rs71658797	1:77967507	A	0.12	[AK5]	UFA	3E-10	0.024	6E-26	-0.004	0.30	0.003	0.39	-0.001	0.53	0.003	0.22	0.006	0.12
rs72892910	6:50816887	T	0.17	TFAP2B-[]---PKHD1	UFA	5E-16	0.023	2E-32	-0.005	0.09	-0.011	8E-6	0.006	0.03	0.009	3E-4	0.010	1E-4
rs6752378	2:25150116	A	0.49	ADCY3-[]--DNAJC27	UFA	1E-60	0.023	7E-55	-0.007	2E-4	-0.003	0.22	0.002	0.25	-4E-4	0.81	0.007	8E-4
rs56186137	16:28825953	G	0.40	[NPIP L1]	UFA	7E-46	0.023	3E-50	-0.010	4E-7	-0.013	2E-11	0.003	0.08	0.010	2E-7	0.008	2E-5
rs7124681	11:47529947	A	0.41	CELF1--[]--PTPMT1	UFA	2E-80	0.022	7E-50	-0.038	2E-97	-0.003	0.07	0.016	5E-15	7E-4	0.79	-0.013	7E-10
rs6602997	15:84521398	T	0.71	[ADA MTSL 3]	UFA	4E-30	0.022	6E-43	-0.005	0.02	-0.003	0.08	0.006	0.005	0.005	0.04	0.004	0.12
rs9358912	6:26211146	G	0.73	HIST1H4E-[]-HIST1H2BG	UFA	7E-26	0.022	5E-39	-0.011	7E-8	-0.017	2E-15	0.005	0.008	0.003	0.14	-0.002	0.42
14:79940130_TA GGAG TTTT CCAG ATCA TTAG	14:79940130	T	0.20	NA	UFA	7E-14	0.022	7E-30	-0.010	1E-5	-0.008	2E-4	0.007	0.004	0.014	2E-8	0.006	0.02

CCAC TTAT ACGG AG_T																		
rs559 31203	17:65 85460 2	T	0.19	[BPTF]	UFA	3E-15	0.021	6E-28	- 0.011	2E-6	- 0.007	5E-4	0.024	3E-20	0.023	1E-19	0.010	1E-4
rs479 0292	17:18 24305	C	0.85	RPA1- -[]-- RTN4 RL1	UFA	4E-9	0.021	6E-24	- 0.007	0.006	- 0.009	3E-4	0.007	0.005	0.011	3E-4	0.002	0.58
rs477 6985	15:68 12302 1	T	0.78	[SKOR 1]	UFA	1E-16	0.020	9E-31	- 0.005	0.01	- 0.006	0.004	0.003	0.10	0.003	0.14	-3E-4	0.95
1:727 67554 _CA_ C	1:727 67554	CA	0.79	NA	UFA	3E-12	0.020	2E-25	- 0.012	3E-8	- 0.011	3E-6	0.011	3E-6	0.006	0.03	0.004	0.17
rs109 38397	4:451 82527	G	0.43	GNPD A2--- []-- GABR G1	UFA	2E-36	0.020	7E-41	- 0.005	0.007	- 0.008	2E-5	-2E-4	0.83	0.009	5E-6	0.003	0.15
rs107 56713	9:158 80555	A	0.56	[CCDC 171]	UFA	2E-31	0.019	1E-37	- 0.003	0.15	- 0.007	5E-4	0.005	0.007	0.006	0.006	5E-4	0.79
rs713 2908	12:50 26314 8	A	0.38	[FAIM 2]	UFA	5E-33	0.019	1E-36	- 0.010	9E-8	- 0.002	0.40	0.003	0.22	7E-4	0.79	0.002	0.34
rs376 4002	12:10 86186 30	C	0.74	[WSC D2]	UFA	1E-18	0.019	2E-29	- 0.001	0.46	- 0.011	2E-7	0.011	1E-6	0.008	7E-4	- 0.001	0.47

rs2112347	5:75015242	T	0.64	<i>POCS-1]---SV2C</i>	UFA	2E-27	0.018	2E-31	-0.018	2E-22	-0.012	6E-11	0.005	0.008	0.005	0.009	-0.005	0.04
rs4876611	8:116671848	G	0.72	<i>[TRPS1]</i>	UFA	3E-27	0.018	7E-28	0.004	0.01	-0.008	9E-5	0.014	6E-10	0.004	0.11	0.004	0.13
rs61888762	11:27709630	G	0.32	<i>[BDNF]</i>	UFA	3E-25	0.018	3E-29	-0.017	1E-18	-0.007	7E-5	0.013	1E-9	0.010	1E-6	0.011	7E-7
rs771025058	18:21122207	AAG	0.54	<i>[NPC1]</i>	UFA	7E-26	0.017	4E-30	-0.015	4E-17	-0.007	3E-4	0.015	5E-15	0.010	4E-7	0.006	0.009
rs4755725	11:43637975	C	0.33	NA	UFA	7E-18	0.017	3E-26	-0.010	7E-7	-0.009	1E-7	0.008	7E-5	0.013	4E-9	0.007	2E-4
rs11666808	19:18383506	T	0.37	<i>[KIAA1683]</i>	UFA	9E-24	0.017	6E-27	-0.006	6E-4	-0.017	4E-18	0.011	3E-9	0.012	2E-9	-0.003	0.08
rs2274224	10:96039597	G	0.57	<i>[PLCE1]</i>	UFA	3E-28	0.017	7E-29	0.001	0.18	-0.007	2E-4	0.009	3E-6	0.012	5E-10	0.012	1E-9
rs8049669	16:69551467	A	0.43	<i>CYB5B--[]--NFAT5</i>	UFA	3E-19	0.016	7E-26	-0.009	1E-6	-0.010	9E-8	0.016	4E-16	0.008	2E-5	0.003	0.09
rs10623997	5:107478679	T	0.76	NA	UFA	2E-8	0.015	2E-16	-0.004	0.13	-0.009	5E-5	0.007	0.001	0.013	2E-7	0.008	0.002
15:73322940_AT_A	15:73322940	A	0.59	NA	UFA	3E-19	0.014	3E-21	-0.010	6E-7	-0.008	4E-5	0.010	3E-6	0.008	2E-4	0.011	5E-8

1:113 20220 3_TCT CTC_T	1:113 20220 3	TCTCT C	0.80	NA	UFA	4E-11	0.014	3E-14	0.003	0.06	- 0.014	2E-9	0.010	1E-5	0.011	4E-6	0.015	1E-9
rs236 660	7:750 50086	C	0.57	NA	UFA	1E-15	0.014	2E-19	- 0.008	7E-7	- 0.002	0.13	0.008	5E-5	0.013	3E-11	0.011	6E-8
rs177 64730	5:127 35752 6	C	0.75	CTXN 3---[]- - SLC12 A2	UFA	2E-12	0.012	8E-12	- 0.017	2E-15	- 0.021	2E-21	0.008	2E-4	0.014	8E-11	0.010	3E-6
rs147 1740	3:136 32827 0	C	0.74	[STAG 1]	UFA	4E-53	0.010	4E-9	- 0.021	3E-25	- 0.053	1E- 140	0.027	5E-33	0.025	2E-27	0.008	2E-4
rs111 22450	1:230 30181 1	T	0.39	[GALN T2]	UFA	1E- 154	0.010	6E-11	- 0.058	5E- 212	- 0.008	3E-4	0.048	3E- 131	0.004	0.02	0.012	3E-9
rs123 69179	12:12 29635 50	C	0.91	[ZCCH C8]	FA	1E-18	0.029	2E-29	0.038	3E-34	- 0.002	0.76	- 0.020	1E-8	- 0.018	4E-7	- 0.011	1E-3
rs468 4847	3:123 86337	T	0.12	SYN2- --[]- PPAR G	FA	7E-42	0.029	3E-37	0.019	6E-12	0.035	6E-33	- 0.025	1E-18	- 0.034	3E-31	- 0.024	1E-16
rs555 16251 0	19:46 18303 1	A	0.82	NA	FA	8E-23	0.024	5E-34	0.010	2E-6	- 0.007	0.04	- 0.012	2E-6	-8E-4	0.57	- 0.005	0.03
rs622 71373	3:150 06654 0	T	0.94	PFN2- --[]- TSC22 D2	FA	8E-10	0.024	2E-14	0.040	4E-26	0.031	5E-14	- 0.043	8E-25	- 0.022	9E-7	- 0.004	0.43

rs729 59041	6:127 45489 3	G	0.95	[RSPO 3]	FA	2E-10	0.023	2E-12	0.050	9E-33	0.018	2E-5	- 0.063	6E-43	- 0.038	9E-16	- 0.029	4E-9
rs121 30231	1:219 63130 4	A	0.41	LYPLA L1--- []--- SLC30 A10	FA	8E-86	0.020	4E-41	0.015	1E-17	0.014	3E-14	- 0.019	2E-21	- 0.015	4E-14	- 0.012	8E-10
rs713 3378	12:12 44095 02	A	0.32	[DNA H10]	FA	3E-89	0.019	4E-33	0.037	2E-78	0.015	5E-14	- 0.029	2E-42	- 0.008	4E-5	0.005	0.05
rs482 1764	22:38 59936 4	G	0.42	[MAF F]	FA	4E-69	0.017	3E-29	0.021	9E-29	0.007	8E-5	- 0.023	2E-29	- 0.017	7E-17	- 0.005	0.03
rs133 89219	2:165 52887 6	T	0.39	GRB1 4--[]-- COBLL 1	FA	7E- 127	0.017	2E-29	0.027	5E-51	0.027	6E-48	- 0.038	4E-84	- 0.023	5E-30	- 0.010	1E-7
rs294 3653	2:227 04777 1	C	0.33	NYAP 2---[]- --IRS1	FA	3E- 125	0.016	1E-23	0.040	2E- 100	0.026	2E-39	- 0.038	3E-76	- 0.025	4E-34	- 0.017	4E-17
rs725 8937	19:33 93880 0	T	0.51	[PEPD]	FA	2E-50	0.016	2E-26	0.014	2E-14	0.012	3E-12	- 0.009	3E-6	- 0.009	8E-6	- 0.013	2E-10
rs726 97297	14:93 06998 9	T	0.82	[RIN3]	FA	6E-11	0.015	8E-15	0.005	0.03	0.004	0.14	- 0.005	0.04	- 0.010	8E-5	- 0.009	9E-4
rs972 283	7:130 46685 4	A	0.49	KLF14 --[]--- MKLN 1	FA	9E-98	0.014	2E-22	0.030	2E-60	0.012	4E-9	- 0.033	2E-62	- 0.012	4E-9	- 0.005	0.009

rs11135038	5:157930133	G	0.27	<i>CLINT1</i> ---[]- -- <i>EBF1</i>	FA	3E-27	0.014	3E-16	0.012	8E-11	0.013	4E-9	- 0.013	3E-10	- 0.008	2E-4	- 0.008	3E-4
rs9851766	3:138121509	A	0.84	[<i>MRA5</i>]	FA	1E-9	0.014	1E-11	0.009	3E-4	0.009	5E-4	- 0.010	4E-4	- 0.009	5E-4	- 0.004	0.12
rs142186653	17:73879851	C	0.23	<i>TRIM47</i> -[]- <i>TRIM65</i>	FA	4E-11	0.012	1E-11	-8E-4	0.62	0.008	1E-3	- 0.010	7E-6	- 0.010	3E-5	- 0.007	0.005
rs987469	4:89706643	C	0.54	[<i>FAM13A</i>]	FA	6E-50	0.012	6E-17	0.020	5E-29	0.009	2E-6	- 0.015	1E-14	- 0.008	4E-5	- 0.009	4E-6
rs2980888	8:126504383	C	0.70	<i>TRIB1</i> --[]	FA	4E-242	0.012	4E-14	0.038	3E-85	0.003	0.22	- 0.085	0E+0	- 0.038	4E-70	- 0.024	2E-28
rs30351	5:55794632	G	0.26	<i>ANKRD55</i> --- []--- <i>MAP3K1</i>	FA	2E-59	0.012	2E-12	0.027	2E-38	0.029	5E-42	- 0.031	9E-44	- 0.018	7E-16	-4E-4	0.70
rs12681990	8:36859186	T	0.84	<i>KCNU1</i> --[]-- - <i>ZNF703</i>	FA	3E-9	0.012	5E-9	0.009	2E-4	0.013	3E-6	- 0.012	1E-6	- 0.010	2E-4	- 0.006	0.06
rs6977416	7:150542711	G	0.67	<i>TME176A</i> --[]- <i>ABP1</i>	FA	8E-27	0.012	3E-14	0.016	7E-17	0.008	2E-4	- 0.012	3E-8	- 0.005	0.007	-1E-4	0.88
rs4976033	5:67714246	A	0.60	<i>PIK3R1</i> ---[]- --	FA	7E-39	0.012	5E-14	0.012	3E-11	0.013	5E-12	- 0.019	2E-21	- 0.013	3E-11	- 0.011	4E-8

				<i>SLC30 A5</i>														
rs124 41543	15:31 68954 3	A	0.29	<i>KLF13 --[]-- OTUD 7A</i>	FA	2E-13	0.012	1E-12	1E-4	0.95	0.007	0.003	- 0.004	0.07	- 0.010	2E-6	- 0.009	2E-4
rs129 40684	17:74 53919	C	0.30	<i>[TNFS F12- TNFSF 13]</i>	FA	0E+0	0.011	1E-11	0.004	0.03	0.173	0E+0	- 0.007	5E-4	0.006	0.009	0.013	4E-10
rs113 22203 8	11:62 38002 7	C	0.72	<i>[EML3]</i>	FA	2E-19	0.011	3E-12	0.011	1E-7	- 0.007	8E-4	- 0.013	4E-9	- 0.008	1E-4	- 0.007	7E-4
rs110 45172	12:20 47022 1	C	0.20	<i>AEBP 2---[]- - PDE3 A</i>	FA	9E-21	0.011	5E-9	0.027	8E-32	0.011	4E-6	- 0.025	9E-25	- 0.004	0.14	- 0.001	0.56
rs280 2774	1:203 52781 2	A	0.55	<i>OPTC- --[]-- ATP2 B4</i>	FA	7E-22	0.011	4E-13	0.007	2E-5	0.007	1E-4	- 0.010	1E-7	- 0.007	3E-4	- 0.005	0.01
rs723 3512	18:42 59507 6	G	0.71	<i>[SETB P1]</i>	FA	3E-16	0.011	8E-11	0.005	0.01	0.008	3E-4	- 0.009	2E-5	- 0.007	6E-4	- 0.005	0.008
rs976 4678	5:118 72666 2	C	0.27	<i>[TNFA IP8]</i>	FA	8E-23	0.010	3E-10	0.016	2E-14	0.003	0.10	- 0.021	7E-22	- 0.006	0.007	- 0.003	0.15
rs108 76529	12:54 42181 0	C	0.37	<i>HOXC 8-- []HOX C6</i>	FA	7E-20	0.010	5E-12	0.008	1E-5	0.010	1E-6	- 0.012	5E-9	- 0.008	4E-5	- 0.003	0.11

rs11664106	18:28 46812	T	0.37	<i>SMCHD1</i> --- [<i>EMI</i> <i>LIN2</i>	FA	9E-22	0.009	5E-9	0.009	1E-5	0.012	2E-9	- 0.013	1E-9	- 0.006	0.003	- 0.002	0.30
rs998584	6:437 57896	C	0.52	<i>VEGFA</i> --- <i>C6orf223</i>	FA	2E-122	0.009	1E-9	0.035	2E-83	0.016	8E-19	- 0.040	4E-96	- 0.017	3E-18	- 0.018	4E-18
rs6029180	20:39 17892 3	G	0.33	[<i>MAFB</i>	FA	3E-16	0.009	2E-8	0.005	0.01	0.003	0.06	- 0.015	2E-14	- 0.013	6E-10	- 0.009	2E-5
rs13132853	4:386 80015	A	0.64	[<i>KLF3</i>	FA	4E-16	0.009	1E-8	0.004	0.09	0.002	0.72	- 0.011	1E-7	- 0.011	9E-8	- 0.007	9E-4
rs573454216	6:139 83742 9	A	0.60	<i>CITED2</i> ---[FA	6E-47	0.009	1E-8	0.019	4E-23	0.010	4E-7	- 0.028	2E-44	- 0.014	1E-11	- 0.008	4E-5
rs4450871	4:499 0298	G	0.44	<i>MSX1</i> ---[<i>CYTL1</i>	FA	2E-24	0.009	1E-8	0.008	5E-7	0.011	3E-8	- 0.014	1E-12	- 0.009	9E-7	- 0.005	0.009
rs11205303	1:149 90641 3	C	0.41	[<i>MTMR11</i>	Conflicting	3E-36	0.019	3E-35	- 0.001	0.54	9E-4	0.93	- 0.004	0.15	0.001	0.48	0.003	0.08
rs1808629	8:734 35964	G	0.31	<i>TRPA1</i> ---[- <i>KCNB2</i>	Conflicting	2E-17	0.017	2E-24	- 0.012	7E-9	- 0.009	6E-6	0.009	1E-5	0.003	0.17	- 0.002	0.19
rs2855818	17:42 29001 5	A	0.24	[<i>UBTF</i>	Conflicting	3E-13	0.016	1E-21	0.002	0.59	- 0.010	9E-6	0.005	0.02	0.004	0.08	- 0.001	0.66
rs1046080	6:315 95882	A	0.72	[<i>PRRC2A</i>	Conflicting	2E-18	0.016	4E-22	- 0.005	0.01	- 0.013	4E-8	0.009	6E-4	0.004	0.24	- 0.011	2E-7

rs11012732	10:21830104	G	0.33	[MLLT10]	Conflicting	1E-21	0.016	2E-24	-0.004	0.02	0.002	0.30	0.002	0.38	8E-4	0.66	-0.011	3E-7
rs10999456	10:72413827	T	0.27	PRF1- -[]-- ADA MTS1 4	Conflicting	1E-13	0.016	2E-21	-9E-4	0.91	-0.003	0.39	0.004	0.06	0.003	0.26	5E-4	0.82
rs7166081	15:67492301	A	0.77	SMAD3- []AAG AB	Conflicting	3E-12	0.016	2E-20	-0.004	0.07	0.003	0.12	0.004	0.06	0.001	0.54	0.002	0.28
rs6938973	6:98421721	C	0.60	MMS22L--- []--- POU3 F2	Conflicting	2E-18	0.016	7E-26	-0.009	2E-7	-0.009	2E-6	0.006	0.001	0.009	1E-5	0.002	0.42
rs72798148	16:29926552	T	0.78	[KCTD13]	Conflicting	1E-8	0.016	7E-18	-0.006	0.003	-0.005	0.01	0.004	0.03	0.004	0.05	-9E-4	0.49
rs9843653	3:49920571	C	0.51	CAMKV--[]- MST1 R	Conflicting	4E-29	0.016	4E-26	-0.019	1E-27	-0.017	1E-20	0.008	4E-5	0.003	0.07	-7E-4	0.80
rs9788550	14:29681138	G	0.75	C14orf23--- []--- PRKD 1	Conflicting	3E-11	0.015	9E-20	-0.005	0.02	-0.007	0.003	0.006	0.007	6E-4	0.77	7E-4	0.79
rs9770544	7:27232126	C	0.18	LOC402470- []-	Conflicting	5E-9	0.015	8E-15	0.003	0.07	0.004	0.08	0.002	0.43	0.002	0.69	0.006	0.03

				<i>HOXA13</i>														
rs200119412	8:77224420	C	0.56	NA	Conflicting	1E-20	0.015	3E-24	-0.001	0.75	-0.007	3E-4	0.004	0.09	-9E-4	0.61	-0.002	0.45
rs17770336	9:28414625	T	0.32	[LINGO2]	Conflicting	3E-14	0.015	2E-21	-0.011	8E-9	-0.006	3E-4	0.008	4E-5	0.008	2E-4	0.003	0.29
rs704061	12:89771903	C	0.45	DUSP6--[]-- - GALNT4	Conflicting	2E-22	0.015	8E-24	0.004	0.07	-2E-4	0.99	0.002	0.30	0.007	0.001	9E-5	0.94
rs3817428	15:89415247	C	0.73	[ACAN]	Conflicting	5E-11	0.015	1E-18	-0.003	0.09	-0.003	0.09	0.004	0.07	9E-4	0.65	-0.003	0.14
rs3045391	22:41867105	T	0.20	[ACO2]	Conflicting	2E-9	0.015	3E-15	-0.005	0.03	0.006	0.01	0.003	0.20	0.005	0.05	0.008	9E-4
rs34898535	16:31025641	C	0.62	STX1B-[]-- STX4	Conflicting	3E-29	0.015	1E-21	-0.010	3E-8	0.007	2E-4	0.015	3E-15	5E-4	0.59	-0.006	0.010
rs1013293	1:62570321	G	0.57	[INADL]	Conflicting	3E-17	0.015	1E-22	-0.009	3E-7	-0.004	0.005	0.009	1E-6	0.008	8E-5	0.005	0.009
rs11165643	1:96924097	T	0.59	[]--- PTBP2	Conflicting	4E-16	0.014	1E-21	-0.005	0.03	-0.007	2E-4	0.004	0.04	0.006	0.003	0.001	0.42
rs56218501	20:46365636	C	0.79	[SULF2]	Conflicting	3E-11	0.014	5E-15	-0.018	7E-17	-0.005	0.04	0.005	0.05	0.006	0.01	0.001	0.71
rs9471333	6:40362023	C	0.45	[LRFN2]	Conflicting	2E-16	0.014	7E-22	-0.006	0.003	-0.008	9E-7	0.007	9E-5	0.004	0.03	0.002	0.46
rs10172678	2:59294558	T	0.40	FANCL---[]	Conflicting	4E-17	0.014	1E-20	-0.008	5E-6	-0.004	0.06	0.012	3E-11	0.011	6E-8	0.005	0.005

rs3215750	2:230633572	TAAA TC	0.33	[TRIP12]	Conflicting	1E-12	0.014	2E-19	-0.006	0.002	-0.005	0.007	0.004	0.02	0.007	0.001	9E-4	0.71
rs9847672	3:131618541	T	0.28	[CPNE4]	Conflicting	3E-11	0.014	3E-18	-0.013	7E-11	-0.007	0.003	0.006	0.001	0.005	0.006	-0.001	0.61
rs12072739	1:98315893	G	0.23	[DPYD]	Conflicting	6E-9	0.014	7E-16	-0.010	5E-6	-0.010	3E-5	0.017	2E-13	0.003	0.21	1E-3	0.54
rs2596121	8:76660225	G	0.59	HNF4G---[]- -- ZFHX4	Conflicting	6E-16	0.014	4E-20	-0.004	0.08	-0.005	0.01	0.003	0.15	-2E-4	0.98	-0.001	0.59
rs2192527	4:18329824	G	0.46	LCORL---[]	Conflicting	4E-17	0.014	4E-21	-0.005	0.004	2E-4	0.94	0.007	4E-4	0.008	4E-5	0.004	0.08
rs59499656	18:40768309	A	0.66	RIT2-- []-- SYT4	Conflicting	2E-13	0.014	2E-18	-0.013	5E-11	-0.004	0.03	0.008	1E-4	0.007	5E-4	0.001	0.44
rs879620	16:4015729	T	0.61	[ADCY9]	Conflicting	7E-17	0.014	1E-19	-0.006	5E-4	-0.004	0.06	0.004	0.11	0.003	0.12	0.007	0.001
rs10756798	9:16739763	C	0.35	[BNC2]	Conflicting	5E-13	0.014	1E-18	-0.009	1E-5	-0.008	8E-5	0.004	0.03	0.005	0.008	0.001	0.42
rs11042030	11:8690718	T	0.72	TRIM66--[]- - RPL27A	Conflicting	2E-9	0.014	6E-17	-0.009	8E-6	-0.005	0.003	0.008	3E-4	0.007	9E-4	7E-4	0.85
rs569541320	19:30286450	GA	0.33	NA	Conflicting	1E-14	0.014	5E-17	-0.005	0.03	-0.004	0.03	0.006	0.002	0.002	0.36	-0.012	8E-9
rs6693294	1:49879122	A	0.31	[AGBL4]	Conflicting	3E-11	0.014	3E-18	-0.005	0.009	-0.003	0.16	0.007	0.001	0.004	0.03	3E-4	0.73

3:185821409_AA_CACA_CACA_CAC_A	3:185821409	A	0.85	NA	Conflicting	3E-16	0.014	2E-10	0.027	8E-25	-0.005	0.11	0.002	0.37	0.014	5E-7	0.008	0.009
rs812949	5:170506141	C	0.73	[RANBP17]	Conflicting	4E-10	0.014	6E-16	-0.009	1E-5	-0.003	0.14	0.004	0.04	0.008	9E-4	-0.001	0.72
rs2678204	1:201800511	G	0.34	[IPO9]	Conflicting	4E-17	0.014	3E-18	-0.009	2E-7	-0.004	0.02	0.010	7E-7	0.004	0.06	0.010	1E-6
rs11907932	20:51148656	A	0.68	ZFP64---[---TSHZ2	Conflicting	7E-11	0.014	2E-17	-0.005	0.02	-0.011	8E-8	0.007	8E-4	0.006	0.02	2E-4	0.97
rs541582524	2:100827641	G	0.59	NA	Conflicting	2E-14	0.014	5E-19	-0.007	3E-5	-0.004	0.009	0.003	0.15	0.006	0.003	0.003	0.18
rs13329943	16:24733751	T	0.73	NA	Conflicting	4E-11	0.013	1E-15	-0.008	3E-4	-1E-4	0.89	0.007	0.001	-6E-4	0.80	-2E-4	0.95
rs57800857	4:140863365	A	0.63	[MAML3]	Conflicting	7E-12	0.013	9E-18	-0.009	1E-6	-0.007	0.002	0.009	2E-5	0.007	6E-4	0.003	0.19
rs1454687	3:94038085	C	0.48	NSUN3---[Conflicting	1E-14	0.013	6E-20	-0.007	7E-5	-0.009	2E-6	0.010	4E-7	0.010	6E-7	0.003	0.16
rs801738	11:65924217	C	0.64	[PACS1]	Conflicting	6E-14	0.013	7E-18	-0.014	6E-13	-0.005	0.01	0.008	4E-5	0.009	3E-5	0.003	0.13
rs200882902	2:228996202	CT	0.33	NA	Conflicting	2E-10	0.013	1E-17	-0.009	2E-5	-0.009	2E-5	0.009	2E-5	0.003	0.10	-2E-4	0.98

rs6575340	14:94023972	A	0.64	[UNC79]	Conflicting	1E-12	0.013	9E-18	-0.009	4E-6	-0.006	8E-4	0.005	0.01	0.003	0.16	0.002	0.55
rs522110	10:99772885	G	0.56	[CRTAC1]	Conflicting	7E-17	0.013	9E-19	-0.013	3E-14	-0.010	1E-7	0.016	3E-17	0.004	0.04	0.001	0.61
rs11079849	17:47090785	C	0.67	[IGF2BP1]	Conflicting	2E-13	0.013	6E-17	-0.010	1E-7	-0.013	2E-10	0.007	4E-4	0.007	0.001	0.001	0.51
rs217672	14:62361021	C	0.27	SNAPC1--[]--SYT16	Conflicting	3E-8	0.013	4E-15	-0.008	3E-4	-0.007	5E-4	0.006	0.004	0.005	0.02	0.002	0.45
13:99119385_TA_A_T	13:99119385	TAA	0.71	NA	Conflicting	6E-9	0.013	6E-16	-0.006	0.007	-0.007	1E-3	0.009	8E-6	0.007	0.004	9E-4	0.74
rs7213608	17:21279289	C	0.33	MAP2K3--[]--KCNJ12	Conflicting	5E-10	0.013	4E-16	-9E-4	0.58	-9E-4	0.60	0.004	0.05	0.007	5E-4	0.002	0.27
rs72634813	1:1537887	C	0.65	C1orf233--[]--MIB2	Conflicting	2E-9	0.013	2E-15	-0.003	0.13	-0.004	0.03	0.003	0.11	0.006	0.004	0.002	0.34
rs58300328	2:69646357	G	0.59	NA	Conflicting	2E-15	0.013	3E-18	-0.006	4E-4	0.002	0.34	0.003	0.28	0.003	0.13	0.002	0.78
rs62217799	20:62347191	T	0.66	NA	Conflicting	3E-16	0.013	9E-16	-0.011	2E-10	-0.016	5E-15	0.005	0.02	0.003	0.09	0.007	7E-4

rs11150745	17:78 757626	A	0.68	[RPTOR]	Conflicting	9E-10	0.013	2E-15	- 0.006	7E-4	- 0.004	0.03	0.002	0.45	0.007	9E-4	0.006	0.01
rs34388845	6:285 78286	G	0.21	SCAN D3-- []-- TRIM 27	Conflicting	9E-16	0.013	3E-12	- 0.017	2E-14	- 0.007	0.002	- 0.008	0.001	- 0.004	0.09	- 0.028	2E-28
14:33298731_CA_C	14:33 298731	C	0.45	[AKAP6]	Conflicting	4E-12	0.013	4E-17	- 0.005	0.006	- 0.003	0.05	0.003	0.09	0.004	0.03	2E-4	0.82
rs12330631	3:123 089834	C	0.63	[ADCY5]	Conflicting	1E-13	0.013	1E-15	- 0.007	3E-5	0.001	0.63	0.003	0.07	0.004	0.03	0.004	0.03
rs394608	21:46 581798	C	0.54	[ADARB1]	Conflicting	1E-13	0.012	7E-17	- 0.008	1E-6	- 0.012	4E-11	0.011	1E-7	8E-4	0.70	- 0.002	0.43
rs9289630	3:141 178670	C	0.39	ZBTB3 8--[]-- RASA 2	Conflicting	5E-15	0.012	5E-17	- 0.005	0.02	- 0.010	6E-8	-8E-4	0.51	9E-4	0.64	0.004	0.07
rs59934506	20:25 373782	C	0.44	NA	Conflicting	1E-13	0.012	4E-16	1E-4	0.90	- 0.005	0.008	0.003	0.09	0.012	2E-10	0.005	0.005
rs2287214	12:10 8090518	G	0.40	[PWP1]	Conflicting	7E-14	0.012	2E-16	0.002	0.41	- 0.001	0.60	- 0.002	0.39	0.008	4E-5	0.004	0.05
rs57989773	6:100 629078	C	0.24	MCHR 2---[]-- SIM1	Conflicting	7E-14	0.012	5E-12	- 0.001	0.40	0.009	4E-5	- 0.013	4E-8	0.006	0.009	- 0.003	0.17

rs3803286	14:103246470	A	0.33	[TRAF3]	Conflicting	1E-13	0.012	6E-15	-0.016	3E-17	-0.005	0.005	0.007	8E-4	-0.001	0.50	-0.005	0.01
rs2474896	6:51760527	T	0.55	[PKHD1]	Conflicting	2E-14	0.012	4E-16	0.003	0.32	-0.003	0.22	2E-4	0.87	0.001	0.59	-2E-4	0.71
rs9512696	13:28012527	G	0.66	[MTIF3]	Conflicting	9E-10	0.012	1E-13	-0.009	9E-7	-0.009	5E-6	0.005	0.006	0.003	0.11	0.001	0.41
rs10169594	2:41637688	C	0.36	SLC8A1---[]-- C2orf91	Conflicting	1E-9	0.012	5E-15	-0.005	0.01	-0.004	0.02	0.005	0.01	0.007	0.002	0.004	0.09
rs13410783	2:36789166	G	0.37	[FEZ2]	Conflicting	2E-11	0.012	8E-15	-0.009	5E-8	-0.004	0.07	0.006	0.002	0.001	0.46	-0.005	0.02
rs3911063	3:85906928	T	0.68	[CADM2]	Conflicting	1E-8	0.012	2E-14	-0.003	0.08	-0.007	4E-4	0.005	0.03	0.005	0.02	0.002	0.17
rs11135450	5:95554016	G	0.67	ELL2-- -[]--- PCSK1	Conflicting	5E-10	0.012	2E-14	-0.008	1E-4	-0.008	3E-5	0.004	0.05	0.005	0.009	0.006	0.003
rs1038088	17:28074563	G	0.52	[SSH2]	Conflicting	3E-14	0.012	1E-15	-0.008	8E-6	-0.001	0.41	-4E-4	0.89	0.007	8E-5	0.007	1E-4
rs3810291	19:47569003	A	0.68	[ZC3H4]	Conflicting	1E-19	0.012	1E-13	-0.015	4E-15	-0.014	6E-13	0.011	1E-7	-0.010	2E-6	-0.009	6E-5
rs4718964	7:70038969	T	0.41	[AUTS2]	Conflicting	2E-12	0.012	2E-15	-0.004	0.04	6E-4	0.60	0.002	0.18	0.005	0.05	0.005	0.03
rs215669	7:32378979	G	0.39	PDE1C--[]-- -LSM5	Conflicting	9E-10	0.012	8E-15	-0.006	6E-4	-0.005	0.003	0.010	2E-6	0.004	0.05	2E-4	0.90
rs238675	1:42470274	G	0.26	HIVEP3--[]--	Conflicting	5E-9	0.012	4E-12	-0.009	4E-6	-0.004	0.03	0.002	0.40	0.001	0.56	0.005	0.03

				- GUCA 2B														
rs19956955	11:130749351	T	0.53	[SNX19]	Conflicting	3E-12	0.012	2E-15	-0.006	5E-4	-0.006	9E-4	0.005	0.007	0.001	0.55	0.002	0.21
rs61782665	1:47692035	A	0.42	[TAL1]	Conflicting	1E-12	0.012	4E-15	-0.007	9E-5	-0.005	0.009	0.003	0.29	0.006	0.001	0.008	3E-5
rs1568488	3:153657951	C	0.60	C3orf79--- []--- ARHG EF26	Conflicting	1E-11	0.012	2E-14	-0.005	0.004	-0.007	1E-4	-2E-4	0.96	-4E-4	0.99	-0.003	0.21
rs1322842	6:20488897	A	0.39	[E2F3]	Conflicting	4E-10	0.012	4E-15	-0.009	3E-6	-0.008	1E-5	0.010	3E-7	0.007	4E-4	0.002	0.29
rs2371767	3:64718258	C	0.27	ADA MTS9 --[]--- MAGI 1	Conflicting	3E-16	0.012	2E-12	0.007	0.003	0.008	8E-4	-0.007	0.002	-0.007	0.003	4E-4	0.64
rs34234296	2:175166636	G	0.61	OLA1- -[]-- SP9	Conflicting	4E-10	0.012	8E-15	-0.006	0.001	-0.008	5E-5	0.012	5E-9	0.006	0.003	0.002	0.35
rs28433072	4:56269683	C	0.46	[TME M165]	Conflicting	4E-19	0.012	1E-14	0.002	0.13	0.005	0.01	-0.004	0.03	-8E-4	0.56	-0.008	6E-5
rs7328213	13:33377830	T	0.55	PDS5 B--[]-- -KL	Conflicting	6E-16	0.012	6E-15	-0.002	0.30	-0.001	0.52	0.007	7E-5	0.013	1E-11	0.002	0.45
rs1441264	13:79580919	A	0.59	RNF2 19--- []---	Conflicting	2E-9	0.012	9E-14	-0.006	0.001	-0.006	0.001	0.003	0.07	0.009	1E-5	0.005	0.02

				<i>RBM2 6</i>														
rs129 6328	4:137 08319 3	A	0.44	[]	Confli cting	1E-11	0.012	6E-15	- 0.005	0.02	- 0.005	0.006	-2E-4	0.90	0.006	0.002	0.005	0.02
rs771 14068 4	16:49 25963	CT	0.33	NA	Confli cting	1E-8	0.012	3E-12	- 0.006	0.002	- 0.003	0.05	0.003	0.08	0.003	0.14	- 0.005	0.02
rs124 77088	2:678 41326	T	0.59	<i>ETAA 1---[]- --C1D</i>	Confli cting	6E-11	0.011	3E-14	-7E-4	0.72	- 0.007	4E-4	0.002	0.27	0.008	7E-5	0.003	0.09
rs106 31643	7:113 01386 5	TTTC	0.38	<i>GPR8 5---[]- -- PPP1 R3A</i>	Confli cting	3E-9	0.011	3E-14	- 0.003	0.08	- 0.003	0.18	0.005	0.006	0.004	0.03	- 0.001	0.40
rs441 792	2:105 40422 1	G	0.49	<i>LOC1 00287 010--- []-- POU3 F3</i>	Confli cting	7E-12	0.011	1E-14	- 0.004	0.02	- 0.003	0.05	0.003	0.10	6E-4	0.97	- 0.006	0.002
rs454 9685	7:393 26478	C	0.67	<i>[POU 6F2]</i>	Confli cting	4E-8	0.011	3E-13	- 0.008	6E-5	- 0.004	0.004	0.007	4E-4	0.002	0.31	- 0.004	0.09
rs384 0590	7:778 27064	G	0.65	<i>[MAG I2]</i>	Confli cting	3E-8	0.011	1E-13	- 0.007	2E-4	- 0.005	0.009	0.003	0.21	0.006	0.002	0.003	0.22
rs793 1311	11:65 28651 6	C	0.22	<i>FRMD 8---[]- SCYL1</i>	Confli cting	2E-10	0.011	4E-10	- 0.008	1E-4	- 0.018	2E-16	0.010	2E-5	- 0.008	5E-4	- 0.005	0.05
rs120 28517	1:666 1732	C	0.67	<i>[KLHL 21]</i>	Confli cting	2E-9	0.011	4E-13	- 0.006	0.002	- 0.005	0.004	0.004	0.06	0.004	0.03	0.007	8E-4

rs72867447	11:13301875	G	0.57	[ARNTL]	Conflicting	1E-12	0.011	5E-14	-0.007	0.003	-0.016	1E-18	0.011	8E-8	0.006	9E-4	0.002	0.30
rs149053776	17:43130624	G	0.38	NA	Conflicting	9E-12	0.011	5E-13	-0.001	0.38	-0.009	5E-6	0.005	0.02	0.001	0.49	0.005	0.01
rs1731260	2:26953354	T	0.47	[KCNK3]	Conflicting	5E-16	0.011	3E-14	-0.003	0.20	0.002	0.46	-0.007	4E-4	0.005	0.02	0.004	0.009
rs2456523	15:53082481	G	0.26	ONECUT1[]- -- WDR72	Conflicting	5E-11	0.011	1E-11	-0.004	0.03	-0.021	1E-22	0.006	0.01	0.003	0.20	3E-4	0.92
rs4377779	6:12117344	T	0.65	[HIVEP1]	Conflicting	1E-11	0.011	1E-12	-0.006	0.002	0.003	0.30	-0.002	0.37	0.001	0.65	0.003	0.13
rs7707628	5:153546900	T	0.35	MFAP3---[]- - GALNT10	Conflicting	2E-11	0.011	9E-13	0.001	0.59	-0.006	0.003	-0.005	0.02	0.002	0.47	-6E-4	0.64
rs17491275	1:39672545	G	0.16	[MACF1]	Conflicting	3E-15	0.011	4E-8	-0.037	1E-52	-0.028	5E-28	0.023	3E-19	0.005	0.03	-0.008	0.003
rs16975918	18:39914522	T	0.32	PIK3C3---[]- --RIT2	Conflicting	4E-8	0.011	4E-12	-0.011	3E-7	-0.004	0.06	0.004	0.10	0.006	0.02	0.001	0.64
rs429343	2:147903382	A	0.42	[]--- ACVR2A	Conflicting	2E-9	0.011	4E-13	-0.009	6E-8	-0.007	9E-5	0.009	2E-6	0.005	0.02	8E-5	0.81
rs1436348	3:104612668	G	0.58	[]--- ALCAM	Conflicting	8E-10	0.011	6E-13	-0.005	0.01	-0.004	0.06	0.004	0.03	4E-4	0.72	-0.004	0.05

rs7925725	11:13 14493 65	C	0.41	<i>SNX19</i> ---[]--- -- <i>NTM</i>	Conflicting	7E-9	0.011	2E-13	- 0.007	3E-5	- 0.004	0.004	0.007	4E-4	0.007	0.001	1E-3	0.83
rs3743861	16:89 81834 0	G	0.58	[<i>FANCA</i>]	Conflicting	4E-9	0.011	1E-13	- 0.005	0.008	- 0.006	0.005	0.008	5E-5	0.007	1E-4	0.006	0.001
rs36090025	10:11 47744 33	A	0.70	[<i>TCF7L2</i>]	Conflicting	2E-21	0.011	1E-11	0.003	0.10	0.012	4E-11	- 0.009	3E-5	- 0.006	0.01	0.008	5E-5
rs2957668	11:10 40438 2	T	0.47	<i>ADM</i> - []-- <i>AMPD3</i>	Conflicting	2E-12	0.011	4E-13	0.003	0.17	- 0.003	0.07	- 0.002	0.25	0.002	0.33	0.001	0.48
rs5849410	3:612 64379	C	0.59	<i>NA</i>	Conflicting	2E-9	0.011	1E-12	- 0.007	1E-3	- 0.006	0.003	0.002	0.33	-5E-5	0.91	2E-4	0.85
6:126927854_GT_G	6:126 92785 4	GT	0.50	<i>NA</i>	Conflicting	6E-22	0.011	4E-13	- 0.003	0.07	0.011	3E-7	0.008	3E-5	0.006	0.002	0.008	8E-5
rs1841025	12:41 84627 2	C	0.48	[<i>PDZRN4</i>]	Conflicting	2E-9	0.011	3E-13	- 0.002	0.32	- 0.005	0.003	7E-4	0.77	0.003	0.05	-5E-4	0.89
rs12951079	17:34 93305 9	G	0.58	[<i>GGNBP2</i>]	Conflicting	3E-9	0.011	1E-12	- 0.005	0.003	0.002	0.12	0.008	5E-5	0.007	2E-4	0.002	0.40
rs67913249	5:432 04126	C	0.66	[<i>NIM1</i>]	Conflicting	2E-8	0.011	3E-11	- 0.006	0.002	- 0.003	0.15	0.010	6E-6	7E-4	0.87	-5E-4	0.60
rs2172131	10:13 39789 62	T	0.42	[<i>JAKMIP3</i>]	Conflicting	2E-9	0.011	1E-12	- 0.004	0.02	- 0.008	4E-4	0.006	0.004	0.004	0.05	0.004	0.02

rs11790018	9:129702842	C	0.63	[RALGPS1]	Conflicting	5E-11	0.011	1E-12	-0.005	0.006	5E-4	0.49	-5E-4	0.85	-0.004	0.05	-0.004	0.18
rs1503526	5:63020706	C	0.48	[]---HTR1A	Conflicting	1E-9	0.011	3E-13	-0.006	7E-4	-0.002	0.30	0.003	0.07	0.004	0.04	0.001	0.33
rs3931548	9:103113652	A	0.38	[TEX10]	Conflicting	9E-9	0.011	4E-12	-0.009	2E-6	-0.005	0.03	0.002	0.32	0.005	0.01	0.005	0.04
rs8074454	17:3981148	C	0.33	[ZZEF1]	Conflicting	6E-12	0.011	3E-11	-0.011	4E-8	-0.010	6E-7	0.002	0.17	-0.003	0.14	-0.005	0.002
rs7630228	3:71681487	T	0.56	FOXP1---[]-EIF4E3	Conflicting	7E-11	0.011	4E-12	-0.013	2E-12	-0.006	0.002	0.008	1E-5	0.002	0.35	-0.005	0.005
rs719802	11:113234679	T	0.39	[TTC12]	Conflicting	3E-9	0.011	6E-12	-0.003	0.06	-0.002	0.40	0.004	0.02	-6E-4	0.78	-1E-5	0.88
rs10792	17:5288179	T	0.30	[RABEP1]	Conflicting	1E-11	0.010	8E-11	-0.003	0.14	-0.012	3E-8	-0.002	0.21	0.005	0.04	-0.005	0.01
rs4894808	3:171833266	G	0.60	[FNDC3B]	Conflicting	3E-13	0.010	8E-12	0.004	0.02	1E-3	0.69	-0.007	6E-4	0.001	0.33	-0.003	0.23
rs2043016	2:198146381	T	0.38	[ANKRD44]	Conflicting	2E-12	0.010	2E-11	-0.005	0.001	-0.006	0.002	-0.004	0.05	-0.001	0.48	0.002	0.32
rs424539	9:14442595	G	0.38	NFIB--[]---ZDHC21	Conflicting	5E-8	0.010	1E-11	-0.003	0.10	-9E-4	0.65	0.005	0.02	0.002	0.28	-0.001	0.53

rs10854853	22:48 874412	T	0.46	[/-- FAM1 9A5	Confli cting	9E-10	0.010	2E-12	- 0.011	2E-7	- 0.008	1E-4	0.006	0.003	0.004	0.04	0.002	0.39
rs4908676	1:773 7099	G	0.46	[CAM TA1]	Confli cting	1E-8	0.010	2E-12	- 0.007	6E-5	- 0.005	0.004	0.006	0.001	0.003	0.09	0.003	0.07
rs12375196	7:103 416541	A	0.42	[RELN]	Confli cting	2E-9	0.010	3E-12	- 0.001	0.36	- 0.002	0.38	-4E-4	0.72	0.005	0.04	0.005	0.005
rs9859077	3:101 136402	G	0.66	[SENP 7]	Confli cting	5E-12	0.010	4E-11	0.006	0.002	- 0.007	3E-4	0.003	0.12	0.009	9E-6	1E-3	0.53
rs9435341	1:107 616641	T	0.34	PRMT 6--[-- NTNG 1	Confli cting	7E-97	0.010	2E-11	- 0.005	0.01	0.046	1E- 122	-8E-4	0.95	0.009	3E-6	0.004	0.06
rs11786089	8:219 75521	G	0.46	[HR]	Confli cting	9E-9	0.010	1E-12	- 0.004	0.01	- 0.006	0.003	0.004	0.01	-2E-4	0.72	-7E-4	0.79
rs529200	3:173 114305	G	0.53	SPAT A16--- [-- NLGN 1	Confli cting	9E-9	0.010	6E-12	- 0.009	7E-7	- 0.005	0.007	0.009	5E-6	0.004	0.02	0.002	0.39
rs9260127	6:299 10478	G	0.45	[HLA- A]	Confli cting	3E-20	0.010	8E-12	- 0.013	4E-13	-6E-4	0.85	- 0.015	7E-14	- 0.007	1E-4	- 0.016	4E-17
rs583893	11:11 8904233	G	0.57	SLC37 A4-[/- - HYOU 1	Confli cting	4E-10	0.010	3E-11	- 0.013	3E-12	- 0.004	0.02	0.008	4E-5	0.009	9E-6	0.003	0.14
rs12945575	17:40 713071	T	0.25	HSD1 7B1- [/-	Confli cting	1E-10	0.010	4E-9	- 0.018	2E-18	- 0.016	1E-14	0.018	2E-16	0.010	3E-5	0.003	0.22

				COAS Y															
rs478 0885	16:20 38000 4	G	0.50	[PDIL T]	Confli cting	6E-11	0.010	8E-12	- 0.005	0.004	7E-4	0.85	6E-5	0.85	0.004	0.02	0.002	0.16	
rs106 81181	9:922 06788	TTTG	0.48	NA	Confli cting	6E-15	0.010	2E-12	- 0.009	4E-6	2E-4	0.88	0.013	7E-12	0.004	0.08	- 0.008	1E-4	
rs121 27506	1:222 07561 4	C	0.68	DUSP 10--- []--- HHIPL 2	Confli cting	9E-11	0.010	8E-11	0.005	0.004	0.003	0.14	- 0.006	0.01	-8E-4	0.67	-7E-5	1.00	
rs675 18031	3:887 42702	G	0.50	NA	Confli cting	2E-8	0.010	1E-12	- 0.008	6E-6	- 0.005	0.006	0.006	0.002	0.008	5E-5	0.004	0.07	
5:639 40500 _CA_ C	5:639 40500	C	0.53	NA	Confli cting	2E-8	0.010	4E-12	- 0.003	0.09	- 0.005	0.005	0.008	9E-5	0.005	0.01	0.002	0.28	
rs279 8297	4:306 4004	A	0.37	GRK4- -[]-- HTT	Confli cting	1E-24	0.010	3E-11	- 0.003	0.02	0.015	3E-15	0.014	1E-12	0.010	6E-7	0.007	8E-4	
rs751 9259	1:664 34743	A	0.53	[PDE4 B]	Confli cting	7E-10	0.010	4E-12	0.001	0.54	- 0.002	0.31	0.003	0.05	0.007	3E-4	0.008	3E-5	
rs678 2581	3:196 97910 6	C	0.56	[DLG1]	Confli cting	2E-10	0.010	9E-12	- 0.002	0.42	0.003	0.17	4E-4	0.79	0.002	0.28	- 0.001	0.53	
rs699 929	3:157 93183 7	A	0.44	NA	Confli cting	2E-8	0.010	6E-12	- 0.005	0.006	- 0.002	0.17	8E-4	0.81	0.002	0.31	0.001	0.54	
rs254 027	5:103 94041 5	A	0.44	[]	Confli cting	4E-9	0.010	9E-12	- 0.011	5E-11	- 0.006	4E-4	0.011	2E-8	0.004	0.03	- 0.002	0.32	

rs10804146	2:206061247	G	0.47	[<i>PARD3B</i>]	Conflicting	4E-9	0.010	1E-11	-0.005	0.02	-0.004	0.04	1E-4	0.93	0.003	0.20	0.003	0.19
rs112454648	10:70347292	A	0.44	[<i>TET1</i>]	Conflicting	4E-10	0.010	8E-11	0.002	0.23	-0.005	0.003	0.005	0.01	0.010	9E-7	0.007	1E-3
rs68177066	13:81104260	C	0.34	<i>SPRY2</i> --[]	Conflicting	7E-12	0.010	3E-10	-0.002	0.26	6E-5	0.86	0.004	0.08	-0.006	0.008	-0.014	6E-12
rs12997625	2:202970250	T	0.53	[<i>LOC100652824</i>]	Conflicting	1E-12	0.010	7E-12	0.002	0.16	-0.005	0.008	0.010	2E-7	0.010	4E-6	0.009	9E-6
3:183513243_AT_TTTT_TTTT_TT_A	3:183513243	ATTTT TTTTT TTTTT TT_A	0.47	NA	Conflicting	1E-8	0.010	7E-11	-0.003	0.24	-6E-4	0.65	0.001	0.70	-0.001	0.87	5E-4	0.87
rs159961	1:8484228	T	0.34	[<i>RERE</i>]	Conflicting	4E-8	0.010	8E-11	-0.004	0.07	0.001	0.66	0.003	0.06	-0.001	0.78	0.001	0.51
rs9319615	17:79072594	A	0.45	[<i>BAIAP2</i>]	Conflicting	3E-8	0.010	3E-11	-0.003	0.24	-0.007	2E-4	0.006	0.003	0.003	0.38	0.001	0.80
rs61791109	3:170734377	C	0.28	[<i>SLC2A2</i>]	Conflicting	3E-8	0.010	1E-9	-1E-3	0.77	-0.012	5E-8	0.012	3E-7	0.012	2E-8	0.012	3E-8
rs11172113	12:57527283	C	0.41	[<i>LRP1</i>]	Conflicting	6E-12	0.010	5E-11	0.007	4E-4	0.002	0.51	-0.002	0.48	0.005	0.008	0.008	4E-5
rs746336168	1:184706212	G	0.48	[<i>EDEM3</i>]	Conflicting	2E-8	0.010	5E-11	3E-4	0.83	-0.008	5E-5	0.003	0.09	0.003	0.16	-7E-4	0.94

rs2717609	8:143769252	A	0.53	<i>PSCA-[]--LY6K</i>	Conflicting	3E-8	0.010	4E-11	-0.003	0.07	-0.003	0.25	0.005	0.01	0.010	5E-7	0.004	0.03
rs6899218	5:178988608	A	0.51	<i>[RUFY1]</i>	Conflicting	8E-10	0.010	1E-11	-2E-4	0.86	-0.007	3E-5	0.008	6E-5	0.001	0.61	8E-5	0.81
rs747489841	16:73095430	AAC	0.36	<i>ZFH3--[]</i>	Conflicting	5E-9	0.010	1E-10	-0.009	9E-7	-0.004	0.01	0.003	0.18	-0.003	0.13	-0.006	0.01
rs33994795	8:9473429	C	0.36	<i>[TNKS]</i>	Conflicting	2E-24	0.010	2E-10	-3E-4	0.94	-0.003	0.16	-0.017	6E-19	0.018	7E-19	0.018	1E-19
rs10496731	2:135597628	T	0.63	<i>[ACMSD]</i>	Conflicting	3E-15	0.010	3E-10	-0.013	3E-12	0.007	6E-4	0.002	0.22	0.003	0.08	0.001	0.38
rs811054	16:72251132	T	0.54	<i>PMFBP1--[]--ZFH3</i>	Conflicting	4E-8	0.010	2E-10	-0.003	0.10	-0.004	0.07	0.011	2E-7	0.005	0.02	0.003	0.12
6:143187255_CA_C	6:143187255	CA	0.51	<i>[HIVEP2]</i>	Conflicting	3E-8	0.010	8E-11	-0.001	0.46	-0.005	0.002	1E-3	0.58	-8E-4	0.67	-9E-4	0.59
rs4668314	2:171631258	G	0.39	<i>SP5--[]-ERICH2</i>	Conflicting	3E-8	0.010	4E-10	-0.009	9E-7	-0.009	7E-7	0.013	2E-11	0.003	0.07	6E-4	0.80
rs564988630	4:83192564	C	0.50	NA	Conflicting	2E-8	0.010	5E-10	-0.003	0.16	2E-4	0.99	-9E-4	0.69	0.001	0.47	-0.002	0.22
rs560547656	15:75443633	C	0.47	NA	Conflicting	3E-11	0.009	3E-10	0.006	0.002	-0.006	3E-4	-0.003	0.27	0.005	0.008	0.005	0.008

rs12432026	14:75282116	G	0.54	[YLP M1]	Conflicting	1E-13	0.009	5E-10	-0.015	2E-17	-0.002	0.37	0.003	0.19	0.001	0.48	-0.006	9E-4
rs2712169	2:217671349	G	0.42	IGFBP5---[]-TNP1	Conflicting	9E-14	0.009	4E-10	0.003	0.24	0.005	0.02	-0.008	1E-4	-0.007	0.002	-0.007	7E-4
rs796663884	6:52426285	CT	0.42	NA	Conflicting	3E-14	0.009	5E-10	0.003	0.12	0.006	0.006	-0.005	0.01	0.001	0.60	-0.008	2E-4
rs79100766	1:151690804	C	0.52	CELF3-[]-RIIAD1	Conflicting	8E-9	0.009	5E-10	0.003	0.03	-0.003	0.18	0.003	0.12	8E-4	0.68	2E-5	0.99
rs3856595	3:66492604	G	0.55	[LRIG1]	Conflicting	1E-9	0.009	4E-9	0.001	0.70	0.003	0.22	-6E-4	0.78	-0.001	0.57	-0.005	0.02
rs143020014	9:86463210	G	0.55	[KIF27]	Conflicting	7E-37	0.009	2E-9	4E-4	0.87	0.022	1E-29	-0.005	0.02	-0.003	0.12	0.012	5E-9
rs17256211	14:23754580	G	0.65	[HOM EZ]	Conflicting	5E-12	0.009	1E-8	-0.001	0.36	0.010	2E-6	-0.005	0.04	0.004	0.12	0.001	0.77
rs505922	9:136149229	C	0.32	[ABO]	Conflicting	7E-120	0.009	2E-8	0.013	7E-11	-0.009	5E-6	-0.013	8E-10	0.026	2E-34	-0.030	3E-43
rs4577503	3:99657922	G	0.41	[CMS S1]	Conflicting	7E-11	0.009	3E-9	0.004	0.07	0.001	0.45	-0.004	0.04	9E-4	0.71	-0.006	0.002
rs4669869	2:12898460	C	0.44	TRIB2--[]	Conflicting	7E-11	0.009	3E-9	0.004	0.05	0.005	0.01	-0.004	0.03	3E-4	0.81	0.003	0.16
rs12927987	16:66720206	T	0.52	[CMT M4]	Conflicting	2E-8	0.009	1E-8	-0.001	0.63	-0.002	0.28	5E-4	0.62	-2E-4	0.93	-0.008	2E-5

rs340025	15:60908307	C	0.58	[RORA]	Conflicting	7E-13	0.009	5E-9	0.002	0.21	-0.010	1E-8	0.010	1E-5	0.017	6E-19	0.010	1E-7
rs7037043	9:77160815	G	0.35	[RORB]	Conflicting	3E-9	0.009	4E-8	0.005	0.003	0.004	0.03	-0.003	0.18	-0.005	0.02	-0.003	0.11
rs7191378	16:58115034	G	0.31	MMP15--[]-C16orf80	Conflicting	1E-8	0.009	2E-8	-0.005	0.01	8E-4	0.56	0.002	0.27	-0.010	2E-6	-0.008	1E-4
rs8071840	17:70721707	G	0.48	[SLC39A11]	Conflicting	6E-9	0.008	2E-8	-9E-4	0.90	-0.006	0.004	1E-4	0.94	-8E-4	0.61	-0.007	1E-4
rs4497915	2:48690596	G	0.54	[PPP1R21]	Conflicting	2E-13	0.008	2E-8	-0.005	0.002	0.006	9E-4	0.003	0.17	0.013	6E-12	0.004	0.03
rs2292238	12:56493822	A	0.59	[ERBB3]	Conflicting	1E-9	0.008	5E-8	-0.010	1E-7	-0.009	1E-6	0.006	0.003	0.011	2E-8	0.012	1E-9
rs4737188	8:64756657	A	0.53	YTHDF3---[]---BHLHE22	Conflicting	4E-8	0.008	3E-8	-0.012	2E-10	-0.011	7E-10	0.010	2E-7	0.004	0.04	8E-4	0.70

Table S3. Colocalisation analysis of six adiposity and metabolic biomarker traits for “unfavourable adiposity” loci, with posterior probability of colocalisation > 0.7. Index SNP: “Unfavourable adiposity” SNP; Traits: Traits showing colocalised association; Posterior probability: Posterior probability of colocalisation; Colocalised SNP: SNP identified with association across traits; Posterior explained by SNP: Proportion of posterior probability explained by colocalised SNP.

CHR	Index SNP	Gene	Traits	Posterior probability	Colocalised SNP	Posterior explained by SNP
17	rs4790292	RPA1--[]--RTN4RL1	SHBG, Triglycerides	0.9993	rs11078597	0.9916
4	rs13107325	[SLC39A8]	BFP, HDL, Triglycerides, ALT, AST	0.9983	rs13107325	1
3	rs1471740	[STAG1]	SHBG, ALT	0.9839	rs687339	0.9105
8	rs4876611	[TRPS1]	BFP, Triglycerides	0.9725	rs4876611	0.3737
5	rs2112347	POC5-[]---SV2C	BFP, HDL	0.9694	rs2307111	0.9438
6	6:34650934	[C6orf106]	Triglycerides, ALT	0.9652	rs185139895	0.6515
12	rs3764002	[WSCD2]	BFP, SHBG, Triglycerides	0.9635	rs3764002	0.9248
18	rs6567160	PMAIP1---[]---MC4R	BFP, SHBG	0.946	rs538656	0.1473
19	rs11666808	[KIAA1683]	SHBG, ALT	0.9455	rs885683	0.1356
14	14:79940130	NA	BFP, ALT	0.944	14:79940130	0.3807
11	rs61888762	[BDNF]	BFP, ALT	0.9123	rs61888762	0.2306
16	rs8049669	CYB5B--[]--NFAT5	BFP, Triglycerides	0.9097	rs10694251	0.2471
15	15:73322940	NA	ALT, AST	0.8948	rs4558379	0.8428
10	rs2274224	[PLCE1]	BFP, Triglycerides, ALT, AST	0.8926	rs2274224	0.2417
18	rs6567160	PMAIP1---[]---MC4R	HDL, Triglycerides	0.8917	rs8089364	0.0574
1	rs539515	FAM5B---[]-SEC16B	ALT, AST	0.8849	rs7523508	0.279
11	rs61888762	[BDNF]	HDL, Triglycerides	0.8779	rs17309930	0.3472
5	rs10623997	NA	HDL, Triglycerides	0.8531	rs256538	0.2694
11	rs4755725	NA	BFP, HDL, ALT	0.7865	rs57951376	0.1175

5	rs17764730	CTXN3---[]--SLC12A2	BFP, HDL, SHBG, ALT, AST	0.7823	rs3749748	0.2312
6	rs9358912	HIST1H4E-[]-HIST1H2BG	HDL, Triglycerides, AST	0.7772	rs76091509	0.4528
11	rs61888762	[BDNF]	SHBG, AST	0.7747	rs71480157	0.0691
16	rs11642015	[FTO]	BFP, HDL, SHBG, ALT, AST	0.7593	rs56094641	0.7168
19	rs11666808	[KIAA1683]	BFP, Triglycerides	0.7427	rs11666808	0.2703
1	1:72767554_CA_C	NA	BFP, HDL, SHBG, Triglycerides	0.7324	rs34361149	0.116
5	rs10623997	NA	ALT, AST	0.7305	rs288237	0.1265
1	1:113202203_TCTCTC_T	NA	BFP, SHBG, ALT, AST	0.7257	1:113181720	0.2319
2	rs143684747	NA	HDL, Triglycerides	0.7191	rs56321614	0.0603
18	rs771025058	[NPC1]	HDL, Triglycerides, ALT	0.7139	rs7239575	0.1674
16	rs8049669	CYB5B--[]--NFAT5	ALT, AST	0.7084	rs78432537	0.4964
12	rs7132908	[FAIM2]	HDL, SHBG	0.7056	rs9669354	0.4722

Table S4. Colocalisation analysis of six adiposity and metabolic biomarker traits for “favourable adiposity” loci, with posterior probability of colocalisation > 0.7. Index SNP: “Favourable adiposity” SNP; Traits: Traits showing colocalised association; Posterior probability: Posterior probability of colocalisation; Colocalised SNP: SNP identified with association across traits; Posterior explained by SNP: Proportion of posterior probability explained by colocalised SNP.

CHR	Index SNP	Gene	Traits	Posterior probability	Colocalised SNP	Posterior explained by SNP
1	rs12130231	NA	ALT, AST	1	rs188273166	1
17	rs12940684	[TNFSF12-TNFSF13]	ALT, AST	0.9994	rs117643180	1
5	rs4976033	PIK3R1---[]---SLC30A5	BFP, HDL, SHBG, Triglycerides, ALT, AST	0.999	rs4976033	1
3	rs62271373	PFN2---[]--TSC22D2	BFP, HDL, SHBG, Triglycerides, ALT	0.9947	rs62271373	1
19	rs555162510	NA	HDL, SHBG	0.9945	rs34255979	0.6435
8	rs2980888	TRIB1--[]	Triglycerides, ALT	0.9937	rs28601761	1
6	rs998584	VEGFA-[]---C6orf223	BFP, HDL, SHBG, Triglycerides, ALT, AST	0.9926	rs998584	1
12	rs7133378	[DNAH10]	BFP, HDL	0.991	rs7133378	1
12	rs7133378	[DNAH10]	SHBG, Triglycerides	0.9872	rs863750	0.3611
15	rs12441543	KLF13--[]--OTUD7A	HDL, SHBG, Triglycerides	0.9866	rs28624578	0.5104
2	rs13389219	GRB14--[]--COBLL1	BFP, HDL, SHBG, Triglycerides, ALT	0.9865	rs13389219	0.9219
12	rs11045172	AEBP2---[]--PDE3A	BFP, HDL, Triglycerides	0.9822	rs11045171	0.5493
7	rs6977416	TMEM176A--[]-ABP1	BFP, HDL	0.9795	rs6977416	0.391
5	rs30351	ANKRD55---[]---MAP3K1	Triglycerides, ALT, AST	0.9775	rs11429307	0.913
12	rs12369179	[ZCCHC8]	HDL, Triglycerides	0.9677	rs2454702	0.1176
17	rs142186653	TRIM47-[]-TRIM65	SHBG, ALT	0.9563	rs73352129	0.5269
20	rs6029180	[]---MAFB	BFP, Triglycerides, ALT, AST	0.9547	rs1883711	0.9995
12	rs10876529	HOXC8--[]HOXC6	BFP, Triglycerides	0.9511	rs10876529	0.105
5	rs9764678	[TNFAIP8]	BFP, HDL, Triglycerides	0.9406	rs5870855	0.3534

8	rs2980888	TRIB1--[]	BFP, HDL, AST	0.9181	rs2980888	0.7557
5	rs30351	ANKRD55---[]---MAP3K1	BFP, HDL, SHBG	0.9179	rs40270	1
4	rs4450871	MSX1---[]--CYTL1	BFP, HDL, SHBG, Triglycerides, ALT	0.9161	rs4450871	1
12	rs7133378	[DNAH10]	ALT, AST	0.9123	rs4930718	0.6021
22	rs4821764	[MAFF]	BFP, HDL, Triglycerides, ALT	0.9102	rs2267373	0.2298
12	rs10876529	HOXC8--[]HOXC6	SHBG, ALT	0.9099	rs143354653	0.6252
12	rs11045172	AEBP2---[]--PDE3A	SHBG, ALT, AST	0.891	rs10841520	0.4452
1	rs12130231	NA	HDL, Triglycerides	0.8839	rs1538742	0.4564
2	rs2943653	NYAP2---[]---IRS1	BFP, HDL, SHBG, Triglycerides, ALT, AST	0.8835	rs2943645	0.8191
11	rs113222038	[EML3]	HDL, Triglycerides	0.8785	rs71458418	0.0875
3	rs4684847	SYN2---[]-PPARG	BFP, SHBG, Triglycerides, ALT, AST	0.8538	rs1801282	0.4245
18	rs7233512	[SETBP1]	BFP, Triglycerides	0.8357	rs7230240	0.1824
4	rs13132853	[KLF3]	BFP, Triglycerides, ALT	0.7701	rs13132853	0.344
1	rs2802774	OPTC--[]--ATP2B4	HDL, SHBG, Triglycerides, ALT	0.7515	rs36043408	0.2103

Table S5. The sex-combined and sex-specific associations of “favourable adiposity” (FA) and “unfavourable adiposity” (UFA) genetic scores with measures of adiposity and biomarkers, C-reactive protein, MRI-derived measures of fat distribution, and cardiometabolic diseases in UK Biobank. LCI: lower 95% confidence interval; UCI: upper 95% confidence interval; P: p-value; P difference: p-value for test of sex difference in association.

Trait	Cluster	Combined				Male				Female				P difference
		Beta	LCI	UCI	P	Beta	LCI	UCI	P	Beta	LCI	UCI	P	
Body fat %	FA	0.014	0.012	0.016	2E-58	0.020	0.018	0.023	6E-53	0.018	0.015	0.020	9E-43	0.15
	UFA	0.020	0.018	0.022	5E-95	0.026	0.024	0.029	1E-78	0.027	0.024	0.030	3E-78	0.91
BMI	FA	0.009	0.007	0.012	3E-15	0.009	0.007	0.012	3E-11	0.010	0.007	0.012	1E-16	0.87
	UFA	0.026	0.020	0.031	4E-22	0.026	0.021	0.032	2E-19	0.026	0.021	0.031	8E-23	0.86
HDL-cholesterol	FA	0.018	0.014	0.022	3E-16	0.018	0.013	0.022	1E-13	0.021	0.016	0.027	9E-14	0.32
	UFA	-0.013	-0.018	-0.008	2E-7	-0.016	-0.022	-0.010	1E-7	-0.013	-0.018	-0.008	6E-7	0.52
Sex-hormone binding globulin	FA	0.016	0.006	0.025	0.001	0.015	0.002	0.028	0.02	0.019	0.010	0.028	3E-5	0.63
	UFA	-0.010	-0.013	-0.006	1E-9	-0.008	-0.012	-0.005	6E-6	-0.012	-0.015	-0.008	2E-11	0.16
Triglycerides	FA	-0.022	-0.027	-0.016	4E-15	-0.019	-0.025	-0.014	5E-11	-0.025	-0.031	-0.018	2E-14	0.23
	UFA	0.010	0.007	0.013	7E-11	0.010	0.007	0.014	4E-11	0.010	0.006	0.013	1E-8	0.76
Aspartate transaminase	FA	-0.008	-0.010	-0.005	2E-9	-0.010	-0.013	-0.007	5E-10	-0.006	-0.009	-0.004	2E-7	0.10
	UFA	0.007	0.004	0.010	1E-5	0.008	0.005	0.011	8E-7	0.006	0.003	0.009	2E-4	0.43
Alanine transaminase	FA	-0.013	-0.016	-0.010	6E-17	-0.013	-0.017	-0.009	5E-11	-0.014	-0.017	-0.011	1E-20	0.72
	UFA	0.009	0.007	0.011	4E-21	0.010	0.008	0.012	3E-17	0.009	0.007	0.012	6E-16	0.75
C-reactive protein	FA	0.004	0.001	0.007	0.005	0.005	0.002	0.007	3E-4	0.004	1E-4	0.007	0.04	0.65
	UFA	0.010	0.008	0.013	3E-14	0.010	0.007	0.013	1E-9	0.011	0.009	0.014	6E-17	0.40
Subcutaneous adipose tissue	FA	0.014	0.010	0.017	1E-17	0.021	0.016	0.026	6E-17	0.011	0.006	0.015	1E-6	0.002
	UFA	0.022	0.018	0.026	1E-22	0.023	0.017	0.030	4E-13	0.025	0.019	0.030	8E-21	0.79
Visceral adipose tissue	FA	-2E-4	-0.005	0.004	0.92	0.006	-5E-4	0.013	0.07	-0.009	-0.015	-0.004	0.001	6E-4
	UFA	0.011	0.008	0.015	2E-12	0.013	0.008	0.017	2E-8	0.016	0.011	0.020	2E-10	0.39
VATSAT ratio	FA	-0.012	-0.016	-0.008	1E-7	-0.018	-0.026	-0.010	6E-6	-0.021	-0.028	-0.013	2E-7	0.69

	UFA	-0.007	-0.010	-0.004	3E-5	-0.014	-0.020	-0.008	9E-6	-0.004	-0.009	8E-4	0.10	0.01
Liver fat	FA	-0.010	-0.014	-0.006	9E-7	-0.008	-0.014	-0.002	0.008	-0.013	-0.017	-0.008	3E-8	0.19
	UFA	0.009	0.006	0.013	2E-8	0.007	0.003	0.011	0.001	0.013	0.008	0.018	7E-8	0.07
Liver volume	FA	-0.006	-0.010	-0.002	0.006	-0.006	-0.011	-4E-4	0.03	-0.006	-0.011	-0.001	0.01	0.90
	UFA	0.013	0.009	0.017	3E-10	0.013	0.008	0.018	3E-7	0.016	0.010	0.021	4E-8	0.49
Pancreas fat	FA	0.002	-0.003	0.007	0.38	0.005	-0.001	0.012	0.10	-0.002	-0.008	0.004	0.54	0.11
	UFA	0.011	0.007	0.014	7E-10	0.010	0.005	0.015	2E-5	0.015	0.009	0.020	8E-8	0.20
Pancreas volume	FA	-0.006	-0.011	-0.002	0.003	-0.007	-0.011	-0.002	0.003	-0.007	-0.012	-0.001	0.02	0.97
	UFA	0.001	-0.003	0.006	0.57	9E-4	-0.005	0.006	0.76	0.002	-0.004	0.008	0.45	0.74
Type 2 diabetes	FA	-1E-3	-0.001	-6E-4	2E-9	-0.001	-0.002	-6E-4	7E-6	-9E-4	-0.001	-6E-4	4E-11	0.45
	UFA	0.001	9E-4	0.001	6E-16	0.001	0.001	0.002	6E-12	9E-4	7E-4	0.001	1E-14	0.03
Heart disease	FA	-8E-4	-0.001	-4E-4	3E-5	-0.001	-0.002	-6E-4	1E-4	-4E-4	-7E-4	-2E-4	0.003	0.02
	UFA	9E-4	6E-4	0.001	2E-7	0.001	9E-4	0.002	6E-7	5E-4	2E-4	9E-4	0.001	0.007
Hypertension	FA	-0.002	-0.002	-7E-4	1E-4	-0.002	-0.003	-9E-4	7E-5	-0.001	-0.002	-5E-4	0.002	0.49
	UFA	0.002	0.002	0.003	4E-8	0.003	0.002	0.004	4E-7	0.002	0.001	0.003	6E-8	0.74
Stroke	FA	-1E-4	-2E-4	4E-5	0.17	1E-5	-2E-4	2E-4	0.92	-2E-4	-3E-4	-2E-5	0.03	0.16
	UFA	3E-4	1E-4	4E-4	5E-4	4E-4	2E-4	6E-4	2E-4	2E-4	2E-5	3E-4	0.03	0.12
Fatty liver disease	FA	-1E-4	-2E-4	-1E-5	0.03	-2E-4	-4E-4	3E-5	0.09	-7E-5	-2E-4	6E-5	0.31	0.32
	UFA	1E-4	4E-5	2E-4	0.004	5E-5	-1E-4	2E-4	0.62	2E-4	7E-5	3E-4	0.002	0.23
Polycystic ovary syndrome	FA	-7E-5	-1E-4	-1E-5	0.02	NA	NA	NA	NA	-7E-5	-1E-4	-1E-5	0.02	NA
	UFA	1E-4	6E-5	2E-4	7E-5	NA	NA	NA	NA	1E-4	6E-5	2E-4	7E-5	NA

Table S6. The association of “favourable adiposity” (FA) and “unfavourable adiposity” (UFA) genetic score with measures of adiposity and biomarkers, C-reactive protein, MRI-derived measures of fat distribution, and cardiometabolic diseases in UK Biobank, FinnGen and published GWAS. LCI: lower 95% confidence interval; UCI: upper 95% confidence interval; P: p-value.

Outcome	Cluster	UK Biobank				FinnGen				Published GWAS			
		Beta	LCI	UCI	P	Beta	LCI	UCI	P	Beta	LCI	UCI	P
Body fat %	FA	0.014	0.012	0.016	2E-58	NA	NA	NA	NA	0.015	0.013	0.018	1E-29
	UFA	0.020	0.018	0.022	5E-95	NA	NA	NA	NA	0.018	0.014	0.021	2E-20
BMI	FA	0.009	0.007	0.012	3E-15	NA	NA	NA	NA	0.009	0.007	0.012	3E-12
	UFA	0.026	0.020	0.031	4E-22	NA	NA	NA	NA	0.025	0.019	0.031	7E-17
HDL-cholesterol	FA	0.018	0.014	0.022	3E-16	NA	NA	NA	NA	0.017	0.014	0.021	9E-21
	UFA	-0.013	-0.018	-0.008	2E-7	NA	NA	NA	NA	-0.013	-0.018	-0.008	4E-8
Sex-hormone binding globulin	FA	0.016	0.006	0.025	0.001	NA	NA	NA	NA	0.008	0.003	0.013	0.001
	UFA	-0.010	-0.013	-0.006	1E-9	NA	NA	NA	NA	-6E-4	-0.003	0.002	0.60
Triglycerides	FA	-0.022	-0.027	-0.016	4E-15	NA	NA	NA	NA	-0.016	-0.022	-0.011	3E-10
	UFA	0.010	0.007	0.013	7E-11	NA	NA	NA	NA	0.010	0.007	0.013	8E-11
Aspartate transaminase	FA	-0.008	-0.010	-0.005	2E-9	NA	NA	NA	NA	-0.002	-0.003	-7E-4	7E-4
	UFA	0.007	0.004	0.010	1E-5	NA	NA	NA	NA	-6E-5	-1E-3	9E-4	0.90
Alanine transaminase	FA	-0.013	-0.016	-0.010	6E-17	NA	NA	NA	NA	-0.002	-0.003	-9E-4	1E-4
	UFA	0.009	0.007	0.011	4E-21	NA	NA	NA	NA	0.001	7E-4	0.002	9E-5
C-reactive protein	FA	0.004	0.001	0.007	0.005	NA	NA	NA	NA	0.003	4E-4	0.005	0.02
	UFA	0.010	0.008	0.013	3E-14	NA	NA	NA	NA	0.009	0.006	0.013	4E-8
Subcutaneous adipose tissue	FA	0.014	0.010	0.017	1E-17	NA	NA	NA	NA	0.008	0.005	0.012	6E-6
	UFA	0.022	0.018	0.026	1E-22	NA	NA	NA	NA	0.012	0.008	0.016	3E-8
Visceral adipose tissue	FA	-2E-4	-0.005	0.004	0.92	NA	NA	NA	NA	-2E-4	-0.003	0.003	0.92
	UFA	0.011	0.008	0.015	2E-12	NA	NA	NA	NA	0.009	0.006	0.013	6E-7
VATSAT ratio	FA	-0.012	-0.016	-0.008	1E-7	NA	NA	NA	NA	-0.010	-0.014	-0.006	2E-6

	UFA	-0.007	-0.010	-0.004	3E-5	NA	NA	NA	NA	-6E-4	-0.004	0.003	0.70
Pericardial adipose tissue	FA	NA	NA	NA	NA	NA	NA	NA	NA	0.002	-0.003	0.006	0.50
	UFA	NA	NA	NA	NA	NA	NA	NA	NA	0.005	0.002	0.009	0.003
Liver fat	FA	-0.010	-0.014	-0.006	9E-7	NA	NA	NA	NA	NA	NA	NA	NA
	UFA	0.009	0.006	0.013	2E-8	NA	NA	NA	NA	NA	NA	NA	NA
Liver volume	FA	-0.006	-0.010	-0.002	0.006	NA	NA	NA	NA	NA	NA	NA	NA
	UFA	0.013	0.009	0.017	3E-10	NA	NA	NA	NA	NA	NA	NA	NA
Pancreas fat	FA	0.002	-0.003	0.007	0.38	NA	NA	NA	NA	NA	NA	NA	NA
	UFA	0.011	0.007	0.014	7E-10	NA	NA	NA	NA	NA	NA	NA	NA
Pancreas volume	FA	-0.006	-0.011	-0.002	0.003	NA	NA	NA	NA	NA	NA	NA	NA
	UFA	0.001	-0.003	0.006	0.57	NA	NA	NA	NA	NA	NA	NA	NA
Type 2 diabetes	FA	-1E-3	-0.001	-6E-4	2E-9	-0.030	-0.039	-0.021	6E-11	-0.031	-0.038	-0.023	8E-15
	UFA	0.001	9E-4	0.001	6E-16	0.032	0.023	0.041	2E-11	0.030	0.022	0.038	3E-13
Heart disease	FA	-8E-4	-0.001	-4E-4	3E-5	-0.016	-0.022	-0.010	9E-8	-0.016	-0.022	-0.010	1E-7
	UFA	9E-4	6E-4	0.001	2E-7	0.006	7E-4	0.012	0.03	0.015	0.010	0.021	1E-7
Hypertension	FA	-0.002	-0.002	-7E-4	1E-4	-0.015	-0.021	-0.008	2E-5	NA	NA	NA	NA
	UFA	0.002	0.002	0.003	4E-8	0.021	0.012	0.029	1E-6	NA	NA	NA	NA
Stroke	FA	-1E-4	-2E-4	4E-5	0.17	-0.009	-0.015	-0.003	0.002	-0.004	-0.008	3E-6	0.05
	UFA	3E-4	1E-4	4E-4	5E-4	0.008	0.002	0.014	0.007	0.008	0.005	0.012	1E-5
Non-alcoholic fatty liver disease	FA	NA	NA	NA	NA	-0.027	-0.051	-0.003	0.03	NA	NA	NA	NA
	UFA	NA	NA	NA	NA	0.016	-0.008	0.040	0.18	NA	NA	NA	NA
Polycystic ovary syndrome	FA	-7E-5	-1E-4	-1E-5	0.02	-0.017	-0.041	0.008	0.19	-0.009	-0.021	0.003	0.13
	UFA	1E-4	6E-5	2E-4	7E-5	0.042	0.017	0.067	1E-3	0.033	0.021	0.045	6E-8

Table S7. DEPICT tissue enrichment results for “unfavourable adiposity” cluster. MeSH: medical subject headings; false discovery rate.

MeSH.term	Name	MeSH.first.level.term	MeSH.second.level.term	Nominal.P.value	False.discovery.rate
A11.872.580	Mesenchymal Stem Cells	Cells	Stem Cells	0.000739	<0.05
A07.541.510.110	Aortic Valve	Cardiovascular System	Heart	0.00157	<0.05
A07.541.510	Heart Valves	Cardiovascular System	Heart	0.00157	<0.05
A11.329.114	Adipocytes	Cells	Connective Tissue Cells	0.00376	<0.20
A02.835.583	Joints	Musculoskeletal System	Skeleton	0.00433	<0.20
A02.835.583.443	Joint Capsule	Musculoskeletal System	Skeleton	0.00433	<0.20
A02.835.583.443.800	Synovial Membrane	Musculoskeletal System	Skeleton	0.00433	<0.20
A10.336.707	Prostate	Tissues	Exocrine Glands	0.01	<0.20
A11.329.171	Chondrocytes	Cells	Connective Tissue Cells	0.01	<0.20
A02.835.232.834.151	Cervical Vertebrae	Musculoskeletal System	Skeleton	0.01	<0.20
A05.360.319.679.690	Myometrium	Urogenital System	Genitalia	0.01	<0.20
A02.835.232.834	Spine	Musculoskeletal System	Skeleton	0.01	<0.20
A11.329.629	Osteoblasts	Cells	Connective Tissue Cells	0.01	<0.20
A10.336	Exocrine Glands	Tissues	Exocrine Glands	0.02	<0.20
A05.360.444	Genitalia Male	Urogenital System	Genitalia	0.02	<0.20

Table S8. DEPICT tissue enrichment results for “favourable adiposity” cluster. MeSH: medical subject headings; false discovery rate.

MeSH.term	Name	MeSH.first.level.term	MeSH.second.level.term	Nominal.P.value	False.discovery.rate
A10.165.114	Adipose Tissue	Tissues	Connective Tissue	0.000213	<0.01
A10.165.114.830.500.750	Subcutaneous Fat Abdominal	Tissues	Connective Tissue	0.000237	<0.01
A10.165.114.830.500	Abdominal Fat	Tissues	Connective Tissue	0.000237	<0.01
A10.165.114.830.750	Subcutaneous Fat	Tissues	Connective Tissue	0.000284	<0.01
A10.165.114.830	Adipose Tissue White	Tissues	Connective Tissue	0.000284	<0.01
A11.329.114	Adipocytes	Cells	Connective Tissue Cells	0.000562	<0.01
A03.556.124.684	Intestine Small	Digestive System	Gastrointestinal Tract	0.00178	<0.05
A03.556.875.500	Esophagus	Digestive System	Gastrointestinal Tract	0.00212	<0.05
A03.734	Pancreas	Digestive System	Pancreas	0.00272	<0.05
A11.329.171	Chondrocytes	Cells	Connective Tissue Cells	0.00294	<0.05
A07.231.114	Arteries	Cardiovascular System	Blood Vessels	0.00322	<0.05
A03.556.875	Upper Gastrointestinal Tract	Digestive System	Gastrointestinal Tract	0.00399	<0.05
A03.556.249.124	Ileum	Digestive System	Gastrointestinal Tract	0.00472	<0.05
A02.835.583.443.800	Synovial Membrane	Musculoskeletal System	Skeleton	0.00709	<0.20
A02.835.583.443	Joint Capsule	Musculoskeletal System	Skeleton	0.00709	<0.20
A02.835.583	Joints	Musculoskeletal System	Skeleton	0.00709	<0.20
A15.378.316.580	Monocytes	Hemic and Immune Systems	Hematopoietic System	0.01	<0.20
A05.810.890	Urinary Bladder	Urogenital System	Urinary Tract	0.01	<0.20
A15.382.812.260	Dendritic Cells	Hemic and Immune Systems	Immune System	0.01	<0.20
A11.066	Antigen Presenting Cells	Cells	Antigen-Presenting Cells	0.01	<0.20
A10.615.789	Serous Membrane	Tissues	Membranes	0.01	<0.20
A02.165	Cartilage	Musculoskeletal System	Cartilage	0.02	<0.20

A03.556.875.875	Stomach	Digestive System	Gastrointestinal Tract	0.02	<0.20
A15.382.812	Mononuclear Phagocyte System	Hemic and Immune Systems	Immune System	0.02	<0.20
A03.556.124.526.767	Rectum	Digestive System	Gastrointestinal Tract	0.02	<0.20
A15.382.680	Phagocytes	Hemic and Immune Systems	Immune System	0.03	<0.20
A15.378	Hematopoietic System	Hemic and Immune Systems	Hematopoietic System	0.03	<0.20
A15.378.316	Bone Marrow Cells	Hemic and Immune Systems	Hematopoietic System	0.03	<0.20
A02.835.583.443.800.800	Synovial Fluid	Musculoskeletal System	Skeleton	0.03	<0.20
A03.556.249.249.209	Cecum	Digestive System	Gastrointestinal Tract	0.03	<0.20
A11.627	Myeloid Cells	Cells	Myeloid Cells	0.03	<0.20
A05.360.319.679.690	Myometrium	Urogenital System	Genitalia	0.03	<0.20
A11.329	Connective Tissue Cells	Cells	Connective Tissue Cells	0.04	<0.20

Table S9. The inverse-variance weighted (IVW), Egger and weighted median (WM) MR analyses for “favourable adiposity” (FA) and “unfavourable adiposity” (UFA) clusters using UK Biobank, FinnGen and published GWAS. SE: standard error; P: p-value; T2D: type 2 diabetes; CAD: coronary artery disease; FLD: fatty liver disease; NAFLD: non-alcoholic fatty liver disease; PCOS: polycystic ovary syndrome.

Trait	Study	Cluster	betaIVW2	sebetaIVW2	tIVW	pIVW	p.hetero	betaEgger	sebetaEgger	tegger	pEgger	egger_int	int_p	betaWM	sebetaWM	tWM	pWM
T2D	UK Biobank	FA	-2.257	0.320	7.055	3E-8	9E-15	-2.653	1.014	2.617	0.01	0.006	0.68	-1.789	0.286	6.263	4E-10
		UFA	1.943	0.174	11.143	2E-13	1E-7	3.137	0.573	5.476	3E-6	-0.026	0.04	1.904	0.190	10.042	1E-23
	FinnGen	FA	-2.159	0.290	7.433	1E-8	3E-11	-1.956	0.899	2.176	0.04	-0.003	0.81	-1.909	0.290	6.581	5E-11
		UFA	1.731	0.201	8.606	6E-10	7E-10	2.585	0.689	3.753	7E-4	-0.018	0.20	1.594	0.200	7.953	2E-15
	Published GWAS	FA	-2.202	0.234	9.402	4E-11	3E-16	-2.186	0.754	2.897	0.007	-2E-4	0.98	-2.120	0.233	9.119	8E-20
		UFA	1.686	0.163	10.324	7E-12	2E-15	2.459	0.528	4.655	5E-5	-0.017	0.13	1.647	0.145	11.371	6E-30
CAD	UK Biobank	FA	-0.635	0.160	3.973	3E-4	1E-8	-0.095	0.498	0.191	0.85	-0.008	0.26	-0.673	0.162	4.156	3E-5
		UFA	0.476	0.105	4.532	6E-5	2E-8	-0.172	0.349	0.491	0.63	0.014	0.06	0.363	0.097	3.735	2E-4
	FinnGen	FA	-1.066	0.219	4.860	2E-5	0.001	-0.131	0.658	0.199	0.84	-0.014	0.14	-1.287	0.257	4.997	6E-7
		UFA	0.286	0.135	2.121	0.04	0.06	0.338	0.474	0.713	0.48	-0.001	0.91	0.447	0.177	2.526	0.01
	Published GWAS	FA	-1.073	0.229	4.677	4E-5	3E-8	0.667	0.690	0.966	0.34	-0.025	0.01	-1.292	0.220	5.875	4E-9
		UFA	0.722	0.134	5.397	6E-6	5E-5	0.693	0.462	1.501	0.14	6E-4	0.95	0.715	0.142	5.025	5E-7
Stroke	UK Biobank	FA	-0.282	0.198	1.427	0.16	0.13	-0.361	0.627	0.575	0.57	0.001	0.90	-0.213	0.254	0.838	0.40
		UFA	0.467	0.154	3.038	0.004	0.004	-0.348	0.518	0.672	0.51	0.018	0.11	0.264	0.191	1.383	0.17
	FinnGen	FA	-0.582	0.213	2.740	0.010	0.14	0.305	0.638	0.478	0.64	-0.013	0.15	-0.475	0.289	1.645	0.10
		UFA	0.350	0.135	2.601	0.01	0.59	-0.230	0.466	0.494	0.62	0.013	0.18	0.209	0.207	1.007	0.31
	Published GWAS	FA	-0.354	0.144	2.461	0.02	0.16	-0.783	0.458	1.707	0.10	0.006	0.33	-0.402	0.183	2.199	0.03
		UFA	0.365	0.094	3.872	5E-4	0.25	-0.357	0.296	1.206	0.24	0.016	0.01	0.195	0.133	1.469	0.14

Hyper tension	UK Bioba nk	FA	-0.569	0.155	3.666	8E-4	0E+0	-0.098	0.486	0.201	0.84	-0.007	0.31	-0.507	0.115	4.394	1E-5
		UFA	0.690	0.113	6.102	5E-7	0E+0	0.408	0.392	1.041	0.30	0.006	0.46	0.740	0.076	9.676	4E-22
	FinnG en	FA	-1.074	0.245	4.381	1E-4	5E-7	-0.283	0.745	0.380	0.71	-0.012	0.27	-1.109	0.231	4.794	2E-6
		UFA	1.109	0.169	6.558	2E-7	4E-6	1.159	0.593	1.956	0.06	-0.001	0.93	1.138	0.170	6.678	2E-11
FLD	UK Bioba nk	FA	-0.863	0.346	2.494	0.02	0.005	-1.384	1.095	1.263	0.22	0.008	0.62	-0.818	0.398	2.056	0.04
		UFA	0.534	0.193	2.758	0.009	0.18	0.075	0.671	0.111	0.91	0.010	0.48	0.476	0.260	1.829	0.07
NAFL D	FinnG en	FA	-1.941	0.871	2.227	0.03	0.07	-1.568	2.700	0.581	0.57	-0.006	0.88	-2.729	1.138	2.398	0.02
		UFA	1.307	0.564	2.317	0.03	0.27	2.568	1.967	1.305	0.20	-0.027	0.51	1.059	0.788	1.344	0.18
PCOS	UK Bioba nk	FA	-1.693	0.698	2.424	0.02	0.67	-1.514	2.186	0.692	0.49	-0.003	0.93	-1.764	1.031	1.711	0.09
		UFA	1.957	0.488	4.014	3E-4	0.32	1.004	1.697	0.592	0.56	0.021	0.56	1.909	0.720	2.650	0.008
	FinnG en	FA	-1.042	0.889	1.171	0.25	0.92	-0.428	2.719	0.157	0.88	-0.009	0.78	-0.997	1.249	0.798	0.42
		UFA	2.317	0.631	3.674	8E-4	0.86	2.643	2.179	1.213	0.23	-0.007	0.86	1.652	0.932	1.772	0.08
	Publis hed GWAS	FA	-0.547	0.516	1.060	0.30	0.07	0.943	1.678	0.562	0.58	-0.022	0.36	-0.334	0.671	0.497	0.62
		UFA	1.820	0.404	4.505	8E-5	0.002	2.878	1.385	2.078	0.05	-0.023	0.43	1.739	0.461	3.770	2E-4

Table S10. The overlap between our UFA and FA variants and previous reported variants with similar pattern. Variants overlapping with Winkler et al. 2018 are RSID matches, whereas those from Pigeyre et al. 2019 are matched by gene and based on the subset of regions they present, which contain only genes previously shown to be associated with both type 2 diabetes and BMI, or type 2 diabetes candidate genes.

SNP	CHR	POS	Cluster	Winkler et al. SNP	Winkler et al. r2	Winkler et al. screen	Winkler et al. classification	Pigeyre et al. region	Pigeyre et al. classification
rs13389219	2	165528876	FA	rs1128249	0.995963	BMI+WHR-	Metabolically rather favourable	118,513-119,273	Metabolically favourable adiposity
rs4684847	3	12386337	FA					11,469-12,231	Metabolically favourable adiposity
rs987469	4	89706643	FA	rs9991328	0.998902301	BMI+WHR-	Metabolically rather favourable		
rs30351	5	55794632	FA	rs459193	0.966821	BMI+WHR+	Metabolically unfavourable		
rs998584	6	43757896	FA	NA	NA	BMI+WHR-	Metabolically rather favourable		
rs10876529	12	54421810	FA	rs2071449	0.949506029	WHRonly-	Metabolically neutral or inconclusive		
rs7133378	12	124409502	FA	rs4765219	0.88702	BMI+WHR-	Metabolically rather favourable		
rs555162510	19	46183031	FA	rs2287019	0.851203676	BMI+WHR+	Metabolically unfavourable		
rs539515	1	177889025	UFA	rs543874	1	BMI+WHR+	Metabolically unfavourable		
rs143684747	2	633053	UFA	rs13021737	0.993122	BMI+WHR+	Metabolically unfavourable		
rs6752378	2	25150116	UFA	rs10182181	1	BMIonly+	Metabolically neutral or inconclusive		
rs10938397	4	45182527	UFA	NA	NA	BMI+WHR+	Metabolically unfavourable		
rs13107325	4	103188709	UFA	NA	NA	BMIonly+	Metabolically neutral or inconclusive		

rs2112347	5	75015242	UFA	NA	NA	BMI+WHR+	Metabolically unfavourable		
rs72892910	6	50816887	UFA	rs2207139	0.868295967	BMI+WHR+	Metabolically unfavourable		
rs236660	7	75050086	UFA	rs1167827	0.881831	BMIonly+	Metabolically neutral or inconclusive		
rs10756713	9	15880555	UFA	rs4740619	0.882797	BMI+WHR+	Metabolically unfavourable		
rs7124681	11	47529947	UFA	rs3817334	0.991856	BMI+WHR+	Metabolically unfavourable		
rs7132908	12	50263148	UFA	rs7138803	0.868750757	BMI+WHR+	Metabolically unfavourable		
rs4776985	15	68123021	UFA	rs16951275	0.961668	BMI+WHR+	Metabolically unfavourable		
rs56186137	16	28825953	UFA	rs3888190	0.986555	BMI+WHR+	Metabolically unfavourable		
rs11642015	16	53802494	UFA	rs1558902	1	BMI+WHR+	Metabolically unfavourable	22,949-23,713	Metabolically deleterious adiposity
rs771025058	18	21122207	UFA	rs1808579	0.836409	BMIonly+	Metabolically neutral or inconclusive		
rs6567160	18	57829135	UFA	NA	NA	BMI+WHR+	Metabolically unfavourable	41,29-42,057	Metabolically deleterious adiposity
rs11666808	19	18383506	UFA	rs12608504	0.962062	WHRonly-	Metabolically neutral or inconclusive		

Fig. S1. Study design.

Fig. S2. Adiposity variants were clustered into 3 groups: (a) 36 “favourable adiposity” variants (FA) where adiposity-increasing alleles were associated with a better metabolic profile (examples include the variant near *PPARG*), and 38 “unfavourable adiposity” variants (UFA) where adiposity-increasing alleles were associated with an adverse metabolic profile (examples include the variant near *FTO*), (b) 180 “conflicting” variants with mixed pattern of association with adiposity and metabolic biomarkers. We considered this cluster of ‘conflicting’ to group any variants that did not belong to the FA or UFA clusters and did not pursue these variants in the rest of the analyses to minimize false discovery. The “conflicting” variants had heterogeneous effects on other metabolic biomarkers compared to FA and UFA clusters.

Fig. S3. The sex-specific effects of 36 “favourable adiposity” and 38 “unfavourable adiposity” variants for (a) body fat %, (b) BMI, (c) HDL-cholesterol (HDL), (d) sex-hormone binding globulin (SHBG), (e) triglycerides, (f) alanine transaminase (ALT), (g) aspartate transaminase (AST), (h) C-reactive protein (CRP), (i) abdominal subcutaneous adipose tissue (ASAT), (j) visceral adipose tissue (VAT), (k) VATSAT ratio, (l) liver volume, (m) liver fat, (n) pancreas volume, (o) pancreatic fat, (p) type 2 diabetes, (q) heart disease, (r) hypertension, (s) stroke, (t) non-alcoholic fatty liver disease.

Fig. S4. The distributions of UFA and FA genetic scores among the UK Biobank participants with and without type 2 diabetes.

Fig. S5. Adiposity-increasing alleles were correlated with lower risk of type 2 diabetes for 33 of the 36 “favourable adiposity” variants, and adiposity-increasing alleles were correlated with higher risk of type 2 diabetes for all 38 “unfavourable adiposity” variants using UK Biobank.

Fig. S6. Adiposity-increasing alleles were correlated with less liver fat for 29 of the 36 “favourable adiposity” variants, and adiposity-increasing alleles were correlated with more liver fat for 31 of the 38 “unfavourable adiposity” variants using UK Biobank.

Fig. S7. “Favourable adiposity” variants had a mixed effect on pancreatic fat, while adiposity-increasing alleles were correlated with higher pancreatic fat for 32 out of the 38 “unfavourable adiposity” variants using UK Biobank.

Fig. S8. The association with measures of adiposity and biomarkers, C-reactive protein (CRP), MRI-derived measures of fat distribution, and cardiometabolic diseases in UK Biobank for “favourable adiposity” variants (a) rs4684847 (*PPARG*), (b) rs12130231 (*LYPLAL1/SLC30A10*), (c) rs11664106 (*EMILIN2*), (d) rs13389219 (*GRB14/COBLL1*), (e) rs2943653 (*NYAP2/IRS1*), (f) rs30351 (*ANKRD55*), (g) rs4450871 (*CYTL1*), and (h) rs7133378 (*DNAH10*). HDL: HDL-cholesterol; SHBG: sex-hormone binding globulin; ALT: alanine transaminase; AST: aspartate transaminase; ASAT: abdominal subcutaneous adipose tissue; VAT: visceral adipose tissue; VATSAT: VATSAT ratio; T2D: type 2 diabetes.

Fig. S9. Adiposity-increasing alleles were correlated with higher C-reactive protein for 27 of the 36 “favourable adiposity” variants and 35 of the 38 “unfavourable adiposity” variants using UK Biobank.

Fig. S10. The association between UFA and FA variants and BMI and WHR. Only 7/36 and 12/36 FA variants are associated with BMI and WHR, respectively. Similarly, while UFA variants are enriched for BMI variants, 7 variants are not associated with BMI and only 14/38 UFA variants are associated with WHR

Fig. S11. The comparison of the multivariate GWAS p-values for 14 variants previously identified as ‘favourable adiposity’ from Ji *et al.* Diabetes, 2019 indicates additional power gained in the current study largely attributable to the availability of other metabolic biomarkers in 451,099 individuals in a single cohort, the UK Biobank.

Supplementary Material

Definition of diseases in UK Biobank

We defined type 2 diabetes cases as individuals who self-reported diabetes on the UK Biobank baseline questionnaire. We included those who were diagnosed at >35 years of age without reporting of insulin use within the first year of diagnosis to exclude other types of diabetes. We defined subjects as hypertensive if systolic blood pressure was >140 mmHg, diastolic blood pressure was >90 mmHg, or blood pressure medication was reported. Control subjects were individuals who did not fulfil these criteria. We defined subjects as having heart disease if they reported angina and/or a heart attack at the interview stage.

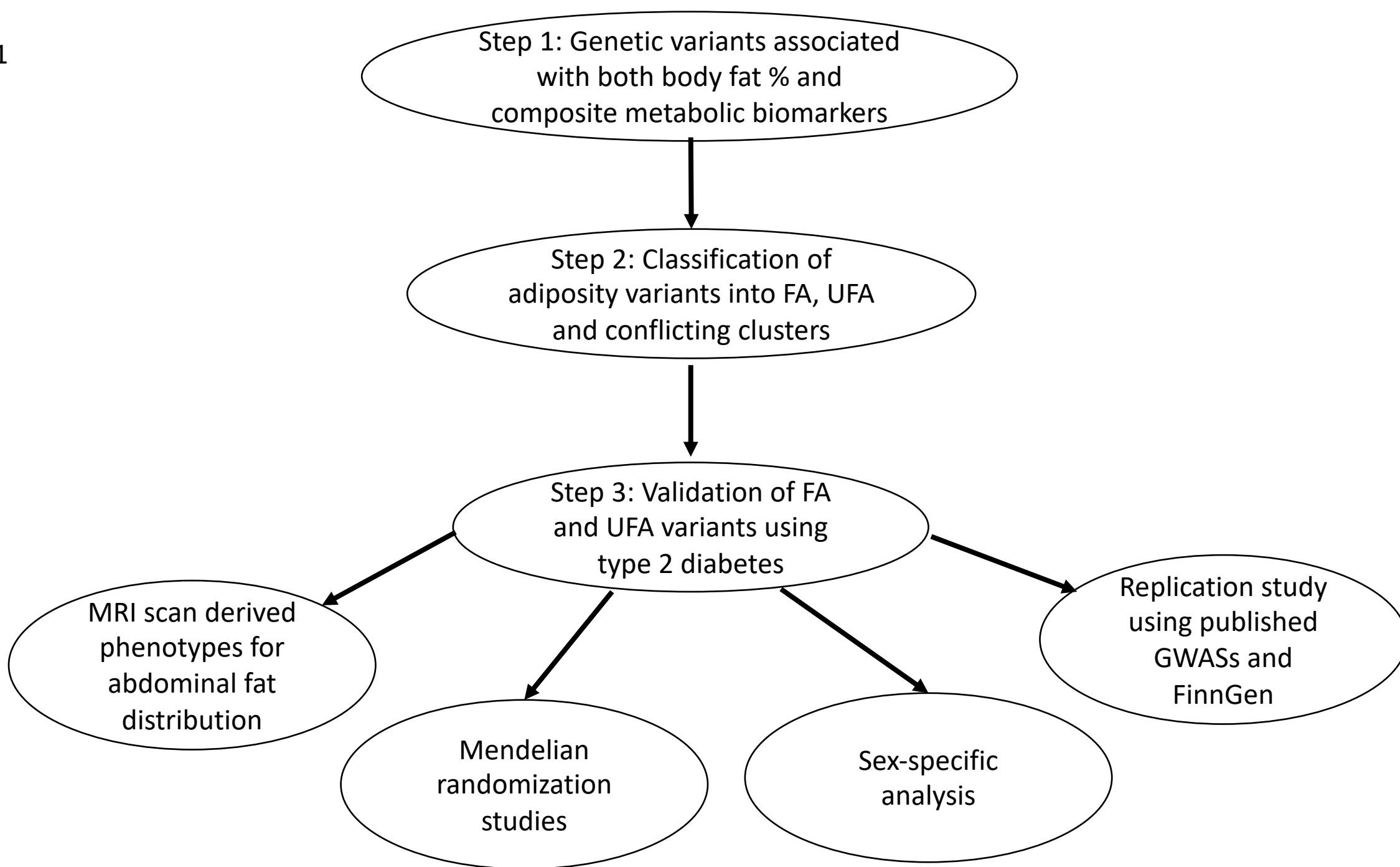
For NAFLD, stroke and PCOS, we defined cases based on ICD10 codes (field number: K76 for NAFLD; E282 for PCOS; I60, I61, I63, and I64 for stroke), ICD9 codes (5715, 5716, 5718, and 5719 for NAFLD; 2564 for PCOS; 430, 431, 434, and 436 for stroke) and if self-reported (1350 for PCOS; 1583, 1081, 1086, and 1491 for stroke). We defined control subjects as individuals without these conditions.

Disease outcomes from FinnGen

Trait	Code	Name	Traits included
Type 2 diabetes	E4_DM2_STRICT	Type 2 diabetes, strict (exclude DM1)	E4_DM2COMA E4_DM2KETO E4_DM2REN E4_DM2OPHTH E4_DM2NEU E4_DM2PERIPH E4_DM2NASCOMP E4_DM2NOCOMP
Heart disease	I9_IHD	Ischaemic heart disease, wide definition	I2[0-5]
Hypertension	FG_HYPERTENSION	Hypertensive diseases (excluding secondary)	I9_HYPTENSESS I9_HYPTENSPUL I9_HYPTENSHR I9_HYPTENS

		ndary)	
Stroke	C_STROKE	STROKE	I9_SAH I9_ICH I9_OTHINTRACRA I9_STR_EXH I9_STR_SAH I9_TIA
Non-alcoholic fatty liver disease	NAFLD	Nonalcoholic fatty liver disease	
Polycystic ovary syndrome	E4_POC S	Polycystic ovarian syndrome	

SF 1



SF 2a

**“Favourable”
adiposity**

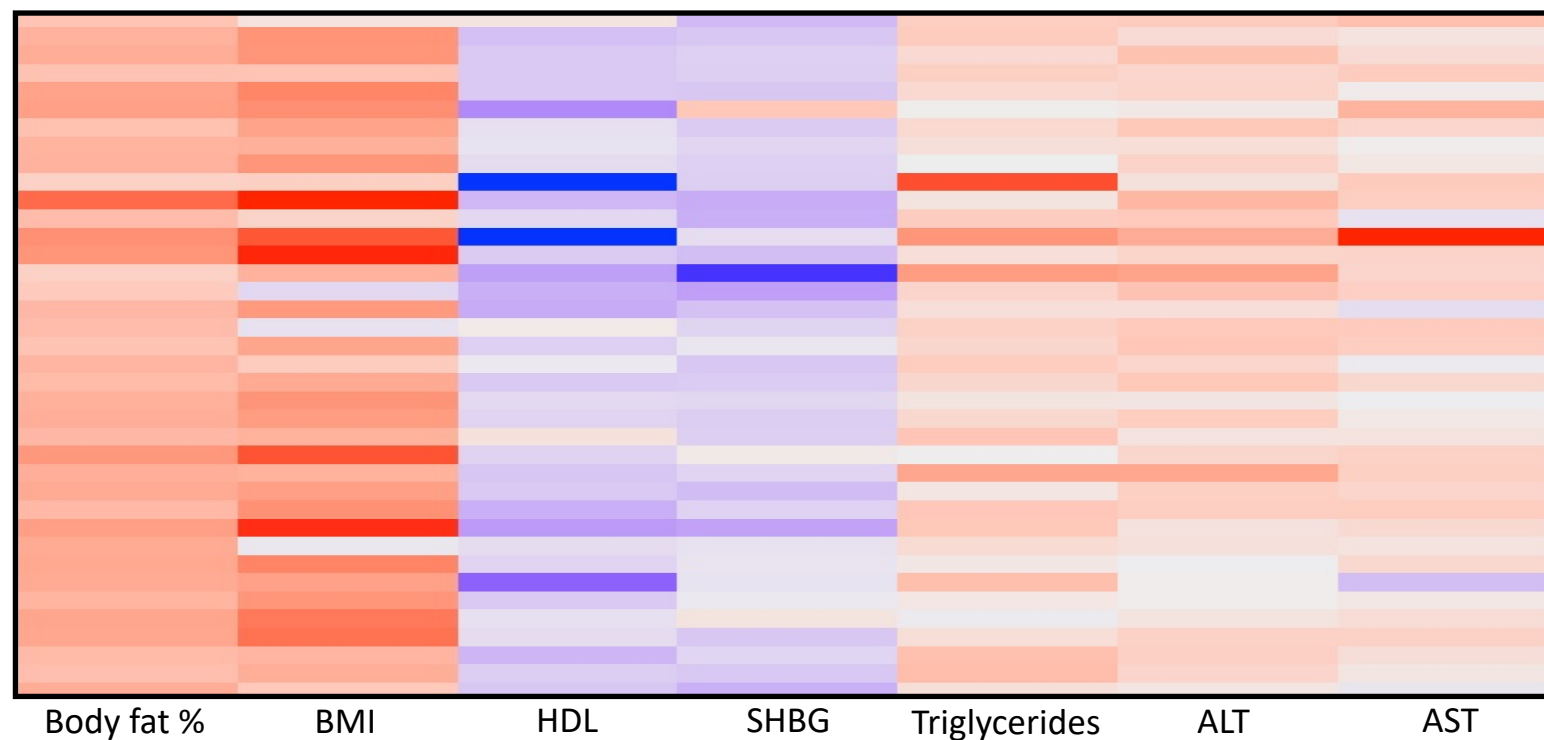
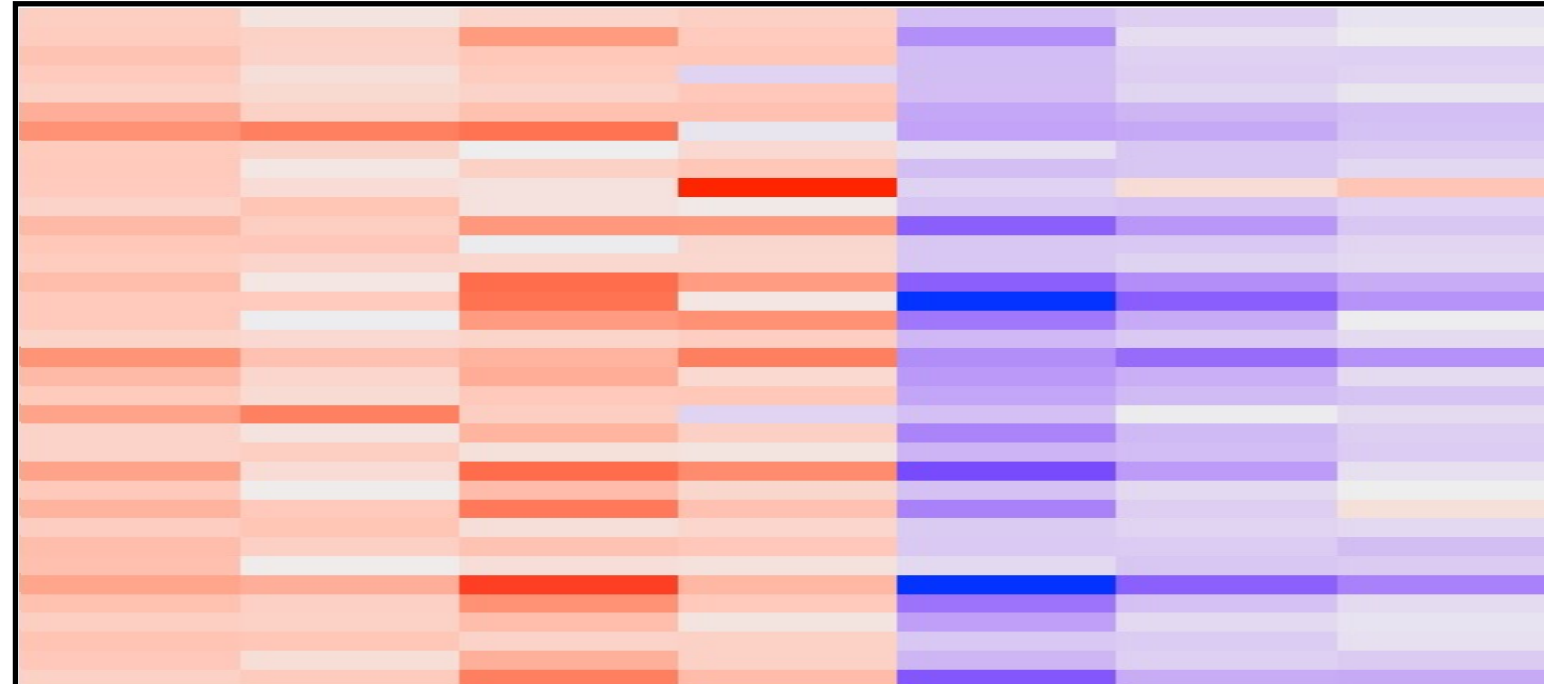
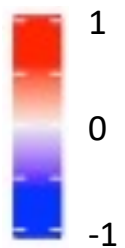
36
variants

→ *PPARG*

**“Unfavourable”
adiposity**

38
variants

→ *FTO*



Body fat %

BMI

HDL

SHBG

Triglycerides

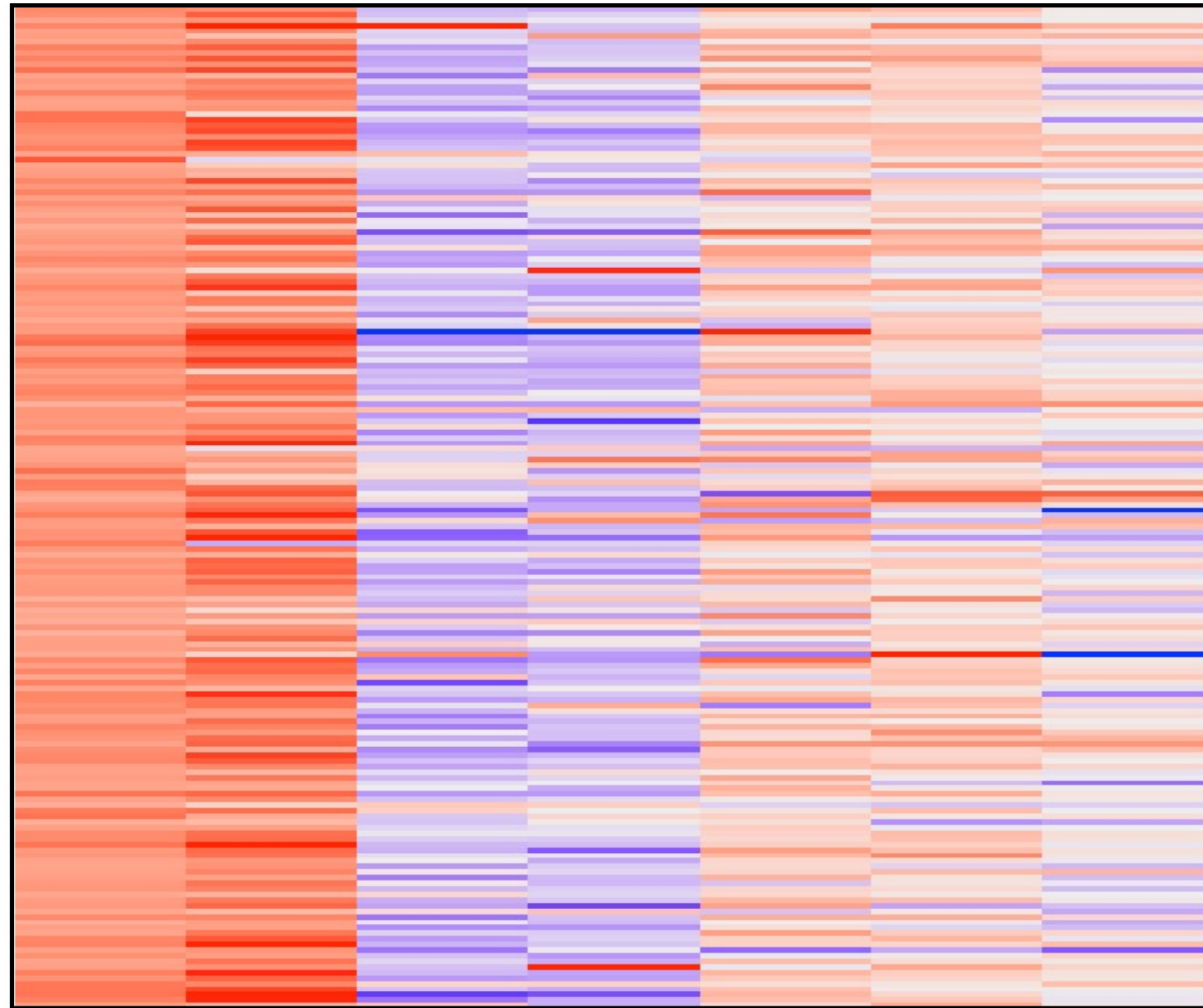
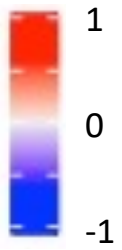
ALT

AST

SF 2b

**Conflicting
cluster**

180
variants



Body fat %

BMI

HDL

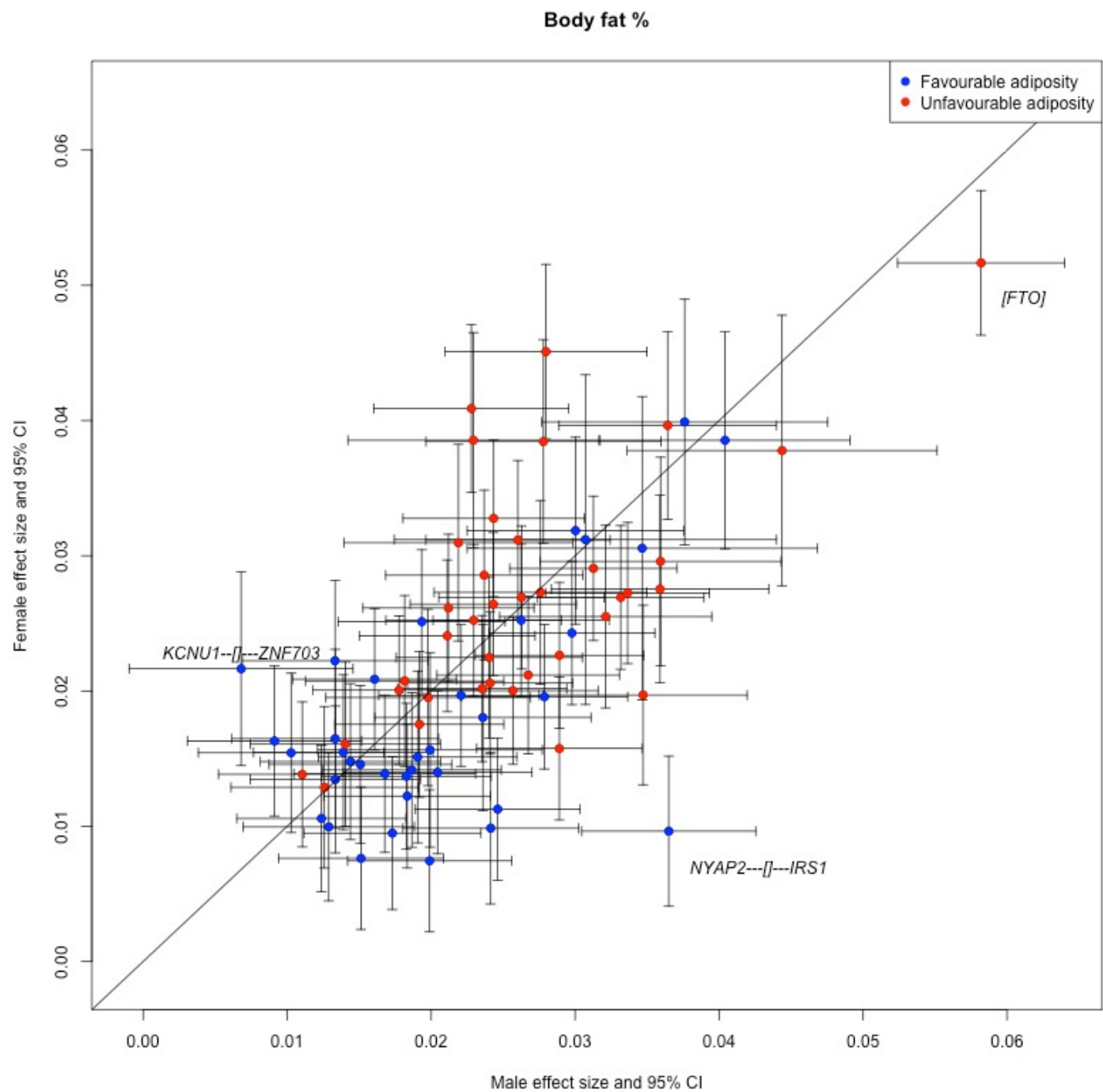
SHBG

Triglycerides

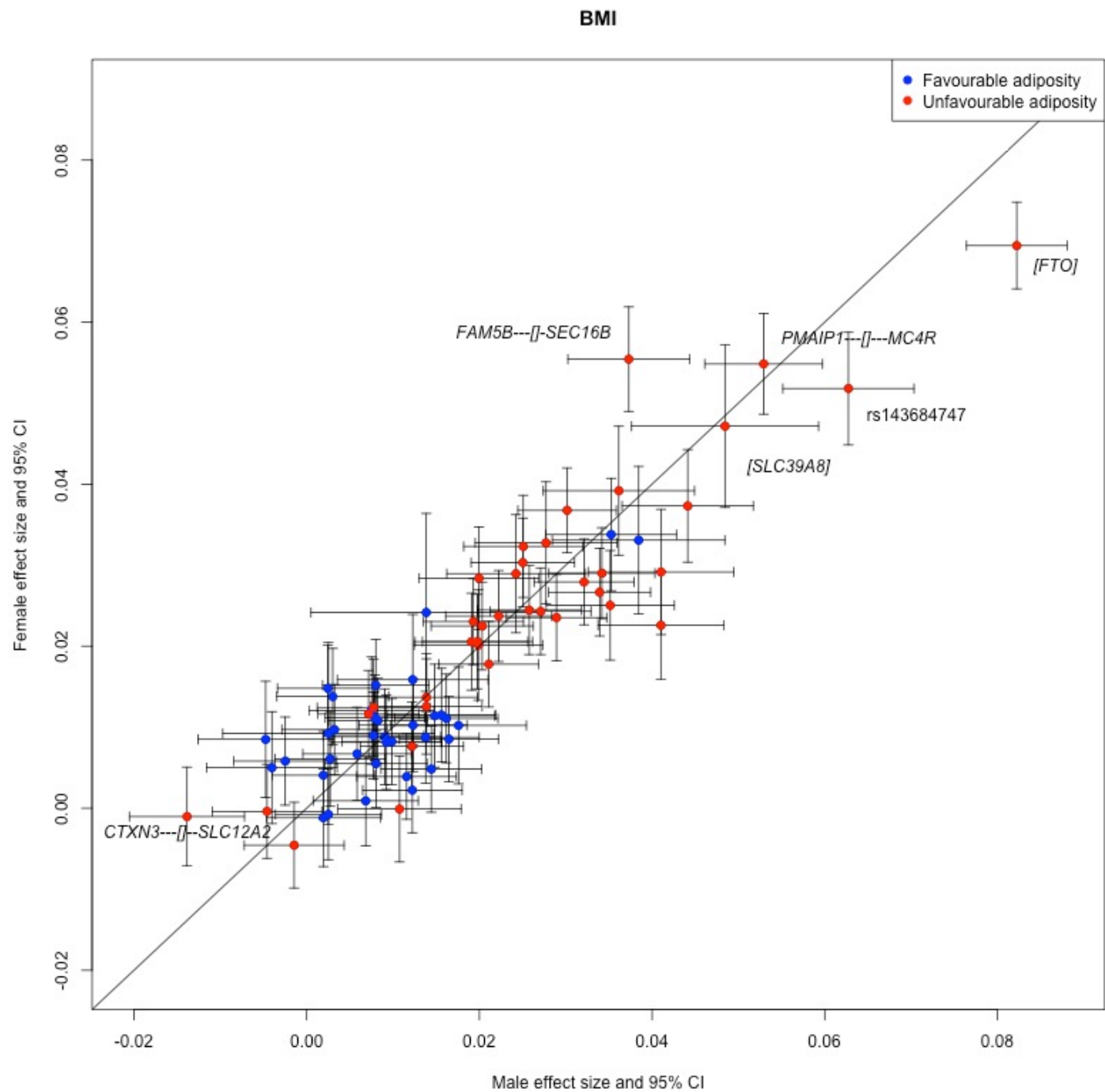
ALT

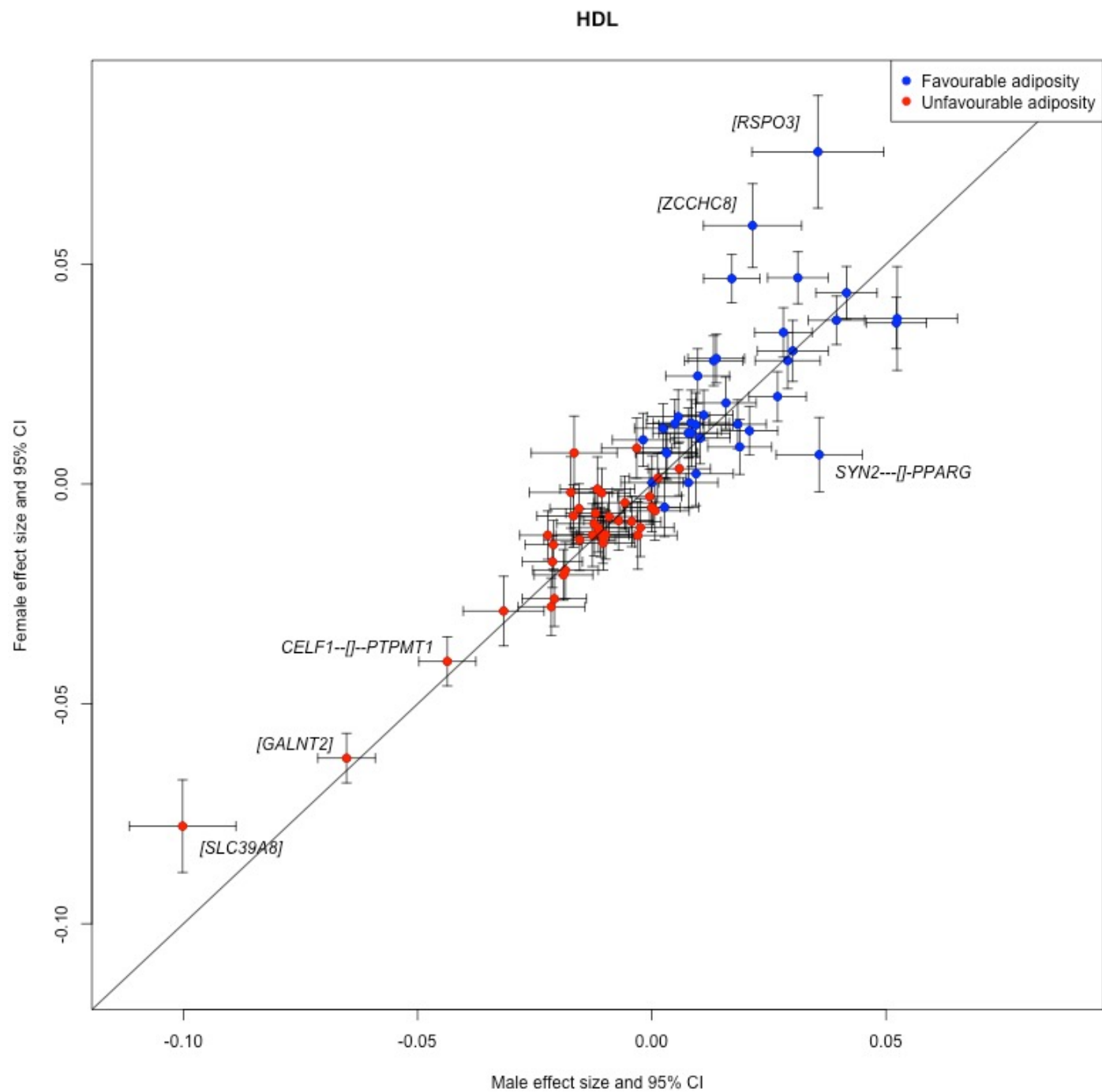
AST

SF 3a



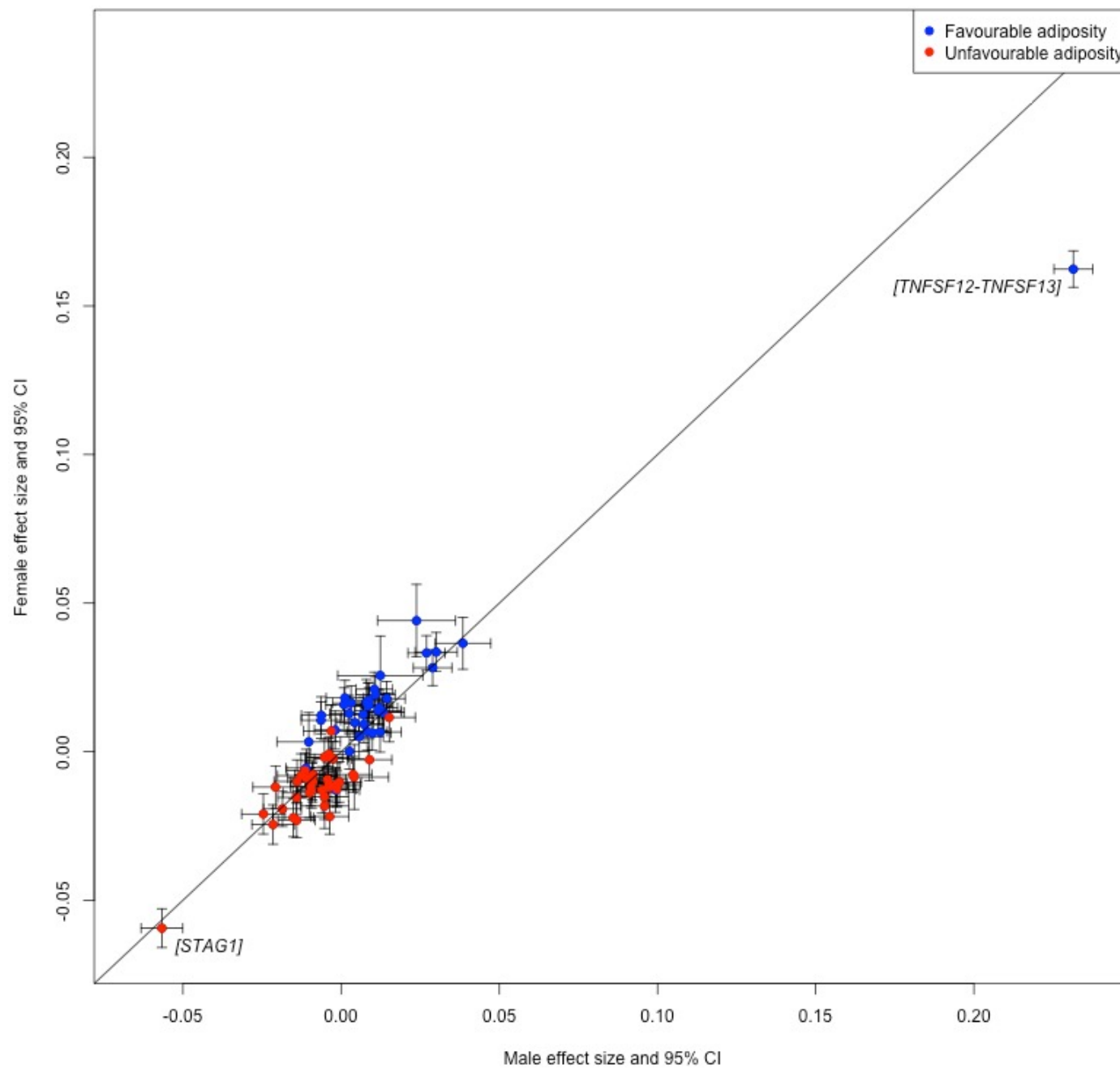
SF 3b





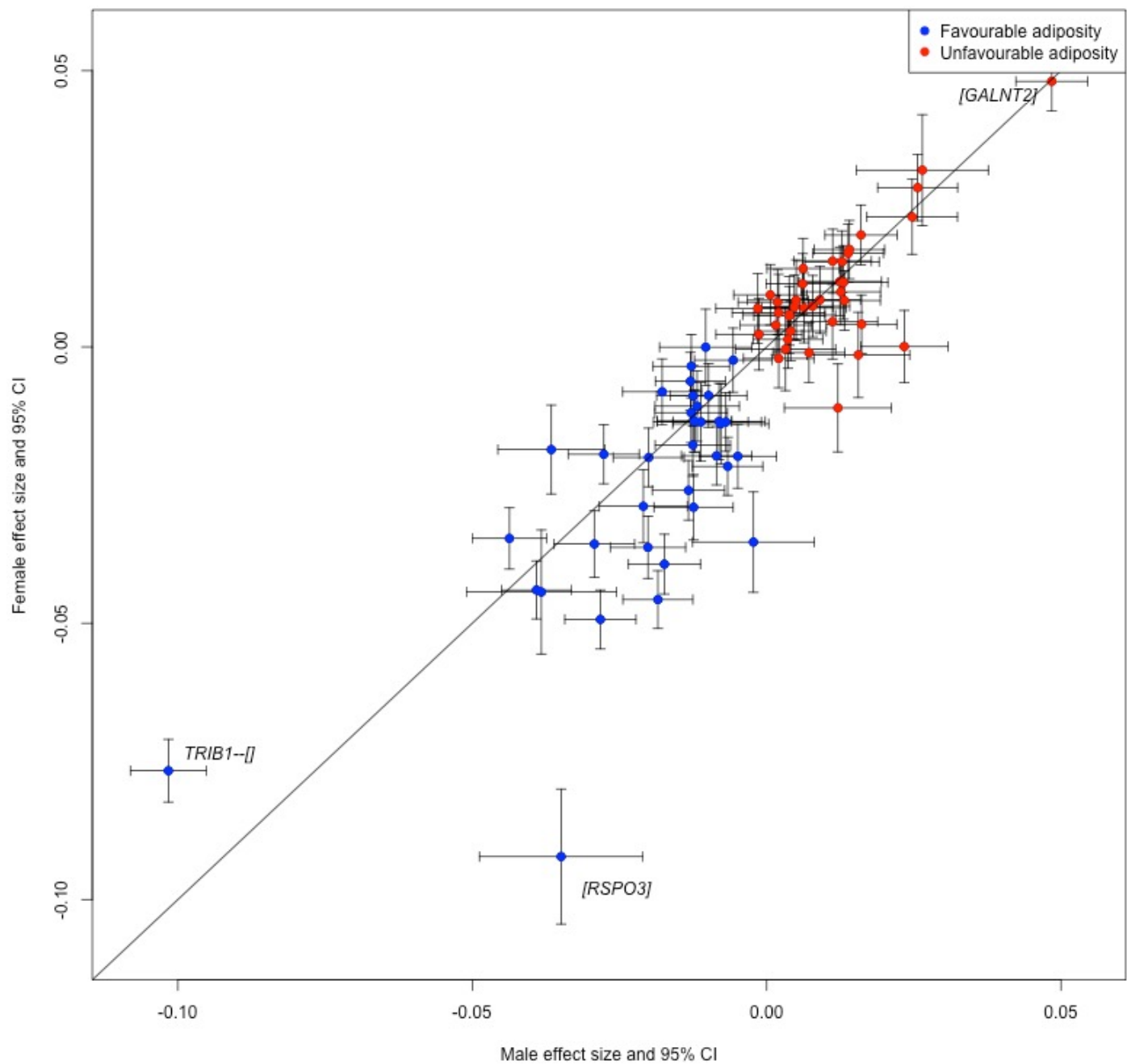
SF 3d

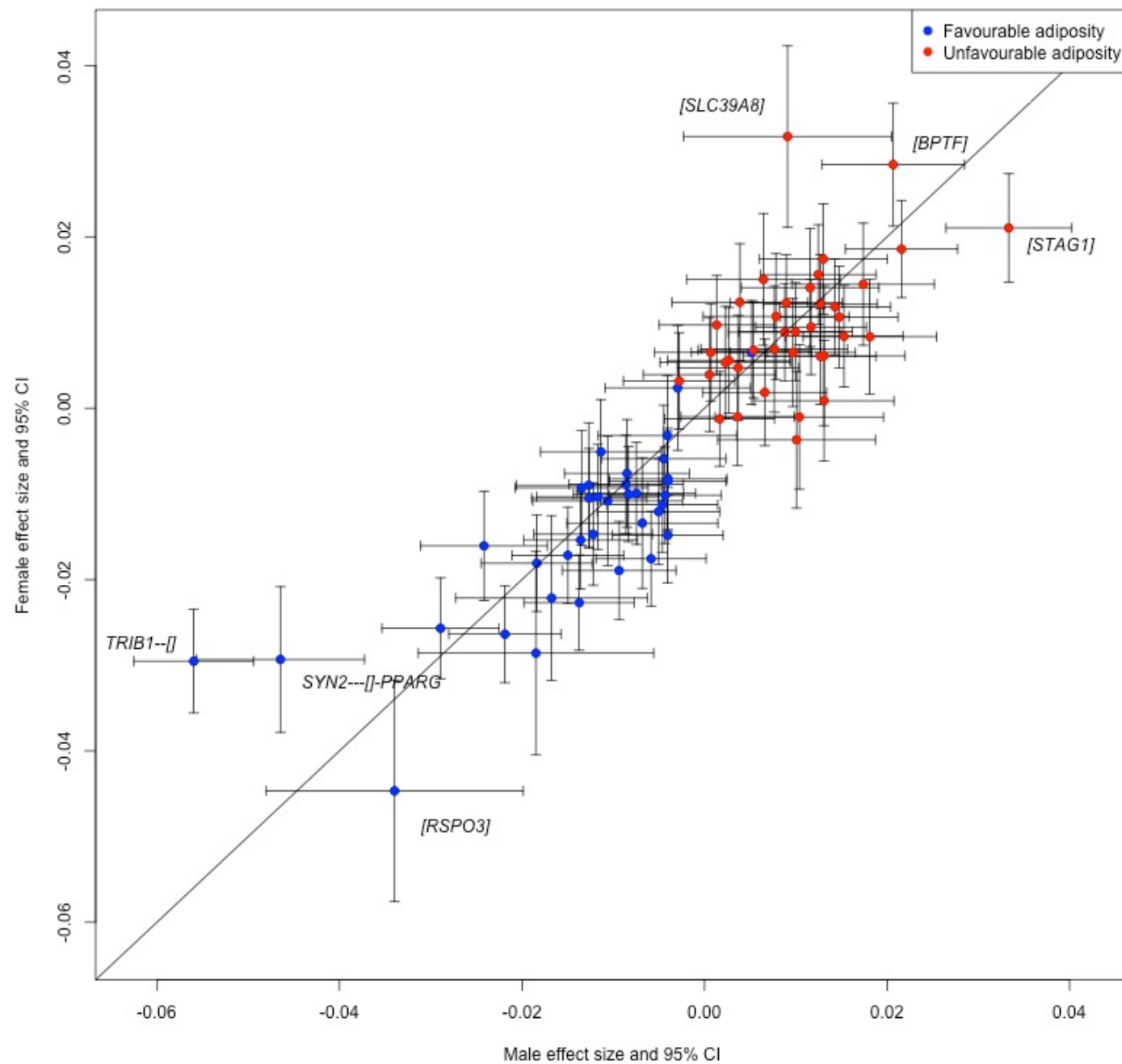
SHBG

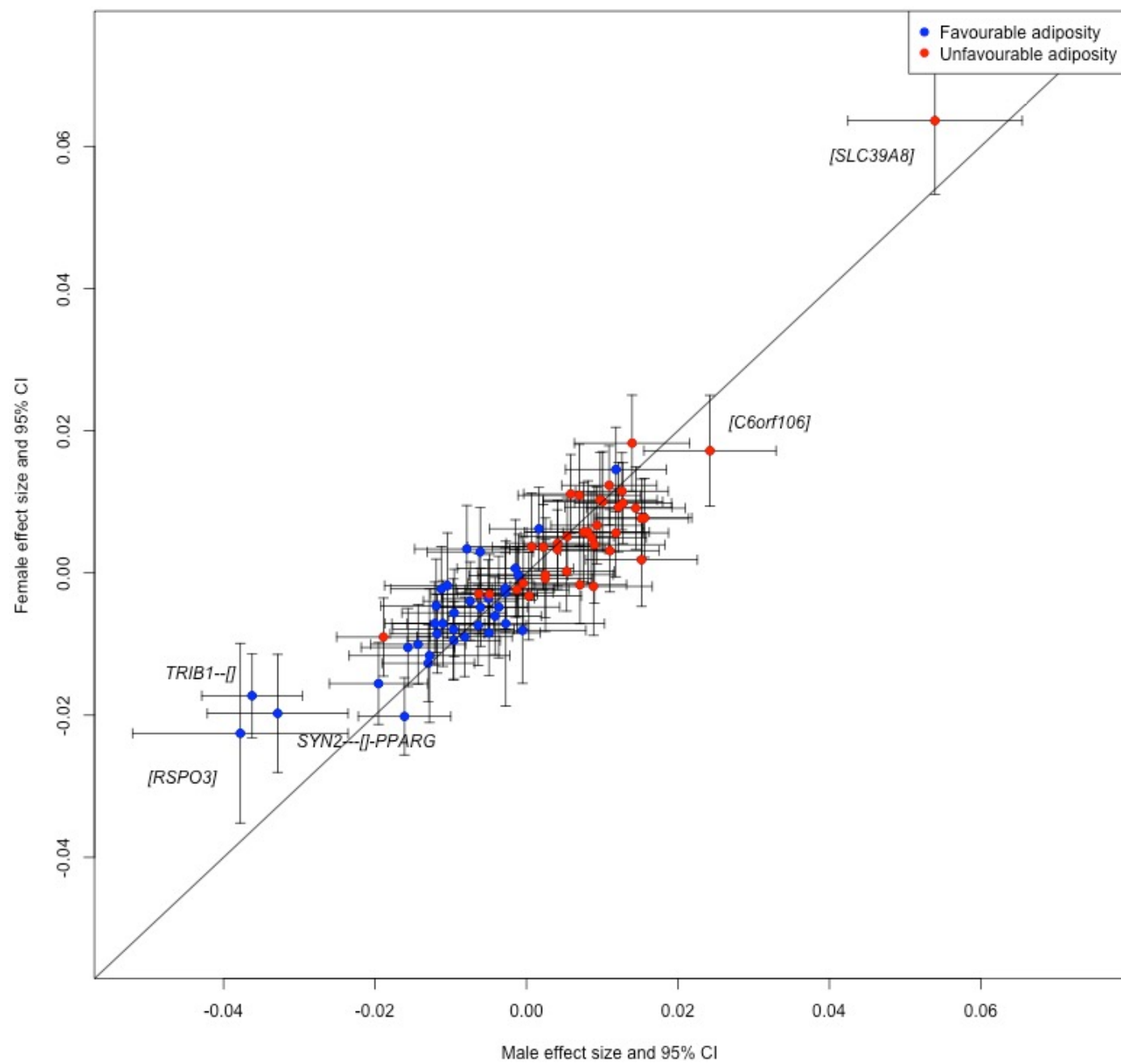


SF 3e

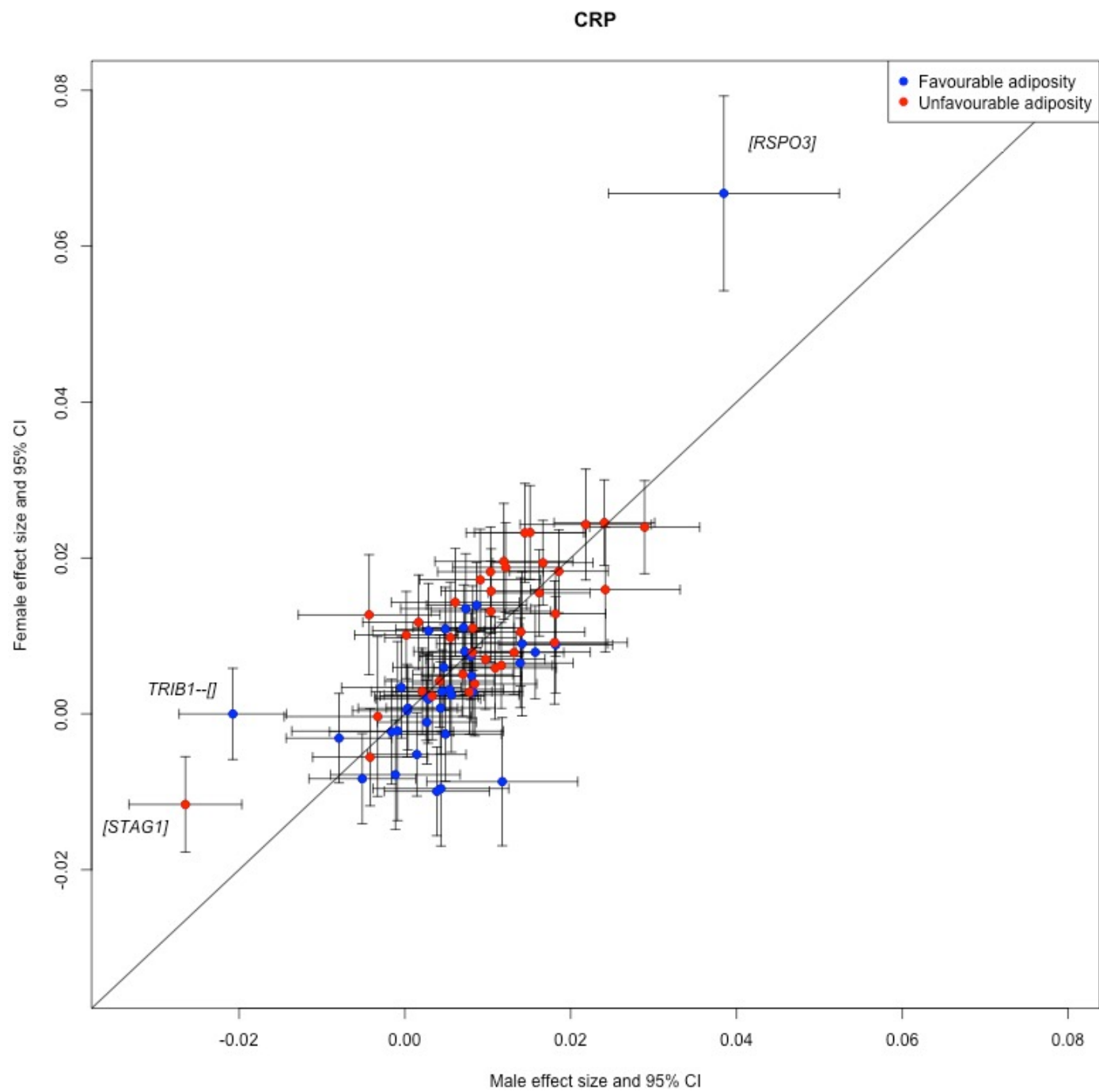
Triglycerides

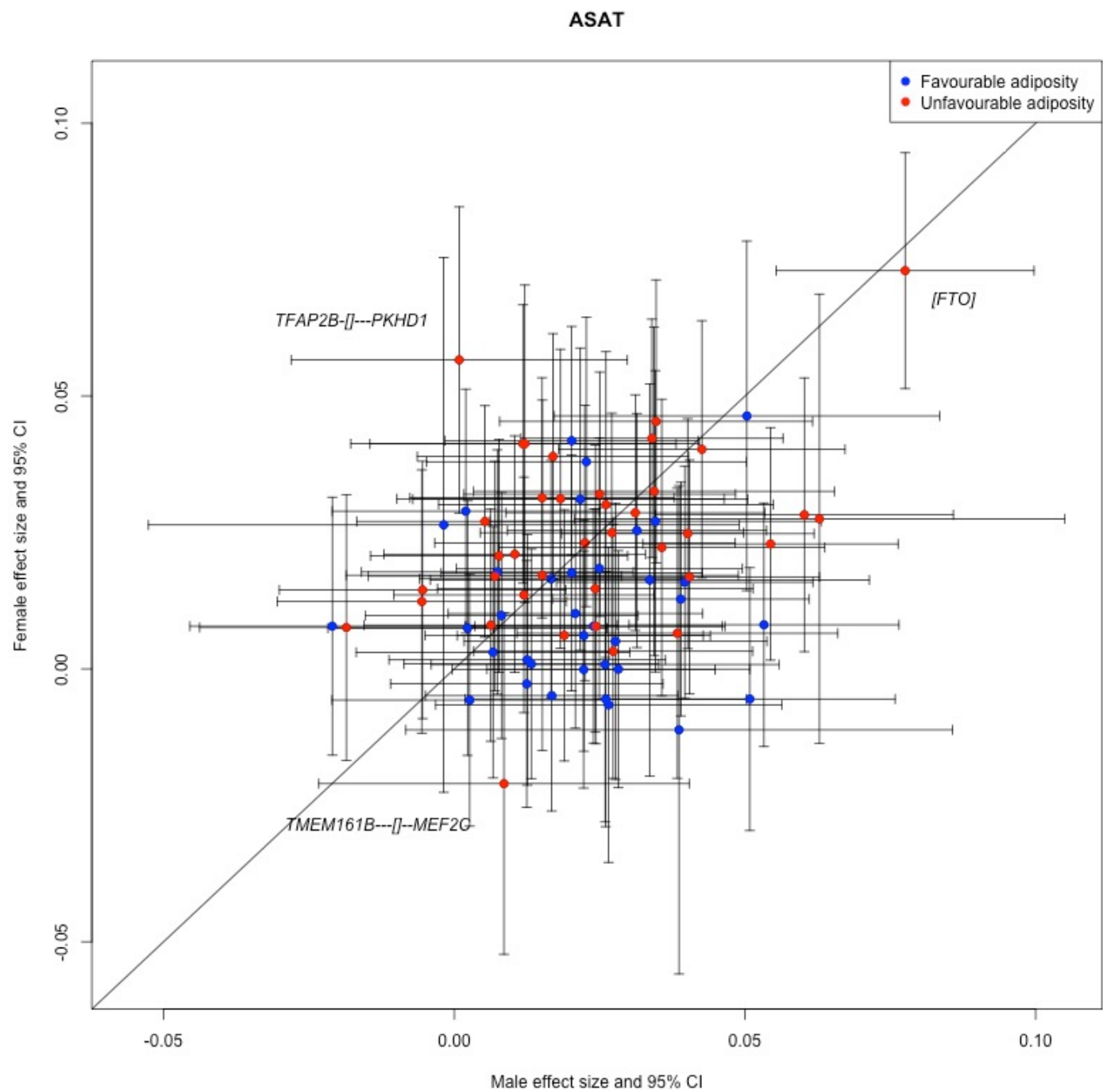




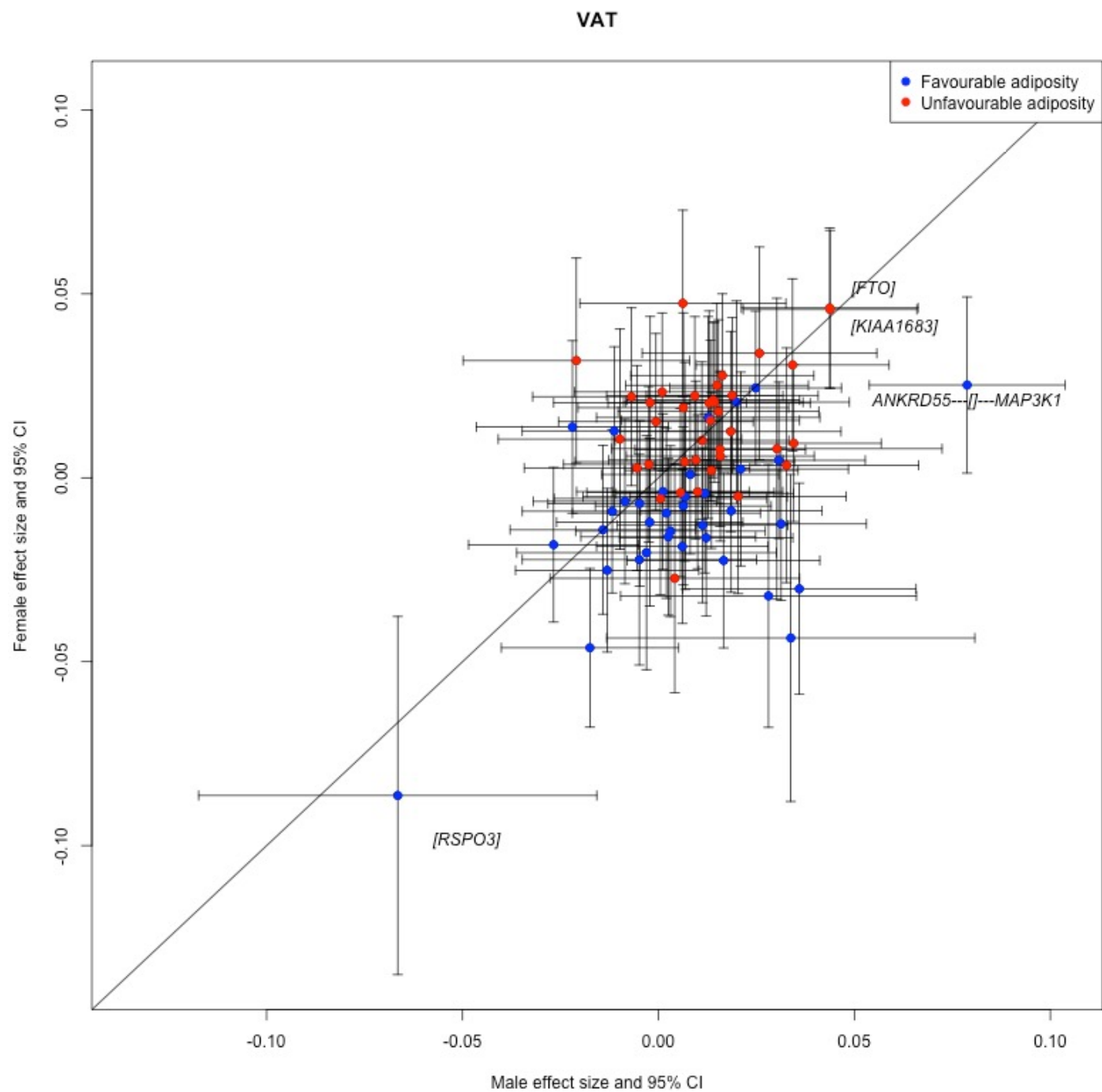


SF 3h

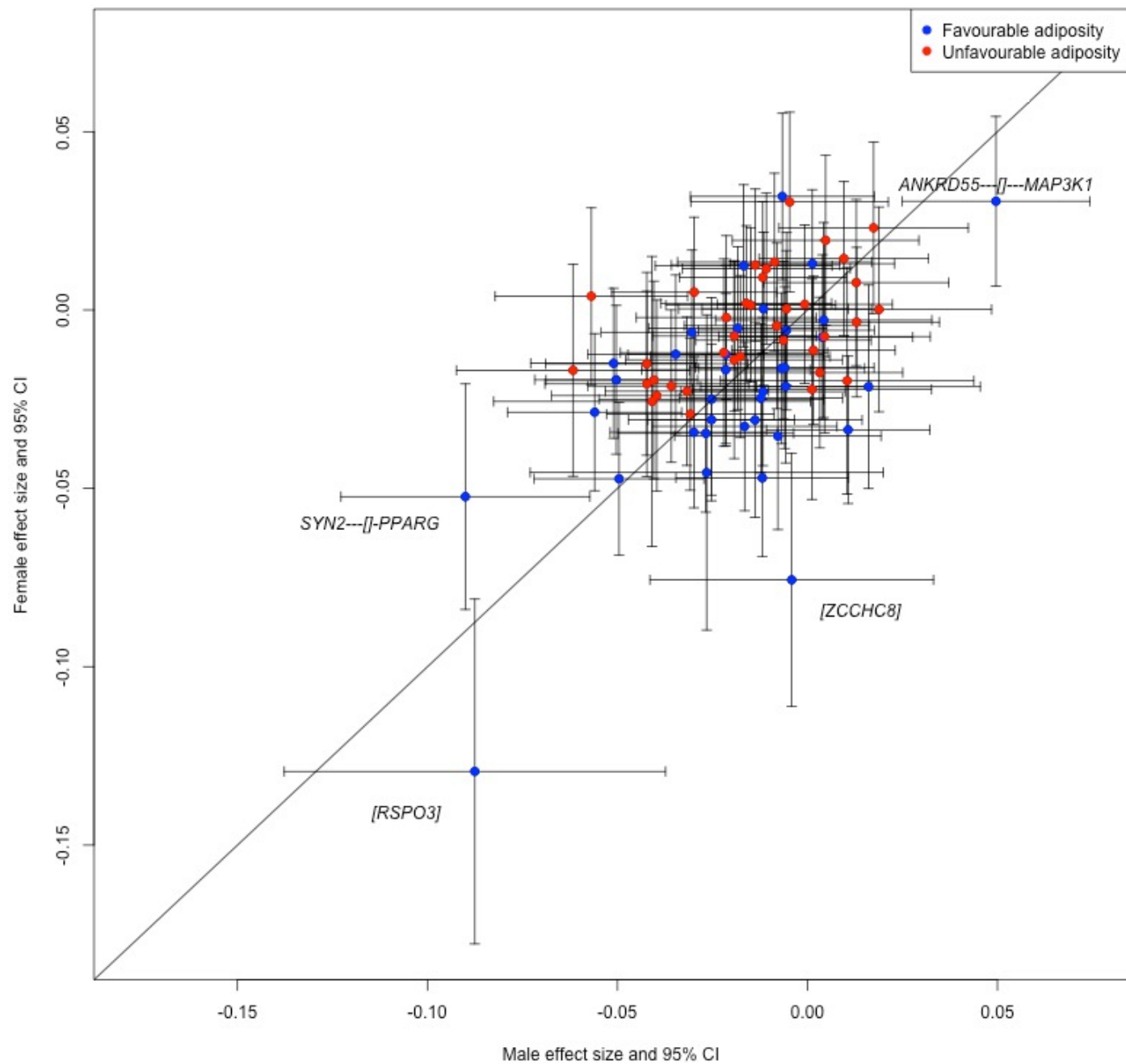


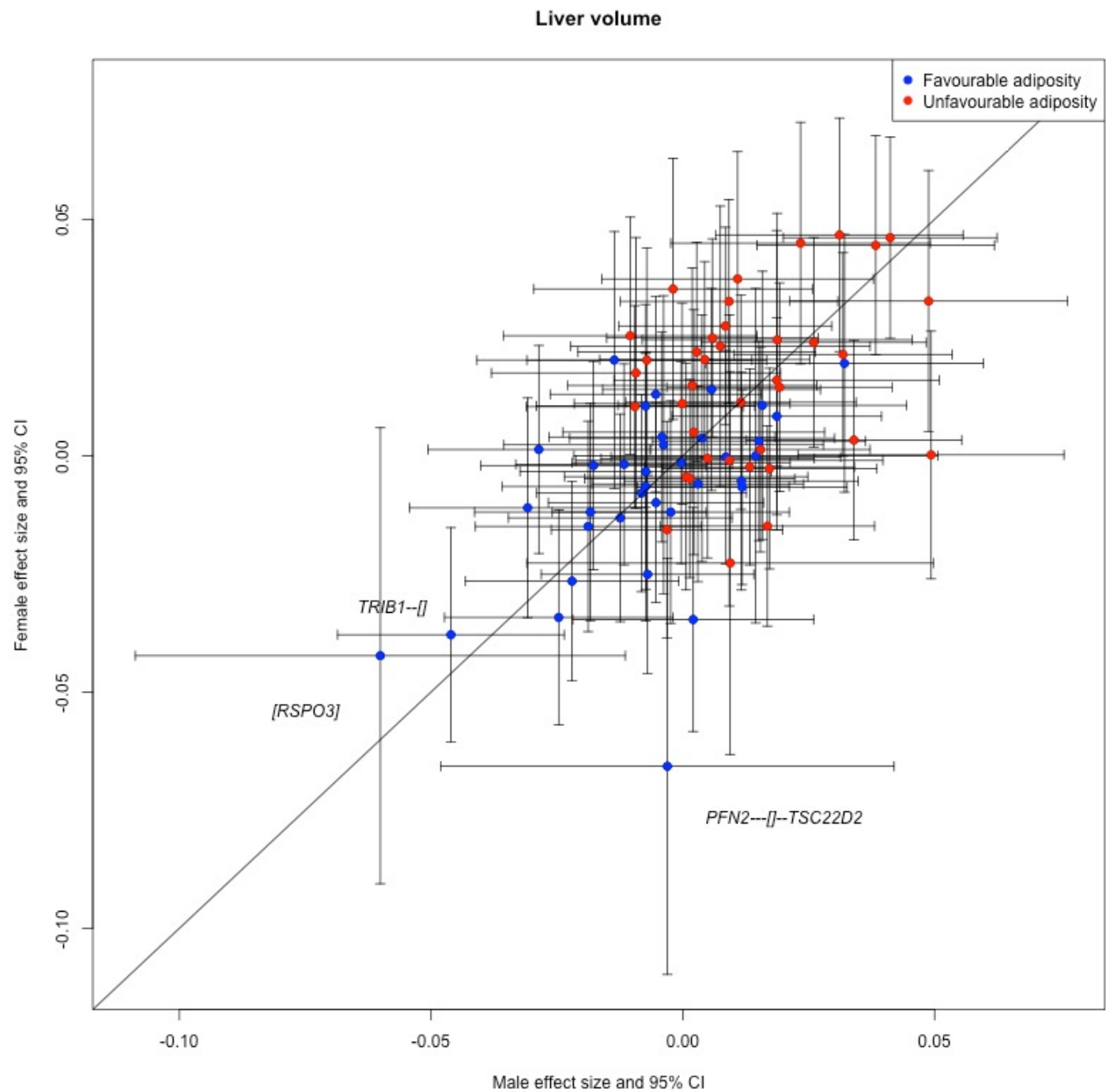


SF 3j



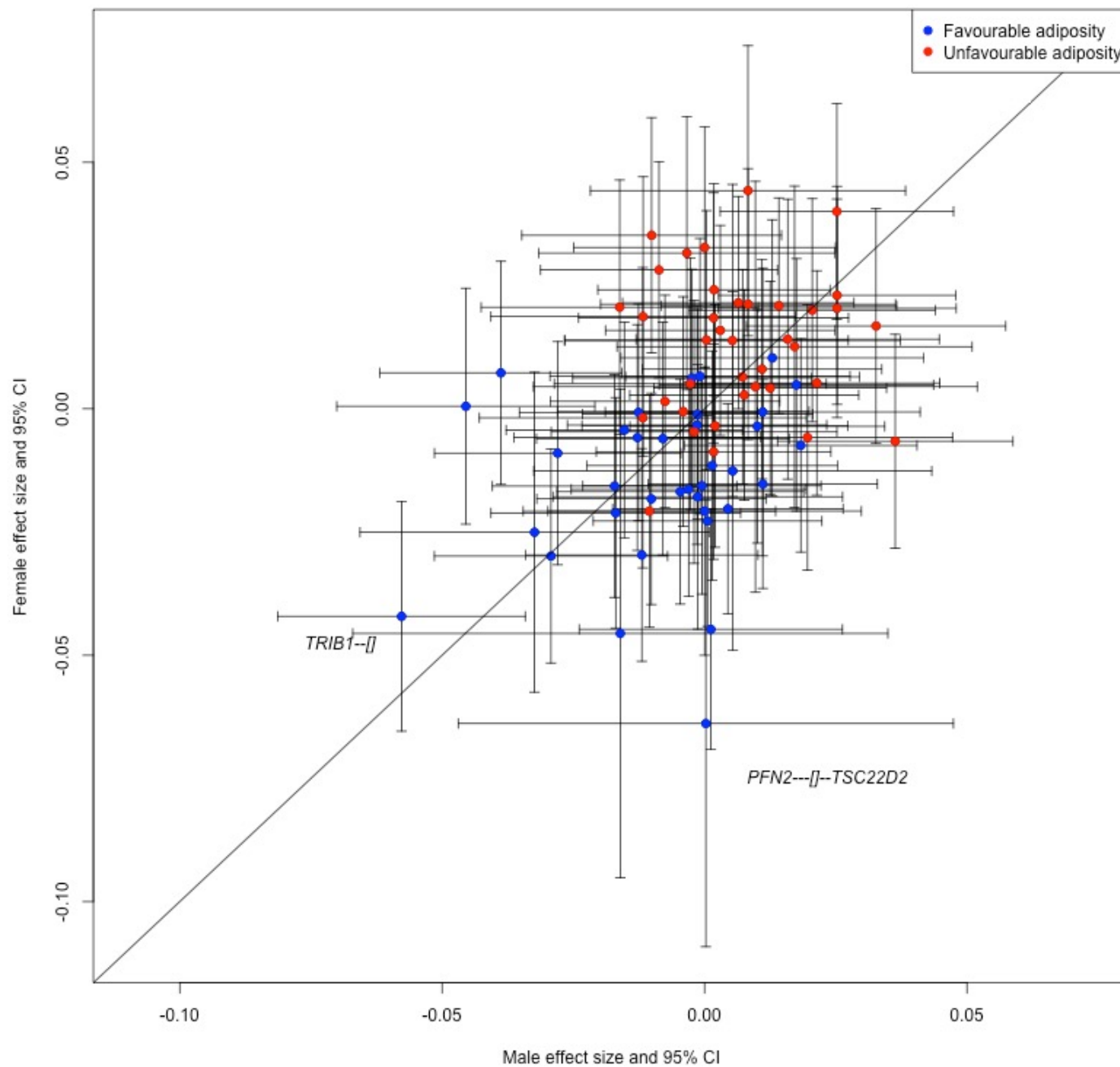
VATSAT



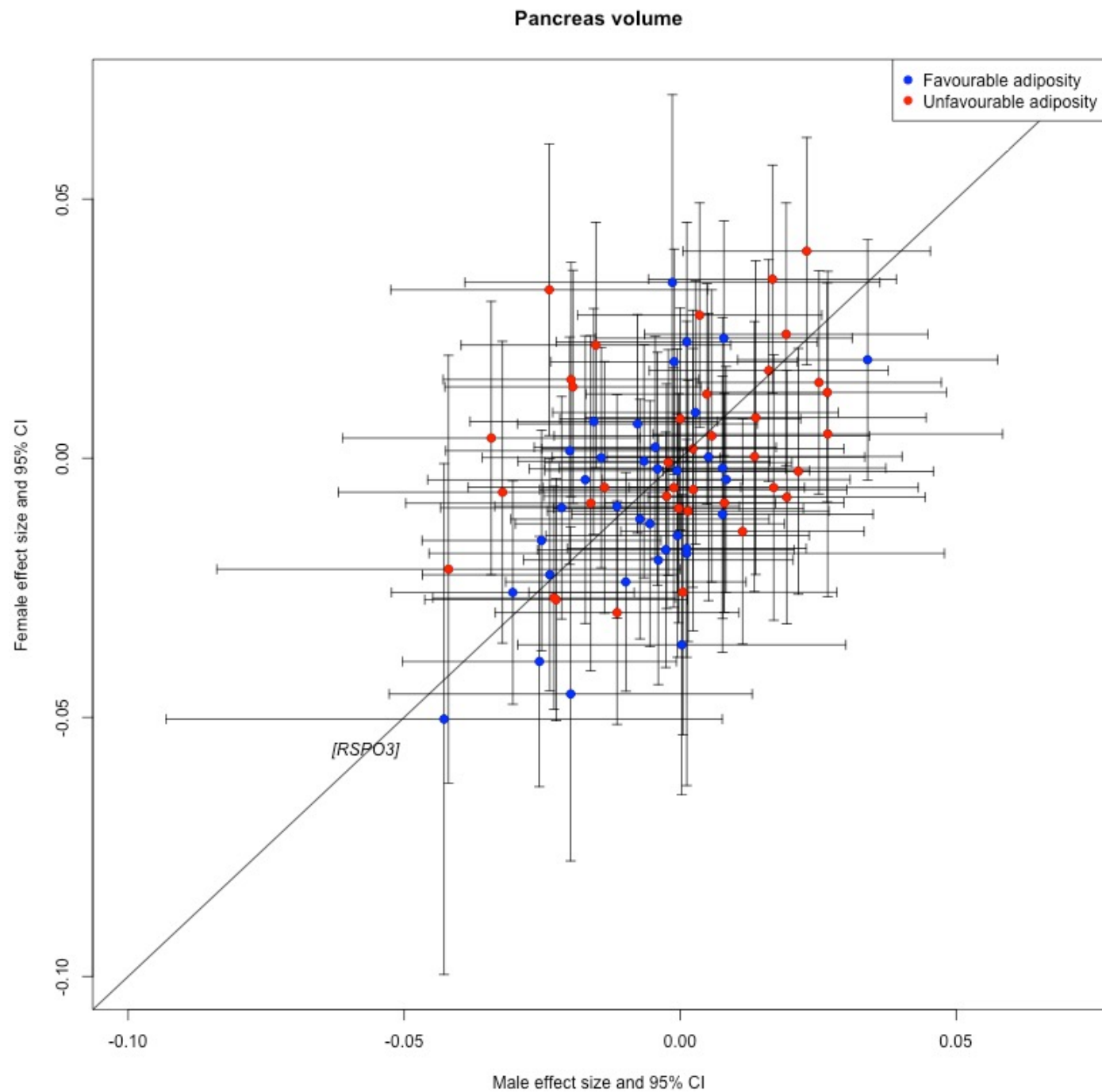


SF 3m

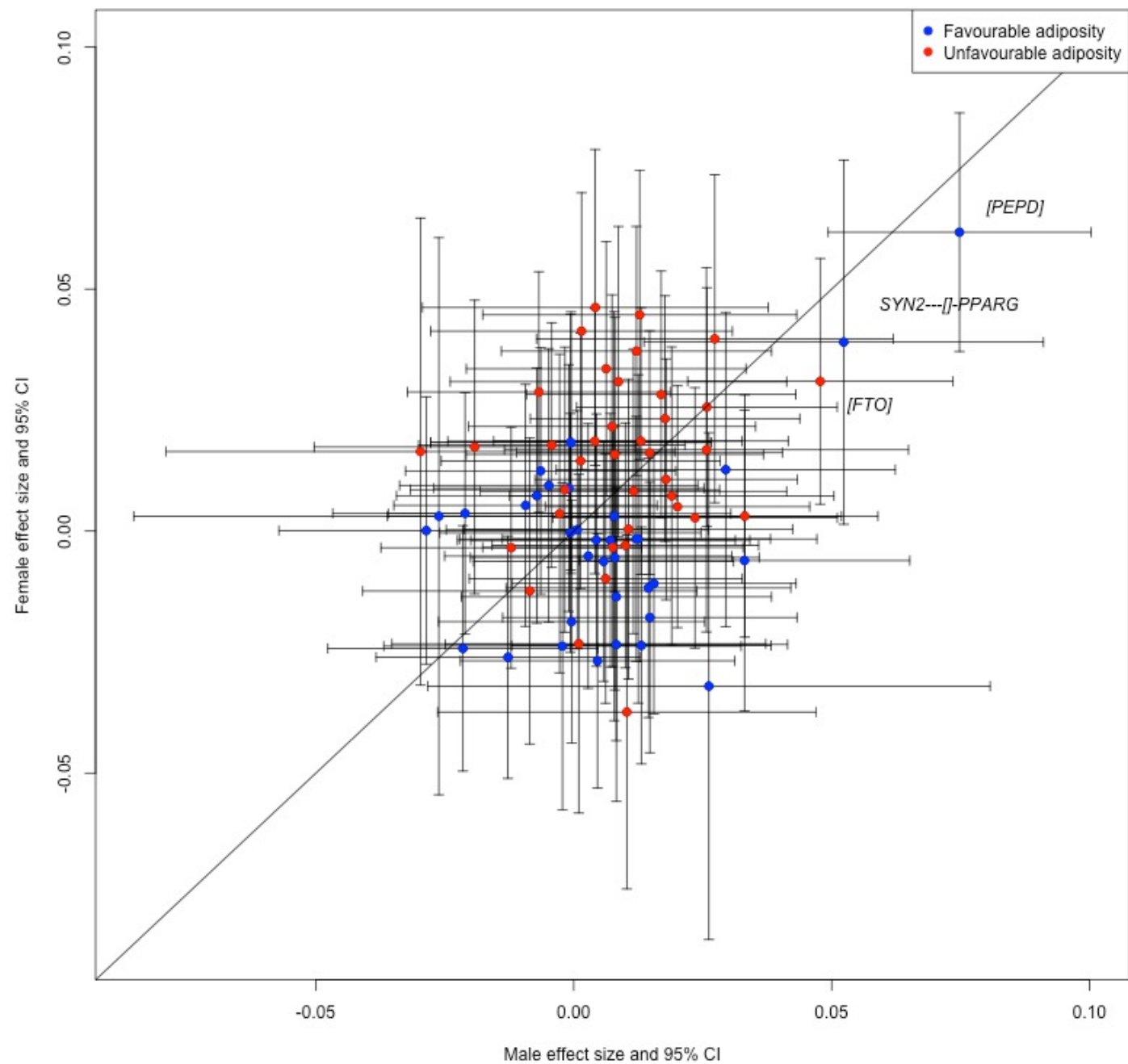
Liver fat

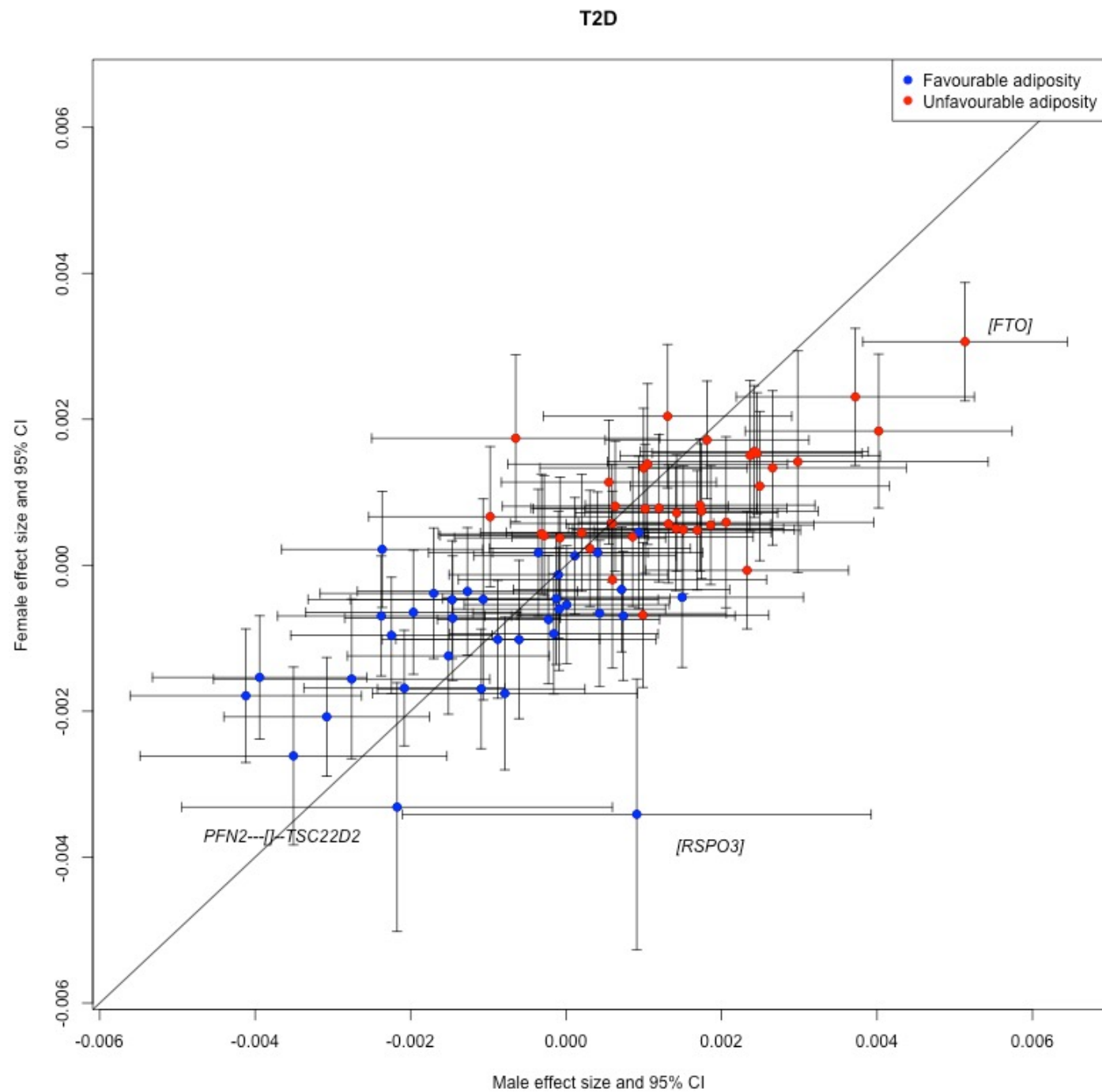


SF 3n



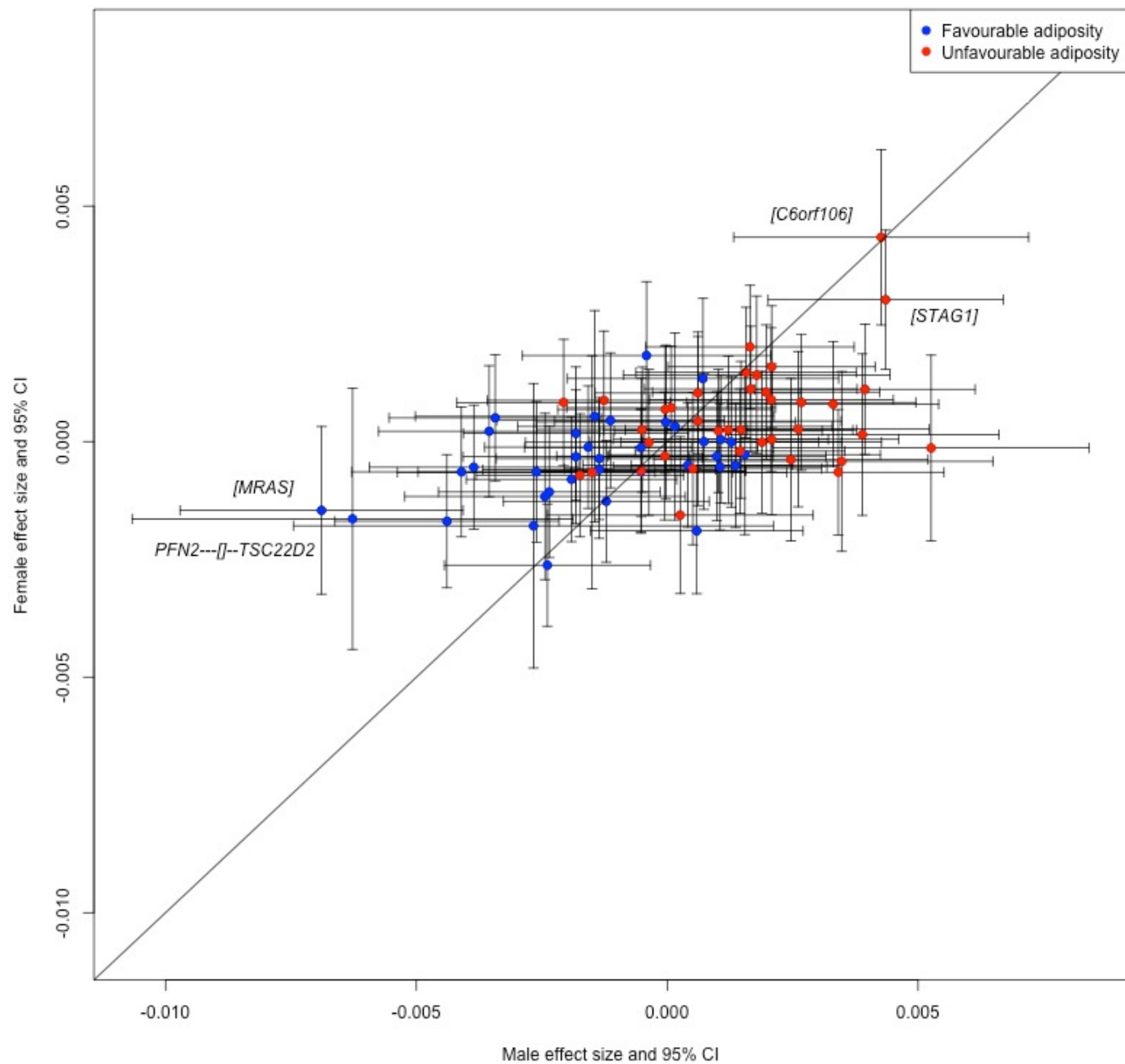
Pancreas fat





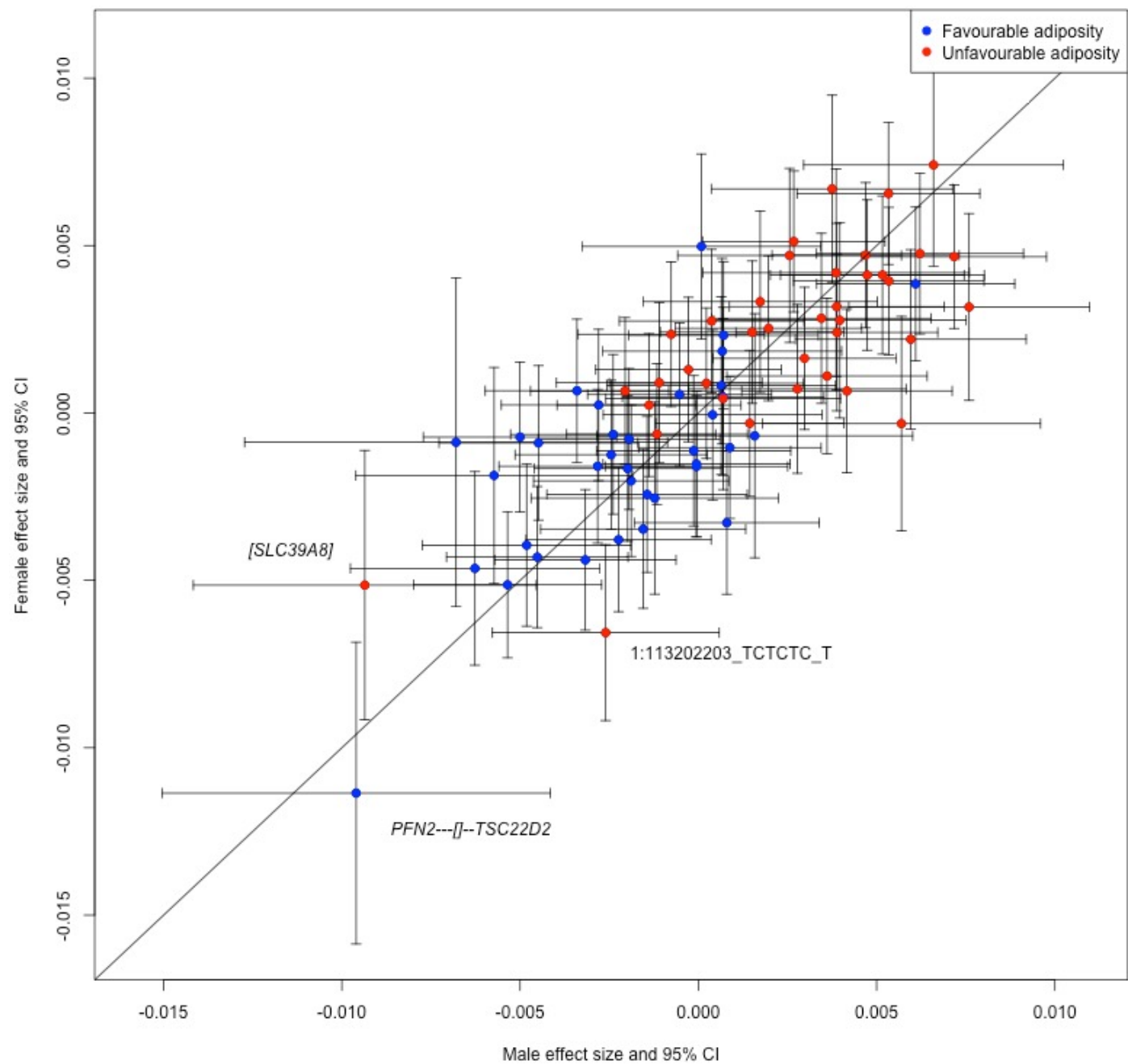
SF 3q

Heart disease

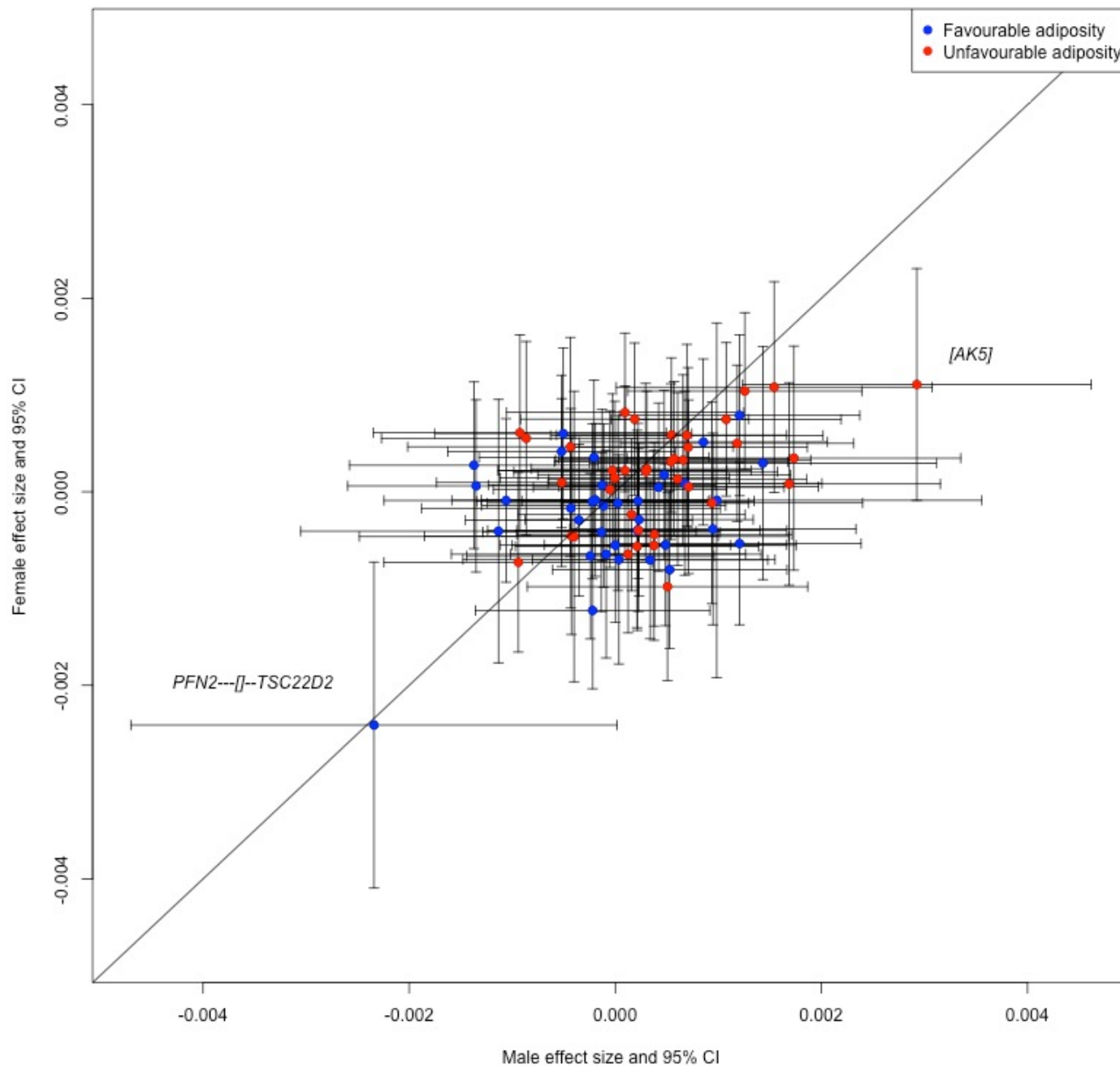


SF 3r

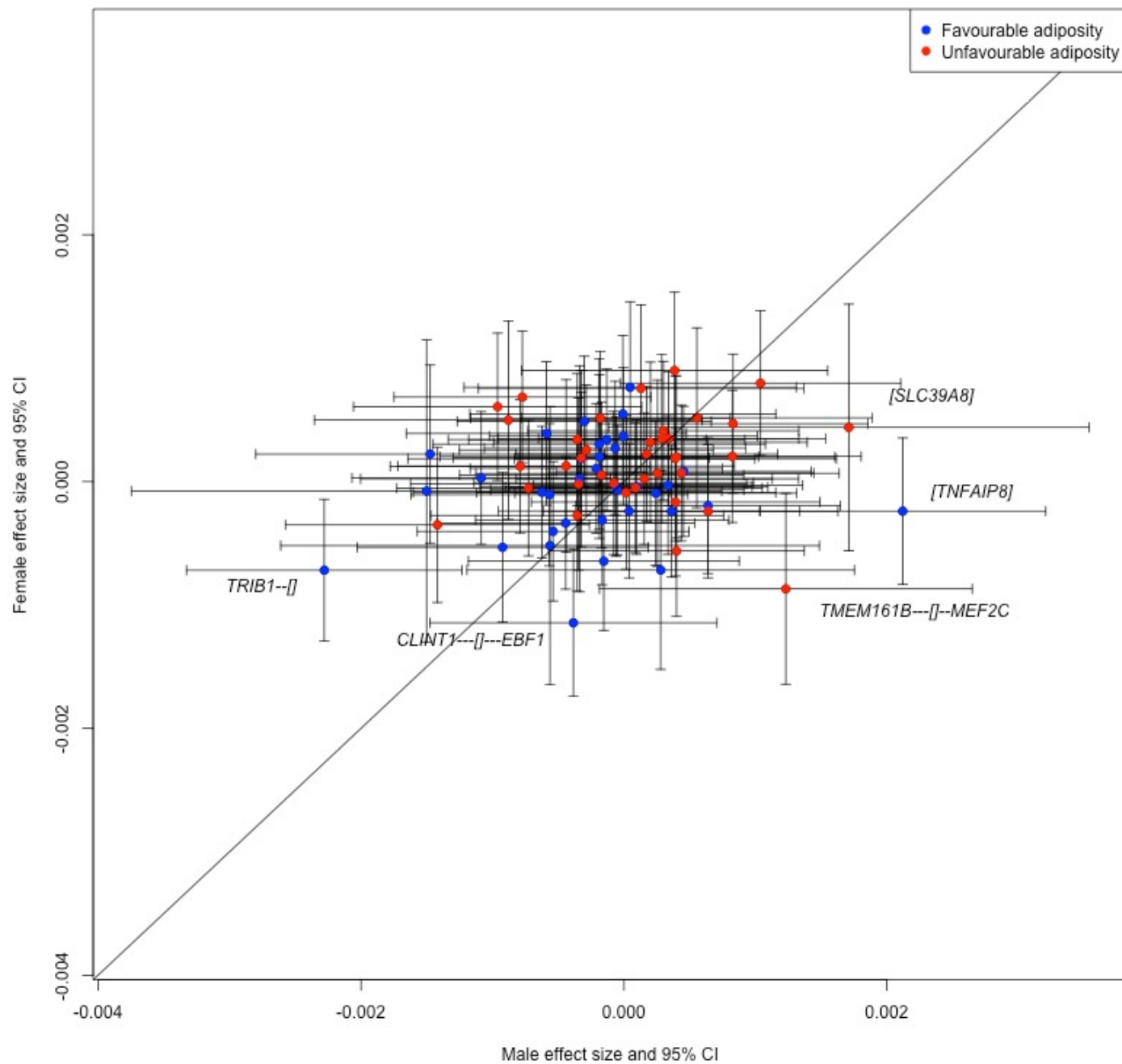
Hypertension



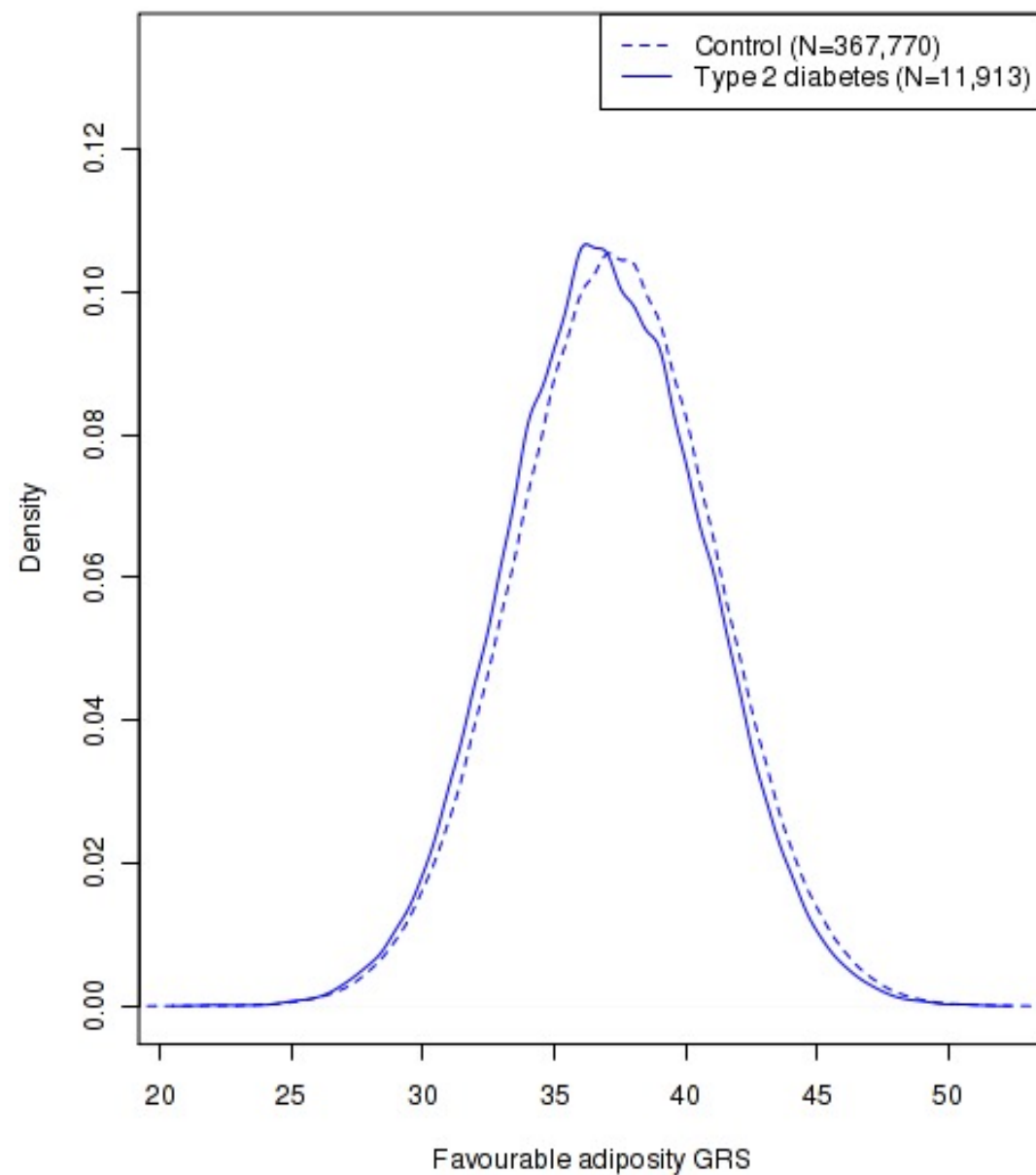
Stroke



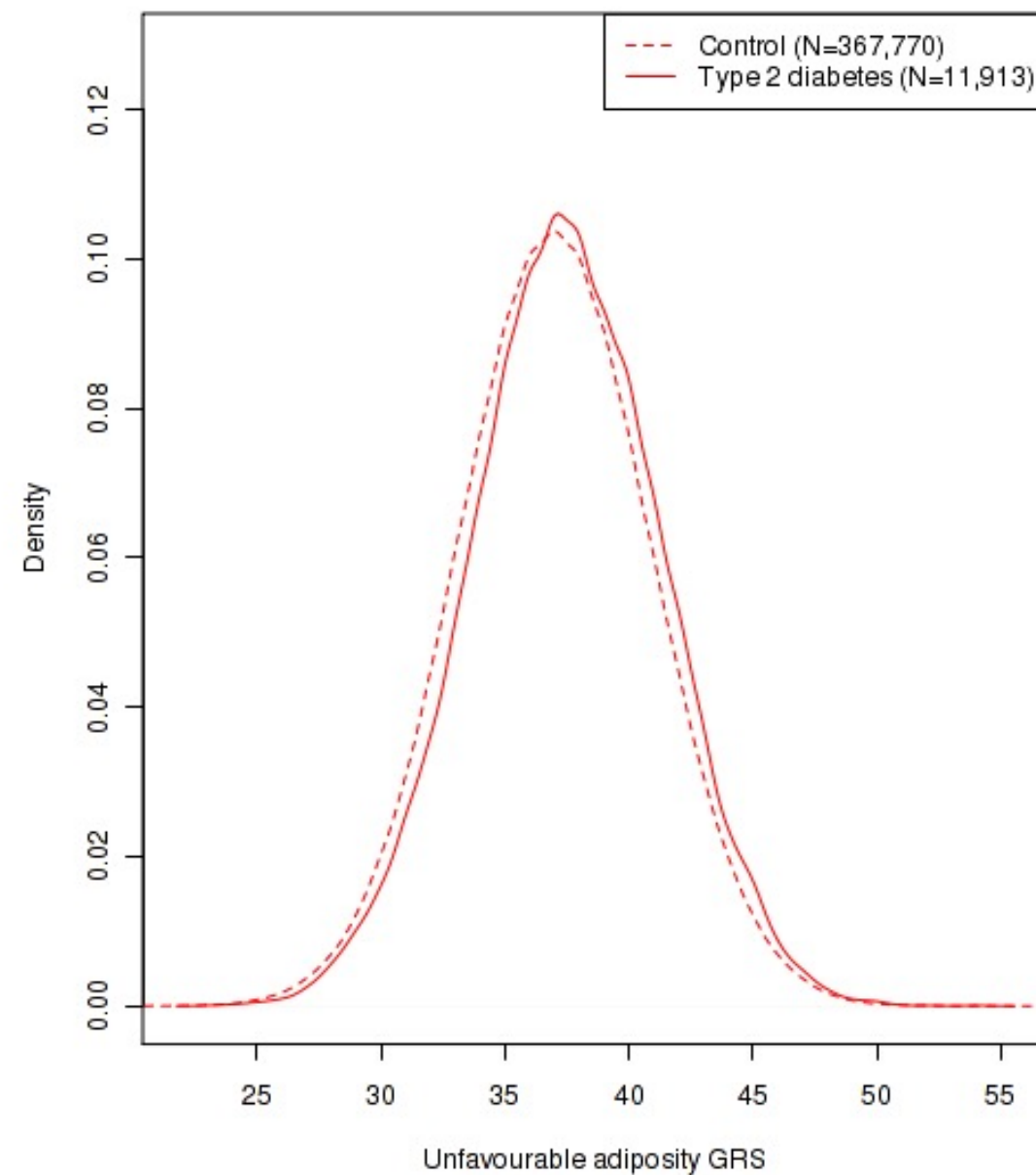
NAFLD

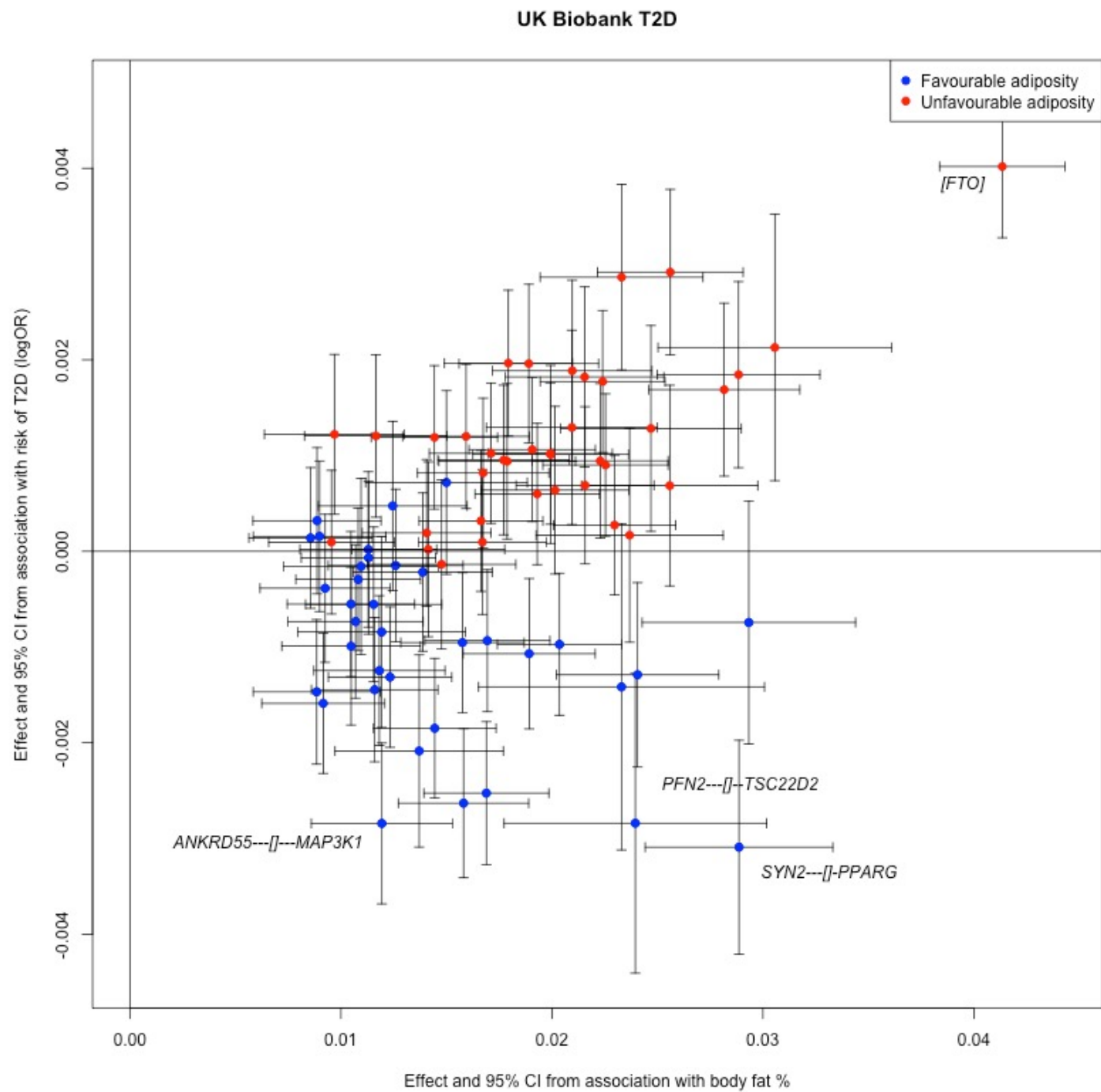


Favourable adiposity

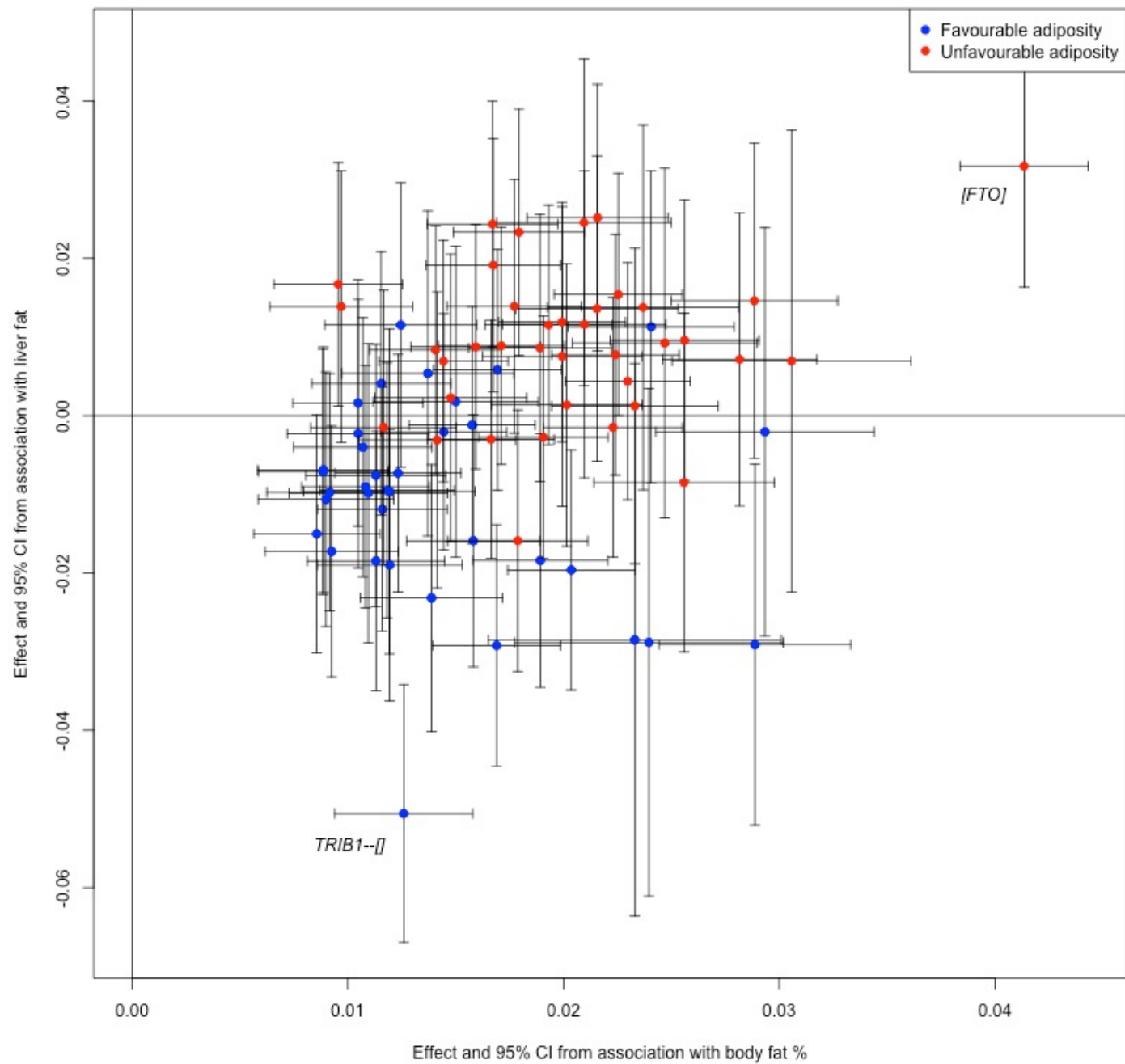


Unfavourable adiposity

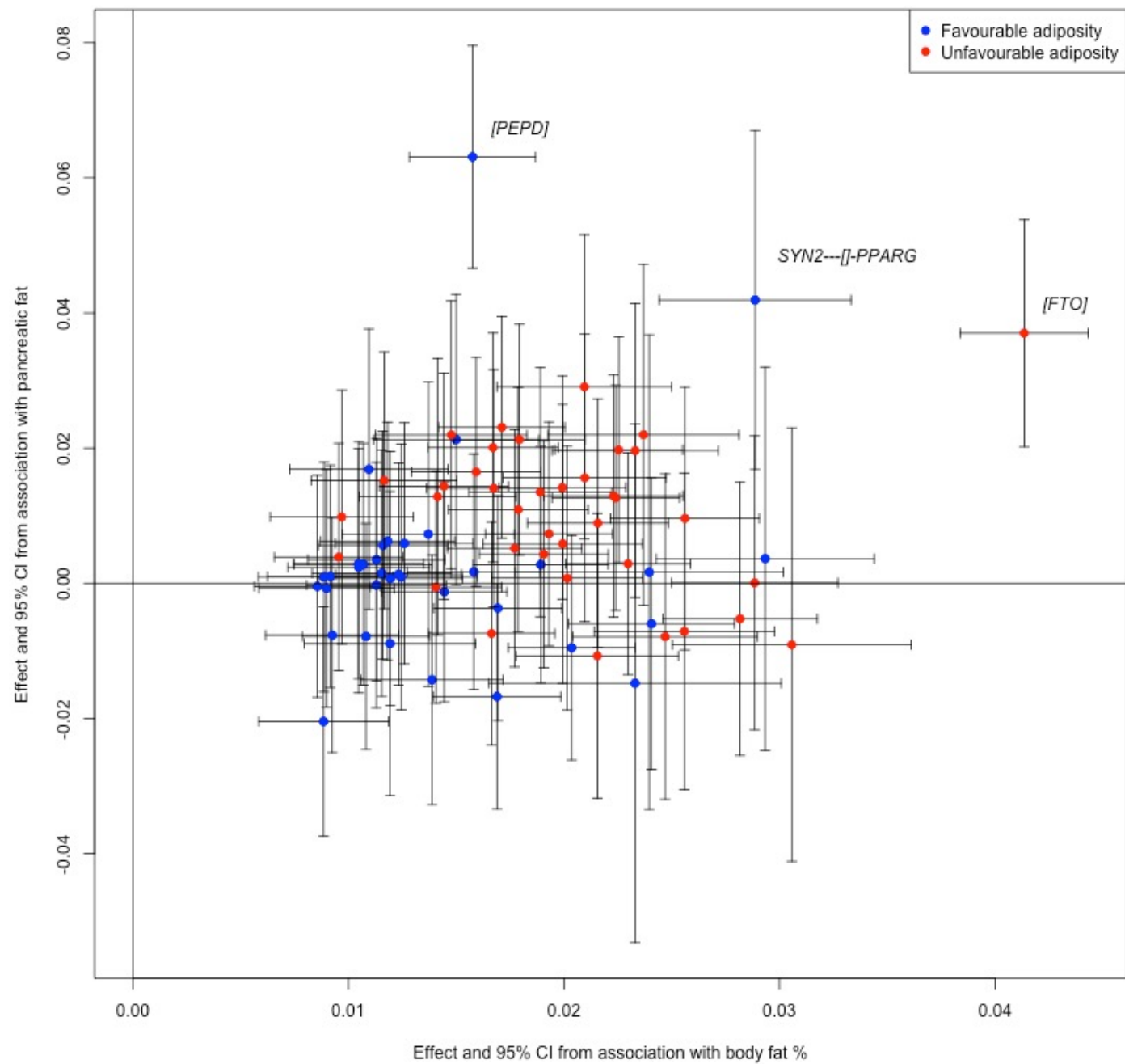




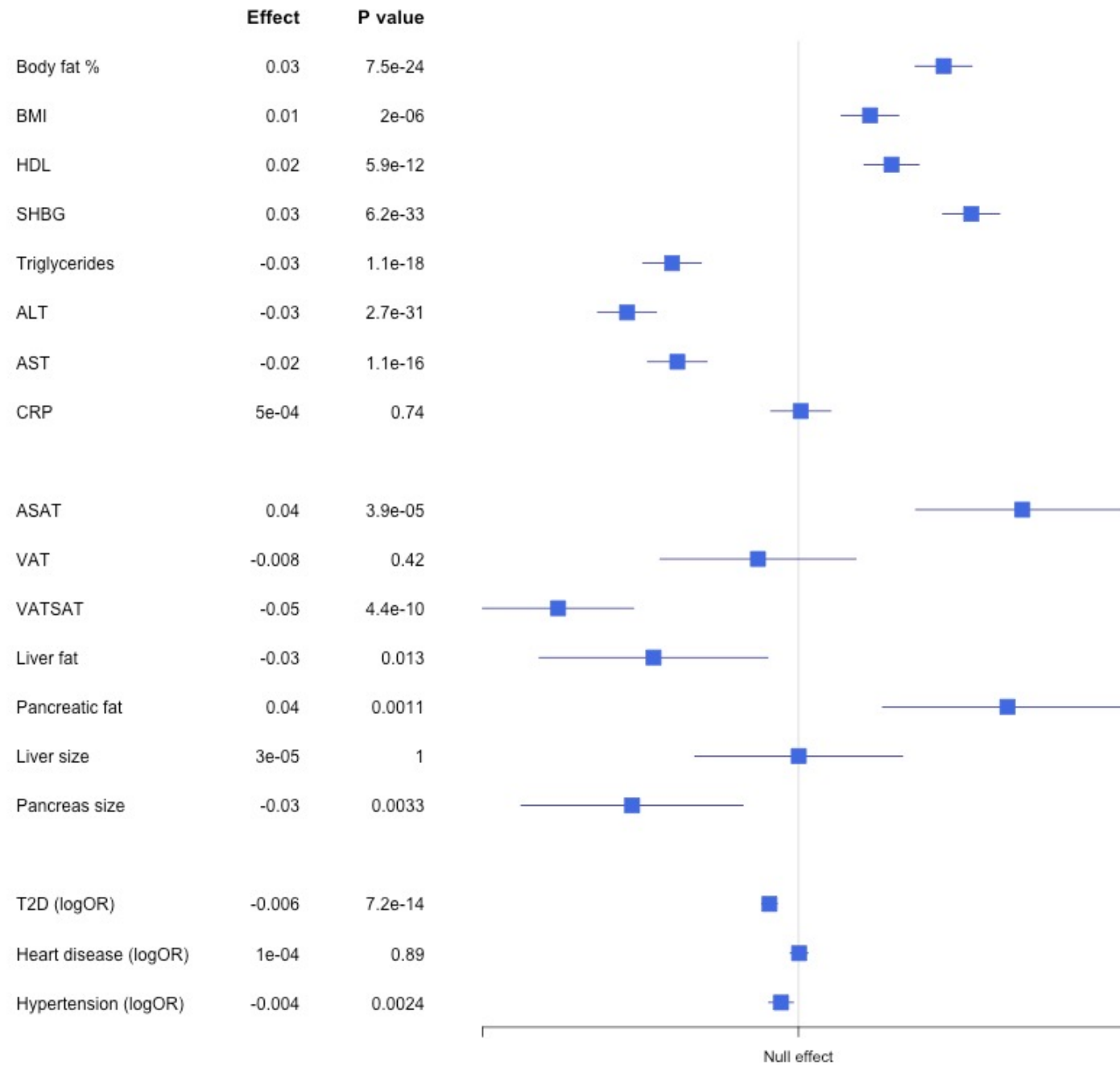
UK Biobank liver fat



UK Biobank pancreas fat

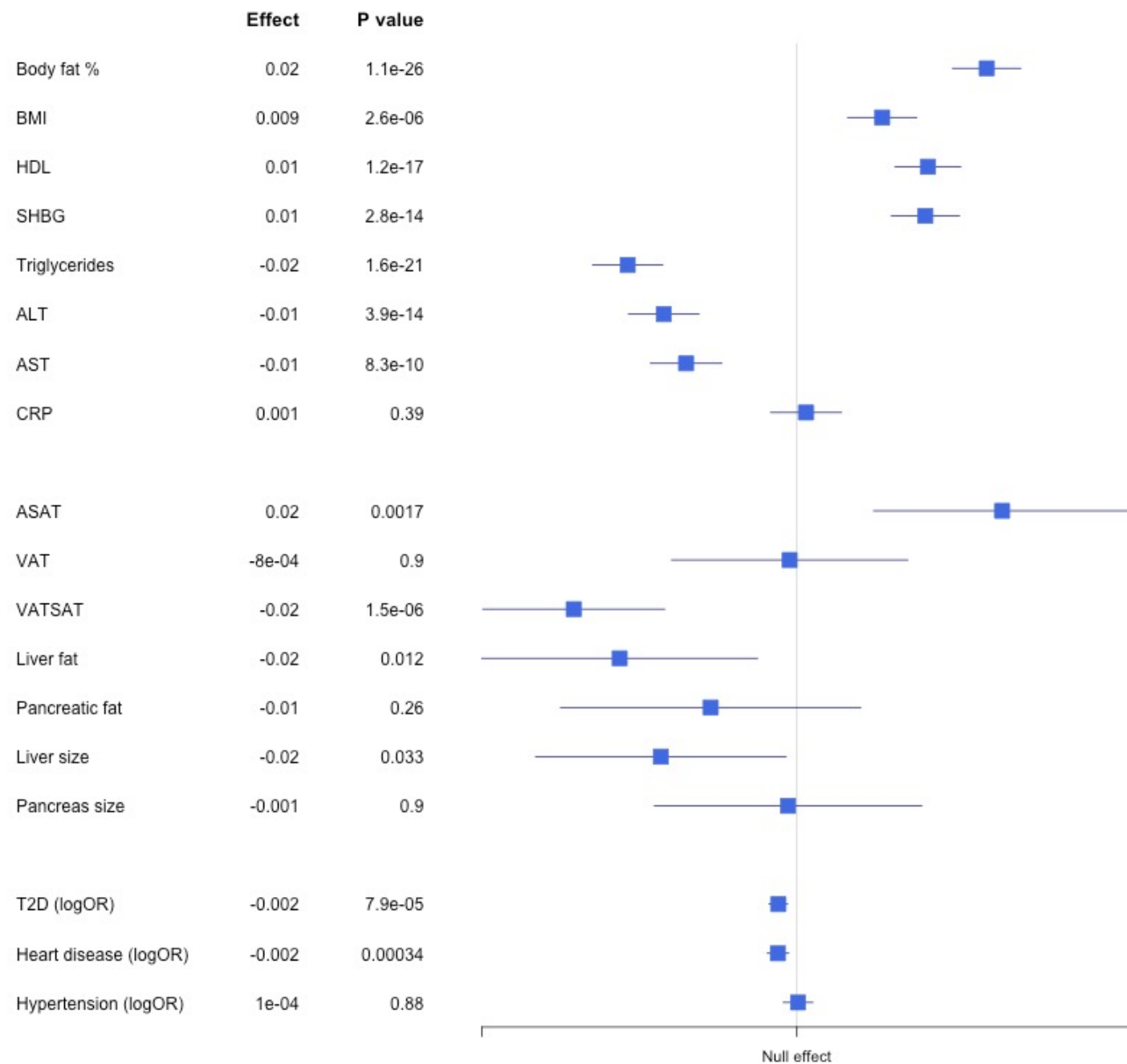


SF 8a



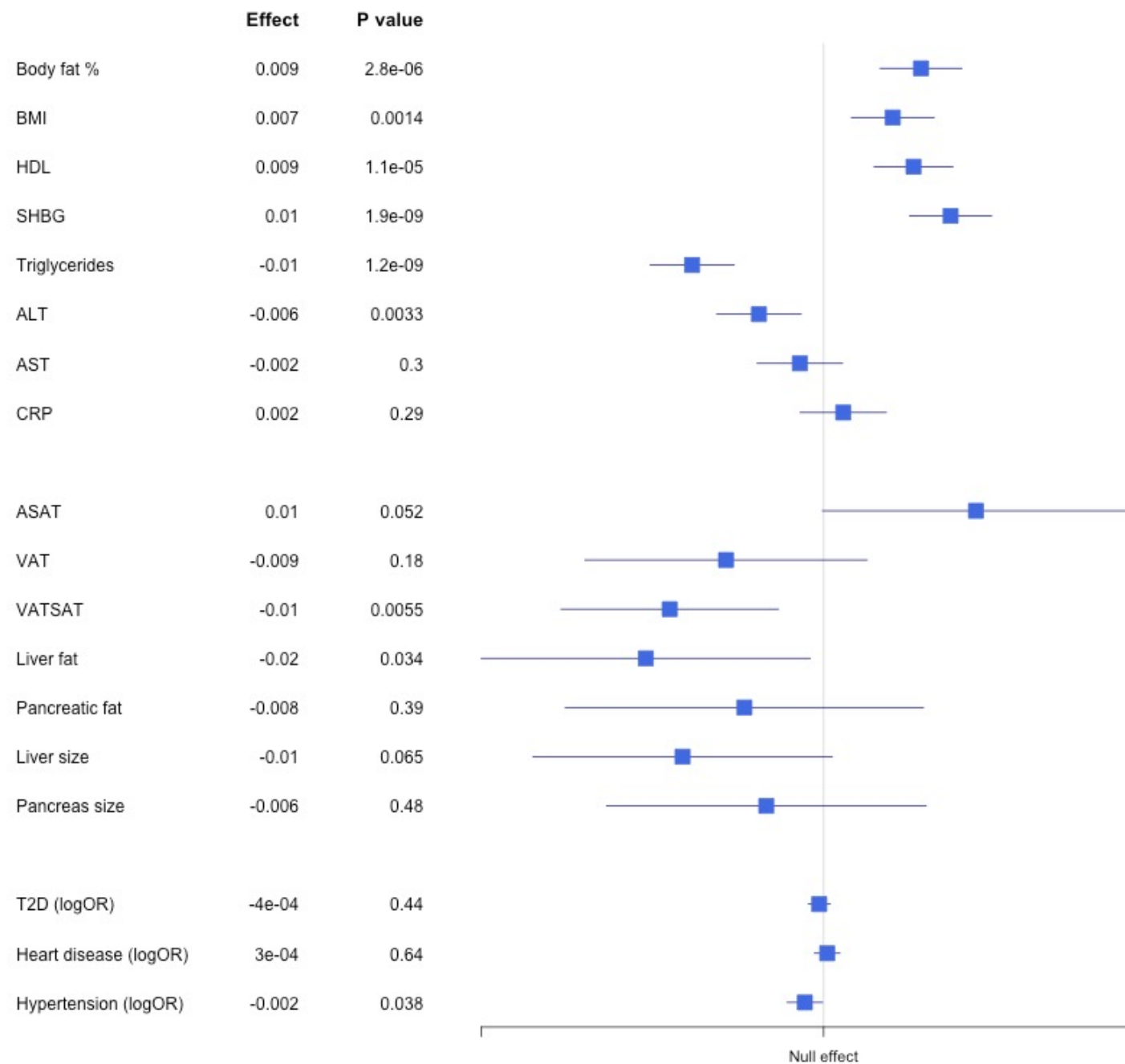
SF 8b

rs12130231 - LYPLAL1---[]---SLC30A10



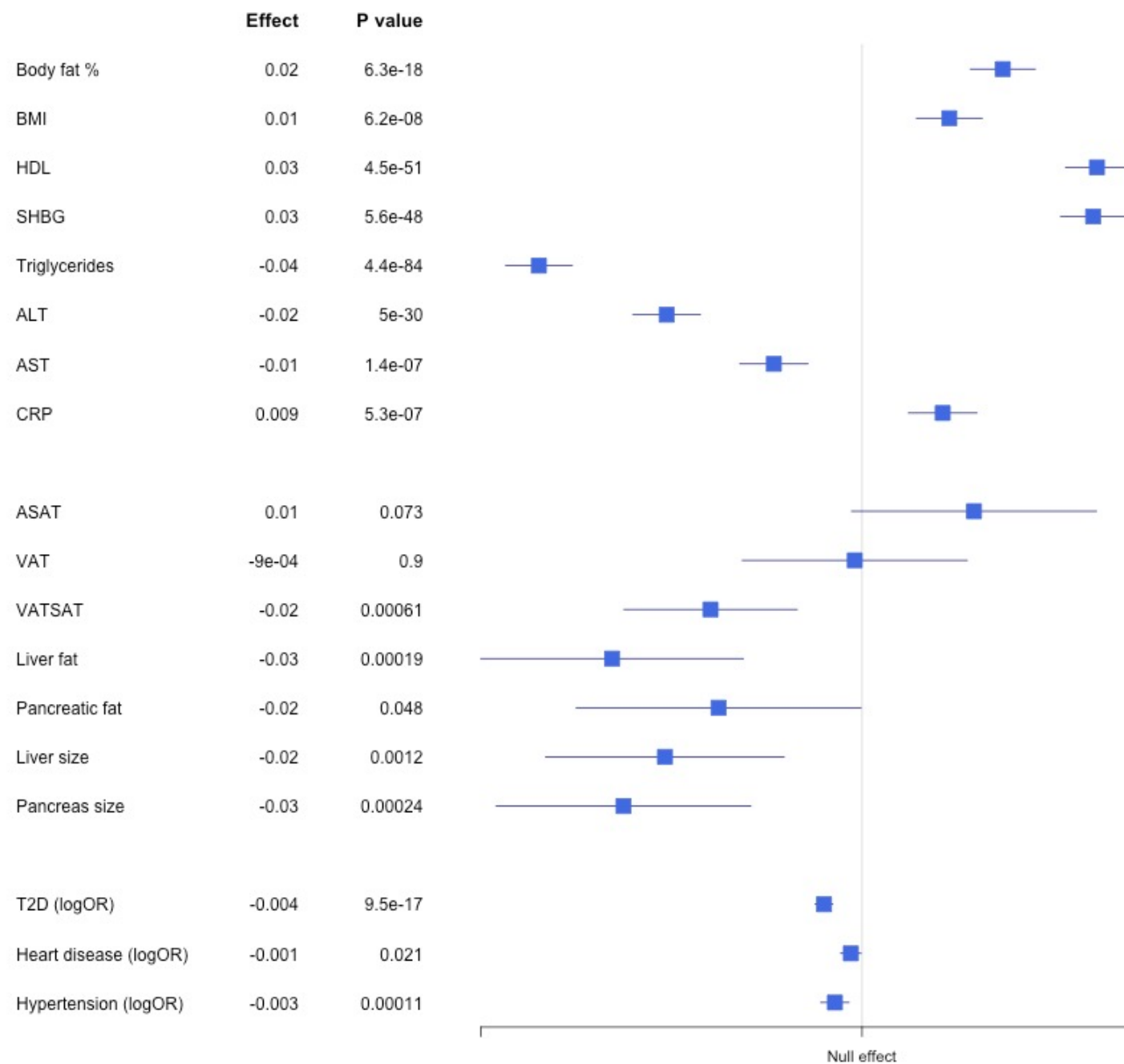
SF 8c

rs11664106 - SMCHD1-EMILIN2



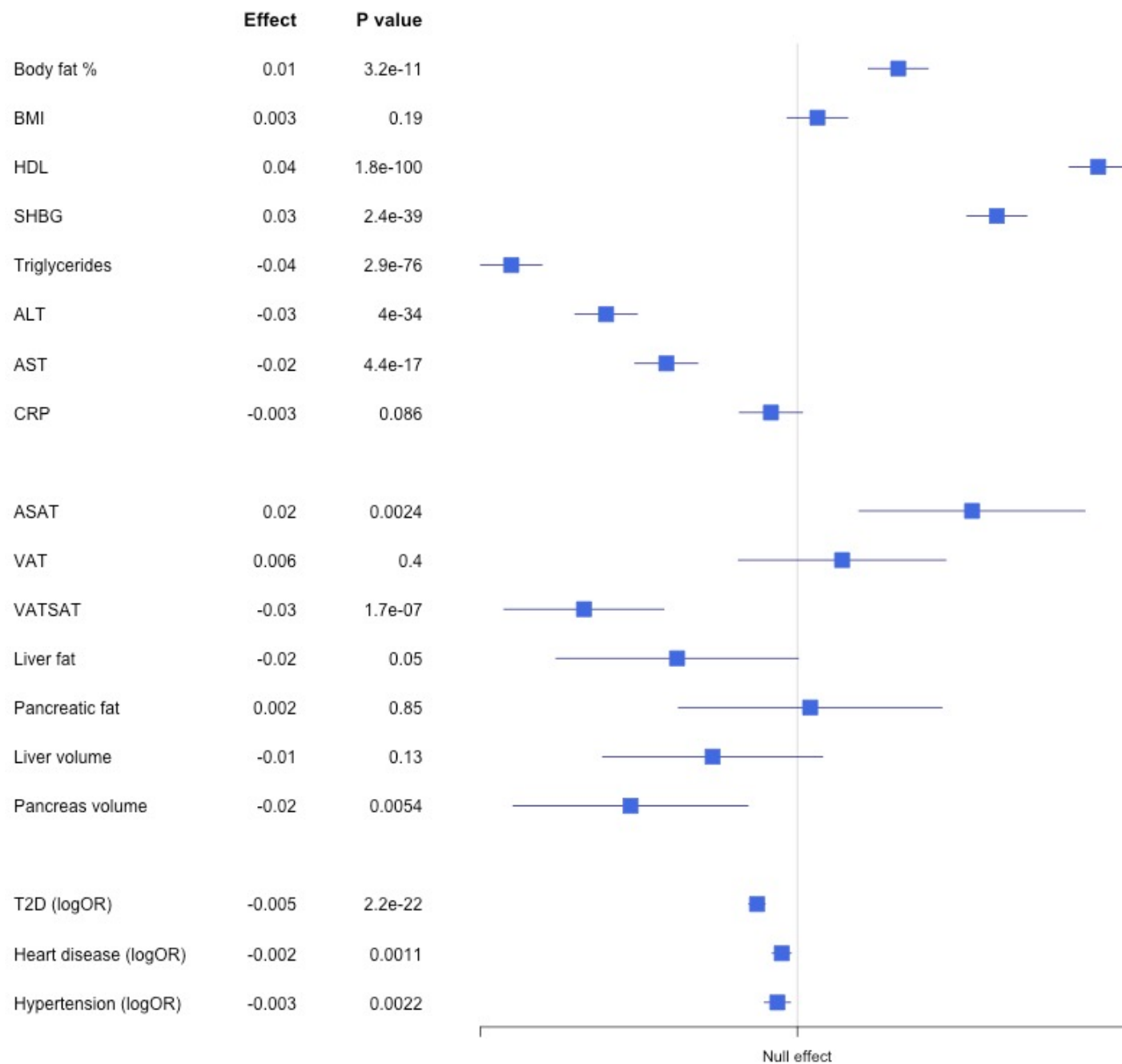
SF 8d

rs13389219 - GRB14--[]--COBLL1



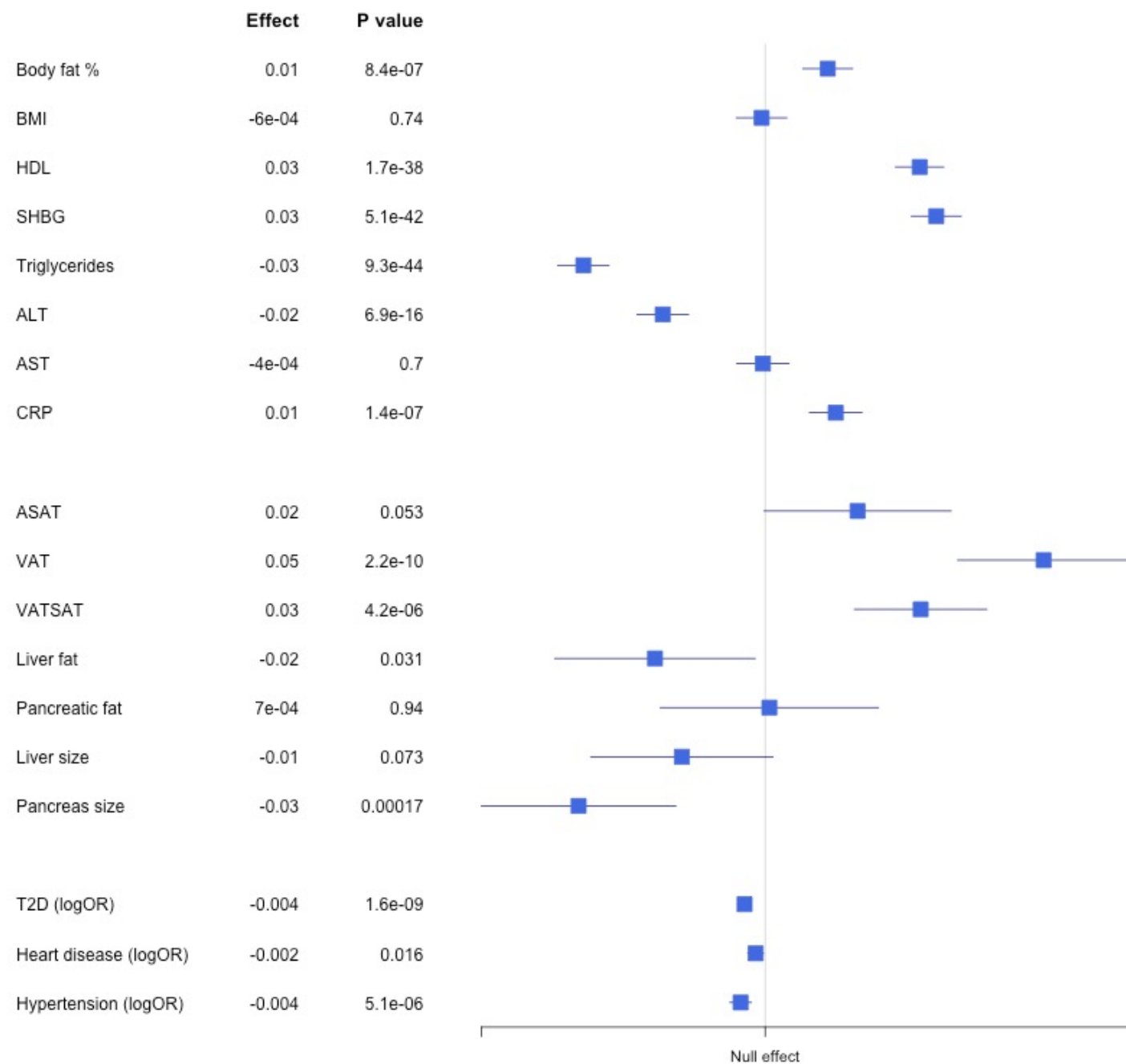
SF 8e

rs2943653 - NYAP2---[]---IRS1



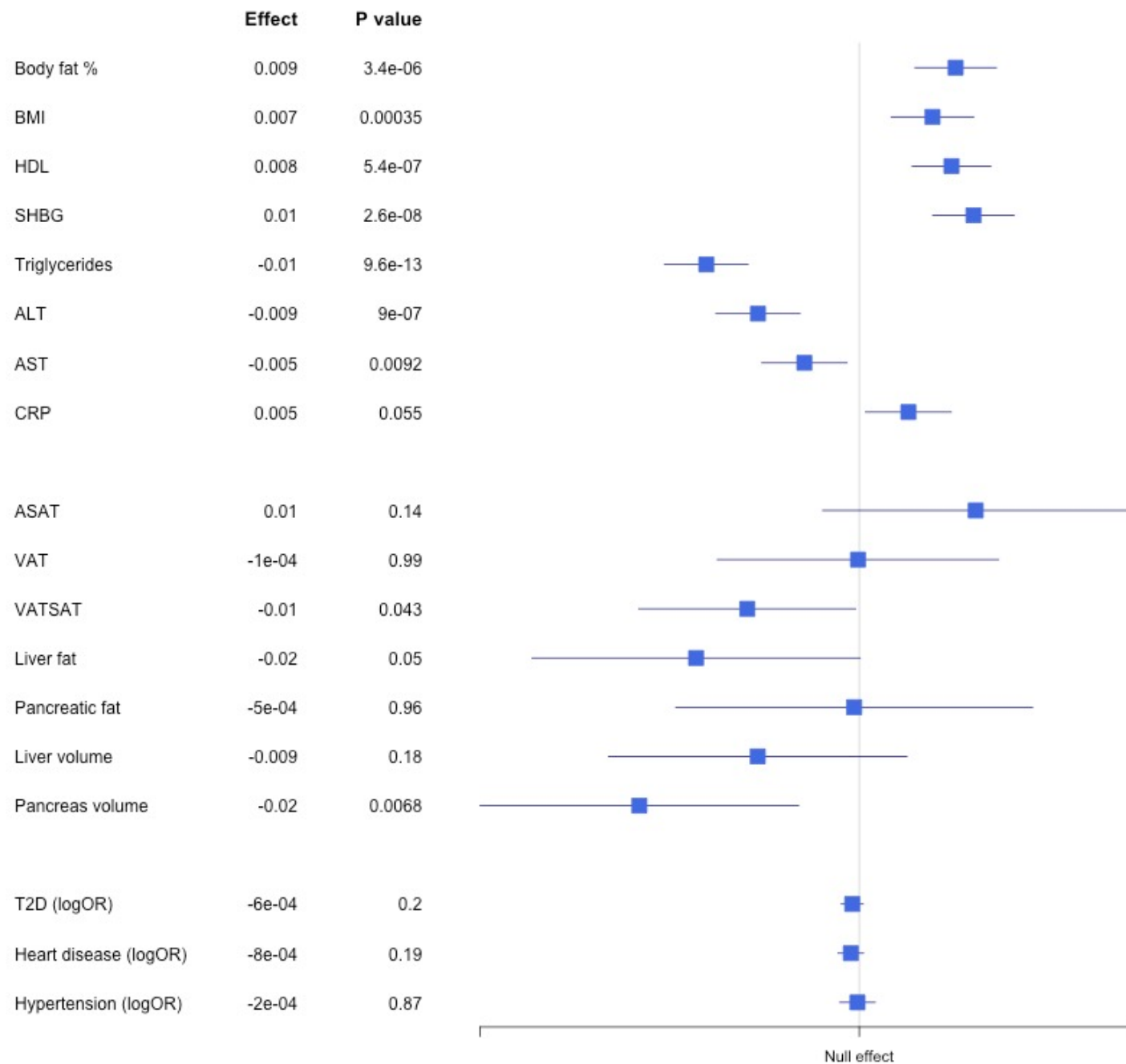
SF 8f

rs30351 - ANKRD55---[]---MAP3K1



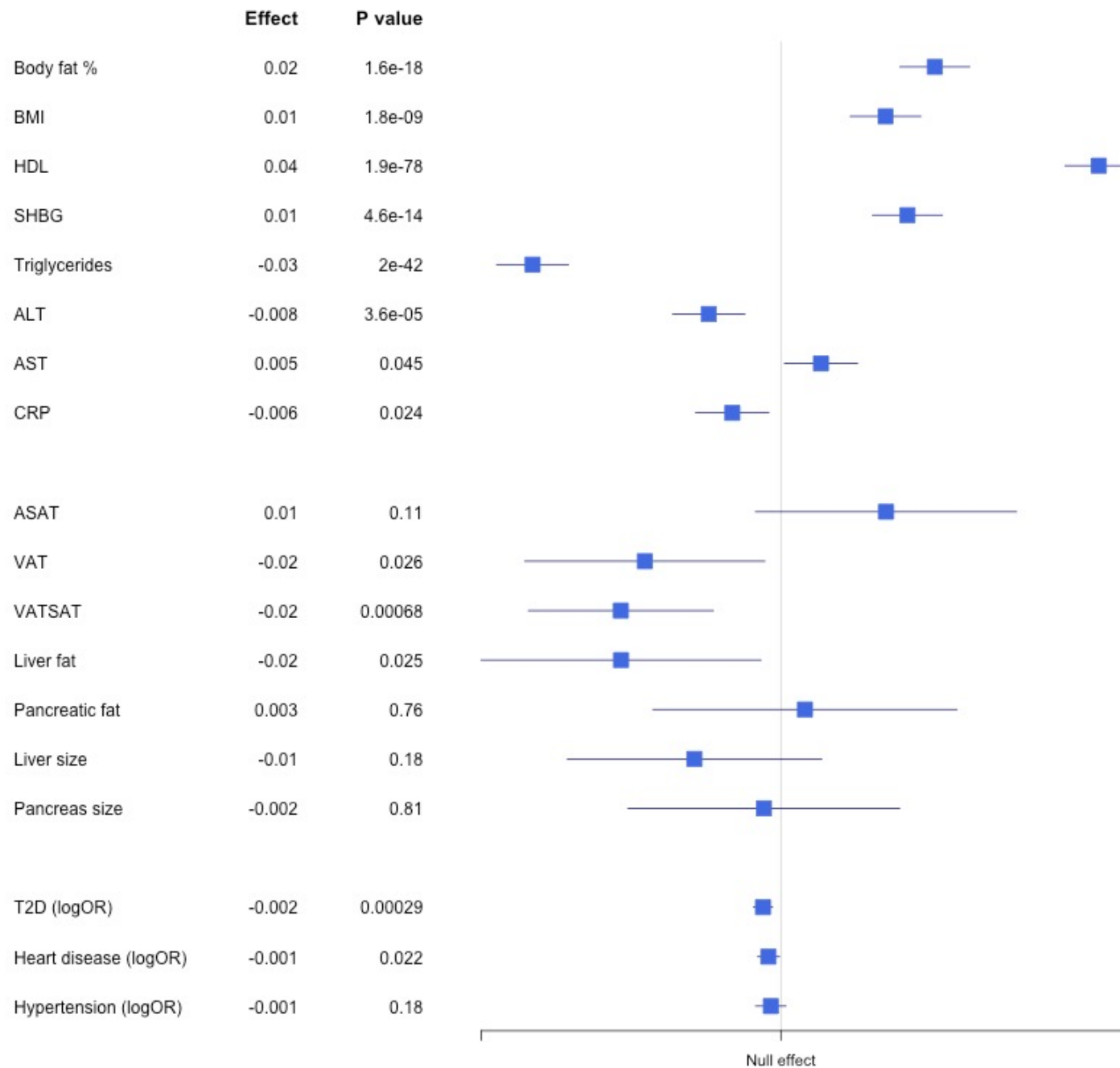
SF 8g

rs4450871 - MSX1---[]--CYTL1



SF 8h

rs7133378 - [DNAH10]



UK Biobank C-reactive protein

