

SUPPLEMENTARY MATERIAL

Genetic risk of obesity as a modifier of associations between neighbourhood environment and body mass index: an observational study of 335 046 UK Biobank participants

Kate E Mason, Luigi Palla, Neil Pearce, Jody Phelan, Steven Cummins

Supplementary Table 1. SNPs included in each polygenic risk score

SNP	Chr	Position	Gene	BMI-increasing allele	Effect size (β coefficient per effect allele, SD units of BMI)	Included in 69-SNP risk score	Included in 91-SNP risk score	Reason for exclusion ^{1,2}
rs1558902	16	52,361,075	<i>FTO</i>	A	0.0818	Yes	Yes	
rs17024393	1	109,956,211	<i>GNAT2</i>	C	0.0658	Yes	Yes	
rs13021737	2	622,348	<i>TMEM18</i>	G	0.0601	Yes	Yes	
rs6567160	18	55,980,115	<i>MC4R</i>	C	0.0556	Yes	Yes	
rs11847697	14	29,584,863	<i>PRKD1</i>	T	0.0492	Yes	Yes	
rs16851483	3	142,758,126	<i>RASA2</i>	T	0.0483	Yes	Yes	
rs543874	1	176,156,103	<i>SEC16B</i>	G	0.0482	Yes	Yes	
rs13107325	4	103,407,732	<i>SLC39A8</i>	T	0.0477	No	No	Possible pleiotropy
rs1516725	3	187,306,698	<i>ETV5</i>	C	0.0451	Yes	Yes	
rs2207139	6	50,953,449	<i>TFAP2B</i>	G	0.0447	Yes	Yes	
rs11030104	11	27,641,093	<i>BDNF</i>	A	0.0414	No	No	Possible pleiotropy
rs12446632	16	19,842,890	<i>GPRC5B</i>	G	0.0403	Yes	Yes	
rs10938397	4	44,877,284	<i>GNPDA2</i>	G	0.0402	Yes	Yes	
rs7899106	10	87,400,884	<i>GRID1</i>	G	0.0395	Yes	Yes	
rs2287019	19	50,894,012	<i>QPCTL</i>	C	0.0360	Yes	Yes	
rs11727676	4	145,878,514	<i>HHIP</i>	T	0.0358	Yes	Yes	
rs16907751	8	81,538,012	<i>ZBTB10</i>	C	0.0350	No	Yes	Identified in secondary meta-analyses only
rs12429545	13	53,000,207	<i>OLFM4</i>	A	0.0334	Yes	Yes	
rs3101336	1	72,523,773	<i>NEGR1</i>	C	0.0334	Yes	Yes	
rs2245368	7	76,446,079	<i>DTX2P1</i>	C	0.0317	Yes	Yes	
rs7138803	12	48,533,735	<i>BCDIN3D</i>	A	0.0315	Yes	Yes	
rs16951275	15	65,864,222	<i>MAP2K5</i>	T	0.0311	Yes	Yes	
rs3888190	16	28,796,987	<i>ATP2A1</i>	A	0.0309	No	No	Possible pleiotropy
rs11191560	10	104,859,028	<i>NT5C2</i>	C	0.0308	Yes	Yes	
rs10182181	2	25,003,800	<i>ADCY3</i>	G	0.0307	Yes	Yes	
rs11057405	12	121,347,850	<i>CLIP1</i>	G	0.0307	Yes	Yes	

SNP	Chr	Position	Gene	BMI-increasing allele	Effect size (β coefficient per effect allele, SD units of BMI)	Included in 69-SNP risk score	Included in 91-SNP risk score	Reason for exclusion ^{1,2}
rs17001654	4	77,348,592	SCARB2	G	0.0306	No	No	Linkage disequilibrium
rs9581854	13	26,915,782	MTIF3	T	0.0298	Yes	Yes	
rs13078960	3	85,890,280	CADM2	G	0.0297	Yes	Yes	
rs3810291	19	52,260,843	ZC3H4	A	0.0283	Yes	Yes	
rs13191362	6	162,953,340	PARK2	A	0.0277	Yes	Yes	
rs3817334	11	47,607,569	MTCH2	T	0.0262	Yes	Yes	
rs2112347	5	75,050,998	POC5	T	0.0261	Yes	Yes	
rs2075650	19	50,087,459	TOMM40	A	0.0258	No	No	Linkage disequilibrium
rs10968576	9	28,404,339	LINGO2	G	0.0249	Yes	Yes	
rs17094222	10	102,385,430	HIF1AN	C	0.0249	Yes	Yes	
rs2121279	2	142,759,755	LRP1B	T	0.0245	Yes	Yes	
rs12566985	1	74,774,781	FPGT	G	0.0242	Yes	Yes	
rs7141420	14	78,969,207	NRXN3	T	0.0235	Yes	Yes	
rs7903146	10	114,748,339	TCF7L2	C	0.0234	No	Yes	Not included in Tyrrell et al's GRS (reason unclear)
rs13201877	6	137,717,234	IFNGR1	G	0.0233	No	Yes	Identified in secondary meta-analyses only
rs10132280	14	24,998,019	STXBP6	C	0.0230	Yes	Yes	
rs1016287	2	59,159,129	LINC01122	T	0.0229	Yes	Yes	
rs657452	1	49,362,434	AGBL4	A	0.0227	Yes	Yes	
rs758747	16	3,567,359	NLRC3	T	0.0225	Yes	Yes	
rs17405819	8	76,969,139	HNF4G	T	0.0224	Yes	Yes	
rs205262	6	34,671,142	C6orf106	G	0.0221	Yes	Yes	
rs7599312	2	213,121,476	ERBB4	G	0.0220	Yes	Yes	
rs11165643	1	96,696,685	PTBP2	T	0.0218	Yes	Yes	
rs12286929	11	114,527,614	CADM1	G	0.0217	Yes	Yes	
rs7243357	18	55,034,299	GRP	T	0.0217	Yes	Yes	
rs12401738	1	78,219,349	FUBP1	A	0.0211	Yes	Yes	
rs17203016	2	207,963,763	CREB1	G	0.0210	No	Yes	Identified in secondary meta-analyses only

SNP	Chr	Position	Gene	BMI-increasing allele	Effect size (β coefficient per effect allele, SD units of BMI)	Included in 69-SNP risk score	Included in 91-SNP risk score	Reason for exclusion ^{1,2}
rs4256980	11	8,630,515	TRIM66	G	0.0209	Yes	Yes	
rs11126666	2	26,782,315	KCNK3	A	0.0207	Yes	Yes	
rs12885454	14	28,806,589	PRKD1	C	0.0207	Yes	Yes	
rs2650492	16	28,240,912	SBK1	A	0.0207	Yes	Yes	
rs1167827	7	75,001,105	HIP1	G	0.0202	Yes	Yes	
rs9914578	17	1,951,886	SMG6	G	0.0201	No	Yes	Identified in secondary meta-analyses only
rs2365389	3	61,211,502	FHIT	C	0.0200	Yes	Yes	
rs2176598	11	43,820,854	HSD17B12	T	0.0198	Yes	Yes	
rs1460676	2	164,275,935	FIGN	C	0.0197	No	Yes	Identified in secondary meta-analyses only
rs2820292	1	200,050,910	NAV1	C	0.0195	Yes	Yes	
rs17724992	19	18,315,825	PGPEP1	A	0.0194	Yes	Yes	
rs1000940	17	5,223,976	RABEP1	G	0.0192	Yes	Yes	
rs2033732	8	85,242,264	RALYL	C	0.0192	Yes	Yes	
rs9925964	16	31,037,396	KAT8	A	0.0192	No	No	Linkage disequilibrium
rs9641123	7	93,035,668	CALCR	C	0.0191	No	Yes	Identified in secondary meta-analyses only
rs2033529	6	40,456,631	TDRG1	G	0.0190	No	Yes	Not included in Tyrrell et al's GRS because unavailable
rs1928295	9	119,418,304	TLR4	T	0.0188	Yes	Yes	
rs3849570	3	81,874,802	GBE1	A	0.0188	Yes	Yes	
rs6091540	20	50,521,269	ZFP64	C	0.0188	No	Yes	Identified in secondary meta-analyses only
rs9400239	6	109,084,356	FOXO3	C	0.0188	Yes	Yes	
rs9374842	6	120,227,364	LOC285762	T	0.0187	No	Yes	Identified in secondary meta-analyses only
rs6804842	3	25,081,441	RARB	G	0.0185	Yes	Yes	
rs12940622	17	76,230,166	RPTOR	G	0.0182	Yes	Yes	
rs29941	19	39,001,372	KCTD15	G	0.0182	Yes	Yes	
rs7164727	15	70,881,044	LOC100287559	T	0.0180	No	Yes	Identified in secondary meta-analyses only
rs4740619	9	15,624,326	C9orf93	T	0.0179	Yes	Yes	
rs1528435	2	181,259,207	UBE2E3	T	0.0178	Yes	Yes	

SNP	Chr	Position	Gene	BMI-increasing allele	Effect size (β coefficient per effect allele, SD units of BMI)	Included in 69-SNP risk score	Included in 91-SNP risk score	Reason for exclusion ^{1,2}
rs11583200	1	50,332,407	ELAVL4	C	0.0177	Yes	Yes	
rs3736485	15	49,535,902	DMXL2	A	0.0176	Yes	Yes	
rs1441264	13	78,478,920	MIR548A2	A	0.0175	No	Yes	Identified in secondary meta-analyses only
rs10733682	9	128,500,735	LMX1B	A	0.0174	Yes	Yes	
rs6477694	9	110,972,163	EPB41L4B	C	0.0174	Yes	Yes	
rs11688816	2	62,906,552	EHBP1	G	0.0172	Yes	Yes	
rs9540493	13	65,103,705	MIR548X2	A	0.0172	No	Yes	Identified in secondary meta-analyses only
rs2080454	16	47,620,091	CBLN1	C	0.0168	No	Yes	Identified in secondary meta-analyses only
rs1808579	18	19,358,886	C18orf8	C	0.0167	Yes	Yes	
rs977747	1	47,457,264	TAL1	T	0.0167	No	Yes	Identified in secondary meta-analyses only
rs6465468	7	95,007,450	ASB4	T	0.0166	No	Yes	Identified in secondary meta-analyses only
rs2836754	21	39,213,610	ETS2	C	0.0164	No	Yes	Identified in secondary meta-analyses only
rs7239883	18	38,401,669	LOC284260	G	0.0164	No	Yes	Identified in secondary meta-analyses only
rs7715256	5	153,518,086	GALNT10	G	0.0163	No	Yes	Identified in secondary meta-analyses only
rs4787491	16	29,922,838	INO80E	G	0.0159	No	Yes	Identified in secondary meta-analyses only
rs492400	2	219,057,996	USP37	C	0.0158	No	Yes	Identified in secondary meta-analyses only
rs2176040	2	226,801,046	LOC646736	A	0.0141	No	Yes	Identified in secondary meta-analyses only

Note: This table is derived from Locke et al (2015), with additional information from Tyrrell et al (2017).

Supplementary Table 2. Results of sensitivity analyses using unweighted genetic risk scores

	69-SNP unweighted imputed GRS (n=332,127)			91-SNP unweighted imputed GRS (n=326,604)		
	Quintile of genetic risk	Mean BMI difference for unit increase in neighbourhood exposure	P-interaction	Quintile of genetic risk	Mean BMI difference for unit increase in neighbourhood exposure	P-interaction
Fast-food proximity (log (base 10) of distance (m) to nearest fast-food outlet)	Q1	-0.094 (-0.229, 0.042)	0.064	Q1	-0.103 (-0.237, 0.030)	0.116
	Q2	-0.123 (-0.250, 0.004)		Q2	-0.130 (-0.254, -0.005)	
	Q3	-0.143 (-0.268, -0.017)		Q3	-0.146 (-0.269, -0.023)	
	Q4	-0.162 (-0.289, -0.034)		Q4	-0.161 (-0.286, -0.037)	
	Q5	-0.191 (-0.327, -0.055)		Q5	-0.186 (-0.319, -0.053)	
Availability of PA facilities (number of formal PA facilities within 1km of home address)	Q1	-0.069 (-0.096, -0.042)	0.119	Q1	-0.069 (-0.096, -0.042)	0.110
	Q2	-0.073 (-0.099, -0.047)		Q2	-0.073 (-0.099, -0.047)	
	Q3	-0.075 (-0.101, -0.050)		Q3	-0.076 (-0.102, -0.050)	
	Q4	-0.078 (-0.104, -0.052)		Q4	-0.078 (-0.104, -0.052)	
	Q5	-0.081 (-0.108, -0.054)		Q5	-0.082 (-0.109, -0.055)	

Supplementary Table 3. Results of sensitivity analyses using an expanded sample including observations from UK Biobank participants of non-White ethnicities

91-SNP weighted imputed GRS (N=374,339)			
	Quintile of genetic risk	Mean BMI difference for unit increase in neighbourhood exposure	P-interaction
Fast-food proximity (log (base 10) of distance (m) to nearest fast-food outlet)	Q1	-0.086 (-0.208, 0.036)	0.026
	Q2	-0.119 (-0.233, -0.005)	
	Q3	-0.140 (-0.252, -0.028)	
	Q4	-0.161 (-0.274, -0.047)	
	Q5	-0.195 (-0.318, -0.073)	
Availability of PA facilities (number of formal PA facilities within 1km of home address)	Q1	-0.068 (-0.095, -0.041)	0.197
	Q2	-0.071 (-0.097, -0.046)	
	Q3	-0.072 (-0.098, -0.046)	
	Q4	-0.074 (-0.100, -0.048)	
	Q5	-0.077 (-0.104, -0.050)	

Supplementary Table 4. Results of sensitivity analyses additionally adjusting for extra 30 genetic ancestry principal components and birth location

P-for-interaction	Fast-food proximity		Availability of PA facilities	
	Adjusted for 40 ancestral PCs	Adjusted for 40 PCs & place of birth	Adjusted for 40 ancestral PCs	Adjusted for 40 PCs & place of birth
69-SNP GRS	0.015	0.030	0.385	0.395
91-SNP GRS	0.028	0.069	0.536	0.550
rs1558902 (FTO)	0.066	0.088	0.928	0.904
rs6567160 (MC4R)	0.009	0.025	0.617	0.766
rs13021737 (TMEM18)	0.999	0.967	0.081	0.063
rs13078960 (CADM2)	0.108	0.142	0.407	0.361
rs10938397 (GNPDA2)	0.306	0.301	0.732	0.964
rs7141420 (NRXN3)	0.519	0.665	0.114	0.155

REFERENCES

1. Tyrrell J, Wood AR, Ames RM, et al. Gene–obesogenic environment interactions in the UK Biobank study. *Int J Epidemiol*. 2017;dyw337. doi:10.1093/ije/dyw337.
2. Locke AE, Kahali B, Berndt SI, et al. Genetic studies of body mass index yield new insights for obesity biology. *Nature*. 2015;518(7538):197-206. doi:10.1038/nature14177.