

SUPPLEMENTARY DATA

Supplementary Table 1. Information of the 97 SNPs included in the study

SNP	Nearest gene	Chromosome	Position	Effect allele	Other allele	β coefficient*
rs1000940	RABEP1	17	5,223,976	G	A	0.019
rs10132280	STXBP6	14	24,998,019	C	A	0.023
rs1016287	LINC01122	2	59,159,129	T	C	0.023
rs10182181	ADCY3	2	25,003,800	G	A	0.031
rs10733682	LMX1B	9	128,500,735	A	G	0.017
rs10938397	GNPDA2	4	44,877,284	G	A	0.04
rs10968576	LINGO2	9	28,404,339	G	A	0.025
rs11030104	BDNF	11	27,641,093	A	G	0.041
rs11057405	CLIP1	12	121,347,850	G	A	0.031
rs11126666	KCNK3	2	26,782,315	A	G	0.021
rs11165643	PTBP2	1	96,696,685	T	C	0.022
rs11191560	NT5C2	10	104,859,028	C	T	0.031
rs11583200	ELAVL4	1	50,332,407	C	T	0.018
rs1167827	HIP1	7	75,001,105	G	A	0.02
rs11688816	EHBP1	2	62,906,552	G	A	0.017
rs11727676	HHIP	4	145,878,514	T	C	0.036
rs11847697	PRKD1	14	29,584,863	T	C	0.049
rs12016871	MTIF3	13	26,915,782	T	C	0.03
rs12286929	CADM1	11	114,527,614	G	A	0.022
rs12401738	FUBP1	1	78,219,349	A	G	0.021
rs12429545	OLFM4	13	53,000,207	A	G	0.033
rs12446632	GPRC5B	16	19,842,890	G	A	0.04
rs12566985	FPGT-TNNI3K	1	74,774,781	G	A	0.024
rs12885454	PRKD1	14	28,806,589	C	A	0.021
rs12940622	RPTOR	17	76,230,166	G	A	0.018
rs13021737	TMEM18	2	622,348	G	A	0.06
rs13078960	CADM2	3	85,890,280	G	T	0.03
rs13107325	SLC39A8	4	103,407,732	T	C	0.048
rs13191362	PARK2	6	162,953,340	A	G	0.028
rs13201877	IFNGR1	6	137,717,234	G	A	0.024
rs1441264	MIR548A2	13	78,478,920	A	G	0.017
rs1460676	FIGN	2	164,275,935	C	T	0.021
rs1516725	ETV5	3	187,306,698	C	T	0.045
rs1528435	UBE2E3	2	181,259,207	T	C	0.018
rs1558902	FTO	16	52,361,075	A	T	0.082
rs16851483	RASA2	3	142,758,126	T	G	0.048
rs16907751	ZBTB10	8	81,538,012	C	T	0.047
rs16951275	MAP2K5	15	65,864,222	T	C	0.031
rs17001654	SCARB2	4	77,348,592	G	C	0.031
rs17024393	GNAT2	1	109,956,211	C	T	0.066
rs17094222	HIF1AN	10	102,385,430	C	T	0.025
rs17203016	CREB1	2	207,963,763	G	A	0.021
rs17405819	HNF4G	8	76,969,139	T	C	0.022
rs17724992	PGPEP1	19	18,315,825	A	G	0.019
rs1808579	C18orf8	18	19,358,886	C	T	0.017
rs1928295	TLR4	9	119,418,304	T	C	0.019
rs2033529	TDRG1	6	40,456,631	G	A	0.019
rs2033732	RALYL	8	85,242,264	C	T	0.019
rs205262G	C6orf106	6	34,671,142	G	A	0.022
rs2075650	TOMM40	19	50,087,459	A	G	0.026
rs2080454	CBLN1	16	47,620,091	C	A	0.017
rs2112347	POC5	5	75,050,998	T	G	0.026
rs2121279	LRP1B	2	142,759,755	T	C	0.025
rs2176040	LOC646736	2	226,801,046	A	G	0.024
rs2176598	HSD17B12	11	43,820,854	T	C	0.02
rs2207139	TFAP2B	6	50,953,449	G	A	0.045

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rs2245368	PMS2L11	7	76,446,079	C	T	0.032
rs2287019	QPCTL	19	50,894,012	C	T	0.036
rs2365389	FHIT	3	61,211,502	C	T	0.02
rs2650492	SBK1	16	28,240,912	A	G	0.021
rs2820292	NAV1	1	200,050,910	C	A	0.02
rs2836754	ETS2	21	39,213,610	C	T	0.017
rs29941A	KCTD15	19	39,001,372	G	A	0.018
rs3101336	NEGR1	1	72,523,773	C	T	0.033
rs3736485	DMXL2	15	49,535,902	A	G	0.018
rs3810291	ZC3H4	19	52,260,843	A	G	0.028
rs3817334	MTCH2	11	47,607,569	T	C	0.026
rs3849570	GBE1	3	81,874,802	A	C	0.019
rs3888190	ATP2A1	16	28,796,987	A	C	0.031
rs4256980	TRIM66	11	8,630,515	G	C	0.021
rs4740619	C9orf93	9	15,624,326	T	C	0.018
rs4787491	INO80E	16	29,922,838	G	A	0.022
rs492400C	USP37	2	219,057,996	C	T	0.024
rs543874G	SEC16B	1	176,156,103	G	A	0.048
rs6091540	ZFP64	20	50,521,269	C	T	0.03
rs6465468	ASB4	7	95,007,450	T	G	0.025
rs6477694	EPB41L4B	9	110,972,163	C	T	0.017
rs6567160	MC4R	18	55,980,115	C	T	0.056
rs657452A	AGBL4	1	49,362,434	A	G	0.023
rs6804842	RARB	3	25,081,441	G	A	0.019
rs7138803	BCDIN3D	12	48,533,735	A	G	0.032
rs7141420	NRXN3	14	78,969,207	T	C	0.024
rs7164727	LOC100287559	15	70,881,044	T	C	0.019
rs7239883	LOC284260	18	38,401,669	G	A	0.023
rs7243357	GRP	18	55,034,299	T	G	0.022
rs758747T	NLRC3	16	3,567,359	T	C	0.023
rs7599312	ERBB4	2	213,121,476	G	A	0.022
rs7715256	GALNT10	5	153,518,086	G	T	0.017
rs7899106	GRID1	10	87,400,884	G	A	0.04
rs7903146	TCF7L2	10	114,748,339	C	T	0.023
rs9374842	LOC285762	6	120,227,364	T	C	0.023
rs9400239	FOXO3	6	109,084,356	C	T	0.019
rs9540493	MIR548X2	13	65,103,705	A	G	0.021
rs9641123	CALCR	7	93,035,668	C	G	0.029
rs977747T	TAL1	1	47,457,264	T	G	0.017
rs9914578	SMG6	17	1,951,886	G	C	0.02
rs9925964	KAT8	16	31,037,396	A	G	0.019

* Obtained from the GWAS meta-analysis by Locke AE et al. Genetic studies of body mass index yield new insights for obesity biology. *Nature* 2015;518:197-206.

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Supplementary Table 2. Information of the SNPs associated with early-life BMI

Proxy SNP	D'	Effect SNP	Chr	Position	Closest gene	BMI increasing / other allele	β coefficient*
rs1558902	1	rs9940128	16	52358255	<i>FTO</i>	A/G	0.083
rs13021737	1	rs12463617	2	619244	<i>TMEM18</i>	C/A	0.100
rs6567160	0.87	rs7234864	18	55885837	<i>MC4R</i>	T/C	0.081
rs12566985	1	rs12142020	1	74772599	<i>TNNI3K</i>	T/A	0.056
rs543874	1	rs591120	1	176169376	<i>SEC16B</i>	C/G	0.050
rs10938397	1	rs13130484	4	44870448	<i>GNPDA2</i>	T/C	0.048

* Obtained from the GWAS of adolescents and young adults by Graff M et al. Genome-wide analysis of BMI in adolescents and young adults reveals additional insight into the effects of genetic loci over the life course. *Hum Mol Genet* 2013;22:3597-3607.

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Supplementary Table 3. Mean BMI and BMI change (standard deviation, kg/m²) at each age in the study sample and overall NHS/HPFS cohorts

Outcome	Study sample	Overall cohorts
Women		
BMI at age 18	21.5 (3.0)	21.3 (3.0)
BMI at age 45	24.5 (4.9)	24.7 (4.7)
BMI at age 50	25.5 (5.0)	25.4 (4.9)
BMI at age 55	26.2 (5.1)	26.0 (5.1)
BMI at age 60	26.8 (5.4)	26.5 (5.3)
BMI at age 65	27.1 (5.4)	26.7 (5.3)
BMI at age 70	26.6 (5.2)	26.5 (5.2)
BMI at age 75	26.1 (5.1)	25.9 (5.0)
BMI at age 80	25.2 (4.8)	25.1 (4.7)
BMI at age 85	24.3 (4.5)	24.3 (4.4)
BMI change from age 18 to 45	3.0 (4.1)	3.4 (4.0)
BMI change from age 45 to 65	2.7 (3.4)	2.6 (3.3)
BMI change from age 65 to 80	-0.9 (3.0)	-0.6 (3.0)
Men		
BMI at age 21	23.1 (2.8)	23.0 (3.0)
BMI at age 45	25.5 (3.5)	25.6 (3.4)
BMI at age 50	25.6 (3.6)	26.0 (3.6)
BMI at age 55	26.0 (3.7)	26.3 (3.6)
BMI at age 60	26.3 (3.6)	26.4 (3.6)
BMI at age 65	26.5 (3.7)	26.3 (3.7)
BMI at age 70	26.3 (3.7)	26.0 (3.7)
BMI at age 75	26.0 (3.6)	25.7 (3.6)
BMI at age 80	25.4 (3.4)	25.1 (3.3)
BMI at age 85	24.6 (3.3)	24.5 (3.3)
BMI change from age 21 to 45	2.5 (2.8)	2.2 (2.6)
BMI change from age 45 to 65	1.0 (2.5)	1.4 (2.2)
BMI change from age 65 to 80	-0.3 (2.1)	-0.3 (2.1)

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Supplementary Table 4. Relationship of GRS with BMI at different ages in women and men.

Outcome	Mean BMI difference per 10 alleles, β (95% CI), kg/m²	<i>P</i> for main effect of GRS	<i>P</i> for sex-GRS interaction
Women			
BMI at age 18	0.76 (0.66 to 0.85)	<0.0001	0.01
BMI at age 45	1.30 (1.11 to 1.49)	<0.0001	0.04
BMI at age 50	1.27 (1.10 to 1.43)	<0.0001	0.01
BMI at age 55	1.32 (1.16 to 1.48)	<0.0001	0.0001
BMI at age 60	1.35 (1.18 to 1.52)	<0.0001	<0.0001
BMI at age 65	1.30 (1.12 to 1.47)	<0.0001	<0.0001
BMI at age 70	1.13 (0.95 to 1.31)	<0.0001	0.0006
BMI at age 75	1.06 (0.85 to 1.27)	<0.0001	0.002
BMI at age 80	0.88 (0.61 to 1.15)	<0.0001	0.05
BMI at age 85	0.86 (0.38 to 1.33)	<0.0001	0.15
Men			
BMI at age 21	0.57 (0.46 to 0.68)	<0.0001	
BMI at age 45	0.91 (0.65 to 1.16)	<0.0001	
BMI at age 50	0.86 (0.65 to 1.08)	<0.0001	
BMI at age 55	0.77 (0.59 to 0.95)	<0.0001	
BMI at age 60	0.72 (0.56 to 0.88)	<0.0001	
BMI at age 65	0.67 (0.52 to 0.82)	<0.0001	
BMI at age 70	0.66 (0.50 to 0.83)	<0.0001	
BMI at age 75	0.60 (0.42 to 0.77)	<0.0001	
BMI at age 80	0.53 (0.31 to 0.74)	<0.0001	
BMI at age 85	0.48 (0.20 to 0.76)	<0.0001	

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Supplementary Table 5. Relationship of GRS with BMI at different ages in women according to age at menopause.

BMI at different ages	Age at menopause, year								<i>P</i> for interaction†
	<45		45-49		50-54		≥55		
	n	β (95% CI)*	n	β (95% CI)*	n	β (95% CI)*	n	β (95% CI)*	
Age 18	952	0.91 (0.60 to 1.21)	2229	0.72 (0.53 to 0.92)	5445	0.77 (0.65 to 0.90)	823	0.52 (0.21 to 0.82)	0.36
Age 45	658	1.39 (0.79 to 1.99)	1495	1.32 (0.93 to 1.71)	3493	1.31 (1.06 to 1.56)	564	0.87 (0.20 to 1.54)	0.62
Age 50	887	1.21 (0.68 to 1.74)	2101	1.40 (1.07 to 1.73)	4996	1.24 (1.02 to 1.45)	777	0.99 (0.38 to 1.60)	0.65
Age 55	975	1.18 (0.66 to 1.71)	2300	1.58 (1.26 to 1.91)	5637	1.28 (1.07 to 1.49)	852	0.96 (0.38 to 1.53)	0.20
Age 60	965	1.15 (0.61 to 1.70)	2284	1.61 (1.27 to 1.95)	5571	1.33 (1.11 to 1.55)	846	1.00 (0.41 to 1.59)	0.24
Age 65	915	1.14 (0.56 to 1.72)	2157	1.53 (1.18 to 1.88)	5336	1.26 (1.03 to 1.48)	805	1.11 (0.49 to 1.74)	0.50
Age 70	736	0.76 (0.14 to 1.38)	1775	1.36 (0.99 to 1.73)	4479	1.08 (0.84 to 1.32)	671	1.19 (0.51 to 1.87)	0.37
Age 75	480	0.88 (0.14 to 1.62)	1300	1.11 (0.68 to 1.54)	3251	1.06 (0.79 to 1.33)	471	0.97 (0.23 to 1.70)	0.95
Age 80	259	0.75 (-0.30 to 1.81)	687	0.96 (0.41 to 1.51)	1835	0.89 (0.55 to 1.23)	241	0.51 (-0.49 to 1.52)	0.86

* β represents the mean BMI difference per 10-allele increment in the GRS.

† *P* for interaction was calculated by the F test with 3 degrees of freedom for the product terms between age at menopause (4 categories) and GRS (continuous).

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Supplementary Table 6. Relationship of eGRS with BMI and BMI change at different ages in women and men.

Outcome	Mean BMI difference per 10 alleles, β (95% CI), kg/m²	P value
Women		
BMI at age 18	0.24 (0.21 to 0.28)	<0.0001
BMI at age 45	0.36 (0.28 to 0.43)	<0.0001
BMI at age 50	0.34 (0.27 to 0.40)	<0.0001
BMI at age 55	0.35 (0.28 to 0.41)	<0.0001
BMI at age 60	0.35 (0.28 to 0.42)	<0.0001
BMI at age 65	0.33 (0.26 to 0.40)	<0.0001
BMI at age 70	0.27 (0.20 to 0.34)	<0.0001
BMI at age 75	0.21 (0.12 to 0.29)	<0.0001
BMI at age 80	0.17 (0.06 to 0.27)	0.002
BMI at age 85	0.30 (0.12 to 0.48)	0.001
BMI change from age 18 to 45	0.11 (0.04 to 0.18)	0.001
BMI change from age 45 to 65	0.01 (-0.05 to 0.07)	0.74
BMI change from age 65 to 80	-0.10 (-0.17 to -0.03)	0.003
Men		
BMI at age 21	0.18 (0.13 to 0.22)	<0.0001
BMI at age 45	0.30 (0.20 to 0.41)	<0.0001
BMI at age 50	0.27 (0.19 to 0.36)	<0.0001
BMI at age 55	0.24 (0.17 to 0.32)	<0.0001
BMI at age 60	0.22 (0.16 to 0.28)	<0.0001
BMI at age 65	0.19 (0.13 to 0.25)	<0.0001
BMI at age 70	0.18 (0.11 to 0.24)	<0.0001
BMI at age 75	0.13 (0.06 to 0.20)	<0.0001
BMI at age 80	0.09 (0.00 to 0.17)	0.05
BMI at age 85	0.08 (-0.03 to 0.19)	0.15
BMI change from age 18 to 45	0.12 (0.04 to 0.21)	0.005
BMI change from age 45 to 65	-0.03 (-0.10 to 0.05)	0.52
BMI change from age 65 to 80	-0.05 (-0.11 to 0.00)	0.07