

## SUPPLEMENTARY MATERIAL

**Supplementary Table S1.** Genetic variants included in the T2D PRS.

SNP	Locus	CHR	Pos	Alt Allele	$\beta$	Odd Ratio	MAF	P-value	N
rs3101336	NEGR1	1	72751185	C	0.018	1.018	0.450	3.07E-02	939912
rs2568958	NEGR1	1	72765116	A	0.022	1.022	0.438	1.64E-04	1082380
rs2815752	NEGR1	1	72812440	A	0.022	1.022	0.388	4.05E-04	1084120
rs10913469	SEC16B	1	177913519	C	0.032	1.033	0.163	1.74E-12	1073630
rs340874	PROX1	1	214159256	C	0.047	1.048	0.475	6.11E-32	1081640
rs2605100	LYPLAL1	1	219644224	G	0.030	1.031	0.213	3.75E-07	1090350
rs12022722	LYPLAL1	1	219651133	T	0.020	1.020	0.413	7.57E-06	917427
rs2820464	LYPLAL1	1	219693220	A	-0.029	0.972	0.175	4.82E-10	927501
rs2785980	LYPLAL1	1	219700519	C	-0.031	0.969	0.175	1.30E-13	1039880
rs4846567	SLC30A10	1	219750717	T	-0.033	0.967	0.125	1.17E-15	1078840
rs6548238	TMEM18	2	634905	C	0.054	1.055	0.113	1.66E-21	1083220
rs7561317	TMEM18	2	644953	G	0.056	1.058	0.238	2.67E-22	1023140
rs780094	GCKR	2	27741237	C	0.053	1.055	0.488	2.05E-34	1082280
rs13389219	GRB14	2	165528876	T	-0.054	0.947	0.400	5.98E-35	1080230
rs7607980	GRB14	2	165551201	C	-0.068	0.935	0.138	1.75E-19	851502
rs1801282	PPARG	3	12393125	G	-0.022	0.978	0.263	4.85E-02	18252
rs11708067	ADCY5	3	123065778	G	-0.072	0.930	0.100	1.06E-44	756464
rs11920090	SLC2A2	3	170717521	A	-0.027	0.974	0.188	1.47E-03	952836
rs4402960	IGF2BP2	3	185511687	T	0.096	1.101	0.425	4.15E-122	1088690
rs7647305	ETV5	3	185834290	C	0.026	1.027	0.213	7.70E-07	965163
rs10938397	GNPDA2	4	45182527	G	0.038	1.039	0.388	5.11E-17	1048050
rs10946398	CDKAL1	6	20661034	C	0.113	1.120	0.375	5.97E-144	1085220
rs2844479	AIF1	6	31572956	C	0.026	1.027	0.500	4.49E-09	1078460
rs2260000	PRRC2A	6	31593476	G	0.020	1.020	0.375	2.71E-05	930840
rs1077393	BAG6	6	31610529	G	0.019	1.019	0.500	1.41E-04	1081460
rs2191349	DGKB	7	15064309	T	0.051	1.053	0.488	1.23E-41	1081160
rs4607517	YKT6	7	44235668	A	0.032	1.032	0.088	2.65E-10	1082060
rs4731702	KLF14	7	130433384	T	-0.037	0.964	0.475	1.09E-20	1075480
rs972283	KLF14	7	130466854	G	0.035	1.036	0.463	5.05E-20	1067780
rs13266634	SLC30A8	8	118184783	T	-0.091	0.913	0.388	2.45E-124	1181190
rs11558471	SLC30A8	8	118185733	G	-0.088	0.916	0.313	8.78E-106	1082770
rs7034200	GLIS3	9	4289050	A	0.040	1.041	0.488	1.20E-23	1070410
rs10811661	GLIS3	9	22134094	C	-0.140	0.869	0.113	2.88E-146	930908
rs1111875	HHEX	10	94462882	T	-0.093	0.912	0.388	7.30E-95	938378
rs5015480	HHEX	10	94465559	T	-0.089	0.915	0.388	1.64E-128	1069430
rs7923837	HHEX	10	94481917	A	-0.094	0.911	0.350	1.62E-75	888616
rs10885122	ADRA2A	10	113042093	G	0.024	1.024	0.125	1.03E-05	1082070
rs7901695	TCF7L2	10	114754088	C	0.207	1.230	0.313	5.82E-226	209644

rs4506565	<i>TCF7L2</i>	10	114756041	T	0.216	1.241	0.313	6.14E-229	208956
rs7903146	<i>TCF7L2</i>	10	114758349	T	0.235	1.265	0.275	2.64E-97	249463
rs5215	<i>KCNJ11</i>	11	17408630	T	-0.056	0.945	0.363	5.74E-52	1192080
rs4074134	<i>BDNF</i>	11	27647285	T	-0.023	0.978	0.150	1.59E-05	937741
rs4923461	<i>BDNF</i>	11	27656910	G	-0.019	0.981	0.150	3.05E-05	931716
rs925946	<i>BDNF</i>	11	27667202	G	0.000	1.000	0.363	2.44E-05	951966
rs10501087	<i>BDNF</i>	11	27670108	C	-0.023	0.977	0.150	2.81E-06	934,105
rs6265	<i>BDNF</i>	11	27679916	T	-0.022	0.978	0.138	9.00E-07	1169040
rs10835211	<i>BDNF</i>	11	27701365	A	0.022	1.103	0.213	1.83E-02	818173
rs11605924	<i>CRY2</i>	11	45873091	C	-0.021	0.979	0.450	4.96E-08	964253
rs10838738	<i>MTCH2</i>	11	47663049	G	0.013	1.013	0.363	5.75E-03	1085580
rs174550	<i>FADS1</i>	11	61571478	C	-0.027	0.973	0.350	1.20E-10	1019910
rs10830963	<i>MTNR1B</i>	11	92708710	G	0.061	1.063	0.225	7.36E-43	1059540
rs7138803	<i>BCDIN3D</i>	12	50247468	A	0.023	1.023	0.425	1.35E-09	1089630
rs8049439	<i>ATXN2L</i>	16	28837515	C	0.019	1.019	0.413	2.76E-05	1191610
rs4788102	<i>SH2B1</i>	16	28873398	A	0.022	1.022	0.413	8.70E-06	933067
rs7498665	<i>SH2B1</i>	16	28883241	G	0.022	1.023	0.400	1.86E-06	1024050
rs6499640	<i>FTO</i>	16	53769677	A	0.027	1.027	0.425	5.97E-08	1080780
rs8050136	<i>FTO</i>	16	53816275	A	0.094	1.098	0.488	8.61E-102	1090360
rs3751812	<i>FTO</i>	16	53818460	T	0.096	1.100	0.488	2.47E-76	935802
rs9939609	<i>FTO</i>	16	53820527	A	0.092	1.096	0.488	5.44E-131	1063990
rs7190492	<i>FTO</i>	16	53828752	G	0.048	1.049	0.325	8.44E-18	937716
rs8044769	<i>FTO</i>	16	53839135	C	0.061	1.062	0.438	2.73E-31	937714
rs633265	<i>MC4R</i>	18	57831468	T	0.039	1.040	0.413	1.05E-18	931300
rs1350341	<i>MC4R</i>	18	57842533	A	0.038	1.039	0.400	5.37E-18	926826
rs17782313	<i>MC4R</i>	18	57851097	C	0.055	1.057	0.238	1.46E-35	1088670
rs12970134	<i>MC4R</i>	18	57884750	A	0.050	1.051	0.300	2.83E-28	1089600
rs29941	<i>KCTD15</i>	19	34309532	G	0.001	1.001	0.338	1.36E-04	1082030
rs11084753	<i>KCTD16</i>	19	34322137	G	0.011	1.011	0.363	2.61E-03	1047670
rs2287019	<i>QPCTL</i>	19	46202172	T	0.021	1.021	0.213	1.00E-04	1149250

T2D = type 2 diabetes, PRS = polygenic risk-score SNP = single nucleotide polymorphism, CHR = , Pos = position based on human genome 19, MAF = minor allele frequency, P value = statistical significant associations of SNPs in GWAS for type 2 diabetes (<https://t2d.hugeamp.org/>), N = Effective sample size from all the dataset where the P-value was significant.

**Supplementary Table S2.** Genetic variants included in the Obesity PRS

SNP	Locus	CHR	Pos	Alt Allele	$\beta$	Odd Ratio	MAF	P-value	N
rs7561317	<i>TMEM18</i>	2	644953	G	0.141	1.151	0.2451	1.38E-04	11743
rs10938397	<i>GNPDA2</i>	4	45182527	G	0.099	1.104	0.4549	2.60E-04	11743
rs7903146	<i>TCF7L2</i>	10	114758349	T	-0.101	0.904	0.2280	3.16E-03	11743
rs4074134	<i>BDNF</i>	11	27647285	T	-0.163	0.850	0.2280	7.37E-06	11743
rs4923461	<i>BDNF</i>	11	27656910	G	-0.163	0.850	0.2232	6.98E-06	11743
rs925946	<i>BDNF</i>	11	27667202	G	-0.088	0.915	0.2610	1.88E-03	11743
rs10501087	<i>BDNF</i>	11	27670108	C	-0.162	0.850	0.2220	8.07E-06	11743
rs6265	<i>BDNF</i>	11	27679916	T	-0.164	0.849	0.2061	1.17E-05	11743
rs10835211	<i>BDNF</i>	11	27701365	A	0.098	1.103	0.1915	2.04E-03	11743
rs8049439	<i>ATXN2L</i>	16	28837515	C	0.087	1.091	0.4305	1.39E-03	11743
rs4788102	<i>SH2B1</i>	16	28873398	A	0.094	1.099	0.4256	5.71E-04	11743
rs7498665	<i>SH2B1</i>	16	28883241	G	0.094	1.099	0.4207	5.65E-04	11743
rs8050136	<i>FTO</i>	16	53816275	A	0.205	1.228	0.4915	9.23E-14	11743
rs3751812	<i>FTO</i>	16	53818460	T	0.206	1.229	0.4902	6.42E-14	11743
rs9939609	<i>FTO</i>	16	53820527	A	0.207	1.231	0.4890	5.07E-14	11743
rs7190492	<i>FTO</i>	16	53828752	G	0.126	1.134	0.3232	5.28E-06	11743
rs8044769	<i>FTO</i>	16	53839135	C	0.162	1.176	0.4195	1.76E-09	11743
rs9921518	<i>IRX3</i>	16	54494424	G	-0.105	0.900	0.2488	6.11E-03	11743
rs17782313	<i>MC4R</i>	18	57851097	C	0.102	1.107	0.1768	3.42E-03	11743
rs12970134	<i>MC4R</i>	18	57884750	A	0.099	1.104	0.2134	3.66E-03	11743
rs29941	<i>KCTD15</i>	19	34309532	G	0.061	1.063	0.3073	2.77E-02	11743

PRS = polygenic risk-score SNP = single nucleotide polymorphism, CHR = , Pos = position based on human genome 19, MAF = minor allele frequency, P value = statistical significant associations of SNPs in GWAS for Obesity (<https://t2d.hugeamp.org/>), N = Effective sample size, DataSet: FinnGen 2018 GWAS: European ancestry ([https://t2d.hugeamp.org/dinspector.html?dataset=GWAS\\_FinnGen\\_eu&phenotype=Obesity](https://t2d.hugeamp.org/dinspector.html?dataset=GWAS_FinnGen_eu&phenotype=Obesity)).

**Supplementary Table S3.** Association of T2D PRS with the baseline metabolic parameters in PolRed.

Metabolic Parameter	$\beta$ (95% CI)	<i>P</i> §
BMI (kg/m <sup>2</sup> )	0.0066 (-0.0020, 0.0112)	<b>0.0053</b>
FFM (kg)	0.0029 (-0.0001, 0.0056)	<b>0.0394</b>
FM (kg)	0.0028 (-0.0003, 0.0053)	<b>0.0293</b>
MM (kg)	-0.0045 (-0.0091, 0.0001)	0.0535
VF (cm <sup>3</sup> )	-0.0004 (-0.0009, 0.0001)	0.0662
SF (cm <sup>3</sup> )	-0.0003 (-0.0007, 0.0001)	0.1360
VAT/SAT ratio	-0.0544 (-0.1436, 0.0348)	0.2310
IPAQ (min/week)	0.0002 (-0.0002, 0.0005)	0.4450
Fasting glucose (mg/dl)	0.0024 (-0.0001, 0.0047)	<b>0.0451</b>
2-hour glucose (mg/dl)	0.0001 (-0.0008, 0.0009)	0.8990
HbA1c (%)	-0.0171 (-0.0629, 0.0288)	0.4650
Fasting insulin (uU/ml)	0.0033 (-0.0003, 0.0063)	<b>0.0320</b>
2-hour insulin (uU/ml)	-0.0001 (-0.0008, 0.0006)	0.7740
Chol (mg/dL)	0.3426 (-0.8705, 1.5558)	0.5790
Tg (mg/dL)	-0.0683 (-0.3109, 0.1744)	0.5800
Hdl (mg/dL)	-0.3415 (-1.5546, 0.8716)	0.5800
Ldl (mg/dL)	-0.3428 (-1.556, 0.8704)	0.5790

BMI: Body mass index; FFM: fat free mass; FM: fat mass; MM: muscle mass; VF: visceral fat; SF: subcutaneous fat; VAT: visceral adipose tissue; SAT: subcutaneous adipose tissue; IPAQ: International Physical Activity Questionnaire; HbA1c: glycated hemoglobin; Chol: total cholesterol; Tg: triglycerides; Hdl: high-density lipoprotein; Ldl: low-density lipoproteins.  $\beta$  values are reported per SD of polygenic score. *P*§ values of 0.05 are in bold and reflect significance after adjustment for multiple testing.

**Supplementary Table S4.** Association of Obesity PRS with the baseline metabolic parameters in PolRed.

Metabolic Parameter	$\beta$ (95% CI)	<i>P</i> §
BMI (kg/m <sup>2</sup> )	0.0141 (-0.0028, 0.0255)	<b>0.0145</b>
FFM (kg)	0.0027 (-0.0259, 0.0312)	0.8539
FM (kg)	0.0043 (-0.0039, 0.0126)	0.3016
MM (kg)	-0.0057 (-0.0522, 0.0409)	0.8111
VF (cm <sup>3</sup> )	0.0013 (-0.0006, 0.0032)	0.1773
SF (cm <sup>3</sup> )	-0.0008 (-0.0020, 0.0005)	0.2489
VAT/SAT ratio	-0.2228 (-0.4980, 0.0523)	0.1121
IPAQ (min/week)	-0.0001 (-0.0006, 0.0003)	0.5656
Fasting glucose (mg/dl)	-0.0033 (-0.0073, 0.0006)	0.0978
2-hour glucose (mg/dl)	0.0003 (-0.0012, 0.0019)	0.6857
HbA1c (%)	0.0371 (-0.0256, 0.0998)	0.2449
Fasting insulin (uU/ml)	0.0017 (-0.0029, 0.0063)	0.4560
2-hour insulin (uU/ml)	0.0004 (-0.0009, 0.0017)	0.5303
Chol (mg/dL)	0.8328 (-0.5718, 2.2374)	0.2445
Tg (mg/dL)	-0.1660 (-0.4469, 0.1149)	0.2460
Hdl (mg/dL)	-0.8329 (-2.2374, 0.5716)	0.2444
Ldl (mg/dL)	-0.8327 (-2.2373, 0.5720)	0.2445

BMI: Body mass index; FFM: fat free mass; FM: fat mass; MM: muscle mass; VF: visceral fat; SF: subcutaneous fat; VAT: visceral adipose tissue; SAT: subcutaneous adipose tissue; IPAQ: International Physical Activity Questionnaire; HbA1c: glycated hemoglobin; Chol: total cholesterol; Tg: triglycerides; Hdl: high-density lipoprotein; Ldl: low-density lipoproteins.  $\beta$  values are reported per SD of polygenic score. *P*§ values of 0.05 are in bold and reflect significance after adjustment for multiple testing.

**Supplementary Table S5.** Association of T2D PRS with changes in metabolic parameters with gender stratification.

Metabolic Parameter	Female (n = 245)		Male (n = 201)	
	$\beta$ (95% CI)	P§	$\beta$ (95% CI)	P§
FFM (kg)	0.0047 (-0.0032, 0.0126)	0.2453	-0.0016(-0.0121, 0.0087)	0.750
FM (kg)	0.0068 (-0.0013, 0.0123)	<b>0.0158</b>	0.0024 (-0.0040, 0.0089)	<b>0.045</b>
MM (kg)	-0.0001 (-0.0004, 0.0002)	0.5088	0.0069 (-0.0079, 0.02180)	0.361
VF (cm <sup>3</sup> )	-0.0006 (-0.0020, 0.0008)	0.4129	0.0009 (-0.0005, 0.0023)	0.214
SF (cm <sup>3</sup> )	0.0004 (-0.0002, 0.0012)	0.1966	-0.0003 (-0.0010, 0.0004)	0.397
VAT/SAT ratio	0.0720 (-0.1583, 0.3023)	0.5384	-0.1753 (-0.4043, 0.05384)	0.133
IPAQ (min/week)	0.0001 (-0.0002, 0.0002)	0.6696	0.0001 (-0.0002, 0.0002)	0.518
Fasting glucose (mg/dl)	-0.0007 (-0.0044, 0.0029)	0.6866	-0.0005 (-0.0036, 0.0025)	0.706
2-hour glucose (mg/dl)	0.0005 (-0.0013, 0.0014)	0.3016	-0.0012 (-0.0030, 0.0005)	0.164
HbA1c (%)	0.105 (0.0081, 0.2018)	0.0937	-0.0011 (-0.1198, 0.1176)	0.985
Fasting insulin (uU/ml)	0.0002 (-0.0041, 0.0045)	0.9248	0.0046 (-0.0004, 0.0097)	0.076
2-hour insulin (uU/ml)	0.0008 (-0.0004, 0.002)	0.202	-0.0008 (-0.0024, 0.0008)	0.328
Chol (mg/dL)	-0.0301 (-0.0798, 0.0195)	0.2337	0.01634 (-0.0055, 0.0382)	0.142
Tg (mg/dL)	0.0056 (-0.0043, 0.01567)	0.2632	-0.0032 (-0.0076, 0.0011)	0.147
Hdl (mg/dL)	0.0278 (-0.0218, 0.0775)	0.2706	-0.0146 (-0.0364, 0.0071)	0.187
Ldl (mg/dL)	0.0298 (-0.0199, 0.0795)	0.2391	-0.016 (-0.0378, 0.0059)	0.151

FFM: fat free mass; FM: fat mass; MM: muscle mass; VF: visceral fat; SF: subcutaneous fat; VAT: visceral adipose tissue; SAT: subcutaneous adipose tissue; IPAQ: International Physical Activity Questionnaire; HbA1c: glycated hemoglobin; Chol: total cholesterol; Tg: triglycerides; Hdl: high-density lipoprotein; Ldl: low-density lipoproteins.  $\beta$  values are reported per SD of polygenic score. P§ values of 0.05 are in bold and reflect significance after adjustment for multiple testing.

**Supplementary Table S6.** Association of Obesity PRS with changes in metabolic parameters with gender stratification.

Metabolic Parameter	Female (n = 245)		Male (n = 201)	
	$\beta$ (95% CI)	P§	$\beta$ (95% CI)	P§
FFM (kg)	0.0020 (-0.0070, 0.0111)	0.657	0.0057 (-0.0064, 0.0180)	0.352
FM (kg)	0.0064 (-0.0001, 0.0128)	<b>0.045</b>	0.0049 (-0.0026, 0.0125,)	<b>0.020</b>
MM (kg)	0.0001 (-0.0001, 0.00052)	0.293	-0.0035 (-0.0211, 0.0140)	0.690
VF (cm <sup>3</sup> )	-0.0005 (-0.0022, 0.00115)	0.536	0.0006 (-0.0010, 0.0023)	0.432
SF (cm <sup>3</sup> )	0.0003 (-0.0004, 0.0012)	0.396	-0.0003 (-0.0012, 0.0005)	0.461
VAT/SAT ratio	0.1525 (-0.1114, 0.4163)	0.256	-0.0907 (-0.3592, 0.1778)	0.506
IPAQ (min/week)	-0.0001 (-0.0002, 0.0002)	0.154	0.0001 (-0.0002, 0.0002)	0.787
Fasting glucose (mg/dl)	0.0029 (-0.0013, 0.0071)	0.181	0.0020 (-0.0015, 0.0057)	0.260
2-hour glucose (mg/dl)	0.0004 (-0.0011, 0.0019)	<b>0.049</b>	0.0021 (-0.0001, 0.0042,)	<b>0.044</b>
HbA1c (%)	0.0851 (-0.0247, 0.1951)	0.128	-0.0939 (-0.2340, 0.0461)	0.187
Fasting insulin (uU/ml)	-0.0039 (-0.0094, 0.0014)	0.154	0.0003 (-0.0056, 0.0063)	0.910
2-hour insulin (uU/ml)	0.0006 (-0.0007, 0.0020)	0.347	0.0001 (-0.0018, 0.0020)	0.908
Chol (mg/dL)	-0.0377 (-0.0942, 0.0187)	0.189	0.0264 (0.0007, 0.0522)	0.044
Tg (mg/dL)	0.0074 (-0.0038, 0.0188)	0.194	-0.0055 (-0.0107, -0.0004)	0.035
Hdl (mg/dL)	0.0391 (-0.01732, 0.0956)	0.173	-0.0260 (-0.0516, -0.0003)	0.047
Ldl (mg/dL)	0.0381 (-0.0183, 0.0947)	0.185	-0.0257 (-0.0515, -0.0001)	0.050

FFM: fat free mass; FM: fat mass; MM: muscle mass; VF: visceral fat; SF: subcutaneous fat; VAT: visceral adipose tissue; SAT: subcutaneous adipose tissue; IPAQ: International Physical Activity Questionnaire; Hba1c: glycated hemoglobin; Chol: total cholesterol; Tg: triglycerides; Hdl: high-density lipoprotein; Ldl: low-density lipoproteins.  $\beta$  values are reported per SD of polygenic score. P§ values of 0.05 are in bold and reflect significance after adjustment for multiple testing.