

Supplementary Information

Supplementary Figure S1: Percentage of AN GWAMA SNPs that also met the p-value threshold in the BMI GWAMA (black dots)

Supplementary Table S1: Meta-analysis of GIANT data sets using (a) full GWAS chip data (HapMap imputed) on N~233,000 and (b) Metabochip on N~88,000 (order of SNPs as in Table 1)

Supplementary Table S2: 39 novel genome-wide significant BMI loci from a European GWAMA primary analysis (GIANT, Locke et al., 2015; Table 1) assessed in the GWAMA for AN (GCAN, Boraska et al., 2014)

Supplementary Table S3: 17 novel genome-wide significant BMI loci from secondary analyses (e.g. non-European, sex specific; GIANT, Locke et al., 2015; Table 2) assessed in a GWAMA for AN (GCAN, Boraska et al., 2014)

Supplementary Table S4: Previously known genome-wide significant BMI loci (GIANT, Locke et al., 2015; Extended Data Table 2) assessed in the AN case-control GWAMA (GCAN, Boraska et al., 2014)

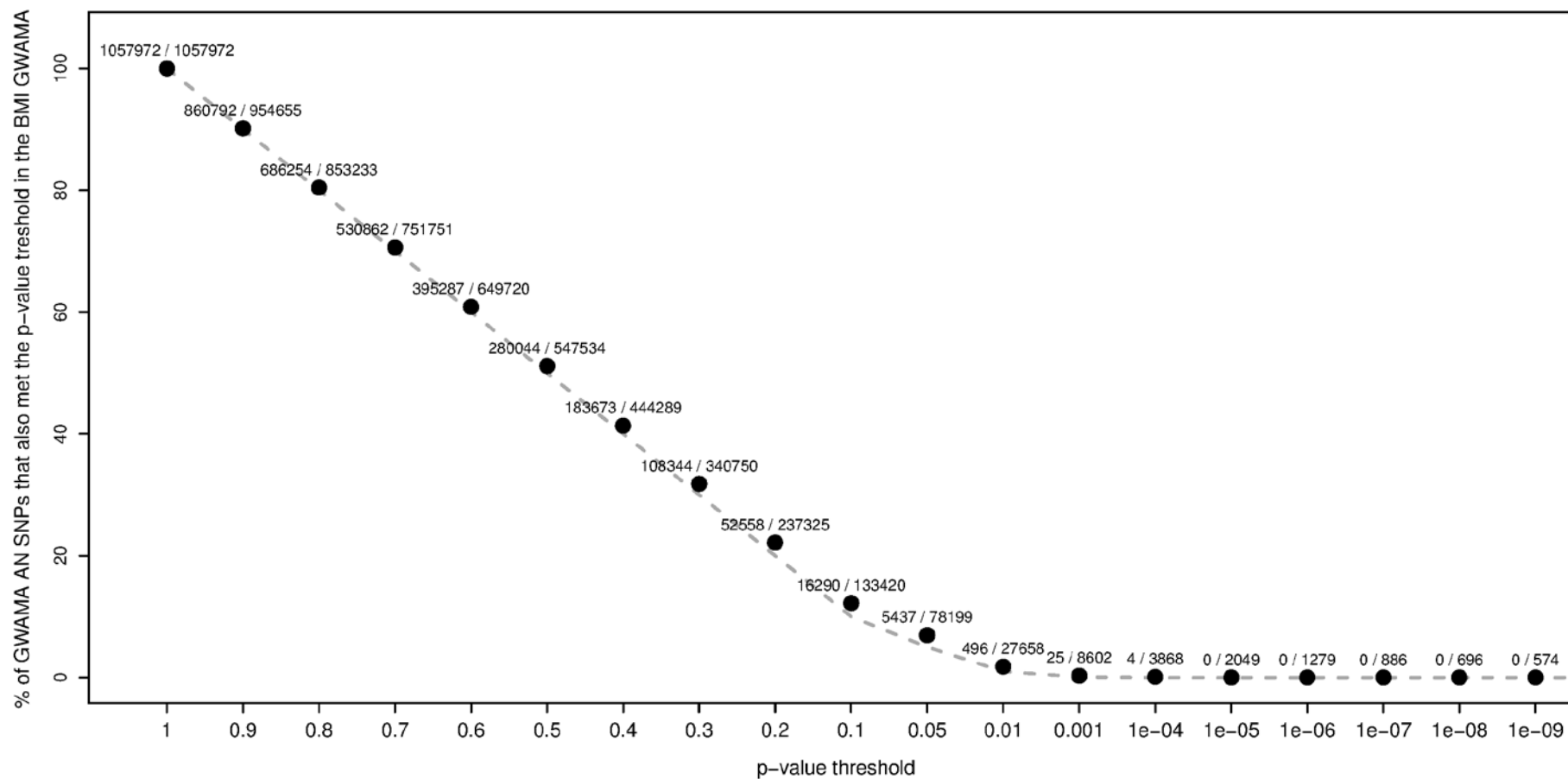
Supplementary Table S5: Genome-wide significant loci for BMI, obesity, childhood obesity not described in Locke et al., 2015 (reviewed in Yazdi et al. 2015, Table 2) assessed in the GWAMA for AN (GCAN, Boraska et al., 2014)

Supplementary Table S6: 68 genome-wide significant WHR loci from a European GWAMA primary analysis (GIANT, Shungin et al., 2015; Tables 1 and 3) assessed in the GWAMA for AN (GCAN, Boraska et al., 2014)

Supplementary Table S7: *In silico* mutation analyses pertaining to the four identified genes (ExAC Browser (Beta); Exome Aggregation Consortium)

Supplementary Table S8: association test of the nine AN / BMI SNPs with adult obesity in GIANT extreme (order of SNPs as in Table 1)

Supplementary Figure S1: Percentage of AN GWAMA SNPs that also met the p-value threshold in the BMI GWAMA (black dots)



The relative frequency is derived for “the absolute number of SNP association signals that meet the p-value threshold on the x-axis in both GWAMAs” / “the absolute number of SNP association signals that meet the p-value threshold on the x-axis in the BMI GWAMA only”. The dashed grey line indicates the expected relative frequency of SNP association signals a given p-value threshold on the x-axis (i.e. “the absolute number of SNP association signals that meet the p-value threshold on the x-axis in the BMI GWAMA only” divided by the total number of 1,057,972 SNPs in the intersection data set of both GWAMAS).

Supplementary Table S1: Meta-analysis of GIANT data sets using (a) full GWAS chip data (HapMap imputed) on N~233,000 and (b) Metabochip on N~88,000 (order of SNPs as in Table 1)

(a)

SNP	Overall					Women			Men		
	EA	Beta	Se	P	N	Beta	P	N	Beta	P	N
rs1561589	0.34	0.0151	0.0041	0.0002126	233684	0.0182	0.0002506	131940	0.0101	0.06284	104455
rs12771627	0.73	-0.0153	0.0043	0.0004029	233437	-0.0176	0.001197	131818	-0.0114	0.05259	104330
rs11245456	0.75	-0.0162	0.0046	0.0003944	233423	-0.0189	0.0008474	131809	-0.0122	0.04986	104325
rs17513613	0.67	-0.017	0.0041	0.00003052	233857	-0.014	0.005912	132029	-0.0201	0.000287	104538
rs17406900	0.48	-0.0142	0.0037	0.0001276	233805	-0.0131	0.005708	132018	-0.0157	0.001606	104497
rs7593917	0.46	-0.0127	0.0037	0.0006116	233851	-0.0109	0.0184	132026	-0.0148	0.002941	104536
rs11691351	0.45	-0.013	0.0037	0.0004526	233969	-0.0115	0.01288	132086	-0.0148	0.002941	104593
rs8102137	0.67	-0.0169	0.0041	0.00003397	233987	-0.014	0.005912	132096	-0.0198	0.0002653	104600
rs7573079	0.45	-0.0125	0.0037	0.000745	233960	-0.0109	0.0184	132078	-0.0146	0.003349	104590

(b)

SNP	Overall					Women			Men		
	EA	Beta	Se	P	N	Beta	P	N	Beta	P	N
rs1561589	0.34	0.0168	0.0057	0.003215	88093	0.0289	0.0001778	39845	0.0063	0.3817	48248
rs12771627	0.74	-0.0179	0.0061	0.003603	87991	-0.0274	0.0009878	39795	-0.0097	0.2158	48196
rs11245456	0.76	-0.0189	0.0064	0.003019	88049	-0.0253	0.002987	39825	-0.014	0.08195	48224
rs17513613	0.67	-0.0114	0.0056	0.04142	88108	-0.0061	0.4227	39854	-0.0174	0.01568	48254
rs17406900	0.50	-0.0118	0.0054	0.02789	88118	-0.0189	0.009662	39852	-0.006	0.376	48266
rs7593917	0.48	-0.014	0.0057	0.01408	80721	-0.027	0.0003221	38126	-0.0021	0.7706	42595
rs11691351	0.48	-0.0118	0.0054	0.02789	88118	-0.022	0.002594	39852	-0.0029	0.6735	48266
rs8102137	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
rs7573079	0.48	-0.0123	0.0054	0.02191	88065	-0.0223	0.002264	39839	-0.0035	0.6111	48226

Supplementary Table S2: 39 novel genome-wide significant BMI loci from a European GWAMA primary analysis (GIANT, Locke et al., 2015; Table 1) assessed in the GWAMA for AN (GCAN, Boraska et al., 2014)

Chromosome / position SNP Notable gene(s) (as annotated by Locke et al., 2015)	BMI increasing alleles (GIANT, Locke et al., 2015; Table 1)			BMI increasing alleles in AN case-control GWAMA (GCAN, Boraska et al., 2014)				
	BMI increasing allele / frequency	β (SE)	p-value	Frequency of reference allele in AN cases	AN risk (odds ratio) for reference allele	p-value	adjusted ^a p-value	Direction of effect ^b + / -
1:49,362,434 rs657452 <i>AGBL4</i>	A / 0.394	0.023 (0.003)	5.48×10^{-13}	A / 0.395	1.026	0.40	1	NE
11:114,527,614 rs12286929 <i>CADM1</i>	G / 0.523	0.022 (0.003)	1.31×10^{-12}	G / 0.523	0.977	0.44	1	NE
10:114,748,339 rs7903146 <i>TCF7L2</i>	C / 0.713	0.023 (0.003)	1.11×10^{-11}	C / 0.709	1.015	0.65	1	NE
14:24,998,019 rs10132280 <i>STXBP6</i>	C / 0.682	0.023 (0.003)	1.14×10^{-11}	A / 0.310	0.976	0.46	1	NE
10:102,385,430 rs17094222 <i>HIF1AN</i>	C / 0.211	0.025 (0.004)	5.94×10^{-11}	T / 0.793	0.988	0.75	1	NE
2:213,121,476 rs7599312 <i>ERBB4</i>	G / 0.724	0.022 (0.003)	1.17×10^{-10}	G / 0.729	0.980	0.56	1	NE
3:61,211,502 rs2365389 <i>FHIT</i>	C / 0.582	0.020 (0.003)	1.63×10^{-10}	^c rs6785875 T / 0.579	0.982	0.55	1	NE

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Supplementary Table S2: 39 novel genome-wide significant BMI loci from a European GWAMA primary analysis (GIANT, Locke et al., 2015; Table 1) assessed in the GWAMA for AN (GCAN, Boraska et al., 2014)

1:200,050,910 rs2820292 <i>NAV1</i>	C / 0.555	0.020 (0.003)	1.83×10^{-10}	A / 0.459	0.993	0.82	1	NE
14:28,806,589 rs12885454 <i>PRKD1</i>	C / 0.642	0.021 (0.003)	1.894×10^{-10}	^c rs11625899 T / 0.338	0.956	0.16	1	NE
3:142,758,126 rs16851483 <i>RASA2</i>	T / 0.066	0.048 (0.008)	3.55×10^{-10}	G / 0.943	0.883	0.06	1	NE
7:75,001,105 rs1167827 <i>HIP1; PMS2L3; PMS2P5; WBSCR16</i>	G / 0.553	0.020 (0.003)	6.33×10^{-10}	G / 0.565	0.975	0.41	1	NE
16:3,567,359 rs758747 <i>NLRC3</i>	T / 0.265	0.023 (0.004)	7.47×10^{-10}	NA	NA	NA	NA	NA
9:119,418,304 rs1928295 <i>TLR4</i>	T / 0.548	0.019 (0.003)	7.91×10^{-10}	T / 0.551	1.010	0.75	1	NE
16:31,037,396 rs9925964 <i>KAT8; ZNF646; VKORC1; ZNF668; STX1B; FBXL19</i>	A / 0.620	0.019 (0.003)	8.11×10^{-10}	^c rs1978487 C / 0.396	1.050	0.12	1	NE

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Supplementary Table S2: 39 novel genome-wide significant BMI loci from a European GWAMA primary analysis (GIANT, Locke et al., 2015; Table 1) assessed in the GWAMA for AN (GCAN, Boraska et al., 2014)

2:26,782,315 rs11126666 <i>KCNK3</i>	A / 0.283	0.021 (0.003)	1.33×10^{-09}	G / 0.735	0.960	0.24	1	NE
16:28,240,912 rs2650492 <i>SBK1; APOBR</i>	A / 0.303	0.021 (0.004)	1.92×10^{-09}	G / 0.712	0.987	0.69	1	NE
3:25,081,441 rs6804842 <i>RARB</i>	G / 0.575	0.019 (0.003)	2.48×10^{-09}	A / 0.429	0.962	0.21	1	NE
9:15,624,326 rs4740619 <i>C9orf93</i>	T / 0.542	0.018 (0.003)	4.56×10^{-09}	T / 0.553	1.030	0.33	1	NE
6:162,953,340 rs13191362 <i>PARK2</i>	A / 0.879	0.028 (0.005)	7.34×10^{-09}	A / 0.880	0.971	0.54	1	NE
15:49,535,902 rs3736485 <i>SCG3; DMXL2</i>	A / 0.454	0.018 (0.003)	7.41×10^{-09}	A / 0.444	0.946	0.07	1	NE
4:77,348,592 rs17001654 <i>NUP54; SCARB2</i>	G / 0.153	0.031 (0.005)	7.76×10^{-09}	C / 0.844	1.033	0.44	1	NE
10:104,859,028 rs11191560 <i>NT5C2; CYP17A1; SFXN2</i>	C / 0.089	0.031 (0.005)	8.45×10^{-09}	T / 0.910	0.940	0.24	1	NE

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Supplementary Table S2: 39 novel genome-wide significant BMI loci from a European GWAMA primary analysis (GIANT, Locke et al., 2015; Table 1) assessed in the GWAMA for AN (GCAN, Boraska et al., 2014)

2:181,259,207 rs1528435 <i>UBE2E3</i>	T / 0.631	0.018 (0.003)	1.20×10^{-08}	T / 0.629	1.039	0.22	1	NE
17:5,223,976 rs1000940 <i>RABEP1</i>	G / 0.320	0.019 (0.003)	1.28×10^{-08}	A / 0.705	0.944	0.09	1	NE
6:40,456,631 rs2033529 <i>TDRG1; LRFN2</i>	G / 0.293	0.019 (0.003)	1.39×10^{-08}	A / 0.715	1.008	0.80	1	NE
1:50,332,407 rs11583200 <i>ELAVL4</i>	C / 0.396	0.018 (0.003)	1.48×10^{-08}	C / 0.379	0.985	0.62	1	NE
6:109,084,356 rs9400239 <i>FOXO3;</i> <i>HSS00296402</i>	C / 0.688	0.019 (0.003)	1.61×10^{-08}	^c rs4946932 C / 0.682	0.959	0.21	1	NE
9:128,500,735 rs10733682 <i>LMX1B</i>	A / 0.478	0.017 (0.003)	1.83×10^{-08}	G / 0.494	1.055	0.08	1	NE
2:62,906,552 rs11688816 <i>EHBP1</i>	G / 0.525	0.017 (0.003)	1.89×10^{-08}	G / 0.512	0.983	0.57	1	NE
12:121,347,850 rs11057405 <i>CLIP1</i>	G / 0.901	0.031 (0.006)	2.02×10^{-08}	^c rs12369179 T / 0.085	1.001	0.99	1	NE

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Supplementary Table S2: 39 novel genome-wide significant BMI loci from a European GWAMA primary analysis (GIANT, Locke et al., 2015; Table 1) assessed in the GWAMA for AN (GCAN, Boraska et al., 2014)

4:145,878,514 rs11727676 <i>HHIP</i>	T / 0.910	0.036 (0.006)	2.55×10^{-08}	NA	NA	NA	NA	NA
3:81,874,802 rs3849570 <i>GBE1</i>	A / 0.359	0.019 (0.003)	2.60×10^{-08}	^c rs11711331 A / 0.327	0.961	0.22	1	NE
9:110,972,163 rs6477694 <i>EPB41L4B; C9orf4</i>	C / 0.365	0.017 (0.003)	2.67×10^{-08}	T / 0.656	0.990	0.75	1	NE
10:87,400,884 rs7899106 <i>GRID1</i>	G / 0.052	0.040 (0.007)	2.96×10^{-08}	A / 0.947	0.915	0.44	1	NE
11:43,820,854 rs2176598 <i>HSD17B12</i>	T / 0.251	0.020 (0.004)	2.97×10^{-08}	^c rs10838184 C / 0.243	1.038	0.30	1	NE
7:76,446,079 rs2245368 <i>PMS2L11</i>	C / 0.180	0.032 (0.006)	3.19×10^{-08}	NA	NA	NA	NA	NA
19:18,315,825 rs17724992 <i>GDF15; PGPEP1</i>	A / 0.746	0.019 (0.004)	3.42×10^{-08}	A / 0.736	1.003	0.94	1	NE
18:55,034,299 rs7243357 <i>GRP</i>	T / 0.812	0.022 (0.004)	3.86×10^{-08}	^c rs9957264 A / 0.165	1.006	0.88	1	NE

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Supplementary Table S2: 39 novel genome-wide significant BMI loci from a European GWAMA primary analysis (GIANT, Locke et al., 2015; Table 1) assessed in the GWAMA for AN (GCAN, Boraska et al., 2014)

8:85,242,264 rs2033732 <i>RALYL</i>	C / 0.747	0.019 (0.004)	4.89×10^{-08}	^c rs733594 T / 0.718	0.962	0.26	1	NE
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^aunadjusted p-values are adjusted for multiplicity by Bonferroni correction for 97 tests

^bDirection of effect: + the BMI increasing allele is less frequently found in AN cases as compared to controls; - the BMI increasing allele is more frequently found in AN cases as compared to controls. Direction of effect was only analyzed for SNPs with a nominal p-value < 0.05 in GCAN

^cProxy SNAP (Broad Institute) with HapMap release 22, CEU population, r2 threshold of 0.8 and a distance limit of 500 kb

NA: not available; NE: not estimated

Supplementary Table S3: 17 novel genome-wide significant BMI loci from secondary analyses (e.g. non-European, sex specific; GIANT, Locke et al., 2015; Table 2) assessed in a GWAMA for AN (GCAN, Boraska et al., 2014)

SNP	Notable gene(s) (as annotated by Locke et al., 2015)	BMI increasing alleles (GIANT, Locke et al., 2015)			BMI increasing alleles in AN case-control GWAMA (GCAN, Boraska et al., 2014)				
		BMI increasing allele / frequency	β (SE)	p-value	Frequency of reference allele in AN cases	AN risk (odds ratio) for BMI increasing allele	p-value	adjusted ^a p-value	Direction of effect ^b + / -
Effect in females									
rs7239883	<i>LOC284260; RIT2</i>	G / 0.391	0.016 (0.003)	1.51×10^{-08}	A / 0.603	0.939	0.04	1	-
rs6465468	<i>ASB4</i>	T / 0.306	0.017 (0.004)	4.98×10^{-08}	G / 0.692	1.025	0.45	1	NE
Effect in males									
rs492400	<i>PLCD4; CYP27A1; USP37; TTLL4; STK36; ZNF142; RQCD1</i>	C / 0.424	0.016 (0.003)	6.78×10^{-09}	C / 0.431	1.029	0.35	1	NE
rs16907751	<i>ZBTB10</i>	C / 0.913	0.035 (0.007)	3.89×10^{-08}	NA	NA	NA	NA	NA
Effect in all ancestries									
rs7164727	<i>LOC100287559;BBS4</i>	T / 0.671	0.018 (0.003)	3.92×10^{-09}	C / 0.313	0.980	0.54	1	NE
rs2080454	<i>CBLN1</i>	C / 0.413	0.017 (0.003)	8.60×10^{-09}	C / 0.381	1.033	0.31	1	NE
rs2836754	<i>ETS2</i>	C / 0.599	0.016 (0.003)	1.61×10^{-08}	T / 0.375	0.994	0.85	1	NE
rs9914578	<i>SMG6; N29617</i>	G / 0.229	0.020 (0.004)	2.07×10^{-08}	^c rs4061660 G / 0.791	0.969	0.40	1	NE
rs977747	<i>TAL1</i>	T / 0.403	0.017 (0.003)	2.18×10^{-08}	T / 0.371	0.933	0.03	1	+
rs1441264	<i>MIR548A2</i>	A / 0.613	0.018 (0.03)	2.96×10^{-08}	A / 0.607	1.011	0.72	1	NE
rs17203016	<i>CREB1; KLF7</i>	G / 0.195	0.021 (0.004)	3.41×10^{-08}	A / 0.810	0.997	0.93	1	NE

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Supplementary Table S3: 17 novel genome-wide significant BMI loci from secondary analyses (e.g. non-European, sex specific; GIANT, Locke et al., 2015; Table 2) assessed in a GWAMA for AN (GCAN, Boraska et al., 2014)

rs13201877	<i>IFNGR1; OLIG3</i>	G / 0.140	0.023 (0.005)	4.29×10^{-08}	^c rs3904532 G / 0.136	0.965	0.42	1	NE
rs1460676	<i>FIGN</i>	C / 0.179	0.020 (0.004)	4.98×10^{-08}	T / 0.832	1.020	0.63	1	NE
European population-based studies									
rs9641123	<i>CALCR; hsa-miR-653</i>	C / 0.430	0.019 (0.004)	2.08×10^{-10}	^c rs10464483 T / 0.405	1.047	0.40	1	NE
rs9374842	<i>LOC285762</i>	T / 0.744	0.019 (0.004)	2.67×10^{-08}	T / 0.742	0.924	0.03	1	+
rs4787491	<i>MAPK3; KCTD13; INO80E; TAOK2; YPEL3; DOC2A; FAM57B</i>	G / 0.510	0.016 (0.004)	2.70×10^{-08}	A / 0.477	0.999	0.98	1	NE
rs9540493	<i>MIR548X2; PCDH9</i>	A / 0.452	0.017 (0.003)	4.97×10^{-08}	A / 0.442	0.996	0.88	1	NE

^a unadjusted p-values are adjusted for multiplicity by Bonferroni correction for 97 tests

^b Direction of effect: + the BMI increasing allele is *less frequently* found in AN cases as compared to controls; - the BMI increasing allele is more frequently found in AN cases as compared to controls. Direction of effect was only analyzed for SNPs with a nominal p-value < 0.05 in GCAN

^c Proxy SNAP (Broad Institute) with HapMap release 22, CEU population, r2 threshold of 0.8 and a distance limit of 500 kb,

NA: not available; NE: not estimated

Supplementary Table S4: 32 previously known genome-wide significant BMI loci (GIANT, Locke et al., 2015; Extended Data Table 2) assessed in the AN case-control GWAMA (GCAN, Boraska et al., 2014)

SNP	Notable gene(s) (as annotated by Locke et al., 2015)	BMI increasing alleles (GIANT, Locke et al., 2015; Extended Data Table 2)			BMI increasing alleles in AN case-control GWAMA (GCAN, Boraska et al., 2014)				
		BMI increasing allele / frequency	β (SE)	p-value for BMI increase	Frequency of BMI increasing in AN cases	AN risk (odds ratio) for BMI increasing allele	p-value	adjusted ^a p-value	Direction of effect ^b + / -
rs1558902	<i>FTO</i>	A / 0.415	0.082 (0.004)	7.51×10^{-153}	^c rs1421085 C / 0.433	1.068	0.03	1	-
rs6567160	<i>MC4R</i>	C / 0.236	0.056 (0.005)	3.93×10^{-53}	^c rs571312 A / 0.242	1.067	0.07	1	NE
rs13021737	<i>TMEM18</i>	G / 0.828	0.060 (0.004)	1.11×10^{-50}	^c rs13012571 C / 0.166	0.916	0.03	1	-
rs10938397	<i>GNPDA2; GABRG1</i>	G / 0.434	0.040 (0.003)	3.21×10^{-38}	^c rs12641981 T / 0.437	1.005	0.86	1	NE
rs543874	<i>SEC16B</i>	G / 0.193	0.048 (0.004)	2.62×10^{-35}	A / 0.819	0.987	0.74	1	NE
rs2207139	<i>TFAP2B</i>	G / 0.177	0.045 (0.004)	4.13×10^{-29}	^c rs943005 T / 0.166	0.949	0.20	1	NE
rs11030104	<i>BDNF</i>	A / 0.792	0.041 (0.004)	5.56×10^{-28}	A / 0.780	0.985	0.68	1	NE
rs3101336	<i>NEGR1</i>	C / 0.613	0.033 (0.003)	2.66×10^{-26}	C / 0.649	1.068	0.04	1	NE
rs7138803	<i>BCDIN3D; FAIM2</i>	A / 0.384	0.032 (0.003)	8.15×10^{-24}	G / 0.622	0.965	0.25	1	NE
rs10182181	<i>ADCY3; POMC; NCOA1</i>	G / 0.462	0.031 (0.003)	8.78×10^{-24}	G / 0.465	1.014	0.65	1	NE
rs3888190	<i>SH2B1; APOB48R; ATXN2L; SBK1; SULT1A2;; TUFM</i>	A / 0.403	0.031 (0.003)	3.14×10^{-23}	C / 0.624	0.965	0.26	1	NE

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Supplementary Table S4: 32 previously known genome-wide significant BMI loci (GIANT, Locke et al., 2015; Extended Data Table 2) assessed in the AN case-control GWAMA (GCAN, Boraska et al., 2014)

rs1516725	<i>ETV5</i>	C / 0.872	0.045 (0.005)	1.89×10^{-22}	^c rs10513801 G / 0.127	1.019	0.68	1	NE
rs12446632	<i>GPRC5B; IQCK</i>	G / 0.865	0.040 (0.005)	1.48×10^{-18}	G / 0.867	1.057	0.21	1	NE
rs2287019	<i>QPCTL; GIPR</i>	C / 0.804	0.036 (0.004)	4.59×10^{-18}	^c rs11672660 T / 0.211	0.990	0.79	1	NE
rs16951275	<i>MAP2K5; LBXCOR1</i>	T / 0.784	0.031 (0.004)	1.91×10^{-17}	^c rs4776982 G / 0.221	0.976	0.50	1	NE
rs3817334	<i>MTCH2; C1QTNF4; SPI1; CELF1</i>	T / 0.407	0.026 (0.003)	5.15×10^{-17}	C / 0.599	0.971	0.35	1	NE
rs2112347	<i>POC5; HMGCR; COL4A3BP</i>	T / 0.629	0.026 (0.003)	6.19×10^{-17}	^c rs3797580 G / 0.282	1.052	0.11	1	NE
rs12566985	<i>FPGT-TNNI3K</i>	G / 0.446	0.024 (0.003)	3.28×10^{-15}	^c rs6604872 C / 0.562	0.972	0.35	1	NE
rs3810291	<i>ZC3H4</i>	A / 0.666	0.028 (0.004)	4.81×10^{-15}	G / 0.317	1.031	0.35	1	NE
rs7141420	<i>NRXN3</i>	T / 0.527	0.024 (0.003)	1.23×10^{-14}	T / 0.532	1.016	0.61	1	NE
rs13078960	<i>CADM2</i>	G / 0.196	0.030 (0.004)	1.74×10^{-14}	^c rs13098327 A / 0.189	0.954	0.23	1	NE
rs10968576	<i>LINGO2</i>	G / 0.320	0.025 (0.003)	6.61×10^{-14}	A / 0.703	0.998	0.95	1	NE
rs17024393	<i>GNAT2; AMPD2</i>	C / 0.040	0.066 (0.009)	7.03×10^{-14}	NA	NA	NA	NA	NA
rs12429545	<i>OLFM4</i>	A / 0.133	0.033 (0.005)	1.09×10^{-12}	G / 0.863	1.124	0.01	0.97	+
rs13107325	<i>SLC39A8</i>	T / 0.072	0.048 (0.007)	1.83×10^{-12}	C / 0.946	0.742	0.26	1	NE
rs11165643	<i>PTBP2</i>	T / 0.583	0.022 (0.003)	2.07×10^{-12}	C / 0.442	0.936	0.03	1	-
rs17405819	<i>HNF4G</i>	T / 0.700	0.022 (0.003)	2.07×10^{-11}	^c rs1462433 A / 0.290	0.911	0.01	1	-
rs1016287	<i>LIC01122</i>	T / 0.287	0.023 (0.003)	2.25×10^{-11}	C / 0.714	1.000	0.99	1	NE
rs4256980	<i>TRIM66; TUB</i>	G / 0.646	0.021 (0.003)	2.90×10^{-11}	^c rs10840100 A / 0.367	1.001	0.97	1	NE

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Supplementary Table S4: 32 previously known genome-wide significant BMI loci (GIANT, Locke et al., 2015; Extended Data Table 2) assessed in the AN case-control GWAMA (GCAN, Boraska et al., 2014)

rs12401738	<i>FUBP1; USP33</i>	A / 0.352	0.021 (0.003)	1.15×10^{-10}	G / 0.674	0.987	0.70	1	NE
rs205262	<i>C6orf106; SNRPC</i>	G / 0.273	0.022 (0.004)	1.75×10^{-10}	G / 0.272	0.976	0.49	1	NE
rs12016871	<i>MTIF3; GTF3A</i>	T / 0.203	0.030 (0.005)	2.29×10^{-10}	^c rs1475221 G / 0.219	1.006	0.86	1	NE
rs12940622	<i>RPTOR</i>	G / 0.575	0.018 (0.003)	2.49×10^{-09}	A / 0.447	0.953	0.12	1	NE
rs11847697	<i>PRKD1</i>	T / 0.042	0.049 (0.008)	3.99×10^{-09}	NA	NA	NA	NA	NA
rs2075650	<i>TOMM40; APOE; APOC1</i>	A / 0.848	0.026 (0.005)	1.25×10^{-08}	A / 0.854	0.968	0.46	1	NE
rs2121279	<i>LRP1B</i>	T / 0.152	0.025 (0.004)	2.31×10^{-08}	C / 0.880	0.897	0.02	1	-
rs29941	<i>KCTD15</i>	G / 0.669	0.018 (0.003)	2.41×10^{-08}	G / 0.686	1.023	0.49	1	NE
rs1808579	<i>NPC1; C18orf8</i>	C / 0.534	0.017 (0.003)	4.17×10^{-08}	C / 0.548	0.986	0.64	1	NE

^a unadjusted p-values are adjusted for multiplicity by Bonferroni correction for 97 tests

^b Direction of effect: + the BMI increasing allele is *less frequently* found in AN cases as compared to controls; - the BMI increasing allele is more frequently found in AN cases as compared to controls

^c Proxy SNAP (Broad Institute) with HapMap release 22, CEU population, r^2 threshold of 0.8 and a distance limit of 500 kb; NA; not available; NE: not estimated

Supplementary Table S5: 32 genome-wide significant loci for BMI, obesity, childhood obesity not described in Locke et al., 2015 (reviewed in Yazdi et al. 2015, Table 2) assessed in the GWAMA for AN (GCAN, Boraska et al., 2014)

Gene / BMI increasing SNP / chromosome / trait (Yazdi et al. 2015; Table 2)	Reference alleles in AN case-control GWAMA (GCAN, Boraska et al., 2014)		
	Reference allele in AN cases	AN risk (odds ratio) for reference allele	Nominal p-value ^b
ADCY9 / rs2531995 / 16 / obesity	T	0.970	0.33
BRE / rs116612809 / 2 / BMI	NA	NA	NA
GNAT2 / rs17024258 / 1 / obesity	NA	NA	NA
GP2 / rs12597579 / 16 / BMI	T	0.991	0.94
GRP120 / rs116454156 / 10 / obesity	NA	NA	NA
HNF4G / rs4735692 / 8 / obesity	^a rs2060604 T	1.088	0.01
HOXB5 / rs9299 / 17 / childhood obesity	T	0.969	0.33
HS6ST3 / rs7989336 / 13 / obesity	^a rs912690 C	1.012	0.70
KCNMA1 / rs2116830 / 10 / obesity	T	0.993	0.85
KLF9 / rs11142387 / 9 / BMI	C	0.964	0.23
LEPR / rs11208659 / 1 / childhood obesity	^a rs11208660 T	0.987	0.81
LPIN2 / rs643507 / 18 / obesity (asthmatic patients)	NA	NA	NA
MAF / rs1424233 / 16 / obesity	C	1.005	0.87
MRPS33P4 / rs13041126 / 20 / obesity	C	1.035	0.31
NPC1 / rs1805081 / 18 / obesity	C	1.017	0.59
NTRK2 / rs1211166 / 9 / BMI	^a rs1187323 C	1.060	0.13
OLFM4 / rs9568856 / 13 / obesity	^a rs4883723 A	1.134	0.0037
OLFM4 / rs9568867 / 13 / obesity	^a rs12429545 A	1.124	0.01
PACS1 / rs564343 / 11 / childhood obesity	G	0.994	0.86
PCSK1 / rs261967 / 5 / BMI, obesity	^a rs261966 C	0.977	0.46
PCSK1 / rs6232 / 5 / BMI, obesity	C	1.262	0.01
PCSK1 / rs6234 / 5 / BMI, obesity	^a rs7713317 G	1.025	0.46

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Supplementary Table S5: 32 genome-wide significant loci for BMI, obesity, childhood obesity not described in Locke et al., 2015 (reviewed in Yazdi et al. 2015, Table 2) assessed in the GWAMA for AN (GCAN, Boraska et al., 2014)

PCSK1 / rs6235 / 5 / BMI, obesity	^a rs7713317 G	1.025	0.46
PRKCH / rs1957894 / 14 / childhood obesity	^a rs1957895 T	0.964	0.48
QPCTL / rs2287019 / 19 / obesity, overweight	^a rs11672660 T	0.990	0.79
RMST / rs11109072 / 12 / childhood obesity	^a rs7963257 G	1.093	0.28
RPL27A / rs11042023 / 11 / obesity	T	1.001	0.98
RPTOR / rs7503807 / 17 / overweight	A	0.958	0.16
SDCCAG8 / rs12145833 / 1 / childhood obesity	G	0.956	0.30
TNKS / rs17150703 / 8 / childhood obesity	A	0.938	0.22
TOMM40, APOE, APOC1 / rs2075650 / 19 / BMI	G	1.033	0.46
ZZZ3 / rs17381664 / 1 / obesity	C	0.984	0.62

^aProxy SNAP (Broad Institute) with HapMap release 22, CEU population, r^2 threshold of 0.8 and a distance limit of 500 kb

^bunadjusted p-values, p-values adjusted for multiplicity by Bonferroni correction for 32 tests are only given if significant after correction

NA: not available

Supplementary Table S6: 68 genome-wide significant WHR loci from a European GWAMA primary analysis (GIANT, Shungin et al., 2015; Tables 1 and 3) assessed in the GWAMA for AN (GCAN, Boraska et al., 2014)

SNP / WHR (Shungin et al., 2015)	Reference alleles in AN case-control GWAMA (GCAN, Boraska et al., 2014)		
	Reference allele in AN cases	AN risk (odds ratio) for reference allele	Nominal p-value ^b
rs905938	C	0.974	0.45
rs10919388	NA	NA	NA
rs1385167	G	0.990	0.83
rs1569135	A	1.004	0.91
rs10804591	A	1.076	0.06
rs17451107	^a rs10049088 T	1.083	0.01
rs3805389	A	0.953	0.17
rs9991328	C	1.039	0.21
rs303084	A	0.978	0.54
rs9687846	^a rs3843467 T	0.964	0.35
rs6556301	NA	NA	NA
rs7759742	^a rs6932542 A	1.027	0.38
rs1776897	G	0.991	0.87
rs7801581	NA	NA	NA
rs7830933	^a rs13273073 T	1.011	0.75
rs12679556	T	1.001	0.98
rs10991437	A	0.986	0.78
rs7917772	G	1.033	0.30
rs11231693	NA	NA	NA
rs4765219	A	1.020	0.54
rs8042543	T	1.027	0.47
rs8030605	A	0.940	0.18

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Supplementary Table S6: 68 genome-wide significant WHR loci from a European GWAMA primary analysis (GIANT, Shungin et al., 2015; Tables 1 and 3) assessed in the GWAMA for AN (GCAN, Boraska et al., 2014)

rs1440372	T	1.011	0.74
rs2925979	T	1.041	0.23
rs4646404	A	0.942	0.06
rs8066985	^a rs1120297 C	0.965	0.24
rs12454712	C	1.001	0.97
rs12608504	A	1.023	0.48
rs4081724	NA	NA	NA
rs979012	T	0.998	0.95
rs224333	G	0.981	0.53
rs6090583	G	0.969	0.31
rs1534696	C	0.961	0.20
rs2645294	C	0.962	0.21
rs714515	A	1.039	0.22
rs2820443	C	1.013	0.70
rs10195252	T	1.005	0.86
rs17819328	G	0.984	0.61
rs2276824	NA	NA	NA
rs2371767	^a rs4616635 C	0.998	0.95
rs1045241	T	0.949	0.12
rs7705502	^a rs17695092 G	1.008	0.80
rs1294410	^a rs1294409 C	0.973	0.39
rs1358980	T	0.983	0.57
rs1936805	C	1.003	0.92
rs10245353	^a rs1055144 T	0.997	0.93

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Supplementary Table S6: 68 genome-wide significant WHR loci from a European GWAMA primary analysis (GIANT, Shungin et al., 2015; Tables 1 and 3) assessed in the GWAMA for AN (GCAN, Boraska et al., 2014)

rs10842707	^a rs718314 G	1.042	0.24
rs1443512	C	1.042	0.26
rs2294239	G	1.028	0.37
rs10925060	NA	NA	NA
rs10929925	^a rs12104582 C	0.966	0.25
rs2124969	^a rs6731260 G	0.978	0.48
rs17472426	G	1.037	0.51
rs7739232	A	1.054	0.38
rs13241538	^a rs13234407 A	0.992	0.79
rs7044106	^a rs1359328 T	1.022	0.56
rs11607976	T	1.071	0.03
rs1784203	^a rs4753523	0.983	0.63
rs1394461	C	0.972	0.44
rs319564	T	0.966	0.27
rs2047937	C	1.035	0.26
rs2034088	T	0.999	0.97
rs1053593	T	0.982	0.56
rs1664789	C	0.993	0.83
rs722585	A	0.995	0.88
rs1144	^a rs4753534	0.941	0.05
rs2398893	G	0.923	0.02
rs4985155{	G	1.071	0.03

^aProxy SNAP (Broad Institute) with HapMap release 22, CEU population, r2 threshold of 0.8 and a distance limit of 500 kb

^bunadjusted p-values, p-values adjusted for multiplicity by Bonferroni correction for 68 tests are only given if significant after correction

NA: not available; NE: not estimated

Supplementary Table S7: *In silico* mutation analyses pertaining to the four identified genes (ExAC Browser (Beta); Exome Aggregation Consortium)*

Gene	Different missense mutations (allele frequencies)	Different nonsense mutations (allele frequencies)	Different frameshift mutations (allele frequencies)
<i>CTBP2</i>	439 (0.0000082 - 0.49)	13 (0.0000083 - 0.082)	29 (0.0000083- 0.002)
<i>CCNE1</i>	99 (0.000008236 - 0.002)	1 (0.000008240)	none
<i>CARF</i>	211 (0.000008281 - 0.091)	9 (0.000008282 - 0.005)	9 (0.000008281 - 0.003)
<i>NBEAL1</i>	578 (0.000008280 - 0.064)	27 (0.000008287 -0.0005)	22 (0.000008281 - 0.009)

Exome Aggregation Consortium (ExAC), Cambridge, MA (URL: <http://exac.broadinstitute.org>) [May, 2015 accessed].

*The data set provided on this website spans 60,706 unrelated individuals sequenced as part of various disease-specific and population genetic studies. The ExAC Principal Investigators and groups that have contributed data to the current release are listed on the website.

All data here are released under a Fort Lauderdale Agreement for the benefit of the wider biomedical community.

Supplementary Table S8: association test of the nine AN / BMI SNPs with adult obesity in GIANT extreme (order of SNPs as in Table 1)

SNP	Gene	extreme BMI			overweight			obesity class I			obesity class II			obesity class III		
		P	Ncases	Ncontrols	P	Ncases	Ncontrols	P	Ncases	Ncontrols	P	Ncases	Ncontrols	P	Ncases	Ncontrols
rs1561589	<i>CTBP2</i>	0.02	7435	7576	0.0083	92546	65729	0.011	32618	64727	0.067	9738	61015	0.08	2544	37624
rs12771627	<i>CTBP2</i>	0.023	6685	6818	0.022	92086	65661	0.005	32350	64659	0.038	9670	60489	0.095	2481	35261
rs11245456	<i>CTBP2</i>	0.013	6635	6760	0.041	92025	65634	0.011	32311	64633	0.014	9657	60484	0.0091	2481	35257
rs17513613	<i>CCNE1</i>	0.053	7139	7289	0.086	90410	64768	0.048	31977	63972	0.026	9601	60401	0.0086	2673	42125
rs17406900	<i>CARF</i>	0.00037	7847	7995	0.069	92976	65801	0.0018	32848	65800	0.019	9867	62474	0.26	2829	45550
rs7593917	<i>NBEAL1</i>	0.00042	7844	7991	0.04	92899	65777	0.0036	32838	65776	0.039	9864	62450	0.24	2830	45583
rs11691351	<i>NBEAL1</i>	0.00037	7850	7996	0.037	92962	65810	0.0034	32829	65809	0.035	9855	62494	0.23	2827	45570
rs8102137	<i>CCNE1</i>	0.049	7142	7290	0.098	89977	64766	0.05	32035	64049	0.021	9627	60445	0.0054	2701	42220
rs7573079	<i>NBEAL1</i>	0.00023	7849	7994	0.042	92989	65822	0.0045	32848	65821	0.023	9867	62495	0.25	2831	45572

Data were derived from Berndt, et al. 2013: extreme BMI upper and lower 5% of the BMI distribution; other controls were subjects with BMI < 25 kg/m² and cases were defined as having BMI ≥ 25 kg/m² for the overweight class, BMI ≥ 30 kg/m² for obesity class I, BMI ≥ 35 kg/m² for obesity class II and BMI ≥ 40 kg/m² for obesity class III