SUPPLEMENTAL MATERIAL

Description of the studies

Myocardial Infarction Genetics Consortium (MIGen)[1]*:* This case-control study included 2,967 cases of early-onset myocardial infarction (MI) (men ≤50 or women ≤60 years old), diagnosed on the basis of autopsy evidence or a combination of chest pain, electrocardiographic evidence, and elevation of cardiac biomarkers, and 3,075 age- and sex-matched controls. Genome-wide genotype data and associated phenotype data were obtained via the database of Genotypes and Phenotypes (dbGaP; http://dbgap.ncbi.nlm.nih.gov; project number #5195). In this study, we performed a discovery analysis of GRS-GRS interactions on myocardial infarction.

Framingham Heart Study (FHS)[2]*:* We included individuals from the FHS Offspring Cohort of 5,124 individuals that were offspring of the original participants and their spouses recruited in 1971. We selected participants aged 35 to 74 years at the time of the exam, who were free of cardiovascular disease (CVD) at that time, and for whom DNA collected during the 1980s and 1990s[3] (3) and complete follow-up information was available. To maximize the number of participants included in the analysis, we set exam 5 as the baseline visit for the Offspring Cohort (3,557 individuals, 1991-95). All coronary events (myocardial infarction, angina, coronary revascularization and death due to coronary artery disease) that occurred during follow-up until the end of 2007 were considered as outcomes of interest. Genome-wide genotype data and associated phenotype data for the FHS sample were also obtained via dbGaP (project number #5195).

FINRISK (FINRISK 1997 & FINRISK 2002): The FINRISK cohorts comprise the respondents of representative, cross-sectional population surveys that have been carried out every 5 years

since 1972 to assess the risk factors of chronic diseases and health behavior in the working age population in 3-5 large study areas of Finland. DNA samples were collected in the following survey years: 1987, 1992, 1997, 2002, 2007, and 2012. The MONICA and EHES (EU) procedures were applied in phenotype collection and a wide spectrum of laboratory tests was carried out from serum and plasma samples. Background information on socioeconomic status, medical history, diet, exercise, anthropometric measures, etc. was collected by questionnaires and during a clinical visit. The cohorts have been followed up by linking them to the national hospital discharge register, causes-of-death register, and cancer register. The study included 5699 individuals from the FINRISK 1997 cohort and 2426 from the FINRISK 2002 cohort.

Estonian Biobank (EGCUT)[4]*:* The Estonian Biobank is the population-based biobank of the Estonian Genome Center at the University of Tartu (www.biobank.ee; EGCUT). The entire project is conducted according to the Estonian Gene Research Act and all of the participants have signed a broad informed consent. The cohort size is up to 50,750 individuals from 18 years of age and up, which closely reflects the age, sex, and geographical distribution of the Estonian population. All of the subjects are recruited randomly by general practitioners and physicians in hospitals. A Computer Assisted Personal interview is completed during 1 - 2 hours visit at a doctor's office, which includes personal, genealogical, educational, occupational history, and lifestyle data. Anthropometric measurements, blood pressure, and resting heart rate are measured and venous blood taken during the visit. Medical history and current health status is recorded according to ICD-10 codes.

The following ICD-9 and ICD-10 codes were initially used to identify potential coronary events in the follow up of the cohorts:

a) Hard ischemic heart disease events (non-fatal and fatal MI and CHD deaths) using the following codes:

i. ICD9: non fatal MI Code 410; CHD death Codes 410-414

ii. ICD10: non fatal MI Codes I21-l22; CHD death Codes I20-I22, I24.8, I24.9, I25

b) All ischemic heart disease events (additionally including angina and coronary revascularization) using the following codes:

i. ICD9: non fatal CHD Codes 410-414; CHD death Codes 410-414

ii. ICD10: non fatal CHD Codes I20-22, I24.8, I24.9, I25; CHD death Codes I20-22, I24.8, I24.9, I25.

Cases with a code of interest were further investigated and categorized by an event committee in the Framingham Heart Study, FINRISK and the Estonian Biobank cohorts.

Statistical analysis: multiplicative and additive interactions

When the effect of one exposure on an outcome depends in some way on the presence or absence of another exposure, there is interaction between the two exposures. Analysis of the presence of interactions may be useful to identify which subgroups of the population would benefit the most from an intervention when resources are limited, and also may provide insight into the mechanisms for the outcome. Interactions can be assessed on different scales, mainly additive or multiplicative, and both of them should be analysed and presented[5]. Consider data on the table below showing the probability of an outcome according to the exposure of two factors (A and B):

	B=0	B=1
A=0	0.10	0.60
A=1	0.90	4.50

Where: p_{00} is the probability of the outcome when the individuals are not exposed to factor A or B (p_{00}=0.10), p_{10} is the probability of the individuals exposed to A but not to B (p_{10}=0.90),

p_{01} is the probability of the individuals exposed to B but not to A (p_{01}=0.60), and p_{11} is the probability of presenting the outcome of those exposed both to A and B (p_{11}=4.50).

A natural way to assess interaction is to measure the extent to which the effect of the combination of the two factors together exceeds the effect of each considered individually:

[1] $$(p_{11} - p_{00}) - [(p_{10} - p_{00}) + (p_{01} - p_{00})] = p_{11} - p_{10} - p_{01} + p_{00}$$

If this difference is nonzero, there is interaction on the additive scale. If the result is > 0, the interaction is positive or "super-additive"; if the result is < 0, the interaction is negative or "sub-additive". For the data in Table 1, we can calculate: 4.50 –0.90 – 0.60 + 0.10 = 3.10, a positive or "super-additive" interaction.

Sometimes, instead of using risk differences to measure effects, one might use risk ratios or odds ratios. In our example: RR_{10} = 0.90 / 0.10 = 9; RR_{01} = 0.60 / 0.10 = 6; RR_{11} = 4.50 / 0.10 = 45.

A measure of interaction on the multiplicative scale for risk ratios could then be taken as:

[2] $$RR_{11} / (RR_{10} \cdot RR_{01})$$

measuring the extent to which, on the risk ratio scale, the effect of both exposures together exceeds the product of the effects of the two exposures considered separately. If the ratio is 1, then the effect of both exposures together is equal to the product of the effect of the two exposures considered separately, that is, there is no interaction on the multiplicative scale. If the ratio is > 1, the multiplicative interaction is positive. If the ratio is < 1, the multiplicative interaction is negative.

In our example: 45 / (9 · 6) = 45 / 54 = 0.83, the multiplicative interaction is negative on the risk ratio scale. In general, measures of multiplicative interaction on the odds ratio and risk ratio scales will be very close to one another whenever the outcome is rare.

We may assess additive interaction from data when only relative risks (or odds ratios) are reported. If we divide eq. [1] by p_{00} we obtain the following:

[3] $$p_{11}/p_{00} - p_{10}/p_{00} - p_{01}/p_{00} + p_{00}/p_{00} = RR_{11} - RR_{10} - RR_{01} + 1$$

This quantity is referred to as the "relative excess risk due to interaction" or RERI[6]. We will assume a super-additive interaction if RERI > 0, a sub-additive interaction if RERI < 0, and an absence of interaction on the additive scale if RERI = 0.

Another commonly used metric to assess the presence of an additive interaction using relative risk values is the "synergy index" that measures the extent to which the risk ratio for both exposures together exceeds 1, and whether this is greater than the sum of the extent to which each of the risk ratios, considered separately, exceeds 1:

[4] $$\text{Synergy Index} = (RR_{11} - 1) / [(RR_{10} - 1) + (RR_{01} - 1)]$$

We will assume a super-additive interaction if this index > 1, a sub-additive interaction if the index < 1, and an absence of interaction on the additive scale if the index = 1.

What differential information do we obtain from the additive and the multiplicative interaction? The additive scale is useful for assessing the public health importance of interventions and the public

health significance of interaction and for targeting subpopulations for which the intervention is most effective. A second reason sometimes given for using additive interaction is that it more closely corresponds to tests for mechanistic interaction. Finally, tests for additive interaction usually are more powerful than tests for multiplicative interaction.

On the other hand, the multiplicative scale is the most natural scale on which to assess interaction for logistic or survival regression models. Second, some authors claim that there is, in general, less heterogeneity on the multiplicative than on the additive scale. Another reason to assess multiplicative interaction is that the relative effect measures are better suited to assessing causality, although the question whether the relative or absolute measure is more useful for assessing causality varies by setting[7].

Supplementary Table 1. Genetic variants identified to be robustly associated with cardiovascular risk factors or coronary endpoints and included in the different genetic risk scores. The associated gene, possible alleles, risk allele, risk allele frequency (RAF), p-value and effect size of the association between each variant and the specific trait of interest, risk allele frequency in the different studies, and references supporting the selection of the genetic variants.

Ischemic heart disease (IHD)

Top SNP	Gene	Chr	Risk allele	RAF	p-value	OR	References
rs11206510	*PCSK9*	1	T	0.85	2.34E-08	1.08	(8,9,10)
rs17114036	*PPAP2B*	1	A	0.92	2.22E-13	1.13	(8,10)
rs646776	*CELSR2-PSRC1-SORT1*	1	T	0.75	9.01E-19	1.11	(9)
rs4845625	*IL6R*	1	T	0.45	3.93E-08	1.05	(10)
rs17464857	*MIA3*	1	T	0.86	4.18E-05	1.06	(10)
rs17465637	*MIA3*	1	C	0.66	3.52E-12	1.08	(8,9)
rs515135	*APOB*	2	C	0.79	3.09E-08	1.07	(10)
rs6544713	*ABCG5-ABCG8*	2	T	0.32	8.88E-07	1.05	(8,10)
rs1561198	*VAMP5-VAMP8-GGCX*	2	T	0.46	6.37E-10	1.06	(10)
rs2252641	*ZEB2-ACO74093.1*	2	C	0.48	5.16E-04	1.03	(9,10)
rs6725887	*WDR12*	2	C	0.11	9.51E-18	1.14	(8,10)
rs9818870	*MRAS*	3	T	0.14	2.21E-06	1.07	(9,10)
rs1878406	*EDNRA*	4	T	0.16	1.24E-06	1.06	(10)
rs7692387	*GUCY1A3*	4	G	0.81	7.35E-09	1.07	(10)
rs273909	*SLC22A4-SLC22A5*	5	G	0.12	1.24E-04	1.06	(10)
rs12526453	*PHACTR1*	6	C	0.71	2.14E-20	1.10	(8,9,10)
rs17609940	*ANKSIA*	6	G	0.82	3.00E-02	1.03	(8,10)
rs10947789	*KCKN5*	6	T	0.78	1.63E-06	1.05	(10)
rs12190287	*TCF21*	6	C	0.62	1.07E-03	1.06	(8,10)
rs2048327	*SLC22A3-LPAL2-LPA*	6	C	0.35	2.46E-09	1.06	(10)
rs3798220	*LPA*	6	C	0.02	4.66E-09	1.42	(8,10)
rs4252120	*PLG*	6	T	0.74	3.32E-03	1.03	(10)
rs2023938	*HDAC9*	7	C	0.10	1.36E-04	1.06	(10)
rs10953541	*BCAP29*	7	C	0.78	1.02E-05	1.05	(9)
rs11556924	*ZC3HC1*	7	C	0.69	5.34E-11	1.08	(8,10)
rs264	*LPL*	8	G	0.85	1.06E-05	1.06	(10)
rs2954029	*TRIB1*	8	A	0.55	2.61E-06	1.04	(8,10)
rs4977574	*CDKN2A, CDKN2B*	9	G	0.49	6.35E-98	1.21	(8,9)
rs579459	*ABO*	9	C	0.21	1.14E-10	1.08	(8,10)
rs2505083	*KIAA1462*	10	C	0.40	1.57E-10	1.06	(10)
rs2047009	*CXCL12*	10	G	0.48	2.75E-11	1.06	(10)
rs501120	*CXCL12*	10	T	0.81	1.39E-11	1.08	(10)
rs11203042	*LIPA*	10	T	0.45	1.22E-04	1.04	(10)
rs1412444	*LIPA*	10	T	0.37	5.15E-12	1.07	(10)
rs12413409	*CYP17A1-CNM2-NT5C2*	10	G	0.89	1.07E-07	1.08	(8,10)
rs974819	*PDGFD*	11	T	0.33	2.44E-10	1.07	(10)
rs964184	*ZNF259, APOA5-*	11	G	0.18	5.60E-05	1.05	(8)

	A4-C3-A1						
rs7136259	*ATP2B1*	12	T	0.43	2.45E-05	1.04	(9)
rs3184504	*SH2B3*	12	T	0.42	1.03E-09	1.07	(8,9,10)
rs9319428	*FLT1*	13	A	0.31	7.13E-05	1.04	(10)
rs4773144	*COLA1-COLA2*	13	G	0.43	3.87E-07	1.05	(8,10)
rs9515203	*COLA1-COLA2*	13	T	0.76	9.33E-10	1.07	(10)
rs2895811	*HHIPL1*	14	C	0.41	1.86E-05	1.04	(8,10)
rs7173743	*ADAMTS7*	15	T	0.56	5.55E-16	1.08	(10)
rs17514846	*FURIN-FES*	15	A	0.44	3.10E-07	1.05	(10)
rs216172	*SMG6*	17	C	0.35	5.07E-07	1.05	(8,10)
rs12936587	*RAI1-PEMT-RASD1*	17	G	0.61	8.24E-04	1.03	(8,10)
rs46522	*UBESZ*	17	T	0.51	1.84E-05	1.04	(8,10)
rs1122608	*LDLR*	19	G	0.77	2.73E-11	1.08	(8,9,10)
rs2075650	*ApoE-ApoC1*	19	G	0.13	1.61E-06	1.07	(10)
rs445925	*ApoE-ApoC1*	19	G	0.90	4.23E-06	1.09	(10)
rs9982601	*Gene desert (KCNE2)*	21	T	0.13	1.33E-13	1.12	(8,9,10)
rs17087335	*REST-NOA1*	4	T	0.21	4.60E-08	1.06	(11)
rs3918226	*NOS3*	7	T	0.06	1.70E-09	1.14	(11)
rs10840293	*SWAP70*	11	A	0.55	1.30E-08	1.06	(11)
rs56062135	*SMAD3*	15	C	0.79	4.50E-09	1.07	(11)
rs8042271	*MFGE8-ABHD2*	15	G	0.93	3.70E-08	1.10	(11)
rs7212798	*BCAS3*	17	C	0.15	1.90E-08	1.08	(11)
rs663129	*PMAIP1-MC4R*	18	A	0.26	3.20E-08	1.06	(11)
rs180803	*POM12IL9P-ADORA2A*	22	G	0.97	1.60E-10	1.20	(11)

LDL

Top SNP	Gene	Chr	Risk allele	RAF	p-value	Effect size (mg/dL)	Reference
rs12027135	*LDLRAP1*	1	T	0.53	$4x10^{-11}$	1.1	(12)
rs2479409	*PCSK9*	1	G	0.3	$2X10^{-28}$	2.01	(12)
rs3850634	*ANGPTL3*	1	T	0.68	$5x10^{-41}$	1.59	(12)
rs629301	*SORT1*	1	T	0.78	$1x10^{-170}$	5.65	(12)
rs2807834	*MOSC1*	1	G	0.68	$6x10^{-11}$	1.09	(12)
rs514230	*IRF2BP2*	1	T	0.52	$9x10^{-12}$	1.13	(12)
rs1367117	*APOB*	2	A	0.3	$4x10^{-114}$	4.05	(12)
rs4299376	*ABCG5/8*	2	G	0.3	$2x10^{-47}$	2.75	(12)
rs12916	*HMGCR*	5	C	0.39	$5x10^{-45}$	2.45	(12)
rs6882076	*TIMD4*	5	C	0.65	$2x10^{-22}$	1.67	(12)
rs3757354	*MYLIP*	6	C	0.78	$1x10^{-11}$	1.43	(12)
rs1800562	*HFE*	6	G	0.94	$6x10^{-10}$	2.22	(12)
rs3177928	*HLA*	6	A	0.16	$2x10^{-15}$	1.83	(12)
rs11153594	*FRK*	6	C	0.59	$3x10^{-9}$	0.89	(12)
rs1564348	*LPA*	6	C	0.17	$2x10^{-17}$	1.95	(12)
rs12670798	*DNAH11*	7	C	0.23	$7x10^{-10}$	1.26	(12)
rs217386	*NPC1L1*	7	G	0.57	$4x10^{-11}$	1.17	(12)
rs2126259	*PPP1R3B*	8	C	0.9	$7x10^{-15}$	2.22	(12)

rs1030431	*CYP7A1*	8	A	0.35	$4x10^{-9}$	0.95	(12)
rs2954022	*TRIB1*	8	C	0.54	$3x10^{-29}$	1.84	(12)
rs11136341	*PLEC1*	8	G	0.4	$4x10^{-13}$	1.4	(12)
rs649129	*ABO*	9	T	0.22	$8x10^{-22}$	2.05	(12)
rs1129555	*GPAM*	10	A	0.29	$2x10^{-9}$	1.08	(12)
rs174583	*FADS1-2-3*	11	C	0.65	$1x10^{-21}$	1.71	(12)
rs964184	*APOA1-C3-A4-A5*	11	G	0.13	$1x10^{-26}$	2.85	(12)
rs11220462	*ST3GAL4*	11	A	0.14	$1x10^{-15}$	1.95	(12)
rs11065987	*BRAP*	12	A	0.58	$1x10^{-9}$	0.97	(12)
rs1169288	*HNF1A*	12	C	0.33	$1x10^{-15}$	1.42	(12)
rs2332328	*NYNRIN*	14	T	0.48	$4x10^{-11}$	1.17	(12)
rs247616	*CETP*	16	C	0.68	$9x10^{-13}$	1.45	(12)
rs2000999	*HPR*	16	A	0.2	$2x10^{-22}$	2	(12)
rs7225700	*OSBPL7*	17	C	0.65	$4x10^{-9}$	0.87	(12)
rs6511720	*LDLR*	19	G	0.89	$4x10^{-117}$	6.99	(12)
rs10401969	*CILP2*	19	T	0.93	$7x10^{-22}$	3.11	(12)
rs4420638	*APOE-C1-C2*	19	G	0.17	$9x10^{-147}$	7.14	(12)
rs2902941	*MAFB*	20	A	0.67	$1x10^{-8}$	0.98	(12)
rs909802	*TOP1*	20	T	0.47	3x10-19	1.41	(12)
rs267733	*ANXA9-CERS2*	1	A	0.84	5x10-9	0.87	(13)
rs12748152	*PIGV-NROB2*	1	T	0.09	3X10-12	0.87	(13)
rs2710642	*EHBP1*	2	A	0.65	6x10-9	0.87	(13)
rs10490626	*INSIG2*	2	G	0.92	2x10-12	0.87	(13)
rs2030746	*LOC84931*	2	T	0.4	9x10-9	0.87	(13)
rs1250229	*FN1*	2	C	0.73	3x10-8	0.87	(13)
rs11563251	*UGT1A1*	2	T	0.12	5x10-8	0.87	(13)
rs7640978	*CMTM6*	3	C	0.91	1x10-8	0.87	(13)
rs17404153	*ACAD11*	3	G	0.86	2x10-9	0.87	(13)
rs6831256	*LRPAP1*	4	G	0.42	2x10-8	0.87	(13)
rs4530754	*CSNK1G3*	5	A	0.54	4x10-12	0.87	(13)
rs4722551	*MIR148A*	7	C	0.2	4x10-14	0.87	(13)
rs10102164	*SOX17*	8	A	0.21	4x10-11	0.87	(13)
rs3780181	*VLDLR*	9	A	0.92	2x10-9	0.87	(13)
rs4942486	*BRCA2*	13	T	0.48	2x10-11	0.87	(13)
rs1801689	*APOH-PRXCA*	17	C	0.04	1x10-11	0.87	(13)
rs314253	*DLG4*	17	T	0.63	3x10-10	0.87	(13)
rs364585	*SPTLC3*	20	G	0.62	4x10-10	0.87	(13)
rs2328223	*SNX5*	20	C	0.21	6x10-9	0.87	(13)
rs5763662	*MTMR3*	22	T	0.04	1x10-8	0.87	(13)
rs4253772	*PPARA*	22	T	0.11	3x10-8	0.87	(13)

HDL

Top SNP	Gene	Chr	Risk allele	RAF	p-value	Effect size (mg/dL)	References
rs1042034	*APOB*	2	T	0.78	1x10-30	-0.9	(12)
rs10808546	*TRIB1*	8	C	0.56	6x10-19	-0.61	(12)

rs12328675	*COBLL1*	2	T	0.87	3x10-10	-0.68	(12)
rs12678919	*LPL*	8	A	0.88	9x10-98	-2.25	(12)
rs12967135	*MC4R*	18	A	0.23	7x10-09	-0.42	(12)
rs13107325	*SLC39A8*	4	T	0.07	7x10-11	-0.84	(12)
rs1515100	*IRS1*	2	A	0.63	2x10-09	-0.46	(12)
rs1532085	*LIPC*	15	G	0.61	3x10-96	-1.45	(12)
rs1689800	*ZNF648*	1	G	0.35	3x10-10	-0.47	(12)
rs16942887	*LCAT*	16	G	0.88	8x10-33	-1.27	(12)
rs17145738	*MLXIPL*	7	C	0.88	1x10-09	-0.57	(12)
rs174601	*FADS1-2-3*	11	T	0.36	2x10-22	-0.73	(12)
rs181362	*UBE2L3*	22	T	0.2	1x10-08	-0.46	(12)
rs1883025	*ABCA1*	9	T	0.25	2x10-33	-0.94	(12)
rs2293889	*TRPS1*	8	T	0.41	6x10-11	-0.44	(12)
rs2652834	*LACTB*	15	A	0.2	9x10-09	-0.39	(12)
rs2814944	*C6orf106*	6	A	0.16	4x10-09	-0.49	(12)
rs2923084	*AMPD3*	11	G	0.17	5x10-08	-0.41	(12)
rs2925979	*CMIP*	16	T	0.3	2x10-11	-0.45	(12)
rs3136441	*LRP4*	11	T	0.85	3x10-18	-0.78	(12)
rs3741414	*LRP1*	12	C	0.76	2x10-08	-0.46	(12)
rs3764261	*CETP*	16	C	0.68	7x10-380	-3.39	(12)
rs4082919	*PGS1*	17	G	0.48	5x10-09	-0.4	(12)
rs4148008	*ABCA8*	17	G	0.32	2x10-10	-0.42	(12)
rs4420638	*APOE-C1-C2*	19	G	0.17	4x10-21	-1.06	(12)
rs4660293	*PABPC4*	1	G	0.23	4x10-10	-0.48	(12)
rs4731702	*KLF14*	7	C	0.52	1x10-15	-0.59	(12)
rs4759375	*SBNO1*	12	C	0.94	8x10-09	-0.86	(12)
rs4765127	*ZNF664*	12	G	0.66	3x10-10	-0.44	(12)
rs4846914	*GALNT2*	1	G	0.4	4x10-21	-0.61	(12)
rs605066	*CITED2*	6	C	0.42	3x10-08	-0.39	(12)
rs6065906	*PLTP*	20	C	0.18	2x10-22	-0.93	(12)
rs643531	*TTC39B*	9	C	0.14	1x10-13	-0.72	(12)
rs6450176	*ARL15*	5	A	0.26	5x10-08	-0.49	(12)
rs7115089	*UBASH3B*	11	C	0.63	3x10-08	-0.31	(12)
rs7134375	*PDE3A*	12	C	0.58	4x10-08	-0.4	(12)
rs7134594	*MVK*	12	C	0.47	7x10-15	-0.44	(12)
rs7241918	*LIPG*	18	G	0.17	3x10-49	-1.31	(12)
rs7255436	*ANGPTL4*	19	C	0.47	3x10-08	-0.45	(12)
rs737337	*LOC55908*	19	C	0.08	3x10-09	-0.64	(12)
rs838880	*SCARB1*	12	T	0.69	3x10-14	-0.61	(12)
rs881844	*STARD3*	17	C	0.34	3x10-14	-0.51	(12)
rs964184	*APOA1-C3-A4-A5*	11	G	0.13	5x10-47	-1.5	(12)
rs9987289	*PPP1R3B*	8	A	0.09	6x10-25	-1.21	(12)
rs1084651	LPA	6	A	0.16	3X10-8	-0.56	(12)
rs386000	LILRA	8	G	0.8	4X10-16	-0.83	(12)
rs1800961	HNF4A	20	T	0.03	1X10-15	-1.88	(12)
rs12748152	*PIGV-*	1	T	0.09	1x10-15	-0.31	(13)

	NROB2						
rs12145743	*HDGF-PMVK*	1	T	0.66	2X10-8	-0.31	(13)
rs4650994	*ANGPTL1*	1	A	0.51	7x10-9	-0.31	(13)
rs1047891	*CPS1*	2	A	0.33	9x10-10	-0.31	(13)
rs2606736	*ATG7*	3	T	0.61	5x10-8	-0.31	(13)
rs2290547	*SETD2*	3	A	0.2	4x10-9	-0.31	(13)
rs2013208	*RBM5*	3	C	0.5	9x10-12	-0.31	(13)
rs13326165	*STAB1*	3	G	0.79	9x1011	-0.31	(13)
rs6805251	*GSK3B*	3	C	0.61	1x10-8	-0.31	(13)
rs17404153	*ACAD11*	3	T	0.14	5x10-9	-0.31	(13)
rs10019888	*C4orf52*	4	G	0.18	5x10-8	-0.31	(13)
rs3822072	*FAM13A*	4	A	0.46	4x10-12	-0.31	(13)
rs2602836	*ADH5*	4	G	0.56	5x10-8	-0.31	(13)
rs1936800	*RSPO3*	6	T	0.51	3x10-10	-0.31	(13)
rs998584	*VEGFA*	6	A	0.49	2x10-11	-0.31	(13)
rs702485	*DAGLB*	7	A	0.55	6x10-12	-0.31	(13)
rs4142995	*SNX13*	7	T	0.38	9x10-12	-0.31	(13)
rs4917014	*IKZF1*	7	T	0.68	1x10-8	-0.31	(13)
rs17173637	*TMEM176A*	7	C	0.12	2x10-8	-0.31	(13)
rs970548	*MARCH8-ALOX5*	10	A	0.74	2x10-10	-0.31	(13)
rs11246602	*OR4C46*	11	A	0.85	2x10-10	-0.31	(13)
rs12801636	*KAT5*	11	G	0.77	3x10-8	-0.31	(13)
rs499974	*MOGAT2-DGAT2*	11	A	0.19	1x10-8	-0.31	(13)
rs4983559	*ZBTB42-AKT1*	14	A	0.6	1x10-8	-0.31	(13)
rs1121980	*FTO*	16	A	0.43	7x10-9	-0.31	(13)
rs17695224	*HAS1*	19	A	0.26	2x10-13	-0.31	(13)
rs731839	*PEPD*	19	G	0.35	3x10-9	-0.31	(13)

TG

Top SNP	Gene	Chr	Risk allele	RAF	p-value	Effect size (mg/dL)	Reference
rs10195252	*COBLL1*	2	T	0.60	$1.63x10^{-10}$	2.01	(12)
rs10401969	*CILP2*	19	T	0.93	$1.61x10^{-29}$	7.83	(12)
rs1042034	*APOB*	2	T	0.78	$1.36x10^{-45}$	5.99	(12)
rs10761731	*JMJD1C*	10	A	0.57	$3.48x10^{-12}$	2.38	(12)
rs11613352	*LRP1*	12	C	0.77	$4.43x10^{-10}$	2.70	(12)
rs11649653	*CTF1*	16	C	0.60	$3.35x10^{-08}$	2.13	(12)
rs11776767	*PINX1*	8	C	0.37	$1.30x10^{-08}$	2.01	(12)
rs12310367	*ZNF664*	12	A	0.66	$1.21x10^{-08}$	2.42	(12)
rs1260326	*GCKR*	2	T	0.41	$6.00x10^{-133}$	8.76	(12)
rs12678919	*LPL*	8	A	0.88	$1.50x10^{-115}$	13.64	(12)
rs1321257	*GALNT2*	1	G	0.39	$2.09x10^{-14}$	2.76	(12)
rs1495743	*NAT2*	8	G	0.22	$4.11x10^{-14}$	2.97	(12)
rs1553318	*TIMD4*	5	C	0.64	$3.68x10^{-12}$	2.63	(12)
rs174546	*FADS1-2-3*	11	T	0.34	$5.41x10^{-24}$	3.82	(12)
rs2068888	*CYP26A1*	10	G	0.53	$2.38x10^{-08}$	2.28	(12)
rs2131925	*ANGPTL3*	1	T	0.68	$8.84x10^{-43}$	4.94	(12)

rs2412710	*CAPN3*	15	A	0.02	$1.87x10^{-08}$	7.00	(12)
rs261342	*LIPC*	15	G	0.22	$2.42x10^{-13}$	2.99	(12)
rs2929282	*FRMD5*	15	T	0.05	$1.63x10^{-11}$	5.13	(12)
rs2943645	*IRS1*	2	T	0.63	$2.35x10^{-08}$	1.89	(12)
rs2954029	*TRIB1*	8	A	0.53	$3.29x10^{-55}$	5.64	(12)
rs439401	*APOE-C1-C2*	19	C	0.64	$1.14x10^{-30}$	5.50	(12)
rs442177	*KLHL8*	4	T	0.59	$8.65x10^{-12}$	2.25	(12)
rs4810479	*PLTP*	20	C	0.24	$4.69x10^{-18}$	3.32	(12)
rs5756931	*PLA2G6*	22	T	0.60	$3.82x10^{-08}$	1.54	(12)
rs645040	*MSL2L1*	3	T	0.78	$2.52x10^{-08}$	2.22	(12)
rs7205804	*CETP*	16	G	0.55	$1.00x10^{-12}$	2.88	(12)
rs7811265	*MLXIPL*	7	A	0.81	$9.00x10^{-43}$	7.91	(12)
rs964184	*APOA1-C3-A4-A5*	11	G	0.13	$7.00x10^{-240}$	16.95	(12)
rs9686661	*MAP3K1*	5	T	0.20	$1.32x10^{-10}$	2.57	(12)
rs2247056	*HLA*	6	C	0.75	1X10-15	2.99	(12)
rs13238203	*TYW1B*	7	C	0.96	1X10-9	7.91	(12)
rs12748152	*PIGV-NROB2*	1	T	0.09	1x10-9	*1.54*	(13)
rs6831256	*LRPAP1*	4	G	0.42	2x10-12	*1.54*	(13)
rs998584	*VEGFA*	6	A	0.49	3x10-15	*1.54*	(13)
rs1936800	*RSPO3*	6	T	0.51	3x10-8	*1.54*	(13)
rs38855	*MET*	7	A	0.53	2x10-8	*1.54*	(13)
rs4722551	*MIR148A*	7	C	0.2	9x10-11	*1.54*	(13)
rs1832007	*AKR1CA*	10	A	0.82	2x10-12	*1.54*	(13)
rs3198697	*PDXDC1*	16	C	0.57	2x10-8	*1.54*	(13)
rs1121980	*FTO*	16	A	0.43	3x10-8	*1.54*	(13)
rs8077889	*MPP3*	17	C	0.22	1x10-8	*1.54*	(13)
rs7248104	*INSR*	19	G	0.58	5x10-10	*1.54*	(13)
rs731839	*PEPD*	19	G	0.35	3x10-9	*1.54*	(13)

BP

Top SNP	Gene	Chr	Risk allele	RAF	p-value	Effect size (mm Hg)	Standardized β	Reference
rs10850411	*TBX5–TBX3*	12	T	0.70	$5.40x10^{-08}$	0.35	0.017	(14)
rs11222084*	*ADAMTS8*	11	T	0.38	$4.00x10^{-04}$	0.26	0.013	(15)
rs12940887	*ZNF652*	17	T	0.38	$1.80x10^{-10}$	0.36	0.018	(14)
rs13002573*	*FIGN*	2	A	0.80	$3.25x10^{-07}$	0.42	0.020	(15)
rs13082711*	*TBX5-TBX3*	12	C	0.22	$1.50x10^{-06}$	0.32	0.016	(14)
rs13107325	*SLC39A8*	4	C	0.95	$3.30x10^{-14}$	0.98	0.048	(14)
rs13139571*	*GUCY1A3-GUCY1B3*	4	C	0.76	$1.20x10^{-06}$	0.32	0.016	(14)
rs1327235	*JAG1*	20	G	0.46	$1.90x10^{-08}$	0.34	0.016	(14)
rs1378942	*CYP1A1-ULK3*	15	C	0.35	$5.70x10^{-23}$	0.61	0.030	(14)
rs1446468	*FIGN*	2	C	0.47	$1.82x10^{-12}$	0.50	0.024	(15)
rs17367504	*MTHFR-NPPB*	1	A	0.85	$8.70x10^{-22}$	0.90	0.044	(14)
rs17477177	*PIK3CG*	7	C	0.28	$5.67x10^{-11}$	0.55	0.026	(15)
rs17608766	*GOSR2*	17	C	0.14	$1.10x10^{-10}$	0.56	0.027	(14)
rs1813353	*CACNB2*	10	T	0.68	$2.60x10^{-12}$	0.57	0.028	(14)
rs2071518*	*NOV*	8	T	0.17	$2.08x10^{-02}$	0.18	0.009	(15)
rs2521501	*FURIN-FES*	15	A	0.31	$5.20x10^{-19}$	0.65	0.032	(14)

rs2782980*	*ADRB1*	10	C	0.80	$7.66x10^{-07}$	0.41	0.019	(15)
rs2932538	*MOV10*	1	G	0.75	$1.20x10^{-09}$	0.39	0.019	(14)
rs319690	*MAP4*	3	T	0.51	$4.74x10^{-08}$	0.42	0.020	(15)
rs3774372*	*ULK4*	3	C	0.17	$3.90x10^{-01}$	0.07	0.003	(14)
rs381815	*PLEKHA7*	11	T	0.26	$5.30x10^{-11}$	0.58	0.028	(14)
rs419076	*MECOM*	3	T	0.47	$1.80x10^{-13}$	0.41	0.020	(14)
rs4373814	*CACNB2*	10	C	0.45	$4.80x10^{-11}$	0.37	0.018	(14)
rs4590817	*C10orf107*	10	G	0.84	$4.00x10^{-12}$	0.65	0.032	(14)
rs633185	*FLJ32810-TMEM133*	11	G	0.72	$1.20x10^{-17}$	0.57	0.028	(14)
rs7129220	*ADM*	11	A	0.11	$3.00x10^{-12}$	0.62	0.031	(14)
rs871606*	*CHIC2*	4	T	0.85	$3.04x10^{-04}$	0.40	0.019	(15)
rs932764	*PLCE1*	10	G	0.44	$7.10x10^{-16}$	0.48	0.024	(14)

Diabetes

Top SNP	Gene	Chr	Risk allele	RAF	p-value	OR	Reference
rs10811661	*CDKN2A/B*	9	T	0.83	$1.45x10^{-10}$	1.19	(16,17,18)
rs11634397	*ZFAND6*	15	G	0.4	$2.40x10^{-09}$	1.06	(16)
rs13292136	*CHCHD9*	9	C	0.93	$2.80x10^{-08}$	1.11	(16)
rs1387153	*MTNR1B*	11	T	0.28	$7.80x10^{-15}$	1.09	(16,17)
rs1470579	*IGF2BP2*	3	C	0.31	$2.17x10^{-09}$	1.14	(17,18)
rs1531343	*HMGA2*	12	C	0.1	$3.60x10^{-09}$	1.1	(16)
rs1552224	*CENTD2*	11	A	0.88	$1.40x10^{-22}$	1.14	(16)
rs231362	*KCNQ1*	11	G	0.52	$2.80x10^{-13}$	1.08	(16)
rs243021	*BCL11A*	2	A	0.46	$2.90x10^{-15}$	1.08	(16)
rs3802177	*SLC30A8*	8	G	0.66	$1.45x10^{-08}$	1.15	(17,18)
rs4457053	*ZBED3*	5	G	0.26	$2.80x10^{-12}$	1.08	(16)
rs5015480	*HHEX/IDE*	10	C	0.58	$1.33x10^{-15}$	1.18	(17,18)
rs7578326	*IRS1*	2	A	0.64	$5.40x10^{-20}$	1.11	(16)
rs10440833	*CDKAL1*	6	A	0.26	$2.00x10^{-22}$	1.25	(17,18)
rs7903146	*TCF7L2*	10	T	0.22	$2.40x10^{-518}$	1.4	(17,18)
rs7957197	*HNF1A*	12	T	0.85	$2.40x10^{-10}$	1.07	(16)
rs8042680	*PRC1*	15	A	0.74	$2.40x10^{-10}$	1.07	(16)
rs896854	*TP53INP1*	8	T	0.48	$9.90x10^{-10}$	1.06	(16)
rs972283	*KLF14*	7	G	0.55	$2.20x10^{-10}$	1.07	(16)
rs849134	*JAZF1*	7	A	0.7	$3X10^{-9}$	1.13	(17)
rs11642841	*FTO*	16	A	0.18	$3x10^{-8}$	1.13	(17)
rs1801214	*WFS1*	4	T	0.27	$3x10^{-8}$	1.13	(16)
rs5219	*KCNJ11*	11	T	0.26	$6.7x10^{-11}$	1.14	(16)

BMI

Top SNP	Gene	Chr	Risk allele	RAF	p-value	Effect size(Kg/m^2)	Reference
rs657452	*AGBL4*	1	A	0.39	$5.48x10^{-13}$	0.023	(19)
rs12286929	*CADM1*	11	G	0.52	$1.31x10^{-12}$	0.022	(19)
rs7903146	*TCF7L2*	10	C	0.71	$1.11x10^{-11}$	0.023	(19)
rs10132280	*STXBP6*	14	C	0.68	$1.14x10^{-11}$	0.023	(19)

rs17094222	*HIF1AN*	10	C	0.21	$5.94x10^{-11}$	0.025	(19)
rs7599312	*ERBB4*	2	G	0.72	$1.17x10^{-10}$	0.022	(19)
rs2365389	*FHIT*	3	C	0.58	$1.63x10^{-10}$	0.02	(19)
rs2820292	*NAV1*	1	C	0.56	$1.83x10^{-10}$	0.02	(19)
rs12885454	*PRKD1*	14	C	0.64	$1.94x10^{-10}$	0.021	(19)
rs16851483	*RASA2*	3	T	0.07	$3.55x10^{-10}$	0.048	(19)
rs1167827	*HIP1; PMS2L3; PMS2P5; WBSCR16*	7	G	0.55	$6.33x10^{-10}$	0.02	(19)
rs758747	*NLRC3*	16	T	0.27	$7.47x10^{-10}$	0.023	(19)
rs1928295	*TLR4*	9	T	0.55	$7.91x10^{-10}$	0.019	(19)
rs9925964	*KAT8;ZNF646; VKORC1*	16	A	0.62	$8.11x10^{-10}$	0.019	(19)
rs11126666	*KCNK3*	2	A	0.28	$1.33x10^{-9}$	0.021	(19)
rs2650492	*SBK1; APOBR*	16	A	0.30	$1.92x10^{-9}$	0.021	(19)
rs6804842	*RARB*	3	G	0.58	$2.48x10^{-9}$	0.019	(19)
rs4740619	*C9orf93*	9	T	0.54	$4.56x10^{-9}$	0.018	(19)
rs13191362	*PARK2*	6	A	0.88	$7.34x10^{-9}$	0.028	(19)
rs3736485	*SCG3; DMXL2*	15	A	0.45	$7.41x10^{-9}$	0.018	(19)
rs17001654	*NUP54; SCARB2*	4	G	0.15	$7.76x10^{-9}$	0.031	(19)
rs11191560	*NT5C2; CYP17A1; SFXN2*	10	C	0.09	$8.45x10^{-9}$	0.031	(19)
rs1528435	*UBE2E3*	2	T	0.63	$1.20x10^{-8}$	0.018	(19)
rs1000940	*RABEP1*	17	G	0.32	$1.28C10^{-8}$	0.019	(19)
rs2033529	*TDRG1; LRFN2*	6	G	0.29	$1.39x10^{-8}$	0.019	(19)
rs11583200	*ELAVL4*	1	C	0.40	$1.48x10^{-8}$	0.018	(19)
rs9400239	*FOXO3; HSS00296402*	6	C	0.69	$1.61x10^{-8}$	0.019	(19)
rs10733682	*LMX1B*	9	A	0.48	$1.83x10^{-8}$	0.017	(19)
rs11688816	*EHBP1*	2	G	0.56	$1.89x10^{-8}$	0.017	(19)
rs11057405	*CLIP1*	12	G	0.90	$2.02x10^{-8}$	0.031	(19)
rs11727676	*HHIP*	4	T	0.91	$2.55x10^{-8}$	0.036	(19)
rs3849570	*GBE1*	3	A	0.36	$2.60x10^{-8}$	0.019	(19)
rs6477694	*EPB41L4B; C9orf4*	9	C	0.37	$2.67x10^{-8}$	0.017	(19)
rs7899106	*GRID1*	10	G	0.05	$2.96x10^{-8}$	0.04	(19)
rs2176598	*HSD17B12*	11	T	0.25	$2.97\ x10^{-8}$	0.02	(19)
rs2245368	*PMS2L11*	7	C	0.18	$3.19\ x10^{-8}$	0.032	(19)
rs17724992	*GDF15; PGPEP1*	19	A	0.75	$3.42\ x10^{-8}$	0.019	(19)
rs7243357	*GRP*	18	T	0.81	$3.86\ x10^{-8}$	0.022	(19)
rs2033732	*RALYL*	8	C	0.75	$4.89x10^{-8}$	0.019	(19)
rs1558902	*FTO*	16	A	0.42	$7.51x10^{-153}$	0.082	(19)
rs6567160	*MC4R*	18	C	0.24	$3.93x10^{-53}$	0.056	(19)
rs13021737	*TMEM18*	2	G	0.83	$1.11x10^{-50}$	0.06	(19)
rs10938397	*GNPDA2; GABRG1*	4	G	0.43	$3.21x10^{-38}$	0.04	(19)
rs543874	*SEC16B*	1	G	0.19	$2.62x10^{-35}$	0.048	(19)
rs2207139	*TFAP2B*	6	G	0.18	$4.13x10^{-29}$	0.045	(19)
rs11030104	*BDNF*	11	A	0.79	$5.56x10^{-28}$	0.041	(19)

rs3101336	*NEGR1*	1	C	0.61	2.66×10^{-26}	0.033	(19)
rs7138803	*BCDIN3D; FAIM2*	12	A	0.38	8.15×10^{-24}	0.032	(19)
rs10182181	*ADCY3; POMC; NCOA1*	2	G	0.46	8.78×10^{-24}	0.031	(19)
rs3888190	*SH281; APOBR; ATXN2L; SBK1; SULT1A2; TUFM*	16	A	0.40	3.14×10^{-23}	0.031	(19)
rs1516725	*ETV5*	3	C	0.87	1.89×10^{-22}	0.045	(19)
rs12446632	*GPRC5B; IQCK*	16	G	0.87	1.48×10^{-18}	0.04	(19)
rs2287019	*QPCTL; G/PR*	19	C	0.80	4.59×10^{-18}	0.036	(19)
rs16951275	*MAP2K5; LBXCOR1*	15	T	0.78	1.91×10^{-17}	0.031	(19)
rs3817334	*MTCH2; C1QTNF4; SPI1; CELF1*	11	T	0.41	5.15×10^{-17}	0.026	(19)
rs2112347	*POC5; HMGCR; COL4A3BP*	5	T	0.63	6.19×10^{-17}	0.026	(19)
rs12566985	*FPGT-TNN/3K*	1	G	0.45	3.28×10^{-15}	0.024	(19)
rs3810291	*ZC3H4*	19	A	0.67	4.81×10^{-15}	0.028	(19)
rs7141420	*NRXN3*	14	T	0.53	1.23×10^{-14}	0.024	(19)
rs13078960	*CADM2*	3	G	0.20	1.74×10^{-14}	0.03	(19)
rs10968576	*LING02*	9	G	0.32	6.61×10^{-14}	0.025	(19)
rs17024393	*GNAT2; AMPD2*	1	C	0.04	7.03×10^{-14}	0.066	(19)
rs12429545	*OLFM4*	13	A	0.13	1.09×10^{-12}	0.033	(19)
rs13107325	*SLC39A8*	4	T	0.07	1.83×10^{-12}	0.048	(19)
rs11165643	*PTBP2*	1	T	0.58	2.07×10^{-12}	0.022	(19)
rs17405819	*HNF4G*	8	T	0.70	2.07×10^{-11}	0.022	(19)
rs1016287	*LINC01122*	2	T	0.29	2.25×10^{-11}	0.023	(19)
rs4256980	*TR/M66; TUB*	11	G	0.65	2.90×10^{-11}	0.021	(19)
rs12401738	*FUBP1; USP33*	1	A	0.35	1.15×10^{-10}	0.021	(19)
rs205262	*C6orf106; SNRPC*	6	G	0.27	1.75×10^{-10}	0.022	(19)
rs9581854	*MTIF3; GTF3A*	13	T	0.20	2.29×10^{-10}	0.03	(19)
rs12940622	*RPTOR*	17	G	0.58	2.49×10^{-09}	0.018	(19)
rs11847697	*PRKD1*	14	T	0.04	3.99×10^{-09}	0.049	(19)
rs2075650	*TOMM40; APOE; APOC1*	19	A	0.85	1.25×10^{-08}	0.026	(19)
rs2121279	*LRP1B*	2	T	0.15	2.31×10^{-08}	0.025	(19)
rs29941	*KCTD15*	19	G	0.67	2.41×10^{-08}	0.018	(19)
rs1808579	*NPC1; C18orf8*	18	C	0.53	4.17×10^{-08}	0.017	(19)
rs9641123	*CALCR; hsa-miR-653*	7	C	0.43	2.80×10^{-10}	0.029	(19)
rs4787491	*MAPK3; KCTD13; INO80E; …*	16	G	0.51	2.70×10^{-8}	0.022	(19)
rs9540493	*MIR548X2; PCDH9*	13	A	0.45	4.97×10^{-8}	0.021	(19)
rs9374842	*LOC285762*	6	T	0.74	2.67×10^{-8}	0.023	(19)

Waist

Top SNP	Gene	Chr	Risk allele	RAF	p-value	Effect size (mg/dl)	References
rs905938	*DCST2*	1	T	0.74	7.30E-10	0.025	(20)
rs10919388	*GORAB*	1	C	0.72	3.20E-09	0.024	(20)
rs1385167	*MEIS1*	2	G	0.15	1.90E-09	0.029	(20)
rs1569135	*CALCRL*	2	A	0.53	5.60E-10	0.021	(20)
rs10804591	*PLXND1*	3	A	0.79	6.60E-09	0.025	(20)
rs17451107	*LEKR1*	3	T	0.61	1.10E-12	0.026	(20)
rs9991328	*FAM13A*	4	T	0.49	4.50E-08	0.019	(20)
rs303084	*SPATA5-FGF2*	4	A	0.8	3.90E-08	0.023	(20)
rs9687846	*MAP3K1*	5	A	0.19	7.10E-08	0.024	(20)
rs6556301	*FGFR4*	5	T	0.36	2.60E-08	0.022	(20)
rs7759742	*BTNL2*	6	A	0.51	4.40E-11	0.023	(20)
rs7801581	*HOXA11*	7	T	0.24	3.70E-10	0.027	(20)
rs7830933	*NKX2-6*	8	A	0.77	7.40E-08	0.022	(20)
rs12679556	*MSC*	8	G	0.25	2.10E-11	0.027	(20)
rs10991437	*ABCA1*	9	A	0.11	1.00E-08	0.031	(20)
rs11231693	*MACROD1-VEGFB*	11	A	0.06	4.50E-08	0.041	(20)
rs4765219	*CCFC92*	12	C	0.67	1.60E-15	0.028	(20)
rs8042543	*KLF13*	15	C	0.78	1.20E-09	0.026	(20)
rs8030605	*RFX7*	15	A	0.14	8.80E-09	0.03	(20)
rs1440372	*SMAD6*	15	C	0.71	1.10E-10	0.024	(20)
rs4646404	*PEMT*	17	G	0.67	1.40E-11	0.027	(20)
rs12608504	*BCL2*	18	A	0.36	8.80E-10	0.022	(20)
rs4081724	*CEBPA*	19	G	0.85	7.40E-12	0.035	(20)
rs979012	*BMP2*	20	T	0.34	3.30E-14	0.027	(20)
rs224333	*GDF5*	20	G	0.62	2.60E-08	0.02	(20)
rs6090583	*EYA2*	20	A	0.48	6.20E-11	0.022	(20)
rs2645294	*TBX15-WARS2*	1	T	0.58	1.70E-19	0.031	(20)
rs714515	*DNM3-PIGC*	1	G	0.43	4.40E-15	0.027	(20)
rs2820443	*LYPLAL1*	1	T	0.72	5.30E-21	0.035	(20)
rs10195252	*GRB14-COBLL1*	2	T	0.59	5.90E-15	0.027	(20)
rs17819328	*PPARG*	3	G	0.43	2.40E-09	0.021	(20)
rs2276824	*PBRM1*	3	C	0.43	3.20E-11	0.024	(20)
rs2371767	*ADAMTS9*	3	G	0.72	1.60E-20	0.036	(20)
rs7705502	*CPEB4*	5	A	0.33	4.70E-14	0.027	(20)
rs1294410	*LY86*	6	C	0.63	2.00E-18	0.031	(20)
rs1358980	*VEGFA*	6	T	0.47	3.10E-27	0.039	(20)
rs1936805	*RSPO3*	6	T	0.51	3.60E-35	0.043	(20)
rs10245353	*NFE2L3*	7	A	0.2	8.40E-16	0.035	(20)
rs10842707	*ITPR2-SSPN*	12	T	0.23	4.40E-16	0.032	(20)
rs1443512	*HOXC13*	12	A	0.24	6.90E-13	0.028	(20)
rs2294239	*ZZNRF3*	22	A	0.59	7.20E-13	0.025	(20)

Schizophrenia

Top SNP	Risk allele	RAF	p-value	OR	References
rs4648845	C	0.527	8.70E-10	1.072	(21)
rs1498232	C	0.296	2.86E-09	1.069	(21)
rs11210892	A	0.323	3.39E-10	1.071	(21)
rs12129573	C	0.358	2.03E-12	1.078	(21)
rs76869799	C	0.036	2.64E-08	1.182	(21)
rs140505938	T	0.836	4.49E-10	1.094	(21)
rs6670165	C	0.184	4.45E-08	1.075	(21)
rs7523273	G	0.685	4.47E-08	1.063	(21)
rs10803138	A	0.762	2.03E-08	1.072	(21)
rs11682175	T	0.458	1.47E-11	1.072	(21)
rs3768644	A	0.899	7.39E-09	1.106	(21)
rs2909457	A	0.407	4.62E-08	1.059	(21)
rs11693094	T	0.542	1.53E-12	1.076	(21)
rs59979824	A	0.663	8.41E-09	1.067	(21)
rs6434928	A	0.357	2.06E-11	1.076	(21)
rs6704641	G	0.805	8.33E-09	1.081	(21)
rs11685299	A	0.674	1.12E-08	1.065	(21)
rs6704768	A	0.448	2.32E-12	1.075	(21)
rs17194490	G	0.156	2.69E-11	1.101	(21)
rs4330281	T	0.52	4.64E-09	1.064	(21)
rs75968099	C	0.324	1.05E-13	1.085	(21)
rs2535627	C	0.529	4.26E-11	1.071	(21)
rs832187	T	0.385	1.43E-08	1.063	(21)
rs7432375	A	0.551	7.26E-11	1.072	(21)
rs9841616	A	0.833	2.35E-08	1.081	(21)
rs215411	T	0.314	3.06E-08	1.064	(21)
rs35518360	A	0.078	7.98E-15	1.167	(21)
rs10520163	C	0.47	1.47E-09	1.065	(21)
rs1106568	A	0.239	9.47E-09	1.071	(21)
rs1501357	T	0.198	5.05E-09	1.08	(21)
rs4391122	A	0.468	1.10E-14	1.085	(21)
rs16867576	G	0.883	4.61E-09	1.101	(21)
rs4388249	C	0.213	3.05E-08	1.076	(21)
rs10043984	C	0.252	1.09E-08	1.069	(21)
rs79212538	G	0.046	7.00E-09	1.155	(21)
rs11740474	A	0.379	3.15E-08	1.062	(21)
rs115329265	G	0.85	3.48E-31	1.205	(21)
rs1339227	T	0.632	2.69E-08	1.062	(21)
rs117074560	T	0.9524	1.64E-09	1.178	(21)
rs12704290	A	0.877	3.33E-10	1.106	(21)
rs6466055	C	0.332	1.13E-09	1.068	(21)
rs211829	C	0.628	3.71E-08	1.061	(21)
rs13240464	C	0.647	3.03E-13	1.083	(21)

rs7801375	A	0.848	4.42E-08	1.082	(21)
rs3735025	C	0.642	3.28E-09	1.066	(21)
rs10503253	C	0.219	1.06E-08	1.073	(21)
rs73229090	A	0.884	2.10E-08	1.101	(21)
rs6984242	A	0.4	5.97E-09	1.063	(21)
rs7819570	G	0.174	1.22E-08	1.079	(21)
rs36068923	A	0.197	2.61E-11	1.088	(21)
rs4129585	C	0.424	1.74E-15	1.087	(21)
rs11139497	T	0.337	3.61E-09	1.069	(21)
rs7893279	G	0.889	1.97E-12	1.125	(21)
rs7907645	G	0.888	1.27E-11	1.143	(21)
rs11027857	G	0.499	2.55E-09	1.064	(21)
rs9420	G	0.311	2.24E-09	1.068	(21)
rs12421382	T	0.666	3.70E-08	1.063	(21)
rs2514218	T	0.686	2.75E-11	1.079	(21)
rs77502336	G	0.322	7.54E-09	1.066	(21)
rs55661361	A	0.665	2.80E-12	1.08	(21)
rs10791097	G	0.46	1.09E-12	1.076	(21)
rs75059851	G	0.797	3.87E-11	1.091	(21)
rs2007044	A	0.376	3.22E-18	1.096	(21)
rs679087	A	0.663	3.91E-08	1.063	(21)
rs324017	A	0.691	2.13E-08	1.066	(21)
rs4240748	C	0.634	4.59E-08	1.06	(21)
rs10860964	C	0.646	4.84E-08	1.06	(21)
rs4766428	C	0.474	1.40E-09	1.068	(21)
rs2851447	C	0.259	1.86E-14	1.093	(21)
rs2068012	T	0.229	1.41E-08	1.072	(21)
rs2332700	G	0.249	4.86E-09	1.073	(21)
rs2693698	A	0.582	4.80E-09	1.065	(21)
rs12887734	G	0.287	1.36E-13	1.088	(21)
rs56205728	G	0.274	4.18E-09	1.074	(21)
rs12903146	G	0.52	3.38E-10	1.067	(21)
rs12148337	C	0.465	1.79E-08	1.06	(21)
rs8042374	G	0.725	2.44E-13	1.093	(21)
rs950169	T	0.743	1.62E-11	1.083	(21)
rs4702	A	0.438	8.30E-14	1.085	(21)
rs9922678	G	0.281	1.28E-08	1.067	(21)
rs7405404	C	0.223	1.01E-09	1.077	(21)
rs12691307	G	0.51	4.55E-11	1.073	(21)
rs12325245	A	0.141	1.87E-08	1.087	(21)
rs8044995	G	0.162	1.51E-08	1.081	(21)
rs4523957	G	0.627	2.86E-10	1.071	(21)
rs8082590	A	0.386	1.77E-08	1.065	(21)
rs78322266	G	0.0292	1.32E-08	1.188	(21)
rs72934570	T	0.9203	1.97E-11	1.145	(21)
rs2905426	T	0.372	3.63E-10	1.071	(21)

rs2053079	A	0.231	4.49E-09	1.074	(21)
rs56873913	G	0.766	4.69E-08	1.071	(21)
rs6065094	A	0.678	1.46E-11	1.078	(21)
rs7267348	T	0.246	4.56E-08	1.067	(21)
rs9607782	T	0.232	2.07E-11	1.087	(21)
rs1023500	C	0.81	3.43E-08	1.076	(21)
rs12845396	A	0.247	2.21E-08	1.056	(21)
rs1378559	C	0.831	1.61E-12	1.09	(21)
rs5937157	T	0.241	1.98E-10	1.066	(21)

* Associated with diastolic blood pressure

Supplementary Table 2. Number of single nucleotide polymorphisms included in the different GRSs. Correlation coefficient between the GRSs in the MIGen study.

GRSs including all the genetic variants of interest

	SNPs N_{total}	GRS_{IHD}	GRS_{TG}	GRS_{BP}	GRS_{HDL}	GRS_{LDL}	GRS_{T2D}	GRS_{BMI}	GRS_{Waist}	GRS_{SCHIZ}
GRS_{IHD}	60	-	0.079	-0.010	-0.034	0.182	-0.002	0.002	-0.007	0.023
GRS_{TG}	44		-	-0.014	-0.391	0.170	0.043	0.014	0.055	-0.004
GRS_{BP}	28			-	0.010	0.011	-0.013	-0.017	0.035	-0.014
GRS_{HDL}	74				-	-0.129	-0.049	-0.024	-0.045	0.006
GRS_{LDL}	58					-	0.008	-0.025	0.000	-0.015
GRS_{T2D}	23						-	0.001	-0.046	-0.007
GRS_{BMI}	81							-	0.029	-0.015
GRS_{Waist}	41								-	-0.024
GRS_{SCHIZ}	98									-

GRSs excluding those genetic variants associated with any other trait different to that of interest

	SNPs N_{total}	GRS_{IHD}	GRS_{TG}	GRS_{BP}	GRS_{HDL}	GRS_{LDL}	GRS_{T2D}	GRS_{BMI}	GRS_{Waist}	GRS_{SCHIZ}
GRS_{IHD}	19	-	0.009	-0.022	-0.007	-0.062	-0.025	-0.050	0.008	.0.002
GRS_{TG}	17		-	0.002	-0.142	0.379	0.002	-0.003	0.123	0.007
GRS_{BP}	11			-	0.049	-0.011	-0.006	-0.074	0.034	0.011
GRS_{HDL}	34				-	-0.008	-0.043	-0.032	-0.083	0.032
GRS_{LDL}	13					-	0.007	0.014	-0.008	-0.003
GRS_{T2D}	11						-	-0.017	-0.022	-0.042
GRS_{BMI}	32							-	-0.010	-0.018
GRS_{Waist}	16								-	0.013
GRS_{SCHIZ}	20									-

GRS: genetic risk scores; SNPs: Single nucleotide polymorphisms; IHD: Ischemic heart disease; TG: Triglycerides; BP: Blood pressure; HDL: High density lipoprotein; LDL: Low density lipoprotein; T2D: Type 2 diabetes; BMI: Body Mass Index; Schiz: Schizophrenia.

Supplementary Table 3. Association Between the Weighted Genetic Risk Scores and Their Corresponding Risk Factors in the Cohorts Included in this Analysis.

GRSs including all the genetic variants of interest				
	FHS*	**FINRISK97**	**FINRISK02**	**EGCUT***
GRS_{LDL}-*	7.16 (0.61)	8.93 (0.44)	14.60 (0.95)	8.92 (0-59)
LDL (mg/dL)	p-value:$2.3x10^{-31}$	p-value: $3.1x10^{-90}$	p-value: $6.3x10^{-51}$	p-value: $8.4x10^{-51}$
GRS_{HDL}-*	-3.58 (0.24)	-3.48 (0.16)	-5.54 (0.35)	-3.56 (0.24)
HDL (mg/dL)	p-value: $4.9x10^{-47}$	p-value: $9.5x10^{-101}$	p-value: $1.1x10^{-54}$	p-value: $8.4x10^{-49}$
GRS_{TG}-*	23.80 (1.82)	18.62 (1.13)	22.11 (1.83)	18.14 (1.43)
TG (mg/dL)	p-value: $5.2x10^{-38}$	p-value: $2.0x10^{-59}$	p-value:$1.1x10^{-32}$	p-value: $3.3x10^{-36}$
GRS_{BP}-*	1.43 (0.31)	0.86 (0.23)	0.88 (0.39)	0.53 (0.20)
SBP (mmHg)	p-value: $3.7x10^{-6}$	p-value: $1.9x10^{-4}$	p-value: 0.023	p-value: $6.7x10^{-3}$
GRS_{BP}-*	0.54 (0.18)	0.30 (0.14)	0.39 (0.23)	0.41 (0.13)
DBP (mmHg)	p-value: $3.4x10^{-3}$	p-value: 0.031	p-value: 0.088	p-value: $1.5x10^{-3}$
GRS_{T2D}-*	0.34 (0.08)	0.16 (0.06)	0.14 (0.07)	0.13 (0.07)
T2D (yes)	p-value: $1.6x10^{-5}$	p-value: $3.2x10^{-3}$	p-value: 0.027	p-value:0.050
GRS_{BMI}-*	0.60 (0.09)	0.60 (0.06)	0.72 (0.10)	0.71 (0.06)
BMI (kg/m^2)	p-value: $1.8x10^{-11}$	p-value: $1.2x10^{-25}$	p-value: $4.7x10^{-12}$	p-value:$5.0x10^{-30}$
GRSs excluding those genetic variants associated with any other trait different to that of interest				
	FHS*	**FINRISK97**	**FINRISK02**	**EGCUT***
GRS_{LDL}-*	0.94 (0.62)	2.35 (0.45)	4.38 (0.99)	2.02 (0.60)
LDL (mg/dL)	p-value:0.129	p-value: $1.9x10^{-7}$	p-value: $1.1x10^{-5}$	p-value: $8.0x10^{-4}$

GRS_{HDL}-*	-1.59 (0.25)	-1.58 (0.17)	-3.03 (0.35)	-1.51 (0.24)
HDL (mg/dL)	p-value: $2.9x10^{-10}$	p-value: $2.4x10^{-21}$	p-value: $6.6x10^{-17}$	p-value: $6.3x10^{-10}$
GRS_{TG}-*	4.29 (1.87)	8.32 (1.16)	10.99 (1.87)	7.99 (1.43)
TG (mg/dL)	p-value: 0.022	p-value: $8.1x10^{-13}$	p-value:$5.0x10^{-9}$	p-value: $2.4x10^{-8}$
GRS_{BP}-*	1.28 (0.30)	0.35 (0.23)	-0.02 (0.39)	0.00 (0.20)
SBP (mmHg)	p-value: $3.1x10^{-5}$	p-value: 0.132	p-value: 0.954	p-value: 1.000
GRS_{BP}-*	0.41 (0.18)	0.15 (0.14)	-0.18 (0.23)	0.06 (0.13)
DBP (mmHg)	p-value: 0.023	p-value: 0.286	p-value: 0.429	p-value: 0.662
GRS_{T2D}-*	0.22 (0.08)	0.09 (0.06)	0.16 (0.07)	0.00 (0.07)
T2D (yes)	p-value: $6.4x10^{-3}$	p-value: 0.103	p-value: 0.020	p-value:0.956
GRS_{BMI}-*	0.26 (0.09)	0.35 (0.06)	0.51 (0.10)	0.50 (0.06)
BMI (kg/m^2)	p-value: $3.6x10^{-3}$	p-value: $1.0x10^{-9}$	p-value: $1.0x10^{-6}$	p-value:$1.3x10^{-15}$

* FHS: Framingham Heart Study; EGCUT: Estonian Biobank; GRS: Genetic risk score; LDL: Low-density lipoprotein; HDL: High-density lipoprotein; TG: Triglycerides; BP: Blood pressure; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; T2D: Type 2 diabetes; BMI: Body Mass Index.

Supplementary Table 4. Association Between the Different Weighted Genetic Risk Scores for Cardiovascular Risk Factors and Ischemic Heart Disease and the Prevalence/Incidence of Hard Ischemic Heart Disease Events (Myocardial Infarction or Ischemic Heart Disease Death).

		MIGen*	***FHS****	***FINRISK1997***	***FINRISK2002***	***EGCUT****	***Meta-analysis***	***p-het‡***
GRS*	OR-RR (95%CI)†	1.51 (1.42, 1.60)	1.37 (1.18, 1.59)	1.25 (1.14, 1.38)	1.26 (1.09, 1.46)	1.18 (1.04, 1.34)	1.37 (1.32, 1.43)	6.8
IHD*	p-value	$8.1x10^{-39}$	$4.8x10^{-05}$	$2.4x10^{-06}$	$1.4x10^{-03}$	$9.5x10^{-03}$	$9.4x10^{-47}$	$x10^{-4}$
GRS	OR-RR (95%CI)	1.16 (1.09, 1.23)	0.90 (0.77, 1.05)	1.02 (0.93, 1.11)	1.05 (0.91, 1.22)	1.07 (0.95, 1.20)	1.09 (1.04, 1.13)	0.010
TG*	p-value	$7.2x10^{-07}$	0.164	0.735	0.492	0.297	$1.1x10^{-4}$	
GRS	OR-RR (95%CI)	1.03 (0.98, 1.10)	1.07 (0.92, 1.25)	1.10 (1.00, 1.21)	0.98 (0.85, 1.14)	0.96 (0.84, 1.08)	1.04 (0.99, 1.08)	0.460
BP*	p-value	0.260	0.371	0.057	0.833	0.492	0.107	
GRS	OR-RR (95%CI)	1.13 (1.07, 1.20)	0.85 (0.73, 0.99)	1.08 (0.98, 1.18)	1.00 (0.87, 1.16)	1.05 (0.93, 1.19)	1.08 (1.03, 1.12)	0.009
HDL*	p-value	$3.2x10^{-05}$	0.034	0.103	0.983	0.396	$6.2x10^{-4}$	
GRS	OR-RR (95%CI)	1.21 (1.14, 1.29)	1.04 (0.89, 1.21)	1.05 (0.96, 1.15)	0.99 (0.86, 1.15)	0.99 (0.87, 1.12)	1.12 (1.07, 1.16)	0.002
LDL*	p-value	$1.2x10^{-10}$	0.660	0.274	0.945	0.844	$3.1x10^{-7}$	
GRS	OR-RR (95%CI)	1.03 (0.97, 1.10)	1.03 (0.89, 1.19)	0.92 (0.84, 1.01)	1.10 (0.95, 1.27)	1.00 (0.88, 1.12)	1.01 (0.97, 1.05)	0.215
T2D*	p-value	0.266	0.714	0.083	0.206	0.947	0.666	
GRS	OR-RR (95%CI)	1.13 (1.06, 1.19)	1.11 (0.95, 1.29)	1.05 (0.96, 1.15)	0.97 (0.84, 1.12)	1.03 (0.91, 1.16)	1.08 (1.04, 1.13)	0.271
BMI*	p-value	$7.7x10^{-05}$	0.179	0.330	0.709	0.619	$2.3x10^{-4}$	
GRS	OR-RR (95%CI)	1.07 (1.00, 1.13)	0.99 (0.85, 1.19)	1.09 (0.99, 1.19)	1.00 (0.87, 1.16)	1.08 (0.96, 1.22)	1.06 (1.02, 1.11)	0.761
WAIST	p-value	0.035	0.714	0.072	0.953	0.196	0.006	
GRS	OR-RR (95%CI)	1.01 (0.95, 1.07)	0.96 (0.82, 1.11)	0.95 (0.86, 1.04)	0.91 (0.78, 1.05)	0.98 (0.86, 1.11)	0.98 (0.94, 1.02)	0.594
SCHIZ	p-value	0.683	0.571	0.281	0.188	0.726	0.395	

*MIGen: Myocardial Infarction Genetics Consortium; FHS: Framingham Heart Study; EGCUT: Estonian Biobank; GRS: Genetic risk score; IHD: Ischemic heart disease; TG: Triglycerides; BP: Blood pressure; HDL: High-density lipoprotein; LDL: Low-density lipoprotein; T2D: Type 2 diabetes; BMI: Body Mass Index; Schiz: Schizophrenia.

† OR-RR (95%CI): Odds ratio/Relative risks (and their 95% confidence intervals) corresponding to the increase in ischemic heart disease risk per standard deviation increase of the genetic risk score, and the P-values of the different reported associations. The OR was estimated in the MIGEN study and the RR in the rest of the studies.

‡ p-het: p-value for heterogeneity between studies.

Supplementary Table 5. Association Between the Weighted Genetic Risk Scores for Cardiovascular Risk Factors and Ischemic Heart Disease and the Incidence of All Ischemic Heart Disease Events (myocardial infarction or ischemic heart disease death or angina or revascularization).

		MIGen*	FHS*	FINRISK1997	FINRISK2002	EGCUT*	Meta-analysis	p-het‡
GRS*	RR (95%CI)†	---	1.32 (1.17, 1.49)	1.23 (1.11, 1.37)	1.29 (1.10, 1.52)	1.08 (0.99, 1.17)	1.19 (1.13, 1.25)	0.026
IHD*	p-value		$9.4x10^{-06}$	$9.6x10^{-05}$	$1.8x10^{-03}$	0.066	$7.9x10^{-03}$	
GRS	RR (95%CI)	---	0.98 (0.87, 1.11)	0.98 (0.88, 1.08)	1.11 (0.94, 1.31)	1.06 (0.98, 1.15)	1.03 (0.97, 1.08)	0.403
TG*	p-value		0.773	0.663	0.201	0.157	0.324	
GRS	RR (95%CI)	---	1.03 (0.91, 1.17)	1.13 (1.02, 1.26)	0.88 (0.74, 1.04)	1.04 (0.95, 1.12)	1.04 (0.99, 1.10)	0.087
BP*	p-value		0.593	0.021	0.121	0.394	0.138	
GRS	RR (95%CI)	---	0.92 (0.81, 1.04)	1.07 (0.97, 1.19)	1.06 (0.90, 1.26)	0.96 (0.89, 1.04)	0.99 (0.94, 1.05)	0.182
HDL*	p-value		0.189	0.181	0.463	0.353	0.819	
GRS	RR (95%CI)	---	1.05 (0.93, 1.19)	1.05 (0.95, 1.16)	1.01 (0.86, 1.19)	0.98 (0.90, 1.07)	1.02 (0.96, 1.07)	0.715
LDL*	p-value		0.431	0.331	0.912	0.680	0.536	
GRS	RR (95%CI)	---	1.05 (0.93, 1.19)	0.91 (0.82, 1.00)	1.19 (1.01, 1.41)	1.01 (0.93, 1.09)	1.00 (0.95, 1.06)	0.033
T2D*	p-value		0.435	0.057	0.034	0.850	0.889	
GRS	RR (95%CI)	---	1.13 (1.00, 1.28)	1.08 (0.98, 1.20)	1.00 (0.85, 1.17)	0.97 (0.90, 1.05)	1.03 (0.98, 1.09)	0.150
BMI*	p-value		0.051	0.127	0.969	0.475	0.246	
GRS	RR (95%CI)	---	1.06 (0.93, 1.19)	1.09 (0.99, 1.21)	1.01 (0.86, 1.19)	1.10 (1.01, 1.19)	1.08 (1.02, 1.14)	0.801
WAIST	p-value		0.394	0.087	0.890	0.024	0.005	
GRS	RR (95%CI)	---	0.99 (0.87, 1.12)	0.96 (0.86, 1.06)	0.91 (0.77, 1.07)	0.99 (0.91, 1.07)	0.97 (0.92, 1.03)	0.824
SCHIZ*	p-value		0.828	0.414	0.262	0.773	0.283	

*MIGen: Myocardial infarction Genetics Consortium; FHS: Framingham Heart Study; EGCUT: Estonian Biobank; GRS: Genetic risk score; IHD: Ischemic heart disease; TG: Triglycerides; BP: Blood pressure; HDL: High-density lipoprotein; LDL: Low-density lipoprotein; T2D: Type 2 diabetes; BMI: Body Mass Index; Schiz: Schizophrenia.

† OR-RR (95%CI): Odds ratio/Relative risks (and their 95% confidence intervals) corresponding to the increase in ischemic heart disease risk per standard deviation increase of the genetic risk score, and the P-values of the different reported associations. The OR was estimated in the MIGEN study and the RR in the rest of the studies.

‡ p-het: p-value for heterogeneity between studies.

Supplementary Table 6. Association Between the Non-pleiotropic Weighted Genetic Risk Scores and the Prevalence/Incidence of Ischemic Heart Disease Events in the Meta-analyses.

		Hard coronary events	**All coronary events**
Non-pleiotropic GRS* IHD*	RR (95%CI)†	1.28 (1.23, 1.34)	1.12 (1.06,1.18)
	p-value	$6.8x10^{-30}$	$2.4x10^{-5}$
Non-pleiotropic GRS TG*	RR (95%CI)	1.02 (0.98, 1.06)	1.00 (0.94,1.06)
	p-value	0.391	0.960
Non-pleiotropic GRS BP*	RR (95%CI)	1.0 (0.96, 1.04)	1.03 (0.97, 1.08)
	p-value	0.981	0.339
Non-pleiotropic GRS HDL*	RR (95%CI)	1.04 (1.00, 1.08)	1.00 (0.95, 1.06)
	p-value	0.074	0.995
Non-pleiotropic GRS LDL*	RR (95%CI)	1.0 (0.96, 1.04)	0.99 (0.94, 1.04)
	p-value	0.919	0.696
Non-pleiotropic GRS T2D*	RR (95%CI)	1.02 (0.98,1.06)	1.00 (0.95, 1.06)
	p-value	0.335	0.875
Non-pleiotropic GRS BMI*	RR (95%CI)	1.03 (0.98, 1.07)	1.02 (0.96, 1.07)
	p-value	0.230	0.576
Non-pleiotropic GRS Waist	RR (95%CI)	1.04 (0.99, 1.08)	1.04 (0.98, 1.09)
	p-value	0.132	0.189
Non-pleiotropic GRS SCHIZ*	RR (95%CI)	0.96 (0.92, 1.00)	0.96 (0.91, 1.01)
	p-value	0.083	0.129

*GRS: Genetic risk score; IHD: Ischemic heart disease; TG: Triglycerides; BP: Blood pressure; HDL: High-density lipoprotein; LDL: Low-density lipoprotein; T2D: Type 2 diabetes; BMI: Body Mass Index; Schiz: Schizophrenia.

† 95%CI: 95% confidence intervals.

Supplementary Table 7. Results of the Meta-analyses for the Multiplicative Interaction Between the Different Genetic Risk Scores of Interest on Ischemic Heart Disease Risk (Hard Events). The Regression Coefficient of the Interaction Terms (Standard Error) is Shown in the Upper-right Part of the Diagonal, and the p-Value of the Multiplicative Interaction and the p-Value for the Heterogeneity Between the Analyzed Studies is Shown in the Lower-left Part of the Diagonal.

	GRS-IHD*	GRS-TG*	GRS-BP*	GRS-HDL*	GRS-LDL*	GRS-T2D*	GRS-BMI*	GRS-Waist	GRS-SCHIZ
GRS-IHD	NA	-0.003 (0.022)	-0.008 (0.022)	-0.003 (0.022)	-0.005 (0.022)	0.022 (0.022)	0.012 (0.022)	0.015 (0.022)	-0.021 (0.022)
GRS-TG	p-value=0.898 p-het†=0.097	NA	-0.028 (0.022)	-0.017 (0.020)	**-0.047** **(0.021)**	0.029 (0.021)	0.035 (0.021)	-0.020 (0.022)	-0.018 (0.022)
GRS-BP	p-value=0.712 p-het=0.411	p-value=0.204 p-het=0.974	NA	-0.021 (0.022)	-0.040 (0.022)	-0.019 (0.022)	-0.013 (0.022)	-0.041 (0.022)	-0.015 (0.022)
GRS-HDL	p-value=0.883 p-het=0.308	p-value=0.406 p-het=0.776	p-value=0.334 p-het=0.695	NA	-0.015 (0.022)	-0.002 (0.021)	0.020 (0.021)	-0.013 (0.021)	-0.024 (0.022)
GRS-LDL	p-value=0.816 p-het=0.802	**p-value=0.027** **p-het=0.011**	p-value=0.066 p-het=0.207	p-value=0.473 p-het=0.228	NA	-0.024 (0.022)	-0.025 (0.021)	-0.009 (0.022)	-0.003 (0.021)
GRS-T2D	p-value=0.305 p-het=0.322	p-value=0.179 p-het=0.065	p-value=0.392 p-het=0.653	p-value=0.909 p-het=0.138	p-value=0.259 p-het=0.103	NA	-0.005 (0.021)	-0.003 (0.022)	0.024 (0.022)
GRS-BMI	p-value=0.589 p-het=0.385	p-value=0.102 p-het=0.179	p-value=0.540 p-het=0.583	p-value=0.340 p-het=0.788	p-value=0.242 p-het=0.781	p-value=0.828 p-het=0.577	NA	-0.007 (0.021)	-0.009 (0.022)
GRS-Waist	p-value=0.483 p-het=0.430	p-value=0.368 p-het=0.379	p-value=0.059 p-het=0.903	p-value=0.537 p-het=0.023	p-value=0.663 p-het=0.368	p-value=0.534 p-het=0.703	p-value=0.730 p-het=0.913	NA	-0.034 (0.021)
GRS-SCHIZ	p-value=0.355 p-het=0.885	p-value=0.408 p-het=0.067	p-value=0.501 p-het=0.242	p-value=0.265 p-het=0.435	p-value=0.901 p-het=0.506	p-value=0.283 p-het=0.186	p-value=0.665 p-het=0.399	p-value=0.111 p-het=0.749	NA

*GRS: Genetic risk score; IHD: Ischemic Heart Disease; TG: Triglycerides; BP: Blood pressure; HDL: High-density lipoprotein; LDL: Low-density lipoprotein; T2D: Type 2 diabetes; BMI: Body Mass Index; Schiz: Schizophrenia.
†P-het: p value for the heterogeneity test.

Supplementary Table 8. Results of the Meta-analyses for the Multiplicative Interaction Between the Different Genetic Risk Scores of Interest on Ischemic Heart Disease Risk (All Events). The Regression Coefficient of the Interaction Terms (Standard Error) is Shown in the Upper-right Part of the Diagonal, and the p-Value of the Multiplicative Interaction and the p-Value for the Heterogeneity Between the Analyzed Studies is Shown in the Lower-left Part of the Diagonal.

	GRS-IHD*	GRS-TG*	GRS-BP*	GRS-HDL*	GRS-LDL*	GRS-T2D*	GRS-BMI*	GRS-Waist	GRS-SCHIZ
GRS-IHD	NA	-0.024 (0.028)	0.022 (0.028)	0.018 (0.028)	0.003 (0.027)	0.070 (0.027)	0.048 (0.027)	0.036 (0.028)	0.012 (0.029)
GRS-TG	p-value=0.395 p-het†=0.517	NA	-0.046 (0.028)	-0.015 (0.025)	**-0.096 (0.028)**	0.034 (0.027)	0.014 (0.027)	0.026 (0.027)	-0.040 (0.028)
GRS-BP	p-value=0.423 p-het=0.881	p-value=0.099 p-het=0.629	NA	0.001 (0.027)	-0.023 (0.028)	0.008 (0.027)	0.009 (0.027)	-0.067 (0.027)	0.018 (0.028)
GRS-HDL	p-value=0.513 p-het=0.666	p-value=0.562 p-het=0.909	p-value=0.973 p-het=0.952	NA	-0.046 (0.027)	0.001 (0.028)	0.008 (0.027)	0.059 (0.027)	-0.046 (0.028)
GRS-LDL	p-value=0.922 p-het=0.478	**p-value=5x10^{-4} p-het=0.252**	p-value=0.397 p-het=0.978	p-value=0.091 p-het=0.541	NA	-0.018 (0.028)	-0.016 (0.027)	0.039 (0.026)	0.002 (0.027)
GRS-T2D	p-value=0.009 p-het=0.495	p-value=0.211 p-het=0.063	p-value=0.757 p-het=0.880	p-value=0.972 p-het=0.180	p-value=0.513 p-het=0.235	NA	-0.023 (0.027)	0.015 (0.027)	0.047 (0.028)
GRS-BMI	p-value=0.078 p-het=0.532	p-value=0.601 p-het=0.217	p-value=0.748 p-het=0.509	p-value=0.779 p-het=0.662	p-value=0.565 p-het=0.693	p-value=0.393 p-het=0.702	NA	-0.013 (0.026)	0.026 (0.028)
GRS-Waist	p-value=0.191 p-het=0.061	p-value=0.343 p-het=0.206	p-value=0.014 p-het=0.634	p-value=0.025 p-het=0.050	p-value=0.131 p-het=0.434	p-value=0.576 p-het=0.101	p-value=0.609 p-het=0.260	NA	-0.020 (0.027)
GRS-SCHIZ	p-value=0.678 p-het=0.942	p-value=0.144 p-het=0.026	p-value=0.515 p-het=0.134	p-value=0.097 p-het=0.504	p-value=0.944 p-het=0.676	p-value=0.092 p-het=0.576	p-value=0.343 p-het=0.727	p-value=0.455 p-het=0.442	NA

*GRS: Genetic risk score; IHD: Ischemic Heart Disease; TG: Triglycerides; BP: Blood pressure; HDL: High-density lipoprotein; LDL: Low-density lipoprotein; T2D: Type 2 diabetes; BMI: Body Mass Index; Schiz: Schizophrenia.
†P-het: p value for the heterogeneity test.

Supplementary Table 9. Results of the sensitivity analyses undertaken to assess whether an individual study influenced the pooled results of the multiplicative GRS_{LDL}·GRS_{TG} and GRS_{LDL}·GRS_{IHD} interaction terms, excluding one study at a time and calculating the multiplicative interaction metrics for the remaining studies considering hard and all coronary events.

	Hard coronary events Regression coefficient (Standard Error)	**All coronary events Regression coefficient (Standard Error)**
GRS_{LDL}·GRS_{TG}		
GRS global analysis	-0.047 (0.021)	-0.096 (0.028)
Global–Excluding MIGEN	-0.116 (0.031)	---
Global–Excluding Framingham	-0.041 (0.022)	-0.097 (0.030)
Global–Excluding FINRISK-1997	-0.018 (0.024)	-0.071 (0.032)
Global–Excluding FINRISK-2002	-0.039 (0.022)	-0.088 (0.029)
Global–Excluding EGCUT	-0.049 (0.023)	-0.142 (0.037)
Non-pleiotropic GRS_{IHD}·GRS_{LDL}		
GRS global analysis	0.064 (0.022)	0.091 (0.028)
Global–Excluding MIGEN	0.079 (0.031)	---
Global–Excluding Framingham	0.058 (0.023)	0.084 (0.031)
Global–Excluding FINRISK-1997	0.073 (0.025)	0.104 (0.033)
Global–Excluding FINRISK-2002	0.072 (0.023)	0.102 (0.030)
Global–Excluding EGCUT	0.047 (0.024)	0.065 (0.037)

GRS: Genetic risk score; LDL: Low density lipoprotein; TG: Triglycerides; IHD: Ischemic Heart Disease.

Supplementary Table 10. Results of the Meta-analyses for the Additive Interaction Between the Different Genetic Risk Scores of Interest on Ischemic Heart Disease Risk (Hard Events). The Synergy Index (and the 95% Confidence Interval) is Shown in the Upper-right Part of the Diagonal; the p-Value of the Additive Interaction and the p-Value for the Heterogeneity Between the Analyzed Studies is Shown in the Lower-left Part of the Diagonal.

	GRS-IHD*	GRS-TG*	GRS-BP*	GRS-HDL*	GRS-LDL*	GRS-T2D*	GRS-BMI*	GRS-Waist	GRS-SCHIZ
GRS-IHD	NA	1.063 (0.919, 1.207)	0.989 (0.842, 1.136)	0.975 (0.803, 1.147)	1.076 (0.933, 1.219)	1.038 (0.883, 1.193)	1.084 (0.938, 1.231)	1.122 (0.981, 1.264)	0.894 (0.736, 1.052)
GRS-TG	p-value=0.392 p-het†=0.063	NA	0.865 (0.552, 1.177)	1.009 (0.499, 1.519)	1.137 (0.900, 1.374)	1.083 (0.760, 1.406)	1.158 (0.880, 1.437)	0.834 (0.523, 1.145)	1.015 (0.664, 1.367)
GRS-BP	p-value=0.879 p-het=0.357	p-value=0.397 p-het=0.983	NA	0.802 (0.338, 1.265)	0.673 (0.385, 0.961)	0.786 (0.174, 1.397)	0.919 (0.589, 1.248)	0.755 (0.332, 1.179)	0.831 (0.060, 1.602)
GRS-HDL	p-value=0.779 p-het=0.196	p-value=0.973 p-het=0.970	p-value=0.402 p-het=0.974	NA	0.793 (0.278, 1.308)	0.824 (0.455, 1.193)	0.839 (0.368, 1.310)	0.453 (-0.265, 1.170)	1.004 (0.642, 1.366)
GRS-LDL	p-value=0.297 p-het=0.399	p-value=0.257 p-het=0.443	p-value=0.026 p-het=0.965	p-value=0.431 p-het=0.882	NA	0.903 (0.612, 1.194)	0.970 (0.755, 1.186)	0.912 (0.666, 1.157)	0.993 (0.683, 1.302)
GRS-T2D	p-value=0.630 p-het=0.418	p-value=0.613 p-het=0.623	p-value=0.492 p-het=0.875	p-value=0.351 p-het=0.542	p-value=0.513 p-het=0.877	NA	0.957 (0.578, 1.335)	0.715 (0.057, 1.373)	0.831 (0.071, 1.591)
GRS-BMI	p-value=0.256 p-het=0.669	p-value=0.266 p-het=0.905	p-value=0.628 p-het=0.888	p-value=0.503 p-het=0.990	p-value=0.788 p-het=0.920	p-value=0.822 p-het=0.902	NA	0.994 (0.690, 1.299)	0.940 (0.474, 1.407)
GRS-Waist	p-value=0.091 p-het=0.489	p-value=0.294 p-het=0.728	p-value=0.258 p-het=0.946	p-value=0.135 p-het=0.990	p-value=0.480 p-het=0.987	p-value=0.396 p-het=0.620	p-value=0.972 p-het=0.975	NA	0.645 (0.032, 1.258)
GRS-SCHIZ	p-value=0.189 p-het=0.959	p-value=0.932 p-het=0.837	p-value=0.667 p-het=0.942	p-value=0.982 p-het=0.787	p-value=0.962 p-het=0.999	p-value=0.663 p-het=0.808	p-value=0.802 p-het=0.944	p-value=0.257 p-het=0.956	NA

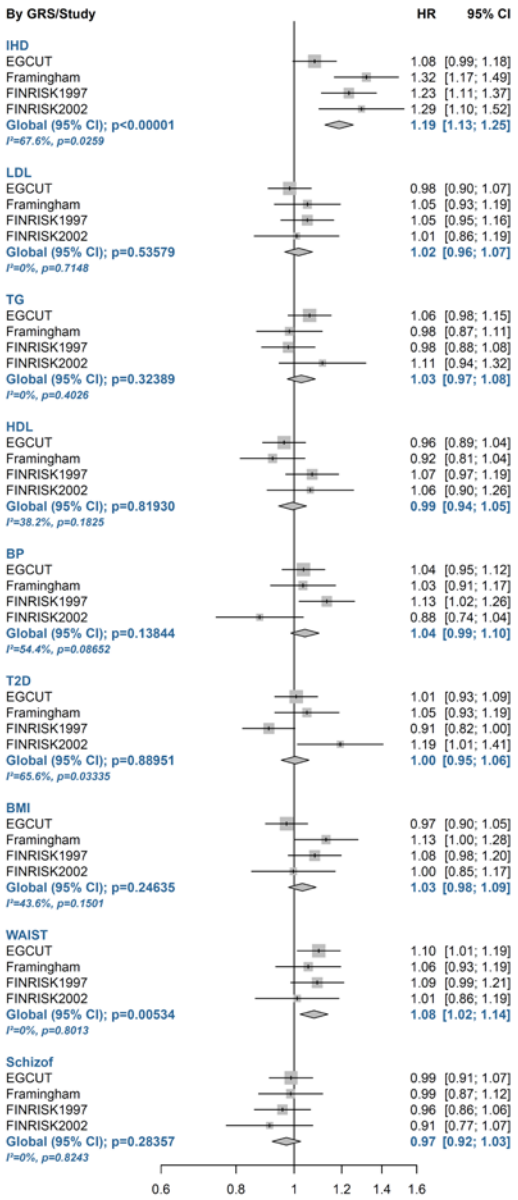
*GRS: Genetic risk score for the traits of interest; IHD: Ischemic Heart Disease; TG: Triglycerides; BP: Blood pressure; HDL: High-density lipoprotein; LDL: Low-density lipoprotein; T2D: Type 2 diabetes; BMI: Body Mass Index; Schiz: Schizophrenia.
†P-het: p value for the heterogeneity between studies.

Supplementary Table 11. Results of the Meta-analyses for the Additive Interaction Between the Different Genetic Risk Scores of Interest on Ischemic Heart Disease Risk (All Events). The Synergy Index (and the 95% Confidence Interval) is Shown in the Upper-right Part of the Diagonal; the p-Value of the Additive Interaction and the p-Value for the Heterogeneity Between the Analyzed Studies is Shown in the Lower-left Part of the Diagonal.

	GRS-IHD*	GRS-TG*	GRS-BP*	GRS-HDL*	GRS-LDL*	GRS-T2D*	GRS-BMI*	GRS-Waist	GRS-SCHIZ
GRS-IHD	NA	0.864 (0.566, 1.162)	1.118 (0.832, 1.404)	0.995 (0.646, 1.344)	0.911 (0.596, 1.227)	1.231 (0.902, 1.561)	1.221 (0.928, 1.514)	1.171 (0.898, 1.445)	0.970 (0.610, 1.330)
GRS-TG	p-value=0.370 p-het†=0.515	NA	0.584 (-0.041, 1.209)	0.781 (-0.020, 1.583)	0.123 (-1.093, 1.340)	0.822 (0.404, 1.241)	1.320 (0.436, 2.203)	1.238 (0.662, 1.814)	0.426 (-1.019, 1.864)
GRS-BP	p-value=0.418 p-het=0.942	p-value=0.192 p-het=0.961	NA	1.149 (0.563, 1.734)	0.880 (0.382, 1.378)	1.007 (0.170, 1.844)	1.017 (0.582, 1.453)	0.666 (0.286, 1.046)	1.270 (0.680, 1.859)
GRS-HDL	p-value=0.977 p-het=0.770	p-value=0.593 p-het=0.996	p-value=0.618 p-het=0.986	NA	0.671 (-0.098, 1.442)	0.705 (-0.111, 1.522)	1.122 (0.578, 1.666)	0.824 (0.163, 1.485)	0.741 (0.028, 1.453)
GRS-LDL	p-value=0.582 p-het=0.526	p-value=0.158 p-het=0.953	p-value=0.636 p-het=0.997	p-value=0.403 p-het=0.674	NA	1.221 (0.475, 1.968)	0.952 (0.460, 1.444)	1.159 (0.487, 1.831)	0.897 (-0.045, 1.839)
GRS-T2D	p-value=0.169 p-het=0.509	p-value=0.406 p-het=0.741	p-value=0.987 p-het=0.928	p-value=0.479 p-het=0.998	p-value=0.561 p-het=0.751	NA	1.000 (0.367, 1.633)	1.104 (0.475, 1.733)	0.841 (0.062, 1.621)
GRS-BMI	p-value=0.139 p-het=0.609	p-value=0.478 p-het=0.902	p-value=0.939 p-het=0.929	p-value=0.660 p-het=0.980	p-value=0.848 p-het=0.937	p-value=1.000 p-het=0.991	NA	0.901 (0.438, 1.365)	0.835 (0.036, 1.634)
GRS-Waist	p-value=0.219 p-het=0.129	p-value=0.418 p-het=0.836	p-value=0.085 p-het=0.773	p-value=0.602 p-het=0.542	p-value=0.642 p-het=0.604	p-value=0.746 p-het=0.395	p-value=0.676 p-het=0.485	NA	0.741 (0.028, 1.453)
GRS-SCHIZ	p-value=0.871 p-het=0.968	p-value=0.432 p-het=0.845	p-value=0.370 p-het=0.974	p-value=0.475 p-het=0.975	p-value=0.830 p-het=0.994	p-value=0.689 p-het=0.789	p-value=0.686 p-het=0.984	p-value=0.475 p-het=0.975	NA

*GRS: Genetic risk score for the traits of interest; IHD: Ischemic Heart Disease; TG: Triglycerides; BP: Blood pressure; HDL: High-density lipoprotein; LDL: Low-density lipoprotein; T2D: Type 2 diabetes; BMI: Body Mass Index; Schiz: Schizophrenia.
†P-het: p value for the heterogeneity between studies.

Supplementary Figure 1. Forest Plot of the Association Between the Different Weighted Genetic Risk Scores for Cardiovascular Risk Factors and Ischemic Heart Disease and the Incidence of All Ischemic Heart Disease Events (Myocardial Infarction, Ischemic Heart Disease Death, Angina and Revascularization) Across Studies and in the Meta-analysis.



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