Supplement Material

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Supplementary Table I. Single nucleotide polymorphisms (SNPs) associated with coronary heart disease							
SNP	**Region**	**Reported Gene(s)**	**Risk allele**	**Risk allele freq. in controls**		**Weight†**	**Reference**
				Study cohorts	**Reference**		
rs646776	1p13.3	*CELSR2, PSRC1, SORT1*	T	0.79	0.81	1.19	1
rs11206510	1p32.3	PCSK9	T	0.84	0.82	1.08	2
rs17465637	1q41	MIA3	C	0.75	0.74	1.14	2
rs6725887	2q33.1	WDR12	C	0.11	0.15	1.14	2
rs2306374	3q22.3	MRAS	C	0.10	0.18	1.12	2
rs12526453	6p24.1	PHACTR1	C	0.56	0.65	1.12	1
rs3798220	6q25.3	LPA	C	0.01	0.02	1.54	2
rs4977574	9p21.3	CDKN2A/B, ANRIL	G	0.43	0.46	1.29	2
rs1746048	10q11.21	CXCL12	C	0.84	0.87	1.09	2
rs3184504	12q24.12	SH2B3	T	0.40	0.44	1.07	2
rs1122608	19p13.2	LDLR	G	0.79	0.77	1.14	2
rs9982601	21q22.11	MRPS6	T	0.13	0.15	1.18	2
rs2259816	12q24.31	HNFA1	T	0.37	0.36	1.08	3
rs17114036	1p32.2	PPAP2B	A	0.89	0.91	1.17	2
rs17609940	6p21.31	ANKS1A	G	0.81	0.75	1.07	2
rs11556924	7q32.2	ZC3HC1	C	0.67	0.62	1.09	2
rs579459	9q34.2	ABO	C	0.22	0.21	1.10	2
rs12413409	10q24.32	CYP17A1, CNNM2, NT5C2	G	0.92	0.89	1.12	2
rs964184	11q23.3	ZNF259, APOA5-A4-C3-A1	G	0.14	0.13	1.13	2
rs4773144	13q34	COL4A1, COL4A2	G	0.40	0.44	1.07	2
rs2895811	14q32.2	HHIPL1	C	0.42	0.43	1.07	2
rs3825807	15q25.1	ADAMTS7	A	0.65	0.57	1.08	2
rs12936587	17p11.2	RASD1, SMCR3, PEMT	G	0.65	0.56	1.07	2
rs216172	17p13.3	SMG6, SRR	C	0.35	0.37	1.07	2

SNP	Region	Reported Gene(s)	Risk allele	Risk allele freq. in controls		Weight†	Reference
				Study cohorts	Reference		
rs46522	17q21.32	UBE2Z, GIP, ATP5G1, SNF8	T	0.55	0.53	1.06	2
rs1412444	10q23.31	LIPA	T	0.42	0.42	1.09	4
rs4380028	15q25.1	ADAMTS7-MORF4L1	C	0.70	0.65	1.07	4
rs10953541	7q22.3	NR	C	0.74	0.80	1.08	4

† Odds ratios from the reference studies were used as weights for the risk allele counts to generate the genetic risk score

Supplementary Table II. Association results for single nucleotide polymorphisms (SNPs) and cardiovascular events									
SNP	**Region**	**Reported Gene(s)**	**Risk allele**	**Coronary heart disease**		**Acute coronary syndrome**		**Cardiovascular disease**	
				HR (95% CI)	**P value**	**HR (95% CI)**	**P value**	**HR (95% CI)**	**P value**
rs646776	1p13.3	*CELSR2, PSRC1, SORT1*	T	1.05 (0.94 , 1.17)	0.37	1.02 (0.90 , 1.15)	0.79	1.02 (0.94 , 1.12)	0.60
rs11206510	1p32.3	PCSK9	T	1.04 (0.93 , 1.17)	0.51	1.07 (0.93 , 1.23)	0.35	1.04 (0.95 , 1.15)	0.40
rs17465637	1q41	MIA3	C	1.04 (0.94 , 1.15)	0.41	1.05 (0.93 , 1.19)	0.40	1.07 (0.98 , 1.16)	0.12
rs6725887	2q33.1	WDR12	C	**1.26 (1.11 , 1.43)**	**0.0003**	**1.21 (1.04 , 1.42)**	**0.02**	**1.13 (1.01 , 1.26)**	**0.03**
rs2306374	3q22.3	MRAS	C	1.00 (0.87 , 1.14)	0.98	1.00 (0.85 , 1.18)	0.97	1.04 (0.93 , 1.16)	0.53
rs12526453	6p24.1	PHACTR1	C	**1.13 (1.04 , 1.23)**	**0.004**	**1.19 (1.07 , 1.32)**	**0.0009**	**1.09 (1.01 , 1.17)**	**0.02**
rs3798220	6q25.3	LPA	C	**1.43 (1.02 , 2.00)**	**0.04**	1.20 (0.77 , 1.86)	0.42	1.21 (0.90 , 1.63)	0.21
rs4977574	9p21.3	CDKN2A/B, ANRIL	G	**1.19 (1.09 , 1.29)**	**5.4×10^{-5}**	**1.16 (1.04 , 1.28)**	**0.005**	**1.19 (1.11 , 1.27)**	**1.3×10^{-6}**
rs1746048	10q11.21	CXCL12	C	**1.31 (1.16 , 1.49)**	**2.2×10^{-5}**	**1.33 (1.14 , 1.54)**	**0.0003**	**1.20 (1.09 , 1.32)**	**0.0004**
rs3184504	12q24.12	SH2B3	T	1.02 (0.94 , 1.12)	0.60	1.04 (0.94 , 1.15)	0.45	1.07 (1.00 , 1.15)	0.06
rs1122608	19p13.2	LDLR	G	1.10 (0.98 , 1.22)	0.10	1.12 (0.98 , 1.27)	0.12	1.02 (0.93 , 1.12)	0.65
rs9982601	21q22.11	MRPS6	T	**1.18 (1.05 , 1.33)**	**0.005**	**1.17 (1.02 , 1.35)**	**0.03**	1.09 (0.98 , 1.20)	0.11
rs2259816	12q24.31	HNF1A	T	1.01 (0.93 , 1.10)	0.83	1.04 (0.94 , 1.16)	0.43	1.00 (0.93 , 1.07)	0.98
rs17114036	1p32.2	PPAP2B	A	1.06 (0.92 , 1.21)	0.43	1.02 (0.87 , 1.20)	0.84	1.02 (0.92 , 1.14)	0.69
rs17609940	6p21.31	ANKS1A	G	1.02 (0.92 , 1.14)	0.72	1.05 (0.92 , 1.20)	0.45	1.01 (0.92 , 1.10)	0.88
rs11556924	7q32.2	ZC3HC1	C	1.01 (0.92 , 1.11)	0.80	1.00 (0.90 , 1.12)	0.98	0.99 (0.92 , 1.07)	0.81
rs579459	9q34.2	ABO	C	1.10 (0.99 , 1.21)	0.07	**1.13 (1.00 , 1.27)**	**0.05**	1.03 (0.95 , 1.12)	0.51
rs12413409	10q24.32	CYP17A1, CNNM2, NT5C2	G	1.04 (0.89 , 1.21)	0.60	1.08 (0.90 , 1.30)	0.43	1.02 (0.90 , 1.16)	0.72

SNP	Region	Reported Gene(s)	Risk allele	Coronary heart disease		Acute coronary syndrome		Cardiovascular disease	
				HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value
rs964184	11q23.3	ZNF259, APOA5-A4-C3-A1	G	1.02 (0.90 , 1.15)	0.78	1.01 (0.88 , 1.17)	0.85	1.05 (0.95 , 1.15)	0.35
rs4773144	13q34	COL4A1, COL4A2	G	**1.10 (1.01 , 1.20)**	**0.03**	1.07 (0.96 , 1.18)	0.21	1.05 (0.98 , 1.12)	0.20
rs2895811	14q32.2	HHIPL1	C	**1.12 (1.03 , 1.22)**	**0.009**	1.10 (0.99 , 1.22)	0.06	1.07 (1.00 , 1.15)	0.06
rs3825807	15q25.1	ADAMTS7	A	**1.13 (1.03 , 1.23)**	**0.008**	**1.12 (1.01 , 1.25)**	**0.04**	**1.10 (1.03 , 1.19)**	**0.008**
rs12936587	17p11.2	RASD1, SMCR3, PEMT	G	**1.11 (1.02 , 1.22)**	**0.02**	1.05 (0.94 , 1.16)	0.41	1.07 (1.00 , 1.16)	**0.05**
rs216172	17p13.3	SMG6, SRR	C	1.06 (0.97 , 1.16)	0.19	1.04 (0.93 , 1.15)	0.50	**1.08 (1.00 , 1.16)**	**0.04**
rs46522	17q21.32	UBE2Z, GIP, ATP5G1, SNF8	T	0.97 (0.89 , 1.06)	0.49	0.98 (0.88 , 1.08)	0.67	0.97 (0.90 , 1.04)	0.37
rs1412444	10q23.31	LIPA	T	0.98 (0.9 , 1.07)	0.63	1.00 (0.90 , 1.11)	0.98	0.94 (0.87 , 1.01)	0.09
rs4380028	15q25.1	ADAMTS7-MORF4L1	C	**1.12 (1.02 , 1.23)**	**0.02**	**1.15 (1.02 , 1.28)**	**0.02**	1.07 (1.00 , 1.16)	0.06
rs10953541	7q22.3	NR	C	1.03 (0.94 , 1.14)	0.50	1.04 (0.92 , 1.17)	0.54	1.02 (0.94 , 1.10)	0.63

Cox proportional hazards model adjusted for sex, total cholesterol, high-density lipiprotein (HDL) cholesterol, body-mass index, systolic blood pressure, blood pressure treatment, smoking and type 2 diabetes; age was used as the timescale.
Abbreviations: HR, Hazard ratio; CI, confidence interval

Supplementary Table III. Reclassification of individuals in four risk categories after addition of genetic risk score (GRS) to a model with traditional risk factors* – sensitivity analysis**

Model without GRS		Model with GRS					
		0-7%	**7-12%**	**12-22%**	**>22%**	**NRI**	**Clinical NRI**
0-7%	**Events**	121	22	0	0	**Events**: 0.04 (P=0.03)	**Events**: 0.10 (P=0.03)
	Nonevents	8564	197	0	0		
	All	8685	219	0	0	**Nonevents**: 0.01 (P=0.0001)	**Nonevents**: 0.14 ($P=3.7\times10^{-12}$)
7-12%	**Events**	15	77	23	0		
	Nonevents	251	689	140	0	**All**: 0.05 (P=0.008)	**All**: 0.24 ($P=9.1\times10^{-7}$)
	All	266	766	163	0		
12-22%	**Events**	0	25	122	43		
	Nonevents	2	182	546	73		
	All	2	207	668	116		
>22%	**Events**	0	0	21	159		
	Nonevents	0	1	92	305		
	All	0	1	113	464		

*Traditional risk factors include sex, total cholesterol, high-density lipiprotein (HDL) cholesterol, body-mass index, systolic blood pressure, blood pressure treatment, smoking and type 2 diabetes; age was used as the timescale in the Cox proportional hazards model.
** Sensitivity of the choice of categories was tested by rising category thresholds by 2%

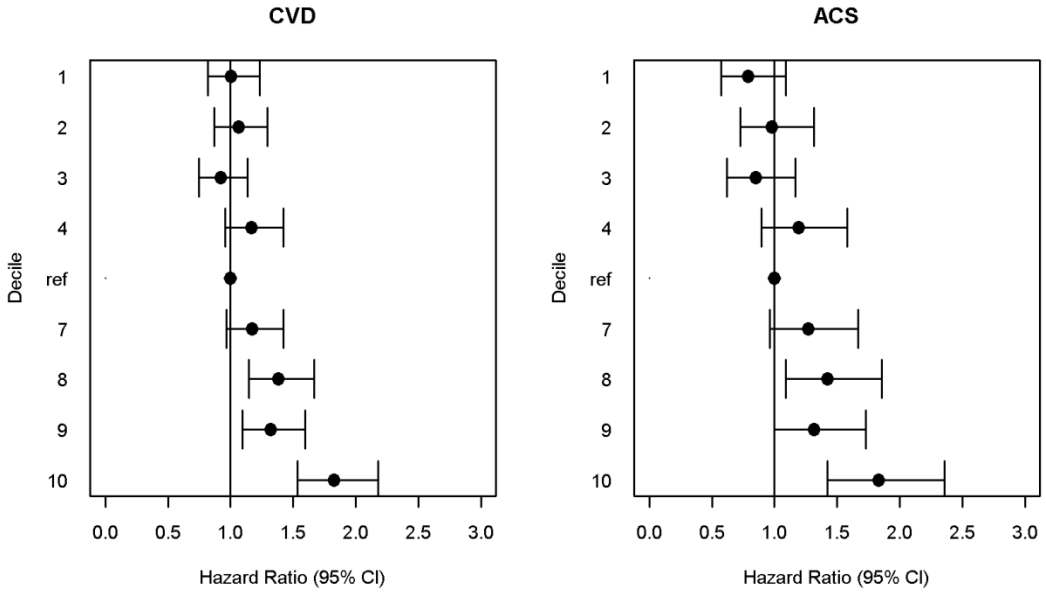
Abbreviations: NRI, net reclassification improvement

Supplementary Table IV. Assessment of over-fitting in discrimination and reclassification measures

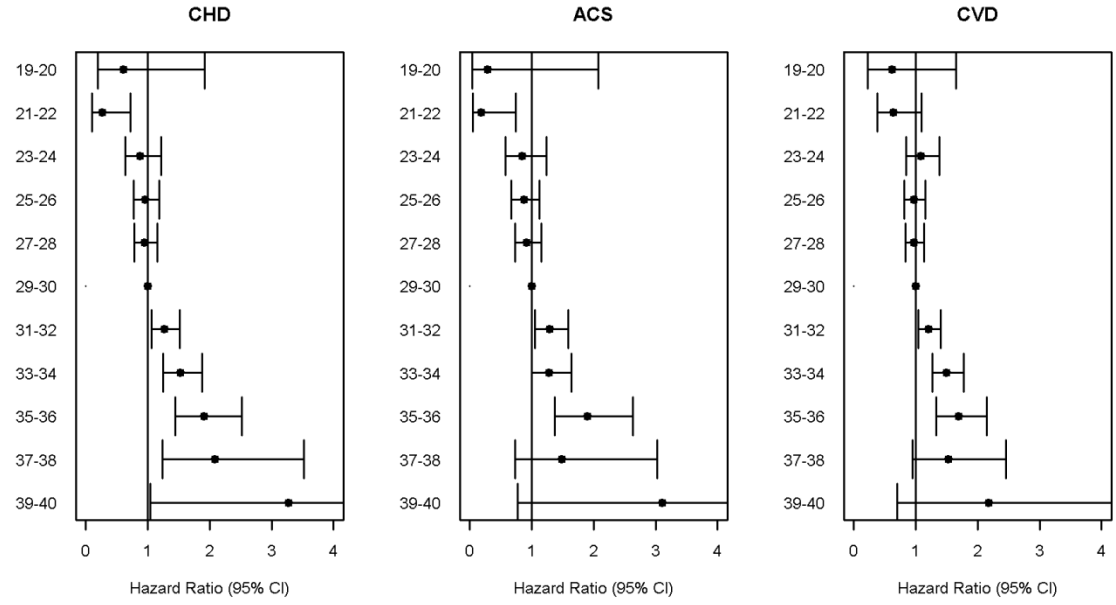
	Effects estimated directly from the test dataset*	**Effects estimated from the training dataset** applied for calculating the linear predictors in the test dataset**
C-index of the model with traditional risk factors	0.859	0.855
C-index change with the addition of the GRS (P-value)	0.004 (P=0.007)	0.004 (P=0.012)
IDI (P-value)	0.007 ($P=4.2\times10^{-5}$)	0.009 ($P=1.3\times10^{-5}$)
NRI (P-value)	0.05 (P=0.01)	0.04 (P=0.05)

* Test dataset: combined FINRISK 1992 and 1997 dataset
** Training dataset: FINRISK 2002 dataset. To justify the comparison with FINRISK 1992 and 1997 datasets, individuals with baseline lipid medication (N=454) were removed from the analysis.
Abbreviations: FR, FINRISK; GRS, genetic risk score; IDI, integrated discrimination index; NRI, net reclassification improvement

Supplementary Figure I. Genetic risk score deciles and risk for cardiovascular disease (CVD) and acute coronary syndrome (ACS).



Supplementary Figure II. Risk allele count and risk for coronary heart disease (CHD), acute coronary syndrome (ACS) and cardiovascular disease (CVD).



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