SUPPLEMENTAL MATERIAL

Polygenic risk score identifies subgroup with higher burden of atherosclerosis and greater relative benefit from statin therapy in the primary prevention setting

Supplementary Tables

Supplementary Figures and Figure Legends

Supplementary Table 1. DNA sequence variants comprising polygenic risk score for coronary heart disease.

					WOSCOPS			BioImage			CARDIA		
Locus	**Implicated Gene(s)**	**Lead SNP**	**Lead Risk Allele**	**CHD OR**	**SNP**	**Risk Allele**	**Frequency**	**SNP**	**Risk Allele**	**Frequency**	**SNP**	**Risk Allele**	**Frequency**
1p13.3	*SORT1*	rs602633	C	1.12	rs602633	C	0.793	rs602633	C	0.793	*rs583104*	*T*	*0.777*
1p32.2	*PPAP2B*	rs17114036	A	1.11	rs17114036	A	0.879	rs17114036	A	0.879	*rs6588635*	*T*	*0.866*
1p32.3	*PCSK9*	rs11206510	T	1.06	rs11206510	T	0.828	rs11206510	T	0.828			
1q21.3	*IL6R*	rs4845625	T	1.06	rs4845625	T	0.451	rs4845625	T	0.451	*rs6689393*	*A*	*0.452*
1q41	*MIA3*	rs17464857	T	1.05	rs17464857	T	0.866	rs17464857	T	0.866			
21q22.11	*KCNE2*	rs9982601	T	1.13	rs9982601	T	0.122	rs9982601	T	0.122			
22q11.23	*POM121L9P-ADORA22B*	rs180803	G	1.02									
2p11.2	*VAMP5-VAMP8-GGCX*	rs1561198	A	1.06	rs1561198	A	0.476	rs1561198	A	0.476	rs1561198	A	0.476
2p21	*ABCG5-ABCG8*	rs6544713	T	1.06	rs6544713	T	0.309	rs6544713	T	0.309			
2p24.1	*APOB*	rs515135	G	1.07	rs515135	G	0.796	rs515135	G	0.796	*rs562338*	*G*	*0.795*
2q22.3	*ZEB2-AC074093.1*	rs2252641	G	1.06	rs2252641	G	0.46	rs2252641	G	0.46	rs2252641	G	0.46
2q33.2	*WDR12*	rs6725887	C	1.12	rs6725887	C	0.13	*rs2351524*	*T*	*0.13*	rs6725887	C	0.13
2q37.1	*KCNJ13-GIGYF2*	rs1801251	A	1.05				rs1801251	A	0.287	*rs283475*	*T*	*0.276*
3q22.3	*MRAS*	rs9818870	T	1.07	rs9818870	T	0.143	rs9818870	T	0.143	rs9818870	T	0.143
4q12	*REST-NOA1*	rs17087335	T	1.06	rs17087335	T	0.186	rs17087335	T	0.186	*rs7687767*	*G*	*0.185*
4q31.22	*EDNRA*	rs1878406	T	1.1	rs1878406	T	0.146				*rs6841581*	*T*	*0.146*
4q32.1	*GUCY1A3*	rs7692387	G	1.08	rs7692387	G	0.795	rs7692387	G	0.795	*rs3796587*	*C*	*0.795*
5q31.1	*SLC22A4-SLC22A5*	rs273909	C	1.07	rs273909	C	0.134	rs273909	C	0.134			
6p21.2	*KCNK5*	rs10947789	T	1.07	rs10947789	T	0.736	rs10947789	T	0.736	*rs6918122*	*C*	*0.746*
6p21.31	*ANKS1A*	rs12205331	C	1.04	rs12205331	C	0.81	rs12205331	C	0.81	*rs17609940*	*G*	*0.811*
6p21.33	*C2*	rs3130683	T	1.09				rs3130683	T	0.968			
6p24.1	*PHACTR1*	rs9369640	A	1.09	rs9369640	A	0.62	rs9369640	A	0.62	rs9369640	A	0.62
6q23.2	*TCF21*	rs12190287	C	1.07	rs12190287	C	0.612						
6q25.3	*LPA*	rs3798220	C	1.28	rs3798220	C	0.01	rs3798220	C	0.01			
6q25.3	*LPA*	rs2048327	G	1.06	rs2048327	G	0.352	rs2048327	G	0.352	rs2048327	G	0.352

6q26	*PLG*	rs4252120	T	1.07	rs4252120	T	0.704	rs4252120	T	0.704	rs4252120	T	0.704
7p21.1	*HDAC9*	rs2023938	G	1.08	rs2023938	G	0.095	rs2023938	G	0.095	*rs10245779*	*C*	*0.1*
7q22.3	*NA*	rs12539895	A	1.08	rs12539895	A	0.188	*rs3815148*	*C*	*0.203*	*rs34084719*	*C*	*0.188*
7q32.2	*ZC3HC1*	rs11556924	C	1.09	rs11556924	C	0.623	rs11556924	C	0.623			
7q36.1	*NOS3*	rs3918226	T	1.14	rs3918226	T	0.014						
8p21.3	*LPL*	rs264	G	1.11	rs264	G	0.851	rs264	G	0.851	*rs271*	*G*	*0.847*
8q24.13	*TRIB1*	rs2954029	A	1.06	rs2954029	A	0.552	rs2954029	A	0.552	*rs2980875*	*A*	*0.548*
9p21.3	*CDKN2A*	rs1333049	C	1.21	rs1333049	C	0.472	rs1333049	C	0.472	rs1333049	C	0.472
9p21.3	*CDKN2A*	rs3217992	A	1.16	rs3217992	A	0.402	rs3217992	A	0.402	rs3217992	A	0.402
9q31.3	*SVEP1*	rs111245230	C	1.14				rs111245230	C	0.032	*rs11791314*	*C*	*0.029*
9q34.2	*ABO*	rs579459	C	1.07	rs579459	C	0.214	rs579459	C	0.214			
10p11.23	*KIAA1462*	rs2505083	C	1.06	rs2505083	C	0.428	rs2505083	C	0.428			
10q11.21	*CXCL12*	rs501120	A	1.07	rs501120	A	0.854	rs501120	A	0.854	*rs671765*	*A*	*0.854*
10q11.21	*CXCL12*	rs2047009	C	1.05	rs2047009	C	0.49				rs2047009	C	0.49
10q23.31	*LIPA*	rs2246833	T	1.06	rs2246833	T	0.358	*rs2246942*	*G*	*0.361*			
10q23.31	*LIPA*	rs11203042	T	1.04	rs11203042	T	0.457	rs11203042	T	0.457	*rs11203041*	*T*	*0.455*
10q24.32	*CYP17A1*	rs12413409	G	1.1	rs12413409	G	0.911	rs12413409	G	0.911	*rs12052058*	*G*	*0.746*
11p15.3	*NA*	rs11042937	T	1.04				rs11042937	T	0.518	rs11042937	T	0.518
11p15.4	*SWAP70*	rs10840293	A	1.06									
11q22.3	*PDGF*	rs974819	A	1.07	rs974819	A	0.279	rs974819	A	0.279	*rs2128739*	*A*	*0.272*
11q23.3	*APOA5-APOA1*	rs9326246	C	1.09	rs9326246	C	0.093	rs9326246	C	0.093	*rs6589566*	*G*	*0.091*
12p13.3	*LRP1*	rs11172113	C	1.06	rs11172113	C	0.388	rs11172113	C	0.388			
12p24.31	*SCARB1*	rs11057830	A	1.08	rs11057830	A	0.165	rs11057830	A	0.165			
12q24.12	*SH2B3*	rs3184504	T	1.07	rs3184504	T	0.464	rs3184504	T	0.464			
13q12.3	*FLT1*	rs9319428	A	1.06	rs9319428	A	0.309	rs9319428	A	0.309			
13q34	*COL4A1*	rs9515203	T	1.08	rs9515203	T	0.766						
13q34	*COL4A1*	rs4773144	G	1.07	rs4773144	G	0.447	rs4773144	G	0.447			
14q32.2	*HHIPL1*	rs2895811	C	1.06	rs2895811	C	0.426	rs2895811	C	0.426			
15q22.33	*SMAD3*	rs17293632	C	1.05				rs17293632	C	0.785	*rs2033784*	*T*	*0.719*
15q25.1	*ADAMTS7*	rs7173743	T	1.07	rs7173743	T	0.535	rs7173743	T	0.535	*rs7168915*	*A*	*0.533*
15q26.1	*MFGE8-ABHD2*	rs8042271	G	1.1									

15q26.1	*FURIN*	rs17514846	A	1.07	rs17514846	A	0.461	rs17514846	A	0.461	*rs1894401*	*G*	*0.469*
16q13	*CETP*	rs247616	C	1.05	rs247616	C	0.708	rs247616	C	0.708			
17p11.2	*RASD1*	rs12936587	G	1.06	rs12936587	G	0.554	rs12936587	G	0.554			
17p13.3	*SMG6*	rs2281727	C	1.04	rs2281727	C	0.369	rs2281727	C	0.369	*rs9895551*	*G*	*0.37*
17q21.32	*UBE2Z*	rs15563	C	1.04	rs15563	C	0.559	rs15563	C	0.559	rs15563	C	0.559
17q23.2	*BCAS3*	rs8080784	C	1.06				rs8080784	C	0.161	*rs7225581*	*A*	*0.161*
18q21.32	*PMAIP1-MC4R*	rs663129	A	1.06	rs663129	A	0.24	*rs571312*	*T*	*0.24*			
19p13.2	*ANGPTL4*	rs116843064	G	1.16				rs116843064	G	0.974			
19p13.2	*LDLR*	rs1122608	G	1.1	rs1122608	G	0.75	rs1122608	G	0.75	rs1122608	G	0.75
19q13.32	*APOE-APOC1*	rs445925	C	1.13	rs445925	C	0.906	rs445925	C	0.906			
19q13.32	*APOE-APOC1*	rs2075650	G	1.11	rs2075650	G	0.131	rs2075650	G	0.131			

A set of 67 independent genomic variants associated with coronary heart disease at stringent statistical thresholds have been found.[1-3] Directly genotyped variants in WOSCOPS were used for analysis. Directly genotyped and imputed proxy variants ($r^2 > 0.8$)[4] in BioImage and CARDIA were included for analysis. Variants in red and italicized are proxy variants. Risk allele frequencies in 1000G phase 3 EUR samples are noted.[4]

Supplementary Table 2. Baseline characteristics in WOSCOPS participants by treatment group.

	Placebo (n = 2,440)	**Statin (n = 2,452)**	***P***
Age, years	55.1 (5.5)	55.2 (5.5)	0.60
Male, %	100.0	100.0	-
BMI, kg/m^2	26.0 (3.1)	26.0 (3.3)	0.99
Family history of CHD, %	5.3	5.7	0.60
Smoking, %	44.0	43.4	0.70
Diabetes mellitus, %	1.0	1.2	0.60
Systolic blood pressure, mmHg	135.8 (17.0)	135.3 (17.5)	0.30
Antihypertensive therapy, %	13.9	14.5	0.59
Total cholesterol, mg/dl	271.8 (22.4)	271.5 (22.8)	0.68
LDL cholesterol, mg/dl	191.8 (17.2)	191.9 (17.5)	0.95
HDL cholesterol, mg/dl	43.9 (9.5)	43.9 (9.3)	0.84
Triglycerides, mg/dl	161.0 (68.0)	158.2 (66.9)	0.15
High polygenic risk score, %	21.0	19.0	0.11
Follow Up, years	13.5 (2.8)	13.7 (2.7)	0.052
Follow Up within trial, years	4.8 (0.7)	4.8 (0.7)	0.15
Follow Up after trial, years	8.7 (2.6)	8.9 (2.4)	0.08

Values are presented as mean (standard deviation) or %. ASCVD = atherosclerotic cardiovascular disease; BMI = body-mass index; HDL = high-density lipoprotein; LDL = low-density lipoprotein.

Supplementary Table 3. Predicted PCE ASCVD 10-year event rates risk by polygenic risk score quintile.

	PCE estimated 10-year ASCVD event rate %		
Polygenic risk score Quintile	**WOSCOPS**	**CARDIA**	**BioImage**
Q1	15.0 (7.6)	1.7 (2.2)	42.1 (18.4)
Q2	15.3 (7.8)	2.1 (2.9)	43.4 (19.2)
Q3	15.0 (8.3)	1.7 (2.4)	43.2 (18.3)
Q4	14.8 (7.9)	1.7 (2.3)	43.0 (18.7)
Q5 (High)	14.5 (7.4)	1.8 (2.0)	42.1 (18.2)

ASCVD = atherosclerotic cardiovascular disease; PCE = ACC/AHA Pooled Cohort Equations; Q = quintile

Supplementary Table 4. Multivariable association of high genetic risk with CHD events in placebo-treated WOSCOPS participants

Variable	HR	CI	*P*
Age	1.30	1.16-1.45	< 0.001
Family history of CHD	1.42	0.93-2.17	0.11
Smoking	1.55	1.25-1.92	< 0.001
Diabetes mellitus	2.10	0.99-4.46	0.054
Systolic blood pressure	0.99	0.89-1.10	0.81
Antihypertensive therapy	1.37	1.03-1.81	0.029
LDL cholesterol	0.97	0.87-1.07	0.52
HDL cholesterol	0.81	0.73-0.91	< 0.001
High CHD polygenic risk score	1.62	1.27-2.05	< 0.001

Continuous variables are standardized to mean = 0 and standard deviation = 1.
CHD = coronary heart disease; CI = confidence interval; HDL = high-density lipoprotein; HR = hazard ratio; LDL = low-density lipoprotein.

Supplementary Table 5. Association of high genetic risk with atherosclerosis traits stratified by self-reported family history of CHD

Self-reported family history				***P* for interaction**
WOSCOPS*: Incident CHD events				
	N	HR (95% CI)	*P*	
Yes	270	1.99 (1.01-3.92)	0.047	
No	4,622	1.43 (1.18-1.73)	< 0.001	
CARDIA: CAC > 0 (Age 18-30 y)				
	N	OR (95% CI)	*P*	
Yes	177	1.44 (0.84-2.44)	0.18	
No	977	1.30 (0.99-1.72)	0.061	
BioImage: Relative Mean carotid artery plaque (Age 55-80 y)				
	N	Estimate (95% CI)	*P*	
Yes	2,531	1.27 (1.01-1.61)	0.04	
No	1,732	1.14 (0.86-1.51)	0.36	

High genetic risk (top quintile of polygenic risk score) was associated with the specified outcome variables for each study stratified by a self-reported family history of CHD. Adjusted for age, sex, diabetes mellitus status, smoking status, LDL cholesterol, HDL cholesterol, systolic blood pressure, antihypertensive medication status, and family history of CHD.

* Placebo-treated participants

CAC = coronary arterial calcification; CHD = coronary heart disease; CI = confidence interval; HR = hazard ratio

Supplementary Table 6. Baseline characteristics for BioImage and CARDIA participants.

	BioImage (n = 4,329)			CARDIA (n = 1,154)		
	High Genetic Risk (n = 866)	**All Others (n = 3,463)**	***P***	**High Genetic Risk (n = 231)**	**All Others (n = 923)**	***P***
Age, years*	69.1 (5.9)	69.1 (6.1)	0.90	40.7 (3.3)	40.8 (3.3)	0.82
Male, %	39.1	45.2	0.002	48.9	48.3	0.93
Family history of CHD, %	60.3	59.1	0.53	16.9	15.0	0.53
Smoking, %	8.0	9.0	0.37	26.7	28.9	0.70
Diabetes mellitus, %	15.7	16.9	0.42	6.1	4.8	0.53
Systolic blood pressure, mmHg	139.1 (19.1)	138.8 (18.4)	0.70	110.4 (13.5)	110.2 (15.5)	0.85
Antihypertensive therapy, %	28.8	27.8	0.61	4.8	4.0	0.74
Total cholesterol, mg/dl	202.4 (37.9)	202.8 (38.0)	0.74	186.3 (32.2)	186.8 (34.5)	0.85
LDL cholesterol, mg/dl	114.0 (33.3)	113.2 (33.4)	0.52	115.1 (29.5)	114.4 (31.6)	0.76
HDL cholesterol, mg/dl	55.4 (15.0)	56.1 (15.7)	0.25	49.0 (15.3)	49.8 (14.4)	0.46
Triglycerides, mg/dl	166.5 (85.7)	171.6 (101.5)	0.13	114.2 (83.3)	114.3 (105.0)	0.99
Statin therapy, %	37.3	33.7	0.06	2.6	2.9	0.96

Values are presented as mean (standard deviation) or %. High genetic risk is defined as the highest quintile of CHD PRS. Differences between continuous variables were tested with Student t-tests and categorical variables with chi-square tests.

* Age for CARDIA is presented at the time of coronary CT scan for CAC.

ASCVD = atherosclerotic cardiovascular disease, CAC = coronary artery calcification, HDL = high-density lipoprotein, LDL = low-density lipoprotein

Supplementary Table 7. Carotid artery plaque burden by polygenic risk score group in BioImage.

Carotid artery plaque burden (mm^2)	High Genetic Risk N = 866		All Others N = 3,463		Relative %
	N	%	N	%	
= 0	153	17.9	689	19.8	-9.8
> 0	710	82.1	2,777	80.2	2.4
> 150	510	59.0	1,973	56.9	3.6
> 300	380	44.0	1,440	41.6	5.9
> 450	293	33.9	1,108	32.0	6.2
> 600	222	25.8	837	24.1	6.7

43 **Supplementary Table 8. Carotid artery plaque burden by polygenic risk score quintile in**
44 **BioImage**
45

Polygenic risk score quintile	Carotid artery plaque Median mm^2 [IQR]	Carotid artery plaque burden Estimate (95% CI, *P*) *
Q1	184 [24, 509]	1
Q2	216 [48, 649]	1.34 (1.07-1.67, *P* =0.01)
Q3	210 [43, 568]	1.32 (1.06-1.66, *P* = 0.01)
Q4	221 [42, 595]	1.29 (1.03-1.62, *P* = 0.02)
Q5 (High)	215 [52, 618]	1.52 (1.22-1.91, *P* <0.001)

46 * Relative to Q1. Adjusted for age, sex, diabetes mellitus status, smoking status, LDL cholesterol, HDL cholesterol,
47 systolic blood pressure, antihypertensive medication status, and family history of CHD
48 CHD = coronary heart disease; CI = confidence interval; HR = hazard ratio; IQR = interquartile range; Q = quintile

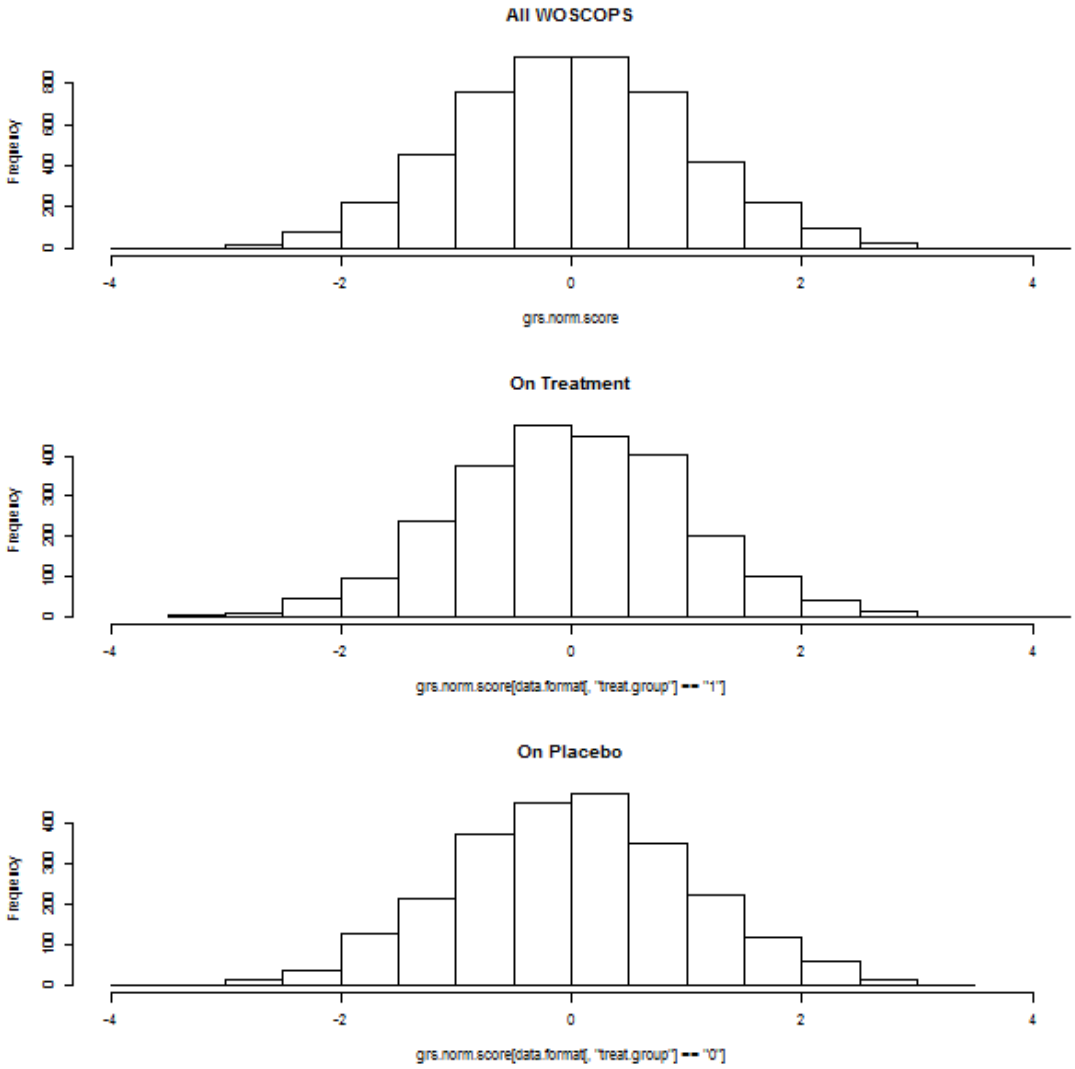
Supplementary Table 9. Comparison of 27-SNP and 57-SNP score association with carotid artery plaque burden in BioImage

Polygenic Risk Score	Relative Effect per SD	95% CI	P
27-SNP score	1.019	0.949-1.093	0.61
57-SNP score	1.097	1.022-1.178	0.01

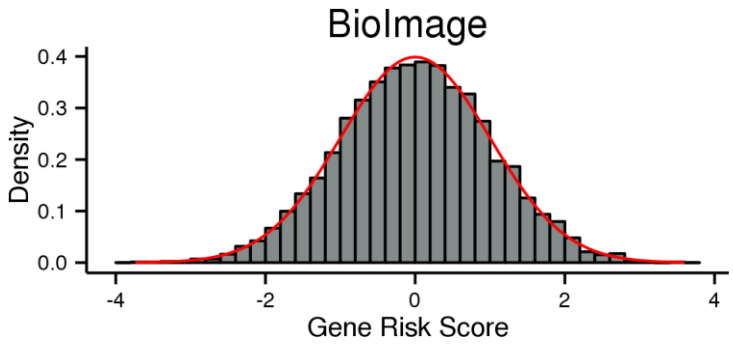
SD = standard deviation; CI = confidence interval

Supplementary Figure 1. Distributions of normalized polygenic risk scores.

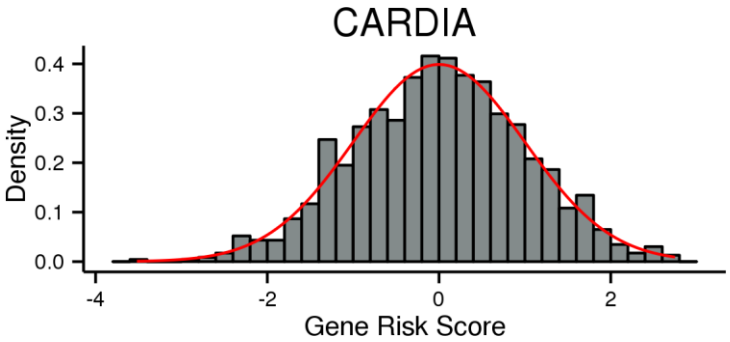
WOSCOPS



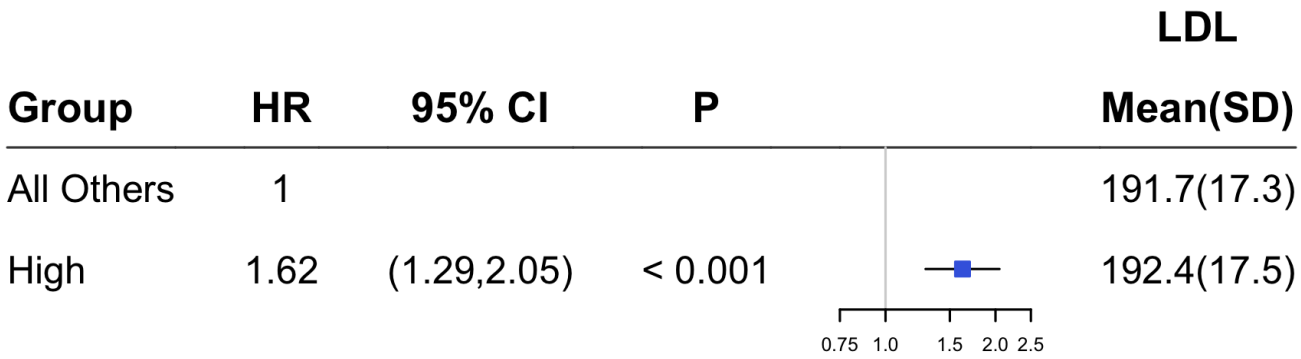
BioImage



CARDIA



Supplementary Figure 2. Risk of incident coronary events in WOSCOPS by polygenic risk score group.



The increased relative risk from high PRS of a first coronary heart disease event in placebo-treated participants of the WOSCOPS is expressed with mean LDL cholesterol values presented. LDL cholesterol is presented as mean (standard deviation) in mg/dl.
CI = confidence interval; HR = hazard ratio, PRS = polygenic risk score; LDL = low-density lipoprotein; SD = standard deviation

Supplementary References

1. CARDIoGRAMplusC4D. A comprehensive 1000 Genomes-based genome-wide association meta-analysis of coronary artery disease. *Nat Genet*. 2015;47:1121-30.

2. CARDIoGRAMplusC4D, Deloukas P, Kanoni S, Willenborg C, Farrall M, Assimes TL, Thompson JR, Ingelsson E, Saleheen D, Erdmann J, Goldstein BA, Stirrups K, Konig IR, Cazier JB, Johansson A, Hall AS, Lee JY, Willer CJ, Chambers JC, Esko T, Folkersen L, Goel A, Grundberg E, Havulinna AS, Ho WK, Hopewell JC, Eriksson N, Kleber ME, Kristiansson K, Lundmark P, Lyytikainen LP, Rafelt S, Shungin D, Strawbridge RJ, Thorleifsson G, Tikkanen E, Van Zuydam N, Voight BF, Waite LL, Zhang W, Ziegler A, Absher D, Altshuler D, Balmforth AJ, Barroso I, Braund PS, Burgdorf C, Claudi-Boehm S, Cox D, Dimitriou M, Do R, Consortium D, Consortium C, Doney AS, El Mokhtari N, Eriksson P, Fischer K, Fontanillas P, Franco-Cereceda A, Gigante B, Groop L, Gustafsson S, Hager J, Hallmans G, Han BG, Hunt SE, Kang HM, Illig T, Kessler T, Knowles JW, Kolovou G, Kuusisto J, Langenberg C, Langford C, Leander K, Lokki ML, Lundmark A, McCarthy MI, Meisinger C, Melander O, Mihailov E, Maouche S, Morris AD, Muller-Nurasyid M, Mu TC, Nikus K, Peden JF, Rayner NW, Rasheed A, Rosinger S, Rubin D, Rumpf MP, Schafer A, Sivananthan M, Song C, Stewart AF, Tan ST, Thorgeirsson G, van der Schoot CE, Wagner PJ, Wellcome Trust Case Control C, Wells GA, Wild PS, Yang TP, Amouyel P, Arveiler D, Basart H, Boehnke M, Boerwinkle E, Brambilla P, Cambien F, Cupples AL, de Faire U, Dehghan A, Diemert P, Epstein SE, Evans A, Ferrario MM, Ferrieres J, Gauguier D, Go AS, Goodall AH, Gudnason V, Hazen SL, Holm H, Iribarren C, Jang Y, Kahonen M, Kee F, Kim HS, Klopp N, Koenig W, Kratzer W, Kuulasmaa K, Laakso M, Laaksonen R, Lee JY, Lind L, Ouwehand WH, Parish S, Park JE, Pedersen NL, Peters A, Quertermous T, Rader DJ, Salomaa V, Schadt E, Shah SH, Sinisalo J, Stark K, Stefansson K, Tregouet DA, Virtamo J, Wallentin L, Wareham N, Zimmermann ME, Nieminen MS, Hengstenberg C, Sandhu MS, Pastinen T, Syvanen AC, Hovingh GK, Dedoussis G, Franks PW, Lehtimaki T, Metspalu A, Zalloua PA, Siegbahn A, Schreiber S, Ripatti S, Blankenberg SS, Perola M, Clarke R, Boehm BO, O'Donnell C, Reilly MP, Marz W, Collins R, Kathiresan S, Hamsten A, Kooner JS, Thorsteinsdottir U, Danesh J, Palmer CN, Roberts R, Watkins H, Schunkert H and Samani NJ. Large-scale association analysis identifies new risk loci for coronary artery disease. *Nat Genet*. 2013;45:25-33.

3. Stitziel NO, Stirrups K, Masca NGD, Erdmann J, Ferrario PG, Konig IR, Weeke PE, Webb TR, Auer PL, Schick UM, Lu Y, Zhang H, Dube MP, Goel A, Farrall M, Peloso GM, Won HH, Do R, Van Iperen E, Kanoni S, Kruppa J, Mahajan A, Scott RA, Willenborg C, Braund PS, J.C. VC, Doney AS, Donnelly LA, Asselta R, Merlini PA, Duga S, Marziliano N, Denny JC, Shaffer CM, El Mokhtari NE, Franke A, Gottesman O, Heilmann S, Hengstenberg C, Hoffmann P, Holmen OL, Hveem K, Jansson JH, Jockel KH, Kessler T, Kriebel J, Laugwitz KL, Marouli E, Martinelli N, McCarthy MI, Van Zuydam NR, Meisinger C, Esko T, Mihailov E, Escher SA, Alver M, Moebus S, Morris AD, Muller-Nurasyid M, Nikpay M, Olivieri O, Perreault LPL, AlQarawi A, Robertson NR, Akinsaya KO, Reilly DF, Vogt TF, Yin W, Asselbergs FW, Kooperberg C, Jackson RD, Stahl E, Strauch K, Varga TV, Waldenberger M, Zeng L, Kraja AT, Liu C, Ehret GB, Newton-Cheh C, Chasman DI, Chowdhury R, Ferrario M, Ford I, Jukema JW, Kee F, Kuulasmaa K, Nordestgaard BG, Perola M, Saleheen D, Sattar N, Surendran P, Tregouet DA, Young R, Howson JMM, Butterworth AS, Danesh J, Ardissino D, Bottinger EP, Erbel R, Franks PW, Girelli D, Hall AS, Hovingh GK, Kastrati A, Lieb W, Meitinger T, Kraus WE, Shah SH, McPherson R, Orho-Melander M, Melander O, Metspalu A, Palmer CNA, Peters

118 A, Rader DJ, Reilly MP, Loos RJ, Reiner AP, Roden DM, Tardif JC, Thompson JR, Wareham NJ,
119 Watkins H, Willer CJ, Kathiresan S, Deloukas P, Samani NJ and Schunkert H. Coding
120 Variation in ANGPTL4, LPL, and SVEP1 and the Risk of Coronary Disease. *N Engl J Med*.
121 2016;374:1134-44.
122 4. Genomes Project C, Auton A, Brooks LD, Durbin RM, Garrison EP, Kang HM, Korbel
123 JO, Marchini JL, McCarthy S, McVean GA and Abecasis GR. A global reference for human
124 genetic variation. *Nature*. 2015;526:68-74.
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