

Online Appendix

Appendix 1

CARDIA genotype filtering and imputation

For the CARDIA GENEVA sub-study, the Beaglecall dataset on dbGaP was used, and samples with a call rate <95% and variants with minor allele frequency <1% were removed. Genotype information for the CARDIA CARE sub-study was filtered to remove samples with a call rate <95% and observed heterozygosity >3 standard deviations from the mean. Variants with minor allele frequency <1% or call rate <95% were removed. Filtered data from both sub-studies was further imputed with the Michigan Imputation Server v1.2.1, using the 1000 Genomes phase 3 v5 reference panel and phased with Eagle v2.4 (36). Self-identified related individuals were removed.

Online Table 1. 142 SNPs included in GRS. Imp Rsq of ‘---’ indicates SNP was genotyped directly and not imputed for analysis.

	rsID	Chr	Position	Effect	Non-Effect	OR	CARDIA GENEVA Effect Allele Freq	CARDIA CARE Effect Allele Freq	MESA Effect Allele Freq	CARDIA GENEVA Imp Rsq	CARDIA CARE Imp Rsq	MESA Imp Rsq
1	rs61776719	1	38461319	A	C	1.04	0.516	0.321	0.411	0.747	0.744	0.766
2	rs56170783	1	57016131	A	C	1.11	0.913	0.953	0.941	0.953	0.789	0.933
3	rs7528419	1	109817192	A	G	1.11	0.777	0.736	0.784	0.959	0.93	0.967
4	rs11806316	1	115753482	G	A	1.04	0.613	0.865	0.795	0.995	0.992	0.996
5	rs11810571	1	151762308	G	C	1.07	0.836	0.587	0.676	0.885	0.971	0.998
6	rs6689306	1	154395946	A	G	1.05	0.432	0.332	0.370	0.959	0.877	0.948
7	rs1892094	1	169094459	C	T	1.04	0.484	0.753	0.645	---	---	---
8	rs6700559	1	200646073	C	T	1.04	0.530	0.689	0.564	---	---	---
9	rs2820315	1	201872264	T	C	1.05	0.304	0.125	0.184	---	---	---
10	rs60154123	1	210468999	T	C	1.04	0.152	0.051	0.157	0.972	0.97	0.977
11	rs67180937	1	222823743	G	T	1.07	0.708	0.317	0.500	0.931	0.976	1.000
12	rs699	1	230845794	G	A	1.04	0.418	0.74	0.648	0.984	0.956	0.983
13	rs16986953	2	19942473	A	G	1.11	0.072	0.13	0.143	0.969	0.943	0.943
14	rs585967	2	21270554	C	A	1.07	0.833	0.717	0.816	0.908	0.952	0.982
15	rs4299376	2	44072576	G	T	1.06	0.306	0.191	0.211	0.625	0.926	0.975
16	rs582384	2	45896437	A	C	1.03	0.558	0.211	0.387	0.87	0.86	0.888
17	rs7568458	2	85788175	A	T	1.06	0.451	0.642	0.499	0.969	0.973	0.989
18	rs17678683	2	145286559	G	T	1.08	0.085	0.031	0.062	---	---	---
19	rs12999907	2	164957251	A	G	1.06	0.810	0.844	0.818	0.975	0.933	0.952
20	rs840616	2	188196469	C	T	1.04	0.638	0.373	0.561	---	---	---
21	rs114123510	2	203831212	A	T	1.13	0.127	0.051	0.075	0.992	0.973	0.981

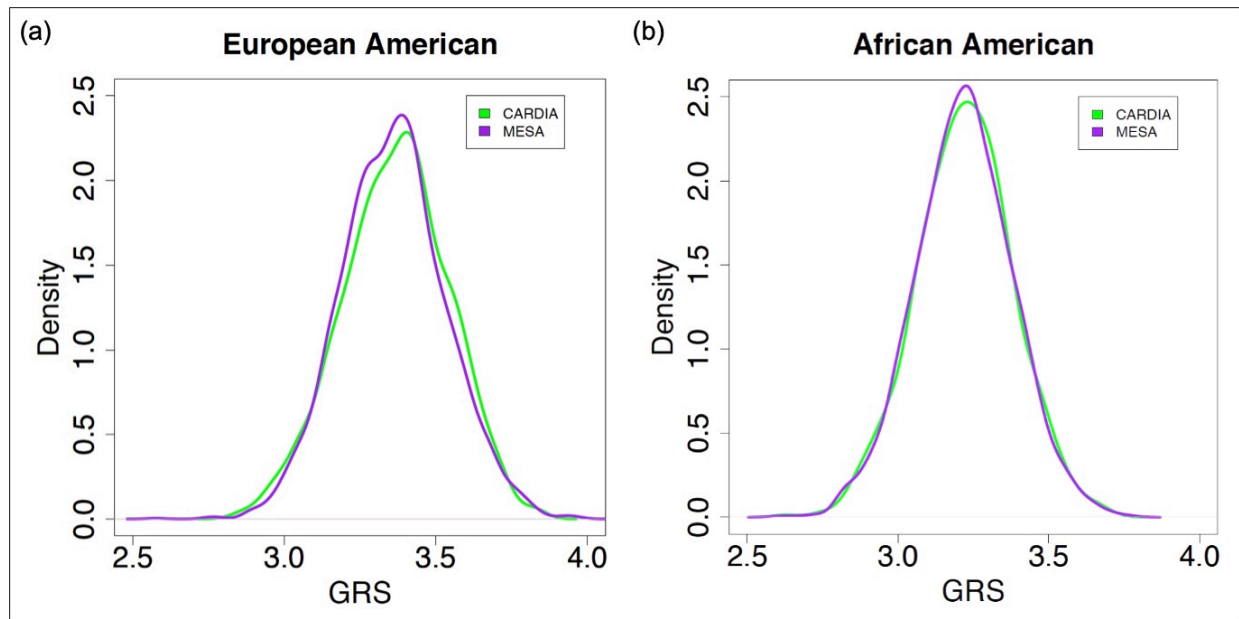
22	rs17517928	2	216291359	C	T	1.06	0.756	0.783	0.796	0.976	0.958	0.961
23	rs2571445	2	218683154	A	G	1.05	0.382	0.275	0.315	0.940	0.882	0.948
24	rs2972146	2	227100698	T	G	1.06	0.635	0.798	0.773	0.961	0.926	0.997
25	rs13003675	2	233584109	T	C	1.04	0.327	0.26	0.293	0.979	0.974	0.997
26	rs11677932	2	238223955	G	A	1.03	0.694	0.789	0.736	0.915	0.931	0.937
27	rs748431	3	14928077	G	T	1.05	0.406	0.333	0.409	0.974	0.964	0.983
28	rs7633770	3	46688562	A	G	1.03	0.414	0.217	0.283	0.968	0.941	0.971
29	rs7617773	3	48193515	T	C	1.04	0.612	0.758	0.694	0.842	0.887	0.968
30	rs7623687	3	49448566	A	C	1.08	0.860	0.857	0.883	0.892	0.945	0.952
31	rs17843797	3	124453022	G	T	1.07	0.115	0.062	0.091	0.994	0.981	0.996
32	rs10512861	3	132257961	G	T	1.04	0.848	0.718	0.787	0.998	0.984	0.994
33	rs667920	3	136069472	T	G	1.05	0.770	0.757	0.775	0.973	0.975	0.994
34	rs139016349	3	138099161	TTTC	T	1.08	0.164	0.325	0.215	0.993	0.979	0.992
35	rs12493885	3	153839866	C	G	1.08	0.864	0.942	0.939	0.886	0.835	0.996
36	rs4266144	3	156852592	G	C	1.03	0.324	0.301	0.388	0.894	0.966	0.991
37	rs12897	3	172115902	G	A	1.04	0.393	0.739	0.582	0.81	0.84	0.864
38	rs72627509	4	57839051	G	C	1.06	0.189	0.127	0.194	0.981	0.969	0.985
39	rs12500824	4	77416627	A	G	1.04	0.362	0.552	0.431	0.982	0.985	0.996
40	rs11099493	4	82587050	A	G	1.04	0.681	0.830	0.757	0.770	0.744	0.800
41	rs3775058	4	96117371	A	T	1.04	0.213	0.301	0.255	---	---	---
42	rs11723436	4	120901336	G	A	1.05	0.316	0.165	0.225	0.922	0.904	0.968
43	rs35879803	4	146782837	C	A	1.05	0.651	0.668	0.729	0.969	0.92	0.964
44	rs6841581	4	148401190	A	G	1.07	0.157	0.255	0.201	---	---	---
45	rs2306556	4	156638573	A	G	1.07	0.814	0.915	0.848	---	---	---
46	rs7696431	4	169687725	T	G	1.04	0.530	0.410	0.418	0.909	0.955	0.99
47	rs1508798	5	9556694	T	C	1.05	0.813	0.808	0.815	---	---	---
48	rs3936511	5	55860781	G	A	1.04	0.169	0.128	0.155	0.824	0.908	0.96
49	rs1800449	5	121413208	T	C	1.07	0.176	0.167	0.174	0.915	0.878	0.934
50	rs77335401	5	131759825	C	T	1.05	0.111	0.040	0.074	0.968	0.949	0.959
51	rs246600	5	142516897	T	C	1.04	0.466	0.347	0.359	---	---	---
52	rs742115	6	11327021	C	T	1.04	0.489	0.334	0.381	0.894	0.838	0.88
53	rs9349379	6	12903957	G	A	1.11	0.420	0.136	0.324	0.883	0.865	0.855
54	rs35541991	6	22583856	C	CA	1.05	0.343	0.201	0.279	0.997	0.995	0.998
55	rs3130683	6	31888367	T	C	1.08	0.859	0.944	0.936	0.924	0.807	0.964
56	rs4472337	6	34769765	T	C	1.06	0.173	0.33	0.207	0.988	0.985	0.995
57	rs1321309	6	36638636	A	G	1.03	0.475	0.223	0.330	0.989	0.994	1.000
58	rs56015508	6	39152041	C	A	1.06	0.781	0.895	0.840	0.868	0.941	0.985
59	rs6905288	6	43758873	A	G	1.05	0.567	0.499	0.570	---	---	---
60	rs9367716	6	57160572	G	T	1.04	0.692	0.667	0.619	0.966	0.935	0.963

61	rs4613862	6	82612271	A	C	1.03	0.534	0.795	0.678	0.983	0.990	0.999
62	rs1591805	6	126717064	A	G	1.04	0.507	0.660	0.463	0.928	0.942	0.968
63	rs12202017	6	134173151	A	G	1.07	0.723	0.688	0.661	0.982	0.973	0.995
64	rs17080091	6	150997401	C	T	1.05	0.934	0.825	0.877	0.996	0.993	0.996
65	rs10455872	6	161010118	G	A	1.31	0.065	0.023	0.030	0.772	0.684	0.717
66	rs10267593	7	1937261	G	A	1.04	0.804	0.647	0.750	0.966	0.96	0.98
67	rs11509880	7	12261911	A	G	1.04	0.321	0.634	0.517	0.993	0.983	0.997
68	rs2107595	7	19049388	A	G	1.08	0.167	0.205	0.216	0.949	0.955	0.957
69	rs112370447	7	107176780	T	C	1.05	0.29	0.222	0.271	0.993	0.994	0.997
70	rs975722	7	117332914	G	A	1.03	0.394	0.761	0.540	---	---	---
71	rs10237377	7	139757136	G	T	1.05	0.647	0.353	0.459	0.838	0.907	0.986
72	rs6997340	8	18286997	T	C	1.04	0.303	0.448	0.393	0.742	---	---
73	rs2083636	8	19865263	T	G	1.05	0.725	0.811	0.783	0.993	0.996	0.999
74	rs10093110	8	106565414	G	A	1.03	0.579	0.424	0.527	---	---	---
75	rs2954029	8	126490972	A	T	1.06	0.549	0.643	0.591	0.978	0.971	0.990
76	rs2891168	9	22098619	G	A	1.19	0.479	0.246	0.386	---	---	---
77	rs944172	9	110517794	C	T	1.04	0.291	0.264	0.236	0.900	0.923	0.974
78	rs111245230	9	113169775	C	T	1.12	0.030	0.012	0.022	0.978	0.828	0.94
79	rs885150	9	124420173	C	T	1.04	0.245	0.089	0.18	0.961	0.966	0.992
80	rs507666	9	136149399	A	G	1.08	0.181	0.110	0.157	0.826	0.978	0.991
81	rs61848342	10	12303813	C	T	1.04	0.36	0.326	0.375	0.935	0.864	0.907
82	rs1887318	10	30321598	T	C	1.06	0.436	0.156	0.304	0.970	0.983	0.992
83	rs1870634	10	44480811	G	T	1.06	0.659	0.440	0.561	0.929	0.957	0.964
84	rs17680741	10	82251514	T	C	1.05	0.719	0.819	0.781	0.985	0.971	0.989
85	rs2246942	10	91004886	G	A	1.08	0.348	0.388	0.391	0.686	0.949	0.993
86	rs11191416	10	104604916	T	G	1.08	0.900	0.921	0.866	---	---	---
87	rs4918072	10	105693644	A	G	1.04	0.277	0.29	0.259	0.968	0.931	0.962
88	rs4752700	10	124237612	G	A	1.03	0.449	0.681	0.528	0.928	0.893	0.943
89	rs10840293	11	9751196	A	G	1.05	0.566	0.492	0.522	0.882	0.931	0.953
90	rs1351525	11	13301548	T	A	1.05	0.704	0.488	0.584	0.991	0.993	1.00
91	rs7116641	11	43696917	G	T	1.03	0.298	0.328	0.298	---	---	---
92	rs12801636	11	65391317	G	A	1.05	0.782	0.755	0.707	---	---	---
93	rs590121	11	75274150	T	G	1.04	0.309	0.437	0.347	0.918	0.931	0.953
94	rs7947761	11	100624599	G	A	1.04	0.277	0.241	0.227	---	---	---
95	rs2839812	11	103673294	T	A	1.06	0.301	0.374	0.345	---	---	---
96	rs964184	11	116648917	G	C	1.05	0.135	0.205	0.212	0.966	---	---
97	rs11838267	12	7175872	T	C	1.05	0.87	0.86	0.879	0.976	0.935	0.982
98	rs10841443	12	20220033	G	C	1.05	0.662	0.332	0.515	0.877	0.866	0.902
99	rs2229357	12	57843711	G	A	1.05	0.776	0.881	0.804	0.954	0.939	0.933

100	rs2681472	12	90008959	G	A	1.07	0.169	0.116	0.158	0.975	0.943	0.961
101	rs7306455	12	95355541	G	A	1.05	0.900	0.884	0.869	---	---	---
102	rs10774625	12	111910219	A	G	1.07	0.489	0.133	0.268	0.633	0.846	0.906
103	rs11830157	12	118265441	G	T	1.03	0.386	0.204	0.316	0.914	0.841	---
104	rs2244608	12	121416988	G	A	1.05	0.330	0.164	0.281	0.964	0.946	0.952
105	rs11057401	12	124427306	T	A	1.05	0.668	0.663	0.704	---	---	---
106	rs1924981	13	29022645	T	C	1.05	0.337	0.287	0.288	0.897	0.876	0.906
107	rs9591012	13	33058333	G	A	1.04	0.642	0.861	0.764	0.983	0.988	1
108	rs11617955	13	110818102	T	A	1.09	0.879	0.945	0.905	---	---	---
109	rs1317507	13	113631780	A	C	1.04	0.249	0.228	0.257	---	---	---
110	rs2145598	14	58794001	G	A	1.03	0.442	0.594	0.476	0.897	0.909	0.947
111	rs3832966	14	75614504	ACCCG	A	1.05	0.478	0.263	0.457	0.974	0.974	0.991
112	rs112635299	14	94838142	G	T	1.15	0.984	0.996	0.991	0.976	0.946	0.968
113	rs6494488	15	65024204	A	G	1.05	0.817	0.389	0.68	0.793	0.935	0.967
114	rs72743461	15	67441750	C	A	1.07	0.783	0.889	0.852	0.926	0.924	0.949
115	rs7164479	15	79123054	T	C	1.07	0.539	0.58	0.568	0.904	0.952	0.997
116	rs2083460	15	89574484	T	C	1.07	0.917	0.417	0.61	0.944	0.94	0.988
117	rs2071382	15	91428197	T	C	1.06	0.494	0.456	0.389	0.937	0.903	0.968
118	rs17581137	15	96146414	A	C	1.04	0.762	0.789	0.769	0.734	---	---
119	rs1050362	16	72130815	A	C	1.04	0.368	0.655	0.464	0.986	0.964	0.997
120	rs33928862	16	75308440	T	TCAGCCTCCTGAG	1.05	0.535	0.291	0.465	0.838	0.887	0.894
121	rs7199941	16	81906423	A	G	1.04	0.399	0.579	0.475	0.983	0.982	0.998
122	rs7500448	16	83045790	A	G	1.06	0.757	0.881	0.813	0.947	0.898	0.93
123	rs113348108	17	2088848	C	CCAGA	1.05	0.301	0.463	0.374	0.985	0.963	0.997
124	rs9897596	17	17593453	T	C	1.04	0.485	0.382	0.507	0.972	0.945	0.977
125	rs13723	17	27941886	G	A	1.04	0.461	0.801	0.595	0.864	0.870	0.913
126	rs76954792	17	30033514	T	C	1.04	0.212	0.087	0.156	0.687	0.920	0.943
127	rs2074158	17	40257163	C	T	1.05	0.169	0.644	0.352	0.828	---	---
128	rs17608766	17	45013271	C	T	1.06	0.137	0.040	0.067	0.822	0.851	0.841
129	rs4643373	17	47123423	T	C	1.05	0.699	0.734	0.732	0.87	0.887	0.935
130	rs8068952	17	59286644	G	C	1.07	0.249	0.745	0.416	0.851	0.927	0.91
131	rs1867624	17	62387091	T	C	1.04	0.617	0.685	0.677	---	---	---
132	rs9964304	18	47229717	C	A	1.04	0.28	0.389	0.326	0.98	0.96	0.976
133	rs35614134	18	57832856	AC	A	1.04	0.224	0.296	0.23	0.978	0.954	0.989
134	rs10417115	19	33386556	C	T	1.07	0.059	0.080	0.068	0.992	0.996	0.990
135	rs138120077	19	41790086	G	GTTATGGTA	1.07	0.135	0.059	0.089	0.67	0.694	0.680
136	rs867186	20	33764554	A	G	1.08	0.910	0.897	0.924	---	---	---
137	rs6102343	20	39924279	A	G	1.04	0.243	0.416	0.301	0.978	0.953	0.977
138	rs3827066	20	44586023	T	C	1.04	0.152	0.064	0.107	0.956	0.931	0.964

139	rs260020	20	57714025	T	C	1.05	0.132	0.32	0.199	0.992	0.985	0.99
140	rs2832227	21	30533076	G	A	1.04	0.139	0.361	0.244	0.991	0.975	0.992
141	rs28451064	21	35593827	A	G	1.14	0.124	0.045	0.064	0.877	0.842	0.915
142	rs180803	22	24658858	G	T	1.18	0.991	0.898	0.951	0.878	0.963	0.944

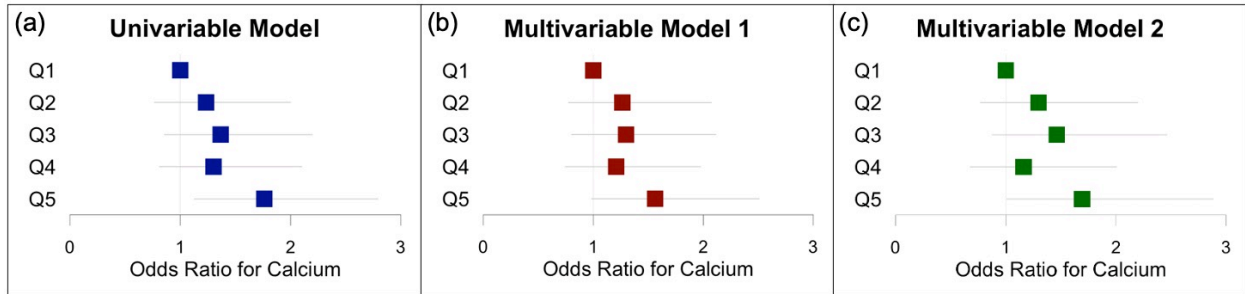
Appendix 2



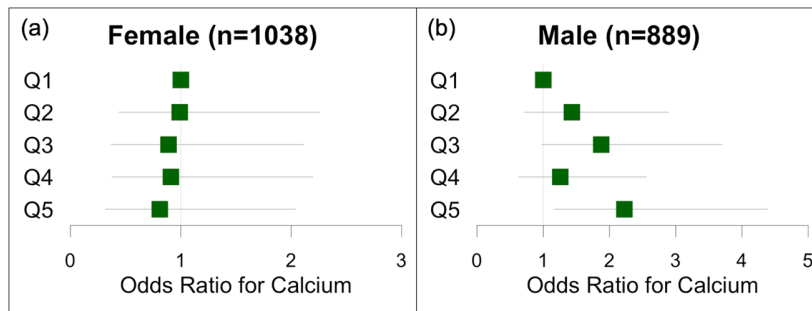
Online Figure 1. Distribution of raw GRS in CARDIA and MESA for self-identified (a) European Americans (CARDIA $n=1251$, MESA $n=2647$) and (b) African Americans (CARDIA $n=676$, MESA $n=1834$).

	Ages 44-54			Ages 55-64			Ages 65-74			Ages 75-84		
	Total	Female	Male	Total	Female	Male	Total	Female	Male	Total	Female	Male
Population	1827	967	860	1908	1008	900	1975	1035	940	935	486	449
Total people	446	149	297	867	340	527	1284	569	715	762	371	391
Low GRS: CAC>0/# People (%)	64/385 (16.6%)	23/208 (11.1%)	41/177 (23.2%)	143/383 (37.3%)	56/200 (28.0%)	87/183 (47.5%)	215/384 (56.0%)	79/182 (43.4%)	136/202 (67.3%)	131/178 (73.6%)	56/88 (63.6%)	75/90 (83.3%)
Int GRS: CAC>0/# People (%)	251/1061 (23.7%)	85/560 (15.2%)	166/501 (33.1%)	508/1138 (44.6%)	193/612 (31.5%)	315/526 (59.9%)	802/1220 (65.7%)	362/652 (55.5%)	440/568 (77.5%)	464/566 (82.0%)	224/290 (77.2%)	240/276 (87.0%)
High GRS: CAC>0/# People (%)	131/381 (34.4%)	41/199 (20.6%)	90/182 (49.5%)	216/387 (55.8%)	91/196 (46.4%)	125/191 (65.4%)	267/371 (72.0%)	128/201 (63.7%)	139/170 (81.8%)	167/191 (87.4%)	91/108 (84.3%)	76/83 (91.6%)
Total CAC>0 rate	24.4%	15.4%	34.5%	45.4%	33.7%	58.6%	65.0%	55.0%	76.1%	81.5%	76.3%	87.1%
High/Low	2.07	1.86	2.13	1.49	1.67	1.38	1.29	1.47	1.21	1.19	1.32	1.1

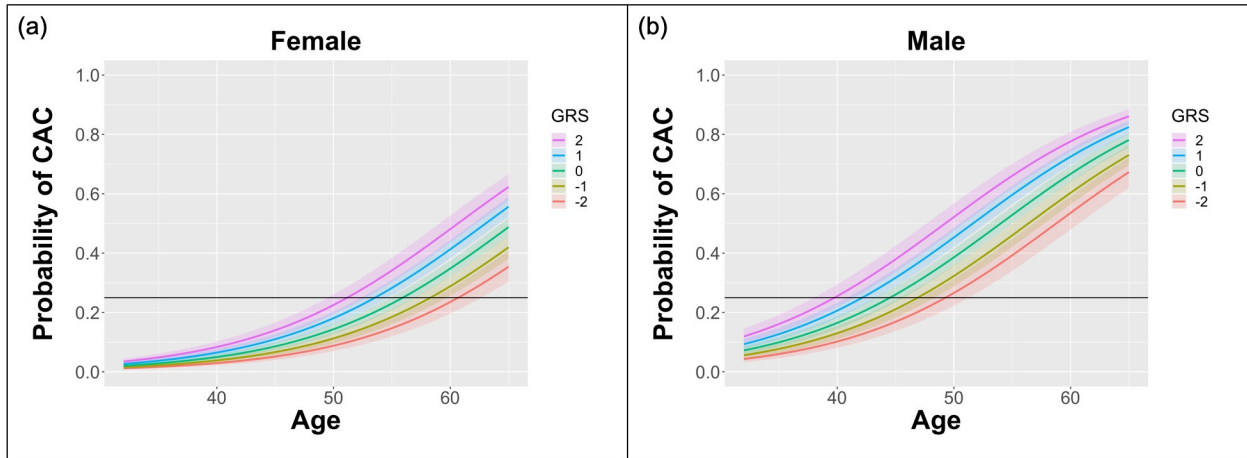
Online Table 2. CAC prevalence in 10-year age categories of the MESA cohort stratified into low (GRS quintile 1), intermediate (GRS quintiles 2-4) and high (GRS quintile 5) genetic risk categories. CAC = coronary artery calcium, GRS = genetic risk score



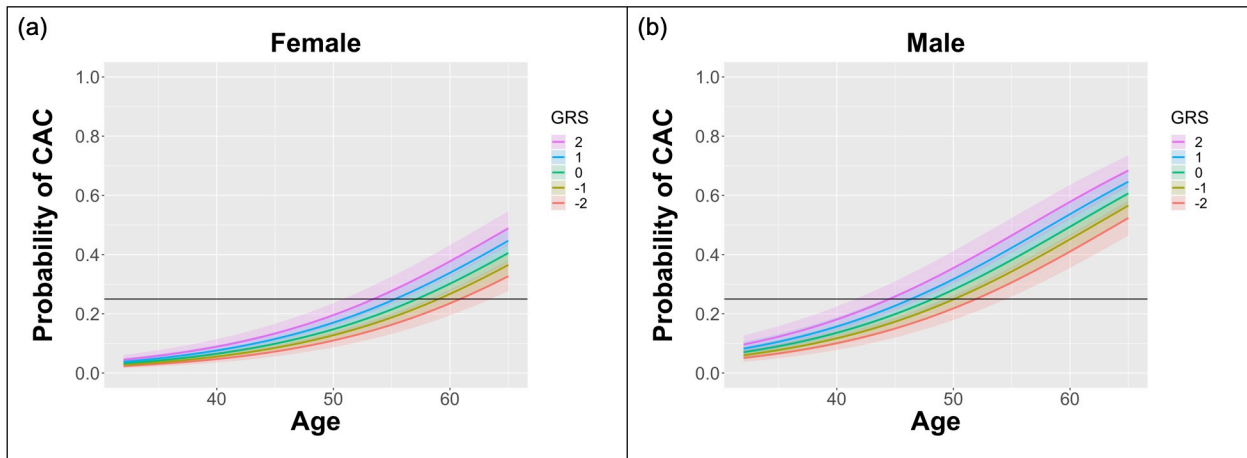
Online Figure 2. CAC risk by GRS quintile in CARDIA (aged 32-47, n=1927). Odds ratio for CAC presence by GRS quintile in the CARDIA cohort under an (a) univariable model, (b) multivariable model including age and sex, and (c) multivariable model including age, sex and other traditional clinical variables (diabetes status, smoking status, LDL-c, HDL-c, systolic blood pressure, antihypertensive therapy status, cholesterol medication status, self-identified race) as covariates. The odds ratio for calcium in GRS quintile 5 compared to GRS quintile 1 was 1.76 (1.13-2.79, $p=0.014$), 1.56 (0.98-2.51, $p=0.061$), and 1.69 (1.01-2.88, $p=0.049$) in the univariable model, the multivariable model including age and sex, and the multivariable model including age, sex, and other traditional clinical variables, respectively.



Online Figure 3. CAC risk by GRS quintile in CARDIA, stratified by sex. Odds ratio for CAC presence by GRS quintile in the (a) female subpopulation and (b) male subpopulation of the CARDIA cohort under a multivariable model including age and other traditional clinical variables (diabetes status, smoking status, LDL-c, HDL-c, systolic blood pressure, antihypertensive therapy status, cholesterol medication status, self-identified race) as covariates. The odds ratio for calcium was significantly larger in GRS quintile 5 compared to quintile 1 in the male subpopulation but not in the female subpopulation.



Online Figure 4. Probability of CAC as a function of age in analysis of European American participants in the CARDIA and MESA cohorts combined (n=3898). The odds ratio for calcium was 1.30 (1.20-1.41, $p=2.71E-10$) per standard deviation from the European American population mean.



Online Figure 5. Probability of CAC as a function of age in analysis of African American participants in the CARDIA and MESA cohorts combined (n=2510). The odds ratio was 1.18 (1.08-1.30, $p=5.32E-4$) per standard deviation from the African American population mean.

Cohort	GRS population mean±SD	Sex	N	Scanning Equation	Scan Age High GRS (+2σ)	Scan Age Low GRS (-2σ)
All	3.31±0.18	Female	4536	Age[scan] = 56.0 - 2.82*GRSn	50.5 (48.8, 52.2)	61.9 (60.2, 63.5)
		Male	4051	Age[scan] = 45.3 - 2.71*GRSn	40.0 (38.1, 41.8)	51.0 (49.2, 52.6)
European American	3.36±0.17	Female	2029	Age[scan] = 55.3 - 2.38*GRSn	50.4 (48.0, 52.7)	59.8 (57.4, 62.2)
		Male	1869	Age[scan] = 44.3 - 2.18*GRSn	39.8 (37.4, 42.0)	48.5 (46.2, 50.7)
African American	3.22±0.16	Female	1385	Age[scan] = 57.6 - 1.83*GRSn	53.8 (50.5, 56.9)	61.1 (57.8, 64.4)
		Male	1125	Age[scan] = 47.5 - 1.80*GRSn	43.9 (39.9, 47.6)	51.1 (47.2, 54.6)

Online Table 3. Scanning equations and recommendation for individuals 2 standard deviations above the population mean and 2 standard deviations below the population mean at a 25% non-zero CAC discovery rate. Equations and ages derived using models that included sex-stratified data. GRS = genetic risk score, GRSn = genetic risk score normalized to the population mean

Variable	All MESA Participants (n=5775)		FH+ (n=2460)		FH- (n=3315)	
	Odds Ratio	p	Odds Ratio	p	Odds Ratio	p
Age	1.10	<2E-16	1.11	<2E-16	1.10	<2E-16
Sex	3.01	<2E-16	2.98	<2E-16	3.03	<2E-16
GRS Q1	1 (ref)	N/A	1 (ref)	N/A	1 (ref)	N/A
GRS Q2	1.24	0.025	1.21	0.20	1.27	0.062
GRS Q3	1.60	1.42E-06	1.40	2.53E-02	1.76	9.60E-06
GRS Q4	1.87	1.56E-10	1.68	4.71E-04	2.03	5.35E-08
GRS Q5	2.68	<2E-16	2.44	3.57E-09	2.89	1.18E-15
0 Traditional Risk Factors	1 (ref)	N/A	1 (ref)	N/A	1 (ref)	N/A
1 Traditional Risk Factor	1.48	1.76E-05	1.39	0.023	1.54	2.48E-04
2 Traditional Risk Factors	2.09	5.48E-15	2.04	1.50E-06	2.12	9.75E-10
>2 Traditional Risk Factors	3.01	<2E-16	2.77	2.00E-09	3.18	2.00E-15
Family History	1.55	1.73E-12	N/A	N/A	N/A	N/A

Online Table 4. Analysis of the family history in combination with traditional risk factors and the GRS in the MESA cohort only. Family history reporting was not consistent between the CARDIA and MESA cohorts. The GRS was predictive of CAC in analysis of all MESA participants with family history reported (n=5775). The GRS remained predictive of CAC in analysis of the MESA cohort stratified by family history status in both individuals who reported family history of an event (n=2460) and in individuals who reported no family history of an event (n=3315).

a. Females 50-60 years (n=954)					
		Age+sex+traditional RFs+GRS			
CAC>0 (events)	Age+sex+traditional RFs	<15%	15-35%	>35%	total
	<15%	12	9	0	21
	15-35%	11	120	24	155
	>35%	0	11	48	59
	total	23	140	72	235
CAC<0 (nonevents)	Age+sex+traditional RFs	<15%	15-35%	>35%	total
	<15%	101	24	0	125
	15-35%	76	401	38	515
	>35%	0	31	48	79
	total	177	456	86	719

b. Males 40-50 years n=931					
		Age+sex+traditional RFs+GRS			
CAC>0 (events)	Age+sex+traditional RFs	<15%	15-35%	>35%	total
	<15%	8	5	0	13
	15-35%	18	120	38	176
	>35%	0	13	37	50
	total	26	138	75	239
CAC<0 (nonevents)	Age+sex+traditional RFs	<15%	15-35%	>35%	total
	<15%	89	31	0	120
	15-35%	90	382	50	522
	>35%	0	20	30	50
	total	179	433	80	692

c. Females 44-54 years (n=1062)					
		Age+sex+traditional RFs+GRS			
CAC>0 (events)	Age+sex+traditional RFs	<10%	10-25%	>25%	total
	<10%	14	3	0	17
	10-25%	8	85	14	107
	>25%	0	6	16	22
	total	22	94	30	146
CAC<0 (nonevents)	Age+sex+traditional RFs	<10%	10-25%	>25%	total
	<10%	267	53	0	320
	10-25%	105	393	31	529
	>25%	0	25	42	67
	total	372	471	73	916

d. Males 34-44 years (n=699)					
		Age+sex+traditional RFs+GRS			
CAC>0 (events)	Age+sex+traditional RFs	<10%	10-25%	>25%	total
	<10%	3	2	0	5
	10-25%	4	63	15	82
	>25%	1	2	16	19
	total	8	67	31	106
CAC<0 (nonevents)	Age+sex+traditional RFs	<10%	10-25%	>25%	total
	<10%	70	22	0	92
	10-25%	79	356	33	468
	>25%	0	5	28	33
	total	149	383	61	593

Online Tables 5a-5d. Reclassification tables between (1) a model that included age, sex, and number of traditional risk factors and (2) a model that included age, sex, number of traditional risk factors, and continuous GRS to predict CAC presence. For the 10-year age range over which most individuals cross a 25% probability threshold, (a) females 50-60 and (b) males 40-50, risk thresholds were 15% and 35%. For the youngest 10-year age category with CAC incidence >10%, (c) females 44-54 and (d) males 34-44, risk thresholds were 10% and 25%.

Appendix 3

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