

SUPPLEMENTAL MATERIAL

Table S1. Background Characteristics Among Individuals Included and Excluded from Analyses Due to Missing Data, the Scottish Family Health Study, 2006-2011.

Characteristics	Excluded (n= 6,176)		Included (n=7,770)		P-value
	n/mean	%/SD	n/mean	%/SD	
Age at baseline evaluation	52.1	16.1	44.3	13.7	<0.001
Ethnicity					<0.001
White	5,691	95.9	7,614	98.0	
Other	246	4.1	156	2.0	
Missing	239		0		
Qualifications					<0.001
College/University degree	1,594	31.0	2,651	34.1	
Other professional or technical qualification	826	16.1	1,559	20.1	
NVQ/HND/HNC or equivalent	472	9.2	661	8.5	
Higher Grade	465	9.1	961	12.4	
Standard Grade/O Level/GCSE	590	11.5	967	12.5	
CSEs, School leavers certificate, other or no qualifications	1,193	23.2	971	12.5	
Missing	1,036		0		
Annual household income, pounds					<0.001
<10,000	509	10.4	517	7.5	
10,000-30,000	1,591	32.4	2,141	31.0	
30,000-50,000	1,151	23.5	1,940	28.1	
50,000-70,000	627	12.8	1,094	15.9	
70,000+	510	10.4	800	11.6	
Prefer not to answer	516	10.5	408	5.9	
Missing	1,272		870		
Parental history of CVD					<0.001
No	1,260	32.0	2,749	35.4	
Yes	2,673	68.0	5,021	64.6	
Missing	2,243		0		
Parental history of diabetes					0.143
No	3,365	85.6	6,568	84.5	
Yes	568	14.4	1,202	15.5	
Missing	2,243		0		

CVD=cardiovascular disease.

Percentages and test of differences in distributions among those with and without the necessary follow-up information are based on observed values and missing categories are not included.

Table S2. Proportion of the Variation in Traits Explained by Variation Between and Within Sibships/Groups of Sisters, the Scottish Family Health Study, 2006-2011.

Characteristics	Proportion explained by variation between sibships	Proportion explained by variation within sibships
Age (years)		
Age at menarche (years)	0.27	0.73
Qualifications (ordered from CSE/school leavers to college/university degree)	0.40	0.60
Current smoking at recruitment (yes versus no)	0.37	0.63
Hours of moderate/vigorous physical activity in the past week	0.48	0.52
Units of alcohol consumed in the past week	0.07	0.93
Adult BMI	0.31	0.69

BMI=body-mass index.

The proportion of variation explained by variation between sibships/groups of sisters estimated using the intra-class correlation coefficient from a random effects linear/logistic regression model.

Table S3. Pairwise Discordance in Traits Between Sibships, the Scottish Family Health Study, 2006-2011.

Characteristics	Number of pairs	%
Difference in age (years) Number of sibling groups=1,541 (Number of women=3,327)		
0-2	584	37.9
3-4	464	30.1
5-6	219	14.2
More than 6	274	17.8
Difference in age at menarche (years) Number of sibling groups=1,541 (Number of women=3,327)		
0	582	37.8
1	331	21.5
2	440	28.6
3	93	6.0
More than 3.0	95	6.2
Discordance in college/university degree Number of sibling groups=1,541 (Number of women=3,327)		
No	1,139	73.9
Yes	402	26.1
Discordance in current smoking at recruitment Number of groups= 1,520 (Number of women= 3,280)		
No	1,235	81.3
Yes	285	18.7
Difference in hours of moderate/vigorous physical activity in the past week Number of sibling groups= 1,332 (Number of women= 2,863)		
0-2.9	524	39.3
3.0-5.9	310	23.2
6.0 or more	498	37.4
Difference in units of alcohol consumed in the past week Number of sibling groups= 1,378 (Number of women= 2,961)		
0-1	304	22.1
2-3	297	21.6
4-5	204	14.8
6 or more	573	41.6
Difference in adult body-mass index Number of sibling groups= 1,513 (Number of women= 3,265)		
0-2	582	38.5
3-4	318	21.0
5-6	233	15.4
More than 6	380	25.1

Table S4. Association Between Age at Menarche and Cardiometabolic Health Outcomes, the Scottish Family Health Study, 2006-2011.

Outcome	Model	Age at menarche	N	Mean/Median	SD/Range	Within-sibships association		Between-sibships association		Bootstrap p-value for the difference in the within and between sibship association
						β	95% CI	β	95% CI	
Systolic blood pressure (mmHg)	Model 1	11 or younger	1,392	127.5	17.2	1.97	-0.16, 4.10	2.08	1.06, 3.10	0.99
		12-13	4,034	124.9	16.5	Ref		Ref		NA
		14-15	1,989	125.6	17.6	-0.02	-1.67, 1.62	-0.47	-1.37, 0.44	0.67
		16 or higher	339	126.6	18.0	-2.50	-5.98, 0.97	0.76	-1.18, 2.69	0.33
	Model 2	11 or younger	1,392	127.5	17.2	1.73	-0.41, 3.86	1.71	0.71, 2.72	0.94
		12-13	4,034	124.9	16.5	Ref		Ref		NA
		14-15	1,989	125.6	17.6	-0.01	-1.66, 1.64	-0.38	-1.28, 0.51	0.74
		16 or higher	339	126.6	18.0	-2.62	-6.10, 0.86	0.81	-1.10, 2.73	0.31
	Model 3	11 or younger	1,189	127.3	17.2	2.26	-0.26, 4.78	1.74	0.68, 2.80	0.78
		12-13	3,474	124.7	16.3	Ref		Ref		NA
		14-15	1,687	125.1	17.3	0.44	-1.45, 2.32	-0.41	-1.35, 0.53	0.54
		16 or higher	285	126.1	17.4	-2.74	-6.52, 1.04	0.31	-1.69, 2.32	0.34
Diastolic blood pressure (mmHg)	Model 1	11 or younger	1,392	79.2	10.1	1.39	0.11, 2.67	1.48	0.83, 2.12	0.98
		12-13	4,034	77.5	9.9	Ref		Ref		NA
		14-15	1,989	77.1	10.0	-0.62	-1.64, 0.41	-0.86	-1.44, -0.28	0.70
		16 or higher	339	77.8	10.1	-0.38	-2.49, 1.73	-0.38	-1.62, 0.85	0.86
	Model 2	11 or younger	1,392	79.2	10.1	1.26	-0.02, 2.55	1.32	0.68, 1.96	0.99
		12-13	4,034	77.5	9.9	Ref		Ref		NA
		14-15	1,989	77.1	10.0	-0.62	-1.64, 0.40	-0.83	-1.40, -0.25	0.75
		16 or higher	339	77.8	10.1	-0.45	-2.57, 1.67	-0.36	-1.58, 0.87	0.89
	Model 3	11 or younger	1,189	79.2	10.1	1.74	0.22, 3.25	1.39	0.71, 2.08	0.75
		12-13	3,474	77.4	9.8	Ref		Ref		NA
		14-15	1,687	77.0	10.1	-0.37	-1.52, 0.78	-0.66	-1.27, -0.05	0.67
		16 or higher	285	77.8	10.3	-0.93	-3.40, 1.54	-0.06	-1.36, 1.24	0.74
HDL cholesterol, (mmol/L)	Model 1	11 or younger	1,338	1.537	0.404	-0.064	-0.109, -0.019	-0.045	-0.074, -0.017	0.65
		12-13	3,851	1.591	0.418	Ref		Ref		NA
		14-15	1,897	1.627	0.405	-0.009	-0.050, 0.033	0.040	0.014, 0.065	0.13
		16 or higher	326	1.646	0.432	-0.025	-0.109, 0.060	0.058	0.004, 0.113	0.21

	Model 2	11 or younger	1,338	1.537	0.404	-0.060	-0.105, -0.015	-0.038	-0.066, -0.010	0.54	
		12-13	3,851	1.591	0.418	Ref		Ref		NA	
		14-15	1,897	1.627	0.405	-0.010	-0.052, 0.032	0.041	0.016, 0.066	0.11	
		16 or higher	326	1.646	0.432	-0.024	-0.108, 0.060	0.066	0.012, 0.120	0.18	
	Model 3	11 or younger	1,146	1.547	0.405	-0.042	-0.093, 0.008	-0.038	-0.067, -0.009	0.96	
		12-13	3,315	1.604	0.415	Ref		Ref		NA	
		14-15	1,615	1.639	0.408	-0.009	-0.057, 0.039	0.037	0.011, 0.063	0.22	
		16 or higher	276	1.674	0.437	-0.017	-0.105, 0.071	0.061	0.005, 0.116	0.24	
	Non-HDL cholesterol (mmol/L)	Model 1	11 or younger	1,338	3.638	1.065	0.196	0.073, 0.319	0.063	-0.004, 0.131	0.20
			12-13	3,851	3.517	1.050	Ref		Ref		NA
14-15			1,897	3.498	1.031	0.021	-0.087, 0.129	-0.100	-0.160, -0.040	0.13	
16 or higher			326	3.583	1.008	-0.035	-0.235, 0.166	-0.030	-0.158, 0.099	0.97	
Model 2		11 or younger	1,338	3.638	1.065	0.202	0.084, 0.321	0.051	-0.015, 0.117	0.13	
		12-13	3,851	3.517	1.050	Ref		Ref		NA	
		14-15	1,897	3.498	1.031	0.012	-0.092, 0.115	-0.106	-0.165, -0.047	0.14	
		16 or higher	326	3.583	1.008	-0.032	-0.217, 0.153	-0.048	-0.174, 0.077	0.88	
Model 3		11 or younger	1,146	3.629	1.068	0.142	0.009, 0.274	0.068	-0.002, 0.137	0.49	
		12-13	3,315	3.491	1.039	Ref		Ref		NA	
		14-15	1,615	3.462	1.021	-0.013	-0.132, 0.105	-0.092	-0.154, -0.030	0.37	
		16 or higher	276	3.539	1.001	0.071	-0.281, 0.139	-0.070	-0.201, 0.061	0.96	
Glucose, (mmol/L)*	Model 1	11 or younger	1,317	4.6	4.3, 4.9	-0.732	-2.418, 0.954	1.349	0.456, 2.241	0.11	
		12-13	3,814	4.5	4.3, 4.8	Ref		Ref		NA	
		14-15	1,876	4.6	4.3, 4.8	0.879	-0.504, 2.262	-0.386	-1.185, 0.413	0.29	
		16 or higher	327	4.6	4.3, 4.8	-0.761	-3.803, 2.281	-0.853	-2.553, 0.846	0.91	
	Model 2	11 or younger	1,317	4.6	4.3, 4.9	-0.338	-1.975, 1.298	1.143	0.287, 1.999	0.23	
		12-13	3,814	4.5	4.3, 4.8	Ref		Ref		NA	
		14-15	1,876	4.6	4.3, 4.8	0.983	-0.352, 2.318	-0.266	-1.032, 0.499	0.27	
		16 or higher	327	4.6	4.3, 4.8	-0.849	-3.941, 2.243	-0.892	-2.521, 0.737)	0.89	
	Model 3	11 or younger	1,126	4.6	4.3, 4.9	-0.022	-2.002, 1.958	1.006	0.125, 1.888	0.43	
		12-13	3,282	4.5	4.3, 4.8	Ref		Ref		NA	
		14-15	1,599	4.6	4.3, 4.8	1.534	0.021, 3.047	-0.212	-0.999, 0.576	0.17	
		16 or higher	276	4.6	4.3, 4.8	-2.585	-6.208, 1.038	-0.721	-2.396, 0.953	0.54	
Body-mass index (kg/m ²)	Model 1	11 or younger	1,374	28.081	6.170	1.687	0.997, 2.377	1.871	1.509, 2.232	0.64	
		12-13	3,997	26.107	5.195	Ref		Ref		NA	
		14-15	1,975	25.048	4.771	-0.477	-0.976, 0.022	-1.343	-1.664, -1.021	0.02	
		16 or higher	334	25.424	5.398	-0.650	-1.693, 0.392	-1.060	-1.749, -0.371	0.73	

	Model 2	11 or younger	1,374	28.081	6.170	1.598	0.919, 2.278	1.742	1.386, 2.098	0.70	
		12-13	3,997	26.107	5.195	Ref		Ref		NA	
		14-15	1,975	25.048	4.771	-0.478	-0.981, 0.024	-1.338	-1.655, -1.022	0.03	
		16 or higher	334	25.424	5.398	-0.670	-1.705, 0.366	-1.187	-1.865, -0.509	0.65	
	Model 3	11 or younger	1,146	3.629	1.068	1.691	0.942, 2.440	1.663	1.295, 2.031	0.94	
		12-13	3,315	3.491	1.039	Ref		Ref		NA	
		14-15	1,615	3.462	1.021	-0.620	-1.172, -0.068	-1.249	-1.576, -0.921	0.16	
		16 or higher	276	3.539	1.001	-1.411	-2.511, -0.311	-0.959	-1.658, -0.260	0.56	
	Waist circumference, (cm)	Model 1	11 or younger	1,364	88.20	15.30	2.907	1.200, 4.614	3.530	2.590, 4.472	0.55
			12-13	3,981	84.48	13.80	Ref		Ref		NA
			14-15	1,966	82.53	12.71	-0.847	-2.240, 0.546	-2.723	-3.560, -1.887	0.07
			16 or higher	335	83.66	14.49	-1.903	-4.576, 0.770	-1.665	-3.455, 0.124	0.83
Model 2		11 or younger	1,364	88.20	15.30	2.752	1.060, 4.444	3.172	2.246, 4.099	0.67	
		12-13	3,981	84.48	13.80	Ref		Ref		NA	
		14-15	1,966	82.53	12.71	-0.868	-2.263, 0.528	-2.755	-3.578, -1.932	0.07	
		16 or higher	335	83.66	14.49	-1.902	-4.569, 0.765	-2.056	-3.817, -0.294	0.98	
Model 3		11 or younger	1,166	87.64	14.97	2.598	0.809, 4.387	3.068	2.108, 4.027	0.72	
		12-13	3,437	84.05	13.46	Ref		Ref		NA	
		14-15	1,672	81.95	12.19	-1.235	-2.710, 0.239	-2.642	-3.496, -1.789	0.20	
		16 or higher	282	83.02	13.90	-3.069	-5.657, -0.481	-1.686	-3.510, 0.137	0.49	

CI=confidence interval; HDL=high-density lipoprotein; SD=standard deviation.

Model 1 Adjusted for age

Model 2 Adjusted for age, ethnicity, qualifications, parental history of cardiovascular disease and parental history of diabetes. Blood pressure further adjusted for use of antihypertensive drugs, cholesterol levels adjusted for lipid lowering drugs and glucose adjusted for use of antidiabetic drugs.

Model 3 Adjusted for age, ethnicity, qualifications, parental history of cardiovascular disease, parental history of diabetes, smoking, alcohol intake and leisure time physical activity. Blood pressure further adjusted for use of antihypertensive drugs, cholesterol levels adjusted for lipid lowering drugs and glucose adjusted for use of antidiabetic drugs.

*Outcome log transformed and the coefficients reflect the percent change in the outcome.

Table S5. Association Between Age at Menarche and 10-Year Risk For Overall Cardiovascular Disease, the Scottish Family Health Study, 2006-2011.

Risk score	Model	Age at menarche	N	Mean	SD	Within-sibships association		Between-sibships association		Bootstrap p-value for the difference in the within and between sibship association
						β	95% CI	β	95% CI	
Framingham risk score *	Model 1	11 or younger	1,076	26.06	0.91	0.09	0.02, 0.17	0.10	0.06, 0.14	0.80
		12-13	3,014	25.94	0.90	Ref		Ref		NA
		14-15	1,543	25.97	0.92	0.02	-0.04, 0.08	-0.03	-0.07, 0.00	0.24
		16 or higher	272	26.07	0.87	-0.03	-0.15, 0.09	0.04	-0.04, 0.12	0.54
	Model 2	11 or younger	1,076	26.06	0.91	0.08	0.00, 0.16	0.09	0.05, 0.13	0.85
		12-13	3,014	25.94	0.90	Ref		Ref		NA
		14-15	1,543	25.97	0.92	0.02	-0.04, 0.08	-0.04	-0.07, 0.00	0.20
		16 or higher	272	26.07	0.87	-0.03	-0.15, 0.09	0.02	-0.05, 0.09	0.68
	Model 3	11 or younger	922	26.04	0.90	0.08	-0.01, 0.17	0.08	0.04, 0.13	0.85
		12-13	2,591	25.92	0.89	Ref		Ref		NA
		14-15	1,312	25.94	0.91	0.02	-0.05, 0.09	-0.02	-0.06, 0.01	0.40
		16 or higher	231	26.01	0.84	-0.04	-0.18, 0.10	0.01	-0.07, 0.08	0.71
NHANES ECG risk equation score †	Model 1	11 or younger	1,076	7.963	0.847	0.030	-0.004, 0.064	0.018	0.001, 0.035	0.62
		12-13	3,054	7.928	0.845	Ref		Ref		NA
		14-15	1,581	7.970	0.880	0.002	-0.025, 0.030	-0.020	-0.035, -0.005	0.27
		16 or higher	265	8.061	0.819	0.003	-0.056, 0.063	0.027	-0.005, 0.059	0.82
	Model 2	11 or younger	1,076	7.963	0.847	0.031	-0.003, 0.065	0.015	-0.002, 0.032	0.52
		12-13	3,054	7.928	0.845	Ref		Ref		NA
		14-15	1,581	7.970	0.880	0.004	-0.024, 0.031	-0.020	-0.035, -0.005	0.24
		16 or higher	265	8.061	0.819	0.003	-0.057, 0.064	0.025	-0.007, 0.057	0.85
	Model 3	11 or younger	919	7.957	0.846	0.044	0.005, 0.083	0.023	0.006, 0.041	0.43
		12-13	2,625	7.914	0.845	Ref		Ref		NA
		14-15	1,336	7.928	0.865	-0.015	-0.047, 0.017	-0.014	-0.030, 0.001	0.93
		16 or higher	224	8.025	0.783	-0.001	-0.073, 0.071	0.027	-0.005, 0.060	0.79

CI=confidence interval; ECG=electrocardiogram; SD=standard deviation.

* The variables included in the Framingham risk score is age, total cholesterol, HDL cholesterol, systolic blood pressure, smoking and diabetes.

† The information included in the NHANES ECG risk score included age, positive deflection of T axis, negative deflection of the T axis, heart rate and corrected QT interval.

Model 1 Adjusted for age

Model 2 Adjusted for age, ethnicity, qualifications, parental history of cardiovascular disease and parental history of diabetes.

Model 3 Adjusted for all of the covariates in Model 2 in addition to smoking (not adjusted for in the analysis of the Framingham risk score since part of the risk calculation), alcohol intake and leisure time physical activity.

Table S6. Associations of Age at menarche With Blood pressure, Cholesterol and Glucose Excluding Individuals On Medications That Might Influence the Outcomes, the Scottish Family Health Study, 2006-2011.

Outcome	Model	Age at menarche	N	Mean/Median	SD/Range	Within-sibships association		Between-sibships association		Bootstrap p-value for the difference in the within and between sibship association
						β	95% CI	β	95% CI	
Systolic blood pressure (mmHg)	Model 1	11 or younger	1,249	126.34	16.66	1.81	-0.40, 4.02	2.21	1.19, 3.24	0.80
		12-13	3,728	123.79	15.72	Ref		Ref		NA
		14-15	1,853	124.56	16.80	-0.07	-1.79, 1.65	-0.26	-1.17, 0.64	0.81
		16 or higher	313	125.04	16.20	-2.69	-6.23, 0.85	0.03	-1.89, 1.96	0.39
	Model 2	11 or younger	1,249	126.34	16.66	1.55	-0.67, 3.77	2.00	0.98, 3.01	0.79
		12-13	3,728	123.79	15.72	Ref		Ref		NA
		14-15	1,853	124.56	16.80	-0.08	-1.79, 1.63	-0.28	-1.18, 0.62	0.83
		16 or higher	313	125.04	16.20	-2.84	-6.39, 0.70	-0.18	-2.09, 1.74	0.40
	Model 3	11 or younger	1,076	126.27	16.75	2.12	-0.53, 4.77	2.05	0.98, 3.13	0.97
		12-13	3,221	123.63	15.55	Ref		Ref		NA
		14-15	1,580	124.13	16.55	0.50	-1.44, 2.44	-0.30	-1.25, 0.65	0.56
		16 or higher	268	124.74	15.83	-2.46	-6.15, 1.23	-0.46	-2.47, 1.56	0.54
Diastolic blood pressure (mmHg)	Model 1	11 or younger	1,249	78.76	9.99	1.29	-0.10, 2.67	1.43	0.77, 2.09	0.88
		12-13	3,728	77.12	9.68	Ref		Ref		NA
		14-15	1,853	76.82	10.0	-0.49	-1.57, 0.60	-0.79	-1.38, -0.21	0.67
		16 or higher	313	77.60	9.86	-0.08	-2.37, 2.21	-0.39	-1.64, 0.85	0.79
	Model 2	11 or younger	1,249	78.76	9.99	1.14	-0.25, 2.53	1.30	0.65, 1.96	0.86
		12-13	3,728	77.12	9.68	Ref		Ref		NA
		14-15	1,853	76.82	10.0	-0.49	-1.57, 0.59	-0.78	-1.36, -0.20	0.70
		16 or higher	313	77.60	9.86	-0.19	-2.49, 2.11	-0.43	-1.66, 0.81	0.81
	Model 3	11 or younger	1,076	78.71	10.02	1.51	-0.13, 3.15	1.34	0.64, 2.04	0.92
		12-13	3,221	76.99	9.65	Ref		Ref		NA
		14-15	1,580	76.72	10.05	-0.20	-1.41, 1.00	-0.64	-1.26, -0.01	0.57
		16 or higher	268	77.65	10.03	-0.24	-2.81, 2.33	-0.11	-1.42, 1.20	0.98
HDL cholesterol, (mmol/L)	Model 1	11 or younger	1,266	1.540	0.408	-0.056	-0.102, -0.010	-0.050	-0.079, -0.021	0.93
		12-13	3,675	1.595	0.415	Ref		Ref		NA
		14-15	1,806	1.626	0.404	-0.013	-0.056, 0.030	0.032	0.006, 0.058	0.18
		16 or higher	308	1.658	0.436	-0.023	-0.116, 0.070	0.055	0.000, 0.110	0.25
	Model 2	11 or younger	1,266	1.540	0.408	-0.054	-0.100, -0.008	-0.042	-0.071, -0.013	0.78
		12-13	3,675	1.595	0.415	Ref		Ref		NA

		14-15	1,806	1.626	0.404	-0.014	-0.057, 0.030	0.034	0.008, 0.060	0.16
		16 or higher	308	1.658	0.436	-0.022	-0.115, 0.071	0.064	0.009, 0.118	0.21
	Model 3	11 or younger	1,101	1.551	0.410	-0.034	-0.087, 0.017	-0.044	-0.074, -0.014	0.77
		12-13	3,173	1.608	0.412	Ref		Ref		NA
		14-15	1,546	1.638	0.408	-0.009	-0.058, 0.040	0.029	0.003, 0.056	0.32
		16 or higher	265	1.679	0.442	-0.009	-0.103, 0.084	0.054	-0.002, 0.111	0.33
Non-HDL cholesterol (mmol/L)	Model 1	11 or younger	1,266	3.657	1.070	0.210	0.087, 0.334	0.062	-0.006, 0.129	0.17
		12-13	3,675	3.530	1.050	Ref		Ref		NA
		14-15	1,806	3.514	1.032	-0.013	-0.122, 0.095	-0.097	-0.157, -0.037	0.31
		16 or higher	308	3.574	1.001	-0.077	-0.270, 0.117	-0.060	-0.188, 0.067	0.97
	Model 2	11 or younger	1,266	3.657	1.070	0.209	0.085, 0.334	0.048	-0.020, 0.115	0.13
		12-13	3,675	3.530	1.050	Ref		Ref		NA
		14-15	1,806	3.514	1.032	-0.011	-0.119, 0.097	-0.101	-0.161, -0.041	0.28
		16 or higher	308	3.574	1.001	-0.086	-0.280, 0.107	-0.066	-0.194, 0.061	0.95
	Model 3	11 or younger	1,101	3.641	1.076	0.142	0.006, 0.279	0.065	-0.006, 0.135	0.49
		12-13	3,173	3.503	1.044	Ref		Ref		NA
		14-15	1,546	3.477	1.020	-0.036	-0.157, 0.086	-0.084	-0.147, -0.021	0.57
		16 or higher	265	3.536	0.989	-0.109	-0.321, 0.102	-0.079	-0.213, 0.054	0.94
Glucose, (mmol/L)*	Model 1	11 or younger	1,305	4.6	4.3, 4.9	-0.71	-2.21, 0.79	0.82	0.03, 1.61	0.20
		12-13	3,780	4.5	4.3, 4.8	Ref		Ref		NA
		14-15	1,864	4.6	4.3, 4.8	1.11	-0.16, 2.37	-0.54	-1.25, 0.17	0.12
		16 or higher	324	4.6	4.3, 4.8	-0.64	-3.72, 2.43	-1.08	-2.59, 0.43	0.99
	Model 2	11 or younger	1,305	4.6	4.3, 4.9	-0.73	-2.22, 0.77	0.80	0.01, 1.59	0.18
		12-13	3,780	4.5	4.3, 4.8	Ref		Ref		NA
		14-15	1,864	4.6	4.3, 4.8	1.13	-0.14, 2.40	-0.54	-1.25, 0.17	0.12
		16 or higher	324	4.6	4.3, 4.8	-0.76	-3.86, 2.34	-1.01	-2.52, 0.50	0.94
	Model 3	11 or younger	1,120	4.6	4.3, 4.9	-0.47	-2.20, 1.25	1.01	0.18, 1.83	0.25
		12-13	3,255	4.5	4.3, 4.8	Ref		Ref		NA
		14-15	1,593	4.6	4.3, 4.8	1.36	-0.14, 2.86	-0.37	-1.11, 0.37	0.16
		16 or higher	274	4.6	4.3, 4.8	-2.64	-6.33, 1.04	-0.55	-2.13, 1.02	0.51

CI=confidence interval; HDL=high-density lipoprotein; SD=standard deviation.

Model 1 Adjusted for age

Model 2 Adjusted for age, ethnicity, qualifications, parental history of cardiovascular disease and parental history of diabetes.

Model 3 Adjusted for age, ethnicity, qualifications, parental history of cardiovascular disease, parental history of diabetes, smoking, alcohol intake and leisure time physical activity.

* Outcome log transformed and the coefficients reflect the percent change in the outcome.

Table S7. Associations of Age at Menarche With Blood Pressure, Cholesterol and Glucose After Adjustment for Body-Mass Index, the Scottish Family Health Study, 2006-2011.

Outcome	Model	Age at menarche	N	Mean /Median	SD/Range	Within-sibships association		Between-sibships association		Bootstrap p-value for the difference in the within and between sibship association
						β	95% CI	β	95% CI	
Systolic blood pressure (mmHg)	Model 1	11 or younger	1,189	127.3	17.2	2.26	-0.26, 4.78	1.74	0.68, 2.80	0.78
		12-13	3,474	124.7	16.3	Ref		Ref		NA
		14-15	1,687	125.1	17.3	0.44	-1.45, 2.32	-0.41	-1.35, 0.53	0.54
		16 or higher	285	126.1	17.4	-2.74	-6.52, 1.04	0.31	-1.69, 2.32	0.34
	Model 2	11 or younger	1,174	127.37	17.19	0.62	-1.88, 3.12	0.55	-0.48, 1.58	0.94
		12-13	3,448	124.71	16.26	Ref		Ref		NA
		14-15	1,674	125.14	17.32	1.10	-0.71, 2.92	0.53	-0.38, 1.45	0.65
		16 or higher	280	126.25	17.50	-1.38	-5.10, 2.34	1.05	-0.90, 2.99	0.48
Diastolic blood pressure (mmHg)	Model 1	11 or younger	1,392	79.2	10.1	1.74	0.22, 3.25	1.39	0.71, 2.08	0.75
		12-13	4,034	77.5	9.9	Ref		Ref		NA
		14-15	1,989	77.1	10.0	-0.37	-1.52, 0.78	-0.66	-1.27, -0.05	0.67
		16 or higher	339	77.8	10.1	-0.93	-3.40, 1.54	-0.06	-1.36, 1.24	0.74
	Model 2	11 or younger	1,174	79.2	10.0	0.52	-0.96, 1.99	0.34	-0.30, 0.99	0.84
		12-13	3,448	77.4	9.8	Ref		Ref		NA
		14-15	1,674	77.0	10.1	0.14	-0.96, 1.23	0.14	-0.43, 0.72	0.91
		16 or higher	280	78.0	10.2	0.55	-1.76, 2.86	0.58	-0.64, 1.80	0.87
HDL cholesterol, (mmol/L)	Model 1	11 or younger	1,338	1.537	0.404	-0.042	-0.093, 0.008	-0.038	-0.067, -0.009	0.96
		12-13	3,851	1.591	0.418	Ref		Ref		NA
		14-15	1,897	1.627	0.405	-0.009	-0.057, 0.039	0.037	0.011, 0.063	0.22
		16 or higher	326	1.646	0.432	-0.017	-0.105, 0.071	0.061	0.005, 0.116	0.24
	Model 2	11 or younger	1,132	1.549	0.404	-0.005	-0.054, 0.045	0.002	-0.026, 0.030	0.87
		12-13	3,292	1.605	0.415	Ref		Ref		NA
		14-15	1,602	1.639	0.408	-0.026	-0.071, 0.020	0.007	-0.018, 0.032	0.38
		16 or higher	271	1.673	0.438	-0.037	-0.126, 0.052	0.030	-0.023, 0.083	0.30
Non-HDL cholesterol (mmol/L)	Model 1	11 or younger	1,338	3.638	1.065	0.142	0.009, 0.274	0.068	-0.002, 0.137	0.49
		12-13	3,851	3.517	1.050	Ref		Ref		NA
		14-15	1,897	3.498	1.031	-0.013	-0.132, 0.105	-0.092	-0.154, -0.030	0.37
		16 or higher	326	3.583	1.008	0.071	-0.281, 0.139	-0.070	-0.201, 0.061	0.96
	Model 2	11 or younger	1,132	3.631	1.067	0.038	-0.091, 0.167	-0.006	-0.074, 0.062	0.68
		12-13	3,292	3.491	1.039	Ref		Ref		NA

		14-15	1,602	3.460	1.023	0.010	-0.106, 0.126	-0.041	-0.102, 0.020	0.55
		16 or higher	271	3.544	1.005	0.005	-0.202, 0.212	-0.028	-0.157, 0.100	0.78
Glucose, (mmol/L)*	Model 1	11 or younger	1,317	4.6	4.3, 4.9	-0.022	-2.002, 1.958	1.006	0.125, 1.888	0.43
		12-13	3,814	4.5	4.3, 4.8	Ref		Ref		NA
		14-15	1,876	4.6	4.3, 4.8	1.534	0.021, 3.047	-0.212	-0.999, 0.576	0.17
		16 or higher	327	4.6	4.3, 4.8	-2.585	-6.208, 1.038	-0.721	-2.396, 0.953	0.54
	Model 2	11 or younger	1,112	4.6	4.3, 4.9	-1.125	-3.057, 0.808	0.516	-0.372, 1.403	0.26
		12-13	3,259	4.5	4.3, 4.8	Ref		Ref		NA
		14-15	1,586	4.6	4.3, 4.8	1.500	0.047, 2.953	0.108	-0.681, 0.897	0.27
		16 or higher	271	4.6	4.3, 4.8	-2.023	-5.570, 1.524	-0.230	-1.902, 1.443	0.58

CI=confidence interval; HDL=high-density lipoprotein; SD=standard deviation.

Model 1 Adjusted for age, ethnicity, qualifications, parental history of cardiovascular disease, parental history of diabetes, smoking, alcohol intake and leisure time physical activity. Blood pressure further adjusted for use of antihypertensive drugs, cholesterol levels adjusted for lipid lowering drugs and glucose adjusted for use of antidiabetic drugs (Model 3 from Supplement Table 4).

Model 2 Adjusted for all covariates in model 1 in addition to adult body-mass index.

*Outcomes log transformed and the coefficients reflect the percent change in the outcome.

Table S8. Association Between Age at Menarche and 10-Year Risk for Cardiovascular Disease After Adjustment for Adult Body-Mass Index, the Scottish Family Health Study, 2006-2011.

Risk score	Model	Age at menarche	N	Mean	SD	Within-sibships association		Between-sibships association		Bootstrap p-value for the difference in the within and between sibship association
						β	95% CI	β	95% CI	
Framingham risk score *	Model 1	11 or younger	922	26.04	0.90	0.08	-0.01, 0.17	0.08	0.04, 0.13	0.85
		12-13	2,591	25.92	0.89	Ref		Ref		NA
		14-15	1,312	25.94	0.91	0.02	-0.05, 0.09	-0.02	-0.06, 0.01	0.40
		16 or higher	231	26.01	0.84	-0.04	-0.18, 0.10	0.01	-0.07, 0.08	0.71
	Model 2	11 or younger	913	26.04	0.90	0.00	-0.08, 0.09	0.02	-0.02, 0.06	0.78
		12-13	2,575	25.92	0.89	Ref		Ref		NA
		14-15	1,304	25.94	0.91	0.04	-0.02, 0.11	0.02	-0.01, 0.06	0.67
		16 or higher	227	26.02	0.84	0.02	-0.11, 0.14	0.04	-0.03, 0.11	0.91
NHANES ECG risk equation †	Model 1	11 or younger	919	7.957	0.846	0.044	0.005, 0.083	0.023	0.006, 0.041	0.43
		12-13	2,625	7.914	0.845	Ref		Ref		NA
		14-15	1,336	7.928	0.865	-0.015	-0.047, 0.017	-0.014	-0.030, 0.001	0.93
		16 or higher	224	8.025	0.783	-0.001	-0.073, 0.071	0.027	-0.005, 0.060	0.79
	Model 2	11 or younger	909	7.961	0.848	0.022	-0.016, 0.059	0.004	-0.014, 0.021	0.45
		12-13	2,607	7.913	0.844	Ref		Ref		NA
		14-15	1,328	7.929	0.864	-0.006	-0.037, 0.026	0.000	-0.015, 0.015	0.94
		16 or higher	220	8.029	0.786	0.005	-0.064, 0.074	0.034	0.002, 0.065	0.75

CI=confidence interval; ECG=electrocardiogram; SD=standard deviation.

* The variables included in the Framingham risk score is age, total cholesterol, HDL cholesterol, systolic blood pressure, smoking and diabetes.

† The information included in the NHANES ECG risk score included age, positive deflection of T axis, negative deflection of the T axis, heart rate and corrected QT interval.

Model 1 Adjusted for age, ethnicity, qualifications, parental history of cardiovascular disease, parental history of diabetes, smoking, alcohol intake and leisure time physical activity (Model 3 from Table 2).

Model 2 Adjusted for all covariates in model 1 in addition to adult body-mass index.

Table S9. Association Between Age at Menarche and Cardiometabolic Health After Restricting the Analysis to Sibships With up to Four Years Age Difference Between Sisters, the Scottish Family Health Study, 2006-2011.

Outcome	Model	Age at menarche	N	Mean/Median	SD/Range	Within-sibships association		Between-sibships association		Bootstrap p-value for the difference in the within and between sibship association
						β	95% CI	β	95% CI	
Systolic blood pressure (mmHg)	Model 1	11 or younger	1,276	127.4	17.1	2.67	0.14, 5.20	1.87	0.84, 2.90	0.69
		12-13	3,757	124.9	16.6	Ref		Ref		NA
		14-15	1,855	125.9	17.8	1.20	-0.76, 3.15	-0.26	-1.17, 0.65	0.25
		16 or higher	313	126.6	18.4	-2.46	-6.58, 1.67	0.28	-1.67, 2.22	0.41
	Model 2	11 or younger	1,276	127.4	17.1	2.35	-0.19, 4.88	1.53	0.52, 2.55	0.70
		12-13	3,757	124.9	16.6	Ref		Ref		NA
		14-15	1,855	125.9	17.8	1.24	-0.71, 3.20	-0.20	-1.09, 0.70	0.27
		16 or higher	313	126.6	18.4	-2.50	-6.65, 1.66	0.26	-1.66, 2.18	0.41
	Model 3	11 or younger	1,090	127.2	17.1	3.01	0.09, 5.93	1.60	0.53, 2.67	0.58
		12-13	3,235	124.7	16.3	Ref		Ref		NA
		14-15	1,569	125.4	17.5	1.75	-0.45, 3.93	-0.24	-1.20, 0.71	0.19
		16 or higher	266	126.2	17.8	1.74	-0.45, 3.93	0.05	-1.98, 2.08	0.29
Diastolic blood pressure (mmHg)	Model 1	11 or younger	1,276	79.2	10.0	1.53	0.03, 3.03	1.38	0.72, 2.03	0.89
		12-13	3,757	77.5	9.9	Ref		Ref		NA
		14-15	1,855	77.1	10.1	0.06	-1.15, 1.26	-0.77	-1.34, -0.19	0.27
		16 or higher	313	77.6	10.2	-0.27	-2.94, 2.40	-0.56	-1.79, 0.68	0.79
	Model 2	11 or younger	1,276	79.2	10.0	1.30	-0.19, 2.79	1.22	0.57, 1.87	0.95
		12-13	3,757	77.5	9.9	Ref		Ref		NA
		14-15	1,855	77.1	10.1	0.07	-1.13, 1.28	-0.74	-1.32, -0.17	0.27
		16 or higher	313	77.6	10.2	-0.30	-2.98, 2.37	-0.55	-1.78, 0.68	0.80
	Model 3	11 or younger	1,090	79.1	10.1	1.93	0.21, 3.66	1.31	0.62, 2.00	0.67
		12-13	3,235	77.3	9.9	Ref		Ref		NA
		14-15	1,569	77.0	10.2	0.30	-1.03, 1.63	-0.63	-1.24, -0.01	0.27
		16 or higher	266	77.7	10.5	-1.08	-4.10, 1.93	-0.18	-1.49, 1.14	0.75
HDL cholesterol, (mmol/L)	Model 1	11 or younger	1,228	1.534	0.405	-0.061	-0.114, -0.008	-0.049	-0.078, -0.020	0.81
		12-13	3,591	1.589	0.414	Ref		Ref		NA
		14-15	1,768	1.625	0.406	-0.022	-0.069, 0.026	0.038	0.013, 0.064	0.08
		16 or higher	300	1.661	0.436	-0.037	-0.139, 0.061	0.073	0.018, 0.127	0.14
	Model 2	11 or younger	1,228	1.534	0.405	-0.061	-0.114, -0.007	-0.042	-0.070, -0.014	0.68
		12-13	3,591	1.589	0.414	Ref		Ref		NA
		14-15	1,768	1.625	0.406	-0.02	-0.071, 0.024	0.039	0.014, 0.065	0.07

	Model 3	16 or higher	300	1.661	0.436	-0.036	-0.137, 0.065	0.083	0.029, 0.137	0.12
		11 or younger	1,053	1.546	0.406	-0.036	-0.097, 0.025	-0.040	-0.069, -0.010	0.88
		12-13	3,089	1.603	0.410	Ref		Ref		NA
		14-15	1,500	1.638	0.409	-0.022	-0.076, 0.032	0.035	0.008, 0.061	0.15
		16 or higher	257	1.684	0.441	-0.024	-0.122, 0.074	0.073	0.017, 0.128	0.20
Non-HDL cholesterol (mmol/L)	Model 1	11 or younger	1,228	3.630	1.056	0.159	0.009, 0.309	0.070	0.002, 0.138	0.49
		12-13	3,591	3.518	1.057	Ref		Ref		NA
		14-15	1,768	3.491	1.025	-0.006	-0.132, 0.120	-0.089	-0.149, -0.028	0.27
		16 or higher	300	3.568	0.996	-0.072	-0.295, 0.151	-0.049	-0.178, 0.080	0.99
	Model 2	11 or younger	1,228	3.630	1.056	0.154	0.009, 0.299	0.055	-0.012, 0.122	0.42
		12-13	3,591	3.518	1.057	Ref		Ref		NA
		14-15	1,768	3.491	1.025	-0.008	-0.130, 0.114	-0.098	-0.157, -0.039	0.24
		16 or higher	300	3.568	0.996	-0.067	-0.273, 0.139	-0.067	-0.193, 0.059	0.94
	Model 3	11 or younger	1,053	3.619	1.059	0.115	-0.046, 0.276	0.059	-0.011, 0.129	0.70
		12-13	3,089	3.490	1.044	Ref		Ref		NA
		14-15	1,500	3.452	1.013	-0.031	-0.166, 0.104	-0.088	-0.150, -0.026	0.49
		16 or higher	257	3.525	0.979	-0.082	-0.314, 0.151	-0.100	-0.232, 0.033	0.85
	Glucose, (mmol/L)*	Model 1	11 or younger	1,207	4.6	4.3, 4.9	-0.62	-2.49, 1.24	1.24	0.34, 2.15
12-13			3,555	4.5	4.3, 4.8	Ref		Ref		NA
14-15			1,747	4.6	4.3, 4.8	-0.22	-1.83, 1.40	-0.20	-1.01, 0.60	0.94
16 or higher			301	4.6	4.3, 4.8	-3.06	-6.54, 0.43	-0.59	-2.30, 1.13	0.32
Model 2		11 or younger	1,207	4.6	4.3, 4.9	-0.51	-2.32, 1.30	1.10	0.24, 1.97	0.22
		12-13	3,555	4.5	4.3, 4.8	Ref		Ref		NA
		14-15	1,747	4.6	4.3, 4.8	0.02	-1.53, 1.56	-0.12	-0.88, 0.65	0.98
		16 or higher	301	4.6	4.3, 4.8	-3.08	-6.61, 0.45	-0.59	-2.23, 1.05	0.29
Model 3		11 or younger	1,033	4.6	4.3, 4.8	0.02	-2.02, 2.05	0.94	0.03, 1.84	0.50
		12-13	3,057	4.5	4.3, 4.9	Ref		Ref		NA
		14-15	1,484	4.6	4.3, 4.8	0.84	-0.86, 2.53	-0.16	-0.97, 0.65	0.48
		16 or higher	257	4.6	4.3, 4.8	-4.14	-8.69, 0.42	-0.57	-2.28, 1.14	0.32
Body-mass index (kg/m ²)		Model 1	11 or younger	1,260	28.0	6.1	1.70	0.87, 2.52	1.88	1.52, 2.25
	12-13		3,721	26.1	5.2	Ref		Ref		NA
	14-15		1,842	25.1	4.8	-0.43	-1.02, 0.17	-1.24	-1.56, -0.92	0.05
	16 or higher		309	25.3	5.3	-0.86	-2.05, 0.34	-1.15	-1.84, -0.47	0.87
	Model 2	11 or younger	1,260	28.0	6.1	1.60	0.78, 2.42	1.76	1.40, 2.11	0.77
		12-13	3,721	26.1	5.2	Ref		Ref		NA
		14-15	1,842	25.1	4.8	-0.42	-1.02, 0.18	-1.24	-1.55, -0.93	0.05
		16 or higher	309	25.3	5.3	-0.87	-2.05, 0.32	-1.29	-1.96, -0.62	0.75

Waist circumference, (cm)	Model 3	11 or younger	1,078	27.8	6.0	1.95	1.09, 2.82	1.68	1.31, 2.05	0.70
		12-13	3,213	25.9	5.0	Ref		Ref		NA
		14-15	1,559	24.9	4.6	-0.75	-1.39, -0.12	-1.12	-1.45, -0.79	0.43
		16 or higher	263	25.0	5.2	-1.73	-2.97, -0.49	-1.13	-1.83, -0.44	0.45
	Model 1	11 or younger	1,249	88.1	15.2	3.07	0.98, 5.18	3.66	2.71, 4.60	0.67
		12-13	3,707	84.4	13.8	Ref		Ref		NA
		14-15	1,833	82.5	12.8	-0.64	-2.37, 1.09	-2.53	-3.36, -1.70	0.13
		16 or higher	309	83.2	14.1	-2.67	-5.75, 0.40	-1.87	-3.64, -0.09	0.71
	Model 2	11 or younger	1,249	88.1	15.2	2.89	0.79, 4.99	3.30	2.37, 4.23	0.76
		12-13	3,707	84.4	13.8	Ref		Ref		NA
		14-15	1,833	82.5	12.8	-0.67	-2.41, 1.06	-2.58	-3.40, -1.77	0.13
		16 or higher	309	83.2	14.1	-2.65	-5.70, 0.40	-2.26	-4.01, -0.51	0.84
Model 3	11 or younger	1,067	87.7	14.9	3.30	1.15, 5.45	3.16	2.19, 4.13	0.92	
	12-13	3,200	83.9	13.4	Ref		Ref		NA	
	14-15	1,555	82.0	12.3	-1.23	-2.95, 0.50	-2.43	-3.29, -1.58	0.33	
	16 or higher	263	82.5	13.5	-3.72	-6.63, -0.81	-2.18	-4.00, -0.35	0.48	

CI=confidence interval; HDL=high-density lipoprotein; SD=standard deviation.

Model 1 Adjusted for age

Model 2 Adjusted for age, ethnicity, qualifications, parental history of cardiovascular disease and parental history of diabetes. Blood pressure further adjusted for use of antihypertensive drugs, cholesterol levels adjusted for lipid lowering drugs and glucose adjusted for use of antidiabetic drugs.

Model 3 Adjusted for all the characteristics in Model 2 in addition to smoking, alcohol intake and leisure time physical activity.

* Outcome log transformed and the coefficients reflect the percent change in the outcome.

Table S10. Association Between Age at Menarche and 10-Year Risk of Cardiovascular Disease After Restricting the Analysis to Sibships With up to Four Years Age Difference Between Sisters, the Scottish Family Health Study, 2006-2011

Risk score	Model	Age at menarche	N	Mean	SD	Within-sibships association		Between-sibships association		Bootstrap p-value for the difference in the within and between sibship association
						β	95% CI	β	95% CI	
Framingham risk score *	Model 1	11 or younger	982	26.06	0.90	0.13	0.05, 0.22	0.09	0.05, 0.13	0.67
		12-13	2,795	25.95	0.90	Ref		Ref		NA
		14-15	1,430	25.98	0.93	0.04	-0.03, 0.11	-0.03	-0.06, 0.01	0.21
		16 or higher	248	26.07	0.90	-0.08	-0.21, 0.05	0.03	-0.05, 0.11	0.28
	Model 2	11 or younger	982	26.06	0.90	0.12	0.03, 0.21	0.08	0.04, 0.12	0.66
		12-13	2,795	25.95	0.90	Ref		Ref		NA
		14-15	1,430	25.98	0.93	0.04	-0.03, 0.11	-0.03	-0.06, 0.01	0.18
		16 or higher	248	26.07	0.90	-0.07	-0.21, 0.06	0.01	-0.06, 0.09	0.42
	Model 3	11 or younger	843	26.04	0.90	0.12	0.02, 0.22	0.08	0.03, 0.12	0.72
		12-13	2,400	25.92	0.90	Ref		Ref		NA
		14-15	1,211	25.95	0.92	0.04	-0.03, 0.12	-0.02	-0.06, 0.02	0.27
		16 or higher	214	26.02	0.86	-0.08	-0.23, 0.07	0.00	-0.08, 0.08	0.47
NHANES ECG risk equation †	Model 1	11 or younger	981	7.97	0.86	0.04	0.00, 0.08	0.02	0.00, 0.04	0.41
		12-13	2,830	7.93	0.85	Ref		Ref		NA
		14-15	1,464	7.98	0.89	-0.01	-0.04, 0.02	-0.01	-0.03, 0.00	0.84
		16 or higher	243	8.08	0.83	-0.02	-0.09, 0.06	0.03	0.00, 0.06	0.49
	Model 2	11 or younger	981	7.97	0.86	0.04	0.00, 0.08	0.02	0.00, 0.03	0.35
		12-13	2,830	7.93	0.85	Ref		Ref		NA
		14-15	1,464	7.98	0.89	-0.01	-0.04, 0.02	-0.01	-0.03, 0.00	0.77
		16 or higher	243	8.08	0.83	-0.02	-0.09, 0.06	0.03	0.00, 0.06	0.54
	Model 3	11 or younger	838	7.97	0.86	0.05	0.01, 0.10	0.02	0.01, 0.04	0.36
		12-13	2,433	7.92	0.85	Ref		Ref		NA
		14-15	1,233	7.94	0.87	-0.03	-0.07, 0.01	-0.01	-0.03, 0.00	0.63
		16 or higher	208	8.03	0.80	-0.02	-0.11, 0.07	0.03	-0.01, 0.06	0.53

CI=confidence interval; ECG=electrocardiogram; SD=standard deviation.

* The variables included in the Framingham risk score is age, total cholesterol, HDL cholesterol, systolic blood pressure, smoking and diabetes.

† The information included in the NHANES ECG risk score included age, positive deflection of T axis, negative deflection of the T axis, heart rate and corrected QT interval.

The estimates are from a mixed effects linear regression analysis.

Model 1 Adjusted for age

Model 2 Adjusted for age, ethnicity, qualifications, parental history of cardiovascular disease and parental history of diabetes.

Model 3 Adjusted for all of the covariates in Model 2 in addition to smoking (not adjusted for in the analysis of the NHANES risk score since part of the risk calculation), alcohol intake and leisure time physical activity.

Table S11. Association Between Age at Menarche and Cardiometabolic Health Outcomes Excluding Individuals of Non-European Ethnicity, the Scottish Family Health Study, 2006-2011.

Outcome	Model	Age at menarche	N	Mean/Median	SD/Range	Within-sibships association		Between-sibships association		Bootstrap p-value for the difference in the within and between sibship association
						β	95% CI	β	95% CI	
Systolic blood pressure (mmHg)	Model 1	11 or younger	1,362	127.7	17.2	1.95	-0.19, 4.08	2.15	1.12, 3.18	0.98
		12-13	3,959	124.9	16.5	Ref		Ref		NA
		14-15	1,943	125.7	17.6	-0.05	-1.71, 1.61	-0.45	-1.36, 0.47	0.69
		16 or higher	334	126.6	18.0	-2.56	-6.09, 0.96	0.87	-1.08, 2.82	0.33
	Model 2	11 or younger	1,362	127.7	17.2	1.82	-0.33, 3.97	1.82	0.75, 2.89	0.91
		12-13	3,959	124.9	16.5	Ref		Ref		NA
		14-15	1,943	125.7	17.6	-0.03	-1.70, 1.64	-0.34	-1.29, 0.62	0.75
		16 or higher	334	126.6	18.0	-2.63	-6.16, 0.90	0.45	-1.57, 2.48	0.32
	Model 3	11 or younger	1,165	127.4	17.3	2.35	-0.19, 4.88	1.74	0.68, 2.80	0.74
		12-13	3,408	124.7	16.3	Ref		Ref		NA
		14-15	1,649	125.2	17.3	0.35	-1.57, 2.26	-0.41	-1.35, 0.53	0.58
		16 or higher	281	126.2	17.4	-3.02	-6.85, 0.81	0.31	-1.69, 2.32	0.29
Diastolic blood pressure (mmHg)	Model 1	11 or younger	1,362	79.2	10.1	1.42	0.14, 2.70	1.49	0.84, 2.15	0.98
		12-13	3,959	77.5	9.9	Ref		Ref		NA
		14-15	1,943	77.1	10.0	-0.62	-1.64, 0.41	-0.84	-1.43, -0.26	0.69
		16 or higher	334	77.8	10.1	-0.41	-2.55, 1.73	-0.22	-1.47, 1.02	0.97
	Model 2	11 or younger	1,362	79.2	10.1	1.38	0.09, 2.66	1.33	0.69, 1.98	0.89
		12-13	3,959	77.5	9.9	Ref		Ref		NA
		14-15	1,943	77.1	10.0	-0.62	-1.64, 0.41	-0.80	-1.38, -0.22	0.74
		16 or higher	334	77.8	10.1	-0.45	-2.61, 1.70	-0.20	-1.44, 1.03	0.99
	Model 3	11 or younger	1,165	79.2	10.1	1.81	0.29, 3.33	1.41	0.72, 2.10	0.67
		12-13	3,408	77.4	9.8	Ref		Ref		NA
		14-15	1,649	77.0	10.1	-0.47	-1.63, 0.69	-0.60	-1.21, 0.02	0.77
		16 or higher	281	77.9	10.3	-1.02	-3.52, 1.48	-0.09	-1.22, 1.40	0.65
HDL cholesterol, (mmol/L)	Model 1	11 or younger	1,309	1.538	0.405	-0.065	-0.110, -0.019	-0.045	-0.074, -0.016	0.62
		12-13	3,779	1.592	0.418	Ref		Ref		NA
		14-15	1,854	1.631	0.402	-0.009	-0.051, 0.033	0.044	0.018, 0.070	0.10
		16 or higher	321	1.645	0.433	-0.032	-0.118, 0.053	0.059	0.004, 0.114	0.18

	Model 2	11 or younger	1,309	1.538	0.405	-0.061	-0.106, -0.016	-0.037	-0.066, -0.009	0.53	
		12-13	3,779	1.592	0.418	Ref		Ref		NA	
		14-15	1,854	1.631	0.402	-0.010	-0.052, 0.032	0.045	0.019, 0.070	0.10	
		16 or higher	321	1.645	0.433	-0.032	-0.118, 0.053	0.067	0.013, 0.120	0.14	
	Model 3	11 or younger	1,122	1.551	0.405	-0.042	-0.094, 0.009	-0.038	-0.067, -0.008	0.93	
		12-13	3,251	1.605	0.415	Ref		Ref		NA	
		14-15	1,580	1.644	0.405	-0.011	-0.059, 0.038	0.040	0.014, 0.066	0.18	
		16 or higher	272	1.674	0.440	-0.028	-0.116, 0.061	0.062	0.006, 0.117	0.20	
	Non-HDL cholesterol (mmol/L)	Model 1	11 or younger	1,309	3.636	1.064	0.209	0.086, 0.332	0.065	-0.003, 0.132	0.17
			12-13	3,779	3.509	1.046	Ref		Ref		NA
14-15			1,854	3.496	1.031	0.034	-0.074, 0.142	-0.093	-0.154, -0.033	0.11	
16 or higher			321	3.586	1.008	-0.025	-0.229, 0.179	-0.011	-0.140, 0.118	0.98	
Model 2		11 or younger	1,309	3.636	1.064	0.213	0.094, 0.331	0.053	-0.014, 0.119	0.11	
		12-13	3,779	3.509	1.046	Ref		Ref		NA	
		14-15	1,854	3.496	1.031	0.025	-0.079, 0.128	-0.098	-0.157, -0.038	0.12	
		16 or higher	321	3.586	1.008	-0.019	-0.207, 0.168	-0.035	-0.161, 0.092	0.88	
Model 3		11 or younger	1,122	3.625	1.067	0.152	0.021, 0.284	0.067	-0.003, 0.137	0.42	
		12-13	3,251	3.483	1.034	Ref		Ref		NA	
		14-15	1,580	3.462	1.021	0.00002	-0.120, 0.120	-0.083	-0.145, -0.020	0.35	
		16 or higher	272	3.547	1.002	0.062	-0.280, 0.151	-0.055	-0.188, 0.077	0.96	
Glucose, (mmol/L)*	Model 1	11 or younger	1,289	4.6	4.3, 4.9	-0.721	-2.422, 0.980	1.376	0.474, 2.277	0.11	
		12-13	3,741	4.5	4.3, 4.8	Ref		Ref		NA	
		14-15	1,832	4.6	4.3, 4.8	0.767	-0.632, 2.165	-0.429	-1.237, 0.380	0.32	
		16 or higher	322	4.6	4.3, 4.8	-0.681	-3.770, 2.407	-0.840	-2.550, 0.870	0.91	
	Model 2	11 or younger	1,289	4.6	4.3, 4.9	-0.291	-1.936, 1.354	1.143	0.280, 2.006	0.25	
		12-13	3,741	4.5	4.3, 4.8	Ref		Ref		NA	
		14-15	1,832	4.6	4.3, 4.8	0.886	-0.464, 2.235	-0.317	-1.090, 0.455	0.30	
		16 or higher	322	4.6	4.3, 4.8	-0.796	-3.942, 2.349	-0.917	-2.553, 0.718	0.88	
	Model 3	11 or younger	1,103	4.6	4.3, 4.9	0.008	-1.986, 2.001	1.010	0.121, 1.890	0.44	
		12-13	3,217	4.5	4.3, 4.8	Ref		Ref		NA	
		14-15	1,563	4.6	4.3, 4.8	1.462	-0.071, 2.994	-0.288	-1.083, 0.507	0.17	
		16 or higher	272	4.6	4.3, 4.8	-2.570	-6.233, 1.093	-0.752	-2.434, 0.930	0.54	
Body-mass index (kg/m ²)	Model 1	11 or younger	1,344	28.080	6.176	1.710	1.018, 2.401	1.848	1.481, 2.214	0.74	
		12-13	3,922	26.115	5.212	Ref		Ref		NA	
		14-15	1,929	25.061	4.767	-0.456	-0.961, 0.049	-1.335	-1.660, -1.009	0.02	
		16 or higher	329	25.423	5.402	-0.667	-1.726, 0.392	-1.057	-1.752, -0.361	0.76	

	Model 2	11 or younger	1,344	28.080	6.176	1.653	0.970, 2.335	1.718	1.358, 2.078	0.84	
		12-13	3,922	26.115	5.212	Ref		Ref		NA	
		14-15	1,929	25.061	4.767	-0.452	-0.961, 0.057	-1.330	-1.650, -1.010	0.02	
		16 or higher	329	25.423	5.402	-0.672	-1.724, 0.380	-1.186	-1.870, -0.503	0.65	
	Model 3	11 or younger	1,122	3.625	1.067	1.736	0.985, 2.488	1.642	1.270, 2.014	0.93	
		12-13	3,251	3.483	1.035	Ref		Ref		NA	
		14-15	1,580	3.462	1.022	-0.628	-1.187, -0.069	-1.237	-1.569, -0.906	0.16	
		16 or higher	272	3.547	1.002	-1.429	-2.545, -0.313	-0.956	-1.660, -0.251	0.55	
	Waist circumference, (cm)	Model 1	11 or younger	1,334	88.23	15.33	3.004	1.301, 4.707	3.513	2.559, 4.467	0.61
			12-13	3,906	84.50	13.82	Ref		Ref		NA
			14-15	1,920	82.54	12.69	-0.767	-2.171, 0.638	-2.730	-3.579, -1.881	0.06
			16 or higher	335	83.68	14.56	-1.938	-4.651, 0.776	-1.621	-3.427, 0.184	0.83
Model 2		11 or younger	1,334	88.23	15.33	2.927	1.237, 4.616	3.155	2.217, 4.094	0.77	
		12-13	3,906	84.50	13.82	Ref		Ref		NA	
		14-15	1,920	82.54	12.69	-0.775	-2.181, 0.631	-2.761	-3.595, -1.926	0.06	
		16 or higher	335	83.68	14.56	-1.909	-4.616, 0.797	-2.018	-3.794, -0.241	0.96	
Model 3		11 or younger	1,142	87.65	14.99	2.716	0.936, 4.498	3.056	2.085, 4.027	0.79	
		12-13	3,371	84.08	13.50	Ref		Ref		NA	
		14-15	1,634	81.95	12.15	-1.266	-2.745, 0.212	-2.638	-3.503, -1.773	0.22	
		16 or higher	278	83.07	13.97	-3.056	-5.683, -0.429	-1.656	-3.495, 0.183	0.52	

CI=confidence interval; HDL=high-density lipoprotein; SD=standard deviation.

Model 1 Adjusted for age

Model 2 Adjusted for age, qualifications, parental history of cardiovascular disease and parental history of diabetes. Blood pressure further adjusted for use of antihypertensive drugs, cholesterol levels adjusted for lipid lowering drugs and glucose adjusted for use of antidiabetic drugs.

Model 3 Adjusted for age, qualifications, parental history of cardiovascular disease, parental history of diabetes, smoking, alcohol intake and leisure time physical activity. Blood pressure further adjusted for use of antihypertensive drugs, cholesterol levels adjusted for lipid lowering drugs and glucose adjusted for use of antidiabetic drugs.

* Outcome log transformed and the coefficients reflect the percent change in the outcome.

Table S12. Association Between Age at Menarche and 10-Year Risk For Overall Cardiovascular Disease Excluding Individuals of Non-European ethnicity, the Scottish Family Health Study, 2006-2011.

Risk score	Model	Age at menarche	N	Mean	SD	Within-sibships association		Between-sibships association		Bootstrap p-value for the difference in the within and between sibship association
						β	95% CI	β	95% CI	
Framingham risk score *	Model 1	11 or younger	1,051	26.07	0.90	0.10	0.02, 0.17	0.11	0.06, 0.15	0.80
		12-13	2,956	25.94	0.90	Ref		Ref		NA
		14-15	1,504	25.97	0.92	0.02	-0.04, 0.08	-0.03	-0.07, 0.003	0.24
		16 or higher	267	26.07	0.86	-0.03	-0.15, 0.09	0.05	-0.03, 0.13	0.48
	Model 2	11 or younger	1,051	26.07	0.90	0.09	0.01, 0.16	0.09	0.05, 0.13	0.88
		12-13	2,956	25.94	0.90	Ref		Ref		NA
		14-15	1,504	25.97	0.92	0.02	-0.04, 0.08	-0.04	-0.07, -0.002	0.20
		16 or higher	267	26.07	0.86	-0.03	-0.15, 0.10	0.03	-0.04, 0.10	0.63
	Model 3	11 or younger	902	26.04	0.90	0.08	-0.01, 0.17	0.09	0.05, 0.13	0.88
		12-13	2,538	25.92	0.89	Ref		Ref		NA
		14-15	1,280	25.94	0.91	0.02	-0.05, 0.09	-0.02	-0.06, 0.01	0.39
		16 or higher	227	26.02	0.83	-0.04	-0.18, 0.10	0.02	-0.06, 0.09	0.66
NHANES ECG risk equation score †	Model 1	11 or younger	1,051	7.971	0.846	0.030	-0.004, 0.064	0.018	0.001, 0.035	0.59
		12-13	2,994	7.931	0.847	Ref		Ref		NA
		14-15	1,544	7.976	0.882	0.005	-0.023, 0.032	-0.019	-0.034, -0.004	0.24
		16 or higher	260	8.056	0.803	0.004	-0.057, 0.065	0.024	-0.008, 0.056	0.85
	Model 2	11 or younger	1,051	7.971	0.846	0.031	-0.004, 0.065	0.016	-0.002, 0.033	0.50
		12-13	2,994	7.931	0.847	Ref		Ref		NA
		14-15	1,544	7.976	0.882	0.006	-0.022, 0.033	-0.019	-0.034, -0.004	0.22
		16 or higher	260	8.056	0.803	0.004	-0.057, 0.066	0.022	-0.010, 0.054	0.89
	Model 3	11 or younger	899	7.966	0.846	0.043	0.004, 0.082	0.023	0.006, 0.041	0.46
		12-13	2,571	7.918	0.847	Ref		Ref		NA
		14-15	1,306	7.935	0.866	-0.016	-0.048, 0.016	-0.013	-0.029, 0.003	1.00
		16 or higher	220	8.024	0.765	-0.002	-0.075, 0.071	0.024	-0.008, 0.057	0.80

CI=confidence interval; ECG=electrocardiogram; SD=standard deviation.

* The variables included in the Framingham risk score is age, total cholesterol, HDL cholesterol, systolic blood pressure, smoking and diabetes.

† The information included in the NHANES ECG risk score included age, positive deflection of T axis, negative deflection of the T axis, heart rate and corrected QT interval.

Model 1 Adjusted for age

Model 2 Adjusted for age, qualifications, parental history of cardiovascular disease and parental history of diabetes.

Model 3 Adjusted for all of the covariates in Model 2 in addition to smoking (not adjusted for in the analysis of the Framingham risk score since part of the risk calculation), alcohol intake and leisure time physical activity.

Table S13. Association Between Age at Menarche and Cardiometabolic Health Outcomes Excluding Non-fasting Individuals, the Scottish Family Health Study, 2006-2011.

Outcome	Model	Age at menarche	N	Mean/ Median	SD/Range	Within-sibships association		Between-sibships association		Bootstrap p-value for the difference in the within and between sibship association
						β	95% CI	β	95% CI	
HDL cholesterol, (mmol/L)	Model 1	11 or younger	1,139	1.543	0.411	-0.075	-0.127, -0.024	-0.038	-0.069, -0.008	0.37
		12-13	3,275	1.591	0.414	Ref		Ref		NA
		14-15	1,599	1.623	0.403	-0.030	-0.078, 0.018	0.039	0.011, 0.066	0.07
		16 or higher	274	1.631	0.429	-0.027	-0.117, 0.062	0.048	-0.009, 0.105	0.30
	Model 2	11 or younger	1,139	1.543	0.411	-0.077	-0.128, -0.025	-0.029	-0.059, 0.001	0.24
		12-13	3,275	1.591	0.414	Ref		Ref		NA
		14-15	1,599	1.623	0.403	-0.031	-0.079, 0.017	0.039	0.012, 0.066	0.06
		16 or higher	274	1.631	0.429	-0.028	-0.118, 0.062	0.057	0.001, 0.114	0.25
	Model 3	11 or younger	971	1.556	0.411	-0.065	-0.125, -0.006	-0.024	-0.055, 0.007	0.39
		12-13	2,809	1.602	0.411	Ref		Ref		NA
		14-15	1,367	1.635	0.408	-0.040	-0.095, 0.015	0.042	0.014, 0.069	0.05
		16 or higher	272	1.652	0.431	-0.045	-0.143, 0.054	0.054	-0.004, 0.112	0.21
Non-HDL cholesterol (mmol/L)	Model 1	11 or younger	1,139	3.630	1.058	0.202	0.064, 0.341	0.047	-0.025, 0.119	0.18
		12-13	3,275	3.530	1.050	Ref		Ref		NA
		14-15	1,599	3.511	1.021	0.059	-0.066, 0.184	-0.099	-0.163, -0.034	0.08
		16 or higher	274	3.589	1.006	-0.057	-0.302, 0.188	-0.028	-0.163, 0.107	0.92
	Model 2	11 or younger	1,139	3.630	1.058	0.204	0.072, 0.337	0.033	-0.038, 0.103	0.11
		12-13	3,275	3.530	1.050	Ref		Ref		NA
		14-15	1,599	3.511	1.021	0.046	-0.075, 0.168	-0.101	-0.164, -0.039	0.10
		16 or higher	274	3.589	1.006	-0.043	-0.267, 0.182	-0.044	-0.176, 0.088	0.98
	Model 3	11 or younger	971	3.619	1.062	0.155	0.003, 0.306	0.042	-0.032, 0.116	0.34
		12-13	2,809	3.510	1.042	Ref		Ref		NA
		14-15	1,367	3.472	1.014	0.055	-0.083, 0.193	-0.104	-0.170, -0.038	0.11
		16 or higher	234	3.560	1.009	-0.075	-0.328, 0.178	-0.046	-0.185, 0.093	0.96
Glucose, (mmol/L)*	Model 1	11 or younger	1,125	4.6	4.3, 4.9	-1.351	-2.916, 0.213	1.229	0.398, 2.059	0.04
		12-13	3,248	4.5	4.3, 4.8	Ref		Ref		NA
		14-15	1,583	4.6	4.3, 4.8	-0.095	-1.577, 1.387	-0.504	-1.246, 0.238	0.80
		16 or higher	275	4.6	4.3, 4.8	-0.560	-4.375, 3.256	-0.589	-2.153, 0.975	0.87

	Model 2	11 or younger	1,125	4.6	4.3, 4.9	-0.865	-2.382, 0.653	1.209	0.398, 2.020	0.10
		12-13	3,248	4.5	4.3, 4.8	Ref		Ref		NA
		14-15	1,583	4.6	4.3, 4.8	0.006	-1.385, 1.398	-0.294	-1.019, 0.430	0.81
		16 or higher	275	4.6	4.3, 4.8	-0.682	-4.505, 3.141	-0.437	-1.964, 1.090	0.80
	Model 3	11 or younger	958	4.6	4.3, 4.9	-0.263	-1.966, 1.440	1.087	0.244, 1.930	0.29
		12-13	2,785	4.5	4.3, 4.8	Ref		Ref		NA
		14-15	1,355	4.6	4.3, 4.8	0.479	-1.024, 1.983	-0.332	-1.084, 0.420	0.54
		16 or higher	234	4.6	4.3, 4.8	-3.115	-7.624, 1.394	-0.155	-1.740, 1.430	0.41

CI=confidence interval; HDL=high-density lipoprotein; SD=standard deviation.

Model 1 Adjusted for age

Model 2 Adjusted for age, ethnicity, qualifications, parental history of cardiovascular disease and parental history of diabetes. Blood pressure further adjusted for use of antihypertensive drugs, cholesterol levels adjusted for lipid lowering drugs and glucose adjusted for use of antidiabetic drugs.

Model 3 Adjusted for age, ethnicity qualifications, parental history of cardiovascular disease, parental history of diabetes, smoking, alcohol intake and leisure time physical activity. Blood pressure further adjusted for use of antihypertensive drugs, cholesterol levels adjusted for lipid lowering drugs and glucose adjusted for use of antidiabetic drugs.

* Outcome log transformed and the coefficients reflect the percent change in the outcome.