

## Supplementary materials

### Genetic studies

Supplementary Table 1. Overview of included genetic studies.

First author	Publication year	Population	Sample size	Outcome
Choi <sup>1</sup>	2019	Koreans	400+1288	CAC score
Lu <sup>2</sup>	2012	Chinese Han	1,515+5,019+15,460+11,472	MI
Iribarren <sup>3</sup>	2018	African, Latino, East-Asian	2,098+4,349+4,804	MI, AP, CABG, PCI, CAD death

List of investigated SNPs: rs602633, rs4845625, rs515135, rs1561198, rs2252641, rs7692387, rs10947789, rs12190287, rs2048327, rs3798220, rs12539895, rs264, rs2954029, rs3217992, rs1333049, rs579459, rs2505083, rs2047009, rs501120, rs2246833, rs12413409, rs974819, rs9326246, rs9319428, rs17216473, rs10507391, rs9515203, rs7173743, rs2281727, rs12936587, rs15563, rs1122608, rs2075650, rs445925, rs2123536, rs1842896, rs9349379, rs9268402, rs12524865, rs9632884, rs10757274, rs1333042, rs1333049, rs7136259, rs11066280, rs10757272

### Logistic regression results for different cut-offs of CAC

Supplementary Table 2. Clinical predictors for minimal CAC (>0).

Variable	Univariate			Multivariate		
	OR	95% CI	p-value	OR	95% CI	p-value
Age	1.13	1.11, 1.16	<0.001	1.13	1.11, 1.16	<0.001
Male gender	3.14	2.29, 4.31	<0.001	2.78	1.91, 4.05	<0.001
SBP avg	1.04	1.03, 1.05	<0.001	1.03	1.01, 1.04	<0.001
DBP avg	1.06	1.04, 1.08	<0.001			

Waist circumference	1.02	1.01, 1.03	0.007			
ALT	1.02	1.01, 1.03	<0.001			
AST	1.04	1.02, 1.06	<0.001			
Alkaline phosphate	1.01	1.00, 1.02	0.004			
Bicarbonate	1.07	1.00, 1.16	0.062			
Bilirubin	1.05	1.02, 1.08	0.002			
LDL	1.62	1.34, 1.95	<0.001	1.41	1.13, 1.76	0.002
Total cholesterol	1.51	1.28, 1.77	<0.001			
GGT	1.01	1.00, 1.02	0.003			
Glucose	2.08	1.57, 2.75	<0.001	1.36	1.02, 1.80	0.031
Hb	1.31	1.17, 1.46	<0.001			
Monocytes	3.43	1.16, 10.17	0.026			
Triglycerides	1.52	1.23, 1.88	<0.001			
Urea	1.35	1.18, 1.55	<0.001			
Steps (1000)	1.05	1.01, 1.09	0.026			
eGFR	0.97	0.96, 0.98	<0.001			
Family history IHD	1.55	0.98, 2.46	0.059			
Exercise weekly	1.66	1.17, 2.35	0.004			
Caffeine daily	1.12	1.03, 1.22	0.011			

Supplementary Table 3. Genetic predictors for minimal CAC (>0).

SNP	Univariate			Multivariate		
	OR	95% CI	p-value	OR	95% CI	p-value
Rs12539895	0.72	0.51, 1.00	0.052	0.67	0.47, 0.95	0.026

Rs2505083	0.72	0.54, 0.96	0.028	0.66	0.49, 0.89	0.006
Rs2047009	0.64	0.50, 0.80	<0.001	0.61	0.48, 0.78	<0.001
Rs974819	1.21	0.96, 1.53	0.099			
Rs9319428	0.80	0.63, 1.01	0.068	0.78	0.61, 1.00	0.049
Rs1333042	0.80	0.63, 1.03	0.079			
Rs11066280	0.80	0.63, 1.03	0.084	0.76	0.59, 0.98	0.036
Rs10757272	0.80	0.63, 1.02	0.069	0.78	0.61, 1.00	0.048

Supplementary Table 4. Clinical and genetic predictors for minimal CAC (>0).

Variable	OR	95% CI	p-value
Age	1.15	1.12, 1.18	<0.001
Gender	3.16	2.08, 4.81	<0.001
SBP avg	1.03	1.02, 1.05	<0.001
LDL cholesterol	1.48	1.16, 1.89	0.002
Rs2505083	0.63	0.43, 0.91	0.014
Rs2047009	0.57	0.43, 0.76	<0.001
Rs10757272	0.66	0.49, 0.89	0.006
Rs12539895	0.56	0.36, 0.85	0.007
Rs11066280	0.71	0.52, 0.96	0.002

Supplementary Table 5. Clinical predictors for mild CAC ( $\geq 10$ ).

Variable	Univariate			Multivariate		
	OR	95% CI	p-value	OR	95% CI	p-value
Age	1.16	1.13, 1.19	<0.001	1.16	1.13, 1.19	<0.001

Gender	3.20	2.25, 4.55	<0.001	2.86	1.88, 4.36	<0.001
SBP avg	1.04	1.03, 1.05	<0.001	1.02	1.01, 1.04	0.002
DBP avg	1.05	1.03, 1.07	<0.001			
Waist circumference	1.02	1.00, 1.03	0.018			
ALT	1.02	1.01, 1.03	0.001			
AST	1.04	1.02, 1.06	<0.001			
Alkaline phosphatase	1.01	1.00, 1.02	0.004			
Bilirubin	1.04	1.01, 1.08	0.005			
LDL	1.41	1.16, 1.72	0.001			
Total cholesterol	1.37	1.15, 1.62	<0.001			
GGT	1.01	1.00, 1.02	0.001			
Glucose	2.15	1.60, 2.87	<0.001	1.47	1.08, 1.99	0.014
Hb	1.33	1.18, 1.51	<0.001			
Neutrophils	0.85	0.73, 0.99	0.042			
Triglycerides	1.51	1.21, 1.88	<0.001			
Urea	1.31	1.13, 1.51	<0.001			
Steps/1000	1.04	1.00, 1.09	0.069			
eGFR	0.97	0.96, 0.98	<0.001			
Family history of IHD	1.69	1.04, 2.74	0.035			
Exercise weekly	1.59	1.08, 2.33	0.019			
Caffeine intake	1.11	1.01, 1.21	0.021			
Income	0.92	0.85, 1.00	0.057			

Supplementary Table 6. Genetic predictors for mild CAC ( $\geq 10$ ).

	Univariate	Multivariate
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SNP	OR	95% CI	p-value	OR	95% CI	p-value
Rs1333049	1.29	1.00, 1.66	0.052			
Rs2047009	0.68	0.53, 0.88	0.003	0.68	0.53, 0.87	0.003
Rs11066280	0.77	0.58, 1.00	0.051	0.75	0.57, 0.99	0.045
Rs10757272	0.79	0.61, 1.04	0.92			

Supplementary Table 7. Clinical and genetic predictors for mild CAC ( $\geq 10$ ).

Variable	OR	95% CI	p-value
Age	1.16	1.12, 1.19	<0.001
Gender	3.80	2.31, 6.24	<0.001
SBP avg	1.03	1.02, 1.05	<0.001
Waist circumference	0.97	0.95, 1.00	0.034
Glucose	1.59	1.12, 2.24	0.009
Rs2047009	0.67	0.49, 0.91	0.010

Supplementary Table 8. Clinical predictors for moderate-severe CAC ( $\geq 100$ ).

Variable	Univariate			Multivariate		
	OR	95% CI	p-value	OR	95% CI	p-value
Age	1.18	1.14, 1.23	<0.001	1.18	1.13, 1.23	<0.001
Male gender	4.64	2.62, 8.22	<0.001	5.36	2.64, 1.088	<0.001
SBP avg	1.04	1.03, 1.06	<0.001	1.04	1.01, 1.06	0.003
DBP avg	1.06	1.03, 1.08	<0.001			
Waist circumference	1.02	1.00, 1.04	0.044			

ALT	1.03	1.01, 1.04	<0.001			
AST	1.05	1.03, 1.07	<0.001			
Alkaline phosphate	1.01	1.00, 1.02	0.097			
Bilirubin	1.05	1.01, 1.09	0.025			
LDL	1.45	1.10, 1.91	0.008			
Total cholesterol	1.48	1.17, 1.88	0.001			
GGT	1.01	1.00, 1.01	0.060			
Glucose	1.97	1.42, 2.72	<0.001	1.67	1.14, 2.45	0.009
Hb	1.31	1.11, 1.57	0.002			
Monocytes	4.44	0.93, 21.16	0.061			
Triglycerides	1.48	1.11, 1.96	0.008			
Urea	1.21	0.98, 1.50	0.070			
Steps/1000	1.09	1.03, 1.16	0.005	1.14	1.04, 1.23	0.002
Minutes asleep (100)	1.29	1.00, 1.67	0.049	1.82	1.31, 2.52	0.002
eGFR	0.98	0.96, 0.99	0.009			
Family history IHD	2.36	1.28, 4.36	0.006	2.57	1.19, 5.58	0.017
Smoking	1.51	0.98, 2.32	0.060			
Exercise weekly	1.76	0.98, 3.16	0.060			
Caffeine daily	1.19	1.06, 1.33	0.002			

Supplementary Table 9. Clinical predictors without activity markers for moderate-severe CAC ( $\geq 100$ ).

Variable	OR	95% CI	p-value
Age	1.19	1.14, 1.24	<0.001
Male gender	3.93	2.07, 7.44	<0.001
SBP avg	1.03	1.01, 1.06	0.002

Family history of IHD	2.33	1.13, 4.80	0.002
AST	1.04	1.01, 1.07	0.005

Supplementary Table 10. Genetic predictors for moderate-severe CAC ( $\geq 100$ ).

SNP	Univariate			Multivariate		
	OR	95% CI	p-value	OR	95% CI	p-value
Rs515135	0.43	0.19, 1.00	0.049	0.43	0.18, 0.99	0.046
Rs1333049	1.39	0.97, 1.99	0.076			
Rs2047009	0.68	0.47, 0.97	0.034	0.68	0.47, 0.97	0.020
Rs9632884	0.68	0.45, 1.03	0.069			
Rs1333042	0.62	0.41, 0.93	0.020			
Rs10757272	0.62	0.41, 0.92	0.018	0.62	0.42, 0.93	0.020

Supplementary Table 11. Clinical and genetic predictors for moderate-severe CAC ( $\geq 100$ ).

Variable	OR	95% CI	p-value
Age	1.18	1.12, 1.23	<0.001
Gender	6.01	2.75, 13.11	<0.001
SBP avg	1.04	1.01, 1.06	0.003
Minutes asleep/100	1.88	1.34, 2.66	<0.001
Glucose	1.62	1.07, 2.46	0.023
Steps/1000	1.12	1.03, 1.22	0.010
Family history of IHD	3.27	1.40, 7.62	0.006
Rs9632884	0.42	0.25, 0.71	0.001
Rs515135	0.33	0.11, 0.98	0.047

Supplementary Table 12. Clinical and genetic predictors without activity markers for moderate-severe CAC ( $\geq 100$ ).

Variable	OR	95% CI	p-value
Age	1.19	1.14, 1.25	<0.001
Male gender	4.13	2.09, 8.16	<0.001
SBP avg	1.04	1.01, 1.06	0.002
AST	1.04	1.01, 1.07	0.012
Family history of IHD	2.80	1.29, 6.06	0.009
Rs515135	0.28	0.10, 0.75	0.011
Rs1333042	0.49	0.31, 0.78	0.003

### Performance comparison

Supplementary Table 13. Performance metrics for minimal CAC ( $>0$ ).

Metric	Clinical	Genetic	Combined
Pseudo R2	0.2536	0.0439	0.2940
LL	-370.1407	-415.53352	-303.63708
AIC	752.2814	845.067	627.2742
AUC*	0.8267 (0.79685, 0.85650)	0.6458 (0.60261, 0.68890)	0.8511 (0.82164, 0.88050)
Brier score	0.1448	0.1934	0.1367

Supplementary Table 14. Performance metrics for mild CAC ( $\geq 10$ ).

Metric	Clinical	Genetic	Combined
Pseudo R2	0.2706	0.0173	0.2865
LL	-306.83257	-374.2413	-261.18015
AIC	623.6651	754.4826	536.3603
AUC*	0.8420 (0.81051, 0.87351)	0.5879 (0.53958, 0.63625)	0.8498 (0.81620, 0.88343)
Brier score	0.1215	0.1669	0.1183

Supplementary Table 15. Performance metrics for moderate-severe CAC ( $\geq 100$ ).

Metric	Clinical	Clinical without lifestyle	Genetic	Combined	Combined without lifestyle
Pseudo R2	0.3411	0.3174	0.0343	0.3786	0.3469
LL	-153.7616	-170.93627	-218.17429	-129.92338	-147.4337
AIC	323.5232	353.8725	444.3486	279.8468	310.8674
AUC	0.8914 (0.85212, 0.93063)	0.8853 (0.85181, 0.91883)	0.6420 (0.57652, 0.70743)	0.9086 (0.87277, 0.94438)	0.8995 (0.86801, 0.93093)
Brier score	0.0570	0.0606	0.0831	0.0570	0.0635

### References

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3. Iribarren C, Lu M, Jorgenson E, et al. Weighted Multi-marker Genetic Risk Scores for Incident Coronary Heart Disease among Individuals of African, Latino and East-Asian Ancestry. *Sci Rep* 2018;8:6853. <https://doi.org/10.1038/s41598-018-25128-x>; PMID: 29717161.