

## SUPPLEMENTAL MATERIALS

**Supplementary Table 1.** Unadjusted incidence rates of atherosclerotic cardiovascular disease and all-cause mortality among those with CAC=0 at baseline (median follow up time 15.9 years) stratified by ASCVD risk

Estimated ASCVD risk	ASCVD			All-Cause Mortality		
	<7.5%	7.5%–<15%	15%–<20%	<7.5%	7.5%–<15%	15%–<20%
Cigarette smoking status						
Never	2.02	5.08	2.73	3.30	10.59	15.00
Former	2.17	4.79	6.85	3.28	11.16	20.14
Current	2.25	11.41	14.64	6.99	14.41	15.31
Diabetes mellitus						
No	2.05	6.11	4.04	3.66	11.84	16.17
Yes	3.31	6.84	16.56	3.97	8.79	20.37
Hypertension						
No	1.91	6.16	2.42	3.20	14.39	13.91
Yes	2.49	6.20	6.44	4.68	10.20	17.29
Aspirin use						
No	2.06	6.03	5.98	3.53	11.32	16.46
Yes	3.22	7.34	5.83	4.00	11.65	19.16
Statin use						
No	2.04	6.25	5.18	3.62	11.54	17.46
Yes	2.78	4.74	8.85	4.41	11.36	14.68
Increased waist circumference						
No	1.77	5.67	5.18	2.75	11.12	21.95
Yes	2.19	6.27	8.85	3.94	11.57	16.06
Family history of premature ASCVD						

No	1.82	6.16	4.91	3.56	10.36	16.11
Yes	3.37	7.36	8.10	2.34	13.91	12.45
Chronic kidney disease						
No	1.92	6.42	6.03	3.56	10.48	17.59
Yes	3.95	4.88	5.40	4.85	17.42	14.67
HDL-C $\leq$ 50 mg/dL						
No	1.96	5.45	5.54	4.09	12.34	13.07
Yes	2.23	6.72	6.12	3.20	10.91	19.75
Triglycerides $\geq$ 150 mg/dL						
No	2.00	5.71	6.51	3.77	11.46	16.53
Yes	2.35	7.32	4.46	3.35	11.63	17.50
LDL-C $\geq$ 130 mg/dL						
No	2.05	6.48	7.92	3.94	13.19	17.50
Yes	2.17	5.64	1.14	3.05	8.42	15.20
Lp(a) $\geq$ 50 mg/dL						
No	1.95	6.73	5.18	3.83	12.06	18.93
Yes	2.68	4.57	7.77	3.00	9.89	10.91
hsCRP $\geq$ 2 mg/L						
No	1.79	5.28	8.39	2.84	11.01	17.23
Yes	2.43	6.99	3.41	4.62	11.95	16.43

Abbreviations: CHD (coronary heart disease); HDL-C (high-density lipoprotein cholesterol); LDL-C (low-density lipoprotein cholesterol); Lp(a) (lipoprotein (a)); hsCRP (high-sensitivity C-reactive protein).

Increased waist circumference is defined as  $\geq$ 90 cm for men or  $\geq$ 80 cm for women



No	2.34	3.39	5.13	8.87	3.02	7.36	11.83	30.78
Yes	3.73	5.96	4.90	0.00	2.78	6.54	12.89	26.23
Chronic kidney disease								
No	2.19	3.70	6.00	6.89	3.02	6.94	13.17	41.39
Yes	5.63	7.30	5.44	11.39	4.66	12.71	20.42	42.27
HDL-C $\leq$ 50 mg/dL								
No	1.45	3.71	5.53	9.18	3.06	6.03	13.48	38.87
Yes	3.24	4.54	6.34	7.79	3.21	9.24	16.66	45.66
Triglycerides $\geq$ 150 mg/dL								
No	2.04	3.50	6.37	8.66	3.16	6.50	15.28	41.68
Yes	3.62	5.59	4.43	8.32	3.10	10.26	13.57	41.83
LDL-C $\geq$ 130 mg/dL								
No	2.53	3.99	5.97	9.94	3.36	7.95	14.68	42.43
Yes	2.27	4.41	5.64	5.11	2.69	7.09	15.19	39.74
Lp(a) $\geq$ 50 mg/dL								
No	2.51	3.77	5.73	7.22	2.88	8.60	14.99	41.47
Yes	2.16	5.36	6.30	13.77	4.24	4.45	14.35	42.61
hsCRP $\geq$ 2 mg/L								
No	2.01	3.70	5.53	5.71	2.54	5.87	14.41	39.26
Yes	2.98	4.53	6.19	12.63	3.89	9.27	15.23	45.20

Abbreviations: CHD (coronary heart disease); HDL-C (high-density lipoprotein cholesterol); LDL-C (low-density lipoprotein cholesterol); Lp(a) (lipoprotein (a)); hsCRP (high-sensitivity C-reactive protein).

Increased waist circumference is defined as  $\geq$ 90 cm for men or  $\geq$ 80 cm for women

**Supplementary Table 3.** Multivariable-adjusted hazard ratios (95% confidence interval) for the association of cardiovascular risk factors and incident atherosclerotic cardiovascular disease and all-cause mortality stratified by sex among those with coronary artery calcium 0 at baseline

	<b>Atherosclerotic Cardiovascular Disease</b>		<b>All-Cause Mortality</b>	
	<b>Women</b>	<b>Men</b>	<b>Women</b>	<b>Men</b>
Cigarette smoking status				
Never	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Former	0.71 (0.40,1.27)	1.56 (0.81,2.98)	0.95 (0.64,1.42)	1.15 (0.74,1.77)
Current	1.69 (0.89,3.22)	<b>2.65</b> <b>(1.23,5.68)</b>	<b>2.75</b> <b>(1.70,4.47)</b>	<b>2.82</b> <b>(1.67,4.47)</b>
Diabetes mellitus	1.45 (0.69,3.09)	1.93 (0.94,3.99)	0.98 (0.57,1.69)	1.40 (0.83,2.38)
Hypertension	1.66 (0.98,2.80)	1.60 (0.86,2.96)	<b>1.52</b> <b>(1.05,2.22)</b>	1.32 (0.86,2.03)
Aspirin use	1.18 (0.65,2.15)	1.03 (0.48,2.22)	0.70 (0.44,1.10)	0.96 (0.59,1.57)
Time varying statin use	0.71 (0.41,1.24)	0.95 (0.49,1.83)	0.88 (0.60,1.28)	0.70 (0.45,1.09)
Waist circumference, per 10 cm	1.07 (0.91,1.25)	1.12 (0.87,1.44)	<b>1.16</b> <b>(1.04,1.30)</b>	0.99 (0.82,1.20)
Family history of premature ASCVD	<b>1.69</b> <b>(1.03,2.77)</b>	0.71 (0.32,1.60)	0.68 (0.43,1.09)	1.10 (0.66,1.85)
Chronic kidney disease	0.97 (0.52,1.82)	1.62 (0.79,3.29)	1.04 (0.69,1.56)	1.37 (0.87,2.17)
HDL-C, per 10 mg/dL	0.88 (0.73,1.05)	0.95 (0.71,1.28)	0.96 (0.85,1.08)	0.95 (0.79,1.15)
Triglycerides, per 10 mg/dL	1.00 (0.96,1.04)	0.99 (0.94,1.04)	0.97 (0.94,1.00)	1.01 (0.98,1.05)

LDL-C, per 10 mg/dL	1.01 (0.93,1.09)	0.97 (0.88,1.07)	0.95 (0.90,1.01)	0.99 (0.93,1.06)
*Lp(a), per 5 mg/dL	0.99 (0.33,2.96)	1.18 (0.30,4.66)	1.29 (0.58,2.90)	1.03 (0.40,2.62)
*hsCRP, per mg/L	0.93 (0.75,1.16)	1.06 (0.80,1.41)	1.10 (0.94,1.29)	1.19 (0.99,1.42)

Abbreviations: SBP (systolic blood pressure); CHD (coronary heart disease); HDL-C (high-density lipoprotein cholesterol); LDL-C (low-density lipoprotein cholesterol); Lp(a) (lipoprotein (a)); hsCRP (high-sensitivity C-reactive protein)

\*Lp(a) and hsCRP are log-transformed

Model is adjusted for age, sex, race/ethnicity, education, presence of healthcare insurance, and all listed risk factors

**BOLDED** items are significant statistically significant ( $P < 0.05$ )

**Supplementary Table 4.** Multivariable-adjusted hazard ratios (95% confidence interval) for the association of cardiovascular risk factors and incident coronary heart disease and stroke among those with coronary artery calcium 0 at baseline

	<b>Coronary Heart Disease</b>	<b>Stroke</b>
Cigarette smoking status		
Never	1.00 (ref)	1.00 (ref)
Former	1.19 (0.68,2.06)	0.98 (0.55,1.73)
Current	<b>2.19 (1.14,4.17)</b>	1.85 (0.93,3.71)
Diabetes mellitus	1.77 (0.89,3.51)	1.56 (0.74,3.25)
Hypertension	1.33 (0.78,2.27)	<b>1.91 (1.09,3.35)</b>
Aspirin use	0.79 (0.40,1.59)	1.62 (0.89,2.94)
Time varying statin use	0.95 (0.55,1.64)	0.70 (0.38,1.30)
Waist circumference, per 10 cm	1.14 (0.96,1.36)	0.98 (0.80,1.19)
Family history of premature ASCVD	1.25 (0.72,2.18)	1.39 (0.78,2.47)
Chronic kidney disease	1.23 (0.66,2.29)	1.27 (0.67,2.43)
HDL-C, per 10 mg/dL	1.01 (0.83,1.23)	0.86 (0.70,1.07)
Triglycerides, per 10 mg/dL	1.01 (0.97,1.05)	0.98 (0.94,1.03)
LDL-C, per 10 mg/dL	1.00 (0.92,1.09)	0.97 (0.89,1.05)
*Lp(a), per 5 mg/dL	0.71 (0.23,2.23)	1.96 (0.59,6.52)
*hsCRP, per mg/L	0.96 (0.76,1.21)	1.03 (0.80,1.31)

Abbreviations: SBP (systolic blood pressure); CHD (coronary heart disease); HDL-C (high-density lipoprotein cholesterol); LDL-C (low-density lipoprotein cholesterol); Lp(a) (lipoprotein (a)); hsCRP (high-sensitivity C-reactive protein).

\*Lp(a) and hsCRP are log-transformed

Model is adjusted for age, sex, race/ethnicity, education, presence of healthcare insurance, and all listed risk factors

**BOLDED** items are significant statistically significant (P < 0.05)