Web Table 1: The correlation between free protein S concentration, clinical and laboratory characteristics

	Correlation with free protein S r	P-value
Age (years)	-0.01	0.476
BMI (kg/m^2)	0.12	<0.001
SBP (mmHg)	0.10	<0.001
DBP (mmHg)	0.09	<0.001
Alcohol (Units/Week)	0.12	<0.001
Lipids		
TC (mmol/L)	0.21	<0.001
TG (mmol/L)	0.18	<0.001
HDL-C (mmol/L)	-0.01	0.526
LDL-C (mmol/L)	0.10	<0.001
Hemostatic and inflammation		
Fibrinogen (g/L)	-0.01	0.708
FVIIa (ng/mL)	-0.05	0.227
FVIIag (% standard)	0.06	0.005
FVIIc (% standard)	0.08	<0.001
FXIIa (ng/mL)	0.14	<0.001
FXpep (pmol/L)	-0.04	0.263
FIXpep (pmol/L)	0.01	0.776
F 1+2 (µmol/L)	0.01	0.643
FpA (µmol/L)	0.05	0.005
Creatinine (µmol/L)	0.03	0.150
CRP (mg/l)	0.07	<0.001

BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressures; TC; Total Cholesterol; TG, Triglyceride; HDL-C, HDL Cholesterol; LDL-C, LDL Cholesterol; FVIIa Factor VII activated; FVIIag, Factor VII antigen; FVIIc, Factor VII coagulant activity; FXIIa, Activated factor XII; FXpep, peptides released upon activation of factor X; FIXpep, Factor IX activation peptide; F 1+2, Factor 1+2; FpA, Fibrinopeptide A; CRP, C-Reactive protein.

Web Table 2: The association between average free protein S CHD and stroke modeled by restricted cubic spline construction

Free Protein S (%)	Median	Number of CHD n (%)	Unadjusted model HR (95% CI), *P*-value	Adjusted model [a] HR (95% CI), *P*-value
CHD				
≤ 97	85	45 (15.2%)	1 (Ref.)	1 (Ref.)
98-106	102	39 (13.1%)	1.32 (0.90, 1.93), 0.154	1.23 (0.83, 1.82), 0.301
107-113	110	68 (22.9%)	1.92 (1.25, 2.92), 0.003	1.72 (1.08, 2.74), 0.022
114-123	120	72 (24.2%)	1.90 (1.27, 2.83), 0.002	1.55 (1.00, 2.42), 0.052
124-194	138	73 (24.6%)	2.56 (1.69, 3.86), <0.001	1.87 (1.18, 2.96), 0.008
P-for trend		<0.001	--	--
Stroke				
≤ 97	85	16 (16.7%)	1 (Ref.)	1 (Ref.)
98-106	102	22 (20.8%)	1.54 (0.70, 3.36), 0.281	1.14 (0.50, 2.56), 0.753
107-113	110	23 (22.9%)	1.17 (0.53, 2.59), 0.698	0.82 (0.35, 1.91), 0.647
114-123	120	19 (18.8%)	1.45 (0.68, 3.10), 0.337	0.94 (0.41, 2.13), 0.883
124-194	138	16 (20.8%)	1.52 (0.66, 3.51), 0.326	0.85 (0.34, 2.15), 0.730
P-for trend		0.628	--	--

Average free protein S, average of 6 annual measures during the study; HR, hazard ratio; CI, confidence interval 95%; Ref., reference group.

Free protein S was modeled by restricted cubic splines with 5 knots (85; 102; 110; 120; 138) at percentiles 5%, 27%, 50%, 73% and 95% in a Cox proportional hazards model. The value of 85 % standard was used as referent for the estimation of all hazard ratios.

[a] Adjusted model for age, clinic, BMI, diabetes, smoking, HDL-C, total cholesterol, systolic blood pressure and lipid/blood pressure lowering medications.