

## **High levels of high-sensitivity C-reactive protein to albumin ratio can increase the risk of cardiovascular disease**

### **Supplementary Material**

Table of contents

Supplementary Table 1. The International Statistical Classification of Diseases and Related Health Problems

10th Revision (ICD-10) coding of the disease.

Supplementary Table 2. Stratified analysis: Cox proportional hazards model analysis of the incidence of end-point events in different CAR groups.

Supplementary Table 3. Cox proportional hazards model analysis of the incidence of end-point events in different CAR groups (sensitivity analysis: hypertensive, hypoglycemic, and lipid-lowering drugs were excluded).

Supplementary Table 4. Cox proportional hazards model analysis of the incidence of end-point events in different CAR groups (sensitivity analysis: hs-CRP>10mg/L were excluded).

Supplementary Table 5. Cox proportional hazards model analysis of the incidence of end-point events in different CAR groups (sensitivity analysis: HbsAg (+) were excluded).

Supplementary Table 6. Cox proportional hazards model analysis of the incidence of end-point events in different CAR groups (competing risk model for death).

Supplementary Table 7. C-index, NRI and IDI of different indicators for end-point events.

Supplementary figure 1. Cumulative Incidence (%) of CVD (2A), myocardial infarction (2B), stroke (2C) and ischemic stroke (2D).

Supplementary figure 2. Cumulative Incidence (%) of hemorrhagic Stroke by CAR.

**Related definitions**

Hypertension: systolic blood pressure  $\geq 140$  mmHg and/or diastolic blood pressure  $\geq 90$  mmHg, or a history of medically diagnosed hypertension who took hypertensive drugs.

Diabetes: fasting blood glucose  $\geq 7.0$  mmol/L, and (or)  $< 7.0$  mmol/L but has a confirmed history of diabetes or is taking hypoglycemic drugs.

Smoker: included smoking cessation and current smoking, and smoking cessation is defined as having smoked but having given up smoking for more than one year; Smoking is defined as smoking at least one cigarette per day on average for the past year.

Alcohol intake: the daily intake of pure alcohol exceeding 36 mL.

Physical exercise: taking physical exercise occasionally or frequently.

Higher education: college degree or above.

Family history of cardiovascular disease: patients' father or mother had a myocardial infarction or stroke.

All-cause death: death due to any cause (except for accidental injury) during the follow-up period, and information on death events was obtained through Kailuan Social Security Information System every year.

Body Mass Index (BMI): calculated by dividing weight (kg) by the square of height (m).

**Supplementary Table 1 The International Statistical Classification of Diseases and Related Health****Problems 10th Revision (ICD-10) coding of the disease**

Diseases	ICD-10
Acute myocardial infarction	I21
Ischemic stroke	I63
Subarachnoid hemorrhage stroke	I60
Cerebral hemorrhage stroke	I61

Supplementary Table 2 Stratified analysis: Cox proportional hazards model analysis of the incidence of end-point events in different CAR groups.

Stratification variables	Groups	Events/total population	Incidence density/10 <sup>3</sup> person-years	CVD	
				HR (95% CI)	P for interaction*
Gender					0.190
Male	Q1	682/11,415	5.83	Ref	
	Q2	779/11,199	6.76	0.96(0.87-1.07)	
	Q3	912/11,858	7.52	1.06(0.96-1.17)	
	Q4	1110/12,031	9.20	<b>1.26(1.14-1.39)</b>	
Female	Q1	91/4199	2.04	Ref	
	Q2	152/4220	3.38	1.17(0.90-1.52)	
	Q3	131/3661	3.36	1.01(0.77-1.33)	
	Q4	168/3484	4.57	1.17(0.90-1.53)	
Age					0.002
<60 years	Q1	448/12,291	3.44	Ref	
	Q2	496/11,028	4.21	1.042(0.92-1.19)	
	Q3	619/11,436	5.07	1.097(0.97-1.24)	
	Q4	754/11,127	6.41	<b>1.33(1.12-1.50)</b>	
≥60years	Q1	325/3323	10.42	Ref	
	Q2	435/4391	10.29	0.96(0.81-1.08)	
	Q3	424/4083	11.09	0.99(0.85-1.15)	
	Q4	524/4388	13.17	<b>1.16(1.00-1.33)</b>	
Taking cardiovascular medicines					0.07
Yes	Q1	280/2770	10.09	Ref	
	Q2	380/3572	10.55	1.02(0.87-1.19)	
	Q3	415/3799	10.92	1.04(0.89-1.21)	

	Q4	530/4215	12.89	<b>1.19(1.02-1.38)</b>
	Q1	493/12,844	3.69	Ref
No	Q2	551/11,847	4.44	0.96(0.85-1.08)
	Q3	628/11,720	5.14	1.05(0.93-1.19)
	Q4	748/11,300	6.43	<b>1.28(1.14-1.44)</b>

Model adjusted for age (continuous), gender (male or female, smoking (yes or no), alcohol intake  $\geq 36$  mL/d (yes or no), physical exercise (yes or no), higher education (yes or no), body mass index ( $< 28$  kg/m<sup>2</sup>,  $\geq 28$  kg/m<sup>2</sup>), hypertension (yes or no), diabetes (yes or no), low-density lipoprotein cholesterol (continuous), high-density lipoprotein cholesterol (continuous), estimated glomerular filtration rate ( $< 60$  mL/min,  $\geq 60$  mL/min), alanine aminotransferase (continuous), hypertensive drugs (yes or no), hypoglycemic drugs (yes or no), and lipid-lowering drugs (yes or no). Abbreviations: CAR, high-sensitivity C-reactive protein to albumin ratio; CVD, cardiovascular disease. Bold font indicated statistical significance with  $p < 0.05$ . \* Multiplicative interaction terms for different arrhythmias and covariates were constructed in the Cox model to calculate  $P$  values for interaction.

**Supplementary Table 3 Cox proportional hazards model analysis of the incidence of end-point events in different CAR groups (sensitivity analysis: hypertensive, hypoglycemic, and lipid-lowering drugs were excluded).**

CAR Groups	Events/total population	Incidence density/103 person-years	Model 1		Model 2		Model 3		Model 4	
			HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>
CVD										
Q1	451/12,501	3.46	Ref		Ref		Ref		Ref	
Q2	513/11,438	4.27	1.07 (0.94-1.22)	0.30	1.01 (0.89-1.14)	0.93	1.01 (0.89-1.14)	0.77	1.01 (0.89-1.14)	0.79
Q3	588/11,342	4.96	1.31 (1.16-1.48)	<0.001	1.11 (0.98-1.25)	0.12	1.11 (0.98-1.25)	0.26	1.11 (0.98-1.25)	0.05
Q4	704/10,906	6.25	1.63 (1.45-1.83)	<0.001	1.34 (1.19-1.51)	<0.001	1.34 (1.19-1.51)	<0.001	1.34 (1.16-1.54)	<0.001
<i>P</i> for trend				<0.001		<0.001		<0.001		<0.001
Increase 1SD			1.09 (1.06-1.12)	<0.001	1.06 (1.03-1.10)	<0.001	1.07 (1.04-1.10)	<0.001	1.05 (1.00-1.09)	0.03
Myocardial Infarction										
Q1	80/12,501	0.61	Ref		Ref		Ref		Ref	
Q2	90/11,438	0.75	1.05 (0.78-1.43)	0.74	0.94 (0.71-1.31)	0.83	0.94 (0.71-1.31)	0.83	0.97 (0.71-1.31)	0.83
Q3	126/11,342	1.06	1.56 (1.19-2.09)	<0.001	1.31 (0.99-1.74)	0.06	1.31 (0.99-1.74)	0.06	1.31 (0.99-1.74)	0.06
Q4	167/10,906	1.48	2.15 (1.65-2.81)	<0.001	1.79 (1.36-2.35)	<0.001	1.79 (1.36-2.35)	<0.001	1.75 (1.28-2.38)	<0.001
<i>P</i> for trend				<0.001		<0.001		<0.001		<0.001
Increase 1SD			1.14 (1.09-1.20)	<0.001	1.13 (1.08-1.20)	<0.001	1.14 (1.08-1.20)	<0.001	1.11 (1.03-1.19)	<0.001
Stroke										
Q1	371/12,501	2.84	Ref		Ref		Ref		Ref	
Q2	423/11,438	3.52	1.07 (0.93-1.24)	0.32	1.01 (0.88-1.17)	0.85	1.01 (0.88-1.17)	0.85	1.01 (0.88-1.17)	0.85
Q3	463/11,342	3.90	1.26 (1.10-1.44)	<0.001	1.06 (0.92-1.22)	0.39	1.06 (0.92-1.22)	0.39	1.06 (0.93-1.22)	0.39
Q4	537/10,906	4.77	1.51 (1.33-1.73)	<0.001	1.24 (1.09-1.42)	<0.001	1.24 (1.09-1.42)	<0.001	1.25 (1.07-1.47)	<0.001
<i>P</i> for trend				<0.001		<0.001		<0.001		0.02
Increase 1SD			1.07 (1.03-1.11)	<0.001	1.05 (1.00-1.09)	0.03	1.05 (1.00-1.09)	0.03	1.03 (0.97-1.08)	0.37
Hemorrhagic stroke										
Q1	56/12,501	0.43	Ref		Ref		Ref		Ref	
Q2	49/11,438	0.41	0.84 (0.57-1.23)	0.37	0.82 (0.56-1.21)	0.31	0.82 (0.56-1.21)	0.31	0.82 (0.56-1.21)	0.32
Q3	60/11,342	0.51	1.09 (0.76-1.57)	0.64	0.97 (0.67-1.40)	0.86	0.97 (0.67-1.40)	0.86	0.97 (0.67-1.40)	0.87
Q4	71/10,906	0.63	1.35 (0.95-1.91)	0.10	1.17 (0.82-1.67)	0.40	1.17 (0.82-1.67)	0.40	1.25 (0.82-1.90)	0.29
<i>P</i> for trend				0.06		0.34		0.33		0.40
Increase 1SD			1.07 (0.97-1.18)	0.18	1.05 (0.94-1.17)	0.38	1.05 (0.94-1.17)	0.38	1.05 (0.92-1.21)	0.52
Ischemic stroke										

Q1	323/12,501	2.48	Ref		Ref		Ref		Ref	
Q2	382/11,438	3.18	1.11 (0.96-1.29)	0.17	1.04 (0.90-1.21)	0.57	1.04 (0.90-1.21)	0.57	1.04 (0.90-1.21)	0.57
Q3	410/11,342	3.46	1.28 (1.10-1.48)	<0.001	1.07 (0.93-1.24)	0.35	1.07 (0.93-1.24)	0.35	1.07 (0.93-1.24)	0.35
Q4	479/10,906	4.25	1.55 (1.34-1.78)	<0.001	1.27 (1.10-1.46)	<0.001	1.27 (1.10-1.46)	<0.001	1.26 (1.07-1.49)	<0.001
<i>P</i> for trend				<0.001		<0.001		0.02		0.02
Increase 1SD			1.07 (1.03-1.11)	<0.001	1.05 (1.00-1.09)	0.04	1.05 (1.00-1.09)	0.04	1.02 (0.96-1.08)	0.50

Model 1 adjusted for age (continuous) and gender (male or female); Model 2 further adjusted for smoking (yes or no), alcohol intake  $\geq 36$  mL/d (yes or no), physical exercise (yes or no), higher education (yes or no), body mass index ( $< 28$  kg/m<sup>2</sup>,  $\geq 28$  kg/m<sup>2</sup>), hypertension (yes or no), diabetes (yes or no), low-density lipoprotein cholesterol (continuous), high-density lipoprotein cholesterol (continuous), estimated glomerular filtration rate ( $< 60$  mL/min,  $\geq 60$  mL/min), alanine aminotransferase (continuous) on the basis of model 1; Model 3 further adjusted for hypertensive drugs (yes or no), hypoglycemic drugs (yes or no), and lipid-lowering drugs (yes or no) on the basis of model 2; Model 4 further adjusted for hs-CRP (continuous) and albumin (continuous) in 2010 based on model 3. Abbreviations: CAR, high-sensitivity C-reactive protein to albumin ratio; CVD, cardiovascular disease; Increase 1SD, increase high-sensitivity C-reactive protein to albumin ratio by 1-unit standard deviation.

**Supplementary Table 4 Cox proportional hazards model analysis of the incidence of end-point events in different CAR groups (sensitivity analysis: hs-CRP>10mg/L were excluded)**

CAR Groups	Events/total population	Incidence density/10 <sup>3</sup> person-years	Model 1		Model 2		Model 3		Model 4	
			HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>
<b>CVD</b>										
Q1	773/15,614	4.79	Ref		Ref		Ref		Ref	
Q2	931/15,419	5.82	1.08 (0.98-1.19)	0.11	1.01 (0.91-1.11)	0.91	1.00 (0.91-1.10)	0.96	1.00 (0.91-1.10)	0.96
Q3	1043/15,519	6.51	1.26 (1.15-1.38)	<0.001	1.07 (0.98-1.18)	0.14	1.07 (0.97-1.18)	0.16	1.07 (0.97-1.18)	0.16
Q4	1067/13,176	7.95	1.52 (1.39-1.67)	<0.001	1.24 (1.13-1.37)	<0.001	1.24 (1.13-1.36)	<0.001	1.24 (1.11-1.38)	<0.001
<i>P</i> for trend				<0.001		<0.001		<0.001		<0.001
Increase 1SD			1.35 (1.26-1.45)	<0.001	1.19 (1.11-1.27)	<0.001	1.18 (1.10-1.27)	<0.001	1.26 (1.12-1.42)	<0.001
<b>Myocardial Infarction</b>										
Q1	143/15,614	0.89	Ref		Ref		Ref		Ref	
Q2	153/15,419	0.96	0.96 (0.76-1.21)	0.72	0.87 (0.69-1.10)	0.24	0.86 (0.69-1.09)	0.21	0.87 (0.69-1.09)	0.22
Q3	215/15,519	1.34	1.40 (1.14-1.73)	<0.001	1.17 (0.94-1.45)	0.15	1.16 (0.94-1.44)	0.17	1.16 (0.94-1.45)	0.16
Q4	255/13,176	1.90	1.95 (1.59-2.40)	<0.001	1.58 (1.28-1.95)	<0.001	1.57 (1.27-1.94)	<0.001	1.62 (1.29-2.04)	<0.001
<i>P</i> for trend				<0.001		<0.001		<0.001		<0.001
Increase 1SD			1.66 (1.44-1.91)	<0.001	1.48 (1.27-1.71)	<0.001	1.47 (1.27-1.47)	<0.001	1.87 (1.46-2.40)	<0.001
<b>Stroke</b>										
Q1	630/15,614	3.90	Ref		Ref		Ref		Ref	
Q2	778/15,419	4.86	1.11 (1.00-1.23)	0.06	1.04 (0.93-1.15)	0.51	1.03 (0.93-1.14)	0.61	1.03 (0.93-1.14)	0.62
Q3	830/15,519	5.18	1.23 (1.11-1.37)	<0.001	1.05 (0.95-1.17)	0.34	1.05 (0.95-1.17)	0.36	1.05 (0.95-1.17)	0.36
Q4	813/13,176	6.06	1.42 (1.28-1.58)	<0.001	1.17 (1.05-1.30)	<0.001	1.16 (1.04-1.29)	<0.001	1.15 (1.02-1.30)	0.02
<i>P</i> for trend				<0.001		<0.001		0.03		0.03
Increase 1SD			1.28 (1.18-1.38)	<0.001	1.12 (1.03-1.21)	<0.001	1.12 (1.03-1.21)	<0.001	1.14 (1.00-1.30)	0.05
<b>Hemorrhagic stroke</b>										
Q1	98/15,614	0.61	Ref		Ref		Ref		Ref	
Q2	92/15,419	0.57	0.85 (0.63-1.13)	0.25	0.81 (0.61-1.08)	0.16	0.81 (0.61-1.07)	0.14	0.81 (0.61-1.07)	0.14
Q3	105/15,519	0.66	1.01 (0.76-1.32)	0.97	0.89 (0.70-1.17)	0.39	0.88 (0.67-1.16)	0.37	0.88 (0.67-1.17)	0.38
Q4	100/13,176	0.75	1.13 (0.85-1.49)	0.40	0.96 (0.72-1.27)	0.76	0.95 (0.71-1.26)	0.70	0.99 (0.71-1.37)	0.94
<i>P</i> for trend				0.24		0.93		0.88		0.93
Increase 1SD			1.18 (0.95-1.47)	0.14	1.05 (0.84-1.32)	0.68	1.04 (0.83-1.31)	0.73	1.15 (0.80-1.67)	0.46
<b>Ischemic stroke</b>										



Q1	548/15,614	3.39	Ref		Ref		Ref		Ref	
Q2	701/15,419	4.38	1.15 (1.02-1.28)	0.02	1.07 (0.95-1.20)	0.26	1.06 (0.95-1.19)	0.32	1.06 (0.95-1.19)	0.32
Q3	745/15,519	4.65	1.27 (1.14-1.41)	<0.001	1.08 (0.97-1.21)	0.17	1.08 (0.97-1.21)	0.18	1.08 (0.96-1.21)	0.19
Q4	731/13,176	5.45	1.47 (1.32-1.64)	<0.001	1.20 (1.07-1.34)	<0.001	1.19 (1.07-1.34)	<0.001	1.19 (1.05-1.35)	<0.001
<i>P</i> for trend				<0.001		<0.001		<0.001		0.01
Increase 1SD			1.29 (1.19-1.40)	<0.001	1.13 (1.04-1.23)	<0.001	1.13 (1.04-1.23)	<0.001	1.16 (1.01-1.33)	0.04

Model 1 adjusted for age (continuous) and gender (male or female); Model 2 further adjusted for smoking (yes or no), alcohol intake  $\geq 36$  mL/d (yes or no), physical exercise (yes or no), higher education (yes or no), body mass index ( $< 28$  kg/m<sup>2</sup>,  $\geq 28$  kg/m<sup>2</sup>), hypertension (yes or no), diabetes (yes or no), low-density lipoprotein cholesterol (continuous), high-density lipoprotein cholesterol (continuous), estimated glomerular filtration rate ( $< 60$  mL/min,  $\geq 60$  mL/min), alanine aminotransferase (continuous) on the basis of model 1; Model 3 further adjusted for hypertensive drugs (yes or no), hypoglycemic drugs (yes or no), and lipid-lowering drugs (yes or no) on the basis of model 2; Model 4 further adjusted for hs-CRP (continuous) and albumin (continuous) in 2010 based on model 3. Abbreviations: CAR, high-sensitivity C-reactive protein to albumin ratio; CVD, cardiovascular disease; Increase 1SD, increase high-sensitivity C-reactive protein to albumin ratio by 1-unit standard deviation.

**Supplementary Table 5 Cox proportional hazards model analysis of the incidence of end-point events in different CAR groups (sensitivity analysis:****HbsAg (+) were excluded)**

CAR Groups	Events/total population	Incidence density/10 <sup>3</sup> person-years	Model 1		Model 2		Model 3		Model 4	
			HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>
<b>CVD</b>										
Q1	600/11,785	4.94	Ref		Ref		Ref		Ref	
Q2	730/11,675	6.02	1.13 (1.01-1.26)	0.03	1.04 (0.93-1.16)	0.50	1.03 (0.92-1.15)	0.63	1.03 (0.92-1.14)	0.64
Q3	846/12,054	6.81	1.29 (1.16-1.43)	<0.001	1.11 (1.00-1.24)	0.04	1.11 (1.00-1.24)	0.05	1.11 (1.00-1.23)	0.05
Q4	1041/12,328	8.33	1.55 (1.40-1.71)	<0.001	1.29 (1.16-1.42)	<0.001	1.28 (1.15-1.41)	<0.001	1.26 (1.11-1.42)	<0.001
<i>P</i> for trend				<0.001		<0.001		<0.001		<0.001
Increase 1SD			1.07 (1.04-1.10)	<0.001	1.05 (1.02-1.08)	<0.001	1.05 (1.02-1.07)	<0.001	1.02 (0.98-1.06)	0.42
<b>Myocardial Infarction</b>										
Q1	117/11,785	0.96	Ref		Ref		Ref		Ref	
Q2	113/11,675	0.93	0.91 (0.70-1.18)	0.47	0.81 (0.63-1.05)	0.12	0.81 (0.62-1.04)	0.10	0.81 (0.62-1.04)	0.10
Q3	169/12,054	1.36	1.32 (1.05-1.68)	0.02	1.12 (0.88-1.42)	0.34	1.12 (0.88-1.42)	0.35	1.12 (0.88-1.42)	0.35
Q4	253/12,328	2.03	1.93 (1.55-2.40)	<0.001	1.59 (1.28-1.99)	<0.001	1.59 (1.27-1.99)	<0.001	1.56 (1.21-2.01)	<0.001
<i>P</i> for trend				<0.001		<0.001		<0.001		<0.001
Increase 1SD			1.12 (1.07-1.17)	<0.001	1.11 (1.05-1.16)	<0.001	1.11 (1.05-1.16)	<0.001	1.05 (0.98-1.13)	0.17
<b>Stroke</b>										
Q1	483/11,785	3.98	Ref		Ref		Ref		Ref	
Q2	617/11,675	5.09	1.18 (1.05-1.33)	<0.001	1.09 (0.97-1.23)	0.15	1.08 (0.96-1.22)	0.20	1.08 (0.96-1.22)	0.21
Q3	679/12,054	5.47	1.28 (1.14-1.44)	<0.001	1.11 (0.99-1.25)	0.07	1.11 (0.99-1.25)	0.08	1.11 (0.99-1.25)	0.08
Q4	789/12,328	6.32	1.46 (1.30-1.63)	<0.001	1.21 (1.08-1.36)	<0.001	1.20 (1.07-1.35)	<0.001	1.18 (1.03-1.36)	0.01
<i>P</i> for trend				<0.001		<0.001		<0.001		0.01
Increase 1SD			1.06 (1.02-1.09)	<0.001	1.03 (0.99-1.06)	0.13	1.03 (0.99-1.06)	0.14	1.00 (0.96-1.05)	0.86
<b>Hemorrhagic stroke</b>										
Q1	73/11,785	0.60	Ref		Ref		Ref		Ref	
Q2	74/11,675	0.61	0.95 (0.69-1.31)	0.75	0.91 (0.95-1.25)	0.55	0.89 (0.65-1.24)	0.55	0.90 (0.65-1.24)	0.50
Q3	82/12,054	0.66	1.03 (0.75-1.41)	0.85	0.92 (0.67-1.27)	0.63	0.92 (0.67-1.26)	0.63	0.92 (0.67-1.27)	0.61
Q4	91/12,328	0.73	1.11 (0.82-1.52)	0.49	0.96 (0.70-1.32)	0.82	0.95 (0.69-1.30)	0.83	1.02 (0.71-1.48)	0.91
<i>P</i> for trend				0.40		0.90		0.85		0.97
Increase 1SD			1.02 (0.92-1.13)	0.68	0.99 (0.89-1.11)	0.92	0.99 (0.89-1.11)	0.90	1.02 (0.88-1.17)	0.81
<b>Ischemic stroke</b>										

			Ref		Ref		Ref		Ref	
Q1	422/11,785	3.47								
Q2	553/11,675	4.56	1.21 (1.07-1.37)	<0.001	1.11 (0.98-1.26)	0.10	1.10 (0.97-1.25)	0.14	1.10 (0.97-1.25)	0.14
Q3	614/12,054	4.94	1.33 (1.18-1.50)	<0.001	1.15 (1.01-1.30)	0.03	1.14 (1.01-1.30)	0.04	1.14 (1.01-1.30)	0.04
Q4	715/12,328	5.72	1.51 (1.34-1.70)	<0.001	1.25 (1.10-1.41)	<0.001	1.24 (1.10-1.40)	<0.001	1.22 (1.06-1.41)	<0.001
<i>P</i> for trend				<0.001		<0.001		<0.001		<0.001
Increase 1SD			1.06 (1.03-1.09)	<0.001	1.03 (1.00-1.07)	0.07	1.03 (1.00-1.07)	0.08	1.01 (0.96-1.06)	0.65

Model 1 adjusted for age (continuous) and gender (male or female); Model 2 further adjusted for smoking (yes or no), alcohol intake  $\geq 36$  mL/d (yes or no), physical exercise (yes or no), higher education (yes or no), body mass index ( $< 28$  kg/m<sup>2</sup>,  $\geq 28$  kg/m<sup>2</sup>), hypertension (yes or no), diabetes (yes or no), low-density lipoprotein cholesterol (continuous), high-density lipoprotein cholesterol (continuous), estimated glomerular filtration rate ( $< 60$  mL/min,  $\geq 60$  mL/min), alanine aminotransferase (continuous) on the basis of model 1; Model 3 further adjusted for hypertensive drugs (yes or no), hypoglycemic drugs (yes or no), and lipid-lowering drugs (yes or no) on the basis of model 2; Model 4 further adjusted for hs-CRP (continuous) and albumin (continuous) in 2010 based on model 3.

Abbreviations: CAR, high-sensitivity C-reactive protein to albumin ratio; CVD, cardiovascular disease; Increase 1SD, increase high-sensitivity C-reactive protein to albumin ratio by 1-unit standard deviation.

**Supplementary Table 6 Cox proportional hazards model analysis of the incidence of end-point events in different CAR groups (competing risk model for death)**

CAR Groups	Model 1		Model 2		Model 3		Model 4	
	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>
Q1	Ref		Ref		Ref		Ref	
Q2	1.01 (0.95-1.08)	0.67	0.98 (0.92-1.05)	0.40	0.98 (0.91-1.04)	0.47	0.97 (0.91-1.04)	0.43
Q3	1.25 (1.17-1.33)	<0.001	1.10 (1.03-1.18)	<0.001	1.10 (1.04-1.18)	<0.001	1.10 (1.03-1.17)	<0.001
Q4	1.58 (1.48-1.68)	<0.001	1.35 (1.27-1.43)	<0.001	1.35 (1.27-1.43)	<0.001	1.25 (1.16-1.34)	<0.001
<i>P</i> for trend		<0.001		<0.001		<0.001		<0.001

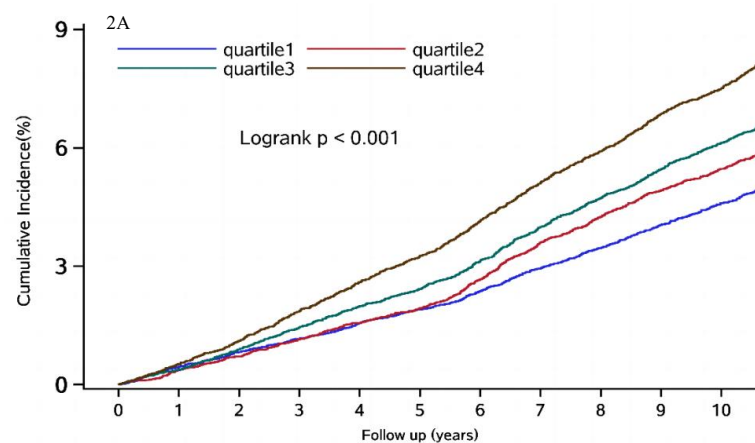
Model 1 adjusted for age (continuous) and gender (male or female); Model 2 further adjusted for smoking (yes or no), alcohol intake  $\geq 36$  mL/d (yes or no), physical exercise (yes or no), higher education (yes or no), body mass index ( $< 28$  kg/m<sup>2</sup>,  $\geq 28$  kg/m<sup>2</sup>), hypertension (yes or no), diabetes (yes or no), low-density lipoprotein cholesterol (continuous), high-density lipoprotein cholesterol (continuous), estimated glomerular filtration rate ( $< 60$  mL/min,  $\geq 60$  mL/min), alanine aminotransferase (continuous) on the basis of model 1; Model 3 further adjusted for hypertensive drugs (yes or no), hypoglycemic drugs (yes or no), and lipid-lowering drugs (yes or no) on the basis of model 2; Model 4 further adjusted for hs-CRP (continuous) and albumin (continuous) in 2010 based on model 3. Abbreviations: CAR, high-sensitivity C-reactive protein to albumin ratio.

Supplementary Table 7 C-index, NRI and IDI of different indicators for end-point events

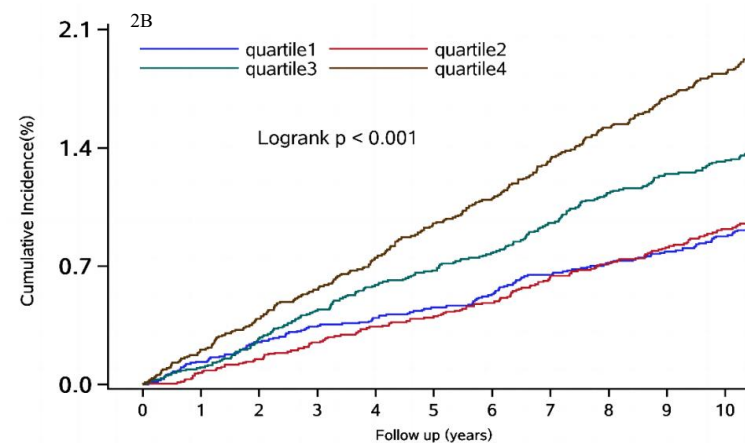
	Predictor	C-Index(95%CI)	Continuous NRI (95%CI)	P	Absolute IDI (95%CI)	P
CVD	China-PAR model	0.7339 (0.7270-0.7406)	Ref		Ref	
	China-PAR model+ hs-CRP	0.7344 (0.7276-0.7411)	0.0711 (0.0477-0.0946)	<0.001	0.0001 (0.0000-0.0002)	0.12
	China-PAR model+ Albumin	0.7339 (0.7271-0.7407)	-0.0090 (-0.0261-0.0081)	0.58	0.0000 (0.0000-0.0000)	0.32
	China-PAR model +CAR	0.7348 (0.7280-0.7416)	0.1366 (0.1049-0.1684)	<0.001	0.0002 (0.0001-0.0004)	<0.001
Myocardial infarction	China-PAR model	0.7578 (0.7437-0.7720)	Ref		Ref	
	China-PAR model+ hs-CRP	0.7596 (0.7454-0.7738)	0.1173 (0.0639-0.1707)	<0.001	0.0001 (0.0000-0.0003)	0.11
	China-PAR model+ Albumin	0.7578 (0.7436-0.7719)	0.0137 (-0.0253-0.0626)	0.39	0.0000 (0.0000-0.0000)	0.10
	China-PAR model +CAR	0.7627 (0.7486-0.7767)	0.2417 (0.1742-0.3092)	<0.001	0.0004 (0.0002-0.0006)	<0.001
Stroke	China-PAR model	0.7324 (0.7247-0.7401)	Ref		Ref	
	China-PAR model+ hs-CRP	0.7327 (0.7250-0.7403)	0.0579 (0.0321-0.0837)	<0.001	0.0000 (-0.0001-0.0001)	0.67
	China-PAR model+ Albumin	0.7325 (0.7249-0.7401)	-0.0198 (-0.0388- (-0.0009))	0.27	0.0000 (0.0000-0.0001)	0.40
	China-PAR model +CAR	0.7328 (0.7252-0.7404)	0.1032 (0.0679-0.1386)	<0.001	0.0001 (0.0000-0.0002)	0.19
Hemorrhagic stroke	China-PAR model	0.7339 (0.7113-0.7564)	Ref		Ref	
	China-PAR model+ hs-CRP	0.7342 (0.7117-0.7567)	0.0331 (-0.0349-0.1012)	0.50	0.0000 (0.0000-0.0000)	1.00
	China-PAR model+ Albumin	0.7343 (0.7117-0.7568)	0.1334 (0.06648-0.2020)	<0.001	0.0000 (0.0000-0.0000)	<0.001
	China-PAR model +CAR	0.7340 (0.7114-0.7565)	0.0667 (-0.0298-0.1632)	0.18	0.0000 (0.0000-0.0001)	0.56
Ischemic stroke	China-PAR model	0.7364 (0.7284-0.7444)	Ref		Ref	
	China-PAR model+ hs-CRP	0.7367 (0.7287-0.7447)	0.0567 (0.0294-0.0839)	<0.001	0.0000 (-0.0001-0.0001)	0.76
	China-PAR model+ Albumin	0.7365 (0.7285-0.7445)	-0.0110 (-0.0380-0.0089)	0.57	0.0000 (0.0000-0.0001)	0.38
	China-PAR model +CAR	0.7369 (0.7289-0.7448)	0.1100 (0.0727-0.1473)	<0.001	0.0001 (0.0000-0.0002)	0.28

Abbreviations: CAR, high-sensitivity C-reactive protein to albumin ratio; China-PAR model, Prediction Model for Atherosclerotic Cardiovascular Disease Risk in China; CVD, cardiovascular disease; hs-CRP, high-sensitivity C-reactive protein; IDI, the integrated discrimination index; NRI, the net reclassification index.

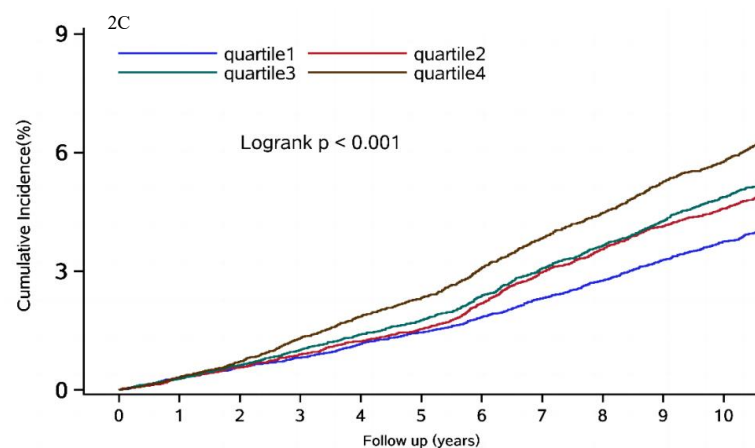
## Supplementary figure 1 Cumulative Incidence (%) of CVD (2A), myocardial infarction (2B), stroke (2C) and ischemic stroke (2D)



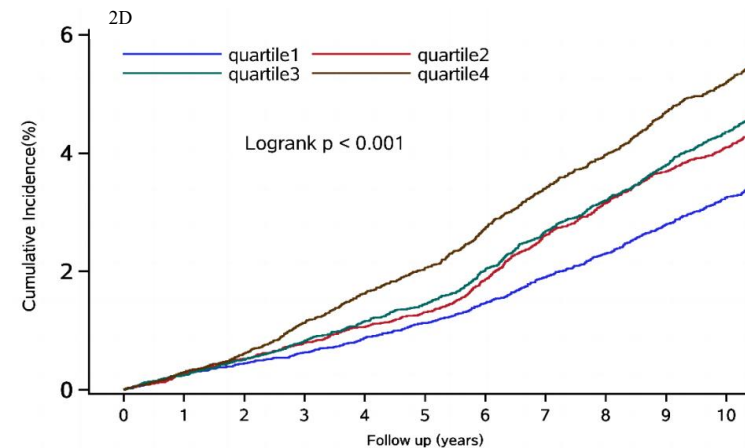
quartile1	15614	15480	15369	15237	15105	14958	14813	14636	14447	14266	14070
quartile2	15419	15320	15192	15040	14888	14748	14534	14284	14056	13813	13582
quartile3	15519	15402	15247	15084	14902	14728	14508	14241	13988	13741	13495
quartile4	15515	15344	15144	14895	14664	14435	14142	13838	13555	13246	12979



quartile1	15614	15480	15369	15237	15105	14958	14813	14636	14447	14266	14070
quartile2	15419	15320	15192	15040	14888	14748	14534	14284	14056	13813	13582
quartile3	15519	15402	15247	15084	14902	14728	14508	14241	13988	13741	13495
quartile4	15515	15344	15144	14895	14664	14435	14142	13838	13555	13246	12979



quartile1	15614	15480	15369	15237	15105	14958	14813	14636	14447	14266	14070
quartile2	15419	15320	15192	15040	14888	14748	14534	14284	14056	13813	13582
quartile3	15519	15402	15247	15084	14902	14728	14508	14241	13988	13741	13495
quartile4	15515	15344	15144	14895	14664	14435	14142	13838	13555	13246	12979



quartile1	15614	15480	15369	15237	15105	14958	14813	14636	14447	14266	14070
quartile2	15419	15320	15192	15040	14888	14748	14534	14284	14056	13813	13582
quartile3	15519	15402	15247	15084	14902	14728	14508	14241	13988	13741	13495
quartile4	15515	15344	15144	14895	14664	14435	14142	13838	13555	13246	12979

Supplementary figure 2 Cumulative Incidence (%) of hemorrhagic stroke

