

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

### **Supplementary Material**

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**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&gt;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)       | P      | HR (95%CI)       | P      | HR (95%CI)       | P      | HR (95%CI)       | P      |
| CVD                   |                         |  |                  |        |                  |        |                  |        |                  |        |
| 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 |
| P 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 |
| Myocardial Infarction |                         |  |                  |        |                  |        |                  |        |                  |        |
| 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 |
| P 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 |
| Stroke                |                         |  |                  |        |                  |        |                  |        |                  |        |
| 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   |
| P 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   |
| Hemorrhagic stroke    |                         |  |                  |        |                  |        |                  |        |                  |        |
| 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   |
| P 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   |
| Ischemic stroke       |                         |  |                  |        |                  |        |                  |        |                  |        |



|                    |            |      |                  |        |                  |        |                  |        |                  |        |
|--------------------|------------|------|------------------|--------|------------------|--------|------------------|--------|------------------|--------|
| 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   |

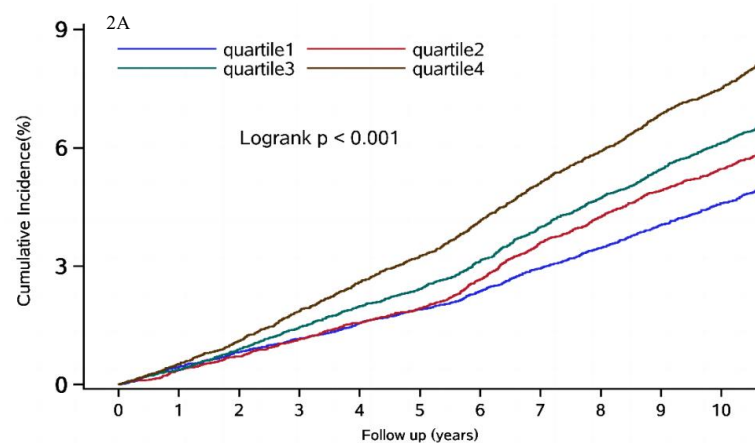
Model 1 adjusted for age (continuous) and gender (male or female); Model 2 further adjusted for smoking (yes or no), alcohol intake  $\geq 36$  mL/d (yes or no), physical exercise (yes or no), higher education (yes or no), body mass index ( $< 28$  kg/m<sup>2</sup>,  $\geq 28$  kg/m<sup>2</sup>), hypertension (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

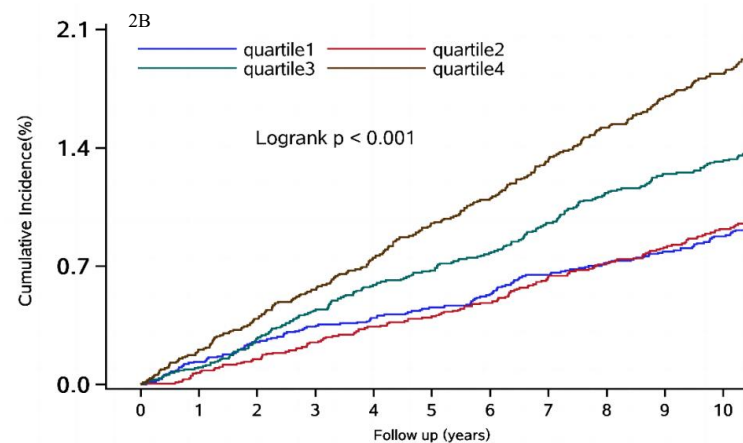
|                       | Predictor                | C-Index(95%CI)         | Continuous NRI (95%CI)       | P      | Absolute IDI (95%CI)    | P      |
|-----------------------|--------------------------|------------------------|------------------------------|--------|-------------------------|--------|
| 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.

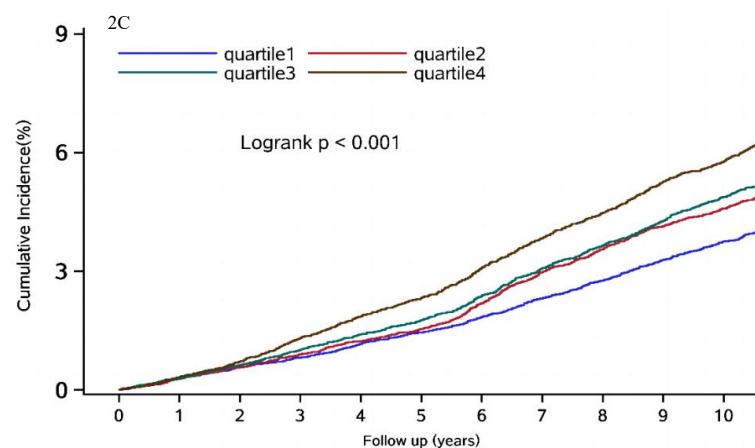
## Supplementary figure 1 Cumulative Incidence (%) of CVD (2A), myocardial infarction (2B), stroke (2C) and ischemic stroke (2D)



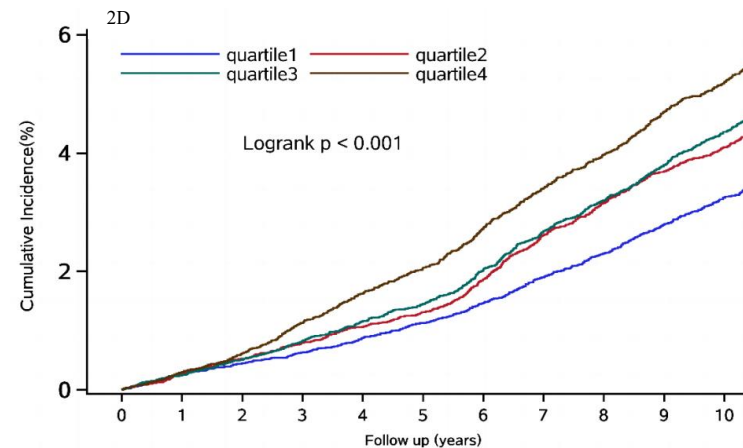
|           |       |       |       |       |       |       |       |       |       |       |       |
|-----------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| quartile1 | 15614 | 15480 | 15369 | 15237 | 15105 | 14958 | 14813 | 14636 | 14447 | 14266 | 14070 |
| 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

