

Supplementary File

Joint association of TyG index and high sensitivity C-reactive protein with cardiovascular disease: a national cohort study

Table S1: Baseline characteristics of the study participants

Characteristics	Group 1	Group 2	Group 3	Group 4
Participants, No.	2412	1917	1826	2503
Age, years, mean (SD)	57.78(8.96)	59.58(9.38)	57.77(8.64)	59.18(8.92)
Sex, Female, n (%)	1165(48.3)	1016(53.0)	770(42.2)	1037(41.4)
Residence, n (%)				
Rural	2023(84.0)	1586(82.7)	1476(81.1)	1891(75.6)
Urban	386(16.0)	331(17.3)	344(18.9)	611(24.4)
Marriage, married, n (%)	2170(90.0)	1696(88.5)	1657(90.7)	2231(89.1)
Educational level, n (%)				
Primary	1632(67.7)	1300(67.8)	1233(67.6)	1668(66.7)
Secondary	511(21.2)	409(21.3)	399(21.9)	525(21.0)
Third	269(11.2)	207(10.8)	191(10.5)	308(12.3)
Smoking status, n (%)				
Never	1451(60.3)	1115(58.2)	1078(59.1)	1513(60.5)
Former	162(6.7)	134(7.0)	134(7.3)	199(8.0)
Current	794(33.0)	667(34.8)	612(33.6)	789(31.5)
Current drinking, n (%)	817(34.0)	703(36.7)	614(33.7)	857(34.3)
BMI ^a , kg/m ²				
Continuous	23.89(6.20)	23.56(5.90)	23.67(5.91)	23.85(6.05)
<23.9	1129(56.5)	896(56.7)	851(56.6)	1142(55.4)
24-27.9	419(21.0)	341(21.6)	332(22.1)	467(22.6)
≥28	452(22.6)	342(21.7)	320(21.3)	453(22.0)
Hypertension, n (%)	1045(43.3)	809(42.2)	781(42.8)	1069(42.7)
Diabetes, n (%)	216(9.0)	170(8.9)	419(22.9)	772(30.8)

Data are presented as the mean (SD) or number (%), as appropriate.

Abbreviations: SD, standard deviation; BMI, body mass index; TyG, triglyceride-glucose index; hsCRP: high-sensitivity C-reactive protein.

^a Calculated as weight in kilograms divided by height in meters squared.

N of missing: BMI (n=1514); residence (n=10); smoking (n=10); drinking (n=13); education (n=6).

Group 1: TyG < median & hs-CRP <1 mg/L; Group 2: TyG < median & hs-CRP ≥1 mg/L; Group 3: TyG ≥ median & hs-CRP <1 mg/L; Group 4: TyG ≥ median & hs-CRP ≥1 mg/L.

Table S2: Risk of cardiovascular disease upon individual exposure stratified by TyG index and hsCRP

	Model 1		Model 2	
	HR (95% CI)	P value	HR (95% CI)	P value
TyG < median	Ref			
TyG ≥ median				
CVD	1.17(1.083-1.264)	<0.001	1.146(1.049-1.252)	0.003
CHD	1.177(1.078-1.286)	<0.001	1.128(1.019-1.248)	0.020
Stroke	1.146(1.001-1.312)	0.049	1.159(0.995-1.35)	0.058
hsCRP <1 mg/L	Ref			
hsCRP ≥1 mg/L				
CVD	1.238(1.145-1.337)	<0.001	1.167(1.071-1.272)	<0.001
CHD	1.263(1.156-1.380)	<0.001	1.176(1.065-1.297)	0.001
Stroke	1.182(1.032-1.354)	0.016	1.199(1.034-1.391)	0.016

Abbreviations: HR, hazard ratio; CI, confidence interval; BMI, body mass index; TyG, triglyceride-glucose index; hsCRP: high-sensitivity C-reactive protein; CVD: cardiovascular disease; CHD: coronary heart disease.

Group 1: TyG < median & hs-CRP <1 mg/L; Group 2: TyG < median & hs-CRP ≥1 mg/L; Group 3: TyG ≥ median & hs-CRP <1 mg/L; Group 4: TyG ≥ median & hs-CRP ≥1 mg/L. Median of TyG: 8.6

Model 1: age and sex adjusted; model 2: age, sex, residence, marriage, education level, BMI level, smoking status, current drinking, hypertension, diabetes were adjusted.

Table S3: Risk of cardiovascular disease upon co-exposure stratified by TyG index and hsCRP

	Model 1		Model 2	
	HR (95% CI)	P value	HR (95% CI)	P value
CVD				
Group 1	Ref			
Group 2	1.210(1.066-1.374)	0.003	1.192(1.036-1.370)	0.014
Group 3	1.284(1.096-1.503)	0.002	1.196(1.001-1.430)	0.049
Group 4	1.157(1.030-1.299)	0.014	1.170(1.029-1.330)	0.016
Group 5	1.279(1.139-1.436)	<0.001	1.200(1.054-1.368)	0.006
Group 6	1.613(1.410-1.846)	<0.001	1.515(1.300-1.766)	<0.001
CHD				
Group 1	Ref			
Group 2	1.232(1.065-1.426)	0.005	1.189(1.012-1.397)	0.035
Group 3	1.415(1.186-1.688)	<0.001	1.362(1.118-1.659)	0.002
Group 4	1.194(1.045-1.363)	0.009	1.191(1.028-1.379)	0.020
Group 5	1.321(1.157-1.507)	<0.001	1.208(1.040-1.403)	0.013
Group 6	1.644(1.410-1.918)	<0.001	1.481(1.241-1.766)	<0.001
Stroke				
Group 1	Ref			
Group 2	1.130(0.909-1.405)	0.271	1.196(0.946-1.513)	0.135
Group 3	1.012(0.758-1.350)	0.936	0.955(0.690-1.321)	0.780
Group 4	1.047(0.855-1.283)	0.656	1.069(0.855-1.337)	0.559
Group 5	1.215(0.995-1.484)	0.056	1.239(0.993-1.546)	0.058
Group 6	1.468(1.160-1.858)	0.001	1.534(1.183-1.989)	0.001

Abbreviations: HR, hazard ratio; CI, confidence interval; BMI, body mass index; TyG, triglyceride-glucose index; hsCRP: high-sensitivity C-reactive protein; CVD: cardiovascular disease; CHD: coronary heart disease.

Group 1: TyG < median & hs-CRP <1 mg/L; Group 2: TyG < median & hs-CRP 1-3 mg/L; Group 3: TyG < median & hs-CRP ≥3 mg/L; Group 4: TyG ≥ median & hs-CRP ≥1 mg/L; Group 5: TyG ≥ median & hs-CRP 1-3 mg/L; Group 6: TyG ≥ median & hs-CRP ≥3 mg/L. Median of TyG: 8.6.

Model 1: age and sex adjusted; model 2: age, sex, residence, marriage, education level, BMI level, smoking status, current drinking, hypertension, diabetes were adjusted.

Table S4: Sensitivity analyses of co-exposure for TyG index and hsCRP in terms of data missing

	Sensitivity analysis 1		Sensitivity analysis 2	
	HR (95% CI)	P value	HR (95% CI)	P value
CVD				
Group 1	Ref			
Group 2	1.193(1.053-1.351)	0.006	1.229(1.098-1.376)	<0.001
Group 3	1.168(1.027-1.327)	0.018	1.138(1.012-1.279)	0.03
Group 4	1.300(1.155-1.462)	<0.001	1.341(1.205-1.491)	<0.001
CHD				
Group 1	Ref			
Group 2	1.245(1.079-1.436)	0.003	1.284(1.129-1.461)	<0.001
Group 3	1.189(1.026-1.377)	0.021	1.171(1.024-1.339)	0.021
Group 4	1.294(1.130-1.481)	<0.001	1.368(1.211-1.546)	<0.001
Stroke				
Group 1	Ref			
Group 2	1.115(0.901-1.380)	0.318	1.092(0.898-1.328)	0.378
Group 3	1.067(0.854-1.335)	0.568	1.027(0.837-1.260)	0.801
Group 4	1.333(1.093-1.628)	0.005	1.262(1.051-1.516)	0.013

Abbreviations: HR, hazard ratio; CI, confidence interval; BMI, body mass index; TyG, triglyceride-glucose index; hsCRP: high-sensitivity C-reactive protein; CVD: cardiovascular disease; CHD: coronary heart disease.

Group 1: TyG < median & hs-CRP <1 mg/L; Group 2: TyG < median & hs-CRP ≥1 mg/L; Group 3: TyG ≥ median & hs-CRP <1 mg/L; Group 4: TyG ≥ median & hs-CRP ≥1 mg/L. Median of TyG index: 8.6

Analyses were adjusted for age, sex, residence, marriage, education level, BMI level, smoking status, current drinking, hypertension, diabetes were adjusted.

Sensitivity analysis 1 was performed among 7 126 participants without any missing data; sensitivity analysis 2 were performed using multiple imputed analyses (5 iterations) by Markov chain Monte Carlo method.

Number of missing: BMI (n=1514); residence (n=10); smoking (n=10); drinking (n=13); education (n=6).

Table S5: Risk of cardiovascular disease upon coexposure stratified by the TyG index and hsCRP among those free of diabetes (7081 participants)

	Model 1		Model 2	
	HR (95% CI)	P value	HR (95% CI)	P value
CVD				
Group 1	Ref			
Group 2	1.255(1.115-1.413)	<0.001	1.227(1.077-1.398)	0.002
Group 3	1.15(1.012-1.308)	0.033	1.174(1.02-1.352)	0.026
Group 4	1.341(1.193-1.507)	<0.001	1.303(1.144-1.483)	<0.001
CHD				
Group 1	Ref			
Group 2	1.297(1.132-1.487)	<0.001	1.261(1.085-1.465)	0.003
Group 3	1.215(1.05-1.406)	0.009	1.229(1.047-1.444)	0.012
Group 4	1.389(1.215-1.588)	<0.001	1.305(1.124-1.516)	<0.001
Stroke				
Group 1	Ref			
Group 2	1.103(0.898-1.354)	0.35	1.132(0.906-1.416)	0.275
Group 3	0.942(0.748-1.187)	0.615	0.988(0.768-1.271)	0.927
Group 4	1.221(0.997-1.495)	0.053	1.323(1.062-1.648)	0.013

Abbreviations: HR, hazard ratio; CI, confidence interval; BMI, body mass index; TyG, triglyceride-glucose index; hsCRP: high-sensitivity C-reactive protein; CVD: cardiovascular disease; CHD: coronary heart disease.

Group 1: TyG < median & hs-CRP <1 mg/L; Group 2: TyG < median & hs-CRP ≥1 mg/L; Group 3: TyG ≥ median & hs-CRP <1 mg/L; Group 4: TyG ≥ median & hs-CRP ≥1 mg/L. Median of TyG index: 8.6

Analyses were adjusted for age, sex, residence, marriage, education level, BMI level, smoking status, current drinking, hypertension were adjusted.

Table S6: Risk of cardiovascular disease upon coexposure stratified by the TyG index and hsCRP further adjusting for medication uses

	CVD		CHD		Stroke	
	HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P
Group 1	Ref					
Group 2	1.191(1.051-1.349)	0.006	1.243(1.078-1.434)	0.003	1.11(0.896-1.374)	0.338
Group 3	1.183(1.042-1.344)	0.009	1.207(1.043-1.397)	0.011	1.083(0.867-1.351)	0.483
Group 4	1.332(1.187-1.494)	0.001	1.327(1.163-1.515)	0.001	1.375(1.132-1.67)	0.001

Abbreviations: HR, hazard ratio; CI, confidence interval; BMI, body mass index; TyG, triglyceride-glucose index; hsCRP: high-sensitivity C-reactive protein; CVD: cardiovascular disease; CHD: coronary heart disease.

Group 1: TyG < median & hs-CRP <1 mg/L; Group 2: TyG < median & hs-CRP ≥1 mg/L; Group 3: TyG ≥ median & hs-CRP <1 mg/L; Group 4: TyG ≥ median & hs-CRP ≥1 mg/L. Median of TyG index: 8.6

Analyses were adjusted for age, sex, residence, marriage, education level, BMI level, smoking status, current drinking, hypertension, antihypertensive medication, diabetes and antidiabetic medication were adjusted.

Figure S1: Flowchart and follow-up setting of this current study

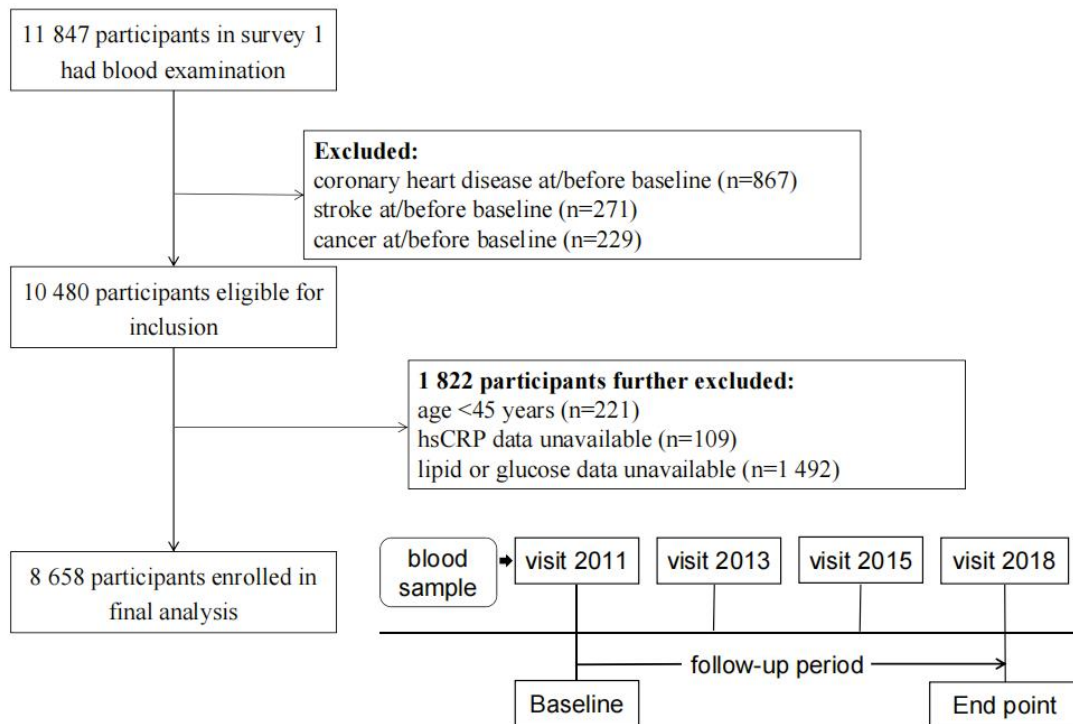
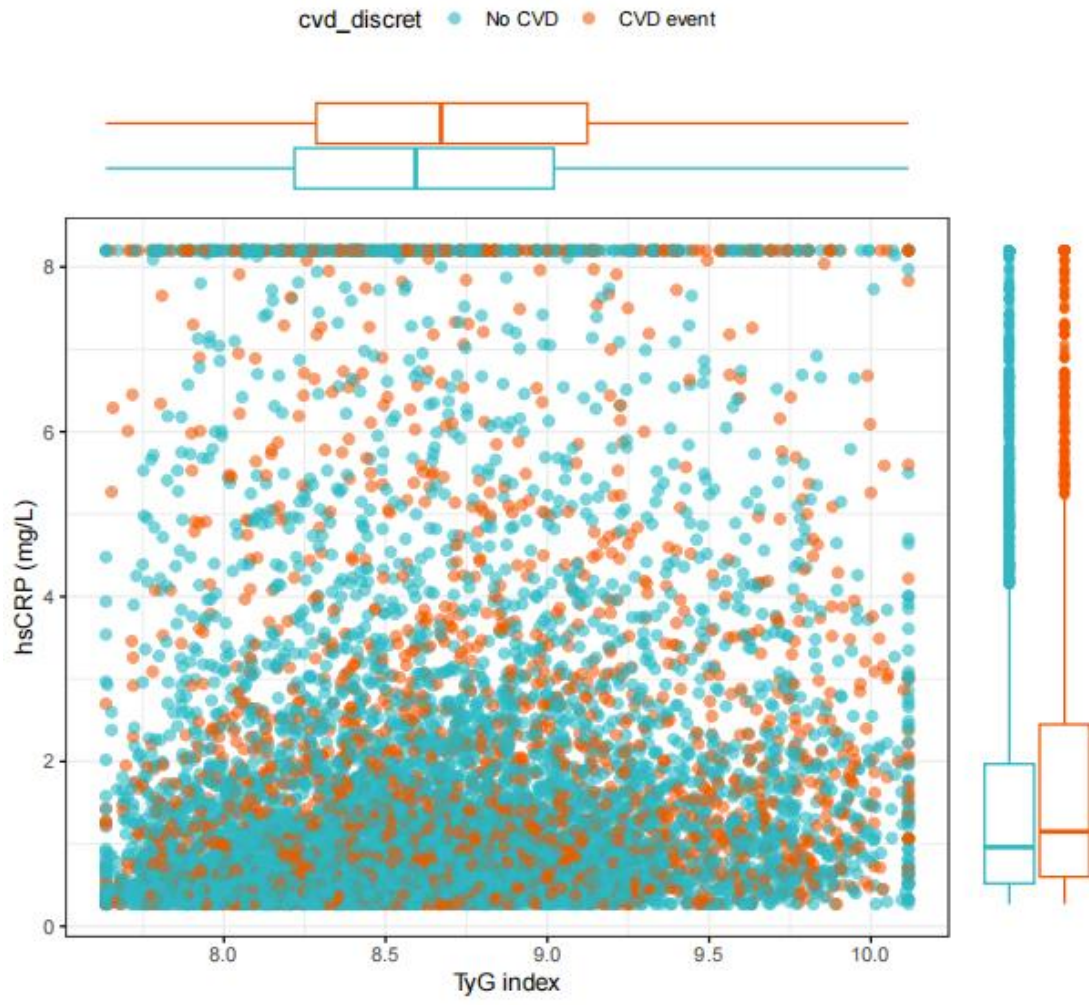
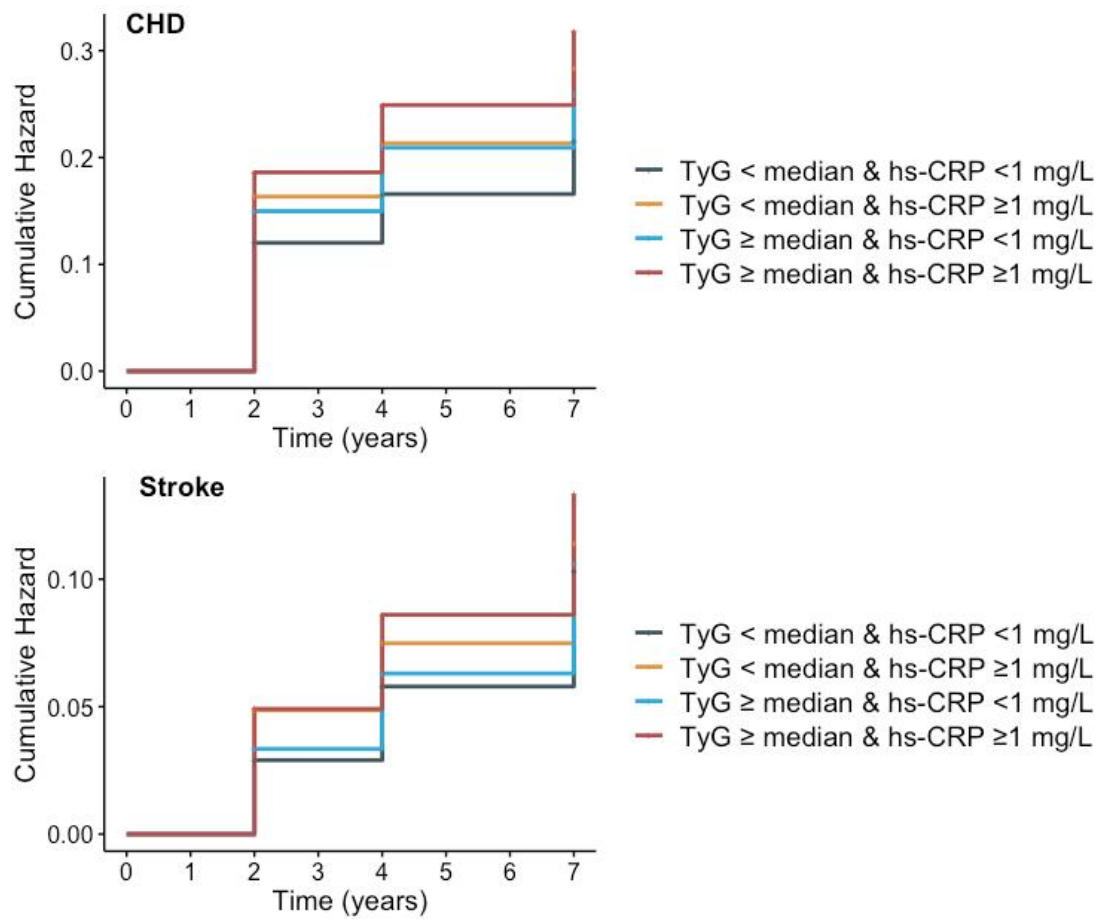


Figure S2: Co-distribution of TyG index and hsCRP stratified by incident cardiovascular diseases or not



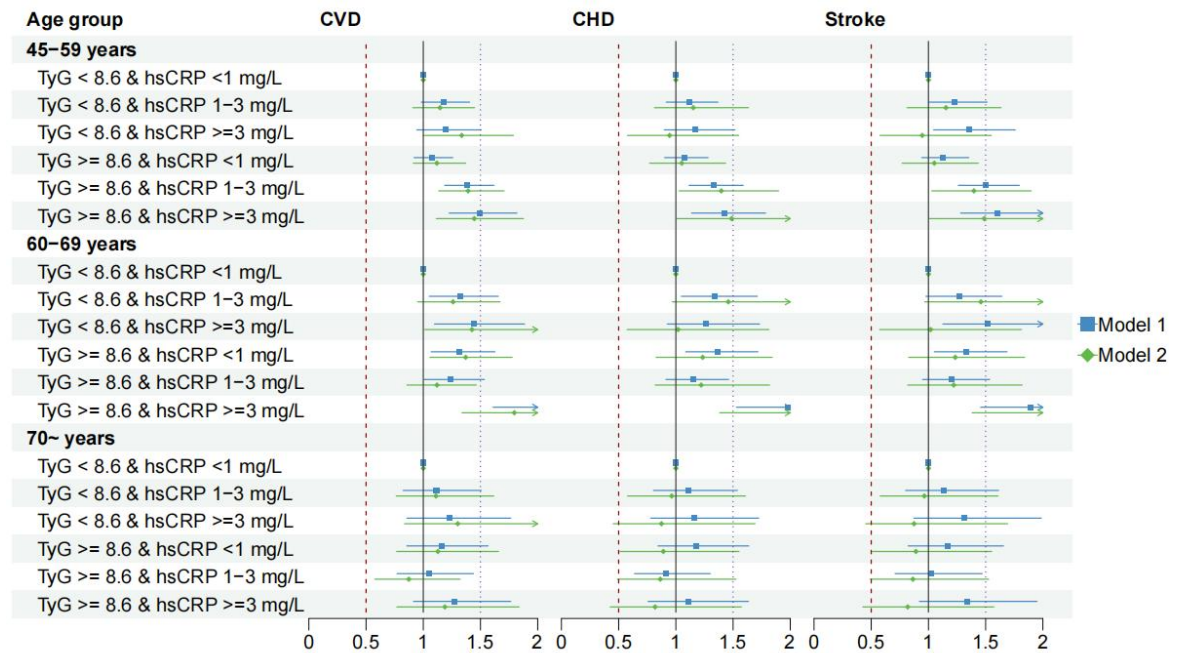
Abbreviations: TyG, triglyceride-glucose index; hsCRP: high-sensitivity C-reactive protein; CVD: cardiovascular disease

Figure S3: K-M plot of coronary heart disease and stroke by TyG index and hsCRP level



Abbreviations: TyG, triglyceride-glucose index; hsCRP: high-sensitivity C-reactive protein; median of TyG index: 8.6

Figure S4: Age-associated risk of TyG index and hsCRP for cardiovascular diseases onset



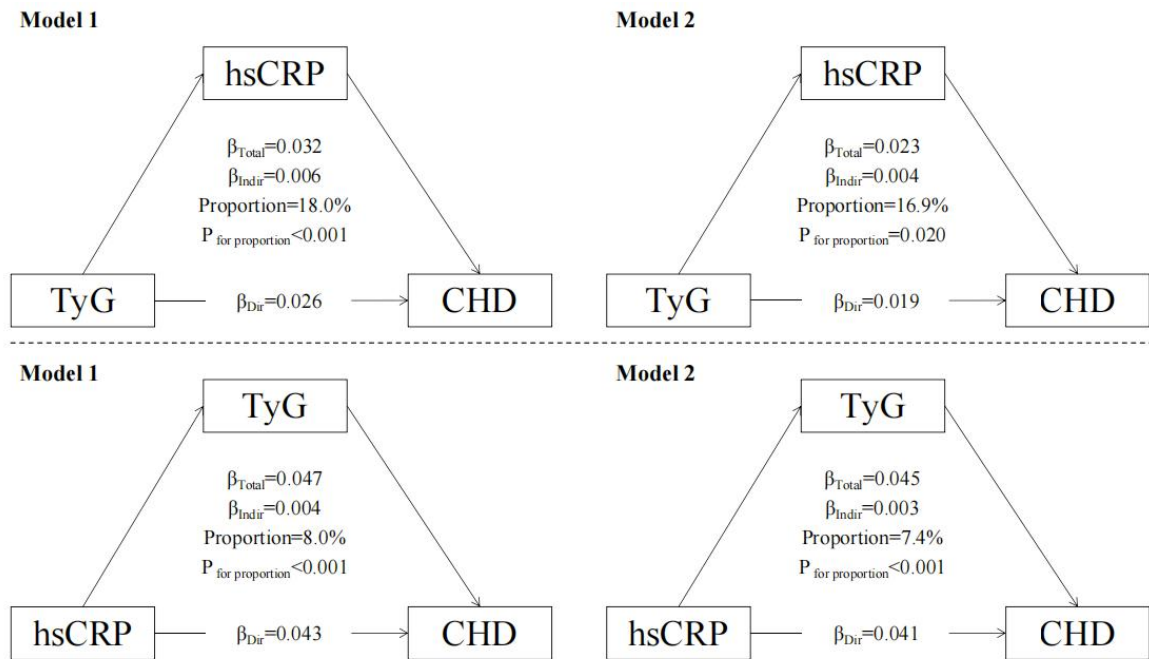
Abbreviations: HR, hazard ratio; CI, confidence interval; BMI, body mass index; TyG, triglyceride-glucose index; hsCRP: high-sensitivity C-reactive protein; CVD: cardiovascular disease; CHD: coronary heart disease.

Number of participants: 45-59 years (n=5 015); 60-69 years (n=2 495); 70~ years (n=1 148)

Dots and lines represent the HR and 95% CI.

Model 1: age and sex adjusted; model 2: age, sex, residence, marriage, education level, BMI level, smoking status, current drinking, hypertension, diabetes were adjusted.

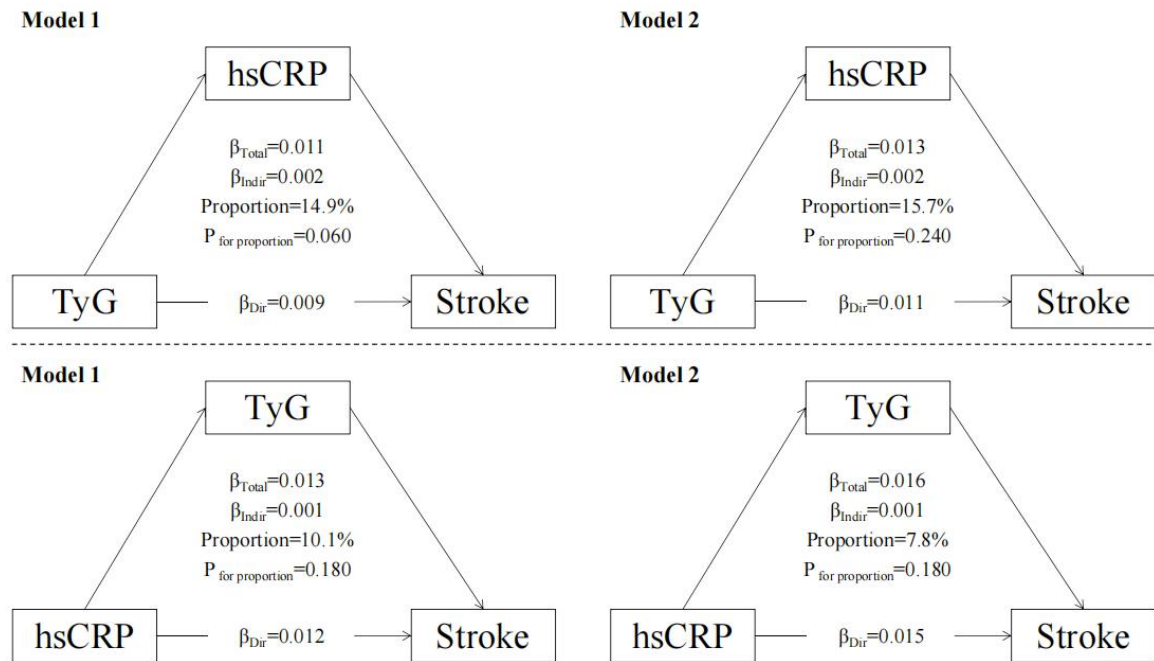
Figure S5: Mutual mediation effects of TyG index and hsCRP on coronary heart disease



Abbreviations: TyG, triglyceride-glucose index; hsCRP: high-sensitivity C-reactive protein

Model 1: age and sex adjusted; model 2: age, sex, residence, marriage, education level, BMI level, smoking status, current drinking, hypertension, diabetes were adjusted.

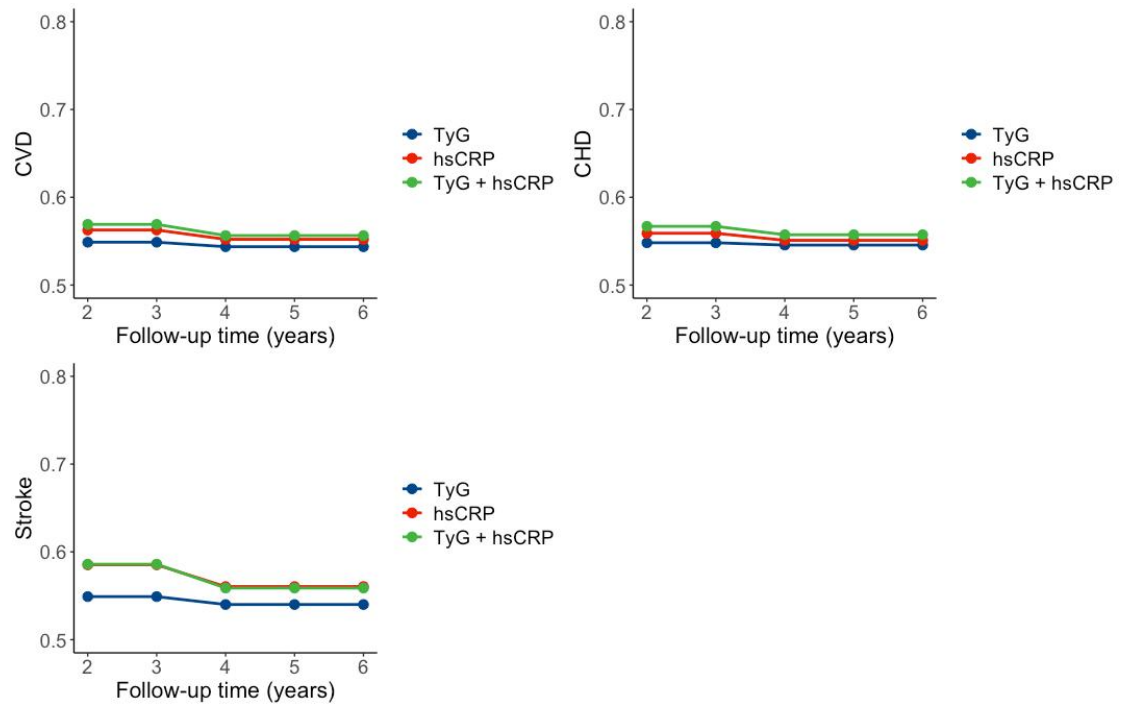
Figure S6: Mutual mediation effects of TyG index and hsCRP on stroke



Abbreviations: TyG, triglyceride-glucose index; hsCRP: high-sensitivity C-reactive protein

Model 1: age and sex adjusted; model 2: age, sex, residence, marriage, education level, BMI level, smoking status, current drinking, hypertension, diabetes were adjusted.

Figure S7: Predictive capacity of TyG index and hsCRP on the cardiovascular risk



Abbreviations: TyG, triglyceride-glucose index; hsCRP: high-sensitivity C-reactive protein