

Supplemental Methods

Study design and sample

Ethical clearance for CHARLS was granted by the Ethics Review Committee of Peking University Health Science Center, while ELSA received clearance from the Joint Research Ethics Committee of University College London. Written informed consent was secured from all participants. The Peking University Ethics Review Committee additionally approved the CHARLS survey (No.irb00001052-11015). Ethical approval for ELSA was granted by the National Research Ethics Service of the National Health Service Research Ethics Committee (Approval Nos.: Wave 4: 07/H0716/48; Wave 5: 09/H0505/124; Wave 6: 11/SC/0374; Wave 7: 13/SC/0532; Wave 8: 15/SC/0526; Wave 9: 17/SC/0588).

Depression

In the CHARLS cohort, the 10-item CES-D version was administered. Items were scored from 0 to 3 based on responses: "The scoring system ranged from 0 points ("rarely or none of the time (<1 day)") to 3 points ("most or all of the time (5–7 days)"), with intermediate scores of 1 point ("some or a little of the time (1–2 days)") and 2 points ("occasionally or a moderate amount of the time (3–4 days)"). Total scores range from 0 to 30, and depression was defined as a score ≥ 10 (1). In the ELSA cohort, an 8-item CES-D version was used, with items answered in a "yes/no" dichotomous format. Total scores range from 0 to 8, and depression was defined as a score ≥ 4 (2).

Statistical analysis

Subgroup differences in the associations of metabolic indices (AIP and TyG) with CMM risk were assessed using multivariable logistic regression. Continuous variables are reported as mean plus or minus standard deviation (SD). To compare differences between groups, Welch's t-test or one-way ANOVA was applied. Frequencies and proportions were used to summarize categorical variables, while Fisher's exact test was applied for group comparisons when expected frequencies were < 5 , otherwise the chi-square test was used(3).

The "segmented" package in R was applied to automatically detect inflection points, and nonlinearity was confirmed using the log-likelihood ratio test (4). Subgroup analyses were carried out using logistic regression models stratified by age, sex, marital status, education, smoking, and drinking. Data analysis was performed in R software (version 4.2.2)(5). Statistical significance was defined as a two-tailed p-value < 0.05 .

References

1. Zhao YH, Hu YS, Smith JP, Strauss J, Yang GH. Cohort profile: the China Health and Retirement Longitudinal Study (CHARLS). *Int J Epidemiol*. 2014;43(1):61–8.
2. Steptoe A, Breeze E, Banks J, Nazroo J. Cohort profile: the English longitudinal study of ageing. *Int J Epidemiol*. 2013;42(6):1640–8.
3. Welch BL. The generalization of 'Student's' problem when several different population variances are involved. *Biometrika*. 1947;34(1–2):28–35.
4. Muggeo VMR. Segmented: an R package to fit regression models with broken-line relationships. *R News*. 2008;8(1):20–5.
5. Team RC. R: A language and environment for statistical computing. R Foundation for Statistical Computing [Internet]. Vienna, Austria; 2022. Available from: <https://www.R-project.org/>.

Supplementary Table SI. Association between AIP and CMM in the CHARLS cohort.

Characteristic	Model 1			Model 2			Model 3		
	OR	95% CI	p-value	OR	95% CI	p-value	OR	95% CI	p-value
AIP (continuous)	3.67	2.73, 4.93	<0.001	3.97	2.93, 5.37	<0.001	3.93	2.91, 5.33	<0.001
AIP									
Q1	—	—		—	—		—	—	
Q2	1.02	0.78, 1.34	0.889	1.01	0.77, 1.33	0.934	1.01	0.77, 1.33	0.954
Q3	1.70	1.32, 2.20	<0.001	1.70	1.31, 2.19	<0.001	1.69	1.31, 2.19	<0.001
Q4	2.55	2.00, 3.26	<0.001	2.65	2.07, 3.40	<0.001	2.61	2.04, 3.35	<0.001
<i>P</i> for trend			<0.001			<0.001			<0.001

Abbreviations: CI = Confidence Interval, OR = Odds Ratio

Model 1 : no covariates were adjusted

Model 2 : adjusted for Age and Gender

Model 3 : adjusted for Age, Gender, Marital status, Education, Smoke, and Drinking status

Supplementary Table SII. Association between TYG and CMM in the CHARLS cohort.

Characteristic	Model 1			Model 2			Model 3		
	OR	95% CI	p-value	OR	95% CI	p-value	OR	95% CI	p-value
TYG (continuous)	2.00	1.76, 2.27	<0.001	2.07	1.82, 2.36	<0.001	2.07	1.82, 2.36	<0.001
TYG									
Q1	—	—		—	—		—	—	
Q2	1.18	0.90, 1.55	0.230	1.17	0.89, 1.54	0.270	1.17	0.89, 1.54	0.274
Q3	1.71	1.32, 2.21	<0.001	1.68	1.29, 2.18	<0.001	1.67	1.28, 2.17	<0.001
Q4	2.78	2.17, 3.56	<0.001	2.87	2.23, 3.69	<0.001	2.86	2.22, 3.69	<0.001
<i>P</i> for trend			<0.001			<0.001			<0.001

Abbreviations: CI = Confidence Interval, OR = Odds Ratio

Model 1 : no covariates were adjusted

Model 2 : adjusted for Age and Gender

Model 3 : adjusted for Age, Gender, Marital status, Education, Smoke, and Drinking status

Supplementary Table SIII. Association between AIP and CMM in the ELSA cohort.

Characteristic	Model 1			Model 2			Model 3		
	OR	95% CI	p-value	OR	95% CI	p-value	OR	95% CI	p-value
AIP (continuous)	3.81	1.51, 9.61	0.005	2.88	1.10, 7.53	0.031	2.88	1.06, 7.82	0.039
AIP									
Q1	—	—		—	—		—	—	
Q2	1.45	0.55, 3.79	0.452	1.53	0.58, 4.05	0.388	1.50	0.55, 4.03	0.426
Q3	2.36	0.96, 5.80	0.061	2.16	0.87, 5.37	0.096	2.16	0.86, 5.45	0.102
Q4	2.90	1.20, 6.99	0.018	2.43	0.99, 5.99	0.052	2.43	0.97, 6.13	0.059
<i>P</i> for trend			0.008			0.039			0.042

Model 1 : no covariates were adjusted

Model 2 : adjusted for Age and Gender

Model 3 : adjusted for Age, Gender, marital status, Education, Smoke, and Drink

Supplementary Table SIV. Association between TYG and CMM in the ELSA cohort.

Characteristic	Model 1			Model 2			Model 3		
	OR	95% CI	p-value	OR	95% CI	p-value	OR	95% CI	p-value
TYG (continuous)	2.61	1.57, 4.34	<0.001	2.40	1.42, 4.06	0.001	2.46	1.42, 4.25	0.001
TYG									
Q1	—	—		—	—		—	—	
Q2	2.10	0.69, 6.43	0.192	2.15	0.70, 6.62	0.182	2.21	0.71, 6.89	0.171
Q3	4.45	1.58, 12.54	0.005	4.27	1.50, 12.10	0.006	4.53	1.57, 13.03	0.005
Q4	5.39	1.94, 14.98	0.001	4.79	1.70, 13.51	0.003	5.18	1.79, 15.03	0.002
<i>P</i> for trend			<0.001			<0.001			<0.001

Model 1 : no covariates were adjusted

Model 2 : adjusted for Age and Gender

Model 3 : adjusted for Age, Gender, marital status, Education, Smoke, and Drink

Supplementary Table SV. Threshold effect analysis of AIP on CMM in the CHARLS cohort.

	OR (95% CI)	<i>P</i> -value
Fitting by standard Logistic regression model	3.67 (2.73, 4.93)	<0.001
Fitting by piecewise Logistic regression model (Break-Point = 0.879)		
AIP < 0.879	4.36 (3.01, 6.32)	<0.001
AIP ≥ 0.879	0.67 (0.05, 9.50)	0.77
Log likelihood ratio		0.179

Supplementary Table SVI. Threshold effect analysis of TYG on CMM in the CHARLS cohort.

	OR (95% CI)	<i>P</i> -value
Fitting by standard Logistic regression model	2.00 (1.76, 2.27)	<0.001
Fitting by piecewise Logistic regression model (Break-Point = 9.939)		
TYG < 9.939	1.88 (1.59, 2.21)	<0.001
TYG ≥ 9.939	3.60 (1.20, 10.82)	0.022
Log likelihood ratio		0.336

Supplementary Table SVII. Threshold effect analysis of AIP on CMM in the ELSA cohort.

	OR (95% CI)	<i>P</i> -value
Fitting by standard Logistic regression model	3.81 (1.51, 9.61)	0.005
Fitting by piecewise Logistic regression model (Break-Point = 0.428)		
AIP < 0.428	5.68 (1.81, 17.82)	0.003
AIP ≥ 0.428	0.03 (0.00, 1290.65)	0.516
Log likelihood ratio		0.271

Supplementary Table SVIII. Threshold effect analysis of TYG on CMM in the ELSA cohort.

	OR (95% CI)	<i>P</i> -value
Fitting by standard Logistic regression model	2.61 (1.57, 4.34)	<0.001
Fitting by piecewise Logistic regression model (Break-Point = 7.244)		
tyg < 7.244	6.48 (1.46, 28.78)	0.014
tyg ≥ 7.244	1.27 (0.42, 3.83)	0.672
Log likelihood ratio		0.196

Supplementary Table SIX. Subgroup analysis AIP in the CHARLS cohort.

Subgroup	N	Crude OR (95% CI)	<i>P</i> value	<i>P</i> for interaction
Overall	3225	3.67 (2.73-4.93)	<0.001	
Age				0.404
< 65	1966	4.49 (3.04-6.62)	<0.001	
≥ 65	1259	3.46 (2.16-5.54)	<0.001	
Gender				0.892
man	1216	3.54 (2.19-5.72)	<0.001	
woman	2009	3.69 (2.53-5.38)	<0.001	
Marital status				0.930
married	2639	3.78 (2.73-5.23)	<0.001	
non-married	586	3.65 (1.77-7.53)	<0.001	
Education				0.625
High school and below	3173	3.69 (2.74-4.97)	<0.001	
Above high school	52	2.20 (0.29-16.92)	0.447	
Smoke				0.229
No	1951	4.30 (2.91-6.36)	<0.001	
Yes	1274	2.98 (1.89-4.70)	<0.001	
Drinking status				0.625
No	1862	3.88 (2.61-5.76)	<0.001	
Yes	1363	3.34 (2.14-5.22)	<0.001	

Supplementary Table SX. Subgroup analysis TYG in the CHARLS cohort

Subgroup	N	Crude OR (95% CI)	<i>P</i> value	<i>P</i> for interaction
Overall	3225	2.00 (1.76-2.27)	<0.001	
Age				0.625
< 65	1966	2.13 (1.81-2.52)	<0.001	
≥ 65	1259	2.00 (1.63-2.45)	<0.001	
Gender				0.219
man	1216	1.80 (1.45-2.22)	<0.001	
woman	2009	2.12 (1.80-2.50)	<0.001	
Marital status				0.678
married	2639	1.99 (1.73-2.29)	<0.001	
non-married	586	2.13 (1.57-2.90)	<0.001	
Education				0.843
High school and below	3173	2.00 (1.76-2.27)	<0.001	
Above high school	52	1.82 (0.70-4.69)	0.218	
Smoke				0.102
No	1951	2.20 (1.86-2.59)	<0.001	
Yes	1274	1.77 (1.45-2.16)	<0.001	
Drinking status				0.324
No	1862	2.10 (1.78-2.48)	<0.001	
Yes	1363	1.84 (1.51-2.25)	<0.001	

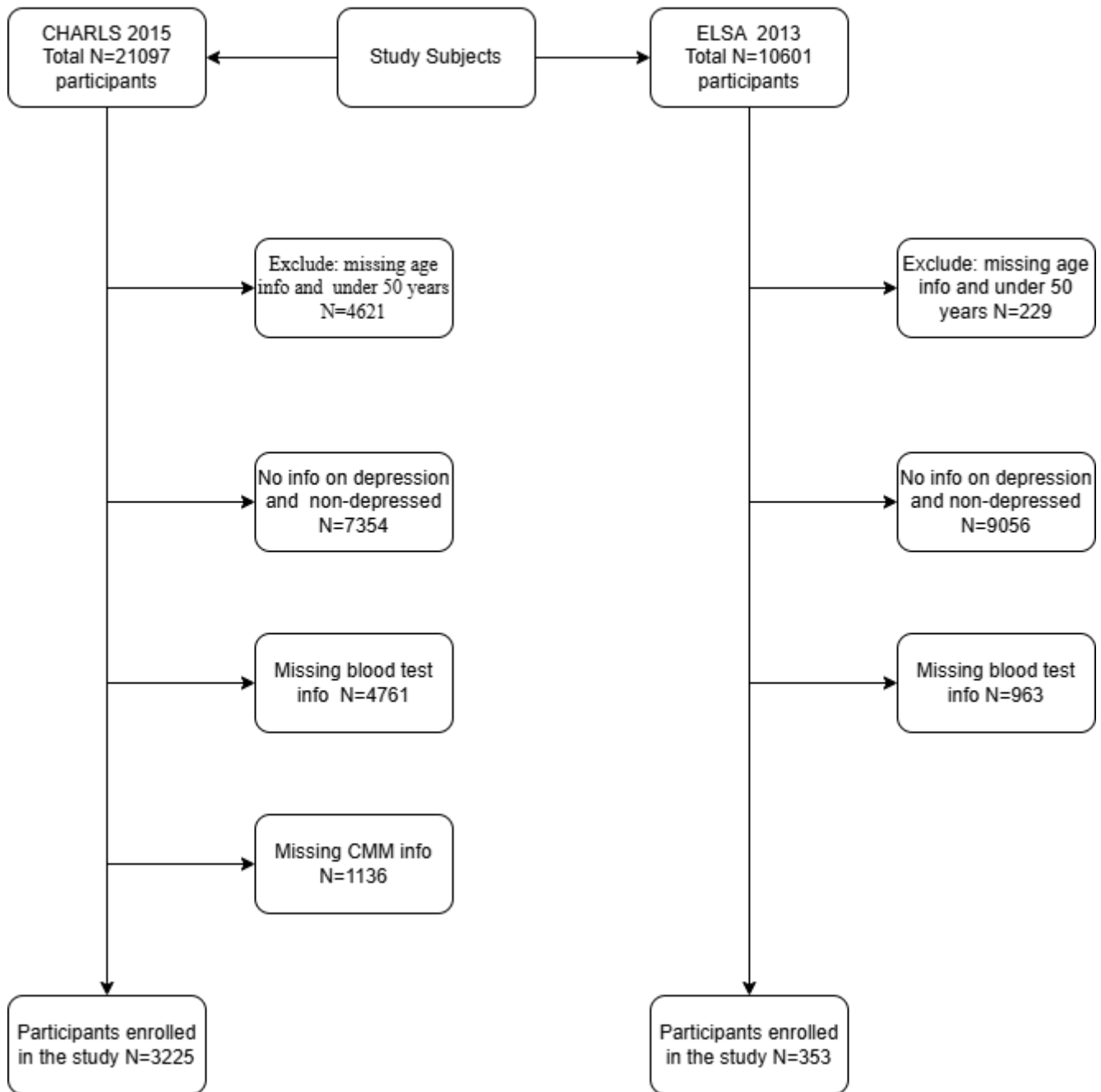
Supplementary Table SXI. Subgroup Analysis AIP in the ELSA cohort

Subgroup	N	Crude OR (95% CI)	<i>P</i> value	<i>P</i> for interaction
Overall	353	3.81 (1.51-9.61)	0.005	
Age				0.450
< 65	199	2.86 (0.93-8.77)	0.067	
≥ 65	154	6.26 (1.14-34.37)	0.035	
Gender				0.264
man	116	1.75 (0.48-6.46)	0.399	
woman	237	5.14 (1.31-20.16)	0.019	
Marital status				0.465
married	193	2.76 (0.74-10.32)	0.130	
non-married	160	5.54 (1.48-20.74)	0.011	
Education				0.850
High school and below	238	3.55 (1.21-10.37)	0.021	
Above high school	115	4.38 (0.65-29.70)	0.130	
Smoke				0.108
No	117	14.64 (2.18-98.31)	0.006	
Yes	236	2.42 (0.81-7.22)	0.113	
Drink				0.437
No	49	9.89 (0.73-133.67)	0.085	
Yes	304	3.27 (1.21-8.88)	0.020	

Supplementary Table SXII. Subgroup Analysis TYG in the ELSA cohort

Subgroup	N	Crude OR (95% CI)	<i>P</i> value	<i>P</i> for interaction
Overall	353	2.61 (1.57-4.34)	<0.001	
Age				0.994
< 65	199	2.57 (1.40-4.71)	0.002	
≥ 65	154	2.55 (0.96-6.78)	0.060	
Gender				0.110
man	116	1.63 (0.82-3.25)	0.163	
woman	237	3.78 (1.76-8.13)	0.001	
Marital status				0.501
married	193	2.19 (1.06-4.54)	0.034	
non-married	160	3.12 (1.52-6.38)	0.002	
Education				0.830
High school and below	238	2.68 (1.49-4.82)	0.001	
Above high school	115	2.34 (0.79-6.90)	0.123	
Smoke				0.018
No	117	8.81 (2.66-29.10)	<0.001	
Yes	236	1.76 (0.96-3.22)	0.067	
Drink				0.294
No	49	5.53 (1.21-25.27)	0.028	
Yes	304	2.33 (1.34-4.03)	0.003	

Supplemental Figure



Supplementary Figure S1. Flow chart of inclusion and exclusion criteria of participants