Association between Life's Essential 8 and hyperuricemia in the elderly in China

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ABSTRACT

Background and Objectives: Life's Essential 8 (LE8) is a comprehensive indicator that evaluates cardiovascular health (CVH). There have been limited studies on the relationship between LE8 and hyperuricemia (HUA). This study explored the association and dose-response relationship between LE8 and HUA among elderly people in China. **Methods and Study Design:** The subjects were the elderly aged 60 and over who participated in the China Health and Nutrition Survey (CHNS) in 2018. The definition of American Heart Association (AHA) was used to measure the score of LE8. Multivariate Logistic regression and restricted cubic spline (RCS) model were used to analyze the association and dose-response relationship between LE8 and HUA. **Results:** A total of 4229 subjects were included, and the prevalence of HUA was 13.2%. The LE8 score was 68.5 points, and physical activity (85.8) and blood pressure (37.6) were the highest and lowest scores, respectively. People with low, medium and high CVH accounted for 5.7%, 77.3% and 17.0%, respectively. Multivariate Logistic regression showed that high CVH in LE8 score reduced the risk of HUA (OR = 0.62, 95%CI = 0.39-0.99) significantly, and the risk decreased by 15% (OR = 0.85, 95%CI = 0.78-0.93) for every 10-point increase in LE8 score. RCS showed a linear dose-response relationship between LE8 and HUA, and the beneficial protective threshold was 68.6 points. The negative association between LE8 score and HUA was more significant in 60-69 years. **Conclusions:** This study suggested that the elderly in 15 provinces of China were at a moderate level of CVH, and a higher LE8 score was beneficial for reducing the risk of HUA.

Key Words: the elderly, Life's Essential 8, hyperuricemia, RCS, CHNS

INTRODUCTION

Hyperuricemia (HUA) is caused by purine metabolic disorder, the prevalence of which has continued to rise in many developed countries and has become an important public health problem.[1, 2] The National Health and Nutrition Examination Survey showed that the death risk of HUA and diabetes was similar.[3] The China Chronic Disease and Risk Factor Surveillance (CCDRFS) in 2018-2019 showed that the prevalence of HUA in the elderly was 11.90%, which was 1.82% higher than that in 2015-2016,[4] and it has become the "fourth highest" after diabetes, hypertension and hyperlipidemia.[5] HUA has attracted more and more attention because of its increasing global trend and the risk of related metabolic diseases. Its prevalence may be affected by many factors, including heredity, lifestyle, diet and metabolic abnormalities.[6, 7]

In 2022, the American Heart Association (AHA) put forward Life's Essential 8 (LE8), which included four healthy behaviors and four health factors.8 It was based on the "Life's Simple 7" proposed in 2010, which added sleep indicator and adjusted the quantification of indicators.[9] At present, there have been some studies on the correlation between LE8 score and cardiovascular diseases (CVD), diabetes and cancer,[10, 11] but there are few studies on the LE8 score and HUA, and the study samples were limited.[12, 13] At the same time, LE8, as an overall cardiovascular health (CVH) evaluation system, had more advantages than single factor analysis. Therefore, our study used the data from China Health and Nutrition Survey (CHNS) in 2018 to analyze the relationship between LE8 score and HUA, and to provide scientific basis for comprehensive prevention and treatment of HUA.

MATERIALS AND METHODS

Study design and subjects

The study used the data of CHNS in 2018. This project started in 1989 and has completed 11 rounds of follow-up in 2018. The demographic characteristics, lifestyle, nutritional status and disease history of people in 15 provinces of China were investigated by stratified multistage cluster random sampling, and some blood biochemical indexes were detected. Each round of survey tracked the same households and indoor members as much as possible. Refer to references for details.[14, 15]

We selected the elderly aged 60 and above as the subjects. The exclusion criteria were as follows: missing demographic data (n=870), missing physical data (n=528), missing blood biochemical data (n=514), missing lifestyle and dietary data (n=38), and included 4229 subjects finally in our study. The project was examined by the Ethics Review Committee of the National Institute for Nutrition and Health, Chinese Center for Disease Control and Prevention (No.2018-004), and all subjects signed informed consent before the investigation. (Figure 1)

Evaluation indicators

Measurement of LE8

According to the definition proposed by AHA, it included 8 indicators, four health behaviors (diet, physical activity, nicotine exposure and sleep), and four health factors ([body mass index (BMI), non-high-density lipoprotein cholesterol (non-HDL-C), blood glucose (BG), and blood pressure (BP)]).[8] The dietary data were collected by 3-day 24-hour dietary recalls and calculated by DASH score,[16] and a total of 9 indicators were included (total fat, saturated fat,

protein, cholesterol, fiber, magnesium, potassium, calcium and sodium) . Each nutrient was calculated as a percentage of energy and was defined as “Intermediate target” and “DASH score target”, respectively. Achieving the “DASH score target” was assigned 1 point, between the “Intermediate target” and the “DASH score target” was assigned 0.5 points, and below the “Intermediate target” was assigned 0 points. The maximum individual total score was 9 points (Supplementary Table 1). Physical activity included four categories: leisure, occupational, transportation and household activities. According to the corresponding metabolic equivalent (MET) of each activity,[17] the level of physical activity was classified as Light-intensity activity (<3METs), Moderate-intensity activity (3~6 METs), and Vigorous-intensity activity (> 6 METs). According to the definition of LE8, the time spent in moderate and vigorous-intensity activity per week was calculated. Nicotine exposure included whether you have smoked or not and the duration of quitting smoking. Sleep included sleep time every day and night. BMI was calculated by weight and height, and its classification criteria were adjusted according to the judgment standard of BMI of Chinese residents.[18] Non-HDL-C was calculated by subtracting HDL-C from total cholesterol (TC).[19] BG was evaluated by asking whether you have diabetes and detecting fasting plasma glucose and HbA1c. BP was determined by measurements and whether or not medication was taken. The subjects should remain seated with the upper arm at the same level as the heart during the measurement. BP was measured with a standard mercury sphygmograph, and systolic and diastolic BP were determined according to the Korotkoff sound. Three consecutive standardized BP measurements were performed for each subject, and the average of the three readings was used as the individual BP value. The specific scores of 8 indicators were shown in Supplementary Table 2.[8]

The score range for each indicator of LE8 was 0 to 100 points, and the final score was the average score of the 8 indicators. The CVH level was determined according to the following rules: low (0~49), moderate (50~79), high (80~100). In this study, the same cut-off point was used to define health behaviors and health factors scores.

Diagnostic criteria for HUA

The fasting venous blood samples of the subjects were taken at the physical examination site, and the uric acid (UA) was detected by enzyme kinetics method in the laboratory (Randox, UKHitachi7600). According to the “Guideline for the diagnosis and management of hyperuricemia and gout in China (2019)”, HUA was diagnosed with UA > 420μmol/L.

Covariate measurement

The demographic data, diet, lifestyle and other information involved in this study were surveyed by unified training and qualified investigators using special questionnaires through face-to-face investigation. Height and weight were measured by SECA206 height meter and electronic weight scale, respectively. The age was divided into two groups (60-69 years and 70~ years). The per capita annual household income was divided into three groups according to the tertile; The education level was divided into three groups: low (primary school and below), middle (middle and high school) and high (university and above); The geographical distribution was divided into east, middle and west according to the three major economic zones in China. Alcohol consumption was divided into yes and no groups based on whether they had consumed alcohol in the past year; Seafood intake was divided by tertile; Triglycerides, urea, and creatinine were also included as covariates, and the specific division criteria were detailed in the literature.[19, 20]

Statistical analysis

Quantitative data were represented by mean and standard deviation (SD), and qualitative data were expressed as percentages (%). ANOVA and Chi-square test were used for statistical tests. Multivariate Logistic regression was used to analyze the association between LE8, health behaviors, health factors scores and HUA, and the influence of each score increased by 10 points on HUA. Considering the smoothness of the curve and the accuracy of the fitting, the restricted cubic spline (RCS) model with five knots was used to analyze the dose-response relationship between each score and HUA and the population density distribution. Model 1 adjusted for age, gender, education, income level, region and areas; Model 2 adjusted for seafood and alcohol intake based on Model 1; Model 3 Adjusted for triglyceride, urea, and creatinine on Model 2. The subgroup analysis of LE8 score and HUA was displayed by Forest Plot. To test the robustness of our findings and to address reverse causality, sensitivity analysis was performed. We excluded subjects with CVD (including myocardial infarction, stroke, and ischemic attack), and repeated our analysis to see whether this change could have influenced our effect estimates. R4.4.0 software was used for data analysis, and the statistical significance was defined as $p < 0.05$.

RESULTS

Baseline characteristics

Among the 4229 subjects, there were 557 patients with HUA, and the prevalence was 13.2%. The basic characteristics of subjects were summarized according to whether they had HUA or not, as shown in Table 1. The average age was 69.1 years old. Low, middle and high CVH accounted for 5.7%, 77.3% and 17.0%, respectively. Compared with non-HUA, people with HUA were older and mostly men and drinkers. In addition, HUA status was statistically significant in the distribution of education level, income, region and CVH.

The score of LE8

The LE8 score was 68.5 points, in which the scores of physical activity and sleep were higher (85.8 and 85.0 points, respectively), and diet and BP were lower (43.3 and 37.6 points, respectively). In terms of total score, those aged 60~69, women, college and above, urban residents and non-drinkers scored relatively high. From the individual scores of each indicator, the scores of BP, BG, sleep and physical activity of people aged 70 and above were lower than those aged 60-69. Men had lower scores on physical activity and nicotine exposure. BP, sleep and physical activity scores were lower in primary and below, low-income people and rural residents. (Table 2)

Association of LE8 levels with HUA

LE8 Score and HUA

The prevalence of HUA in high CVH (7.10%) was significantly lower than that in moderate (13.7%) and low CVH (24.4%) (Figure 2) . After adjusting all covariates, taking the low CVH as a reference, the risk of HUA in high CVH decreased by 38% (OR = 0.62, 95%CI = 0.39-0.99), respectively. Every increase of 10 points reduced the risk of HUA by 15% (OR = 0.85, 95%CI = 0.78-0.93) (Table 3).

RCS showed that there was an overall negative linear correlation between LE8 score and HUA (*p*-nonlinear = 0.38), and the beneficial protective threshold was 68.6 points (OR = 1). The LE8 score of this population mostly clustered between 60 and 80 points (Figure 3A).

Health behaviors score and HUA

The prevalence of HUA in high health behaviors (10.7%) was significantly lower than that in moderate (14.0%) and low health behaviors (20.9%) (Figure 2). Taking the low health

behaviors group as a reference, no correlation was found between health behaviors and HUA (Table 3).

RCS showed that the overall association (*p*-overall=0.26) and non-linear association (*p*-nonlinear = 0.23) of health behaviors score were not statistically significant with HUA. The health behaviors scores of this population mostly clustered between 75 and 100 points (Figure 3B).

Health factors score and HUA

The prevalence of HUA in high health factors (6.6%) was significantly lower than that in moderate (13.2%) and low health factors (18.5%) (Figure 2). Taking the low health factors group as a reference, the risk of HUA in moderate and high health factors was reduced by 24% (OR = 0.76, 95%CI = 0.60-0.95) and 61% (OR = 0.39, 95%CI = 0.27-0.56), respectively. Every increase of 10 points reduced the risk of HUA by 14% (OR = 0.86, 95%CI = 0.81-0.92) (Table 3).

RCS showed that there was an overall nonlinear association between health factors score and HUA (P-nonlinear=0.04), and the beneficial protective threshold was 63.66 points (OR = 1). The health factors score of this population mostly clustered between 50 and 75 points (Figure 3C).

Subgroup analysis

There was no significant association between LE8 score and HUA in subjects aged 70 years and above, with college and above, with middle income, living in urban areas, and with alcohol consumption. For each other stratification, the association was statistically significant. In addition, the negative correlation between LE8 score and HUA was stronger in 60-69 years (OR = 0.81, 95%CI = 0.73-0.90) (Figure 4).

Sensitivity analysis

Sensitivity analysis showed that the association of LE8, health behaviors and health factors score with HUA were similar to our main analysis. Compared with the low group, the risk of HUA in high CVH and high health factors decreased by 37% (OR = 0.63, 95%CI = 0.39-1.01) and 61% (OR = 0.39, 95%CI = 0.27-0.57), respectively (Table 4).

DISCUSSION

In this study, LE8 score and health factors score of the elderly in 15 provinces of China were negatively correlated with HUA, and the beneficial protective threshold was about 65 points. The negative correlation between LE8 score and HUA was more significant in lower age groups.

In our study, the LE8 score was 68.5 points, which was in the moderate level, and the high CVH accounted for 16.98%. According to the data of CCDRFS in 2015, the high CVH of the elderly aged 60 and over in China accounts for 15.2%.21 Among American adults, the CVH score for those aged 65-79 was 63.3 points, and the high CVH accounts for 11.0% in the elderly aged 65 and above.[22, 23] In addition, BP score of the elderly was the lowest, followed by diet in our study. According to the CHNS in 2015, the prevalence of elevated BP among the elderly was 71.3%. Therefore, early prevention of hypertension in the elderly should be emphasized to reduce the occurrence of hypertension related diseases. In addition, the physical and mental functions of the elderly may also decline with aging, such as decreased chewing and digestive abilities, and delayed taste responses. Therefore, the elderly should consume foods with high nutrient density, easy digestion, absorption, utilization, and rich in high-quality protein, and participate in outdoor activities actively to maintain a healthy weight.[24]

In this study, high CVH in LE8 score reduced the risk of HUA by 38%. An analysis of the Kailuan study (mainly for coal miners) found that the LE8 score in the top quartile group was related to a 36% reduction in the risk of HUA.[12] A Chinese ethnic cohort study found that high CVH reduced the risk of HUA by 55%, and the minimum threshold of beneficial association was 66.9 points, which was close to the results of this study.[13] At present, few studies have explored the association between LE8 and HUA, but previous studies on LS7 and UA suggested that ideal CVH was beneficial to improve the state of HUA. Studies have shown that ideal CVH reduced the risk of HUA by 54%,[13] and the more ideal CVH indicators, the lower the risk of HUA.[25] A National Nutrition Survey in America showed a significant negative correlation between CVH score and UA ($\beta = -0.041$, $p < 0.001$).[26]

At present, the correlation mechanism between LE8 and HUA is unclear, and there are some explanations. Obesity was an independent risk factor for HUA,[7] and the risk of HUA increased with the increase of BMI.[27] Adipose tissue could upregulate xanthine oxidoreductase activity, thereby increasing uric acid production from purines. Additionally, pentose phosphate pathway activation during fatty acid synthesis in adipose tissue contributed to increased uric acid production.[28] Insulin resistance (IR) can affect UA transport in the

kidney, leading to increased UA reabsorption. In addition, IR may lead to the increase of lipolysis and the decrease of lipoprotein lipase activity in adipose tissue, which may lead to excessive production of UA.[29] The interaction between elevated UA and hypertension can be explained by the increase of oxidative stress related to UA production.[30] The association between dyslipidemia and HUA may be related to IR, oxidative stress, inflammation, etc., leading to UA accumulation. Studies have found that the ratio of non-HDL-C to HDL-C (NHHR) had a high predictive value for HUA.[31]

Although our study did not find the association between the health behaviors score and HUA, previous studies have found the influence of dietary habits and lifestyle on HUA, which may be related to the interaction between different behaviors. Studies have found that infrequent consumption of milk and soy products and short sleep time were risk factors for HUA. It was suggested that patients with HUA should actively limit the intake of fried foods, alcohol, and foods rich in purine, increase the intake of milk and soy products, and increase the sleep time.[32] The relationship between sleep and HUA was still controversial, with some reports showing a negative correlation33 and some showing a U-shaped curve correlation.[34] Sleep could promote the decomposition of nucleotides by affecting the level of catecholamine, leading to more endogenous UA production. In addition, sleep had a significant impact on inflammatory mediators, which induced chronic inflammatory diseases. UA, as an activator of immune system, participated in the inflammatory response of the body. Therefore, the choice of sleep time should take into account other issues caused by excessive sleep time. Meta-analysis found that moderate-to-vigorous intensity physical activity and sedentary were negatively and positively associated with the risk of HUA, respectively, and the risk thresholds were 15 MET-h/w and 25h/w, respectively.[35] Some studies have suggested that the potential risk of smoking on HUA may be attributed to oxidative stress, and may be related to the intensity and duration of smoking and concurrent health behaviors.[36] A limited protective effect of smoking against HUA has also been reported, which may be related to xanthine oxidase inactivation by cyanide in cigarettes,[37] but this should not be interpreted as an endorsement of smoking, as the health risks of smoking were well documented.

In subgroup analysis, our study found that the negative correlation between LE8 score and HUA was more significant in younger (60-69 years vs. ≥70 years [OR, the same below] :0.81 vs. 0.92). In similar studies, it also found that the correlation between LE8 and HUA was more significant among women, younger and non-drinkers.[12, 13] These findings further indicated that LE8 increased the sensitivity of differences between individuals and

populations. In addition, after excluding subjects with CVD, our repeated analysis was consistent with the main analysis, further reflecting the robustness of the study results.

At present, there are many indicators for CVH scores, such as Framingham risk score, systemic coronary risk evaluation, Reynolds risk score, China-PAR model, and so on.[38] These indicators included demographic characteristics, lifestyle, blood biochemical indicators and disease status to evaluate the risk of CVD. In this study, LE8 was used to synthesize a variety of eight health behaviors and health factors. The main advantage was that each indicator was quantified in detail through scientific algorithms, which increased the sensitivity of individual differences, and provided strong support for the development of more efficient health intervention measures.

However, there are still some restrictions: firstly, in this study, the 3-day 24-hour dietary recalls may have recall bias, and usually cannot assess the daily dietary intake, but it is more accurate than the food frequency questionnaire in calculating nutrients; Secondly, the variable of whether to accept lipid therapy was not investigated in our study, so the score may be slightly higher; Finally, smoking in AHA standard referred to all nicotine exposure, including electronic cigarettes and atomizers in addition to traditional cigarettes, but this part has not been investigated in this study so we should be cautious when comparing similar studies. In addition, the DASH score used in this study, MEPA score and the Kailuan version of the score used in other studies, most of which used food or nutrient intake to evaluate diet, but related studies have found that dietary habits or diet types also have an effect on HUA. Therefore, in future studies, the effect of diet types on HUA can be further considered. In addition, more mechanistic studies are still needed to further explore the interaction between LE8 components.

Conclusions

The overall CVH status of elderly people in 15 provinces of China was at a moderate level. LE8 and health factors score were negatively correlated with HUA, and the beneficial protective threshold was about 65 points. It was recommended to adhere to the optimal level of LE8 score to reduce the risk of HUA effectively.

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CONFLICT OF INTEREST AND FUNDING DISCLOSURE

The authors declare no conflict of interest.

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Table 1. Baseline characteristics of the subjects

	Overall (n=4229)	Non-HUA (n=3672)	HUA (n=557)	*p* value
Age, years†	69.1±6.7	69.0±6.6	70.0±7.0	<0.05
Age strata‡				<0.05
60~69	2643 (62.5)	2331 (63.5)	312 (56.0)	
70~	1586 (37.5)	1341 (36.5)	245 (44.0)	
Gender‡				<0.05
Men	1976 (46.7)	1571 (42.8)	405 (72.7)	
Women	2253 (53.3)	2101 (57.2)	152 (27.3)	
Education‡				<0.05
Primary and below	2143 (50.7)	1892 (51.5)	251 (45.1)	
Middle and high	1580 (37.4)	1349 (36.7)	231 (41.5)	
College and above	506 (12.0)	431 (11.7)	75 (13.5)	
Income‡				<0.05
Low	1410 (33.3)	1266 (34.5)	144 (25.8)	
Middle	1409 (33.3)	1198 (32.6)	211 (37.9)	
High	1410 (33.3)	1208 (32.9)	202 (36.3)	
Region‡				<0.05
Central	1060 (25.1)	934 (25.4)	126 (22.6)	
Eastern	1964 (46.4)	1723 (46.9)	241 (43.3)	
Western	1205 (28.5)	1015 (27.5)	190 (34.1)	
Area‡				0.07
Urban	1584 (37.5)	1356 (36.9)	228 (40.9)	
Rural	2645 (62.5)	2316 (63.1)	329 (59.1)	
Drinking‡				<0.05
No	3268 (77.3)	2912 (79.3)	356 (63.9)	
Yes	961 (22.7)	760 (20.7)	201 (36.1)	
CVH‡				<0.05
Low	242 (5.7)	183 (5.0)	59 (10.6)	
Moderate	3269 (77.3)	2822 (76.9)	447 (80.2)	
High	718 (17.0)	667 (18.1)	51 (9.2)	

†mean ± SD, ‡percent (%).

Table 2. Scores of 8 indicators of LE8 with different characteristics

	Health Factors				Health behaviors				LE8 Score
	BMI	non-HDL-C	BP	BG	Sleep	PA	NE	Diet	
Age									
60~69	76.2*	70.2	40.8*	67.4*	86.3*	88.8*	76.7*	45.6*	69.0*
70~	80.1	71.8	32.3	65.3	82.9	80.9	80.3	47.5	67.6
Gender									
Men	78.6	75.2*	36.8	66.5	86.0*	81.2*	56.5*	45.7	65.8*
Women	76.8	77.0	38.4	66.6	84.2	89.9	96.9	46.9	70.8
Education									
Primary and above	78.6[a]	70.5	36.0[b]	68.0[a]	82.5[b]	85.9[b]	80.9[a]	46.4	68.6[b]
Middle and high	76.6[b]	70.9	38.7[a]	65.2[b]	87.2[a]	84.9[b]	73.3[b]	45.7	67.8[b]
College and above	77.2	72.1	41.4[a]	64.5[b]	89.2[a]	88.3[a]	80.8[a]	48.2	70.2[a]
Income									
Low	79.8[a]	71.2	37.4[b]	68.2[a]	83.1[b]	83.0[c]	76.0[b]	51.3[a]	68.7
Middle	76.2[b]	71.1	37.0[b]	66.8	85.9[a]	86.4[b]	79.6[a]	44.0[b]	68.4
High	76.9[b]	70.2	38.5[a]	64.7[b]	86.1[a]	88.2[a]	78.5	43.6[b]	68.4
Region									
Central	77.9[a]	71.1	35.5[b]	67.9[a]	85.8[a]	85.6	80.2[a]	46.7[a]	68.8
Eastern	75.8[b]	71.4	36.0[b]	65.8[b]	85.2	86.0	77.0[b]	48.7[a]	68.2
Western	80.4[a]	69.7	42.1[a]	66.7	84.1[b]	85.7	77.7	42.0[b]	68.6
Area									
Urban	77.1	70.2	40.6*	64.1*	86.7*	86.7*	81.5*	44.6*	68.9*
Rural	78.0	71.2	35.8	68.1	84.0	85.4	76.0	47.4	68.2
Drinking									
No	77.4	69.8[a]	38.6[a]	66.4	85.1	85.9	87.0[a]	46.7	69.6[a]
Yes	78.6	74.2	34.2	67.2	84.7	85.7	47.6	44.9	64.6
Total	77.6	70.8	37.6	66.6	85.0	85.8	78.0	46.3	68.5

BMI: body mass index; BP: blood pressure; BG: blood glucose; PA: Physical activity; NE: nicotine exposure.
a,b,c: different letters indicate statistical significance, same letters and no letters indicate no statistical significance
*:$p<0.05$

Table 3. Association of the LE8 scores with HUA

	Model 1		Model 2		Model 3	
	OR(95%CI)	*p* value	OR(95%CI)	*p* value	OR (95%CI)	*p* value
LE8 Score						
Low	1.00	/	1.00	/	1.00	/
Moderate	0.63 (0.46-0.87)	<0.05	0.63 (0.46-0.87)	<0.05	0.86 (0.60-1.21)	0.39
High	0.35 (0.23-0.54)	<0.05	0.35 (0.23-0.54)	<0.05	0.62 (0.39-0.99)	<0.05
Per 10 points increase	0.79 (0.75-0.84)	<0.05	0.80 (0.75-0.84)	<0.05	0.85 (0.78-0.93)	<0.05
Health behaviors Score						
Low	1.00	/	1.00	/	1.00	/
Moderate	0.81 (0.61-1.08)	0.15	0.81 (0.61-1.08)	0.16	0.84 (0.62-1.14)	0.25
High	0.79 (0.58-1.07)	0.13	0.82 (0.60-1.11)	0.20	0.90 (0.65-1.24)	0.51
Per 10 points increase	0.94 (0.89-1.00)	<0.05	0.95 (0.90-1.01)	0.07	0.97 (0.92-1.03)	0.38
Health factors Score						
Low	1.00	/	1.00	/	1.00	/
Moderate	0.61 (0.49-0.75)	<0.05	0.61 (0.50-0.76)	<0.05	0.76 (0.60-0.95)	<0.05
High	0.27 (0.19-0.38)	<0.05	0.27 (0.19-0.38)	<0.05	0.39 (0.27-0.56)	<0.05
Per 10 points increase	0.79 (0.75-0.84)	<0.05	0.80 (0.75-0.84)	<0.05	0.86 (0.81-0.92)	<0.05

*Model 1 adjusted for age, gender, education, income level, region and areas; Model 2 adjusted for seafood and alcohol intake based on Model 1; Model 3 Adjusted for triglyceride, urea, and creatinine on Model 2

Table 4. Sensitivity analysis of LE8 scores and HUA

	Model 1		Model 2		Model 3	
	OR(95%CI)	*p* value	OR(95%CI)	*p* value	OR (95%CI)	*p* value
LE8 Score						
Low	1.00	/	1.00	/	1.00	/
Moderate	0.61 (0.44-0.85)	<0.05	0.61 (0.44-0.85)	<0.05	0.86 (0.60-1.25)	0.43
High	0.34 (0.22-0.53)	<0.05	0.35 (0.23-0.54)	<0.05	0.63 (0.39-1.01)	0.06
Per 10 points increase	0.75 (0.69-0.81)	<0.05	0.76 (0.70-0.82)	<0.05	0.85 (0.78-0.93)	<0.05
Health behaviors Score						
Low	1.00	/	1.00	/	1.00	/
Moderate	0.75 (0.56-1.00)	0.05	0.75 (0.56-1.01)	0.06	0.80 (0.59-1.10)	0.17
High	0.75 (0.55-1.03)	0.08	0.78 (0.57-1.07)	0.13	0.89 (0.64-1.25)	0.51
Per 10 points increase	0.93 (0.88-0.99)	<0.05	0.94 (0.89-1.00)	<0.05	0.97 (0.91-1.03)	0.30
Health factors Score						
Low	1.00	/	1.00	/	1.00	/
Moderate	0.62 (0.50-0.77)	<0.05	0.62 (0.50-0.78)	<0.05	0.77 (0.60-0.97)	<0.05
High	0.27 (0.19-0.38)	<0.05	0.27 (0.19-0.38)	<0.05	0.39 (0.27-0.57)	<0.05
Per 10 points increase	0.79 (0.75-0.84)	<0.05	0.79 (0.75-0.84)	<0.05	0.86 (0.80-0.92)	<0.05

*Model 1 adjusted for age, gender, education, income level, region and areas; Model 2 adjusted for seafood and alcohol intake based on Model 1; Model 3 Adjusted for triglyceride, urea, and creatinine on Model 2

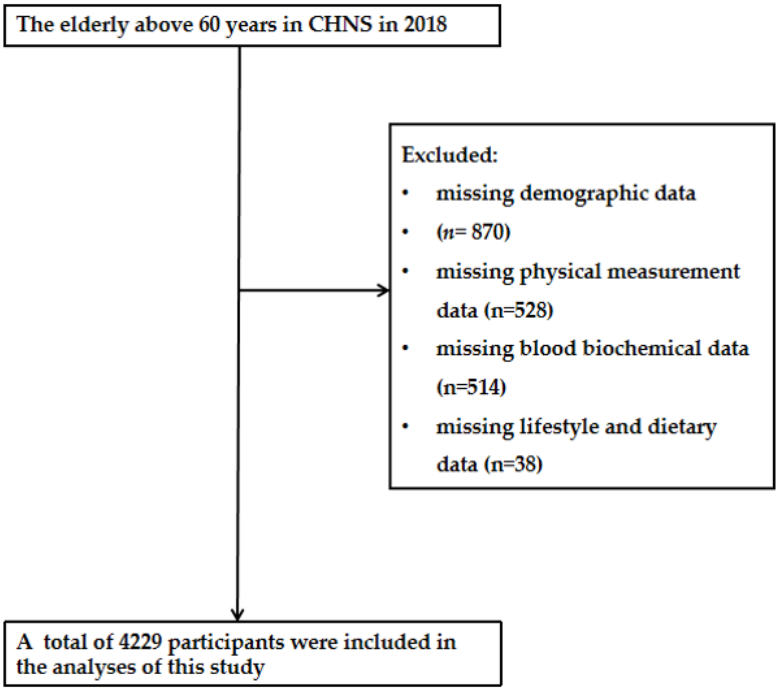

Figure 1. Flowchart of subjects.

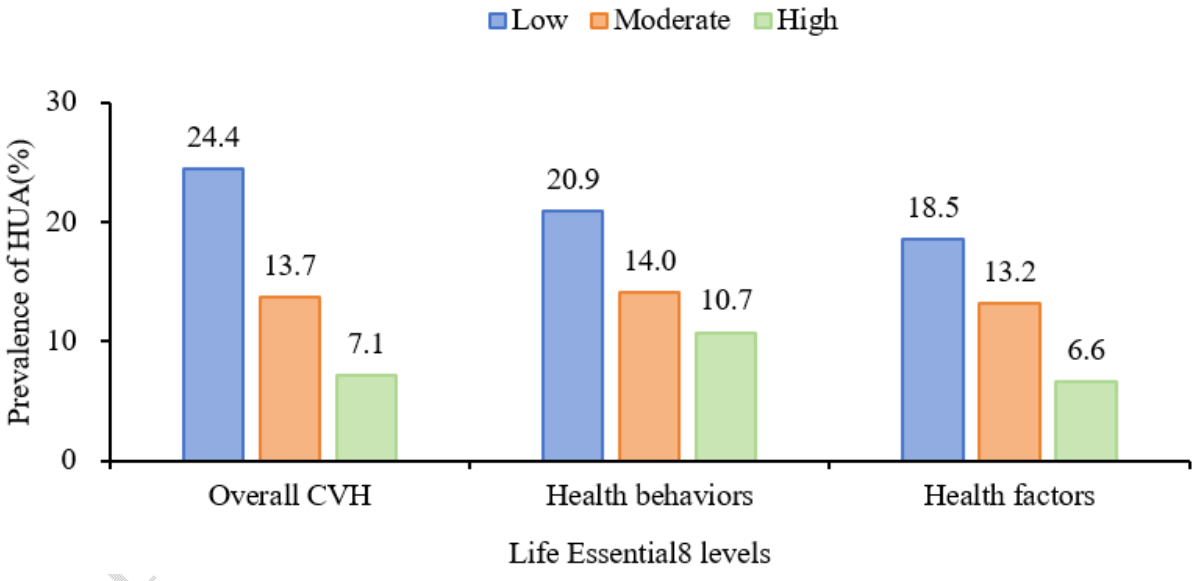

Figure 2. Prevalence of HUA in different levels of LE8 scores

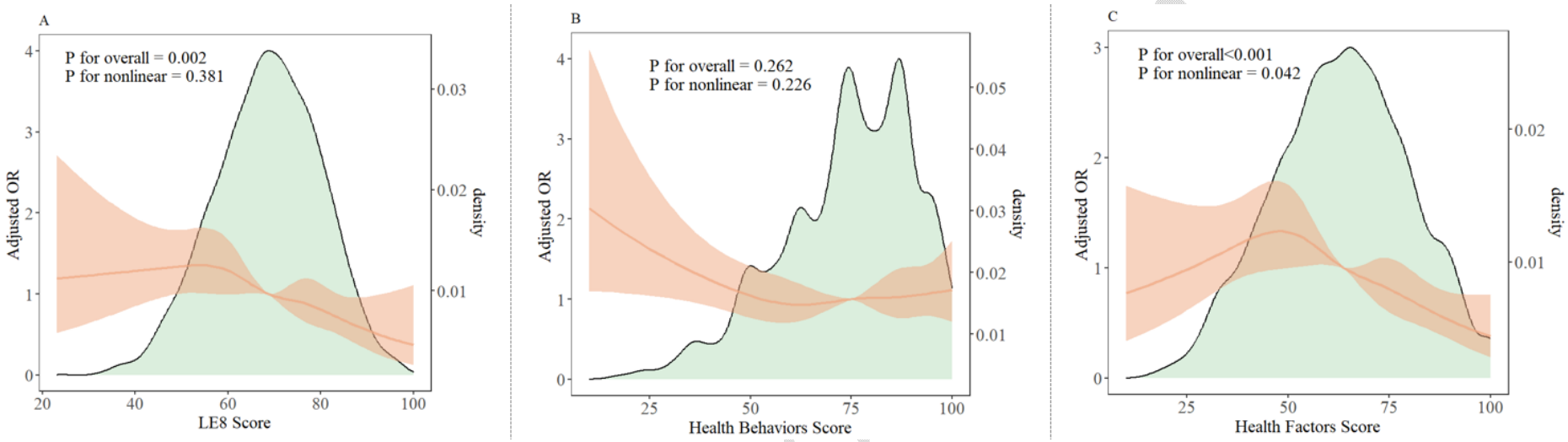

Figure 3. Population density and dose-response relationships between LE8 score (A), Health Behaviors score (B), Health Factors Score (C), and HUA

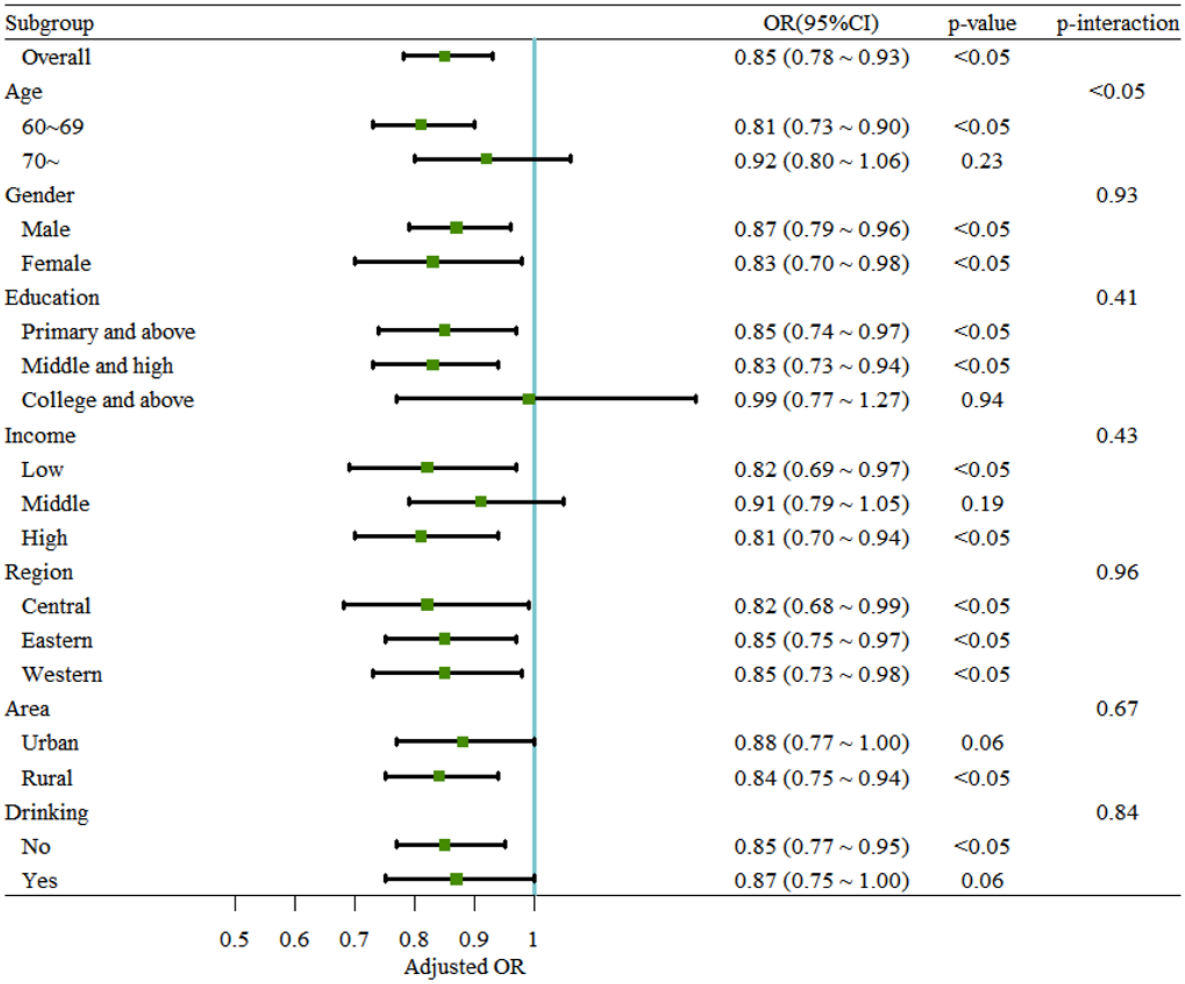

Figure 4. Subgroup analysis of the association between LE8 score and HUA. The ORs was calculated for each 10-point increase in LE8 score. Each stratification was adjusted for age, gender, education, income level, region, areas, seafood, alcohol intake, triglyceride, urea, and creatinine

Supplementary Table

Supplementary Table 1. Nutrient Targets for DASH Score

Nutrient	DASH score target	Intermediate target
Saturated fat	6% of energy	11% of energy
Total fat	27% of energy	32% of energy
Protein	18% of energy	16.5% of energy
Cholesterol	71.4 mg/1000 kcal	107.1 mg/1000 kcal
Fiber	14.8 g/1000 kcal	9.5 g/1000 kcal
Magnesium	238 mg/1000 kcal	158 mg/1000 kcal
Calcium	590 mg/1000 kcal	402 mg/1000 kcal
Potassium	2238 mg/1000 kcal	1534 mg/1000 kcal
Sodium	1143 mg/1000 kcal	1286 mg/1000 kcal

[†]The total score was 9 points, with 1 point for meeting the DASH score target, 0.5 points for being between the intermediate target and DASH score target, and 0 points for being below the intermediate target.

Supplementary Table 2. Quantitative assessment of LE8

Indicators	Quantification
Health factors	
BMI (kg/m^2)	
<24.0	100
24.0-27.9	70
28.0-34.9	30
35.0-39.9	15
≥40.0	0
Non-HDL-C (mg/dL)	
<130	100
130-159	60
160-189	40
190-219	20
≥220	0
Blood pressure (mm/Hg)	
<120/80	100
120-129/80	75
130-139 or 80-89	50
140-159 or 90-99	25
≥160 or ≥100	0
If drug-treated level, subtract 20 points	
Blood glucose (mg/dL) or HbA1c (%)	
No diabetes and FBG <100 (or HbA1c <5.7)	100
No diabetes and FBG:100-125 (or HbA1c: 5.7-6.4)	60
Diabetes with HbA1c <7.0	40
Diabetes with HbA1c: 7.0-7.9	30
Diabetes with HbA1c: 8.0-8.9	20
Diabetes with HbA1c: 9.0-9.9	10
Diabetes with HbA1c: ≥10.0	0
Health behaviors	
Sleep (hours)	
7 - <9	100
9 - <10	90
6 - <7	70
5 - <6 or ≥10	40
4 - <5	20
<4	0
Physical activity (min/week)	
≥150	100
120-149	90
90-119	80
60-89	60
30-59	40
1-29	20
0	0
Nicotine exposure	
Never smoker	100
Former smoker, quit ≥5y	75
Former smoker, quit 1 - <5y	50
Former smoker, quit <1y	25
Current smoker	0
Diet	
≥95th percentile	100
75th-94th percentile	80
50th-74th percentile	50
25th-49th percentile	25
1st-24th percentile	0

[†]The total score was 9 points, with 1 point