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Complete List of Authors:	Li, Ruiqiang; Hebei Medical University Zhan, Wenqiang; Shanghai Jiao Tong University School of Medicine Huang, Xin; Hebei Medical University Zhang, Zechen; Hebei Medical University Zhou, Meiqi; Hebei Medical University Bao, Wei; Hebei Medical University Huang, Feifei; Chinese Center for Disease Control and Prevention National Institute for Nutrition and Health Ma, Yuxia; Hebei Medical University,
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Association of Dietary Inflammatory Index(DII) and Depression in the elderly over 55 years in Northern China

Ruiqiang Li[1]; Wenqiang Zhan[2]; Xin Huang[1]; Zechen Zhang[1]; Meiqi Zhou[1]; Wei Bao[1]; Feifei Huang[3]; Yuxia Ma[1]*

Ruiqiang Li and Wenqiang Zhan contributed equally to this work.

Affiliations:

1.Department of Nutrition and Food Hygiene, School of Public Health, Hebei Medical University, Hebei Province Key Laboratory of Environment and Human Health, Shijiazhuang, China

2.School of Public Health, Shanghai Jiao Tong University School of Medicine, Shanghai 200025, PR China

3 National Institute for Nutrition and Health, Chinese Center for Disease Control and Prevention, No. 27, Nanwei Road, Xicheng District, Beijing, China

Correspondence address:

Yuxia Ma.

Department of Nutrition and Food Hygiene, School of Public Health, Hebei Medical University, Hebei Province Key Laboratory of Environment and Human Health, Shijiazhuang, China

Email: 2669909599@qq.com

Abstract

Objectives: Our study aimed to assess the association between the Dietary inflammation index (DII) and depression in the elderly over 55 years in Northern China.

Methods: We analyzed the data of 2022 Chinese adults aged 55 and over from a community-based neurological disease cohort study from 2018 to 2019. A validated semi-quantitative food frequency questionnaire was used to assess eating habits at the time of inclusion. Multiple logistic regression was used for analysis, and social demographics, lifestyle, and health-related factors were adjusted.

Results: A higher incidence of depression were observed among individuals in the highest quartile of the dietary inflammatory index. Individuals in the highest quartile of DII were more likely to be patients with obesity, hypertension and to be less daily energy intake. Participants in the most pro-inflammatory group (quartile 4) suffer the risk of depression was significantly higher than the participants in the most anti-inflammatory group (quartile 1) (OR 1.53; 1.37–1.82; P-trend=0.01). The subgroup analysis of BMI showed that there is a significant association between DII and the risk of depression in overweight and obese people($P<0.05$). The RCS results show that the OR value of depression possesses an upward trend with the increase of the DII

score.

Conclusions: Aged patients with depression present a higher potential for dietary inflammation. Pro-inflammatory diets might increase the risk of depressive symptoms. Further research in different populations is crucial to confirm the association between DII and depression.

Strengths and limitations of this study

This study is the first study to explore the association between DII and depression in the elderly over 55 years in China;

The dietary consumption level is estimated based on the FFQ covering the past 12 months, which may have a certain recall bias;.

Only 22 food parameters can be used in the DII calculations in this study, and there may be deviations in the estimation of the possibility of dietary inflammation.

1. Introduction

Due to rapid economic growth and changes in lifestyles, China is undergoing a rapid epidemiological transition from infectious diseases to non-communicable diseases (NCDs). Mental disorders such as depression are an important but often overlooked non-communicable disease, and it is becoming an increasingly serious cause of disability and disease burden. [1]These conditions are common in the general population, especially the elderly. For example, 7.73% of elderly people aged 55 and over in China suffered from depression (major depressive

disorder [MDD] and dysthymia) in the previous month, and the prevalence is 3.5 times and 1.4 times that of adults aged 18 -39 and 40-54 years. [2]

Systemic inflammation is becoming an important factor in the etiology of mental illnesses such as depression and anxiety. [3]According to reports, systemic chronic low-grade inflammation is related to the progression of MDD by affecting monoaminergic and glutamatergic neurotransmission. However, before the first episode of depression, whether various pro-inflammatory cytokines are abnormally elevated remains unclear. [4]Some studies have shown that the association between diet and mental health disorders may be mediated by the inflammatory properties of diet. [5]The current treatment of depression is not considered to be effective in all cases. So far, there are few nutritional programs in the guidelines for the treatment of depression. Recently, due to the pro-inflammatory and anti-inflammatory properties of nutrients, people are paying more and more attention to the protective and regulating effects that diet may have in common mental disorders (including depression).[6]However, there are limited data on the role of dietary inflammation potential in this regard.[7]

The Dietary Inflammation Index (DII) is a tool used to quantify the dietary inflammation potential of an individual's diet. Its goal is to assess the impact of diet-related inflammation on health outcomes. [8]Thus, the purpose of this work was to examine the association between the inflammatory potential of habitual diets and depressive outcomes.

2. Methods

2.1. Study Population

Participants came from the Community Cohort Study of Nervous System Diseases

(CCSNSD) project under the National Key Research and Development Program, the National Key Research and Development Program, and the Precision Medicine Project Nervous System Disease Cohort Research (CCSNSD) project. The project is undertaken by the Institute of Nutrition and Health of the Chinese Center for Disease Control and Prevention, in cooperation with the Center for Disease Control and Prevention. The project uses a multistage random cluster sampling method to draw samples. The protocol of this study was reviewed and approved by the Institutional Review Board of the National Institute for Nutrition and Health (No. 2017020, November 6, 2017).In addition, written informed consent was obtained for each participant before the survey.[9] The present study focuses on elderly people over 55 years of age in the cohort study. In the current analysis, We included data from participants who had complete dietary information and diagnostic information for depression. Finally, a total of 2022 participants participated in the analysis.

2.2. Patient and Public Involvement

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. Written informed consent was obtained from all participants.

2.3. Depression

We defined depression according to the Geriatric Depression Scale (GDS), this scale is one of the most widely used scales to assess the depression of the elderly. [10]It consists of 30

self-assessment items with yes/no response options. A score of 0-10 indicates no depression, a score of 11-20 indicates mild depression, and a score of 21-30 indicates severe depression. [11]

2.4. Assessment of Food Consumption

Dietary consumption is assessed by a validated semi-quantitative FFQ, covering 81 foods, Participants were asked about the frequency of habitual consumption the number of each item in the past 12 months, and choose from five types of frequencies(Daily, weekly, monthly, yearly, or never) and consumption in the past 12 months. For consumers, their consumption of each food group or item is calculated based on their reported average consumption frequency and quantity.

2.5. Diet and Dietary Inflammatory Index

The Dietary Inflammation Index (DII) aims to provide a quantitative method for assessing the effect of diet on health outcomes. [12]It is the characteristic of DII to objectify the inflammatory characteristics of specific dietary intake. [13]When calculating the E-DII score, the dietary information of each study participant is first linked to a regionally representative database that provides a global estimate of the average intake of each of the 45 parameters, and the standard deviation considered in the DII definition. Then, by subtracting the energy-adjusted regional representative database average from the number of reports, and then dividing that value by the standard deviation of the parameters used to derive the participant's z-score relative to the standard global average. These z-scores are converted to percentages (expressed as a ratio; that is, the value goes from 0 to 1), and then centered on doubling and subtracting 1. These extra steps avoid inappropriate weighting.DII scores range from negative tail to positive tail, more negative values indicate anti-inflammatory properties and corrected scores indicate pro-inflammatory properties.

[14]Energy adjusted DII (E-DII) food intake per 1,000 calories is used to explain the effect of total intake on energy intake. For this, the energy standardized version requires a world database. [15]Twenty-two of the 45 possible food parameters were used for DII calculation based on the FFQ in this study(carbohydrates, protein, fat, alcohol, fiber, cholesterol, saturated fat, monounsaturated fat, polyunsaturated fat, niacin, thiamine, riboflavin, vitamin B12, vitamin B6, iron, magnesium, zinc, selenium, vitamin A, vitamin C, vitamin E and folic acid).

2.6. Covariates

We adjusted the variables previously identified as potential confounders in the literature. Personal background characteristics including self-reported age (yearly), gender (female or male), an education level (illiterate, elementary school, junior high school and above), employment status(yes or no); health-related variables including tobacco smoking (yes or no), alcohol drinking (yes or no), physical activity (yes or no), daily energy intake(kcal), diabetes (yes or no), hypertension (yes or no), We use a cut-off value of 28 kilograms per square meter (kg/m2) of China's body mass index (BMI) to determine obesity. [16]

2.7. Statistical Analysis

Data were expressed as mean (SD/SEM) and n (%) for continuous variables and categorical variables, respectively. The differences between groups were analyzed by analysis of variance of continuous variables and chi-square test of categorical variables. Logistic regression analysis is used to simulate the association between depressed people and people in different DII quartiles, and OR(95% CI) was calculated to evaluate the relationship between depression and the DII score. We utilized a subgroup analysis of BMI to optimize the robustness of the statistical test. (BMI

159 <18.5,18.5-24.0,24-28,≥30 kg/m2).Restricted cubic splines were used to evaluate the correlation
160 between the DII and the risk of depression. All statistical analyses were performed using the
161 software package R (http://www.R-project.org, The R Foundation). A two-tailed p-value of <0.05
162 was considered statistically significant.

163 **3. Results**

164 From the Community Cohort Study on Specialized Nervous System Diseases, the study
165 included 2022 elderly participants (median [IQR] age, 64 [60-70] years; 775 [38.3%] males) from
166 2017 to 2018. Mean (SD) and range of the DII in the included population were 1.70 (1.42) and －
167 5.20 to ＋5.68. Clinical and demographic characteristics according to quartiles of DII are
168 presented in Table 1. A higher incidence of depression was observed among individuals in the
169 highest quartile of the dietary inflammatory index, and thus the most pro-inflammatory diet.
170 Individuals in the highest quartile of DII were more likely to be patients with obesity,
171 hypertension and to be less daily energy intake. No differences in sex, employment status,
172 physical activities, diabetes, tobacco smoking, or alcohol drinking were observed between groups.

173 Table 2 shows the OR and 95% CI of depression according to the quartile of DII. When DII
174 is expressed as a quartile, the results obtained by adjusting for confounding factors and modeling
175 DII as a categorical variable for depression indicate that there is a direct association. Participants
176 in the most pro-inflammatory group (quartile 4) suffer the risk of depression was significantly
177 higher than the participants in the most anti-inflammatory group (quartile 1) (OR 1.53; 1.37–1.82;
178 P-trend=0.01).

179 Stratified logistic regression analysis (Table 3) revealed body mass index(BMI) differences

in the associations between dietary inflammatory potential and depression outcomes(BMI<18.50kg/m^2; 18.50 ⩽ BMI<24.00; BMI ⩾ 28.00). Increased risk of depression were (OR 1.25,95%CI 1.08-1.46; OR 1.39, 95%CI 1.19-1.52) observed among the overweight and obese study participants, respectively. Comparing the highest to the lowest quartile of DII, the association with depression remained in the fully adjusted model ($P < 0.05$, comparing highest to lowest tertile of DII). No associations were observed among the underweight and normal-weight participants. The RCS results show that the OR value of depression possesses an upward trend with the increase of the DII score($P < 0.05$)(Figure 1).

4. Discussion

As far as we know, this is the first study in China to investigate the association between depression and DII as a representative indicator of the potential for dietary inflammation. We found that patients with depression had higher DII scores compared to the control group without depression. The association between DII and depression observed in this study suggests that the potential of an inflammatory diet plays an important role in depression.

The significant association between DII and depression observed in the current study broadly supports a related study that studied 254 depression patients in the UK and found that compared with the disease-free control group, these patients'DII scores were higher.[17] Other reports have found that compared with other types of severe mental illness, people with depression have higher levels of dietary inflammation and are more likely to show worse indicators of physical health.[18]

Depression (or clinical depression) is a widespread and severe mood disorder worldwide.[19]

Among the elderly, depression is the most common mental disorder, and it is becoming more common. Depression also reduces the ability of the elderly to recover.[20] Therefore, the National Institute of Mental Health in the United States regards depression in the elderly as a major public health problem, leading to significant and continuous growth in health care expenditures. In addition, depression is often associated with an increased risk of other diseases (such as heart disease) and mortality in the elderly.[21-22] Therefore, personalized early depression detection is essential for the physical and mental health of the elderly. Effective and individualized prediction of the onset of depression can inform intervention strategies in time to prevent depression in the elderly and further reduce the cost of medical care.

As we all know, inflammation is related to depression. In the early 1990s, the macrophage theory was first hypothesized as depression, especially when these cells are activated by any damage (M1 cells).[23] There is increasing evidence that the role of M1 cells (including microglia and central nervous system macrophages) in depression has accumulated, because peripheral M1 cells may be the main source of increased cytokines in depression. Changes in the peripheral immune system of depression, impaired cellular immunity, and elevated levels of pro-inflammatory cytokines.[24-26] For example, cytokines may affect neurotransmitter metabolism, neuroendocrine function, and regional brain activity. All of these factors may be related to the onset of depression. related. However, it should be noted that in studies that adjusted the analysis of serum cytokine levels, DII® was still significantly associated with the onset of depression. These findings may indicate that unhealthy (pro-inflammatory) diets independently contribute to the onset of depression, leading to important clinical consequences. Diet seems to be an important goal in preventing depression. Some observational studies have reported that a

healthy diet (such as the Mediterranean diet) is associated with a lower incidence of depression in adults. Our research further confirms these findings, suggesting that a healthy diet may be necessary to prevent depression. A recent randomized controlled trial of adults with depressive symptoms showed that using a Mediterranean diet significantly reduced depressive symptoms. In addition, it can be assumed that there is a synergistic anti-inflammatory effect between antidepressants and the Mediterranean or longevity diet, thus opening up areas for potential preventive interventions or early interventions that can target the inflammatory pathway before or when mild symptoms appear.[27-29]

The subgroup analysis of BMI showed that there is a significant association between DII and the risk of depression in overweight and obese people. Eating behavior related to mood may be the underlying mechanism of the relationship between depression and obesity. Several mechanisms can explain the link between depression and obesity in this pathway. In particular, emotional eating, food reward processes, increased brain monoamine activity, and the inflammatory potential of the diet may also be related to the depression-obesity link. Future studies must be conducted to examine whether the intake of pro-inflammatory foods can enhance the emotional state of patients with atypical depression under psychosocial stress.[30-31]

Among the strengths of our study are a large number of participants over 55 years with evaluable data; information about diet and lifestyle factors; and various confounding factors. To the best of our knowledge, the current study is the first to explore the association between DII and depression in the elderly over 55 years in China. None of the 30 items in the GDS was somatic, thus avoiding the confusion of somatic symptoms with physical disturbances that were common in the elderly.[32] The limitation is also of note. Firstly, due to all of the participants recruited into

the cohort are from the same province, the true state of the nation's elderly may not be accurately reflected. Another potential limitation is that among the 45 food parameters, only 22 food parameters can be used in the DII calculations in this study, and there may be deviations in the estimation of the possibility of dietary inflammation. Furthermore, the dietary consumption level is estimated based on the FFQ covering the past 12 months, which may have a certain recall bias.

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Conflict of interest

The authors declare that they have no conflict of interest.

Ethical approval

All procedures involving participants were approved by the institutional review board of the National Institute for Nutrition and Health, Chinese Center for Disease Control and Prevention (approval number: 2017-020).

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Data availability statement

No additional data available.

Author Contributions

Ma and Li had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Concept and design: Ma, Li.

Acquisition, analysis, or interpretation of data: All authors.

Drafting of the manuscript: Ma, Li, Zhan

Critical revision of the manuscript for important intellectual content: All authors.

Statistical analysis: Li, Zhan, Zhou, Zhang,Huang.

Obtained funding: Ma, Huang.

Administrative, technical, or material support: Huang, Wang, Lv,Huang.

Supervision: Ma

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Figure legend

Figure 1 Restricted cubic splines for the nonlinear relationship between the risk of depression and increased dietary inflammation index.

Table 1 Baseline characteristics of the Community Cohort Study of Nervous System Diseases (CCSNSD) project population across quartiles of the DII score

Characteristic	Frequency (%) or Mean(SD)				P-value
	Quartile 1 （n=504）	Quartile 2 （n=506）	Quartile 3 （n=504）	Quartile 4 （n=508）	
Age (years)					<0.001
	68.36±0.33	66.10±0.34	63.85±0.31	64.67±0.32	
Sex					0.394
Male	201(39.9%)	191(37.7%)	190(37.7%)	193(38.0%)	
Female	303(60.1%)	315(62.3%)	314(62.3%)	315(62.0%)	
BMI（kg/m2）					
BMI<18.50 (underweight)	9(1.8%)	22(4.3%)	13(2.6%)	12(2.4%)	0.010

18.50≤BMI<24.00 (normal weight)	171(33.9%)	210(41.5%)	208(41.3%)	177(14.8%)	
24.00≤BMI<28.00 (overweight)	215(42.7%)	194(38.3%)	184(36.5%)	187(36.8%)	
BMI≥28.00 (obese)	109(21.6%)	80(15.8%)	99(19.6%)	132(26.0%)	
Employment					0.120
No	444(88.1%)	430(85.0%)	417(82.7%)	464(85.4%)	
Yes	60(11.9%)	76(15.0%)	87(17.3%)	74(14.6%)	
Education					0.034
Illiteracy	129(25.6%)	137(27.1%)	111(22.0%)	120(23.6%)	
Primary school	181(35.9%)	163(32.2%)	150(29.8%)	155(30.5%)	
Junior high school/above	194(38.5%)	206(40.7%)	243(48.2%)	233(45.9%)	
Daily energy intake (kcal)					<0.001
	1530.08±15.69	1344.05±14.65	1638.82±13.84	1301.62±14.04	
Tobacco Smoking					0.213
No	409(81.2%)	430(85.0%)	432(85.7%)	426(83.9%)	
Yes	95(18.8%)	76(15.0%)	72(14.3)	82(16.1%)	
Alcohol Drinking					0.344
No	460(91.3%)	448(88.5%)	459(91.1%)	452(89.0%)	
Yes	44(8.7%)	58(11.5%)	45(8.9%)	56(11.0%)	
Physical activities					0.894
No	309(61.3%)	309(61.1%)	305(60.5%)	319(62.8%)	
Yes	195(38.7%)	197(38.9%)	199(39.5)	189(37.2%)	
Diabetes					0.444
No	418(82.9%)	436(86.2%)	430(85.3%)	424(83.5%)	

	Yes	86(17.1%)	70(13.8%)	74(14.7%)	84(16.5%)	
Depression						<0.001
	No	394(78.2%)	390(77.1%)	387(76.8%)	378(74.4%)	
	Yes	110(21.8%)	116(22.9%)	117(23.2%)	130(25.6%)	
Hypertension						<0.001
	No	205(40.7%)	222(43.9%)	231(45.8%)	195(38.4%)	
	Yes	299(59.3%)	284(56.1%)	273(54.2%)	313(61.6%)	

Quartile 1:-5.20 to 0.94;Quartile 2:0.95,1.95;Quartile 3:1.96 to 2.69;Quartile 4:2.70 to 5.68

Table 2 Logistic regression analysis of the association between DII and depression.

	Quartile 1（n=504）	Quartile 2（n=506）	Quartile 3（n=504）	Quartile 4（n=508）
Model 1	1 [reference]	1.29(1.09-1.42)	1.36(1.13-1.52)	1.43(1.29-1.68)
Model 2	1 [reference]	1.33(1.12-1.46)	1.40(1.27-1.65)	1.51(1.31-1.75)
Model 3	1 [reference]	1.31(1.20-1.43)	1.39(1.25-1.63)	1.53(1.37-1.82)

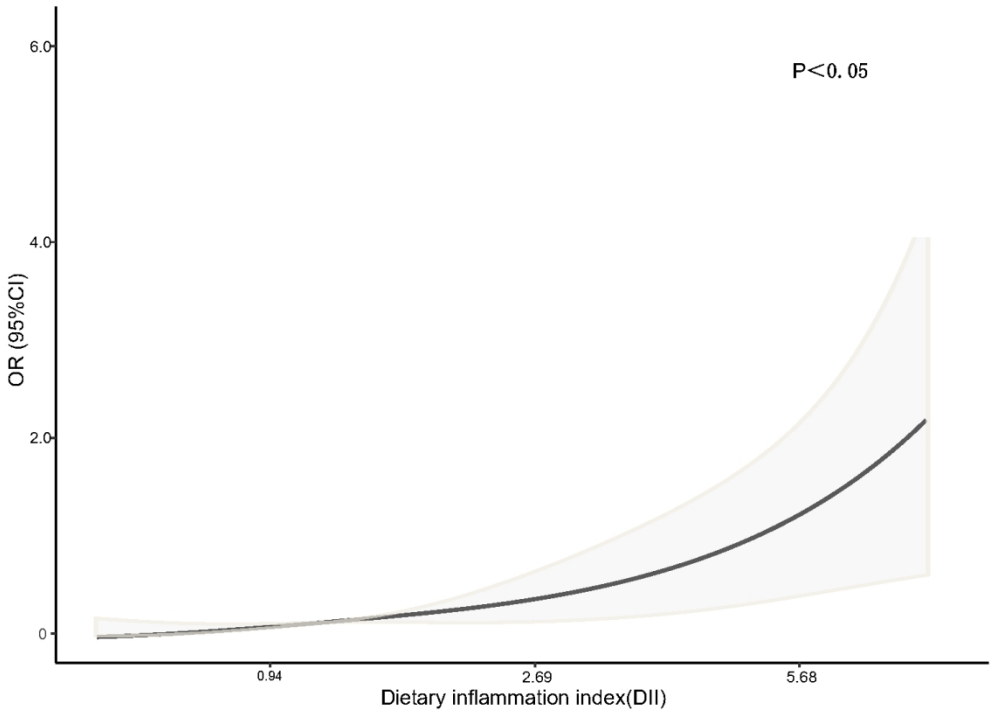
Model 1 is not adjusted; Model 2 adjusts age, sex, BMI, employment, education, daily energy intake, daily energy intake, tobacco smoking, alcohol drinking and physical activities; Model 3 adjusts age, sex, BMI, employment, education, daily energy intake, daily energy intake, tobacco smoking, alcohol drinking, physical activities, diabetes and hypertension.

Table 3 Body mass index stratified analysis of the association between DII and depression

	Model 1	Model 2	Model 2
BMI<18.50 (underweight)			
Quartile 1（n=9）	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)

Quartile 2（n=22）	1.09(0.89-1.15)	1.06(0.76-1.15)	1.03(0.83-1.27)
Quartile 3（n=13）	1.06(0.83-1.12)	1.12(0.89-1.37)	1.20(0.90-1.32)
Quartile 4（n=12）	1.13(1.02-1.22)	1.16(0.91-1.58)	1.35(0.98-1.53)
P-trend	0.53	0.32	0.12
18.50≤BMI<24.00 (normal weight)			
Quartile 1（n=171）	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)
Quartile 2（n=210）	1.02(0.73-1.16)	0.98(0.87-1.12)	1.01(0.86-1.12)
Quartile 3（n=208）	1.19(0.81-1.28)	1.03(0.90-1.16)	1.13(0.90-1.25)
Quartile 4（n=177）	1.27(0.91-1.36)	1.23(0.96-1.51)	1.26(0.92-1.48)
P-trend	0.23	0.35	0.29
24.00≤BMI<28.00 (overweight)			
Quartile 1（n=215）	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)
Quartile 2（n=194）	1.09(0.89-1.25)	1.08(1.01-1.26)	1.10(1.03-1.29)
Quartile 3（n=184）	1.13(1.02-1.32)	1.15(1.05-1.29)	1.21(1.09-1.37)
Quartile 4（n=187）	1.25(1.08-1.46)	1.31(1.11-1.52)	1.35(1.13-1.56)
P-trend	0.03	0.01	0.006
BMI≥28.00 (obese)			
Quartile 1（n=109）	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)
Quartile 2（n=80）	1.08(1.01-1.19)	1.15(1.05-1.29)	1.18(1.09-1.35)
Quartile 3（n=99）	1.21(1.10-1.39)	1.28(1.13-1.46)	1.32(1.19-1.58)
Quartile 4（n=132）	1.39(1.19-1.52)	1.42(1.21-1.62)	1.56(1.23-1.78)
P-trend	0.008	0.005	0.003

413



Restricted cubic splines for the nonlinear relationship between the risk of depression and increased dietary inflammation index.

203x152mm (192 x 192 DPI)

STROBE Statement—Checklist of items that should be included in reports of ***case-control studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	3-4
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls	4
		(*b*) For matched studies, give matching criteria and the number of controls per case	4
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5
Bias	9	Describe any efforts to address potential sources of bias	6
Study size	10	Explain how the study size was arrived at	6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6
		(*b*) Describe any methods used to examine subgroups and interactions	6
		(*c*) Explain how missing data were addressed	6
		(*d*) If applicable, explain how matching of cases and controls was addressed	6
		(*e*) Describe any sensitivity analyses	6-7
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	7
		(b) Give reasons for non-participation at each stage	7
		(c) Consider use of a flow diagram	7
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	7
		(b) Indicate number of participants with missing data for each variable of interest	7
Outcome data	15*	Report numbers in each exposure category, or summary measures of exposure	7

Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	7
		(*b*) Report category boundaries when continuous variables were categorized	7
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	7
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	7-8
Discussion			
Key results	18	Summarise key results with reference to study objectives	8
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	10
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	8-9
Generalisability	21	Discuss the generalisability (external validity) of the study results	8-9
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	11

*Give information separately for cases and controls.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

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Association of Dietary Inflammatory Index(DII) and Depression in the elderly over 55 years in Northern China

Ruiqiang Li[1]; Wenqiang Zhan[2]; Xin Huang[1]; Zechen Zhang[1]; Meiqi Zhou[1]; Wei Bao[1]; Feifei Huang[3]; Yuxia Ma[1]*

Ruiqiang Li and Wenqiang Zhan contributed equally to this work.

Affiliations:

1.Department of Nutrition and Food Hygiene, School of Public Health, Hebei Medical University, Hebei Province Key Laboratory of Environment and Human Health, Shijiazhuang, China

2.School of Public Health, Shanghai Jiao Tong University School of Medicine, Shanghai 200025, PR China

3 National Institute for Nutrition and Health, Chinese Center for Disease Control and Prevention, No. 27, Nanwei Road, Xicheng District, Beijing, China

Correspondence address:

Yuxia Ma.

Department of Nutrition and Food Hygiene, School of Public Health, Hebei Medical University, Hebei Province Key Laboratory of Environment and Human Health, Shijiazhuang, China

Email: 2669909599@qq.com

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Abstract

Objectives: Our study aimed to assess the association between the Dietary Inflammatory Index (DII) and depression in the elderly over 55 years in Northern China.

Methods: We analyzed the data of 2022 Chinese adults aged 55 and over from a community-based neurological disease cohort study from 2018 to 2019. A validated semi-quantitative food frequency questionnaire was used to assess eating habits at the time of inclusion. Multiple logistic regression was used for analysis, and social demographics, lifestyle, and health-related factors were adjusted.

Results: Among the included population, the prevalence of depression was 23.39%. Mean (SD) and range of the DII in the included population were 1.70 (1.42) and -5.20 to +5.68. Participants in the most pro-inflammatory group (quartile 4) suffer the risk of depression was significantly higher than the participants in the most anti-inflammatory group (quartile 1) (OR 1.53; 1.37–1.82; P-trend=0.01). The subgroup analysis of BMI showed that there is a significant association between DII and the risk of depression in overweight and obese people($P < 0.05$). The restricted cubic spline (RCS) results show that the OR value of depression possesses an upward trend with the increase of the DII score.

Conclusions: Aged patients with depression present a higher potential for dietary inflammation. Pro-inflammatory diets might increase the risk of depressive symptoms. Further research in different populations is crucial to confirm the association between DII and depression.

Keywords: Dietary Inflammatory Index, depression, elderly.

Article summary

Strengths and limitations of this study:

1.Among the strengths of our study are a large number of participants over 55 years with evaluable data; information about diet and lifestyle factors; and various confounding factors.

2.To the best of our knowledge, the current study is the first to explore the association between DII and depression in the elderly over 55 years in China.

3.Due to all of the participants recruited into the cohort are from the same province, the true state of the nation's elderly may not be accurately reflected. 4.Another potential limitation is that among the 45 food parameters, only 22 food parameters can be used in the DII calculations in this study,

5.Owing to disease-related conditions such as diabetes and high blood pressure are only based on confounding factors reported by participants, the results may be unreliable.

1. Introduction

Due to rapid economic growth and changes in lifestyles, China is undergoing a rapid epidemiological transition from infectious diseases to non-communicable diseases (NCDs). Mental disorders such as depression are an important but often overlooked non-communicable disease, and it is becoming an increasingly serious cause of disability and disease burden. [1]These conditions are common in the general population, especially the elderly. For example, 7.73% of elderly people aged 55 and over in China suffered from depression (major depressive disorder [MDD] and dysthymia) in the previous month, and the prevalence is 3.5 times and 1.4 times that of adults aged 18 -39 and 40-54 years. [2]

Systemic inflammation is becoming an important factor in the etiology of mental illnesses

such as depression and anxiety. [3] Approximately one-quarter of patients with major depression (MDD) show evidence of systemic inflammation. [4]Moreover, some studies have shown that chronic low-grade inflammation of the whole body can affect monoaminergic and glutamate neurotransmission, which may adversely affect the cognitive function of patients with bipolar disorder or major depression. However, before the first episode of depression, whether various pro-inflammatory cytokines are abnormally elevated remains unclear. [5,6]Some studies have shown that the association between diet and mental health disorders may be mediated by the inflammatory properties of diet. [7]The current treatment of depression is not considered to be effective in all cases. So far, there are few nutritional programs in the guidelines for the treatment of depression. Recently, due to the pro-inflammatory and anti-inflammatory properties of nutrients, people are paying more and more attention to the protective and regulating effects that diet may have in common mental disorders (including depression). [8]However, there are limited data on the role of dietary inflammation potential in this regard. [9]The long-term unhealthy diet leads to a decline in the quality of the diet, which may create a pro-inflammatory environment in the human body, thereby creating conditions for the occurrence and development of various chronic inflammatory diseases. DII, as a tool that can assess the potential of dietary inflammation, provides the possibility to test this hypothesis. [10]

Meanwhile, inflammation has important physiological effects on mood and behavior. Kynurenine metabolism is hypothesized to be a pathway connecting inflammation and depression, partly because of the effect of kynurenine metabolites on the neurotransmission of glutamate in the central nervous system. [11]Some studies have shown that inflammation may affect the interconnection of the hypothalamus with areas important for cognition and emotion, and it may

cause the hypothalamus-pituitary-adrenal (HPA) axis to be dysregulated and affect the monoaminergic system. [12]

The Dietary inflammatory index (DII) was developed and verified by researchers at the University of South Carolina in Columbia to assess the inflammatory potential of an individual's diet. The initial DII score was based on the results of articles published from 1950 to 2007 that assessed the impact of specific foods on specific inflammatory markers (specific inflammatory markers include IL-1β, IL-4, IL-6, IL-10, TNF-α and CRP), significantly increase IL-1β, IL-6, TNF-α or CRP, or decrease IL-4 or IL-10 to "+1", which is pro-inflammatory; significantly reduce IL-1β, IL-6, TNF -α or CRP, or increase IL-4 or IL-10 to "-1", which is an anti-inflammatory effect. In 2014, South Carolina researchers improved the DII score from 2007 to 2010, and the improved scoring system applied 45 food parameters. [13]

The relationship between diet, inflammation and mental health is of increasing interest, and the link between diet and mental health disorders may be mediated by the inflammatory properties of diet. [14,15] As a tool to assess the potential of dietary inflammation, the relationship between DII and mental disorders is worthy of discussion and research. Moreover, a study has shown that people with the lowest levels of DII have a lower risk of being at the highest levels of mental health disorders. [14]

Although the number of patients with depression has increased in recent years, compared with other developed countries, there are relatively few studies on depression in China. [16] Therefore, it is urgent to explore the relationship between DII and depression risk in the Chinese elderly. The Dietary Inflammatory Index (DII) is a tool used to quantify the dietary inflammation

potential of an individual's diet. Its goal is to assess the impact of diet-related inflammation on health outcomes. [17]Thus, the purpose of this work was to examine the association between the inflammatory potential of habitual diets and depression. Moreover, the use of DII as an indicator to directly and reasonably connect the three of nutrition, inflammation and depression, may have clinical and public health significance for the development of new nutritional psychiatric methods to promote good mental health.

2. Methods

2.1. Study Population

Participants came from the Community Cohort Study of Nervous System Diseases (CCSNSD) project under the National Key Research and Development Program, the National Key Research and Development Program, and the Precision Medicine Project Nervous System Disease Cohort Research (CCSNSD) project. The project is undertaken by the Institute of Nutrition and Health of the Chinese Center for Disease Control and Prevention, in cooperation with the Center for Disease Control and Prevention. The project uses a multistage random cluster sampling method to draw samples. The protocol of this study was reviewed and approved by the Institutional Review Board of the National Institute for Nutrition and Health (No. 2017020, November 6, 2017).

In allusion to subjects recruited in the CCSNSD cohort, the samples eligible for inclusion were (1) 55 years old and older, (2) resident population living in the sampled community, (3) absence of clinically diagnosed depression, (4) be able to perform a normal depression assessment, (5) completed data of sociodemographic characteristics, disease history, and food

frequency questionnaire (FFQ). We excluded subjects because of (1) no depression assessment results, (2) lack of baseline status such as education and physical activities, (3) nutrient deficiency, (4) abnormal energy intake, (5) people with other psychological disorders. Finally, a total of 2022 participants were involved in the analysis.

2.2. Patient and Public Involvement

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. Written informed consent was obtained from all participants.

2.3. Depression

We defined depression according to the Geriatric Depression Scale (GDS), this scale is one of the most widely used scales to assess the depression of the elderly. [18]It consists of 30 self-assessment items with yes/no response options. A score of 0-10 indicates no depression, a score of 11-20 indicates mild depression, and a score of 21-30 indicates severe depression. [19]

2.4. Assessment of Food Consumption

Dietary consumption is assessed by a validated semi-quantitative FFQ, covering 81 foods, Participants were asked about the frequency of habitual consumption the number of each item in the past 12 months, and choose from five types of frequencies(Daily, weekly, monthly, yearly, or never) and consumption in the past 12 months. For consumers, their consumption of each food group or item is calculated based on their reported average consumption frequency and quantity.

2.5. Assessment of DII score

The Dietary Inflammatory Index (DII) aims to provide a quantitative method for assessing the effect of diet on health outcomes. [20]It is the characteristic of DII to objectify the inflammatory characteristics of specific dietary intake. [21]

The calculation of the dietary inflammatory index links the personal dietary data obtained in each clinical study with the global average intake. The specific formula is: Z score = (daily intake of this kind of dietary ingredient or nutrient-this kind of dietary ingredient or the global average per capita daily intake of nutrients)/The standard deviation of the global average per capita daily intake of this dietary ingredient or nutrient. Then convert the Z score to a percentile system (to reduce the influence of outlier effects), double the obtained percentile value and subtract "1" to achieve a symmetrical distribution centered on "0". Finally, multiply by the total inflammatory score of each dietary component, and combine the results to obtain the personal dietary inflammatory index score. DII scores range from negative tail to positive tail, more negative values indicate anti-inflammatory properties and corrected scores indicate pro-inflammatory properties. [14]Energy adjusted DII (E-DII) food intake per 1,000 calories is used to explain the effect of total intake on energy intake. For this, the energy standardized version requires a world database. [22]Twenty-two of the 45 possible food parameters were used for DII calculation based on the FFQ in this study(carbohydrates, protein, fat, β-Carotene, fiber, cholesterol, saturated fat, monounsaturated fat, polyunsaturated fat, niacin, thiamine, riboflavin, vitamin B12, vitamin B6, Fe, magnesium, zinc, selenium, vitamin A, vitamin C, vitamin E and folic acid).

The appendix of the DII

$Zscore$ = [(daily mean intake - global daily mean intake)/standard deviation]

$Zscore^1 = Zscore \rightarrow$(converted to a percentile score)×2-1

DII = $\sum Zscore^1 \times$ the inflammatory effect score of each dietary component

2.6. Covariates

We adjusted the including self-reported age (yearly), gender (female or male), an education level (illiterate, elementary school, junior high school and above), employment status(yes or no); health-related variables including tobacco smoking (yes or no), alcohol drinking (yes or no), physical activity (yes or no), daily energy intake(kcal), diabetes (yes or no), hypertension (yes or no), We use a cut-off value of 28 kilograms per square meter (kg/m2) of China's body mass index (BMI) to determine obesity. [23]

2.7. Statistical Analysis

Data were expressed as mean (SD/SEM) and n (%) for continuous variables and categorical variables, respectively. The differences between groups were analyzed by analysis of variance of continuous variables and chi-square test of categorical variables. Logistic regression analysis is used to simulate the association between depressed people and people in different DII quartiles, and OR(95% CI) was calculated to evaluate the relationship between depression and the DII score. We utilized a subgroup analysis of BMI to optimize the robustness of the statistical test. (BMI <18.5,18.5-24.0,24-28,≥30 kg/m2).Restricted cubic splines were used to evaluate the correlation between the DII and the risk of depression. All statistical analyses were performed using the software package R (http://www.R-project.org, The R Foundation). A two-tailed p-value of <0.05

was considered statistically significant.

3. Results

From the Community Cohort Study on Specialized Nervous System Diseases, the study included 2022 elderly participants (median [IQR] age, 64 [60-70] years; 775 [38.3%] males) from 2017 to 2018. Mean (SD) and range of the DII in the included population were 1.70 (1.42) and − 5.20 to + 5.68. Clinical and demographic characteristics according to quartiles of DII are presented in Table 1. A higher incidence of depression was observed among individuals in the highest quartile of the dietary inflammatory index, and thus the most pro-inflammatory diet. Individuals in the highest quartile of DII were more likely to be patients with obesity, hypertension and to be less daily energy intake. No differences in sex, employment status, physical activities, diabetes, tobacco smoking, or alcohol drinking were observed between groups. We also compared baseline characteristics of depressed and non-depressed patients, and found differences in gender, employment status, and physical activity between the two groups ($P<0.05$) (Supplementary Table 1). At the same time, no significant difference was observed between the nutrients between the two groups (Supplementary Table 2).

Table 2 shows the OR and 95% CI of depression according to the quartile of DII. When DII is expressed as a quartile, the results obtained by adjusting for confounding factors and modeling DII as a categorical variable for depression indicate that there is a direct association. Participants in the most pro-inflammatory group (quartile 4) suffer the risk of depression was significantly higher than the participants in the most anti-inflammatory group (quartile 1) (OR 1.53; 1.37–1.82; P-trend=0.01).

Stratified logistic regression analysis (Table 3) revealed body mass index(BMI) differences in the associations between dietary inflammatory potential and depression outcomes(BMI<18.50kg/m^2; 18.50 ⩽ BMI<24.00; BMI ⩾ 28.00). Increased risk of depression were (OR 1.25,95%CI 1.08-1.46; OR 1.39, 95%CI 1.19-1.52) observed among the overweight and obese study participants, respectively. Comparing the highest to the lowest quartile of DII, the association with depression remained in the fully adjusted model ($P < 0.05$, comparing highest to lowest tertile of DII). No associations were observed among the underweight and normal-weight participants. The RCS results show that the OR value of depression possesses an upward trend with the increase of the DII score($P < 0.05$) (Figure 1). At the same time, a subgroup analysis of people of different genders showed that the pro-inflammatory diet is a risk factor for depression in elderly women ($P < 0.05$) (Supplementary Table 3).

4. Discussion

As far as we know, this is the first study in China to investigate the association between depression and DII as a representative indicator of the potential for dietary inflammation. We found that patients with depression had higher DII scores compared to the control group without depression. The association between DII and depression observed in this study suggests that the potential of an inflammatory diet plays an important role in depression.

The significant association between DII and depression observed in the current study broadly supports a related study that studied 254 depression patients in the UK and found that compared with the disease-free control group, these patients'DII scores were higher.[24] Other reports have found that compared with other types of severe mental illness, people with depression have higher

levels of dietary inflammation and are more likely to show worse indicators of physical health.[25]

Depression (or clinical depression) is a widespread and severe mood disorder worldwide.[26] Among the elderly, depression is the most common mental disorder, and it is becoming more common. Depression also reduces the ability of the elderly to recover.[27] Therefore, the National Institute of Mental Health in the United States regards depression in the elderly as a major public health problem, leading to significant and continuous growth in health care expenditures. In addition, depression is often associated with an increased risk of other diseases (such as heart disease) and mortality in the elderly.[28-29] Therefore, personalized early depression detection is essential for the physical and mental health of the elderly. Effective and individualized prediction of the onset of depression can inform intervention strategies in time to prevent depression in the elderly and further reduce the cost of medical care. A study in US women also applied reduced rankregression (RRR) (using CRP, IL-6, and TNF-A as response variables) and found that higher scores in inflammatory dietary patterns, including sugary beverages, refined grains, red meat, dietary soft drinks, margarine, and other vegetables and fish, were associated with higher depressive symptoms. In addition, three studies using prior DII observed a statistically significant positive association between higher DII scores and higher depressive symptoms.[30-31]

As we all know, inflammation is related to depression. In the early 1990s, the macrophage theory was first hypothesized as depression, especially when these cells are activated by any damage (M1 cells).[32] There is increasing evidence that the accumulation of M1 cells (including microglia and central nervous system macrophages) plays a critical role in the pathogenesis of depression, as peripheral M1 cells may be the main source of cytokine increase in depression.Due

to changes in the peripheral immune system of depression, cellular immunity is impaired, resulting in increased levels of pro-inflammatory cytokines.[33-34] For example, cytokines may affect neurotransmitter metabolism, neuroendocrine function, and regional brain activity. All of these factors may be related to the onset of depression. related. However, it should be noted that in studies that adjusted the analysis of serum cytokine levels, DII® was still significantly associated with the onset of depression. These findings may indicate that unhealthy (pro-inflammatory) diets independently lead to the onset of depression, further leading to important clinical consequences. Dietary intervention seems to be an important goal in preventing depression. Some observational studies have reported that a healthy diet (such as the Mediterranean diet) is associated with a lower incidence of depression in adults. Our research further confirms these findings, suggesting that a healthy diet may be necessary to prevent depression. A recent randomized controlled trial of adults with depressive symptoms showed that using a Mediterranean diet significantly reduced depressive symptoms. In addition, it can be assumed that there is a synergistic anti-inflammatory effect between antidepressants and the Mediterranean diet or the longevity diet, so as to propose prevention and intervention before or when mild symptoms appear.[35-38]

The lifetime prevalence of major depressive disorder (MDD) and depressive symptoms in women is higher than in men. Studies have shown that the estimated number of women with mood disorders is about twice that of men. Stressful life events, health and lifestyle factors, and a history of premenstrual dysphoria are related to the prevalence of MDD and depressive symptoms during menopausal transition.[39-40] A number of evidences indicate that changes in reproductive hormone levels are predisposing factors for depression in women who are susceptible to depression. The immune response changes with aging. For women, menopause is an important life

event that changes the immune response, because the ovarian hormone estrogen has anti-inflammatory effects and plays a protective role in innate immunity. It is worth noting that the epidemic of depression increases the risk of vascular diseases such as coronary heart disease and atherosclerosis by activating inflammation and causing endothelial cell dysfunction. Although men have a higher risk of cardiovascular disease than women during the entire life cycle, as the frequency of depressive symptoms increases, women's cardiovascular risk in later life increases significantly. Studies have shown that there are significant gender differences in the gene expression patterns of white blood cells in patients with late-life depression (LLD). DEGs in white blood cells of LLD patients are related to innate immune function, especially in women. Since inflammation is known to be related to the pathophysiology of MDD and depressive symptoms, changes in the activity of the innate immune system may contribute to the pathophysiology of female LLD. In addition, MDD itself or diseases that are comorbid with MDD may lead to increased inflammatory activity, especially in elderly women. In contrast, inflammation may be an uncommon feature in the pathophysiology of male LLD.[40-42]

The subgroup analysis of BMI showed that there is a significant association between DII and the risk of depression in overweight and obese people. Eating behavior related to mood may be the underlying mechanism of the relationship between depression and obesity. Several mechanisms can explain the link between depression and obesity in this pathway. In particular, emotional eating, food reward processes, increased brain monoamine activity, and the inflammatory potential of the diet may also be related to the depression-obesity link. Future studies must be conducted to examine whether the intake of pro-inflammatory foods can enhance the emotional state of patients with atypical depression under psychosocial stress.[43-44]

Among the strengths of our study are a large number of participants over 55 years with evaluable data; information about diet and lifestyle factors; and various confounding factors. To the best of our knowledge, the current study is the first to explore the association between DII and depression in the elderly over 55 years in China. None of the 30 items in the GDS was somatic, thus avoiding the confusion of somatic symptoms with physical disturbances that were common in the elderly.[45] The limitation is also of note. Firstly, due to all of the participants recruited into the cohort are from the same province, the true state of the nation's elderly may not be accurately reflected. Another potential limitation is that among the 45 food parameters, only 22 food parameters can be used in the DII calculations in this study, and there may be deviations in the estimation of the possibility of dietary inflammation. Furthermore, the dietary consumption level is estimated based on the FFQ covering the past 12 months, which may have a certain recall bias. Finally, owing to disease-related conditions such as diabetes and high blood pressure are only based on confounding factors reported by participants, the results may be unreliable.

Author Contributions

Ma and Li had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Concept and design: Ma, Li.

Acquisition, analysis, or interpretation of data: All authors.

Drafting of the manuscript: Ma, Li, Zhan

Critical revision of the manuscript for important intellectual content: All authors.

Statistical analysis: Li, Zhan, Zhou, Zhang, Huang.

Obtained funding: Ma, Huang.

Administrative, technical, or material support: Huang, Wang, Bao, Zhou.

Supervision: Ma

Conflict of interest

The authors declare that they have no conflict of interest.

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Data availability statement

No additional data available.

Ethical approval

All procedures involving participants were approved by the institutional review board of the National Institute for Nutrition and Health, Chinese Center for Disease Control and Prevention (approval number: 2017-020).

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contribution to scientific research in the field of nutrition.

Reference

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Figure legend

Figure 1 Restricted cubic splines for the nonlinear relationship between the risk of depression and increased Dietary Inflammatory Index.

Table 1 Baseline characteristics of the Community Cohort Study of Nervous System Diseases (CCSNSD) project population across quartiles of the DII score

Characteristic	Frequency (%) or Mean(SD)				P-value
	Quartile 1 (n=504)	Quartile 2 (n=506)	Quartile 3 (n=504)	Quartile 4 (n=508)	
Age (years)					<0.001
	68.36±0.33	66.10±0.34	63.85±0.31	64.67±0.32	
Sex					0.394
Male	201(39.9%)	191(37.7%)	190(37.7%)	193(38.0%)	
Female	303(60.1%)	315(62.3%)	314(62.3%)	315(62.0%)	
BMI（kg/m2）					0.006
BMI<24.00 (normal)	180(35.7%)	232(45.8%)	221(43.9%)	189(17.2%)	
24.00≤BMI<28.00 (overweight)	215(42.7%)	194(38.3%)	184(36.5%)	187(36.8%)	
BMI≥28.00 (obese)	109(21.6%)	80(15.8%)	99(19.6%)	132(26.0%)	
Employment					0.120
No	444(88.1%)	430(85.0%)	417(82.7%)	464(85.4%)	
Yes	60(11.9%)	76(15.0%)	87(17.3%)	74(14.6%)	
Education					0.034
Illiteracy	129(25.6%)	137(27.1%)	111(22.0%)	120(23.6%)	

Primary school	181(35.9%)	163(32.2%)	150(29.8%)	155(30.5%)	
Junior high school/above	194(38.5%)	206(40.7%)	243(48.2%)	233(45.9%)	
Tobacco Smoking					0.213
No	409(81.2%)	430(85.0%)	432(85.7%)	426(83.9%)	
Yes	95(18.8%)	76(15.0%)	72(14.3)	82(16.1%)	
Alcohol Drinking					0.344
No	460(91.3%)	448(88.5%)	459(91.1%)	452(89.0%)	
Yes	44(8.7%)	58(11.5%)	45(8.9%)	56(11.0%)	
Physical activities					0.894
Moderate	309(61.3%)	309(61.1%)	305(60.5%)	319(62.8%)	
Vigorous	195(38.7%)	197(38.9%)	199(39.5)	189(37.2%)	
Diabetes					0.444
No	418(82.9%)	436(86.2%)	430(85.3%)	424(83.5%)	
Yes	86(17.1%)	70(13.8%)	74(14.7%)	84(16.5%)	
Depression					＜0.001
No	394(78.2%)	390(77.1%)	387(76.8%)	378(74.4%)	
Yes	110(21.8%)	116(22.9%)	117(23.2%)	130(25.6%)	
Hypertension					＜0.001
No	205(40.7%)	222(43.9%)	231(45.8%)	195(38.4%)	
Yes	299(59.3%)	284(56.1%)	273(54.2%)	313(61.6%)	

Quartile 1:-5.20 to 0.94;Quartile 2:0.95,1.95;Quartile 3:1.96 to 2.69;Quartile 4:2.70 to 5.68

Table 2 Logistic regression analysis of the association between DII and depression.

	Quartile 1（n=504）	Quartile 2（n=506）	Quartile 3（n=504）	Quartile 4（n=508）
Model 1	1 [reference]	1.29(1.09-1.42)	1.36(1.13-1.52)	1.43(1.29-1.68)
Model 2	1 [reference]	1.33(1.12-1.46)	1.40(1.27-1.65)	1.51(1.31-1.75)
Model 3	1 [reference]	1.31(1.20-1.43)	1.39(1.25-1.63)	1.53(1.37-1.82)

Model 1 is not adjusted; Model 2 adjusts age, sex, BMI, employment, education, daily energy intake, daily energy intake, tobacco smoking, alcohol drinking and physical activities; Model 3 adjusts age, sex, BMI, employment, education, tobacco smoking, alcohol drinking, physical activities, diabetes and hypertension.

Table 3 Body mass index stratified analysis of the association between DII and depression

	Model 1	Model 2	Model 2
BMI<24.00 (normalweight)			
Quartile 1（n=180）	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)
Quartile 2（n=232）	1.08(0.92-1.18)	1.06(0.82-1.16)	1.05(0.86-1.18)
Quartile 3（n=221）	1.12(0.86-1.25)	1.15(0.92-1.28)	1.18(0.92-1.26)
Quartile 4（n=189）	1.16(0.95-1.28)	1.21(0.96-1.46)	1.32(0.98-1.52)
P-trend	0.28	0.16	0.08
24.00≤BMI<28.00 (overweight)			
Quartile 1（n=215）	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)
Quartile 2（n=194）	1.09(0.89-1.25)	1.08(1.01-1.26)	1.10(1.03-1.29)
Quartile 3（n=184）	1.13(1.02-1.32)	1.15(1.05-1.29)	1.21(1.09-1.37)
Quartile 4（n=187）	1.25(1.08-1.46)	1.31(1.11-1.52)	1.35(1.13-1.56)
P-trend	0.03	0.01	0.006
BMI≥28.00 (obese)			
Quartile 1（n=109）	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)

Quartile 2（n=80）	1.08(1.01-1.19)	1.15(1.05-1.29)	1.18(1.09-1.35)
Quartile 3（n=99）	1.21(1.10-1.39)	1.28(1.13-1.46)	1.32(1.19-1.58)
Quartile 4（n=132）	1.39(1.19-1.52)	1.42(1.21-1.62)	1.56(1.23-1.78)
P-trend	0.008	0.005	0.003

Model 1 is not adjusted;

Model 2 adjusts age, sex, BMI, employment, education, daily energy intake, daily energy intake, tobacco smoking, alcohol drinking and physical activities;

Model 3 adjusts age, sex, BMI, employment, education, tobacco smoking, alcohol drinking, physical activities, diabetes and hypertension.

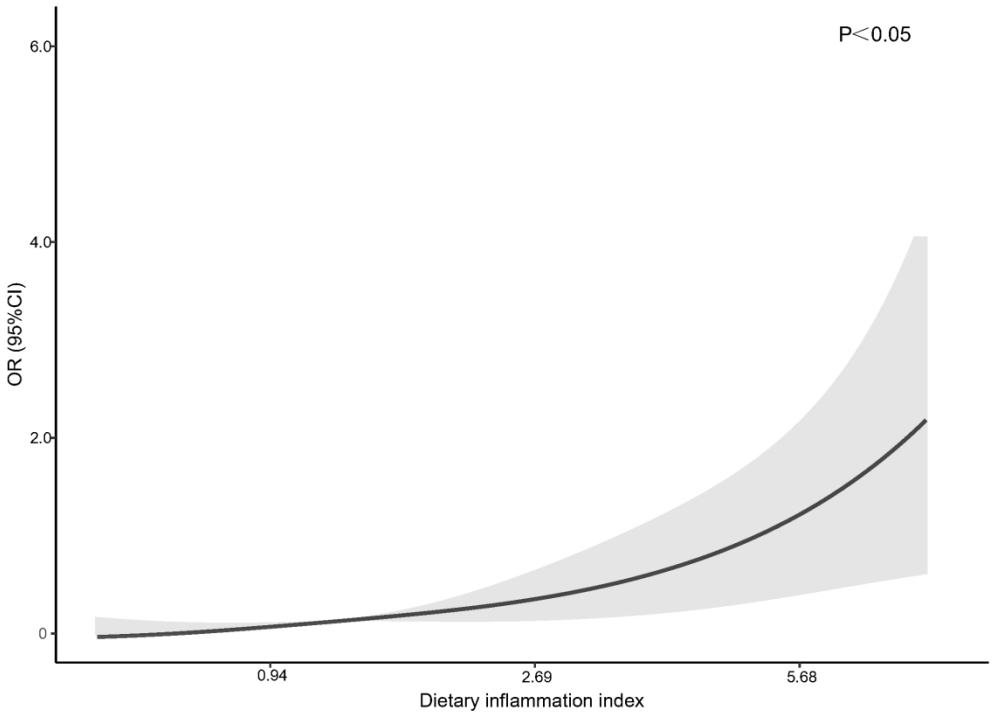

Figure 1

203x152mm (300 x 300 DPI)

Supplementary Table 1 Baseline characteristics of the Community Cohort Study of Nervous System Diseases (CCSNSD) project population across depression status

Characteristic	Non-Depression(n=1549)	Depression(n=473)	P-Value
Age (years)			0.541
	65.69±0.17	65.93±0.16	
Sex			＜0.001
Male	626(40.4%)	149(31.5%)	
Female	923(59.6%)	324(68.5%)	
BMI（kg/m2）			0.411
BMI<18.50 (underweight)	39(2.5%)	17(3.6%)	
18.50≤BMI<24.00 (normal weight)	593(38.3%)	173(36.6%)	
24.00≤BMI<28.00 (overweight)	623(40.2%)	183(38.7%)	
BMI≥28.00 (obese)	294(19.0%)	100(21.1%)	
Employment			0.014
No	1305(84.2%)	420(88.8%)	
Yes	244(15.8%)	53(11.2%)	
Education			0.873
Illiteracy	385(24.9%)	112(23.7%)	
Primary school	495(32.0%)	154(32.6%)	
Junior high school/above	669(43.2%)	207(43.8%)	
Tobacco Smoking			0.472
No	1295(83.6%)	402(85.0%)	
Yes	254(16.4%)	71(15.0%)	
Alcohol Drinking			0.257
No	1387(89.5%)	432(91.3%)	
Yes	162(10.5%)	41(8.7%)	
Physical activities			＜0.001
No	1009(65.1%)	233(49.3%)	
Yes	540(34.9%)	240(50.7%)	
Diabetes			0.412
No	801(51.7%)	237(50.1%)	
Yes	748(48.3%)	236(49.9%)	
Hypertension			0.334
No	628(40.5%)	180(38.1%)	
Yes	921(59.5%)	293(61.9%)	

Supplementary Table 2 Nutrient content of study participants.

Characteristic	Median(IQR)		p-Value
	Non-depression（n=1563）	Depression（n=459）	
Carbohydrates (g)	192.21(159.62-235.27)	194.70(161.45-237.93)	0.444
Protein (g)	53.61(43.04-66.12)	54.53(43.69-67.67)	0.373
Total fat (g)	34.77(27.09-44.23)	35.21(27.51-45.62)	0.412
β-Carotene (μg)	1459.28(748.00-2677.97)	1560.46(795.40-2738.40)	0.300
Fiber (g)	8.70(6.38-11.54)	8.87(6.61-11.83)	0.150
Cholesterol (mg)	389.57(233.05-436.60)	388.02(238.10-434.77)	0.989
Saturated fat (g)	4.00(2.58-6.02)	4.18(2.63-6.05)	0.655
Monounsaturated fat (g)	5.84(4.17-7.64)	5.98(4.14-7.75)	0.618
Polyunsaturated fats (g)	4.63(2.79-6.93)	4.92(2.84-7.07)	0.475
Niacin (mg)	8.83(6.85-10.97)	8.84(6.95-11.13)	0.702
Thiamine (mg)	0.71(0.56-0.89)	0.72(0.58-0.89)	0.506
Riboflavin (mg)	0.66(0.51-0.83)	0.67(0.51-0.85)	0.324
Vitamin B12 (μg)	0.22(0.14-0.34)	0.22(0.14-0.32)	0.892
Vitamin B6 (mg)	0.07(0.05-0.10)	0.07(0.05-0.10)	0.182
Fe (mg)	15.58(12.20-19.11)	15.90(12.52-19.33)	0.409
Magnesium (mg)	215.78(165.89-266.09)	218.40(169.30-270.06)	0.166
Zinc (mg)	7.15(5.66-8.68)	7.29(5.77-8.83)	0.383
Selenium (μg)	40.42(33.25-48.11)	40.86(32.89-49.39)	0.511
Vitamin A (RE)	430.36(283.91-660.48)	443.76(274.19-683.98)	0.505
Vitamin C (mg)	49.68(27.47-84.84)	52.51(28.11-89.54)	0.482
Vitamin E (mg)	11.74(8.24-14.95)	12.07(8.26-15.81)	0.177
Folic acid (μg)	115.79(83.57-153.99)	119.97(85.02-159.85)	0.370

Supplementary Table 3 Gender stratified analysis of the association between DII and depression

	Model 1	Model 2	Model 2
Male			
Quartile 1（n=201）	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)
Quartile 2（n=191）	1.12(0.88-1.26)	1.09(0.85-1.20)	1.05(0.79-1.23)
Quartile 3（n=190）	1.08(0.81-1.17)	1.15(0.90-1.28)	1.11(0.92-1.25)
Quartile 4（n=193）	1.18(1.02-1.26)	1.21(0.96-1.42)	1.26(0.97-1.46)
P-trend	0.62	0.46	0.12
Female			
Quartile 1（n=303）	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)
Quartile 2（n=315）	1.08(0.92-1.16)	1.12(1.03-1.27)	1.21(1.13-1.36)
Quartile 3（n=314）	1.17(1.02-1.28)	1.24(1.08-1.41)	1.35(1.22-1.48)
Quartile 4（n=315）	1.25(1.12-1.36)	1.39(1.15-1.48)	1.46(1.28-1.62)
P-trend	0.042	0.012	0.006

STROBE Statement—Checklist of items that should be included in reports of ***case-control studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	3-4
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls	4
		(*b*) For matched studies, give matching criteria and the number of controls per case	4
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5
Bias	9	Describe any efforts to address potential sources of bias	6
Study size	10	Explain how the study size was arrived at	6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6
		(*b*) Describe any methods used to examine subgroups and interactions	6
		(*c*) Explain how missing data were addressed	6
		(*d*) If applicable, explain how matching of cases and controls was addressed	6
		(*e*) Describe any sensitivity analyses	6-7
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	7
		(b) Give reasons for non-participation at each stage	7
		(c) Consider use of a flow diagram	7
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	7
		(b) Indicate number of participants with missing data for each variable of interest	7
Outcome data	15*	Report numbers in each exposure category, or summary measures of exposure	7

Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	7
		(*b*) Report category boundaries when continuous variables were categorized	7
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	7
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	7-8
Discussion			
Key results	18	Summarise key results with reference to study objectives	8
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	10
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	8-9
Generalisability	21	Discuss the generalisability (external validity) of the study results	8-9
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	11

*Give information separately for cases and controls.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

BMJ Open

Association of Dietary Inflammatory Index(DII) and Depression in the elderly over 55 years in Northern China: analysis of data from a multicentre, cohort study

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Primary Subject Heading:	Mental health
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Association of Dietary Inflammatory Index(DII) and Depression in the elderly over 55 years in Northern China: analysis of data from a multicentre, cohort study

Ruiqiang Li[1]; Wenqiang Zhan[2]; Xin Huang[1]; Zechen Zhang[1]; Meiqi Zhou[1]; Wei Bao[1]; Feifei Huang[3]; Yuxia Ma[1]*

Ruiqiang Li and Wenqiang Zhan contributed equally to this work.

Affiliations:

1.Department of Nutrition and Food Hygiene, School of Public Health, Hebei Medical University, Hebei Province Key Laboratory of Environment and Human Health, Shijiazhuang, China

2.School of Public Health, Shanghai Jiao Tong University School of Medicine, Shanghai 200025, PR China

3 National Institute for Nutrition and Health, Chinese Center for Disease Control and Prevention, No. 27, Nanwei Road, Xicheng District, Beijing, China

Correspondence address:

Yuxia Ma.

Department of Nutrition and Food Hygiene, School of Public Health, Hebei Medical University, Hebei Province Key Laboratory of Environment and Human Health, Shijiazhuang, China

Email: 2669909599@qq.com

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Abstract

Objectives: Our study aimed to assess the association between the Dietary Inflammatory Index (DII) and depression in the elderly over 55 years in Northern China.

Methods: We analyzed the data of 2022 Chinese adults aged 55 and over from a community-based neurological disease cohort study from 2018 to 2019. A validated semi-quantitative food frequency questionnaire was used to assess eating habits at the time of inclusion. Multiple logistic regression was used for analysis, and social demographics, lifestyle, and health-related factors were adjusted.

Results: Among the included population, the prevalence of depression was 23.39%. Mean (SD) and range of the DII in the included population were 1.70 (1.42) and -5.20 to +5.68. Participants in the most pro-inflammatory group (quartile 4) suffer the risk of depression was significantly higher than the participants in the most anti-inflammatory group (quartile 1) (OR 1.53; 1.37–1.82; P-trend=0.01). The subgroup analysis of BMI showed that there is a significant association between DII and the risk of depression in overweight and obese people($P < 0.05$). The restricted cubic spline (RCS) results show that the OR value of depression possesses an upward trend with the increase of the DII score.

Conclusions: Aged patients with depression present a higher potential for dietary inflammation. Pro-inflammatory diets might increase the risk of depressive symptoms. Further research in different populations is crucial to confirm the association between DII and depression.

Keywords: Dietary Inflammatory Index, depression, elderly.

Article summary

Strengths and limitations of this study:

1.Among the strengths of our study are a large number of participants over 55 years with evaluable data; information about diet and lifestyle factors; and various confounding factors.

2.To the best of our knowledge, the current study is the first to explore the association between DII and depression in the elderly over 55 years in China.

3.Due to all of the participants recruited into the cohort are from the same province, the true state of the nation's elderly may not be accurately reflected. 4.Another potential limitation is that among the 45 food parameters, only 22 food parameters can be used in the DII calculations in this study,

5.Owing to disease-related conditions such as diabetes and high blood pressure are only based on confounding factors reported by participants, the results may be unreliable.

1. Introduction

Due to rapid economic growth and changes in lifestyles, China is undergoing a rapid epidemiological transition from infectious diseases to non-communicable diseases (NCDs). Mental disorders such as depression are an important but often overlooked non-communicable disease, and it is becoming an increasingly serious cause of disability and disease burden. [1]These conditions are common in the general population, especially the elderly. For example, 7.73% of elderly people aged 55 and over in China suffered from depression (major depressive disorder [MDD] and dysthymia) in the previous month, and the prevalence is 3.5 times and 1.4 times that of adults aged 18 -39 and 40-54 years. [2]

Systemic inflammation is becoming an important factor in the etiology of mental illnesses such as depression and anxiety. [3] Approximately one-quarter of patients with major depression (MDD) show evidence of systemic inflammation. [4]Moreover, some studies have shown that chronic low-grade inflammation of the whole body can affect monoaminergic and glutamate neurotransmission, which may adversely affect the cognitive function of patients with bipolar disorder or major depression. However, before the first episode of depression, whether various pro-inflammatory cytokines are abnormally elevated remains unclear. [5,6]Some studies have shown that the association between diet and mental health disorders may be mediated by the inflammatory properties of diet. [7]The current treatment of depression is not considered to be effective in all cases. So far, there are few nutritional programs in the guidelines for the treatment of depression. Recently, due to the pro-inflammatory and anti-inflammatory properties of nutrients, people are paying more and more attention to the protective and regulating effects that diet may have in common mental disorders (including depression). [8]However, there are limited

data on the role of dietary inflammation potential in this regard. [9]The long-term unhealthy diet leads to a decline in the quality of the diet, which may create a pro-inflammatory environment in the human body, thereby creating conditions for the occurrence and development of various chronic inflammatory diseases. DII, as a tool that can assess the potential of dietary inflammation, provides the possibility to test this hypothesis. [10]

Meanwhile, inflammation has important physiological effects on mood and behavior. Kynurenine metabolism is hypothesized to be a pathway connecting inflammation and depression, partly because of the effect of kynurenine metabolites on the neurotransmission of glutamate in the central nervous system. [11]Some studies have shown that inflammation may affect the interconnection of the hypothalamus with areas important for cognition and emotion, and it may cause the hypothalamus-pituitary-adrenal (HPA) axis to be dysregulated and affect the monoaminergic system. [12]

The Dietary inflammatory index (DII) was developed and verified by researchers at the University of South Carolina in Columbia to assess the inflammatory potential of an individual's diet. The initial DII score was based on the results of articles published from 1950 to 2007 that assessed the impact of specific foods on specific inflammatory markers (specific inflammatory markers include IL-1β, IL-4, IL-6, IL-10, TNF-α and CRP), significantly increase IL-1β, IL-6, TNF-α or CRP, or decrease IL-4 or IL-10 to "+1", which is pro-inflammatory; significantly reduce IL-1β, IL-6, TNF -α or CRP, or increase IL-4 or IL-10 to "-1", which is an anti-inflammatory effect. In 2014, South Carolina researchers improved the DII score from 2007 to 2010, and the improved scoring system applied 45 food parameters. [13]

The relationship between diet, inflammation and mental health is of increasing interest, and

the link between diet and mental health disorders may be mediated by the inflammatory properties of diet. [14,15] As a tool to assess the potential of dietary inflammation, the relationship between DII and mental disorders is worthy of discussion and research. Moreover, a study has shown that people with the lowest levels of DII have a lower risk of being at the highest levels of mental health disorders. [14]

Although the number of patients with depression has increased in recent years, compared with other developed countries, there are relatively few studies on depression in China. [16] Therefore, it is urgent to explore the relationship between DII and depression risk in the Chinese elderly. The Dietary Inflammatory Index (DII) is a tool used to quantify the dietary inflammation potential of an individual's diet. Its goal is to assess the impact of diet-related inflammation on health outcomes. [17]Thus, the purpose of this work was to examine the association between the inflammatory potential of habitual diets and depression. Moreover, the use of DII as an indicator to directly and reasonably connect the three of nutrition, inflammation and depression, may have clinical and public health significance for the development of new nutritional psychiatric methods to promote good mental health.

2. Methods

2.1. Study Population

Participants came from the Community Cohort Study of Nervous System Diseases (CCSNSD) project under the National Key Research and Development Program, the National Key Research and Development Program, and the Precision Medicine Project Nervous System Disease Cohort Research (CCSNSD) project. The project is undertaken by the Institute of Nutrition and Health of the Chinese Center for Disease Control and Prevention, in cooperation with the Center

for Disease Control and Prevention. The project uses a multistage random cluster sampling method to draw samples. The protocol of this study was reviewed and approved by the Institutional Review Board of the National Institute for Nutrition and Health (No. 2017020, November 6, 2017).

In allusion to subjects recruited in the CCSNSD cohort, the samples eligible for inclusion were (1) 55 years old and older, (2) resident population living in the sampled community, (3) absence of clinically diagnosed depression, (4) be able to perform a normal depression assessment, (5) completed data of sociodemographic characteristics, disease history, and food frequency questionnaire (FFQ). We excluded subjects because of (1) no depression assessment results, (2) lack of baseline status such as education and physical activities, (3) nutrient deficiency, (4) abnormal energy intake, (5) people with other psychological disorders. Finally, a total of 2022 participants were involved in the analysis.

2.2. Patient and Public Involvement

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. Written informed consent was obtained from all participants.

2.3. Depression

We defined depression according to the Geriatric Depression Scale (GDS), this scale is one of the most widely used scales to assess the depression of the elderly. [18]It consists of 30 self-assessment items with yes/no response options. A score of 0-10 indicates no depression, a score of 11-20 indicates mild depression, and a score of 21-30 indicates severe depression. [19]

2.4. Assessment of Food Consumption

Dietary consumption is assessed by a validated semi-quantitative FFQ, covering 81 foods, Participants were asked about the frequency of habitual consumption the number of each item in the past 12 months, and choose from five types of frequencies(Daily, weekly, monthly, yearly, or never) and consumption in the past 12 months. For consumers, their consumption of each food group or item is calculated based on their reported average consumption frequency and quantity.

2.5. Assessment of DII score

The Dietary Inflammatory Index (DII) aims to provide a quantitative method for assessing the effect of diet on health outcomes. [20]It is the characteristic of DII to objectify the inflammatory characteristics of specific dietary intake. [21]

The calculation of the dietary inflammatory index links the personal dietary data obtained in each clinical study with the global average intake. The specific formula is: Z score = (daily intake of this kind of dietary ingredient or nutrient-this kind of dietary ingredient or the global average per capita daily intake of nutrients)/The standard deviation of the global average per capita daily intake of this dietary ingredient or nutrient. Then convert the Z score to a percentile system (to reduce the influence of outlier effects), double the obtained percentile value and subtract "1" to achieve a symmetrical distribution centered on "0". Finally, multiply by the total inflammatory score of each dietary component, and combine the results to obtain the personal dietary inflammatory index score. DII scores range from negative tail to positive tail, more negative values indicate anti-inflammatory properties and corrected scores indicate pro-inflammatory properties. [14]Energy adjusted DII (E-DII) food intake per 1,000 calories is used to explain the effect of total intake on energy intake. For this, the energy standardized version requires a world

database. [22]Twenty-two of the 45 possible food parameters were used for DII calculation based on the FFQ in this study(carbohydrates, protein, fat, β-Carotene, fiber, cholesterol, saturated fat, monounsaturated fat, polyunsaturated fat, niacin, thiamine, riboflavin, vitamin B12, vitamin B6, Fe, magnesium, zinc, selenium, vitamin A, vitamin C, vitamin E and folic acid).

The appendix of the DII

$Zscore$ = [(daily mean intake - global daily mean intake)/standard deviation]

$Zscore^1$ = $Zscore$→(converted to a percentile score)×2-1

DII = $\sum Zscore^1$ × the inflammatory effect score of each dietary component

2.6. Covariates

We adjusted the including self-reported age (yearly), gender (female or male), an education level (illiterate, elementary school, junior high school and above), employment status(yes or no); health-related variables including tobacco smoking (yes or no), alcohol drinking (yes or no), physical activity (yes or no), daily energy intake(kcal), diabetes (yes or no), hypertension (yes or no), We use a cut-off value of 28 kilograms per square meter (kg/m2) of China's body mass index (BMI) to determine obesity. [23]

2.7. Statistical Analysis

Data were expressed as mean (SD/SEM) and n (%) for continuous variables and categorical variables, respectively. The differences between groups were analyzed by analysis of variance of continuous variables and chi-square test of categorical variables. Logistic regression analysis is used to simulate the association between depressed people and people in different DII quartiles, and OR(95% CI) was calculated to evaluate the relationship between depression and the DII score. We utilized a subgroup analysis of BMI to optimize the robustness of the statistical test. (BMI

199 <18.5,18.5-24.0,24-28,≥30 kg/m2).Restricted cubic splines were used to evaluate the correlation
200 between the DII and the risk of depression. All statistical analyses were performed using the
201 software package R (http://www.R-project.org, The R Foundation). A two-tailed p-value of <0.05
202 was considered statistically significant.

203 **3. Results**

204 From the Community Cohort Study on Specialized Nervous System Diseases, the study
205 included 2022 elderly participants (median [IQR] age, 64 [60-70] years; 775 [38.3%] males) from
206 2017 to 2018. Mean (SD) and range of the DII in the included population were 1.70 (1.42) and −
207 5.20 to + 5.68. Clinical and demographic characteristics according to quartiles of DII are
208 presented in supplementary Table 1. A higher incidence of depression was observed among
209 individuals in the highest quartile of the dietary inflammatory index, and thus the most
210 pro-inflammatory diet. Individuals in the highest quartile of DII were more likely to be patients
211 with obesity, hypertension and to be less daily energy intake. No differences in sex, employment
212 status, physical activities, diabetes, tobacco smoking, or alcohol drinking were observed between
213 groups. We also compared baseline characteristics of depressed and non-depressed patients, and
214 found differences in gender, employment status, and physical activity between the two groups (P
215 < 0.05) (Supplementary Table 2). At the same time, no significant difference was observed
216 between the nutrients between the two groups (Supplementary Table 3).

217 Table 1 shows the OR and 95% CI of depression according to the quartile of DII. When DII
218 is expressed as a quartile, the results obtained by adjusting for confounding factors and modeling
219 DII as a categorical variable for depression indicate that there is a direct association. Participants
220 in the most pro-inflammatory group (quartile 4) suffer the risk of depression was significantly

higher than the participants in the most anti-inflammatory group (quartile 1) (OR 1.53; 1.37–1.82; P-trend=0.01).

Stratified logistic regression analysis (Table 2) revealed body mass index(BMI) differences in the associations between dietary inflammatory potential and depression outcomes(BMI<18.50kg/m^2; 18.50 ⩽ BMI<24.00; BMI ⩾ 28.00). Increased risk of depression were (OR 1.25,95%CI 1.08-1.46; OR 1.39, 95%CI 1.19-1.52) observed among the overweight and obese study participants, respectively. Comparing the highest to the lowest quartile of DII, the association with depression remained in the fully adjusted model (P＜0.05, comparing highest to lowest tertile of DII). No associations were observed among the underweight and normal-weight participants. The RCS results show that the OR value of depression possesses an upward trend with the increase of the DII score(P＜0.05) (Figure 1). At the same time, a subgroup analysis of people of different genders showed that the pro-inflammatory diet is a risk factor for depression in elderly women (P＜0.05) (Table 3).

4. Discussion

As far as we know, this is the first study in China to investigate the association between depression and DII as a representative indicator of the potential for dietary inflammation. We found that patients with depression had higher DII scores compared to the control group without depression. The association between DII and depression observed in this study suggests that the potential of an inflammatory diet plays an important role in depression.

The significant association between DII and depression observed in the current study broadly supports a related study that studied 254 depression patients in the UK and found that compared with the disease-free control group, these patients'DII scores were higher.[24] Other reports have

found that compared with other types of severe mental illness, people with depression have higher levels of dietary inflammation and are more likely to show worse indicators of physical health.[25]

Depression (or clinical depression) is a widespread and severe mood disorder worldwide.[26] Among the elderly, depression is the most common mental disorder, and it is becoming more common. Depression also reduces the ability of the elderly to recover.[27] Therefore, the National Institute of Mental Health in the United States regards depression in the elderly as a major public health problem, leading to significant and continuous growth in health care expenditures. In addition, depression is often associated with an increased risk of other diseases (such as heart disease) and mortality in the elderly.[28-29] Therefore, personalized early depression detection is essential for the physical and mental health of the elderly. Effective and individualized prediction of the onset of depression can inform intervention strategies in time to prevent depression in the elderly and further reduce the cost of medical care. A study in US women also applied reduced rankregression (RRR) (using CRP, IL-6, and TNF-A as response variables) and found that higher scores in inflammatory dietary patterns, including sugary beverages, refined grains, red meat, dietary soft drinks, margarine, and other vegetables and fish, were associated with higher depressive symptoms. In addition, three studies using prior DII observed a statistically significant positive association between higher DII scores and higher depressive symptoms.[30-31]

As we all know, inflammation is related to depression. In the early 1990s, the macrophage theory was first hypothesized as depression, especially when these cells are activated by any damage (M1 cells).[32] There is increasing evidence that the accumulation of M1 cells (including microglia and central nervous system macrophages) plays a critical role in the pathogenesis of

depression, as peripheral M1 cells may be the main source of cytokine increase in depression.Due to changes in the peripheral immune system of depression, cellular immunity is impaired, resulting in increased levels of pro-inflammatory cytokines.[33-34] For example, cytokines may affect neurotransmitter metabolism, neuroendocrine function, and regional brain activity. All of these factors may be related to the onset of depression. related. However, it should be noted that in studies that adjusted the analysis of serum cytokine levels, DII® was still significantly associated with the onset of depression. These findings may indicate that unhealthy (pro-inflammatory) diets independently lead to the onset of depression, further leading to important clinical consequences. Dietary intervention seems to be an important goal in preventing depression. Some observational studies have reported that a healthy diet (such as the Mediterranean diet) is associated with a lower incidence of depression in adults. Our research further confirms these findings, suggesting that a healthy diet may be necessary to prevent depression. A recent randomized controlled trial of adults with depressive symptoms showed that using a Mediterranean diet significantly reduced depressive symptoms. In addition, it can be assumed that there is a synergistic anti-inflammatory effect between antidepressants and the Mediterranean diet or the longevity diet, so as to propose prevention and intervention before or when mild symptoms appear.[35-38]

The lifetime prevalence of major depressive disorder (MDD) and depressive symptoms in women is higher than in men. Studies have shown that the estimated number of women with mood disorders is about twice that of men. Stressful life events, health and lifestyle factors, and a history of premenstrual dysphoria are related to the prevalence of MDD and depressive symptoms during menopausal transition.[39-40] A number of evidences indicate that changes in reproductive hormone levels are predisposing factors for depression in women who are susceptible to

depression. The immune response changes with aging. For women, menopause is an important life event that changes the immune response, because the ovarian hormone estrogen has anti-inflammatory effects and plays a protective role in innate immunity. It is worth noting that the epidemic of depression increases the risk of vascular diseases such as coronary heart disease and atherosclerosis by activating inflammation and causing endothelial cell dysfunction. Although men have a higher risk of cardiovascular disease than women during the entire life cycle, as the frequency of depressive symptoms increases, women's cardiovascular risk in later life increases significantly. Studies have shown that there are significant gender differences in the gene expression patterns of white blood cells in patients with late-life depression (LLD). DEGs in white blood cells of LLD patients are related to innate immune function, especially in women. Since inflammation is known to be related to the pathophysiology of MDD and depressive symptoms, changes in the activity of the innate immune system may contribute to the pathophysiology of female LLD. In addition, MDD itself or diseases that are comorbid with MDD may lead to increased inflammatory activity, especially in elderly women. In contrast, inflammation may be an uncommon feature in the pathophysiology of male LLD.[40-42]

The subgroup analysis of BMI showed that there is a significant association between DII and the risk of depression in overweight and obese people. Eating behavior related to mood may be the underlying mechanism of the relationship between depression and obesity. Several mechanisms can explain the link between depression and obesity in this pathway. In particular, emotional eating, food reward processes, increased brain monoamine activity, and the inflammatory potential of the diet may also be related to the depression-obesity link. Future studies must be conducted to examine whether the intake of pro-inflammatory foods can enhance the emotional state of patients

with atypical depression under psychosocial stress.[43-44]

Among the strengths of our study are a large number of participants over 55 years with evaluable data; information about diet and lifestyle factors; and various confounding factors. To the best of our knowledge, the current study is the first to explore the association between DII and depression in the elderly over 55 years in China. None of the 30 items in the GDS was somatic, thus avoiding the confusion of somatic symptoms with physical disturbances that were common in the elderly.[45] The limitation is also of note. Firstly, due to all of the participants recruited into the cohort are from the same province, the true state of the nation's elderly may not be accurately reflected. Another potential limitation is that among the 45 food parameters, only 22 food parameters can be used in the DII calculations in this study, and there may be deviations in the estimation of the possibility of dietary inflammation. Furthermore, the dietary consumption level is estimated based on the FFQ covering the past 12 months, which may have a certain recall bias. Finally, owing to disease-related conditions such as diabetes and high blood pressure are only based on confounding factors reported by participants, the results may be unreliable.

Author Contributions

Ma and Li had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Concept and design: Ma, Li.

Acquisition, analysis, or interpretation of data: All authors.

Drafting of the manuscript: Ma, Li, Zhan

Critical revision of the manuscript for important intellectual content: All authors.

Statistical analysis: Li, Zhan, Zhou, Zhang, Huang.

Obtained funding: Ma, Huang.

Administrative, technical, or material support: Huang, Wang, Bao, Zhou.

Supervision: Ma

Conflict of interest

The authors declare that they have no conflict of interest.

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Data availability statement

No additional data available.

Ethical approval

All procedures involving participants were approved by the institutional review board of the National Institute for Nutrition and Health, Chinese Center for Disease Control and Prevention (approval number: 2017-020).

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Figure legend

Figure 1 Restricted cubic splines for the nonlinear relationship between the risk of depression and increased Dietary Inflammatory Index.

Table 1 Logistic regression analysis of the association between DII and depression.

	Quartile 1（n=504）	Quartile 2（n=506）	Quartile 3（n=504）	Quartile 4（n=508）
Model 1	1 [reference]	1.29(1.09-1.42)	1.36(1.13-1.52)	1.43(1.29-1.68)
Model 2	1 [reference]	1.33(1.12-1.46)	1.40(1.27-1.65)	1.51(1.31-1.75)
Model 3	1 [reference]	1.31(1.20-1.43)	1.39(1.25-1.63)	1.53(1.37-1.82)

Model 1 is not adjusted; Model 2 adjusts age, sex, BMI, employment, education, daily energy intake, daily energy intake, tobacco smoking, alcohol drinking and physical activities; Model 3 adjusts age, sex, BMI, employment, education, tobacco smoking, alcohol drinking, physical activities, diabetes and hypertension.

Table 2 Body mass index stratified analysis of the association between DII and depression

	Model 1	Model 2	Model 3
BMI<24.00 (normalweight)			
Quartile 1（n=180）	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)
Quartile 2（n=232）	1.08(0.92-1.18)	1.06(0.82-1.16)	1.05(0.86-1.18)
Quartile 3（n=221）	1.12(0.86-1.25)	1.15(0.92-1.28)	1.18(0.92-1.26)
Quartile 4（n=189）	1.16(0.95-1.28)	1.21(0.96-1.46)	1.32(0.98-1.52)
P-trend	0.28	0.16	0.08
24.00≤BMI<28.00 (overweight)			
Quartile 1（n=215）	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)
Quartile 2（n=194）	1.09(0.89-1.25)	1.08(1.01-1.26)	1.10(1.03-1.29)
Quartile 3（n=184）	1.13(1.02-1.32)	1.15(1.05-1.29)	1.21(1.09-1.37)
Quartile 4（n=187）	1.25(1.08-1.46)	1.31(1.11-1.52)	1.35(1.13-1.56)
P-trend	0.03	0.01	0.006
BMI≥28.00 (obese)			
Quartile 1（n=109）	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)
Quartile 2（n=80）	1.08(1.01-1.19)	1.15(1.05-1.29)	1.18(1.09-1.35)
Quartile 3（n=99）	1.21(1.10-1.39)	1.28(1.13-1.46)	1.32(1.19-1.58)
Quartile 4（n=132）	1.39(1.19-1.52)	1.42(1.21-1.62)	1.56(1.23-1.78)
P-trend	0.008	0.005	0.003

Model 1 is not adjusted;

Model 2 adjusts age, sex, employment, education, daily energy intake, daily energy intake, tobacco smoking, alcohol drinking and physical activities;

Model 3 adjusts age, sex, employment, education, tobacco smoking, alcohol drinking, physical activities, diabetes and hypertension.

Table 3 Gender stratified analysis of the association between DII and depression

	Model 1	Model 2	Model 3

Male			
Quartile 1（n=201）	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)
Quartile 2（n=191）	1.09(0.87-1.21)	0.98(0.62-1.12)	1.06(0.90-1.19)
Quartile 3（n=190）	1.06(0.68-1.15)	1.08(0.89-1.18)	1.14(0.98-1.28)
Quartile 4（n=193）	1.12(0.91-1.27)	1.16(0.98-1.32)	1.26(1.02-1.36)
P-trend	0.41	0.28	0.06
Female			
Quartile 1（n=303）	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)
Quartile 2（n=315）	0.96(0.81-1.08)	1.07(1.01-1.18)	1.12(1.04-1.28)
Quartile 3（n=314）	1.08(0.96-1.25)	1.17(1.06-1.31)	1.21(1.08-1.35)
Quartile 4（n=315）	1.17(1.02-1.35)	1.26(1.08-1.37)	1.36(1.15-1.42)
P-trend	0.042	0.028	0.016

Model 1 is not adjusted;

Model 2 adjusts age, BMI, employment, education, daily energy intake, daily energy intake, tobacco smoking, alcohol drinking and physical activities;

Model 3 adjusts age, BMI, employment, education, tobacco smoking, alcohol drinking, physical activities, diabetes and hypertension.

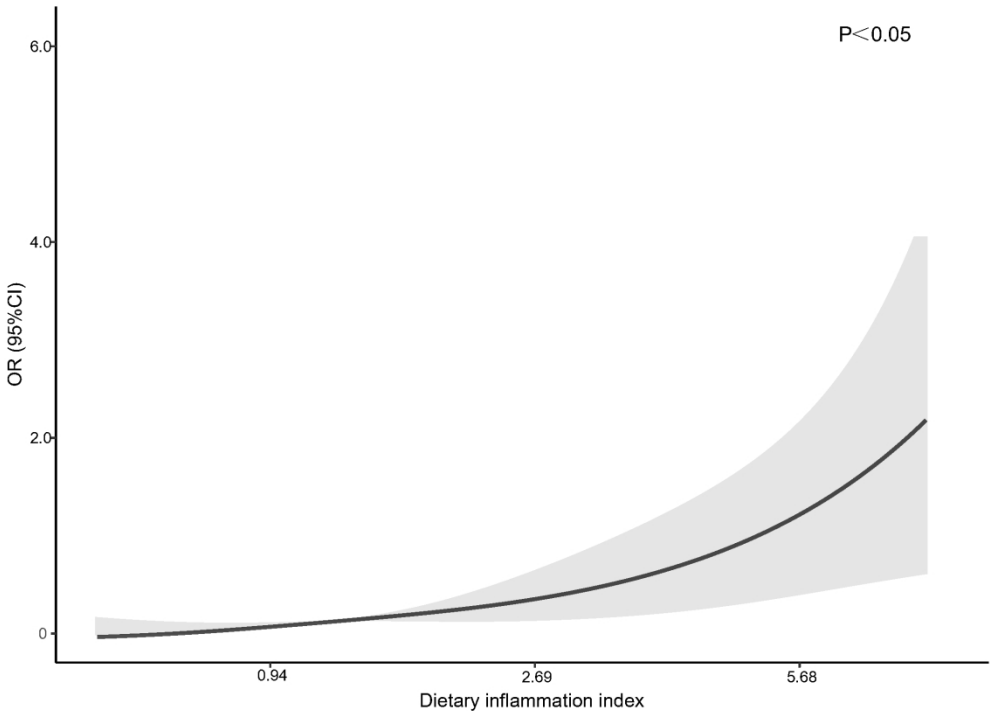

Figure 1

203x152mm (300 x 300 DPI)

Supplementary Table 1 Baseline characteristics of the Community Cohort Study of Nervous System Diseases (CCSNSD) project population across quartiles of the DII score

Characteristic	Frequency (%) or Mean(SD)				P-value
	Quartile 1（n=504）	Quartile 2（n=506）	Quartile 3（n=504）	Quartile 4（n=508）	
Age (years)					<0.001
	68.36±0.33	66.10±0.34	63.85±0.31	64.67±0.32	
Sex					0.394
Male	201(39.9%)	191(37.7%)	190(37.7%)	193(38.0%)	
Female	303(60.1%)	315(62.3%)	314(62.3%)	315(62.0%)	
BMI（kg/m2）					0.006
BMI<24.00 (normal)	180(35.7%)	232(45.8%)	221(43.9%)	189(17.2%)	
24.00≤BMI<28.00 (overweight)	215(42.7%)	194(38.3%)	184(36.5%)	187(36.8%)	
BMI≥28.00 (obese)	109(21.6%)	80(15.8%)	99(19.6%)	132(26.0%)	
Employment					0.120
No	444(88.1%)	430(85.0%)	417(82.7%)	464(85.4%)	
Yes	60(11.9%)	76(15.0%)	87(17.3%)	74(14.6%)	
Education					0.034
Illiteracy	129(25.6%)	137(27.1%)	111(22.0%)	120(23.6%)	
Primary school	181(35.9%)	163(32.2%)	150(29.8%)	155(30.5%)	
Junior high school/above	194(38.5%)	206(40.7%)	243(48.2%)	233(45.9%)	
Tobacco Smoking					0.213
No	409(81.2%)	430(85.0%)	432(85.7%)	426(83.9%)	
Yes	95(18.8%)	76(15.0%)	72(14.3)	82(16.1%)	
Alcohol Drinking					0.344
No	460(91.3%)	448(88.5%)	459(91.1%)	452(89.0%)	
Yes	44(8.7%)	58(11.5%)	45(8.9%)	56(11.0%)	
Physical activities					0.894
Moderate	309(61.3%)	309(61.1%)	305(60.5%)	319(62.8%)	
Vigorous	195(38.7%)	197(38.9%)	199(39.5)	189(37.2%)	
Diabetes					0.444
No	418(82.9%)	436(86.2%)	430(85.3%)	424(83.5%)	
Yes	86(17.1%)	70(13.8%)	74(14.7%)	84(16.5%)	
Depression					<0.001
No	394(78.2%)	390(77.1%)	387(76.8%)	378(74.4%)	
Yes	110(21.8%)	116(22.9%)	117(23.2%)	130(25.6%)	
Hypertension					<0.001
No	205(40.7%)	222(43.9%)	231(45.8%)	195(38.4%)	
Yes	299(59.3%)	284(56.1%)	273(54.2%)	313(61.6%)	

Quartile 1:-5.20 to 0.94;Quartile 2:0.95,1.95;Quartile 3:1.96 to 2.69;Quartile 4:2.70 to 5.68

Supplementary Table 2 Baseline characteristics of the Community Cohort Study of Nervous System Diseases (CCSNSD) project population across depression status

Characteristic	Non-Depression(n=1549)	Depression(n=473)	P-Value
Age (years)			0.541
	65.69±0.17	65.93±0.16	
Sex			＜0.001
Male	626(40.4%)	149(31.5%)	
Female	923(59.6%)	324(68.5%)	
BMI（kg/m2）			0.411
BMI<18.50 (underweight)	39(2.5%)	17(3.6%)	
18.50≤BMI<24.00 (normal weight)	593(38.3%)	173(36.6%)	
24.00≤BMI<28.00 (overweight)	623(40.2%)	183(38.7%)	
BMI≥28.00 (obese)	294(19.0%)	100(21.1%)	
Employment			0.014
No	1305(84.2%)	420(88.8%)	
Yes	244(15.8%)	53(11.2%)	
Education			0.873
Illiteracy	385(24.9%)	112(23.7%)	
Primary school	495(32.0%)	154(32.6%)	
Junior high school/above	669(43.2%)	207(43.8%)	
Tobacco Smoking			0.472
No	1295(83.6%)	402(85.0%)	
Yes	254(16.4%)	71(15.0%)	
Alcohol Drinking			0.257
No	1387(89.5%)	432(91.3%)	
Yes	162(10.5%)	41(8.7%)	
Physical activities			＜0.001
No	1009(65.1%)	233(49.3%)	
Yes	540(34.9%)	240(50.7%)	
Diabetes			0.412
No	801(51.7%)	237(50.1%)	
Yes	748(48.3%)	236(49.9%)	
Hypertension			0.334
No	628(40.5%)	180(38.1%)	
Yes	921(59.5%)	293(61.9%)	

Supplementary Table 3 Nutrient content of study participants.

Characteristic	Median(IQR)		p-Value
	Non-depression（n=1563）	Depression（n=459）	
Carbohydrates (g)	192.21(159.62-235.27)	194.70(161.45-237.93)	0.444
Protein (g)	53.61(43.04-66.12)	54.53(43.69-67.67)	0.373
Total fat (g)	34.77(27.09-44.23)	35.21(27.51-45.62)	0.412
β-Carotene (μg)	1459.28(748.00-2677.97)	1560.46(795.40-2738.40)	0.300
Fiber (g)	8.70(6.38-11.54)	8.87(6.61-11.83)	0.150
Cholesterol (mg)	389.57(233.05-436.60)	388.02(238.10-434.77)	0.989
Saturated fat (g)	4.00(2.58-6.02)	4.18(2.63-6.05)	0.655
Monounsaturated fat (g)	5.84(4.17-7.64)	5.98(4.14-7.75)	0.618
Polyunsaturated fats (g)	4.63(2.79-6.93)	4.92(2.84-7.07)	0.475
Niacin (mg)	8.83(6.85-10.97)	8.84(6.95-11.13)	0.702
Thiamine (mg)	0.71(0.56-0.89)	0.72(0.58-0.89)	0.506
Riboflavin (mg)	0.66(0.51-0.83)	0.67(0.51-0.85)	0.324
Vitamin B12 (μg)	0.22(0.14-0.34)	0.22(0.14-0.32)	0.892
Vitamin B6 (mg)	0.07(0.05-0.10)	0.07(0.05-0.10)	0.182
Fe (mg)	15.58(12.20-19.11)	15.90(12.52-19.33)	0.409
Magnesium (mg)	215.78(165.89-266.09)	218.40(169.30-270.06)	0.166
Zinc (mg)	7.15(5.66-8.68)	7.29(5.77-8.83)	0.383
Selenium (μg)	40.42(33.25-48.11)	40.86(32.89-49.39)	0.511
Vitamin A (RE)	430.36(283.91-660.48)	443.76(274.19-683.98)	0.505
Vitamin C (mg)	49.68(27.47-84.84)	52.51(28.11-89.54)	0.482
Vitamin E (mg)	11.74(8.24-14.95)	12.07(8.26-15.81)	0.177
Folic acid (μg)	115.79(83.57-153.99)	119.97(85.02-159.85)	0.370

STROBE Statement—Checklist of items that should be included in reports of ***case-control studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	3-4
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls	4
		(*b*) For matched studies, give matching criteria and the number of controls per case	4
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5
Bias	9	Describe any efforts to address potential sources of bias	6
Study size	10	Explain how the study size was arrived at	6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6
		(*b*) Describe any methods used to examine subgroups and interactions	6
		(*c*) Explain how missing data were addressed	6
		(*d*) If applicable, explain how matching of cases and controls was addressed	6
		(*e*) Describe any sensitivity analyses	6-7
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	7
		(b) Give reasons for non-participation at each stage	7
		(c) Consider use of a flow diagram	7
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	7
		(b) Indicate number of participants with missing data for each variable of interest	7
Outcome data	15*	Report numbers in each exposure category, or summary measures of exposure	7

Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	7
		(*b*) Report category boundaries when continuous variables were categorized	7
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	7
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	7-8
Discussion			
Key results	18	Summarise key results with reference to study objectives	8
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	10
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	8-9
Generalisability	21	Discuss the generalisability (external validity) of the study results	8-9
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	11

*Give information separately for cases and controls.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.