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## Shellfish-based dietary patterns and cognition in the Chinese senior population: A cross-sectional study in Qingdao, China

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## ABSTRACT

**Background and Objectives:** This study aims to investigate the association between dietary patterns and cognitive function among older adults with lower educational backgrounds living in China. **Methods and Study Design:** We analyzed data from the 2018 Health Survey of individuals aged over 50 in Chengyang, Qingdao, China. Questionnaires were used to collect information on the behaviors and lifestyles of the elderly. The Montreal Cognitive Assessment (MoCA) was administered to evaluate cognition, with a total score of less than 19 indicating cognitive impairment for participants with low educational attainment. Using Principal Component Analysis, we identified three dietary patterns: Shellfish, Fruit, and Red Meat. Cross-sectional data regarding dietary intake, cognition, and demographics from 964 participants was analyzed using multivariate regression models to explore the relationship between dietary patterns and cognitive function. **Results:** Our findings indicated that the 'Shellfish-based' dietary pattern ("Shellfish" DP) was significantly associated with cognitive function in both the third quartile (Q3: Odds Ratio=0.58, 95% CI: 0.36-0.93,  $p<0.05$ ) and the fourth quartile (Q4: OR=0.54, 95% CI: 0.33-0.87,  $p<0.05$ ). Furthermore, stratified analysis based on specific covariates revealed that significant results among individuals with a BMI of less than 25 kg/m<sup>2</sup> (OR=0.57, 95% CI: 0.33-0.99,  $p<0.05$ ). No significant interaction effects were observed between shellfish dietary intake and various subgroups (all interaction  $p > 0.05$ ). **Conclusions:** Our research demonstrates that "Shellfish" DP is negatively correlated with cognitive decline among the elderly population. This correlation is particularly significant in individuals with BMI < 25kg/m<sup>2</sup>, as well as among women and under the age of 65. However, no interaction was observed between the shellfish DP and the various subgroups. These findings can effectively guide older adults in optimizing their dietary structures, thereby safeguarding their cognition.

**Key Words:** cognitive decline, dietary pattern, dementia, principal component analysis, aging

## INTRODUCTION

Memory loss and slow thinking, both associated with cognitive decline, are becoming increasingly serious as the population ages.<sup>1, 2</sup> Currently, China is experiencing the fastest population aging in the world;<sup>3</sup> projections indicating the number of individuals aged 65 and older will exceed 150 million by 2030.<sup>4</sup> This substantial elderly population will exert significant pressure on social and economic development.<sup>5</sup> Moreover, it is concerning that

cognitive decline encompasses more than merely memory loss; it also leads to a decline in daily living abilities, a deterioration of social skills, and other serious consequences. These include falling injuries,<sup>6</sup> anxiety,<sup>7</sup> depression,<sup>8</sup> and social disengagement<sup>9</sup> are notable examples. These factors collectively contribute to a diminished quality of life and compromised living experiences, particularly among older populations.<sup>10</sup> Genetic,<sup>11, 12</sup> metabolic,<sup>13</sup> vascular conditions and metabolic syndromes,<sup>14, 15</sup> lifestyle and social factors jointly affect cognitive decline and dementia risk in the elderly, especially in non-urban areas.<sup>16</sup> The prevention of cognitive impairment in older adults has emerged as a significant public health concern.

The impact of modifiable factors, such as diet, on preventing cognitive decline has been extensively researched.<sup>17</sup> Several research indicated that healthy eating patterns, particularly the Mediterranean diet, may significantly contribute to the prevention and management of cognitive decline.<sup>18, 19</sup> Román et al indicates that polyphenols extracted from fruits and vegetables can effectively modulate hyper phosphorylation and beta-amyloid aggregation in animal models of Alzheimer's disease (AD).<sup>20-22</sup> This suggest that regular consumption of plant-based foods may mitigate the risk of cognitive impairment and enhance overall brain health.<sup>21</sup> Bioactive compounds found in plant foods including vitamins, polyphenols, various phytochemicals and unsaturated fatty acids, have been demonstrated to enhance neurogenesis, synaptic plasticity and neuronal survival by mitigating oxidative stress and neuroinflammation.<sup>22</sup> In addition to fruit consumption, the intake of mushrooms has been reported to slow neurodegeneration, potentially due to the role of ergothioneine in protecting neuroplasticity and reducing oxidative stress.<sup>23</sup> Additionally, some studies have indicated that the consumption of processed red meat may negatively impact the cognitive health of older adults, whereas the consumption of lean red meat and white meat has been associated with improved cognitive functioning.<sup>24-26</sup> It has long been posited that the consumption of marine fish rich in omega-3 fatty acids, such as salmon, tuna, and sardines, may confer protection against cognitive decline, including Alzheimer's disease.<sup>27-29</sup> However, other evidence suggests that the relationship between marine fish consumption and cognitive function may be more complex than previously understood, this protective effect could be influenced by various factors, including genetic predispositions and socioeconomic status,<sup>30</sup> highlighting the need for further research to elucidate these relationships.

The applicability of existing dietary research to the Chinese population is limited, as typical Chinese dietary patterns are distinct and rarely observed in other cultures.<sup>31</sup> Shellfish hold significant cultural importance in Chinese diets, especially in coastal regions such as

Qingdao<sup>32, 33</sup> This culinary tradition provides a unique context for investigating diet-cognition relationships, as regular shellfish consumption represents both a nutritional practice and a culturally reinforced behavior. Longitudinal evidence suggests that increased fish consumption may slow the cognitive decline process in China elderly people, however, the protective effect has not been observed across all age groups.<sup>34</sup> Research conducted among the Hong Kong population did not demonstrate significant links between cognitive health and the intake of vegetables, antioxidants, fish, or phytoestrogens.<sup>35</sup> In contrast, diets rich in nuts, vegetables, and fruits have been associated with a reduced risk of cognitive impairment.<sup>36</sup> Notably, a study on elderly Chinese individuals ( $\geq 90$  years) found that only legumes and animal oils were linked to the prevalence of mild cognitive impairment.<sup>37</sup> Given that individual dietary components often exert subtle effects,<sup>38</sup> dietary patterns provide a more comprehensive overview of overall diet and health.<sup>39</sup> A cross-sectional study conducted in suburban Qingdao utilized exploratory factor analysis to elucidate Chinese dietary patterns and their relationship with cognitive function.<sup>40</sup> This approach enables us to better understand how these modifiable factors may effectively prevent or manage cognitive decline and dementia within this population.

## MATERIALS AND METHODS

### *Study subjects*

In this cross-sectional study, all participants resided in Chengyang District, Qingdao City, Shandong Province, for at least five years between May and September 2018. Utilizing cluster random sampling as the sampling method, a total of 1,064 middle-aged and older participants were recruited. Data on participants' demographics, cognition, diet, health history, and lifestyle were collected through a questionnaire. A standardized protocol was employed, and trained investigators administered the questionnaire in a comfortable setting. Face-to-face interviews were conducted with consideration for participants' educational backgrounds.

The questionnaire was developed based on existing research and theoretical frameworks. Biometric data, including weight, height, BMI, blood pressure, and glucose levels, were measured, and blood samples were collected following an overnight fast. Furthermore, data were collected from 1,033 participants, applying the following Inclusion criteria: (1) permanent Han Chinese residents of Qingdao ( $\geq 5$  years); (2) aged  $\geq 50$  years; (3) agree and sign the written informed consent. Exclusion criteria: (1) individuals under 50 years of age; (2) insufficient investigation data; (3) inability to comprehend or provide informed consent for the study; (4) prior diagnoses of dementia or significant cognitive impairment (Figure 1). This

analysis specifically targets older community populations with lower educational attainment, utilizing data from 964 participants whose education levels were below the middle school equivalent (years 7-9) or below the equivalent of year 6. Data entry was performed using EpiData and subsequently verified. This study was approved by the Medical Ethics Committee of Qingdao Municipal Center for Disease Control and Prevention in Qingdao, China (ID: 201804, approval data July 12, 2018). All subjects signed informed consent forms.

### ***Cognitive assessment***

Participants' cognitive function was evaluated by the Chinese version of Montreal Cognitive Assessment,<sup>41</sup> which comprises seven components: visual space (0-5 points), naming (0-3 points), attention (0-6 points), language (0-3 points), abstract ability (0-2 points), delayed recall (0-5 points) and orientation (0-6 points). The total score for the assessment is 30 points, with a cutoff point of <26 points defined as optimal for identifying Mild Cognitive Impairment (MCI).<sup>42</sup> It is more sensitive than the MMSE and is widely used in China.<sup>43</sup> Generally, a MoCA score of 25 or lower often indicates possible cognitive impairment, whereas a score above 26 reflects a normal level of cognitive function.<sup>42</sup> Meta-analytic evidence suggests that a cutoff score of 23 should be adopted, as it demonstrates greater diagnostic accuracy.<sup>44</sup> However, research on the use of MoCA among the Chinese population indicates that for participants with relatively lower educational background, a cut off score of 19 is optimal, as it exhibits higher sensitivity and accuracy in detecting cognitive decline and mild cognitive impairment (MCI).<sup>45</sup> Given that all subjects in our study had less than 12 years of education, we added one point to each participant's total MoCA score at the time of data collection.<sup>42</sup> Subsequently, for analysis based on their MoCA performances: (1) Low cognitive performance defined as scores below 19, and (2) Normal cognitive performance, defined as scores of 19 or higher (ranging from 19 to 30). The cross-sectional data was divided into case (Low cognitive performance group, n = 167) group and control (normal cognitive performance group, n = 797) group.

### ***Dietary data***

We examined the frequency of intake for 12 food groups based on local food habits, including shellfish, saltwater fish, garlic, fruits, vegetables, red meat, nuts, white meat, tea, milk, yogurt, and coffee. Respondents could select from six frequency options: 'less than once per week', 'one to three times per week', 'four to six times per week', 'once per day', 'two to three times per day', and 'four times per day or more'. The reported frequencies for these 12 food groups

were subsequently converted into weekly intakes using the *China Food Composition*.<sup>46</sup> Additionally, we calculated the total energy intake for each food category, expressed in kcal/week.

### ***Demographic data and other covariates***

The demographic data we measured included age, biological sex (male, female), educational years ( $\leq 6$  years, 7-9 years), and marital status (married/living with partner, live alone/widowed/divorced/separated/never married). Biometric data encompassed the body mass index (BMI), which was calculated using participants' height (m) and weight (kg) based on the following categories:  $< 25 \text{ kg/m}^2$ ,  $25\text{-}30 \text{ kg/m}^2$ , and  $\geq 30 \text{ kg/m}^2$ .

Diabetes mellitus was determined by a fasting blood glucose concentration exceeding 7.0 mmol/L, or a self-reported history of diabetes mellitus, or current use of glucose-lowering medication. Hypertension was defined as a systolic blood pressure  $\geq 140 \text{ mm Hg}$  and/or diastolic blood pressure  $\geq 90 \text{ mm Hg}$  without antihypertensive medication, a self-reported history of hypertension, or current use of antihypertensive medication. Diabetes and hypertension were defined based on self-reported physician diagnoses and were defined as yes or no.

Lifestyle data included the frequency of smoking, alcohol consumption, and physical activity, each categorized as: 'never' (never engaged), 'former' (ceased within the past year), and 'current' (currently engaged).

### ***Statistical analysis***

#### **Descriptive statistics**

The Kolmogorov-Smirnov normality test was first applied to assess continuous variables' normality. Normally distributed ones were reported as Mean  $\pm$  SD, and non-normally distributed ones were described by median and IQR. Two independent samples t-tests were used for normally distributed variables to compare means between low and normal cognitive performance groups, while the Mann-Whitney U test was used for non-normally distributed variables. Chi-square tests were employed to assess differences in categorical variables' distribution between the two groups. The grouping of each variable and the prevalence results of cognitive decline between groups were presented in Table 1.

### **Principal component analysis**

The current study employed exploratory factor analysis on the 12 food groups under investigation to identify three major dietary patterns, which collectively accounted for 36.9% of the total dietary variance (Table 2). The factor scores for each dietary pattern were estimated by summing the weighted food group intakes multiplied by their respective factor loadings.<sup>47, 48</sup> Each dietary pattern (DP) was named based on the food group with the highest factor loadings in the pattern analysis. These patterns were rotated using the maximum variance method to enhance clustering.

### **Logistic regression**

In our study, each dietary pattern was categorized into four groups based on quartiles, which were further divided into two categories: low and normal cognitive performance. This categorization was based on the cognitive score, with scores above 19 to 30 classified as normal cognitive performance and those below 19 classified as low cognitive performance. Binary logistic regression was subsequently conducted by us to investigate the association between different dietary patterns and cognitive decline. In the crude model (Model 1), we intentionally excluded demographic, biometric, and lifestyle data to prevent these covariates from obscuring the relationship between dietary patterns and cognitive decline. Model 2 subsequently adjusted for age and sex to evaluate their influence on the association. Finally, a fully adjusted model (Model 3) incorporating all covariates was fitted, with the results presented in Table 3.

### **Stratified analysis**

Based on the results of the binary logistic regression, we subsequently examined the interaction between "Shellfish" DP and all other covariates (Age, Gender, Education and BMI). The threshold for significance was set at a  $p$ -value of 0.05. The covariates that interacted with "Shellfish" DP served as the basis for the stratified analysis, through which the relationship between "Shellfish" DP and cognitive decline was re-evaluated; the results are presented in Figure 2. All statistical analyses were conducted using IBM SPSS Statistics version 26.0, and the forest plot was generated drawn using R 4.2.3.

## RESULTS

### *Characteristics of study population*

This analysis included data from 964 participants, of whom 17.3% were categorized as having cognitive impairment (MoCA score <19), while 82.7% exhibited normal cognitive function (MoCA score  $\geq 19$ ). The mean MoCA score was  $23.1 \pm 4.9$ .

We compared data between two groups: individuals with low cognitive function and those with normal cognition. Significant differences were observed in age, gender, educational level, marital status, blood pressure, smoking frequency, and alcohol consumption frequency. As illustrated in Table 1, individuals with low cognitive function were more likely to be older adults (the mean age was  $71.9 \pm 7.5$ ), predominantly male, educational level below 6 years, non-married, and be either past smokers or current alcohol consumers.

### *Principal component analysis of dietary patterns*

The finalized factor loading matrices for the three dietary patterns, along with their respective variances and interpretations of cumulative variance, were presented in Table 2. Each DP was named according to the input food group with the highest factor loadings in the pattern,<sup>49</sup> and three dietary patterns in this study were “Shellfish”, “Fruits” and “Red Meat”. After that, factor scores were used as the basis for ranking participants for each dietary pattern from lowest to highest, and this ranking was used to create quartiles for subsequent statistical analysis.<sup>38</sup> The characteristic foods of this dietary pattern include shellfish (factor load 0.62), saltwater fish (0.62), and garlic (0.52), reflecting the traditional dietary habit of coastal residents to consume shellfish in combination with fish. Although labeled the 'Shellfish' model, this dietary pattern reflects a typical coastal diet centered on seafood, particularly shellfish and saltwater fish, and is characterized by the use of seasonings like garlic. In this study, it is referred to as the Shellfish DP.

### *Association between dietary patterns and cognitive decline*

In the context of cognitive decline, the unadjusted crude model (Model 1), which did not account for any covariates, demonstrated a significant protective effect of quartile 3 (OR=0.58, 95% CI: 0.36-0.93,  $p < 0.05$ ) and quartile 4 (OR=0.54, 95% CI: 0.33-0.87,  $p < 0.05$ ) of the "Shellfish" DP when compared to quartile 1. Model 2, adjusted for age and gender, revealed that while the effect sizes for quartiles 3 and 4 changed slightly, the overall significance of the association remained unchanged. After adjusting for all covariates in Model 3, a negative correlation was still observed for quartile 3 (OR=0.61, 95% CI: 0.39-



0.97,  $p < 0.05$ ) and quartile 4 (OR=0.56, 95% CI: 0.34-0.94,  $p < 0.05$ ) of the "Shellfish" DP in relation to cognitive decline. In contrast, neither the crude model, nor model 1 adjusted for covariates, identified an association between "Fruit" DP, "Red Meat" DP and cognitive decline. The results are presented in Table 3.

### *Stratified analyses by selected covariates*

Covariates that exhibited significant interaction with "shellfish" DP served as the basis for stratification. A stratified analysis was conducted on the study population to further investigate the relationship between "shellfish" DP and cognitive decline across different levels. In the stratified analysis model, all covariates in this study were adjusted and illustrated through a forest plot (Figure 2).

Within the context of "shellfish" DP, a weekly intake of 50-100 g demonstrated a significant protective effect against cognitive decline in individuals under 65 years old and female subgroup, with OR of 0.37 (95% CI: 0.16-0.81,  $p < 0.05$ ) and 0.55 (95% CI: 0.35-0.88,  $p < 0.05$ ), respectively. A similar protective effect was observed in individuals with a body mass index (BMI) of less than 25 kg/m<sup>2</sup>, with an OR of 0.57 (95% CI: 0.33-0.99,  $p < 0.05$ ). However, no significant interaction was found between each group and bud intake frequency.

## **DISCUSSION**

This cross-sectional analysis suggest a protective effect of "Shellfish" DP on the decline in cognitive function among middle-aged and elderly individuals with low levels of education in China. We observed a significant protective effect of "Shellfish" DP on cognitive decline in the crude model, which did not adjust for covariates and the fully adjusted model. Furthermore, in the stratified analysis, the third quartile (Q3) of "Shellfish" DP remained significantly protective against cognitive decline in both the solitary and BMI groups with values less than 25 kg/m<sup>2</sup>. By exploring these associations, this study contributes to the existing evidence and suggests that increased consumption of "Shellfish" DP may serve as a non-pharmaceutical intervention to protect older individuals with lower educational backgrounds from developing cognitive decline.<sup>27</sup>

Extensive evidence underscores the role of healthy eating in health promotion, especially for older adults who are more susceptible to health issues. The human brain is susceptible to oxidative damage. Thus, foods rich in antioxidants can mitigate cognitive decline in older individuals, regardless of particularly regarding its significance dementia.<sup>50</sup> The potential benefits of fish consumption on cognitive functioning have been extensively discussed in

literature. While physiological and metabolic research has supported its role in anti-inflammation,<sup>51, 52</sup> this body of knowledge remains inconsistent, particularly regarding its effectiveness across different age groups.<sup>34</sup> One study utilizing longitudinal and clinical trial data have yielded mixed findings regarding the contribution of (fatty) fish intake to cognitive health in older populations.<sup>28, 29</sup>

Furthermore, a prior study focusing on an illiterate community-dwelling older Chinese population did not identify significant associations between increased fish intake and improved cognitive function.<sup>53</sup> The study also suggests a potential association between increased consumption of saltwater fish and a reduced risk of developing dementia; however a dose-response relationship has not been established.<sup>54</sup> Furthermore, participants who consumed “Shellfish” DP were found to be less likely to experience cognitive decline. In our factor analysis, the two foods with the highest factor loadings in the “Shellfish” DP were shellfish and saltwater fish. Although the result was derived from cross-sectional data and should not be interpreted as indicative of causal relationships, it nonetheless provides valuable insights, particularly within the local context. This evidence suggests that incorporating saltwater fishery products into future clinical and public health strategies may benefit cognitive health in older adults, particularly in communities where shellfish and saltwater fish are affordable and accessible.

Following the factor analysis of the 12 food groups, we examined the relationship between each DP and cognitive decline using binary logistic regression. Our results indicated that the “Shellfish” DP had a significant protective effect against the decline in cognitive function. In our study, the three food groups with factor loadings greater than 0.5 in the “Shellfish” DP were shellfish,<sup>48</sup> saltwater fish, and garlic. Previous evidence has indicated that increased garlic intake may offer potential protective effects against certain metabolic conditions,<sup>55</sup> and may also reduce the risk of all-cause mortality within the Chinese population.<sup>56</sup> The observed protective association between the “Shellfish” DP and cognitive preservation may be further explained by synergistic interactions between bioactive components within this dietary pattern. Beyond the previously discussed omega-3 fatty acids abundant in marine sources, emerging evidence highlights the complementary neuroprotective roles of other dietary constituents. For instance, aged garlic extract (AGE), a key component of the “Shellfish” DP in this population, has demonstrated potent antioxidative and anti-inflammatory properties in experimental models, reducing  $\beta$ -amyloid deposition and tau hyperphosphorylation—hallmark pathologies of Alzheimer’s disease.<sup>57</sup> This aligns with our findings, suggesting that regular garlic consumption within the shellfish-centric dietary pattern may contribute to the

observed cognitive benefits through multiple molecular pathways. In China, particularly in the suburban areas of Shandong, the consumption of raw or cooked garlic in each meal is both popular and prevalent. Given this dietary pattern, future research could investigate whether and how garlic intake affects the cognitive health of older populations in this region, potentially serving as a culturally appropriate strategy for community health promotion.

Notably, the coastal geographical context of Qingdao provides unique dietary advantages, as shellfish and saltwater fish are rich sources of docosahexaenoic acid (DHA), an omega-3 fatty acid critical for neuronal membrane integrity and synaptic plasticity. Furthermore, while our study did not directly assess vitamin A intake, recent preclinical research demonstrates that vitamin A supplementation counteracts high-fat diet-induced cognitive deficits in APP/PS1 mice by reducing amyloid- $\beta$  plaque burden and enhancing synaptic protein expression.<sup>58</sup> Experimental studies in murine models have shown that DHA supplementation modulates hippocampal lipid profiles and mitigates neurodegeneration induced by high-fat diets, particularly in ApoE genotypes associated with Alzheimer's risk.<sup>59</sup> This mechanistic evidence supports our epidemiological findings, suggesting that the benefits of the "Shellfish" DP may be enhanced in populations with genetic predispositions to lipid metabolism dysregulation. Given that shellfish naturally contain retinoids and carotenoids (precursors to vitamin A), the "Shellfish" DP may indirectly support neuroprotection through this additional pathway. Emerging evidence suggests that dietary patterns similar to the "Shellfish" DP—rich in anti-inflammatory nutrients—may mitigate diabetes-related cognitive risks. A recent cross-sectional study demonstrated that higher dietary diversity combined with marine-sourced omega-3s improved cognitive performance in elderly T2DM patients, potentially counteracting hyperglycemia-induced neural damage.<sup>60</sup> These findings collectively underscore the multifactorial nature of dietary interventions, where combinatorial effects of omega-3s, garlic-derived compounds, and fat-soluble vitamins may synergistically attenuate neuroinflammation and oxidative stress, which are key drivers of cognitive decline.

This study presents several strengths. A reasonably large sample size enhanced the reliability of our statistical analyses. We conducted a comprehensive examination of various demographic and biometric variables, as well as lifestyle patterns, which were utilized as covariates to bolster the robustness of our results. However, this study has limitations, and the findings should be interpreted with caution. Firstly, due to its cross-sectional design, we cannot draw causal inferences from the reported associations. The sample population exhibited a disproportionate gender distribution, with a higher number of female participants compared to male participants, suggesting biological plausibility transcends sex differences,

the female predominance (68%) may limit generalizability to male populations. A post-hoc gender-stratified analyses revealed consistent effect sizes across subgroups ( $p$  for interaction=0.335). This imbalance reflects China's sex-specific longevity patterns.<sup>61</sup> Experimental evidence indicates estrogen may enhance DHA bioavailability,<sup>62</sup> suggesting that further biological plausibility for sex-differential dietary effects requiring mechanistic exploration. While we aimed to exclude individuals with dementia, it is possible that undiagnosed early-stage dementia patients were inadvertently included in our study. A significant proportion of our participants had limited educational backgrounds, which restricted our ability to further explore the relationships between educational level and cognitive function. Although examining nutrient intake was not the primary objective of this study, it is noteworthy that we did not collect information on nutrient intake. Consequently, we were unable to investigate the potential reasons behind the association between diet and cognitive function. Although no collinearity was detected, covariates may still have implicitly influenced the results. For instance, individuals with higher levels of education are likely to possess greater knowledge about nutrition and health, as well as better access to higher-quality food options, such as saltwater fish, nuts, and fresh fruits and vegetables. Additionally, they may exhibit greater literacy regarding healthy lifestyles and preventative measures related to dementia. Future studies should prioritize mechanistic investigations into garlic's neuroprotective potential, particularly given experimental evidence from aged garlic extract (AGE) studies demonstrating  $\beta$ -amyloid reduction and anti-tau hyperphosphorylation effects in Alzheimer's models. Our cross-sectional design inherently limits causal inference; the observed association between shellfish consumption and cognitive function may reflect reverse causality, wherein cognitively intact individuals are better able to maintain seafood-rich diets. Although we excluded participants with advanced dementia, preclinical cognitive decline may still influence dietary habits. Longitudinal cohorts that track dietary changes and cognitive trajectories are necessary to establish temporality. Furthermore, the neuroprotection conferred by marine-based diets likely operates through synergistic pathways:

1. Bioactive lipid mediation: Shellfish-derived DHA is incorporated into neuronal membranes, enhancing membrane fluidity and promoting the expression of synaptic proteins such as PSD-95 and synaptophysin.<sup>63</sup>
2. Oxidative stress mitigation: Selenium and astaxanthin found in crustaceans upregulate Nrf2-mediated antioxidant enzymes, including superoxide dismutase (SOD) and catalase (CAT), thereby reducing lipid peroxidation in the hippocampus.<sup>64</sup>

3. Anti-inflammatory cascade: Omega-3 fatty acids inhibit the activation of the NLRP3 inflammasome, while organosulfides from garlic suppress COX-2/PGE2 signaling, collectively attenuating neuroinflammation. This tripartite mechanism underscores the multimodal potential of marine diets in combating age-related cognitive decline.<sup>65</sup>

## **Conclusion**

Our research confirmed the negative correlation between shellfish consumption and cognitive decline. Meanwhile, it also identified an optimal dietary pattern to safeguard cognitive function among various subgroups, including those under 65 years of age, women, and individuals with a BMI < 25 kg/m<sup>2</sup>. This finding would contribute to the updating of dietary patterns guidelines based on cognitive function for the elderly.

## **CONFLICT OF INTEREST AND FUNDING DISCLOSURE**

The authors declare no conflict of interest.

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**Table 1.** Demographics and bivariate analysis results of frequency of dietary intake and cognitive decline.

Variables	Number of Subjects (N)	MoCA Scores N (%) / M $\pm$ SD		p <sup>a</sup>
		Low cognitive performance	Normal cognitive performance	
Age	964	71.9 $\pm$ 7.5	65.7 $\pm$ 7.0	<0.01
< 65 years		36 (8.5)	386 (91.5)	
$\geq$ 65 years		131 (24.1)	411 (75.9)	
Gender	964			<0.01
Female		129 (77.3)	506 (63.5)	
Male		38 (22.8)	291 (36.5)	
Education years	963			<0.01
$\leq$ 6 years		155 (92.8)	483 (60.7)	
7-9 years		12 (7.2)	313 (39.3)	
Marital status	952			<0.01
Married/living with partner		117 (70.1)	690 (87.9)	
Widowed/divorced/separated/never married		50 (29.9)	95 (12.1)	
BMI	964			0.07
< 25 kg/m <sup>2</sup>		76 (45.5)	333 (41.8)	
25-30 kg/m <sup>2</sup>		70 (41.9)	399 (50.1)	
$\geq$ 30 kg/m <sup>2</sup>		21 (12.6)	65 (8.2)	
Diabetes <sup>b</sup>	949	40 (24.0)	171 (21.5)	0.46
Hypertension <sup>c</sup>	964	107 (64.1)	377 (47.3)	<0.01
Shellfishd	964			<0.01
< 50g		82 (49.1)	323 (40.5)	
50-100g		77 (46.2)	423 (53.2)	
$\geq$ 100g		8 (4.7)	51 (6.3)	
Frequency of smoking	958			0.02
Never		131 (78.9)	549 (69.3)	
Former		14 (8.4)	132 (16.7)	
Current		21 (12.7)	111 (14.0)	
Frequency of alcohol consumption	962			<0.01
Never		129 (77.3)	499 (62.8)	
Former		6 (3.59)	28 (3.5)	
Current		32 (19.2)	268 (33.7)	
Frequency of physical activity	960			0.11
Never		37 (22.3)	131 (16.5)	
Former		111 (66.9)	588 (74.1)	
Current		18 (10.8)	75 (9.4)	

M, mean; SD, standard deviation; BMI, body mass index.

a Numbers in bold indicate significant findings (p<0.05).

b DM history was based on self-report diagnosis, use of blood sugar lowering medications, or fasting blood glucose  $\geq$  7.0mmol/L.

c Hypertension history was based on self-report diagnosis, anti-hypertensive use, systolic blood pressure  $\geq$  140 mmHg, or diastolic blood pressure  $\geq$  90 mmHg.

**Table 2.** Principal component analysis of 12 food groups: Unraveling dietary patterns in elderly nutrition studies.

Food group	Dietary pattern		
	Shellfish	Fruits	Red meat
Shellfish	0.62	0.04	0.06
Saltwater fish	0.62	-0.03	0.27
Garlic	0.52	0.40	-0.10
Fruits	-0.05	0.68	0.11
Vegetables	0.06	0.55	0.58
Red meat	-0.01	0.03	0.82
Nuts	0.10	0.41	0.08
White meat	0.43	-0.25	0.03
Tea	0.49	0.32	-0.39
Milk	0.10	0.03	0.38
Yogurt	-0.22	0.40	-0.18
Coffee	0.02	0.24	0.01
Explained variance (%)	15.3	11.6	10.0
Cumulative variance (%)	15.3	26.9	36.9

Extraction method: principal component analysis.

Rotation method: varimax with Kaiser normalization.

Factor predictive value ( $-0.4 \leq x \leq 0.4$ ) are present in regular type.

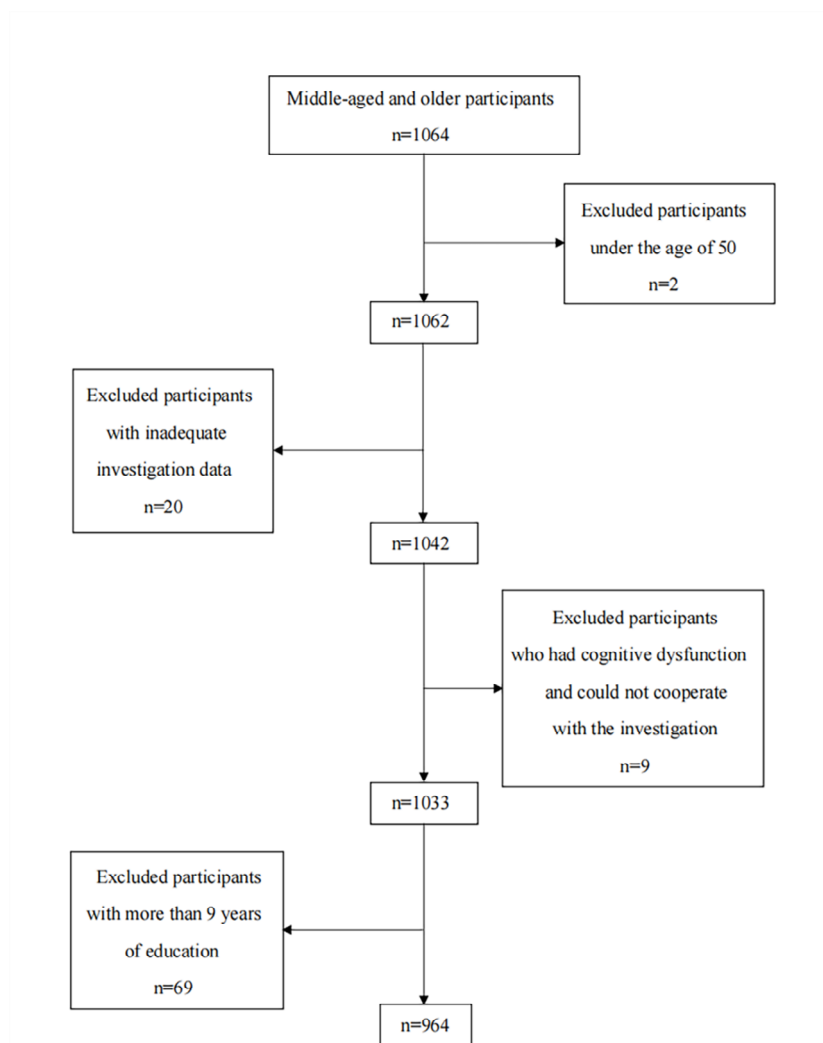
Factor loadings with a high predictive value ( $> 0.5$ ) are presented in boldface type.

**Table 3.** Multivariable logistic regression between dietary patterns and the risk of cognitive decline.

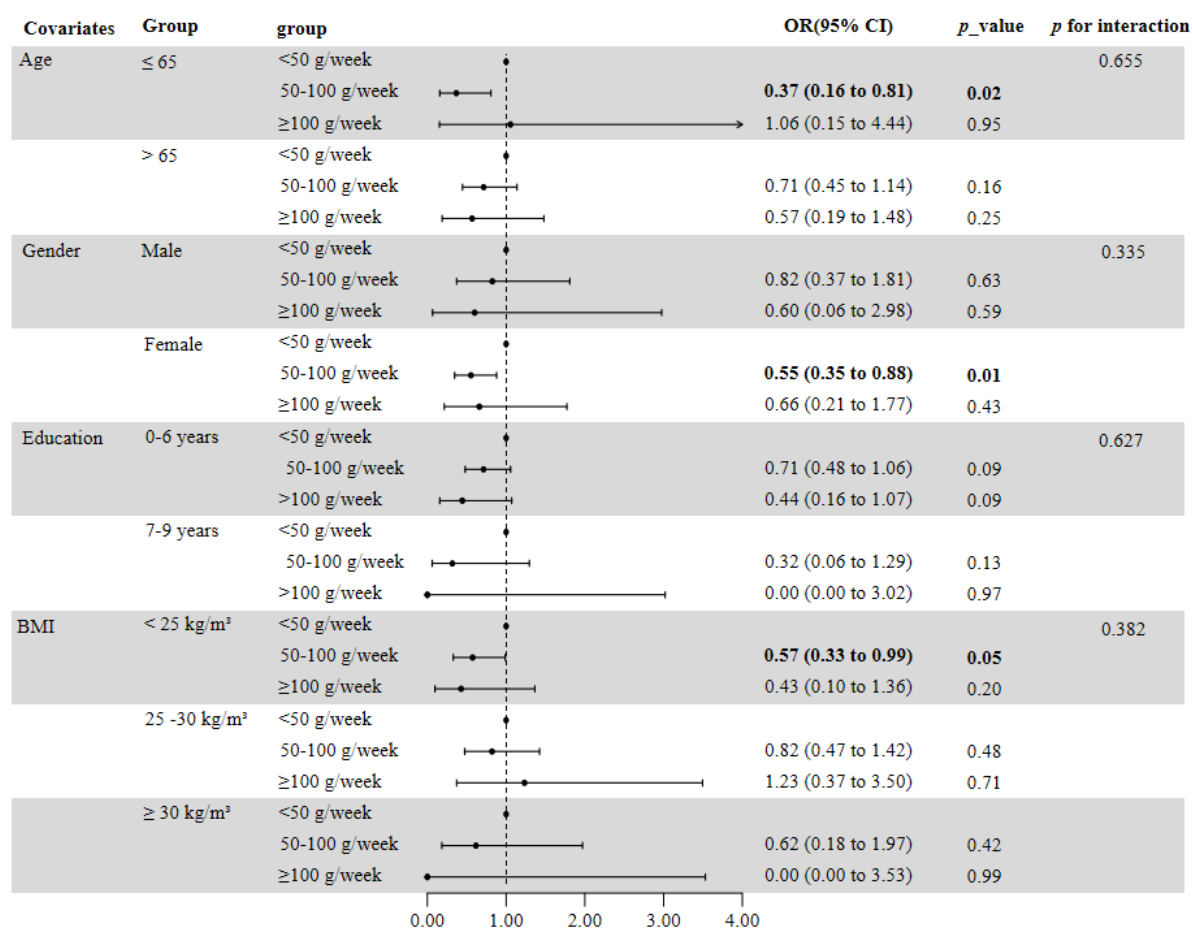
Dietary patterns	Model 1 (95%CI)	<i>p</i>	Model 2 (95%CI)	<i>p</i>	Model 3 (95%CI)	<i>p</i>
Shellfish						
Q1	1.00 (Ref.)		1.00 (Ref.)		1.00 (Ref.)	
Q2	0.88 (0.56, 1.36)	0.58	0.83 (0.52,1.31)	0.42	0.94 (0.59, 1.51)	0.82
Q3	0.58 (0.36, 0.93)	0.03	0.54 (0.31,0.90)	0.02	0.61 (0.39, 0.97)	0.04
Q4	0.54 (0.33, 0.87)	0.01	0.53 (0.29,0.96)	0.04	0.56 (0.34, 0.94)	0.03
Fruit						
Q1	1.00 (Ref.)		1.00 (Ref.)		1.00 (Ref.)	
Q2	0.97 (0.61, 1.53)	0.91	1.01 (0.62,1.66)	0.95	1.22 (0.73, 2.05)	0.44
Q3	0.86 (0.54, 1.38)	0.55	0.83 (0.50,1.37)	0.47	1.14 (0.67, 1.93)	0.61
Q4	0.72 (0.44, 1.16)	0.18	0.73 (0.38,1.41)	0.37	1.02 (0.59, 1.78)	0.92
Red Meat						
Q1	1.00 (Ref.)		1.00 (Ref.)		1.00 (Ref.)	
Q2	0.72 (0.45, 1.16)	0.19	0.81 (0.48,1.35)	0.42	0.83 (0.48, 1.42)	0.51
Q3	0.97 (0.61, 1.53)	0.91	1.06 (0.63,1.77)	0.83	1.09 (0.65, 1.84)	0.73
Q4	0.77 (0.48, 1.23)	0.28	0.86 (0.48,1.52)	0.60	1.11 (0.64, 1.89)	0.70

CI, confidence interval; OR, odds ratio; Q, quartile; Ref, reference.

Model 1: unadjusted covariates; Model 2: adjusted for age and gender; Model 3: adjusted for age and gender educational level, marital status, body mass index (BMI), diabetes, hypertension, frequency of smoking, frequency of alcohol consumption, frequency of physical activity and other dietary variables. 3Boldface indicates  $p < 0.05$ .



**Figure 1.** Flow chart of screening for qualified participants.



**Figure 2.** Forest plot of adjusted odds ratio for the associations between “Shellfish” pattern and changes in cognitive function stratified by selected covariates(Age, Gender and BMI). All models were adjusted for age, gender, education level, marital status, BMI, diabetes, hypertension, frequency of smoking, frequency of alcohol consumption, frequency of physical activity. CI, confidence interval; OR, odds ratio; BMI, body mass index. Factor with a prominent  $p$ -values ( $p < 0.05$ ) are presented in boldface type.