Original Article

The relationship between dietary complexity and cognitive function in Guangxi, China: A cross-sectional study

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Background and Objectives: The composition of the human diet is complex and diverse, and the relationship between dietary composition and cognitive decline has not been adequately studied. Therefore, this study explored the possible association between food items and the risk of cognitive impairment. **Methods and Study Design:** This cross-sectional study was based on an ecological longevity cohort and included 2881 participants (1086 men and 1795 women) aged ≥30 years between December 2018 and November 2019. The association between food items and the risk of cognitive impairment was explored using the Bayesian kernel machine regression (BKMR) learning model. **Results:** Finally, 2881 participants (1086 men and 1795 women) were included. In all participants, the multivariable logistic analysis showed that fresh fruit consumption was associated with cognitive function (OR=0.999, 95% CI: 0.998-0.999, *p*=0.021). Using the BKMR model, none of the 18 food items were significantly correlated with cognitive function among women. In men, when the other food items were fixed at the 25th, 50th, and 75th percentile values (P25, estimate=-0.239; P50, estimate=-0.210; P75, estimate=-0.158), there was a negative correlation between fresh fruit consumption and the predicted risk of cognitive function disorders. **Conclusions:** Men displayed a negative association between fresh fruit consumption and the risk of cognitive function disorders, but this was not apparent among women.

Key Words: cognitive impairment, diet, machine learning, sex, fruit, vegetable

INTRODUCTION

Cognitive impairment is a neurocognitive disorder that affects learning ability, memory, sensorimotor function, language, attention, and problem-solving skills, gradually affecting the quality of life and functioning, and its prevalence might increase due to global population aging.[1,2] There are several possible causes of cognitive decline.[3]

Diet can modulate the incidence of various conditions like hyperlipidemia, hyperglycemia, hypertension, and neurodegenerative diseases, and specific dietary habits might have protective effects on the development of these conditions and, subsequently, on brain function.[4,5] Dietary approaches can reduce the risk of dementia,[6] and nutritional epidemiological investigations examined the effect of single food groups or nutrients on health, such as the use of olive oil in the Mediterranean diet being associated with a reduced risk of cognitive dysfunction,[7,8] as also appears for omega-3 polyunsaturated fatty acids and age-related cognitive impairment.[9] Of importance, human dietary habits and foods are so that food patterns and items rather than single nutrients should be the preferred consideration.

Statistical models investigating the correlation between nutrition and cognitive function have been described, and there are correlations between dietary habits and diseases

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assessed from the perspective of dietary patterns.[10] Factor analysis, principal component analysis, cluster analysis, and dietary index score methods are available to assess the relationship between diet and health, but these methods also have obvious limitations and do not adequately extract information from the complex dietary data.[10] Therefore, there is a need to develop new odelling approaches to determine the appropriateness of models for assessing relationships between dietary intake and diseases.[11] The Bayesian kernel machine regression (BKMR) model proposed by Bobb et al[12] has advantages in assessing the exploration of combined exposure of mixtures with outcome response, nonlinearity, and interaction relationships and can consider the exposure-response relationships of single food items, mixtures, and outcomes, facilitating exposure-response relationship research.

The literature suggests a correlation between dietary factors and cognitive function.[6,13] No previous study used the BKMR model to perform a cross-sectional study of the association between food items and the risk of cognitive decline. Therefore, this study aimed to use the BKMR model to explore the possible correlations between food items (considering the effects of single factors and overall combined exposures on outcomes) and the risk of cognitive impairment in adults >30 years of age.

METHODS

The study was based on an ecological longevity cohort 14 in Gongcheng Yao Autonomous County, Guangxi, China, that recruited 4356 residents aged >30 years between December 2018 and November 2019 in two towns of Gongcheng (Lianhua Town and Li Mu Town). The study was approved by the Ethics and Human Discipline Committee of Guilin Medical University (No. 20180702-3). The study was conducted in accordance with the guidelines outlined in the Declaration of Helsinki, and each participant signed a written informed consent prior to the original epidemiological survey.

The following subjects were excluded: a) <30 years old; b) did not complete the physical examination, c) serious disease or type 1 diabetes, d) unreasonable energy intake (men: <800 kcal/day or >8000 kcal/day; women: <600 kcal/day or >6000 kcal/day));[15] e) missing information from the questionnaire.

Institutional review board statement

The study was reviewed and approved by the ethics committee of the School of Medicine of Guilin Medical College, and informed consent forms were signed for the participation system (No. 20180702-3 and July 2, 2018).

Dietary intake

The dietary assessment was performed using the Food Frequency Questionnaire (FFQ), referring to the reported literature on dietary frequency questionnaires.[16,17] The 108 foods in the questionnaire were divided into 17 groups,[16,18] and the dietary grouped measurements were log-transformed to ensure that the dietary data did not violate the model's assumptions about homoscedasticity and normal distribution of the response variable by adding the constant 1 to the 17 groups of dietary values to shift the minimum of the distribution to 1 (ensuring that it was a non-negative observation).[19] Furthermore, for calculating the Z-scores, the dietary data must be log-transformed without missing values to enter the model.[20]

The energy and nutrient contents of foods were referenced in the "Chinese Food Composition Table" (2009).[21] The participants were asked to recall and report their average frequency of consumption and estimated portion size in the previous year, using either the traditional Chinese weight unit (1 tael = 0.050 kg) or the natural unit (one bowl = 300 mL). In addition, the frequency of dietary intake was categorized as non (never or occasionally), less than once a day (1-3 times/month, 1-2 times/week, 3-4 times/week, 5-6 times/week), once a day, 2 times/day, and ≥3 times/day. The selected frequency categories were converted into daily intakes and used for further analysis. Daily intake = dosage/each time × frequency of intake. Various ingredients required for oil tea were purchased from the local market, and the amounts of various ingredients were weighed sequentially using an electronic balance to an accuracy of 0.0001 kg. Oil tea is a distinctive flavor of Guilin. Oil tea is prepared by frying tea leaves with garlic, salt, ginger, chili, and possibly other ingredients in an iron wok. Water is added and boiled for a while with the mixture till the broth (the oil tea) is ready. It is then sieved and served with other foods.[22]

Cognitive function assessment

The Chinese version of the Simple Mental State Examination (MMSE) was used to assess cognitive status.[23] The MMSE has a total score of 30 points and consists of six components: time and place orientation, attention, memory, language, and visual structure.[24] The lower the score, the worse the cognitive ability. Based on the participants' performance on the MMSE and the number of years of formal education, the participants were divided into cognitively normal and cognitively impaired (CI) groups using the following cutoff values: ≤17 for uneducated individuals, ≤20 for individuals with primary school education, and ≤24 for individuals with junior high school or higher education.[25]

Data collection and definition

All subjects underwent a physical examination and a demographic baseline survey that included sex (man, woman), age (30-59, 60-99 years),[26] ethnicity (Han, Yao, and others), diabetes, physical activity, marital status, years of education, agricultural activities, alcohol consumption, smoking, body mass index (BMI), and hyperlipidemia.

The most recent recommendations of the American Diabetes Association for diabetes were used to define the following variables of interest: fasting blood glucose (FPG) ≥126 mg/dL (7.0 mmol/L) or history of diabetes.[27] Physical activity was measured by labor status according to the Physical Activity Guidelines (PAG) recommended grading scale for labor intensity: light (mainly sitting, standing, or unable to work properly), moderate (mainly general conditions), and energetic (mainly heavy labor).[28] The marital status was divided into two groups: married or cohabiting, unmarried or divorced (widowed, divorced, separated). Education had to be considered,[29-32] and the number of years of education was divided into three groups: no formal education, primary school education, and junior high school or higher. Agricultural activities were defined as people engaged in farming (plowing, planting, weeding). Alcohol consumption was defined as drinking >0.050 kg of alcohol at least once a month. Smoking was defined as currently smoking at least one cigarette a day. Body mass index (BMI) was calculated by dividing the weight by height squared (kg/m^2). Overweight was defined as 23.0-27.5 kg/m^2,[33] and obesity was defined as ≥27.5 kg/m^2. Hyperlipidemia was defined as total cholesterol >5.72 mmol/L and triglycerides >1.70 mmol/L.[34] Hyperglycemia was defined as FPG >6 mmol/L.[35,36]

Statistical analysis

All statistical analyses were performed in SPSS 20.0 (IBM Corp., Armonk, NY, USA) and Microsoft-R-Open (4.0.2). Categorical variables were analyzed using the chi-square test. Nonnormal continuous variables were compared using the Wilcoxon test. The association between a single food item and cognitive function impairment was assessed using logistic regression, and then a logistic regression model including all variables was fitted to assess the association between food items and cognitive function. All models were adjusted for covariables. Restricted cubic spline (RCS) plots were used to show the trends in variables with significance in the logistic regression section, and used Spearman correlation analysis to observe the correlations between variables. The RCS plots were used to determine whether there were nonlinear associations between food items and cognitive function. Given the limited ability of the regression model to represent a high-dimensional parameter space containing nonlinearities and interactions, the BKMR model was applied in the second stage of the analysis. The methods for calculating the summary parameters are available through the R "bkmr" package.[12,37] The aim was to assess the possible interaction between exposure to food items and cognitive impairment with a nonlinear dose-dependent relationship, implemented using a Markov chain Monte Carlo algorithm for 50,000 iterations.[15,38] Potential interactions between a food group and food group-specific exposure-response curves were shown when exposure dosage for all other food groups were maintained at the median or 25^{th} or 75^{th} percentile. Two-sided *p*-values <0.05 were considered statistically significant.

RESULTS

Finally, 2881 participants (1086 men and 1795 women) were included in the study. Table 1 presents the clinical and demographic characteristics of the participants; 52% of the population was 60 years and older, with more women than men. Yao participants accounted for 74.9%. The population with primary school education dominated, with 50.9%. Moderate physical activity accounted for the majority (56.8%). The non-smoking group accounted for 81.5%, the non-drinking group accounted for 67.4%, and more people had normal cognitive functions (n=2009) than cognitive impairment (n=872). All variables were significantly different between the CI and normal groups, except for BMI (all $p<0.05$).

The characteristic distribution of food items in different populations is shown in Supplementary table 1. Oil tea intake was significantly higher in men than in women ($p<0.001$). Egg intake was higher in women than in men ($p<0.001$). Alcohol intake was significantly higher in men than in women ($p<0.001$). For fresh fruit intake, no significant significance was observed among the different groups.

In the whole study population, the univariable logistic regression analyses showed fresh fruits (OR=0.999, 95% CI: 0.998-0.999, $p=0.004$), fish, seafood, & aquatic products (OR=0.994, 95% CI: 0.988-0.999, $p=0.029$), and eggs (OR=0.996, 95% CI: 0.993-0.999, $p=0.018$) were associated with cognitive function. In the multivariable logistic regression analysis, fresh fruits were associated with cognitive function (OR=0.999, 95% CI: 0.998-0.999, $p=0.021$) (Table 2).

In Supplementary table 2, the multivariable logistic regression model showed that stem vegetables (OR=0.993, 95% CI: 0.987-0.998, $p=0.014$), gourd vegetables (OR=1.001, 95% CI: 1.000-1.003, $p=0.038$), and fresh fruits (OR=0.999, 95% CI: 0.998-0.999, $p=0.033$) were associated with cognitive function in men. No significant correlations were seen in women (Supplementary table 3).

The food items that significantly ”orre'ated with cognitive function in the logistic regression model were selected for analysis. The results showed a nonlinear association between fresh fruits and cognitive function in all participants ($p<0.001$), men ($p=0.045$), and women ($p=0.002$) (Supplementary figure 1). Spearman's correlation coefficient was used to evaluate the correlations between each pair of foods (Figure 1). The correlations were ranked from strong to weak, and the results showed no significant correlations between the 18 foods consumed by all participants and by men and women.

The BKMR model was used to examine the association between food items and the risk of cognitive dysfunction. Supplementary figure 2 demonstrates that this association was estimated as a potentially nonlinear exposure-response relationship as the values of all 18 food items changed from the median to a specific quartile. Indeed, among all participants, a small number of food items (root vegetables, stem vegetables, and white meat) had a nonlinear relationship with cognitive function. In the man population, only the consumption of fresh fruit had a nonlinear relationship with cognitive function, while the other food items showed a linear relationship with cognitive impairment. In women (Supplementary figure 2C), no linear trends were found in predicting the risk of cognitive dysfunction.

We estimated the change in predicted risk of disease for single food item changes in the man population while fixing all other factors (17 other food items) at the 25^{th}, 50^{th} (median), or P75th percentile, and there might be a significant correlation between dietary intake of fresh fruit when associated with cognitive impairment at P25, P50, and P75, along with a possible protective effect (P25, estimate=-0.239; P50, estimate=-0.210; P75, estimate=-0.178) (Figure 2).

We did not observe any interaction between cognitive function and the 18 food items after comparing the single exposure health risk when all other exposures were fixed at P75, and all other exposures were fixed at P25 (Figure 3). In addition, no overall effect of the mixture of food

Table 1. Characteristics of the 2881 study participants

Characteristics	All (n=2881)	CI (n=872)	Normal (n=2009)	$p^{\dagger}$
Sex				
Man	1086 (37.7)[§]	232 (26.6)	854 (42.5)	<0.001
Woman	1795 (62.3)	640 (73.4)	1155 (57.5)	
Age				
30-59	1383 (48.0)	237 (28.2)	1146 (72.8)	<0.001
60-99	1498 (52.0)	635 (72.8)	863 (43.0)	
Ethnicity				
Han	568 (19.7)	212 (24.3)	356 (17.7)	<0.001
Yao	2158 (74.9)	611 (70.1)	1547 (77.0)	
Other	155 (5.4)	49 (5.6)	106 (5.3)	
Education				
No formal education	428 (14.9)	428 (49.1)	0 (0)	<0.001
Primary School Education	1465 (50.9)	257 (29.5)	1208 (60.1)	
Junior high school and above	988 (34.3)	187 (21.4)	801 (39.9)	
Occupation				
Famer	2670 (92.7)	836 (95.9)	1834 (91.3)	<0.001
Other	211 (7.3)	36 (4.1)	175 (8.7)	
Physical activity				
Light	1181 (41)	438 (50.2)	743 (37.0)	<0.001
Moderate	1636 (56.8)	425 (48.7)	1211 (60.3)	
Vigorous	64 (2.2)	9 (1.0)	55 (2.7)	
Smoking				
No	2347 (81.5)	740 (84.9)	1607 (80.0)	0.002
Yes	534 (18.5)	132 (15.1)	402 (20.0)	
Drinking				
No	1941 (67.4)	598 (68.6)	1343 (66.8)	0.363
Yes	940 (32.6)	274 (31.4)	666 (33.2)	
BMI[‡]				
≤23	1659 (57.6)	533 (61.1)	1126 (56.0)	0.009
23-27.5	995 (34.5)	287 (32.9)	708 (35.2)	
≥27.5	227 (7.9)	52 (6.0)	175 (8.7)	
Hyperlipidemia				
No	1439 (49.9)	403 (46.2)	1036 (51.6)	0.008
Yes	1442 (50.1)	469 (53.8)	973 (48.4)	
Hyperglycemia				
No	2746 (95.3)	813 (93.2)	1933 (96.2)	0.001
Yes	135 (4.7)	59 (6.8)	76 (3.8)	

[†] p values from a $\chi 2$ test for categorical variables. All tests were 2-sided.
[‡] Body mass index: weight (kg)/height (m)^2
[§] Values are expressed as median (interquartile range).

Table 2. Multiple logistic regression, all participants

Food items	Single-component model [a, b]			Multi-component model [a, c]		
	OR	95% CI	p	OR	95% CI	p
Oil tea	0.9999	0.9996-1.0002	0.6652	1.0000	0.9997-1.0003	0.8038
Rice, noodles and corn	1.0001	0.9999-1.0004	0.2581	1.0002	1.0000-1.0005	0.1037
Root vegetables	1.0001	0.9990-1.0011	0.9239	1.0003	0.9992-1.0013	0.6449
Green vegetables	0.9995	0.9985-1.0004	0.2600	0.9997	0.9987-1.0006	0.5022
Stem vegetables	0.9988	0.9967-1.0009	0.2532	0.9990	0.9967-1.0013	0.4047
Gourd vegetable	1.0001	0.9993-1.0008	0.8525	1.0005	0.9997-1.0013	0.2321
Fresh fruits	0.9993	0.9988-0.9998	0.0037	0.9994	0.9988-0.9999	0.0214
Pulses, beans and peas	1.0001	0.9988-1.0013	0.9246	1.0011	0.9997-1.0026	0.1211
Nuts	1.0013	0.9995-1.0031	0.1562	1.0019	0.9993-1.0045	0.1475
Read meat and offal	1.0000	0.9985-1.0015	0.9682	1.0004	0.9988-1.0019	0.6540
White meat	0.9955	0.9892-1.0018	0.1614	0.9973	0.9909-1.0038	0.4126
Preserved meat	0.9973	0.9905-1.0042	0.4498	1.0005	0.9931-1.0079	0.9049
Fish, seafood and aquatic products	0.9940	0.9886-0.9994	0.0291	0.9957	0.9901-1.0013	0.1355
Eggs	0.9963	0.9932-0.9994	0.0178	0.9974	0.9942-1.0007	0.1256
Milk and yogurts	0.9997	0.9983-1.0011	0.6956	1.0000	0.9986-1.0014	0.9883
Mushrooms	0.9887	0.9773-1.0003	0.0572	0.9935	0.9826-1.0046	0.2484
Alcoholic drinks	0.9997	0.9988-1.0007	0.5820	0.9998	0.9989-1.0008	0.7444
Oil and other dressings	0.9999	0.9982-1.0016	0.8959	1.0002	0.9985-1.0019	0.8423

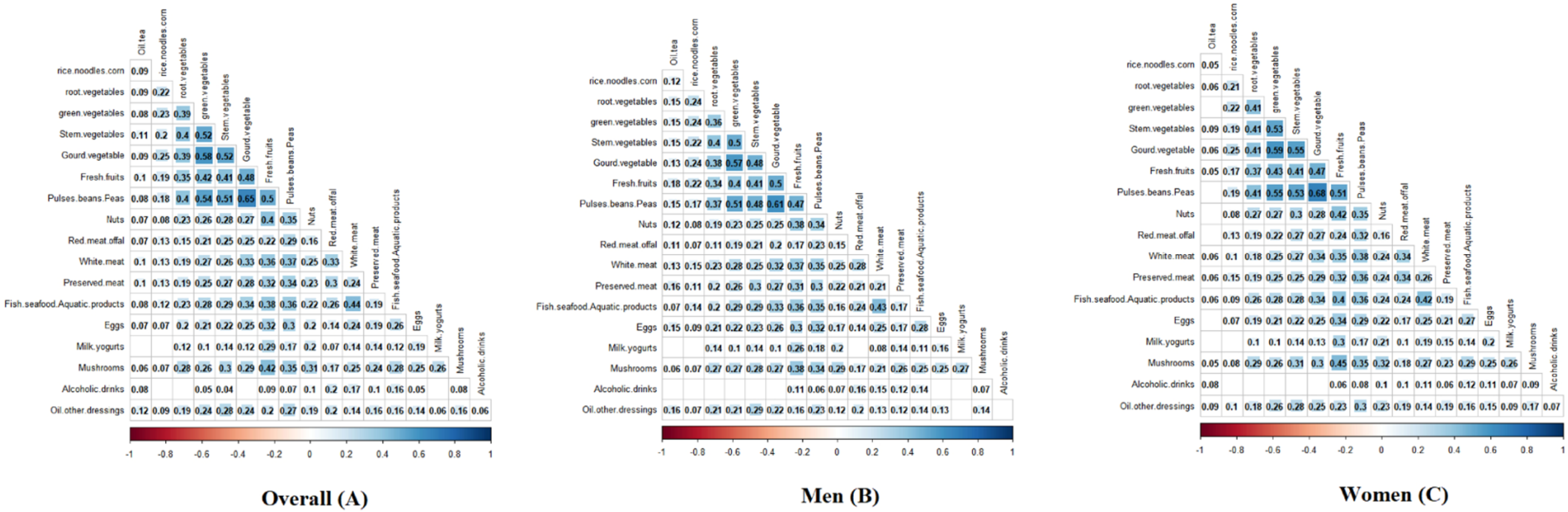

Figure 1. Correlation matrix between food groupings for food items. (A) Overall. (B) Men. (C) Women.

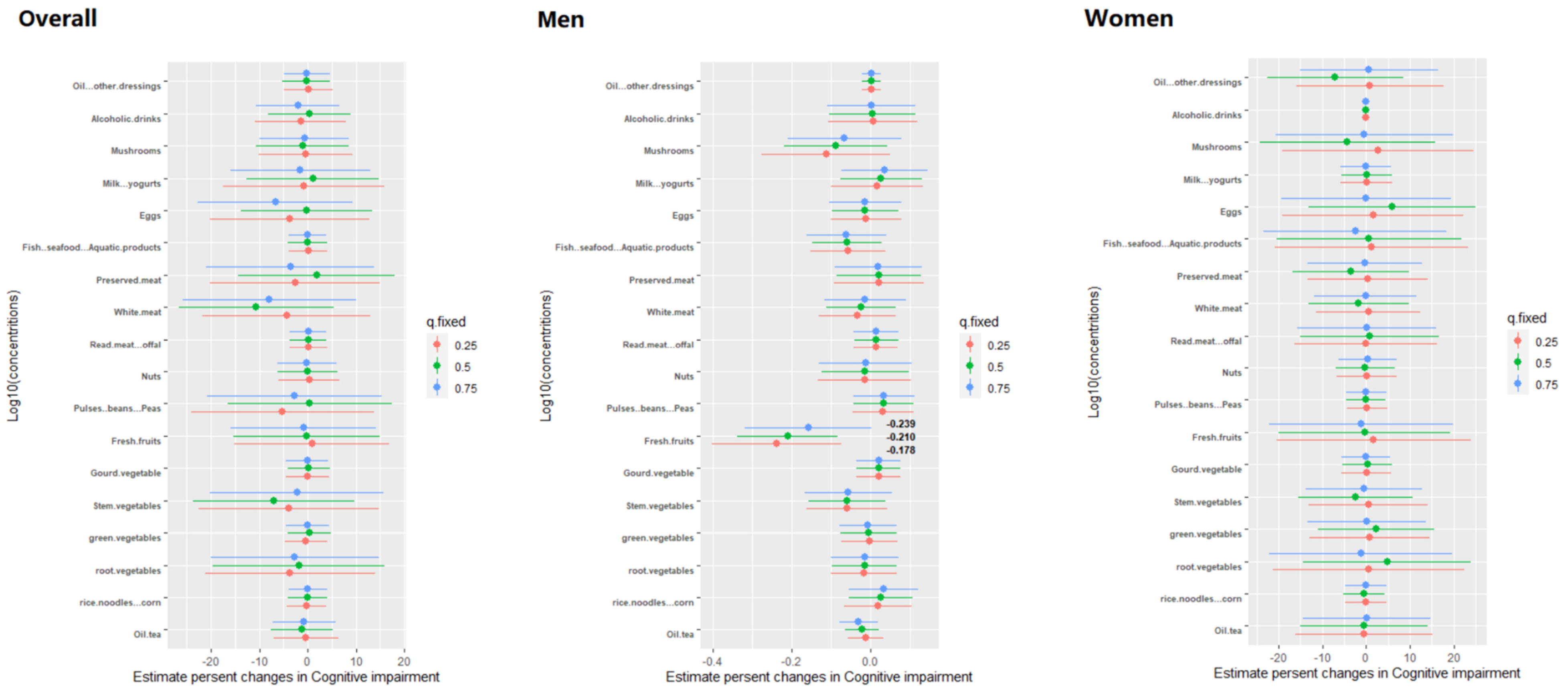

Figure 2. Effect of a single exposure of individual food items on cognitive (estimates and 95% confidence intervals) by Bayesian core machine regression model. (A) Overall. (B) Men. (C) Women. Models adjusted for sex (man/woman), and/or age (30-59 years/≥60 years), ethnicity (Han/Yao/other), literacy (≤6 years/>6 years) and/or smoking (yes/no), alcohol consumption (yes/no), body mass index (<23/23-27.49/≥27.5 kg/m^2), and agricultural physical activity (yes/no).

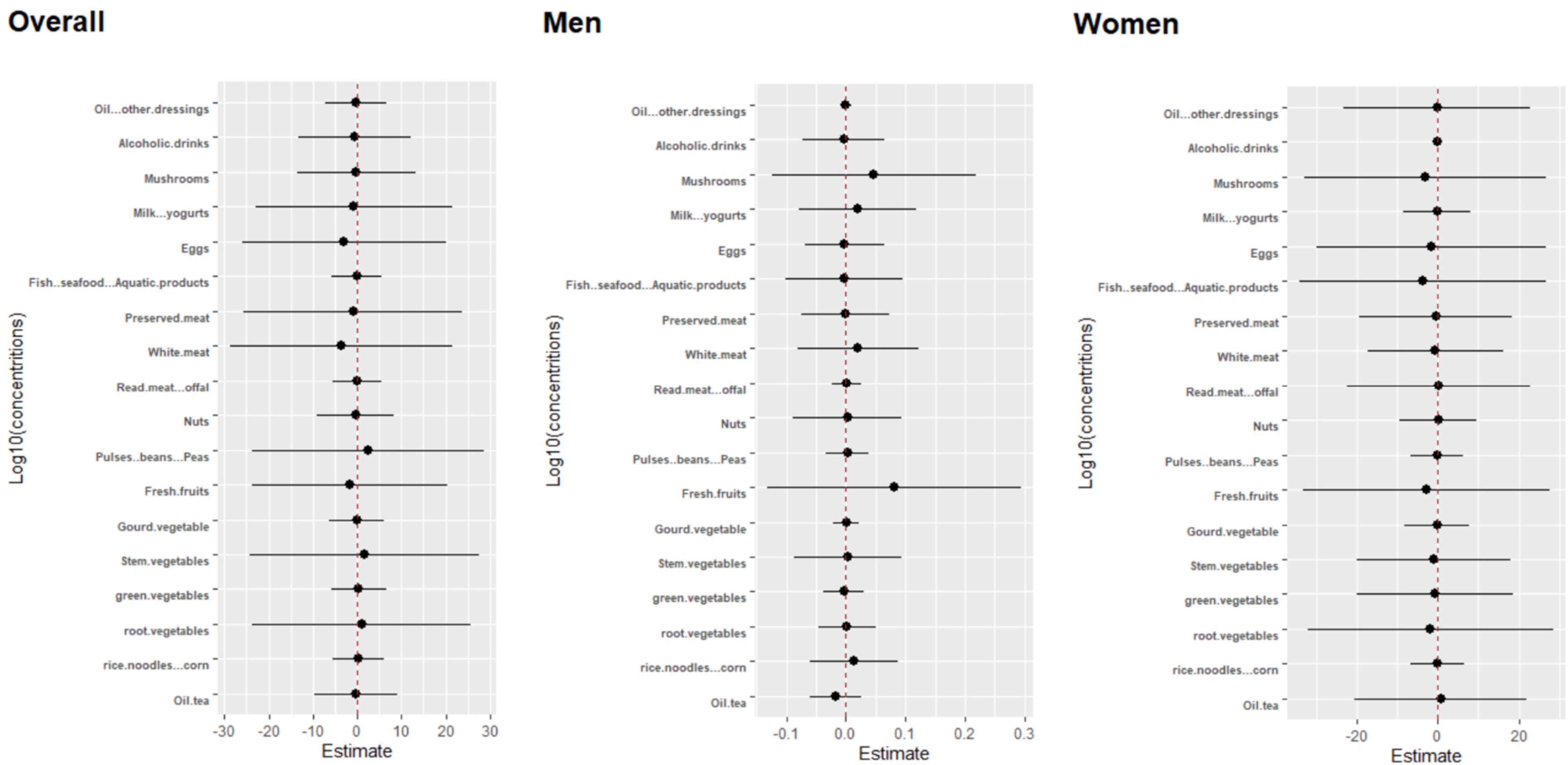

Figure 3. Single exposure health risk when all other exposures are fixed at the 75th percentile compared to single exposure health risk when all other exposures are fixed at the 25th percentile. (A) Overall. (B) Men. (C) Women. Models adjusted for sex (man/woman), and/or age (30-59 years/≥60 years), ethnicity (Han/Yao/other), literacy (≤6 years/>6 years) and/or smoking (yes/no), alcohol consumption (yes/no), body mass index (<23/23-27.49/≥27.5 kg/m2), and agricultural physical activity (yes/no).

items was observed on cognitive function based on the concentration of all foods fixed at P50. Nevertheless, when the concentration of foods was less than P40 in men, it was possible to observe an overall positive effect of the mixture of food items on cognitive function (P25, estimate=7.667; P30, estimate=0.168; P35, estimate=0.126; P40, estimate=0.079). In all participants, when the concentration of all factors was fixed at P35, it was observed that the overall food item mixture was likely to have a positive effect on cognitive function (P35, estimate=15.844) (Figure 4).

DISCUSSION

For the first time, this study used the BKMR learning model to explore the possible correlations between food items and the risk of cognitive impairment. The results suggest that men displayed a negative correlation between fresh fruit consumption and the risk for cognitive function disorders, but no correlations were observed in women.

The BKMR R package provides a generic, open-source implementation of BKMR, an R-based language with flexible and parsimonious and estimated multivariable exposure-response functions and variable selection for potentially high-dimensional vectors of exposures and allows for group variable selection parties that can accommodate highly correlated exposures. In the setting of large numbers of exposures and binary outcomes, the Probit BKMR implementation can correctly identify variables included in the exposure-response function and produce interpretable quantities on a scale of potentially continuous outcomes or on a scale of outcome probabilities. The dichotomous outcome implementation exploits the potentially normal specification of probabilistic regression and is computationally advantageous for Bayesian kernel regression inference. This newly developed software, integrated suite of tools, and extended methodology allow BKMR to be used in many epidemiological applications where multiple risk factors have complex health effects.[12] The machine learning approach to exploring the nonlinear relationship between combined multi-factor

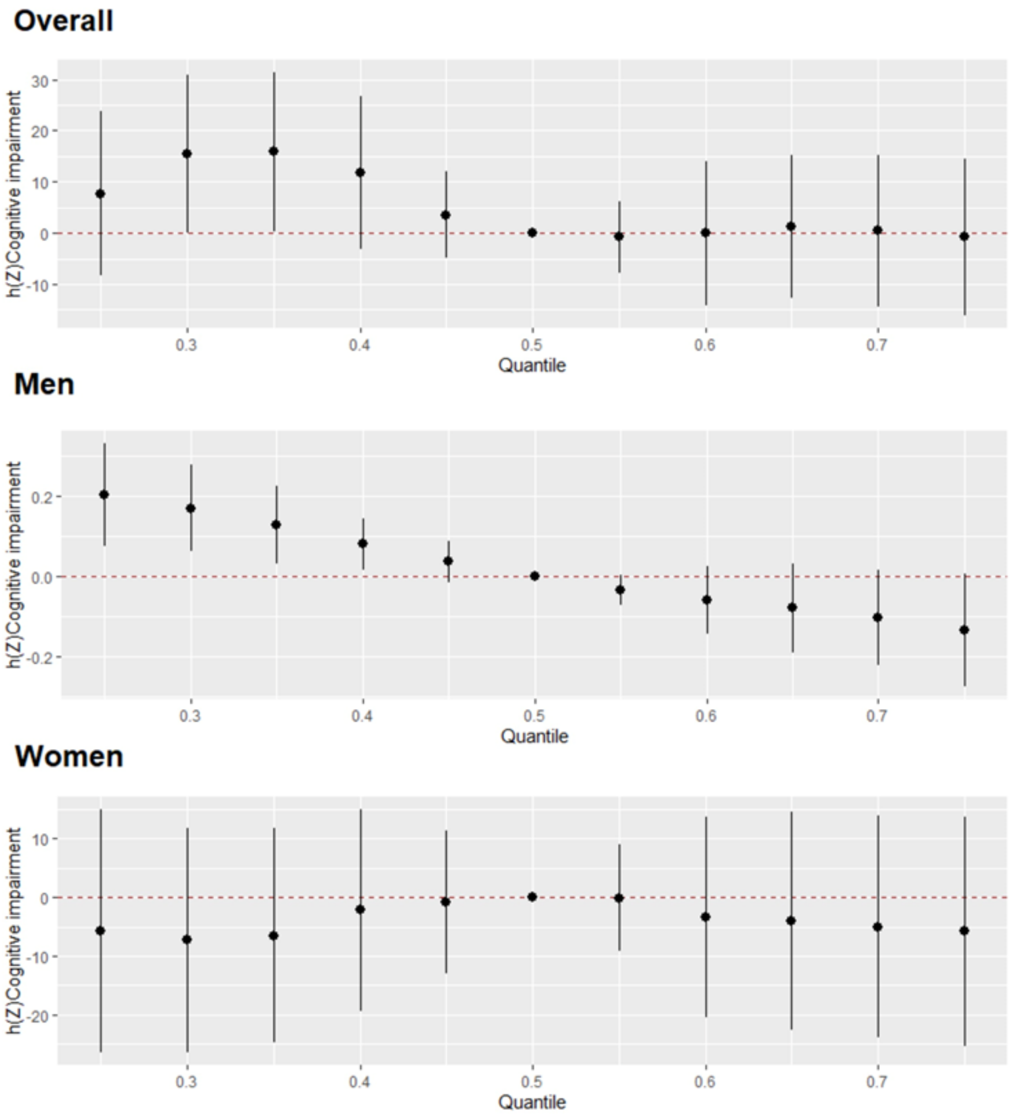

Figure 4. Overall associations and 95% confidence intervals with food item mixtures, including oil tea. (A) All participants; (B) men; (C) women. H (Z) can be interpreted as the relationship between food and potential continuous outcomes, and estimates are labeled at the bottom of the figure. Data were estimated by Bayesian kernel machine regression while adjusting for and/or sex (man/woman), and/or age (30-59 years/≥60 years), ethnicity (Han/Yao/other), literacy (≤6 years/>6 years) and/or smoking (yes/no), alcohol consumption (yes/no), body mass index (<23/23-27.49/≥27.5 kg/m^2), and agricultural physical activity (yes/no).

exposures and disease allows researchers to assess the impact of mixtures on disease and individual factors and interaction relationships. From environmental epidemiology to nutritional epidemiology, mostly used to explore correlations between combined exposures to metal elements and predicted disease risk, multidimensional exposure-response effects can be modeled.[39-41]

This study applied the BKMR model to the data of 2881 participants (1086 men and 1795 women to assess the possible correlations between the cumulative intake of 18 food items and the predicted risk of cognitive dysfunction in a population from an ethnic minority area in Gongcheng County, Guangxi, China. The analysis results varied by sex because of significant differences in dietary intake, as previously observed.[15]

A higher dietary quality might reduce the risk of chronic diseases.[42] The present study found that low fresh fruit consumption in men was the main dietary risk factor for cognitive impairment, showing a nonlinear relationship with outcome variables. Some studies hypothesize that there is a synergistic effect of fruit and whole-grain diets to mitigate cognitive impairment.[43] In a traditional study examining fruit and cognitive decline, a possible correlation between long-term adherence to a diet with high consumption of fruits and vegetables and better cognitive performance in an elderly population was found,[44] as in the present study. Fruit consumption is much higher in men without cognitive impairment than in men with cognitive decline, and higher fruit consumption reduces the risk of cognitive impairment.[45] Higher fruit and vegetable juice intakes are also associated with a reduced risk of Alzheimer's disease in Japanese Americans followed for more than 7 years.[46]

On the other hand, we found no significant correlations with the predicted risk of cognitive dysfunction among the 18 food items in the women included in the present study. Such results are not unexpected, as a study of dietary patterns and cognitive function correlated with a nine-year follow-up showed that dietary patterns characterized by dietary scores such as the AMED, HEI-2010, AHEI-2010, or DASH were not significantly associated with cognitive decline in older women.[47] In addition, participants' adherence to a healthy dietary pattern of eating habits did not change the risk of cognitive decline in hypertensive women.[47] Another study did not find any association between diet and the incidence of MCI or dementia in women.[48] One specific study noted no correlation between long-term gluten intake and cognitive function scores.[49] The lack of association could be because of the errors in the measurement and assessment of cognitive function by investigators in large epidemiological surveys and the wide variety of ways of assessing cognitive function and diet. The present study used the MMSE questionnaire, which adds to the difficulty of finding more reliable evidence for exploring factors influencing cognitive function and food items, but it must be acknowledged that the ways of assessing cognitive function are limited.[50-52] The present study did not detect a correlation between any of the 18 food items and cognitive decline in women, possibly because of the lack of follow-up (cross-sectional study) and also because education influences cognitive decline and nutrition patterns,[53] possibly masking the relationship between both cognitive ability and food items. There were no significant correlations between the pre-defined 18 food items and cognitive decline in women (Supplementary figure 3). It is possible that the inconsistent content of dietary questionnaires and inconsistent definitions of food groups in different epidemiological surveys led to biased results during data analysis, and some studies have pointed out that high consumption of red meat might be a protective factor for cognitive function in women,[15] but it was not observed here.

Beyond differences in food items between men and women, interactions of the sex hormonal physiology and dietary responsiveness might be important. Female hormones possess protective effects that can delay the development of cognitive impairment.[54,55] These protective effects of sex hormones could mask or attenuate the impact of food items on cognitive functions. The lack of correlation in the whole study population is probably due to such an attenuation, but further studies are necessary. Of note, data about menopause were not available. In addition, phytoestrogens from the diet have different effects among non-menopausal women, menopausal women, and men,[56,57] but data about phytoestrogens were unavailable in the present study. Especially, future studies should examine non-menopausal vs. menopausal women and women with a wide range of menopause duration.

The BKMR model incorporates a complex model of diet that yields less biased estimates and ranks the results for the contribution of food items, an important feature given that there are many exposure variables to deal with, and it avoids traditional linear models that yield statistically significant results that might be due to chance.[15] We extended the application of BKMR to assess the health effects of complex dietary patterns, with model results that are more robust than those of standard linear regression. This study is the first application of BKMR to investigate the relationship between total diet and cognitive function health outcomes.

Nevertheless, this study has limitations. Because of the cross-sectional nature of the study, causality could not be determined. The present study was designed after the mother study was completed, limiting the available data to those planned in the original study. Among others, the menopausal status of the women was not available. Only food items were considered, and the possible contribution of specific nutrients or other food components was not assessed. Of note, phytoestrogens are known to have several metabolic effects in men and women,[56,57] but the mother study did not collect specific data on soy/tofu or phytoestrogens.

Conclusion

In conclusion, using a BKMR model, fresh fruit consumption was found to be negatively correlated with the risk of cognitive impairment in men but not observable in women.

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AUTHOR DISCLOSURES

The authors declare no conflict of interest.

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Supplementary table 1. Intake of food groups with different group characteristics

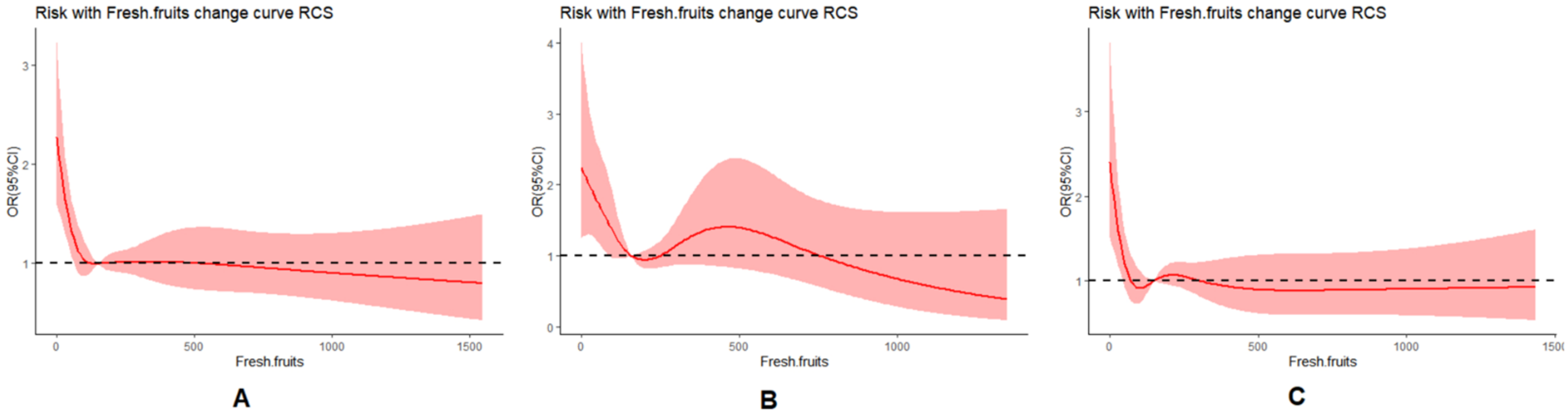
Dietary Group	Male			Female		
	CI (n=232)	Normal (n=854)	*p*	CI (n=640)	Normal (n=1155)	*p*
Oil tea	481.00 (301.00-721.00)	501 (321.00-721.00)	0.077	361.00 (241.00-641.00)	361.00 (241.00-641.00)	0.690
Rice, noodles and corn	547.97 (368.16-811.14)	580.48 (401.00-836.75)	0.289	510.53 (339.96-720.88)	507.07 (352.29-720.79)	0.754
Root vegetables	19.23 (5.78-52.46)	25.05 (7.58-67.80)	0.027	19.92 (4.95-61.39)	30.88 (12.57-73.46)	<0.001
Green vegetables	71.52 (31.14-132.70)	78.26 (39.81-140.81)	0.116	60.44 (28.29-111.36)	73.26 (37.16-133.15)	<0.001
Stem vegetables	20.69 (10.49-43.86)	27.59 (12.41-52.84)	0.004	20.89 (9.77-44.91)	27.92 (12.92-54.18)	<0.001
Gourd vegetable	54.59 (29.50-128.74)	62.64 (27.30-119.36)	0.679	47.03 (20.73-102.79)	62.51 (30.59-116.07)	<0.001
Fresh fruits	119.69 (50.51-275.82)	170.78 (80.33-350.22)	<0.001	106.53 (42.92-236.10)	179.35 (79.90-361.79)	<0.001
Pulses, beans and peas	42.09 (20.73-87.71)	49.58 (21.49-94.78)	0.312	33.88 (15.70-82.14)	49.07 (23.42-93.05)	<0.001
Nuts	5.00 (1.39-13.23)	6.88 (1.99-19.13)	0.034	3.40 (1.00-10.86)	6.66 (2.37-16.02)	<0.001
Read meat and offal	51.00 (20.79-101.00)	51.00 (21.70-101.00)	0.729	26.00 (11.00-51.00)	27.96 (11.85-57.58)	0.003
White meat	7.58 (2.64-14.15)	10.86 (4.29-17.44)	0.002	4.75 (1.82-10.86)	7.58 (2.64-14.15)	<0.001
Preserved meat	4.29 (1.00-8.61)	4.87 (1.49-13.33)	0.173	3.02 (1.00-7.58)	4.70 (1.53-12.51)	<0.001
Fish, seafood and aquatic products	7.58 (4.01-18.91)	10.86 (4.29-20.73)	0.007	5.93 (1.80-10.86)	7.58 (3.43-20.73)	<0.001
Eggs	14.02 (5.34-41.09)	22.70 (8.50-51.00)	0.002	18.29 (5.34-48.74)	30.46 (11.65-57.00)	<0.001
Milk and yogurts	1.00 (1.00-17.44)	1.00 (1.00-27.30)	0.065	1.00 (1.00-17.44)	4.29 (1.00-33.88)	<0.001
Mushrooms	2.32 (1.00-4.80)	2.97 (1.00-5.93)	0.010	1.72 (1.00-4.29)	2.97 (1.00-5.93)	<0.001
Alcoholic drinks	20.73 (1.00-171.05)	4.62 (1.00-142.24)	0.080	1.00 (1.00-1.00)	1.00 (1.00-1.00)	0.542
Oil and other dressings	63.11 (40.92-91.55)	64.76 (44.08-97.40)	0.267	54.11 (37.80-82.00)	64.71 (43.00-93.00)	<0.001

Supplementary table 2. Multiple logistic regression, males

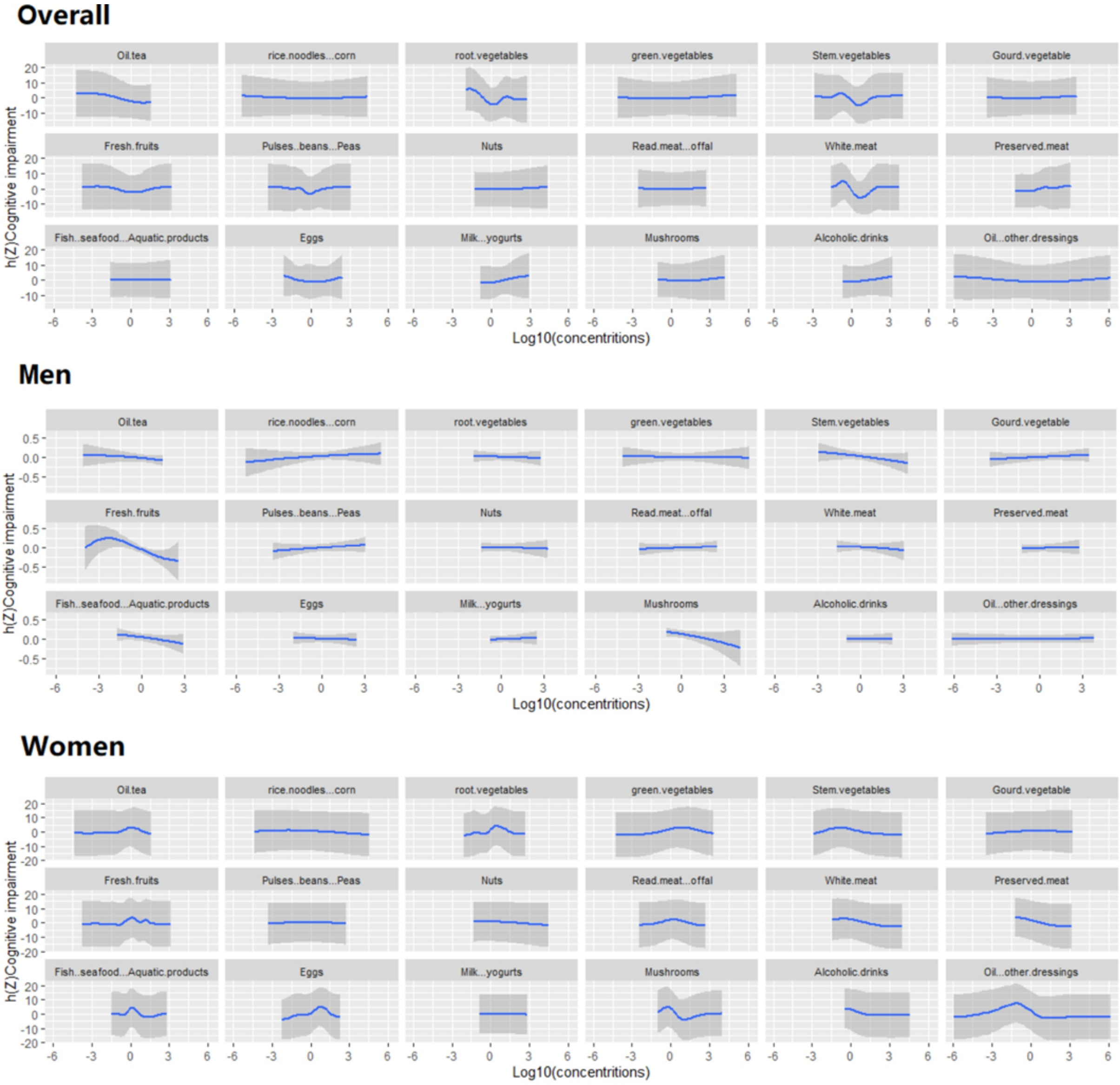
Dietary Factor	Single-Component Model [a,b]			Multi-Component Model [a,c]		
	OR	95% CI	*p*	OR	95% CI	*p*
Oil tea	0.9996	0.9991-1.0001	0.1453	0.9997	0.9991-1.0002	0.1932
Rice, noodles and corn	1.0001	0.9997-1.0005	0.6092	1.0003	0.9999-1.0007	0.0977
Root vegetables	0.9987	0.9967-1.0007	0.1898	0.9990	0.9971-1.0010	0.3276
Green vegetables	0.9991	0.9976-1.0006	0.2427	0.9997	0.9984-1.0011	0.7041
Stem vegetables	0.9944	0.9896-0.9993	0.0248*	0.9930	0.9874-0.9985	0.0136*
Gourd vegetable	1.0003	0.9994-1.0012	0.4884	1.0013	1.0001-1.0025	0.0375*
Fresh fruits	0.9989	0.9980-0.9997	0.0079*	0.9990	0.9980-0.9999	0.0334*
Pulses, beans and peas	1.0000	0.9979-1.0021	0.9974	1.0017	0.9995-1.0039	0.1247
Nuts	0.9975	0.9901-1.0048	0.4984	1.0000	0.9935-1.0066	0.9946
Read meat and offal	1.0010	0.9992-1.0029	0.2710	1.0013	0.9993-1.0033	0.1975
White meat	0.9991	0.9921-1.0061	0.7937	0.9992	0.9921-1.0063	0.8202
Preserved meat	0.9969	0.9869-1.0070	0.5424	1.0017	0.9908-1.0128	0.7575
Fish, seafood and aquatic products	0.9953	0.9879-1.0027	0.2160	0.9964	0.9887-1.0041	0.3541
Eggs	0.9974	0.9922-1.0026	0.3299	0.9999	0.9944-1.0054	0.9669
Milk and yogurts	1.0002	0.9975-1.0029	0.8934	1.0006	0.9978-1.0035	0.6642
Mushrooms	0.9747	0.9481-1.0022	0.0708	0.9843	0.9601-1.0091	0.2127
Alcoholic drinks	0.9998	0.9988-1.0008	0.6511	0.9996	0.9985-1.0007	0.5033
Oil and other dressings	1.0009	0.9982-1.0036	0.5114	1.0016	0.9988-1.0044	0.2614

Supplementary table 3. Multiple logistic regression, females

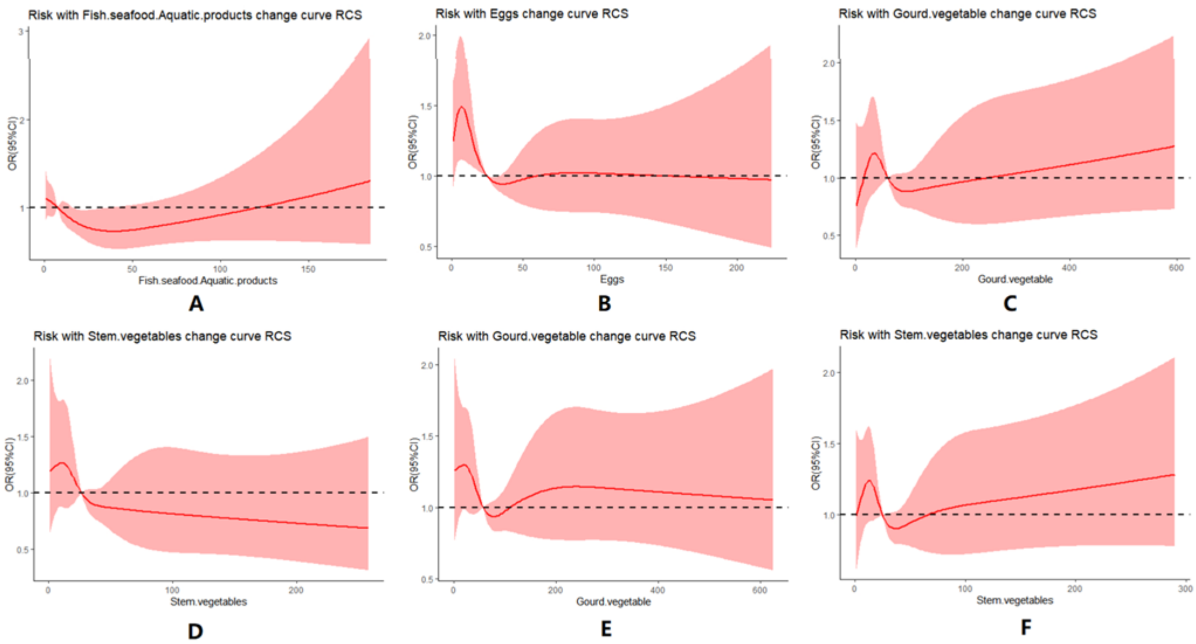
Dietary Factor	Single-component model [a,b]			Multi-component model [a,c]		
	OR	95% CI	*p*	OR	95% CI	*p*
Oil tea	1.0000	1.0000-1.0000	0.6300	1.000	1.000-1.001	0.466
Rice, noodles and corn	1.0000	1.0000-1.0010	0.2530	1.000	1.000-1.001	0.188
Root vegetables	1.0010	1.0000-1.0020	0.1500	1.001	1.000-1.003	0.094
Green vegetables	1.0000	0.9990-1.0010	0.6510	1.000	0.998-1.001	0.791
Stem vegetables	1.0000	0.9980-1.0020	0.9990	1.000	0.998-1.002	0.727
Gourd vegetable	1.0000	0.9980-1.0010	0.5670	1.000	0.998-1.001	0.597
Fresh fruits	1.0000	0.9990-1.0000	0.0940	1.000	0.999-1.000	0.195
Pulses, beans and peas	1.0000	0.9990-1.0020	0.8920	1.001	0.999-1.003	0.169
Nuts	1.0020	0.9990-1.0050	0.1500	1.003	0.999-1.007	0.165
Read meat and offal	0.9980	0.9960-1.0010	0.1690	0.999	0.996-1.001	0.365
White meat	0.9880	0.9770-0.9990	0.0390	0.992	0.980-1.005	0.216
Preserved meat	0.9970	0.9870-1.0070	0.5360	1.002	0.991-1.012	0.752
Fish, seafood and aquatic products	0.9920	0.9850-1.0000	0.0490	0.995	0.987-1.004	0.265
Eggs	0.9960	0.9920-1.0000	0.0290	0.997	0.993-1.001	0.140
Milk and yogurts	0.9990	0.9980-1.0010	0.4970	1.000	0.998-1.001	0.643
Mushrooms	0.9930	0.9810-1.0060	0.2890	0.996	0.984-1.009	0.594
Alcoholic drinks	0.9980	0.9930-1.0020	0.3140	0.998	0.994-1.002	0.363
Oil and other dressings	0.9990	0.9970-1.0020	0.6110	1.000	0.997-1.002	0.677



Supplementary figure 1. Dose-response relationship between fresh fruits and cognitive function. (A) Overall. (B) Men. (C) Women. The solid and dashed shaded lines in the figure represent the dose-response curves and 95% confidence intervals, respectively. The relationship has been adjusted for sex (man/woman), and/or age (30-59 years/260 years), ethnicity (Han/Yao/other), education (S6 years/>6 years), and/or smoking (yes/no), alcohol consumption (yes/no), BMI (<23/23-27.49/27.5 kg/m^2), and agricultural physical activity (yes/no).



Supplementary figure 2. Univariable exposure-response functions and 95% confidence intervals (shaded areas) for food items, with other elements held at the median. (A) Overall. (B) Men. (C) Women. H (Z) can be interpreted as the relationship between food items and potential outcomes. Data were subjected to Bayesian adjustment for sex (man/woman), and/or age (30-59 years/≥60 years), ethnicity (Han/Yao/other), literacy (≤6 years/>6 years), and/or smoking (yes/no), alcohol consumption (yes/no), body mass index (<23/23-27.49/≥27.5 kg/m^2), and agricultural physical activity (yes/no).



Supplementary figure 3. Dose-response relationship between food items and cognitive function. (A-B) Overall. (C-D) Men. (E-F) Women. The solid and dashed shaded lines in the figure represent the dose-response curves and 95% confidence intervals, respectively.