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# Dietary patterns and cognitive decline among Chinese older adults

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# Abstract

**Background**—Prospective evidence of associations of dietary patterns with cognitive decline is limited and inconsistent. We examined how cognitive changes among Chinese older adults relate to either an adapted Mediterranean diet score or factor analysis-derived dietary patterns.

**Methods**—This prospective cohort study comprised 1650 adults 55 years who completed a cognitive screening test at two or more waves of the China Health and Nutrition Survey in 1997, 2000 or 2004. Outcomes were repeated measures of global cognitive scores, composite cognitive z-scores (standardized units [SU]), and standardized verbal memory scores (SU). Baseline diet was measured by 24-hour recalls over three days. We used linear mixed-effects models to evaluate how changes in cognitive scores were associated with adapted Mediterranean diet score and two dietary pattern scores derived from factor analysis.

**Results**—Among adults 65 years, compared with participants in the lowest tertile of adapted Mediterranean diet, those in the highest tertile had a slower rate of cognitive decline (difference in mean standardized unit [SU] change/year  $\beta$ =0.042; 95% CI: 0.002, 0.081). A wheat-based diverse diet derived by factor analysis shared features of the adapted Mediterranean diet, with the top tertile associated with slower annual decline in global cognitive function ( $\beta$ =0.069 SU/year; 95% CI: 0.023, 0.114). We observed no associations among adults <65 years.

**Conclusions**—Our findings suggest a potential role of an adapted Mediterranean diet or a wheat-based diverse diet with similar components as a modifiable dietary factor to reduce the rate of cognitive decline in later life in the Chinese population.

Conflicts of Interest: No authors declare a conflict of interest.

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# INTRODUCTION

Population aging and the burden of dementia is a global issue. However, no effective treatments currently are available to change the progression of dementia, highlighting the significance of prevention. Modifiable lifestyle changes including dietary interventions could translate into a great reduction in the burden of dementia,<sup>1</sup> where the pre-symptomatic phase and the early stage of cognitive decline are thought to be critical periods to intervene to prevent progression to dementia. Previous studies evaluating the relationship between single foods or nutrients with cognitive decline and dementia offered inconsistent evidence.<sup>2</sup> Since foods are consumed together in complex combinations, evaluating dietary exposures as dietary patterns may allow us to better capture the role of diet in cognitive health, as this approach can accommodate the multidimensionality of the diet.

Several mechanisms linking the Mediterranean diet to cognitive health have been proposed, including lowering oxidative stress, reducing inflammation, preventing against vascular comorbidity, and protection against cerebrovascular diseases.<sup>3</sup> Although a 2013 systematic review of seven unique cohorts suggested that greater adherence of Mediterranean diet may be associated with slower cognitive decline, research on this topic is limited, and results have been inconsistent.<sup>4</sup> The review reported beneficial associations especially among studies with large sample size, long follow-up and older baseline ages. However, several recent prospective studies, published subsequent to this review, found no associations between adherence to Mediterranean diet and cognitive change among adults at least 65 years old. 5-7 It has been hypothesized that these inconsistencies may be explained by residual confounding, as beneficial effects may be attributable to other healthy lifestyle factors correlated with Mediterranean diet adherence in Western populations.<sup>7</sup> Others have suggested that the varied results may instead be due to population differences in levels of intake of key Mediterranean diet components, which may indicate that benefits of this dietary pattern may not translate across food cultures.<sup>5</sup> Alternatively, it has also been suggested that some recent null findings could be explained by limited variability in cognitive decline due to high levels of education in some cohorts.<sup>6</sup> The current study seeks to address these issues, by exploring the relationship between this dietary pattern and cognitive decline in a population diverse in terms of age at baseline, education, and levels of food intakes.

The traditional Mediterranean diet is characterized by high intake of vegetables, fruit, legumes, nuts, cereals, fish; olive oil as the primary source of monounsaturated fatty acid; and a low intake of meat and meat products. Despite the use of different sources of oils and much lower intake of dairy products,<sup>8,9</sup> the traditional Chinese diet and other Asian diets have been suggested to share the majority of common elements of the Mediterranean diet, in that both are characterized by a high intake of plant based foods and a low intake of meats and fat.<sup>8,10</sup> However, it remains unknown whether the benefits of adhering to a Mediterranean-style diet will be observed in a non-Western population where the specific types and amounts of food, as well as the lifestyle correlates of this dietary pattern, may be substantially different from those in the Western populations previously studied. Evidence from diverse populations could also strengthen evidence supporting a possible etiological

role of the Mediterranean dietary pattern in delaying cognitive decline by reducing concern that associations may reflect residual confounding by correlated health behaviors.

Meanwhile, associations with dietary patterns derived in the study population may be helpful in identifying the extent to which foods included in *a priori* diet scores such as the Mediterranean diet are eaten in combination, as well as in highlighting important dietary factors not reflected in such dietary scores. Therefore, the current study examined prospectively the relation between both adherence to an adapted Mediterranean diet —based on higher intakes of vegetables, legumes and nuts, fruits, grains, fish, dairy products, and lower intake of red meats and animal-source cooking fats, and low to moderate consumption of alcohol— and dietary patterns derived using factor analysis and cognitive decline among a sample of older, community-dwelling Chinese men and women. We hypothesized that the adapted Mediterranean diet would be beneficially related to cognitive changes over time, and that a Chinese dietary pattern which shared features of the adapted Mediterranean diet would also predict slower progression of cognitive decline. To our knowledge, while a few studies have explored select food groups and nutrients, the current study is among the first to prospectively examine the association between dietary patterns and cognitive decline in non-Western populations.

# METHODS

### Subjects

The China Health and Nutrition Survey (CHNS) is a prospective ongoing open cohort study established in 1989. A multistage, random cluster process was utilized to draw samples from nine provinces of China that are substantially different geographically and in economic development. The CHNS was designed to be representative of each of the 9 provinces covered, and to provide data from randomly selected households in areas with diverse economic and demographic characteristics, but was not designed to be nationally representative.<sup>11</sup>

In 1997, 2000 and 2004, cognitive assessments were conducted among CHNS participants who were community dwellers aged 55 y or older. Data collection also included demographic, socioeconomic, lifestyle, physical activity, diet, and health information. Among the 2408 adults with at least one wave of measurement (participation rate for a baseline cognitive test among eligible CHNS participants 73%), 1677 (70%) had at least two measurement occasions of cognitive function. Among these, 1650 had no missing dietary information and were included in this study. A wide array of characteristics was evaluated and presented among participants completing one vs. two or more waves of cognitive tests to evaluate sample selectivity.

All participants in CHNS provided written informed consent. The institutional review committees of the University of North Carolina at Chapel Hill and the National Institute of Nutrition and Food Safety, Chinese Center for Disease Control and Prevention approved this study.

#### Assessments

**Cognitive function**—The CHNS adopted the cognitive screening items from part of the Telephone Interview for Cognitive Status–modified,<sup>12</sup> which have been used in population based studies including the U.S. and Chinese populations.<sup>13,14</sup> The same cognitive screening test was used in the 3 waves of the CHNS among adults aged at least 55 y. The test assessed immediate and delayed recall of a 10-word list, counting backward from 20, serial 7 subtraction, and orientation. Scores for immediate and delayed recall ranged from 0 to 10. Counting backward and serial 7's were used to assess attention and calculation, with scores ranging from 0 to 7. Orientation was assessed by asking the participant the current date (1 point each for year, month and date), and to name the tool usually used to cut paper (1 point). Higher scores on all items suggest better cognitive performance.

The outcomes of interest were repeated measures of: 1) the global cognitive score, the sum of the scores of all cognitive testing items which ranges from 0 to 31 points; 2) the composite z-score (in standardized unit [SU]); and 3) verbal memory score (in SU) which combined immediate and delayed 10-word recall. The vast majority of studies using brief cognitive screening measures such as the Telephone Interview for Cognitive Status-modified and the Mini-Mental State Examination use the total raw score (i.e. our global cognitive score) as their outcome measure.<sup>12,13,15</sup> Consistent with this, we used the total score (i.e. global cognitive score) on our abbreviated version of the Telephone Interview for Cognitive Status-modified as one of the outcome measures. We constructed the composite score as an alternative global cognitive measure by averaging z-scores of verbal memory items and the other items assessing attention, calculation and orientation. We constructed this score for two reasons; first, to reduce the influence of the memory component, which has additional points and is more influential in the global score than other domains, and second, to allow direct comparison with other studies. Other studies have also previously derived memory subscales part from the Telephone Interview for Cognitive Status and made a standardized verbal memory score.<sup>5,7</sup>

**Dietary assessment and adapted Mediterranean Dietary score**—Food intakes were estimated based on in-person 24-hour dietary recalls over three consecutive days by trained interviewers.<sup>16,17</sup> Food models and pictures were used to aid quantification. All food intake was expressed in g/day. The dietary information measured at the same wave as the first cognitive test was used in our study for the adapted Mediterranean dietary score and factor analysis. A validation study among a sample of non-CHNS participants in one of the CHNS survey provinces has been described elsewhere.<sup>17</sup>

We modified the components of the Mediterranean diet scale to adapt to the Chinese food culture and the distribution of food intake based on 24-hour recalls (see eTable 1 for food examples). We defined fiber-rich grains based on the fiber to carbohydrate ratio, where the cutoff point was similar to the ratio recommended to identify fiber-rich whole grains from the American Heart Association.<sup>18</sup> To replace the beneficial component defined based either on intakes of olive oil or a high monounsaturated-to-saturated fat ratio, we defined animal-source cooking fats as a negative component in the adapted Mediterranean diet scale. Data on specific fats were not yet available in the CHNS, and olive oil is not widely consumed.

Animal-source cooking fats, known to have high saturated fats,<sup>19</sup> are commonly used for cooking in China;<sup>20</sup> saturated fats have been suggested to predict worse cognitive outcomes in older adults.<sup>21,22</sup> For each beneficial component—namely vegetables, legumes and nuts, fruits, fiber-rich grains, fish, and dairy products—a value of 1 was assigned to people who consumed above the sex-specific median or any amount when the percentage of consumers did not reach half of the sample. A value of 0 was given otherwise. Since the highest consumption of dairy products (mainly milk) was no more than 1 serving/day, we considered dairy products at this low consumption level as beneficial, consistent with current literature on both cognitive and cardiometabolic outcomes.<sup>23,24</sup> For components presumed to be harmful, which included red and processed meat as well as animal-source cooking fats, a value of 1 was given to people who consumed below the sex-specific median or were nonconsumers, and 0 otherwise. For alcohol, 1 point was assigned to men whose alcohol consumption was 10–50g/d and women 5–25g/d, vs. 0 for the other levels of intake.<sup>25</sup> The possible range of adapted Mediterranean diet scores was 0 to 9, with higher scores indicating greater adherence.

Principal component analysis: diet patterns—We used principal component analysis (PCA) to derive underlying dietary patterns among all 1650 participants, and to assess whether there was a preexisting consumption pattern within the population under study that was similar to Mediterranean dietary patterns. Food items included in PCA derived dietary patterns were grouped in a behaviorally as well as nutritionally meaningful way, yielding more refined groups.<sup>16</sup> After removing food groups with less than 5% consumers overall, to accommodate a high proportion of non-consumers for several food groups and to allow for consistent comparisons across groups, each of the 34 food and condiment groups was categorized as a binary variable (consumer/nonconsumer for food groups with less than 50% of consumers; or above/below median for those with higher intakes) and included in PCA.<sup>26</sup> We derived dietary patterns based on the polychoric correlation matrix and orthogonal varimax rotation in STATA. On the basis of eigenvalue>1.0, scree plot (eFigure 1) and interpretability, 2 factors were retained (see eTable 2 for food examples and factor loading), which together accounted for 23% of the variance in intakes (12% and 11% for pattern 1 and 2 respectively). Other population-based studies have reported similar proportions of the variance explained.<sup>27,28</sup> The Wheat-based Diverse diet (pattern 1) was characterized by high intakes of wheat buns, deep-fried wheat, nuts, fruits, moderate-to-high fat red meat, poultry and game, egg, fish, dairy, sugar, vinegar, soy sauce, plant oil, and with low intake of animal-source cooking fats. The Rice/pork pattern (pattern 2) was characterized by high intakes of rice, low fat red meats, low fat pork, moderate-to-high fat pork, organ meats, poultry and game, fish, and low intakes of wheat flour, wheat buns, and coarse grain. Each participant received a separate score for each individual dietary pattern, with a higher score indicating a greater adherence. Since the Wheat-based Diverse diet (pattern 1) shared important features of the adapted Mediterranean diet including grains, nuts, fruits, fish, dairy, and low consumption of animal-source cooking fats, we hypothesized that a higher adherence to the Wheat-based Diverse diet would be associated with a slower cognitive decline. Since there is no convincing evidence to support a link between cognitive function and either rice intake, or meat intakes at the moderate levels of consumption in this

population, we hypothesized that the Rice/pork diet (pattern 2) would not strongly predict differences in the rate of cognitive decline.

**Covariates**—We selected covariates based on known factors associated with cognitive decline and potential confounders between dietary patterns and the outcome. All non-dietary covariates were collected at the time of the first cognitive measure which includes age, gender, region (south/north), urbanization index (a multicomponent continuous scale),<sup>29</sup> education (highest level of education attained primary vs. less), annual household income per capita (inflated to 2011, 5,000 yuan vs. less), current smoking (yes/no), body mass index (BMI, calculated by measured weight and height), hypertension (measured mean *SBP/DBP 140/90 mm Hg* or self-report of anti-hypertension medications), history of chronic diseases including myocardial infarction, stroke or diabetes (self-report). Physical activity was self-reported based on hours per week spent in different occupational, household, transportation and leisure-time activities, which were converted into metabolic equivalent-hours per week and included in the model as tertiles.

#### Statistical analysis

**Missing data imputation**—Among 1650 participants, 169 had missing baseline covariates. Multiple imputation was used to impute missing covariates, with 5 datasets generated. The estimates from each datasets were pooled to generate a single set of estimates following Rubin's rules.<sup>30</sup> Although there is debate on how many datasets to generate, 3–5 imputations have been suggested to be sufficient to obtain stabilized results; gains have been found to rapidly diminish after the first few imputations.<sup>31</sup> All statistical analysis was performed by STATA (version 11.2; STATACorp).

**Sample characteristics**—We classified adherence to the adapted Mediterranean diet based on approximate tertiles, with low adherence for scores of 0–2, middle adherence with a score 3, and relatively high adherence with scores of 4–9. We examined baseline characteristics of participants by tertiles of adapted Mediterranean diet scores. We also compared the degree of similarity between adapted Mediterranean diet and PCA-derived dietary patterns using pairwise Pearson correlation tests.

**Longitudinal data analysis**—We used linear mixed-effects models to evaluate the relationship between dietary patterns and rate of cognitive change over time. To account for inter-individual differences in baseline cognitive function and rate of change, the intercept and slope were fitted with random-effects components. The predictors were the adapted Mediterranean diet score as a continuous variable and in tertiles; or scores of each PCA-derived dietary pattern in tertiles with trend analysis.

Our first mixed-effects model was only adjusted for time. In model 2, we adjusted for covariates considered as potential confounders or risk factors for cognitive decline: age, gender, region, urbanization index, education, annual household income per capita, physical activity, current smoking, total energy intake, time, and the interaction between time and all covariates. In model 3, we further adjusted for body mass index and hypertension, and time interactions with the above covariates, both of which may be either confounders or

We examined whether the relationship between adapted Mediterranean diet or PCA-derived dietary patterns and cognitive decline was modified by one key factor, age, based on our prior knowledge that the association between Mediterranean diet and cognitive decline was more evident in studies of populations at older ages.<sup>4</sup> Age interactions have been found in other studies on diet and cognitive decline, including some evaluating dietary fat,<sup>7,32</sup> and our previous study assessing fish intake.<sup>33</sup> The cutoff of 65y was selected based on results using 5-y age group categories (55–59, 60–64, 65–69, and 70 y).

In sensitivity analyses, first, we excluded participants with the lowest 10% baseline cognitive scores who may be categorized as having cognitive impairment. Second, we estimated the associations after excluding adults with a self-reported history of diabetes (3%), self-reported history of myocardial infarction (1%) or stroke (2%). Third, to alleviate concerns related to measurement error in using a limited number of dietary recalls to estimate alcohol consumption, we created an alternative alcohol component score considering drinking alcohol in the past year as beneficial (asked separately from the dietary recall, yes/no) and the alternative adapted Mediterranean diet continuous scores were analyzed. Fourth, although orthogonal rotation is more commonly used in PCA studies to obtain uncorrelated dietary patterns, we also derived dietary patterns using oblique rotation and tested their associations with cognitive decline. Moreover, since 28% of participants shared a residence, we allowed for clustering by household to account for the potential non-independence of data in models that included a random intercept. Finally, we repeated the main analyses with 30 imputed datasets to test whether the imputed results were stabilized.

To explore how each food group contributes to the relation of adapted Mediterranean diet and cognitive health, we also estimated the association between each component of the adapted Mediterranean diet score and cognitive change over time, as well as the association with the score after removing each component respectively.

# RESULTS

#### **Baseline characteristics of participants**

Baseline characteristics of participants in the analytic sample (n=1650) and eligible participants who were not included (n=716) were compared (eTable 3). CHNS participants who were not included were similar to those included in the analysis regarding to gender, education, household income, BMI or the consumption of any of the adapted Mediterranean diet components, but were more likely to be older and live in the North.

Since age modified the association between adapted Mediterranean diet scores and cognitive decline (p=0.01) all subsequent analysis were stratified by age 55–64 y at baseline (n=1046), and 65 y (n=604). Among participants aged 65 y in the analysis sample, higher tertiles of adapted Mediterranean diet scores were associated with: a greater likelihood of being male, residing in Northern China, and having completed education beyond primary school; higher

household income, prevalence of hypertension, higher BMI, and energy intake; and lower dietary energy density (Table 1). Adapted Mediterranean diet scores in this group were not associated with age, urbanization index, smoking, and physical activity. Characteristics of higher vs lower adherence of adapted Mediterranean diet among those aged <65 y were similar to those for age 65 y, with the exception of an association with age and the urbanization index, and the absence of differences in gender, household income, and hypertension.

#### Correlations between adapted Mediterranean diet and PCA-derived dietary patterns

The adapted Mediterranean diet score and Wheat-based Diverse (pattern 1) dietary score were positively correlated (r=0.47). 51% (n=273) of participants in the highest tertile of the adapted Mediterranean diet were also in the highest tertile of Wheat-based Diverse diet. The Rice/Pork (pattern 2) and the adapted Mediterranean diet scores were negatively correlated (r=-0.18).

#### Associations between adapted Mediterranean diet and cognitive decline

The average follow-up duration among all participants was 5.3 years. The mean annual rate of global cognitive change among adults <65 y and 65 y was a decline of 0.3 point and 0.5 point respectively. In both unadjusted linear mixed-effects model (model 1) and adjusted model (model 2) which controlled for demographic, socioeconomic and lifestyle factors, a higher adapted Mediterranean diet score was associated with slower decline of cognitive function among adults 65+ y (Table 2). In model 3 we further adjusted for BMI, hypertension and their interactions with time, results materially remained the same. Among adults 65+ y: compared to those with low adherence of adapted Mediterranean diet, the rate of global cognitive decline with middle level adherence and with high adherence was slower by 0.13 points per year (95% CI: -0.11, 0.38) and 0.28 points per year (95% CI: 0.02, 0.54) respectively. Similarly, participants in the highest tertile of adapted Mediterranean diet had a slower rate of decline in composite scores ( $\beta$ =0.042; 95% CI: 0.002, 0.081) and verbal memory scores ( $\beta$ =0.047, 95% CI: 0.003, 0.091), equivalent to differences observed among subjects 1.6 and 2.0 years younger in age respectively. Continuous adapted Mediterranean diet scores were associated with decline in global scores, composite scores or verbal memory scores. We did not find any association of adapted Mediterranean diet with cognitive test items for adults below age 65 y. Multiple sensitivity analyses did not alter our conclusions e.g. excluding subjects with the lowest 10% baseline cognitive scores, or using 30 imputed data sets.

We applied the fully-adjusted mixed-effects model to explore the influence of each food component that made up the adapted Mediterranean diet scores (Table 3). Among adults aged 65+ y, the rate of cognitive decline was slower by 0.34 points comparing fish consumers (95% CI: 0.11, 0.56) vs. nonconsumers. Fruit consumers had a slower rate of cognitive decline by 0.28 points per year (95% CI: -0.02, 0.59) vs. nonconsumers. Consumers of animal-source cooking fats were associated with faster decline by -0.31 points per year (95% CI: -0.55, -0.07) vs. nonconsumers. We did not find any relation between consumption of vegetables, legumes, fiber-rich grains, dairy products, red meat or alcohol with cognitive decline after multivariable adjustment. The findings derived by

removing each component respectively from the adapted Mediterranean diet continuous scores also suggested that fish, animal-source cooking fats, and fruits were most influential to our results.

#### Associations between PCA-derived dietary patterns and cognitive decline

Among those 65 years and older, compared to subjects in the lowest tertile of Wheat-based Diverse diet (pattern 1), the rate of global cognitive decline among those in the highest tertile was slower by 0.42 points per year (95% CI: 0.12, 0.73; Table 4); the rate of composite score decline for the highest tertile was slower by 0.07 points per year (95% CI: 0.02, 0.11), which is equivalent to the mean disparity in scores observed for a 1.7-year difference in age. We observed no association of Rice/Pork (pattern 2) with any cognitive outcomes. We did not find any association between PCA derived dietary patterns and cognitive decline among adults aged 55–64 y, similar to findings for the adapted Mediterranean diet.

## DISCUSSION

This large prospective cohort study is among the first to examine the association between dietary patterns and cognitive decline in a non-Western population. Our results have shown that an adapted Mediterranean dietary pattern may reduce the rate of cognitive decline among adults 65 years and older. Moreover, a factor analysis-derived dietary pattern rich in wheat, fish, fruits, nuts, and dairy, as well as low in animal cooking fats, which we labeled a wheat-based diverse diet, was also associated with slower decline of global cognitive function for adults aged 65y. Although this pattern shared some common components with the adapted Mediterranean diet score, both the food groups included and methods used to derive the scores differed. For both dietary patterns, we did not observe a relationship with cognitive change among adults aged 55 to 64 y.

A systematic review which summarized evidence through January 2012 suggested that greater adherence to a Mediterranean diet is associated with slower cognitive decline and a lower risk of Alzheimer's disease based on results from up to 7 independent cohorts.<sup>4</sup> Several recent observational studies, however, showed inconsistent evidence on the association between Mediterranean diet and cognitive decline.<sup>5–7</sup> For example, in one study, Mediterranean diet adherence was associated with cognitive status at baseline, but not with cognitive decline;<sup>6</sup> two other studies reported no association between adherence to this diet pattern and either subsequent cognition,<sup>6</sup> or cognitive change over time.<sup>5,7</sup> The limited number of cohorts, the inconsistent evidence, and concerns about potential residual confounding all indicate the need to assess this relationship in other populations with diverse patterns of intake. Although randomized trials suggest increasing intake of foods such as olive oil and nuts are beneficial,<sup>34</sup> whether components of the Mediterranean diet widely consumed in non-Western cultures may reduce the rate of cognitive decline remains unclear.

In contrast to several recent studies, we found an adapted Mediterranean dietary pattern consumed by community-dwelling older adults in China, as well as a pattern that shared several components of this pattern derived using factor analysis, to be associated with slower cognitive decline. Compared with previous studies in Western populations, in this population from China, dietary intakes based on 3-day recalls reflected a markedly lower percentage of

consumers of fruits, dairy products, and alcohol. Population differences in consumption patterns could influence the magnitude of associations with dietary pattern scores which are characterized based on relative differences in intake. Nonetheless, our findings suggesting cognitive benefits of adherence to the Mediterranean diet-like pattern are consistent with a number of studies in Western populations.<sup>15,35,36</sup> Moreover, consistent results with the wheat-based diverse diet derived using factor analysis, which shared several components with the adapted Mediterranean diet, supported the findings for the adapted Mediterranean diet in this sample. The two dietary patterns retained from factor analysis are comparable with previous findings among all CHNS adults,<sup>26</sup> and are similar to several patterns identified in the China National Nutrition and Health Survey, which reported a pattern characterized by high intakes of rice and moderate intakes of animal foods, as well as a pattern characterized by high intakes of fruit, eggs, poultry and seafood.<sup>26,37</sup> It is worth noting that although the wheat-based diverse diet was also characterized by deep-fried wheat and moderate-to-high fat red meats, the level of intake in this Chinese population remained low with a mean intake of 4g/day and 35g/d respectively. Indeed, a pooled analysis of Asian cohort studies found that red meat intake, which is much lower than that in the US, was inversely associated with cardiovascular mortality in Asian men and with cancer mortality in Asian women.38

Another important question was whether all aspects of the Mediterranean diet or selected food components confer the observed cognitive benefits. Analyses evaluating individual food item with cognitive decline and the influence of removing each food component one at a time suggested that in our sample the benefits of adapted Mediterranean diet mainly come primarily from higher consumption of fish and fruit, and lower intake of animal-source cooking fats. Prior evidence regarding effects of fruit consumption has been limited and mixed, perhaps in part due to variable levels of intake.<sup>2</sup> However, most prior studies suggested that higher fish consumption favored better cognitive health (detailed findings for this cohort provided elsewhere<sup>33</sup>), and a few studies have reported higher intake of late-life saturated fat to be associated with faster cognitive decline.<sup>21,22</sup> Interestingly, the *a posteriori* diet patterns in this population were not distinguished by differences in intakes of vegetables. Analysis of associations with food groups indicated that it was not drivers of the associations observed with the adapted Mediterranean diet score. Supplementary analyses showed that unlike the weak negative association with total and leafy vegetables, nonleafy vegetables—which had greater intake variability—tended to associate with a slower rate of cognitive decline, although associations did not reach significance. These findings highlight the potential contribution of comparative analyses of the type implemented here to gain further insights on the dietary components that may underlie links between diet patterns and health outcomes in different populations.

Our observation that the association between greater adherence to the adapted Mediterranean diet and a reduced rate of cognitive decline was evident among adults aged 65 y and older but not among younger participants might reflect that for accruing cognitive benefits, long-term exposure to a healthier diet is needed. It is also possible that the relatively narrow scope of cognitive screening items adopted in CHNS may not be sensitive enough to detect associations in a younger age group in which the rate of cognitive decline is relatively slow, as observed in our study and others.<sup>39</sup>

Another limitation of the current study applies to all observational studies, namely that some residual confounding is possible despite adjusting for a wide array of covariates. Although included participants were more likely to be older and living in the North compared to those who were not included, adapted Mediterranean diet components were not related to eligibility for inclusion in the analytic sample. Thus, while it cannot be ruled out, selection bias was not a strong concern. In addition, compared to food frequency questionnaires, the use of 24-hour dietary recalls over three days limited our ability to estimate the habitual intakes of foods that are episodically consumed. The measurement error in the estimate of episodically consumed foods such as fish and alcohol is likely to be random, which could attenuate associations. Finally, the issue of how to handle cognitive impairment at baseline is inherent in all prospective epidemiological studies on late life cognition that rely on self-reported exposure information. Generally recall error due to cognitive impairment is thought to bias results towards the null.<sup>40</sup> Nevertheless, we did sensitivity analyses in which we excluded those with the lowest 10% baseline scores and found results unchanged.

Major strengths of this study include the use of longitudinal data, the use of two scoring methods to evaluate overall cognitive function which increased our confidence in the robustness of the findings, and the use of a population-based sample from CHNS which imparts the ability to generalize the results to the Chinese population.

In conclusion, results from this population-based sample suggested that adherence to an adapted Mediterranean dietary pattern was associated with a slower cognitive decline among community-dwelling Chinese adults 65 years and older. Fish, fruits, and lower intakes of animal-source cooking fats may be primarily responsible for the observed associations. Similar global cognitive benefits were observed to be associated with a preexisting dietary pattern in this sample, characterized by food components similar to those in adapted Mediterranean diet. Further study, including more randomized clinical trials, are needed to confirm this finding.

#### Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Baseline characteristics of participants by tertile of adapted Mediterranean diet score<sup>a,b</sup>

	Amo	ng all (n=1	(020)	Age at ei	1try<65 y (	n=1046)	Age at e	ntry 65 y	(n=604)
Characteristics	Low	Middle	High	Low	Middle	High	Low	Middle	High
No. of subjects	538	538	574	327	330	389	211	208	185
Baseline global cognitive score, points	18.7	19.1	19.9	19.7	20.0	21.0	17.4	17.9	17.8
Age, $y$	64.0	63.6	62.9	59.5	59.2	59.0	70.9	70.6	71.1
Women, %	52	52	47	50	53	49	54	51	44
North region, %	25	35	40	28	35	37	21	35	48
Urbanisation index	57.1	58.5	60.3	54.8	57.3	59.1	60.7	60.4	62.8
Graduated from primary or above, %	41	44	55	47	54	61	31	28	42
Household income per capita 5000yuan/yr, %	30	37	41	37	41	42	19	29	40
Current smoking, %	33	30	30	37	32	32	27	25	28
Physical activity, %									
low	33	35	33	22	24	23	50	51	54
medium	33	32	36	35	34	39	29	28	30
high	35	34	31	43	42	38	21	21	16
Hypertension, %	39	41	43	36	33	37	44	54	54
Body mass index, <i>kg/m</i> <sup>2</sup>	22.2	22.7	23.5	22.5	22.7	23.5	21.7	22.6	23.7
Height, <i>cm</i>	156.4	158.0	159.8	157.6	158.5	159.7	154.7	157.2	160.0
Total caloric intake, <i>kcal</i>	1361.6	1412.4	1583.3	1389.8	1482.9	1618.7	1318.0	1300.6	1509.0
Dietary energy density, kcal/g	2.3	2.1	1.9	2.3	2.1	1.9	2.3	2.1	2.0
Adapted Mediterranean diet score components									
Vegetables, g/d	185.7	216.7	256.8	192.9	233.5	272.6	175.7	192.7	226.2
Legumes and nuts, g/d	22.7	41.1	58.9	22.9	42.1	61.1	22.3	39.6	54.6
Fruits consumer, %	б	12	28	б	10	29	4	14	27
Fiber-rich grains consumer, %	4	16	34	б	17	31	4	15	38
Fish consumer, %	17	36	60	18	34	58	16	38	64
Dairy products consumer, %	0	б	11	0	ю	11	-	б	13
Alcohol, g/d	1.6	2.0	4.5	1.3	1.9	4.3	2.1	2.1	4.9
Red meat and processed meat, g/d	57.9	46.8	42.5	55.8	49.9	43.5	60.8	42.3	40.5

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	Ame	ng all (n=1	(020)	Age at e	ntry<65 y (	n=1046)	Age at 6	entry 65 y	(n=604)
Characteristics	Low	Middle	High	Low	Middle	High	Low	Middle	High
Animal-source cooking fats consumer, %	53	24	7	54	25	8	52	21	9
<i>a</i>									

Values are mean unless otherwise noted.

 $b_{\rm L}$  Low adherence for the adapted Mediterranean diet: 0–2; Medium: 3; High: 4–9.

#### Table 2

Mean difference in rate of change in cognitive function over 5 years by tertile of adapted Mediterranean diet scores and an increase of 1 point of the score<sup>a-d</sup>

	All participants (n=1650)	Age at entry<65 (n=1046)	Age at entry 65 (n=604)
Global scores			
Mean annual change (points/y)	-0.41	-0 34	-0.53
(points, y)	в (95% CI)	в (95% CI)	в (95% CI)
M. 1.1.16	P (7070 CI)	P (7070 C1)	p (30% Cl)
Model 1	٥	0	0
Low	0	0 00 ( 0.00 0.27)	0
Medium	0.10 (-0.04, 0.25)	0.09 (-0.09, 0.27)	0.10 (-0.15, 0.35)
High	0.06 (-0.09, 0.20)	-0.07 (-0.25, 0.11)	0.28 (0.03, 0.53)
Medi score (0–9)	0.03 (-0.02, 0.08)	-0.01 (-0.07, 0.05)	0.09 (0.01, 0.18)
Model $2^{f}$			
Low	0	0	0
Medium	0.07 (-0.08, 0.21)	0.05 (-0.13, 0.23)	0.12 (-0.12, 0.37)
High	0.01 (-0.14, 0.16)	-0.12 (-0.29, 0.06)	0.30 (0.04, 0.56)
Medi score (0-9)	0.01 (-0.04, 0.06)	-0.03 (-0.09, 0.03)	0.10 (0.01, 0.18)
Model 3g			
Low	0	0	0
Medium	0.07 (-0.08, 0.21)	0.05 (-0.13, 0.23)	0.13 (-0.11, 0.38)
High	0.00 (-0.14, 0.15)	-0.12 (-0.30, 0.06)	0.28 (0.02, 0.54)
Medi score (0-9)	0.01 (-0.04, 0.06)	-0.03 (-0.09, 0.03)	0.10 (0.01, 0.18)
Composite scores			
Mean annual change (SUs/y)	-0.063	-0.052	-0.084
Model 1 <sup>e</sup>			
Low	0	0	0
Medium	0.016 (-0.005, 0.038)	0.016 (-0.010, 0.043)	0.014 (-0.024, 0.051)
High	0.012 (-0.010, 0.033)	-0.006 (-0.031, 0.020)	0.041 (0.004, 0.079)
Medi score (0-9)	0.006 (-0.001, 0.013)	0.000 (-0.008, 0.009)	0.014 (0.002, 0.026)
Model $2^f$			
Low	0	0	0
Medium	0.011 (-0.010, 0.032)	0.010 (-0.015, 0.035)	0.017 (-0.020, 0.054)
High	0.004 (-0.017, 0.025)	-0.013 (-0.038, 0.013)	0.043 (0.004, 0.083)
Medi score (0-9)	0.003 (-0.004, 0.010)	-0.003 (-0.011, 0.006)	0.014 (0.001, 0.027)
Model 3 <sup>g</sup>			
Low	0	0	0
Medium	0.011 (-0.010, 0.032)	0.010 (-0.016, 0.035)	0.018 (-0.019, 0.056)
High	0.003 (-0.018, 0.024)	-0.013 (-0.039, 0.012)	0.042 (0.002, 0.081)
Medi score (0-9)	0.002 (-0.005, 0.009)	-0.003 (-0.011, 0.006)	0.014 (0.001, 0.027)

Verbal memory scores

	All participants (n=1650)	Age at entry<65 (n=1046)	Age at entry 65 (n=604)
Mean annual change (SUs/y)	-0.055	-0.048	-0.068
Model 1 <sup>e</sup>			
Low	0	0	0
Medium	0.013 (-0.013, 0.039)	0.008 (-0.025, 0.040)	0.019 (-0.022, 0.060)
High	0.001 (-0.024, 0.026)	-0.021 (-0.052, 0.011)	0.043 (0.001, 0.084)
Medi score (0-9)	0.002 (-0.006, 0.011)	-0.004 (-0.015, 0.006)	0.014 (0.000, 0.027)
Model $2^{f}$			
Low	0	0	0
Medium	0.008 (-0.018, 0.034)	0.001 (-0.031, 0.033)	0.022 (-0.020, 0.064)
High	-0.004 (-0.030, 0.022)	-0.029 (-0.062, 0.004)	0.047 (0.003, 0.091)
Medi score (0-9)	0.000 (-0.008, 0.009)	-0.007 (-0.018, 0.004)	0.015 (0.001, 0.030)
Model 3 <sup>g</sup>			
Low	0	0	0
Medium	0.008 (-0.018, 0.033)	0.002 (-0.031, 0.034)	0.024 (-0.018, 0.066)
High	-0.004 (-0.031, 0.022)	-0.029 (-0.062, 0.004)	0.047 (0.003, 0.091)
Medi score (0-9)	0.000 (-0.009, 0.009)	-0.008 (-0.019, 0.003)	0.016 (0.001, 0.030)

<sup>a</sup>Age modified the association between adapted Mediterranean diet and change in global cognitive scores (p=0.01).

 $b_{\rm Low}$  adherence for the adapted Mediterranean diet: 0–2; Medium: 3; High: 4–9.

<sup>C</sup>Global cognitive score combined results of immediate and delayed recall of a 10-word list, counting backward from 20, serial 7 subtraction, and orientation. Composite scores were computed by averaging baseline z-scores of memory scores and the rest of the cognitive scores. Verbal memory score combined results of immediate and delayed recall of a 10-word list.

 ${}^d\!A$  positive  $\beta$  coefficient indicates slower rate of decline in cognitive function.

<sup>e</sup>Model 1 was unadjusted.

f Model 2 adjusted for age, gender, education (graduated from primary/less), region (south/north), urbanization index, annual household income per capita (5,000 yuan/less), total energy intake, physical activity (tertile), current smoking (yes/no), time (year since baseline), and time interactions with each covariate.

 $g^{g}$ Model 3 adjusted for model 2 covariates plus for body mass index (linear and squared terms) and hypertension, and time interactions with each covariate.

				Adjus	sted mean difference $(95\%)$	$\operatorname{CI}^{p-d}$
	Median or percentage as specified	Comparison group vs. reference group	Scoring criteria	All (n=1650)	Age at entry<65 (n= 1046)	Age at entry 65 (n=604)
Vegetables	231g/d for male; 210g/d for female	Above sex-specific median vs. less	1 point for comparison group; 0 otherwise	-0.09 (-0.21, 0.04)	-0.09 (-0.24, 0.06)	-0.11 (-0.33, 0.10)
Legumes and nuts	42g/d for male; 40g/d for female	Above sex-specific median vs. less	Same as above	-0.05 (-0.18, 0.07)	$0.00 \ (-0.15, \ 0.15)$	-0.14 (-0.35, 0.08)
Fruits	15% consumer	Consumer vs. non-consumer	Same as above	0.12 (-0.05, 0.29)	0.03 (-0.17, 0.23)	0.28 (-0.02, 0.59)
Fiber-rich grains	18% consumer	Consumer vs. non-consumer	Same as above	-0.08 (-0.25, 0.09)	-0.12 (-0.33, 0.88)	0.02 (-0.27, 0.31)
Fish	38% consumer	Consumer vs. non-consumer	Same as above	0.10 (-0.03, 0.23)	-0.03 (-0.19, 0.12)	$0.34\ (0.11,\ 0.56)$
Dairy products	5% consumer	Consumer vs. non-consumer	Same as above	0.10 (-0.20, 0.40)	0.01 (-0.36, 0.37)	0.22 (-0.29, 0.74)
Alcohol	6% with low-to- moderate consumption	10–50g/day for men and 5–25g/day for women vs. other	Same as above	0.10 (-0.16, 0.36)	0.05 (-0.27, 0.38)	0.25 (-0.20, 0.71)
Red meat and processed meat	50g/d for male; 47g/d for female	Above sex-specific median vs less	0 point for comparison group; 1 otherwise	0.03 (-0.10, 0.17)	0.08 (-0.08, 0.25)	-0.05 (-0.28, 0.18)
Animal-source cooking fats	27% consumer	Consumer vs. non-consumer	Same as above	-0.13 (-0.27, 0.01)	-0.05 (-0.22, 0.12)	-0.31 (-0.55, -0.07)
$^{a}$ Age modified the association be $b_{}$	tween Mediterranean diet s	core and change in global cognitive score	es ( <i>p</i> =0.01).			

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Global score combined results of immediate and delayed recall of a 10-word list, counting backward from 20, serial 7 subtraction, and orientation.

<sup>C</sup>Model adjusted for model 3 covariates, including age, gender, region (south/north), urbanisation index, education (graduated from primary/less), annual household income per capita (5,000 yuan/less), total energy intake, time, physical activity (tertile), current smoking (yes/no), body mass index (linear and squared terms) and hypertension, and time interactions with each covariate.

 $d_{A}$  positive  $\beta$  coefficient indicates slower rate of decline in cognitive performance.

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Mean difference in rate of change in global cognitive scores of each food group in adapted Mediterranean diet<sup>a</sup>

Table 3

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# Table 4

Adjusted mean difference in rate of change in cognitive score according to factor analysis-based dietary patterns  $a^{-d}$ 

	Α	attern 1: Wheat-based divers Mean difference (95% CI	e diet )		Pattern 2: Rice/pork Mean difference (95% CI)	
	All (n=1650)	Age at entry<65 (n=1046)	Age at entry 65 (n=604)	All (n=1650)	Age at entry<65 (n=1046)	Age at entry 65 (n=604)
Global s	cores					
T1	0	0	0	0	0	0
T2	$0.115 \left(-0.036, 0.265\right)$	$0.144 \left(-0.041, 0.330\right)$	0.054 (-0.217, 0.404)	-0.048 (-0.219, 0.123)	-0.101 (-0.307, 0.105)	0.094 (-0.217, 0.404)
T3	$0.164 \left(-0.016, 0.343\right)$	0.020 (-0.205, 0.246)	0.424 (0.119, 0.730)	-0.022 $(-0.213, 0.169)$	-0.063 (-0.296, 0.169)	0.147 (-0.197, 0.491)
P-trend	0.12	0.89	0.011	0.19	0.21	0.43
Composi	ite scores					
T1	0	0	0	0	0	0
T2	0.019 (-0.002, 0.041)	$0.024 \ (-0.003, \ 0.050)$	0.011 (-0.029, 0.050)	-0.007 $(-0.032, 0.018)$	-0.014 (-0.043, 0.016)	0.012 (-0.034, 0.059)
T3	0.026 (0.000, 0.052)	0.003 (-0.029, 0.035)	0.069 (0.023, 0.114)	-0.003 (-0.031, 0.025)	-0.006 (-0.040, 0.027)	0.018 (-0.034, 0.069)
P-trend	0.08	0.98	0.009	0.22	0.17	0.63
Verbal m	nemory scores					
T1	0	0	0	0	0	0
T2	0.012 (-0.015, 0.039)	0.017 (-0.018, 0.051)	0.002 (-0.043, 0.046)	-0.007 (-0.038, 0.023)	-0.018 (-0.056, 0.020)	0.018 (-0.034, 0.071)
T3	0.020 (-0.012, 0.052)	0.003 (-0.039, 0.044)	0.050 (-0.002, 0.101)	$-0.004 \ (-0.038, \ 0.030)$	-0.017 (-0.060, 0.026)	0.032 (-0.026, 0.090)
P-trend	0.32	0.75	0.045	0.21	0.39	0.19

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b Global cognitive score combined results of immediate and delayed recall of a 10-word list, counting backward from 20, serial 7 subtraction, and orientation. Composite scores were computed by averaging baseline z-scores of memory scores and the rest of the cognitive scores. Verbal memory score combined results of immediate and delayed recall of a 10-word list.

<sup>c</sup> Model adjusted for model 3 covariates, including age, gender, region (south/north), urbanisation index, education (graduated from primary/less), annual household income per capita (5,000 yuan/less), total energy intake, physical activity (tertile), current smoking (yes/no), body mass index (linear and squared terms), hypertension, time (year since baseline), and time interactions with each covariate.

 $d^{}_{}$  A positive  $\beta$  coefficient indicates slower rate of decline in cognitive performance.