

SUPPLEMENTARY MATERIAL

Methods

Study Design and Sample

This cohort study utilized data from the CLHLS, an ongoing national longitudinal study initiated in 1998. The study utilized a multi-phase, regionally stratified random sampling approach spanning 22 Chinese provinces, with subsequent data collection waves carried out in 2000, 2002, 2005, 2008–2009, 2011–2012, 2014, and 2017–2018. Detailed sampling procedures are documented in prior studies^[1,2]. In order to address the absence of objective medical data such as biomarkers in the CLHLS, urine and blood samples were collected from participants who had provided consent during three time periods: 2008–2009, 2011–2012, and 2014. These in-depth surveys were called the biomarker sub-study of CLHLS.

The subjects deemed eligible for inclusion in this study were required to meet the following criteria: at the time of the baseline measurement, they were required to be 65 years of age or older, and they were required to have complete data. The detailed exclusion criteria are outlined below: subjects were excluded due to age < 65 years ($n = 600$); subjects were excluded due to mild cognitive impairment at baseline ($n = 12,423$); subjects with stroke, Parkinson's disease and dementia at baseline were excluded ($n = 3,531$), subjects were excluded due to missing data on years of education ($n = 309$); and subjects were excluded due to missing data on specific types and intakes of staple foods ($n = 3,990$), and covariates ($n = 2,476$). Participants who enrolled in the 2018 wave were not included as no follow-up data were available. Finally, the total number of participants included in this study was 21,283. The PLT and PDW data were obtained from the biomarker sub study of CLHLS, excluding participants with missing PLT and PDW biomarkers and

those with MCI at the time of biomarker measurement, this resulted in a total of 1,323 participants. Due to the limited number of individuals who primarily consume coarse cereals ($n = 12$), mediation analysis was confined to the mediation effects of PLT and PDW on the relationship between staple foods consumption and MCI in elderly individuals whose dietary staples are rice and wheat ($N = 1,311$), as shown in Supplementary Figure S1.

The CLHLS study was approved by the Institutional Review Board, Duke University (Pro00062871), and the Biomedical Ethics Committee, Peking University (IRB00001052–13074). All participants gave written informed consent.

Assessment of Types and Intakes of Staple Foods

Dietary consumption was assessed using a validated semi-quantitative food frequency questionnaire (FFQ), wherein participants were queried regarding the types of foods consumed and their frequency of consumption. Staple foods were categorized as rice, coarse cereals, and wheat based on responses to "What is the main grain as staple food at present?" Daily intake of these staple foods was determined through responses to "What is the average daily intake of the staple food?". Total staple foods intake was calculated as the sum of the reported daily intake of rice, coarse cereals, and wheat.

Outcome Ascertainment

Cognitive function was assessed using the Chinese version of the Mini-Mental State Examination (MMSE) in each survey. This version was adapted and validated based on the scale originally developed by Folstein et al^[3]. Scores on the MMSE range from 0 to 30, with higher scores

denoting greater cognitive ability. It consists of 13 questions that evaluate various cognitive domains, including registration, orientation, calculation and attention, recall, and language abilities. For more detailed information on the Chinese version of the MMSE, please refer to the relevant published literature^[4].

Mild cognitive impairment was diagnosed using a modified version of the Petersen criteria^[5]: (1) cognitive status as assessed by the MMSE, with cutoff scores of ≤ 17 for individuals without formal education, ≤ 20 for those with 1–6 years of education, and ≤ 24 for those with 7 or more years of education; (2) absence of dementia, Alzheimer disease, psychiatric disorders, cerebral damage, or other physical diseases resulting in cognitive impairment; (3) functional status, indicated by having little or no difficulty in daily activities as measured by the activities of daily living (ADL) scale^[6]. The follow-up period for each participant was calculated from baseline to the earliest occurrence of MCI, death, loss to follow-up, or the end of the study period.

Covariates

Potential confounders considered in the analysis included age, sex, body weight, living areas (rural vs. urban), ethnicity (Han vs. others), marital status (married, divorced, widowed, and unmarried), live alone (yes vs. no), fruit intake (always or almost every day, often, sometimes or occasionally, rarely or never), vegetable intake (always or almost every day, often, sometimes or occasionally, rarely or never), smoking status (current, former, and never), alcohol consumer status (yes vs. no), physical activity (current, former, and never), self-reported health (poor, fair, and good), history of coronary heart disease (yes vs. no), history of diabetes (yes vs. no), and history of hypertension (yes vs. no).

Statistical Analysis

The baseline characteristics were reported as mean \pm standard deviation (SD) for continuous variables and frequency (percentages) for categorical variables. Statistical significance was assessed using independent t-test and analysis of variance for continuous variables and chi-squared tests for categorical variables. Cox proportional hazard regression models were conducted to assess the hazard ratios (*HRs*) and 95% confidence intervals (*CI*s), which were used to assess the associations of types (rice as the reference) and intakes (increase per SD) of staple foods with the incidence of mild cognitive impairment. The proportional hazards assumption was tested by analyzing Schoenfeld residuals for each exposure and covariate. Additionally, the sampling weights of the CLHLS were applied to adjust for non-response bias and the over-sampling of specific populations. Subgroup analyses were stratified by sex, age and living areas to explore the association of types of staple foods and intakes of staple foods with mild cognitive impairment within these subgroups. Additionally, a restricted cubic spline analysis with three knots placed at the 5th, 50th, and 95th percentiles was performed, using the recommended daily intake of staple foods (300 g) as a reference point, in order to assess potential non-linear relationships between staple foods intakes and MCI. Bootstrap analysis was used to assess the mediation effects of PLT and PDW on the relationships between staple foods consumption and MCI in elderly individuals.

Four sensitivity analyses were conducted. Firstly, participants with mild cognitive impairment within three years of baseline were excluded in order to reduce the potential for reverse causal relationships. Secondly, there may be region cluster due to the sample design. Therefore, a multilevel Cox proportional hazard regression model was performed with province as a random term. Thirdly, to examine the influence of death on the association of types and intakes of staple

foods with MCI, a competing risk cox proportional hazard regression models was performed with death as a competing risk factor. Fourth, we analyzed the associations of types and intakes of staple foods with mild cognitive impairment in mediation analysis sub-samples with adjustment for PLT and PDW.

A two-tailed *P*-value of ≤ 0.05 was considered statistically significant. All analyses were performed using SAS 9.4 (SAS Institute Inc., Cary, NC, United States) and R 4.3.3.

REFERENCES

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Supplementary Table S1. Baseline characteristics of all participants

Characteristics	Total samples (<i>N</i> = 21,283)	Types of staple foods			<i>P</i>
		Rice (<i>n</i> = 16,343)	Coarse cereals (<i>n</i> = 905)	Wheat (<i>n</i> = 4,035)	
Age (years, mean ± SD) ^a	85.17 ± 10.89	85.21 ± 10.86	85.58 ± 11.26	84.92 ± 10.89	0.165
Body weight (kg, mean ± SD) ^a	49.69 ± 10.87	48.80 ± 10.46	51.89 ± 11.77	52.78 ± 11.66	< 0.001
Intakes of staple foods (g/d, mean ± SD) ^a	313.79 ± 129.99	302.29 ± 123.08	356.05 ± 140.51	350.85 ± 145.06	< 0.001
Sex (<i>n</i> (%)) ^b					0.099
Male	9,822 (46.15)	7,508 (45.94)	399 (44.09)	1,915 (47.46)	
Female	11,461 (53.85)	8,835 (54.06)	506 (55.91)	2,120 (53.85)	
Ethnicity (<i>n</i> (%)) ^b					< 0.001
Han	19,871 (93.37)	15,107 (92.44)	796 (87.96)	3,968 (98.34)	
Others	1,421 (6.63)	1,236 (7.56)	109 (12.04)	67 (1.66)	
Living areas (<i>n</i> (%)) ^b					< 0.001
Urban	8,774 (41.23)	7,075 (43.29)	357 (39.45)	1,342 (33.26)	
Rural	12,509 (58.77)	9,268 (56.71)	548 (60.55)	2,693 (66.74)	
Marital status (<i>n</i> (%)) ^b					0.006
Married	7,427 (34.90)	5,610 (34.33)	307 (33.92)	1,510 (37.42)	
Divorced	115 (0.54)	98 (0.60)	3 (0.33)	14 (0.35)	
Widowed	13,497 (63.42)	10,444 (63.91)	585 (64.64)	2,468 (61.16)	
Unmarried	244 (1.15)	191 (1.17)	10 (1.10)	43 (1.07)	
Education level (<i>n</i> (%)) ^b					< 0.001
Illiterate	12,752 (59.92)	9,499 (58.12)	582 (64.31)	2,671 (66.20)	
Elementary school education	6,415 (30.14)	5,197 (31.80)	225 (24.86)	993 (24.61)	
Middle school education and above	2,116 (9.94)	1,647 (10.08)	98 (10.83)	371 (9.19)	
Living alone (<i>n</i> (%)) ^b					0.192
Yes	3,015 (14.17)	2,353 (14.40)	117 (12.93)	545 (13.51)	
No	18,268 (85.83)	13,990 (85.60)	788 (87.07)	3,490 (86.49)	
Fruit intake (<i>n</i> (%)) ^b					
Always or almost every day	2,780 (13.06)	2,079 (12.72)	120 (13.26)	581 (14.40)	< 0.001
Often	3,758 (17.66)	2,675 (16.37)	168 (18.56)	915 (22.68)	
Sometimes or occasionally	9,713 (45.64)	7,608 (46.55)	422 (46.63)	1,683 (41.71)	
Rarely or never	5,032 (23.64)	3,981 (24.36)	195 (21.55)	856 (21.21)	
Vegetable intake (<i>n</i> (%)) ^b					< 0.001
Always or almost every day	13,910 (65.36)	11,056 (67.65)	512 (56.57)	2,342 (58.04)	
Often	4,566 (21.45)	3,240 (19.83)	252 (27.85)	1,074 (26.62)	
Sometimes or occasionally	2,326 (10.93)	1,695 (10.37)	127 (14.03)	504 (12.49)	

Characteristics	Total samples (N = 21,283)	Types of staple foods			P
		Rice (n = 16,343)	Coarse cereals (n = 905)	Wheat (n = 4,035)	
Rarely or never	481 (2.26)	352 (2.15)	14 (1.55)	115 (2.85)	
Smoking status (n (%)) ^b					< 0.001
Current	4,440 (20.86)	3,348 (20.49)	176 (19.45)	916 (22.70)	
Former	3,007 (14.13)	2,233 (13.66)	109 (12.04)	665 (16.48)	
Never	13,836 (65.01)	10,762 (65.85)	620 (68.51)	2,454 (60.82)	
Alcohol consumption status (n (%)) ^b					0.994
Yes	4,837 (22.73)	3,717 (22.74)	205 (22.65)	915 (22.68)	
No	16,446 (77.27)	12,626 (77.26)	700 (77.35)	3,120 (77.32)	
Physical activity (n (%)) ^b					0.127
Current	6,984 (32.81)	5,323 (32.57)	326 (36.02)	1,335 (33.09)	
Former	1,163 (5.46)	902 (5.52)	37 (4.09)	224 (5.55)	
Never	13,136 (61.72)	10,118 (61.91)	542 (59.89)	2,476 (61.36)	
Self-reported health (n (%)) ^b					< 0.001
Poor	2,011 (9.45)	1,548 (9.47)	69 (7.62)	394 (9.45)	
Fair	6,837 (32.12)	5,523 (33.79)	255 (28.18)	1,059 (26.25)	
Good	12,435 (58.43)	9,272 (56.73)	581 (64.20)	2,582 (63.99)	
History of coronary heart disease (n (%)) ^b					0.003
Yes	1,548 (7.27)	1,135 (6.94)	78 (8.62)	335 (8.30)	
No	19,735 (92.73)	15,208 (93.06)	827 (91.38)	3,700 (91.70)	
History of diabetes (n (%)) ^b					0.023
Yes	366 (1.72)	275 (1.68)	26 (2.87)	66 (1.61)	
No	20,917 (98.28)	16,068 (98.32)	897 (97.13)	3,970 (98.39)	
History of hypertension (n (%)) ^b					< 0.001
Yes	12,026 (56.51)	9,061 (55.44)	499 (55.14)	2,466 (61.12)	
No	9,257 (43.49)	7,282 (44.56)	406 (44.86)	1,569 (38.88)	

Note: ^a These variables were compared between three groups using analysis of variance. ^b These variables were compared between three groups using chi-square test.

Supplementary Table S2. Baseline characteristics of all participants and mediation analysis sub-sample

Characteristics	Total samples (<i>N</i> = 21,283)	Mediation analysis sub-samples (<i>n</i> = 1,311)	<i>P</i>
Age (years, mean ± SD) ^a	85.17 ± 10.89	83.11 ± 11.17	< 0.001
Body weight (kg, mean ± SD) ^a	49.69 ± 10.87	51.42 ± 12.28	< 0.001
Intakes of staple foods (g/d, mean ± SD) ^a	313.79 ± 129.99	313.17 ± 135.59	0.869
Sex (<i>n</i> (%)) ^b			0.060
Male	9,822 (46.15)	640 (48.82)	
Female	11,461 (53.85)	671 (51.18)	
Ethnicity (<i>n</i> (%)) ^b			< 0.001
Han	19,871 (93.37)	1,146 (87.41)	
Others	1,421 (6.63)	165 (12.59)	
Living areas (<i>n</i> (%)) ^b			< 0.001
Urban	8,774 (41.23)	222 (16.93)	
Rural	12,509 (58.77)	1,089 (83.07)	
Marital status (<i>n</i> (%)) ^b			< 0.001
Married	7,427 (34.90)	607 (46.30)	
Divorced	115 (0.54)	6 (0.46)	
Widowed	13,497 (63.42)	684 (52.17)	
Unmarried	244 (1.15)	14 (1.07)	
Education level (<i>n</i> (%)) ^b			0.246
Illiterate	12,752 (59.92)	766 (58.43)	
Elementary school education	6,415 (30.14)	423 (32.27)	
Middle school education and above	2,116 (9.94)	122 (9.31)	
Living alone (<i>n</i> (%)) ^b			< 0.001
Yes	3,015 (14.17)	259 (19.76)	
No	18,268 (85.83)	1,052 (80.24)	
Fruit intake (<i>n</i> (%)) ^b			< 0.001
Always or almost every day	2,780 (13.06)	135 (10.30)	
Often	3,758 (17.66)	384 (29.29)	
Sometimes or occasionally	9,713 (45.64)	493 (37.60)	
Rarely or never	5,032 (23.64)	299 (22.81)	
Vegetable intake (<i>n</i> (%)) ^b			< 0.001
Always or almost every day	13,910 (65.36)	692 (52.78)	
Often	4,566 (21.45)	486 (37.07)	
Sometimes or occasionally	2,326 (10.93)	100 (7.63)	
Rarely or never	481 (2.26)	33 (2.52)	
Smoking status (<i>n</i> (%)) ^b			< 0.001
Current	4,440 (20.86)	280 (21.36)	
Former	3,007 (14.13)	114 (8.70)	
Never	13,836 (65.01)	917 (69.95)	
Alcohol consumption status (<i>n</i> (%)) ^b			0.041
Yes	4,837 (22.73)	266 (20.29)	

Characteristics	Total samples (<i>N</i> = 21,283)	Mediation analysis sub-samples (<i>n</i> = 1,311)	<i>P</i>
No	16,446 (77.27)	1,045 (79.91)	
Physical activity (<i>n</i> (%)) ^b			< 0.001
Current	6,984 (32.81)	286 (21.82)	
Former	1,163 (5.46)	70 (5.34)	
Never	13,136 (61.72)	955 (72.85)	
Self-reported health (<i>n</i> (%)) ^b			< 0.001
Poor	2,011 (9.45)	174 (13.27)	
Fair	6,837 (32.12)	476 (36.31)	
Good	12,435 (58.43)	661 (50.42)	
History of coronary heart disease (<i>n</i> (%)) ^b			0.057
Yes	1,548 (7.27)	77 (5.87)	
No	19,735 (92.73)	1,234 (94.13)	
History of diabetes (<i>n</i> (%)) ^b			0.463
Yes	366 (1.72)	19 (1.45)	
No	20,917 (98.28)	1,292 (98.55)	
History of hypertension (<i>n</i> (%)) ^b			0.251
Yes	12,026 (56.51)	762 (58.12)	
No	9,257 (43.49)	549 (41.88)	

Note: ^a These variables were compared between two groups using t-test. ^b These variables were compared between two groups using chi-square test.

Supplementary Table S3. The mediation effects of PLT and PDW on the associations of intakes of staple foods (per SD) with mild cognitive impairment ($N = 1,311$)

Mediator	Intakes of staple foods	Total Effect (95% CI)	<i>P</i>	Direct Effect (95% CI)	<i>P</i>	Indirect Effect (95% CI)	<i>P</i>	Proportion Mediated (%)	<i>P</i>
PLT	Rice	0.051 (-0.043, 0.187)	0.388	0.072 (-0.025, 0.207)	0.192	-0.021 (-0.038, -0.007)	< 0.001	-27.54	0.388
	Wheat	0.299 (0.143, 0.454)	< 0.001	0.244 (0.093, 0.402)	0.004	0.055 (0.026, 0.092)	< 0.001	18.25	< 0.001
	Total staple foods	0.141 (0.029, 0.251)	< 0.001	0.124 (0.018, 0.231)	0.016	0.017 (0.004, 0.032)	0.012	12.25	0.012
PDW	Rice	0.059 (-0.038, 0.199)	0.356	0.080 (-0.024, 0.218)	0.176	-0.021 (-0.039, -0.007)	< 0.001	-26.15	0.356
	Wheat	0.298 (0.134, 0.444)	0.004	0.289 (0.128, 0.432)	0.004	0.009 (-0.004, 0.027)	0.172	2.88	0.168
	Total staple foods	0.132 (0.026, 0.247)	0.004	0.137 (0.031, 0.253)	0.004	-0.005 (-0.015, 0.006)	0.400	-3.53	0.404

Note: ^a Age, sex, body weight, ethnicity, living areas, marital status, education level, living alone, fruit intake, vegetable intake, smoking status, alcohol consumption status, physical activity, self-reported health, history of coronary heart disease, history of diabetes, and history of hypertension were adjusted

PLT: platelet count, PDW: platelet distribution width.

Supplementary Table S4. Associations of types and intakes of staple foods with mild cognitive impairment excluding participants newly diagnosed with mild cognitive impairment within three years after baseline ($N = 18,754$)^a

Subgroups	HR (95% CI)	P
Types of staple foods		
Rice	1.000	
Coarse cereals	0.943 (0.675, 1.319)	0.733
Wheat	1.231 (1.062, 1.427)	0.006
Intakes of staple foods		
Rice	1.017 (0.938, 1.102)	0.681
Coarse cereals	1.010 (0.949, 1.076)	0.746
Wheat	1.079 (1.002, 1.163)	0.045
Total staple foods	1.034 (0.976, 1.096)	0.259

Note:^a Age, sex, body weight, ethnicity, living areas, marital status, education level, living alone, fruit intake, vegetable intake, smoking status, alcohol consumption status, physical activity, self-reported health, history of coronary heart disease, history of diabetes, and history of hypertension were adjusted

Supplementary Table S5. Associations of types and intakes of staple foods with mild cognitive impairment using multilevel model with province as a random term ($N = 21,283$)^a

Subgroups	HR (95% CI)	P
Types of staple foods		
Rice	1.000	
Coarse cereals	1.100 (0.897, 1.350)	0.344
Wheat	1.187 (1.039, 1.357)	0.014
Intakes of staple foods		
Rice	1.015 (0.949, 1.085)	0.653
Coarse cereals	1.034 (0.993, 1.077)	0.103
Wheat	1.071 (1.010, 1.136)	0.024
Total staple foods	1.033 (0.987, 1.081)	0.158

Note:^a Age, sex, body weight, ethnicity, living areas, marital status, education level, living alone, fruit intake, vegetable intake, smoking status, alcohol consumption status, physical activity, self-reported health, history of coronary heart disease, history of diabetes, and history of hypertension were adjusted

Supplementary Table S6. Associations of types and intakes of staple foods with mild cognitive impairment from competing risk model with death as a competing risk factor ($N = 21,283$)

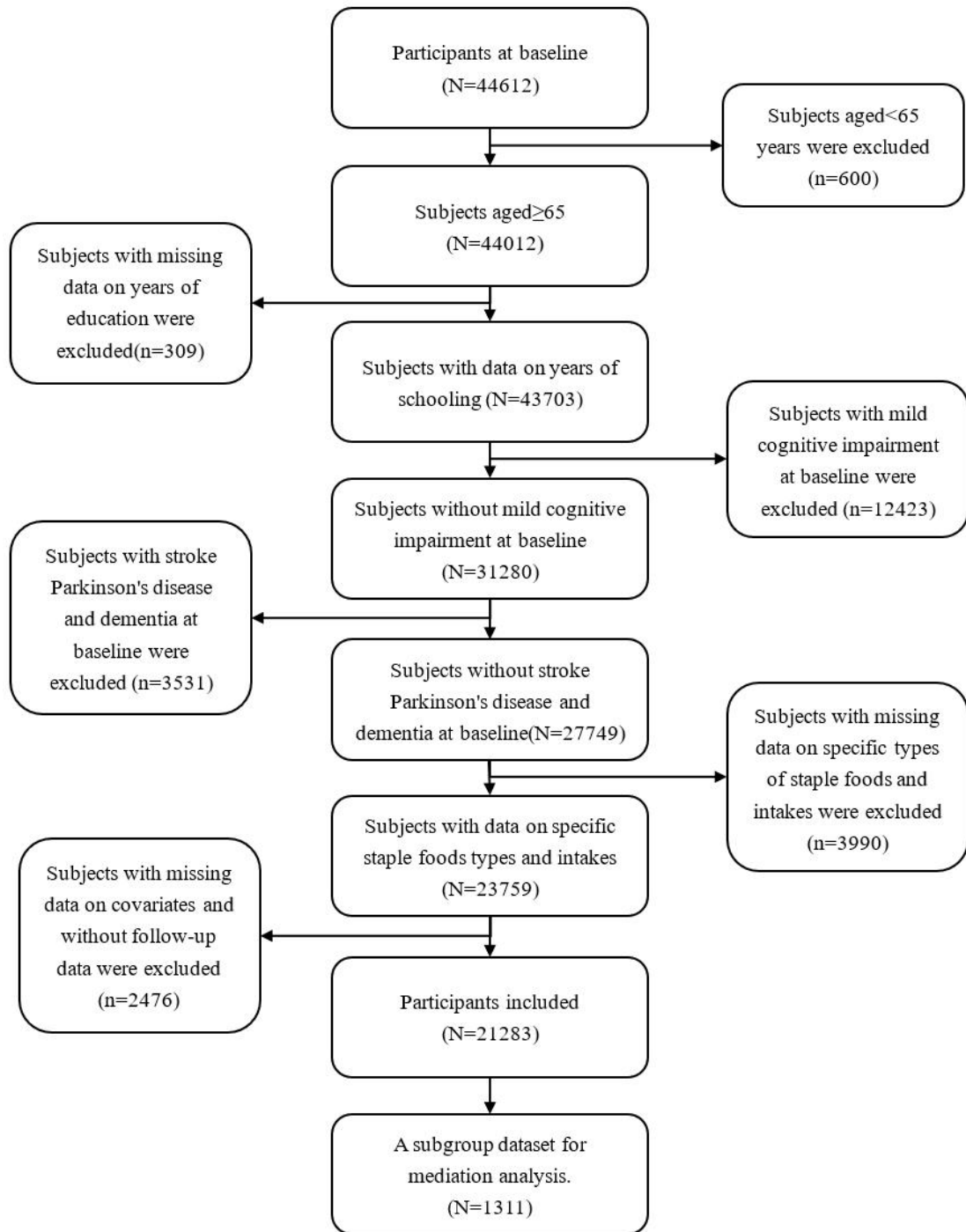
Subgroups	HR (95% CI)	P
Types of staple foods		
Rice	1.000	
Coarse cereals	1.096 (0.975, 1.232)	0.125
Wheat	1.126 (1.055, 1.201)	< 0.001
Intakes of staple foods		
Rice	1.039 (1.003, 1.077)	0.034
Coarse cereals	1.029 (1.003, 1.055)	0.027
Wheat	1.072 (1.037, 1.108)	< 0.001
Total staple foods	1.044 (1.017, 1.071)	0.001

Note: ^a Age, sex, body weight, ethnicity, living areas, marital status, education level, living alone, fruit intake, vegetable intake, smoking status, alcohol consumption status, physical activity, self-reported health, history of coronary heart disease, history of diabetes, and history of hypertension were adjusted.

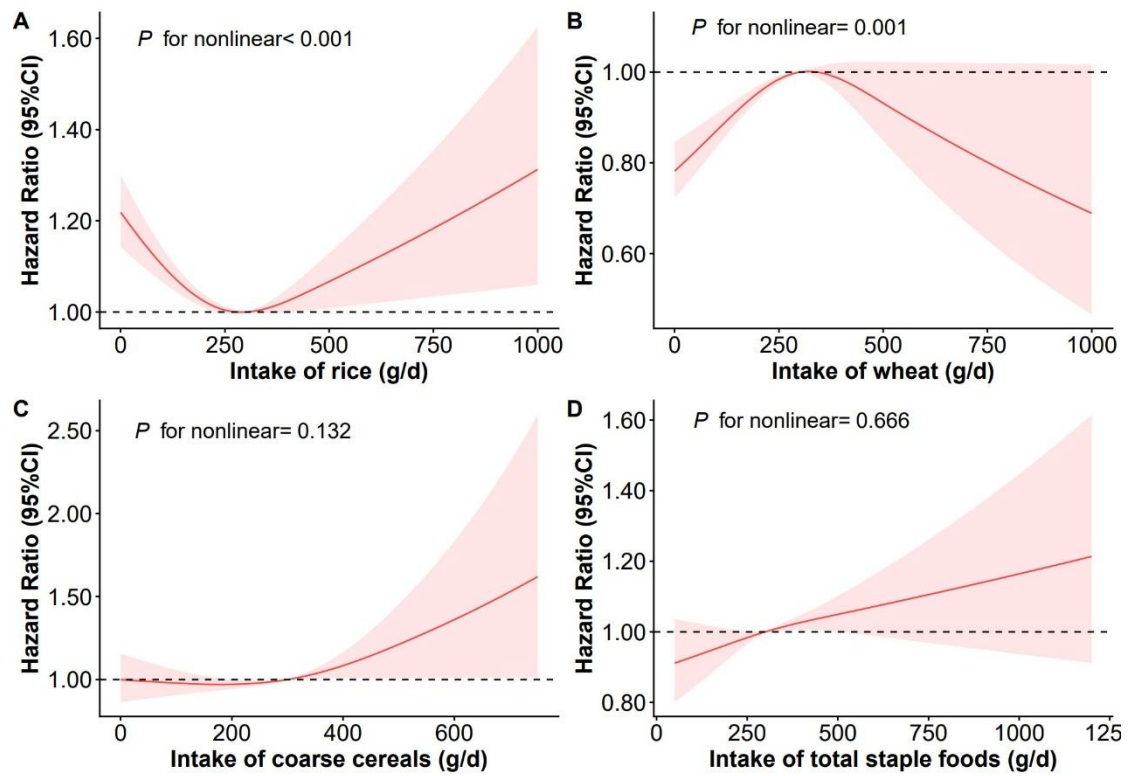
Supplementary Table S7. Associations of types and intakes of staple foods with mild cognitive impairment in the sub-samples of mediation analysis ($N = 1,311$) ^a

Subgroups	HR (95% CI)	P
Types of staple foods		
Rice	1.000	
Wheat	2.846 (1.462, 5.541)	0.002
Intakes of staple foods		
Rice	0.913 (0.713, 1.168)	0.468
Wheat	1.591 (1.182, 2.142)	0.002
Total staple foods	1.160 (0.913, 1.474)	0.224

Note: ^a Age, sex, body weight, ethnicity, living areas, marital status, education level, living alone, fruit intake, vegetable intake, smoking status, alcohol consumption status, physical activity, self-reported health, history of coronary heart disease, history of diabetes, history of hypertension, platelet count and platelet distribution width were adjusted



Supplementary Figure S1. Flowchart of the study population.



Supplementary Figure S2. The non-linear relationship between staple food intake and mild cognitive impairment. A) indicates intake of rice; B) indicates intake of wheat; C) indicates intake of coarse cereals; D) indicates intake of total staple foods. Age, sex, body weight, ethnicity, living areas, marital status, education level, living alone, fruit intake, vegetable intake, smoking status, alcohol consumption status, physical activity, self-reported health, history of coronary heart disease, history of diabetes, and history of hypertension were adjusted.