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Quantity and variety of fruit and vegetable intake in midlife and cognitive impairment in late life: a prospective cohort study

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Abstract

There is limited evidence on fruit and vegetable intake in relation to cognitive function. This study aimed to evaluate the associations of quantity and variety in fruit and vegetable intake in midlife with cognitive impairment in late life. We used data from 16 737 participants of the Singapore Chinese Health Study, a population-based cohort study. The participants provided dietary data at recruitment at median age of 52·5 (range: 45–74) years and also participated in the third follow-up interview 20 years later at median age of 72·2 (range: 61–96) years. Quantity and variety of fruits and vegetables consumed at baseline were measured using a validated FFQ. Cognitive impairment at the third follow-up was defined using a Singapore-modified version of Mini-Mental State Examination. About 14·3 % participants had cognitive impairment. In multivariable logistic regression models, comparing extreme quartiles for intake of fruits and vegetables combined, the OR (95 % CI) associated with cognitive impairment was 0·83 (95 % CI: 0·73, 0·95; *P*-trend = 0·006) for quantity and 0·76 (95 % CI: 0·67, 0·87; *P*-trend< 0·001) for variety scores. Independently, those with increased variety of fruit intake or higher quantity of vegetable intake also had significantly 22 % and 15 % reduced odds of cognitive impairment, respectively. Finally, compared with those with low intake for both quantity and variety, those with both high quantity and variety for fruits and vegetables had 23 % reduction in odds of cognitive impairment. In conclusion, increase in quantity and variety of fruits and vegetables in midlife may reduce the risk of cognitive impairment in late life.

Key words: Fruit: Vegetable: Cognitive function: Cohort study: Chinese: Diet

As a result of global population ageing, the number of people living with dementia will almost double every 20 years and is estimated to reach 131·5 million in 2050 worldwide[1]. A healthful diet is among the first steps to preserve cognitive function in ageing[2]. Dietary guidelines from the WHO and many countries have recently emphasised that, on top of eating enough, increasing the variety in the consumption of fruits and vegetables is also important in improving health[3–5]. Previous studies have revealed that a higher consumption of fruits and vegetables is likely to reduce the incidence of dementia[6,7]. However, the independent effect of these two food groups on cognitive function has yet to be established[8]. Besides, there is evidence that some specific subtypes of fruits and vegetables, such as green leafy vegetables[9,10] and berries[11], are associated with cognitive function or risk of dementia. However, very few studies have reported a comprehensive examination of subtypes of fruits and vegetables[10,12]. Moreover, it is unclear whether increasing the variety in fruits and vegetables, independent of the quantity of intake, could further prevent cognitive impairment. Finally, the types of fruits and vegetables consumed commonly in

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different populations may vary due to sociocultural factors such as religion, traditional beliefs and food preferences, as well as socio-economic factors such as cost, availability and ease of accessibility, which are all factors that can influence the diversity in fruits and vegetables between Asian and Western populations[13]. Given that most of previous studies were done in Western countries, studies among understudied Asian populations are necessary.

In this study, we investigated the associations of fruits and vegetables at midlife, in quantity as well as in variety, with cognitive impairment in late life in a population-based cohort of Chinese residing in Singapore.

Material and methods

Study population

The Singapore Chinese Health Study is a population-based cohort study established between 1993 and 1998 by a recruitment of 63 257 participants aged 45–74 years from 2 major dialect groups of Chinese (the Hokkiens and the Cantonese) in Singapore. Face-to-face interviews were conducted at baseline to collect dietary data and other information. Details of the study design have been reported previously[14,15].

The participants were contacted over the phone to update information (but not including diet) for two follow-up interviews in 1999–2004 and 2006–2010. The third follow-up interview was conducted in-person among surviving participants aged 61–96 years (n 45 109) from 2014 but was terminated prematurely in February 2016 due to limited funding. A total of 17 107 participants were successfully interviewed at their homes, and cognitive function was evaluated for the first time in this visit. For the main analysis, those with incomplete cognitive examination (n 159) and those with implausible energy intake (<2508 or >12 540 kJ/d for women and <2926 or >15 466 kJ/d for men; n 211) from the dietary examination at baseline were excluded, leaving 16 737 participants in the final analyses (Fig. 1).

This study was conducted according to the guidelines laid down in the Declaration of Helsinki, and all procedures involving human subjects were approved by the Institutional Review Board at the National University of Singapore (ethics number: NUS-IRB Reference Code: L04-026). Written informed consent was obtained from all subjects.

Dietary exposures and covariates

At baseline recruitment, home visits were conducted to interview the participants and collect information about demographics, lifestyle factors, usual dietary habits and medical history using structured questionnaires. A medical history of cancer was further verified by linkage to the nationwide Singapore Cancer Registry database.

Dietary data were collected using a 165-item semi-quantitative FFQ. This questionnaire was subsequently validated among a subset of 810 participants in this cohort, and details have been described elsewhere[14,16,17]. A total of 14 fruits and 25 vegetables were included (online Supplemental Table 1).

We summated quantity (weight in grams) of fruits and vegetables for each participant by including the relevant food items consumed alone and from mixed dishes or juices as previously described[16,17]. Fruits were further categorised as low-glycaemic-index fruits, moderate-glycaemic-index fruits, and high-glycaemic-index fruits according to carbohydrate quality. Vegetables were categorised as light green vegetables, dark green vegetables, cruciferous vegetables, yellow-orange vegetables, tomato products and mushrooms[16,17]. All food items were adjusted for total energy intake using the residual method[18]. Specific subgroups have been related to risk of other diseases such as diabetes in our previous studies[16,17], and categorisations of individual fruits/vegetables into these various subgroups are shown in Supplemental Table 1. In keeping with other research of the same topic[10,19], white potatoes were not counted as a vegetable in this study because they are nutritionally high in starchy carbohydrates.

The variety scores of fruits and vegetables were calculated by summing up the number of items eaten at least once a month in the FFQ, which is in line with previous studies[20]. The total score theoretically ranged from 0 to 39 (up to fourteen for fruits and twenty-five for vegetables).

Cognition measurement

Cognitive function was measured at participants' homes by trained interviewers using a Singapore-modified version of Mini-Mental State Examination (SM-MMSE), which has previously been validated in the Singapore population[21]. The total score of this test ranged from 0 to 30, with higher scores indicating better cognition. Given that more than 60 % of the participants had no formal education or only had primary school education, education-specific cut points (less than 18 scores for people with no formal education; 21 scores for primary school education and 25 scores for secondary school or higher education) from the Shanghai Dementia Survey were used to define cognitive impairment, since the participants in this Shanghai study had comparable education levels as those in our study[22].

Statistical analysis

Reasonably, people who consumed a wider variety of fruits and vegetables also consumed a higher quantity of these food items (the Spearman correlation coefficients between variety and quantity were 0·47 for fruits and 0·39 for vegetables, $P < 0·001$, see online Supplemental Table 2). To evaluate the association of variety with cognitive impairment independent of quantity, we regressed the variety scores on the absolute intake quantities to derive the residuals of variety scores and then added a constant (the predicted variety score for the mean absolute intake quantity of the study population) to the residuals to provide an intuitive sense of variety scores[19,23]. Expectantly, the Spearman correlation coefficients between variety scores and quantity were reduced to 0·11 for fruits and 0·08 for vegetables after adjustment (see online Supplemental Table 2).

The baseline characteristics across the quartiles of quantity and variety scores in total fruit and vegetable intake were

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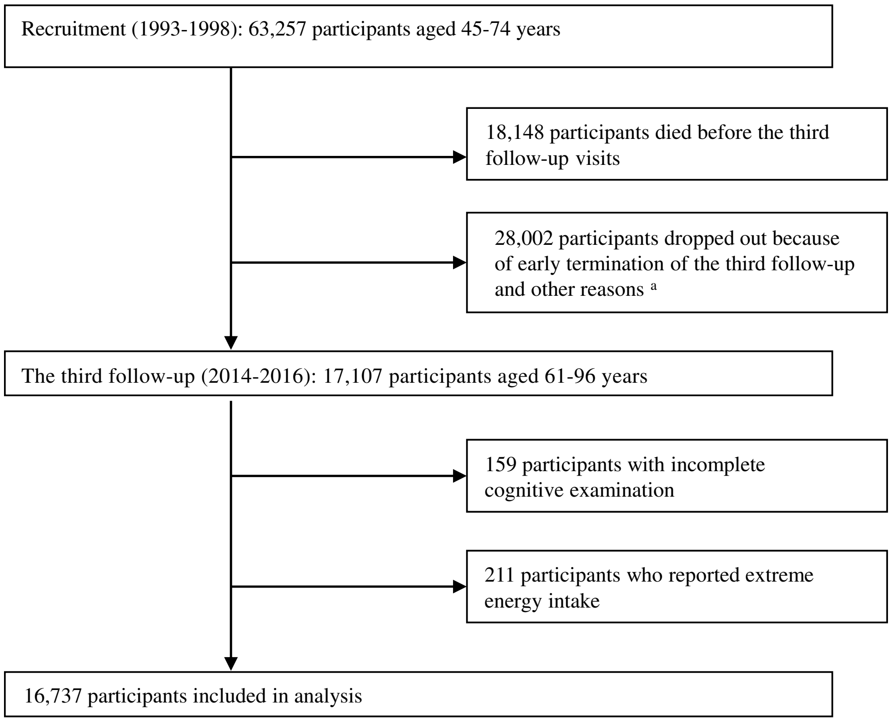

Fig. 1. Flow chart of the inclusion of participants in the analyses. [a]The third follow-up was terminated and only conducted for 2 years, while the original schedule was for 5 years. Besides, we sent 1–2 invitation letters to the subjects before the third follow-up investigation, some participants could not be contacted due to reasons such as moving out of the government housing estates, some were unable to participate in the third follow-up visit due to serious diseases, and severe cognitive impairment or clinically diagnosed dementia.

compared using the χ^2 test for categorical variables or the Kruskal–Wallis rank test for continuous variables. The pairwise correlations between fruits and vegetables and with other foods were assessed using the Spearman correlation coefficients. Multivariable logistic regression models were performed to calculate OR and 95 % CI of cognitive impairment according to quartiles of quantity and variety in fruit and vegetable intake. In model 1, we adjusted for age at cognitive assessment (continuous) and a comprehensive list of baseline covariates: sex, education level (no formal education, primary school, secondary school, or diploma/college and higher), marital status (married, separated/divorced, widowed or never married), dialect group (Hokkien or Cantonese), BMI (<18·5, 18·5–22·9, 23·0–27·4 or ≥27·5 kg/m^2), total energy intake (kJ/d), cigarette smoking status (never, former or current smokers), alcohol consumption (never/monthly, weekly or daily drinkers), physical activity level (<0·5, 0·5–3·9 or ≥4·0 h of moderate or vigorous activities per week), sleep duration (≤5, 6, 7, 8 or ≥9 h/d), baseline history of hypertension, diabetes, heart attack, stroke and cancer (yes or no), weekly supplement use (yes or no) and dietary intakes of red meats, poultry, fresh fish/shellfish, preserved fish/shellfish, dairy products and nuts (g/d). The dietary factors in the models were chosen based on their significant associations with cognitive impairment in our previous studies[24–26]. In model 2, fruit intake and vegetable intake were mutually adjusted to examine their independent associations with cognitive impairment. Linear trend was assessed by including median values of quartile categories as continuous variables in the models. We further conducted a number of sensitivity analyses to test the robustness of our results: (1) excluding 4155 participants with cancer, CVD, diabetes or hypertension at baseline; (2) excluding 896 participants aged 65 years and older at baseline; (3) using the commonly used cut point of <24 to define cognitive impairment[27] and (4) excluding 874 participants with a medical history of stroke at the third follow-up. The dose–response relationship between the quantity of fruit and vegetable intake and cognitive impairment was additionally evaluated using restricted cubic spline models. Generalised linear models were also performed to calculate the least-squares mean SM-MMSE scores and differences across quartiles. Finally, we categorised the participants into four groups by using the median value to define high and low categories for quantity and variety scores for fruits and vegetables combined, and for fruits and vegetables separately. We used this variable to study the joint effect of quantity and variety in intake of fruits and vegetables in association with cognitive impairment. To evaluate the potential effect of loss to follow-up, our previous studies have compared the baseline characteristics between participants who attended and who did not attend the third follow-up visits. Here, we further compared the intake levels of fruits and vegetables using the Kruskal–Wallis rank test.

All statistical analyses were performed using SAS (version 9.4; SAS Institute, Inc.).

Results

The median ages of participants (*n* 16 737) were 52.5 years at baseline and 72.2 years at assessment of cognition. The median (interquartile range) intake of total fruits and vegetables combined was 308.4 (220.6–419.4) g/d for quantity and 24.6 (20.6–28.1) for variety scores. Participants with higher quantity and wider variety of intake in fruits and vegetables combined were more likely to be women, to have had higher educational levels, and to eat more fresh fish/shellfish, dairy products and nuts. Meanwhile, they were less likely to smoke or drink (Table 1). The Spearman correlation coefficients for pairwise comparisons of fruit and vegetables with other food groups were generally low (online Supplemental Table 3).

A total of 2397 (14·3 %) participants were identified to have cognitive impairment after 20 years of follow-up. As shown in Table 2, a higher quantity of intake in fruits and vegetables combined was associated with lower odds of cognitive impairment (highest *v.* lowest quartile: OR 0·83 (95 % CI: 0·73, 0·95; *P*-trend = 0·006)). When fruits and vegetables were examined separately and adjusted for each other, higher quantities of intake in vegetables (highest *v.* lowest quartile: OR 0·85 (95 % CI: 0·74, 0·98; *P*-trend = 0·02)) and fruits (highest *v.* lowest quartile: OR 0·91 (95 % CI: 0·79, 1·04; *P*-trend =0·12)) were independently associated with lower odds of cognitive impairment, although the risk estimate of fruit intake was no longer statistically significant after adjusting for vegetable intake in model 2. Higher variety score of fruits and vegetables combined was also associated with lower odds of cognitive impairment (highest *v.* lowest quartile: OR 0·76 (95 % CI: 0·67, 0·87; *P*-trend < 0·001)). When examined separately and mutually adjusted for each other, higher variety scores in intake of fruits (highest *v.* lowest quartile: OR 0·78 (95 % CI:0·68, 0·90; *P*-trend < 0·001)) and of vegetables (highest *v.* lowest quartile: OR 0·87 (95 % CI: 0·76, 1·00; *P*-trend =0·08)) were independently associated with lower odds of cognitive impairment, although the risk estimate of vegetable intake was of borderline significance after adjusting for fruit intake in model 2. The findings were robust in various sensitivity analyses (online Supplemental Table 4). When we conducted the analyses for subgroups, inverse associations were observed for moderate-glycaemic-index fruits, light-green vegetables and mushrooms (online Supplemental Table 5).

As shown in Fig. 2, inverse association (OR (95 % CI) per SD increment = 0·91 (95 % CI: 0·86, 0·96; *P* < 0·001)) was most prominently observed at lower levels of fruit intake (0–300 g/d), and the OR plateaued off to become non-significant estimates at higher intake levels (*P*-overall = 0·008, *P*-nonlinearity = 0·005). Conversely, total vegetable intake was linearly associated with cognitive impairment throughout the examined range in this cohort (*P*-overall = 0·02, *P*-nonlinearity = 0·64) and the OR (95 % CI) per SD increment was 0·93 (95 % CI: 0·88, 0·98; *P* = 0·007).

As shown in Table 3, differences in least-squares means of SM-MMSE scores comparing extreme quartiles in intake quantity were 0·21 (*P*-trend = 0·003) for total intake of fruits and vegetables, and 0·23 (*P*-trend < 0·001) for intake of vegetables, which were equivalent to 1·2 and 1·3 years younger in cognition when compared with the effect estimate for age in the same model (β = -0·18), respectively. Differences in least-squares means of SM-MMSE scores comparing extreme quartiles of variety were 0·43 for total fruits and vegetables, 0·39 for fruits and 0·23 for vegetables (all *P*-trend < 0·001), which were equivalent to 2·4, 2·2 and 1·3 years younger in cognition, respectively.

The median quantity for intake of fruits and vegetables combined and separately for fruits and vegetables were 308·4 g/d, 194·0 g/d and 105·3 g/d, respectively. Correspondingly, the median variety scores were 24·6 for fruits and vegetables combined, 6·7 for fruits and 17·8 for vegetables. We used these cut-offs to categorise participants into groups with high (above median) and low (below median) scores. As shown in Table 4, compared with participants with low scores in variety and quantity, those who were high in both variety and quantity had the lowest odds of cognitive impairment, and the results were the same for total fruits and vegetables, and for fruits and vegetables separately.

Discussion

In this study conducted among Singapore Chinese, having higher quantity and wider variety in the consumption of fruits and vegetables in midlife was associated with lower odds of cognitive impairment in late life. The joint association of higher quantity and variety with lower odds of cognitive impairment was observed for fruits and vegetables, emphasising the importance of a higher intake of fruits and vegetables in both quantity and variety simultaneously.

Fruit and vegetables are the major source of vitamins and phytochemicals with potent bioactivity[28], and their health benefits regarding their associations with cognitive-related outcomes, such as cognitive impairment and dementia, have attracted much attention[7,29]. Our finding was consistent with the previous studies that higher quantity of total fruit and vegetable intake was associated with lower odds of cognitive impairment. Considering fruits and vegetables separately, inverse association was observed for vegetable intake in many studies from Western countries[9,30,31], while the association between fruit intake and cognitive function was less clear from existing evidence[8]. In our study, an inverse linear association was observed between quantity of vegetable intake and odds of cognitive impairment, which concurs with the associations observed in populations of Western countries[9,30,31]. Folate and antioxidants, both occurring naturally with great levels in green leafy vegetables, have been linked to better cognition and lower risk of dementia in observational studies[32,33]. Consistently, light-green vegetables had a significant inverse association with cognitive impairment in this study. The Shiitake mushrooms are a feature of many Asian cuisines. Results from the current study and the Ohsaki Cohort 2006 Study in Japan[34] both suggested that a greater consumption of mushroom was significantly associated with a lower risk of incident dementia, although studies in the USA did not observe significant associations[10,31]. The diversity in intake levels may account for the inconsistent findings between Asian and Western populations.

As for fruits, our findings showed an inverse association between the quantity of fruit intake and cognitive impairment,

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Table 1. Characteristics of the study population by quartiles of quantity and variety in total FV intake (Median values and interquartile ranges or frequencies and percentages)

	Quantity of total FV intake							Variety of total FV intake				
	All		Q1		Q4			Q1		Q4		
	Median or frequency	Interquartile range or percentage	Median or frequency	Interquartile range or percentage	Median or frequency	Interquartile range or percentage	*P*	Median or frequency	Interquartile range or percentage	Median or frequency	Interquartile range or percentage	*P*
n	16 737		4184		4184			4184		4184		
Age at baseline, years	52·5	48·2–57·7	53·3	48·4–58·6	51·8	48·1–56·7	<0·001	52·5	48·2–58·2	52·3	48·1–57·1	0·003
Age at cognitive test, years	72·2	68·0–77·3	73·2	68·2–78·2	71·5	67·7–76·5	<0·001	72·0	67·8–77·4	72·2	68·2–77·2	0·14
BMI, kg/m^2	23·0	21·1–24·8	23·0	20·8–24·5	23·1	21·2–25·0	<0·001	23·1	21·1–24·8	23·0	21·1–24·7	0·02
Female	9903	59·2	1892	45·2	2667	63·7		2346	56·1	2512	60·0	<0·001
Father dialect												
Cantonese	8341	49·8	1924	46·0	2227	53·2	<0·001	2027	48·5	2086	49·9	0·04
Hokkien	8396	50·2	2260	54·0	1957	46·8		2157	51·6	2098	50·1	
Education												
No formal education	3137	18·7	935	22·4	570	13·6	<0·001	879	21·0	667	15·9	<0·001
Primary school	7504	44·8	2050	49·0	1704	40·7		1900	45·4	1839	44·0	
Secondary school	4851	29·0	1005	24·0	1483	35·4		1158	27·7	1314	31·4	
Higher education	1245	7·4	194	4·6	427	10·2		247	5·9	364	8·7	
Current smoker	2182	13·0	1003	24·0	310	7·4	<0·001	714	17·1	474	11·3	<0·001
Daily drinker	454	2·7	235	5·6	60	1·4	<0·001	156	3·7	94	2·3	<0·001
6–8 h of sleep	14 470	86·5	3554	84·9	3623	86·6	0·01	3434	82·1	3787	90·5	<0·001
<0·5 h of physical activity	10 593	63·3	2768	66·2	2357	56·3	<0·001	2837	67·8	2463	58·9	<0·001
Weekly supplement use	1285	7·7	209	5·0	474	11·3	<0·001	322	7·7	328	7·8	0·38
Hypertension	3244	19·4	714	17·1	874	20·9	<0·001	875	20·9	741	17·7	0·002
Diabetes	817	4·9	190	4·5	201	4·8	0·59	232	5·5	155	3·7	<0·001
Hearth attack	351	2·1	86	2·1	104	2·5	0·1866	106	2·5	80	1·9	0·15
Stroke	82	0·5	22	0·5	23	0·6	0·8412	34	0·8	13	0·3	0·0022
Cancer	318	1·9	63	1·5	81	1·9	0·17	83	2·0	83	2·0	0·87
Total energy intake, kJ/d	6291·7	5068·7–7870·5	6938·4	5440·3–8606·6	6564·3	5378·0–8128·0	<0·001	6155·9	4803·7–7888·1	6340·6	5184·9–7846·3	<0·001
Quantity of total FV intake, g/d	308·4	220·6–419·4	165·0	118·0–196·2	520·6	460·7–618·7	<0·001	283·3	183·8–427·3	319·6	247·7–403·8	<0·001
Quantity of fruit intake, g/d	194·0	121·7–289·4	79·5	43·1–110·6	383·3	321·0–470·3	<0·001	183·5	99·9–314·8	199·5	141·9–271·9	<0·001
Quantity of vegetable intake, g/d	105·3	79·3–137·7	75·7	55·8–96·5	140·4	106·4–183·9	<0·001	90·1	64·3–124·1	111·6	88·3–141·3	<0·001
Variety score of total FV intake	24·6	20·6–28·1	23·0	18·9–26·7	24·4	20·5–27·7	<0·001	17·9	15·5–19·4	30·5	29·2–32·3	<0·001
Variety score of fruit intake	6·7	4·9–8·5	5·8	4·0–7·6	6·7	4·9–8·5	<0·001	4·4	3·1–5·6	9·3	8·2–10·6	<0·001
Variety score of vegetable intake	17·8	15·0–20·3	16·8	13·8–19·7	18·0	15·3–20·3	<0·001	13·1	11·2–14·8	21·5	20·1–22·9	<0·001
Red meat, g/d	28·9	19·6–39·7	31·0	19·7–43·9	25·0	15·7–35·0	<0·001	27·8	18·3–39·1	29·8	20·7–40·6	<0·001
Poultry, g/d	19·5	11·8–28·5	19·2	11·1–29·3	17·8	9·9–26·6	<0·001	17·9	10·5–27·3	20·9	13·3–29·5	<0·001
Fresh fish and shellfish, g/d	51·2	36·2–67·8	47·2	32·0–63·6	52·7	36·1–71·6	<0·001	48·1	33·4–66·4	51·6	37·5–67·5	<0·001
Preserved fish and shellfish, g/d	2·2	1·1–4·1	2·1	0·8–3·9	2·1	0·9–4·1	<0·001	1·9	0·8–3·5	2·6	1·4–4·5	<0·001
Dairy products, g/d	30·1	12·4–84·8	24·6	5·0–60·7	32·1	12·7–109·0	<0·001	30·1	11·5–68·0	30·5	13·6–95·1	0·03
Nuts, g/d	2·0	0·9–3·4	1·7	0·5–3·0	2·0	0·9–3·6	<0·001	1·8	0·7–3·2	2·1	1·1–3·5	<0·001

FV, fruit and vegetable.

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Table 2. Multivariable-adjusted odds ratios for cognitive impairment by quartiles of fruit and vegetable (FV) intake (Odds ratios and 95 % confidence intervals)

	Quantity and variety of FV intake							
		Q2		Q3		Q4		
	Q1	OR	95 % CI	OR	95 % CI	OR	95 % CI	*P*-trend*
Quantity of total FV intake								
Median, g/d	164·98	264·89		356·47		520·64		
Case/*n*	674/4184	607/4184		562/4185		554/4184		
Model 1†	1·00	0·90	0·79, 1·02	0·82	0·72, 0·93	0·83	0·73, 0·95	0·006
Quantity of fruit intake								
Median, g/d	76·30	158·84		235·08		383·44		
Case/*n*	665/4184	612/4184		550/4185		570/4184		
Model 1†	1·00	0·93	0·82, 1·06	0·84	0·74, 0·96	0·88	0·77, 1·00	0·04
Model 2‡	1·00	0·95	0·83, 1·08	0·86	0·75, 0·99	0·91	0·79, 1·04	0·12
Quantity of vegetable intake								
Median, g/d	62·62	92·56		119·41		169·11		
Case/*n*	653/4184	623/4184		582/4185		539/4184		
Model 1†	1·00	0·92	0·81, 1·05	0·87	0·76, 0·99	0·83	0·72, 0·95	0·006
Model 2‡	1·00	0·93	0·82, 1·06	0·88	0·77, 1·01	0·85	0·74, 0·98	0·02
Variety score of total FV intake								
Median	17·87	22·76		26·31		30·46		
Case/*n*	697/4184	577/4184		554/4185		569/4184		
Model 1†	1·00	0·77	0·68, 0·88	0·75	0·66, 0·86	0·76	0·67, 0·87	<0·001
Variety score of fruit intake								
Median	3·69	5·85		7·58		9·76		
Case/*n*	736/4184	582/4184		550/4185		529/4184		
Model 1†	1·00	0·81	0·71, 0·92	0·80	0·70, 0·91	0·75	0·66, 0·86	<0·001
Model 2‡	1·00	0·82	0·73, 0·93	0·83	0·72, 0·94	0·78	0·68, 0·90	<0·001
Variety score of vegetable intake								
Median	12·94	16·53		19·07		21·95		
Case/*n*	651/4184	566/4184		584/4185		596/4184		
Model 1†	1·00	0·81	0·71, 0·92	0·83	0·73, 0·94	0·81	0·71, 0·92	0·002
Model 2‡	1·00	0·84	0·74, 0·95	0·87	0·76, 1·00	0·87	0·76, 1·00	0·08

* Linear trend was assessed by including median values of intake groups as continuous variables in models.
† Model 1 was adjusted for age at cognitive assessment, sex, level of education, marital status, dialect group, BMI, total energy intake, cigarette smoking status, alcohol consumption, physical activity level, sleep durations, baseline history of hypertension, diabetes, heart attack, stroke, cancer, dietary intakes of red meat, poultry, dairy products, nuts, fresh fish/shellfish, preserved fish/shellfish and weekly supplement use.
‡ In model 2, fruit intake and vegetable intake were mutually adjusted in their respective models.

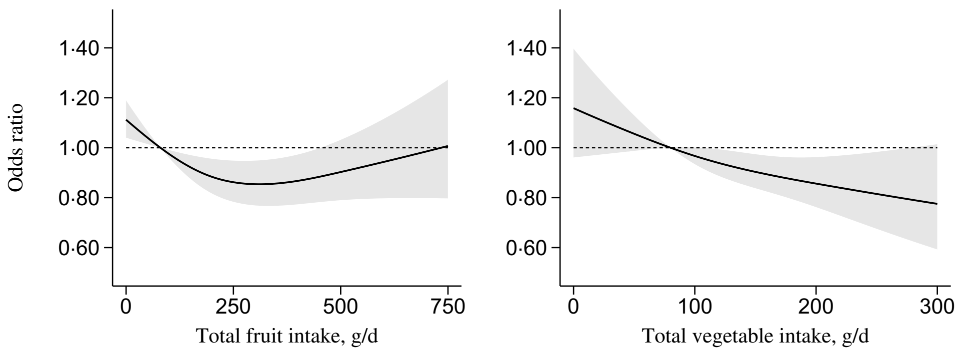

Fig. 2. Dose-dependent associations of quantities in fruit and vegetable intake with cognitive impairment. Notes: Covariates in the restricted cubic spline regression model were the same as in the final models of Table 2. Panel A. Nonlinear association was observed for fruit intake (*P*-overall = 0·008, *P*-nonlinearity = 0·005). For fruit intake within the range of 0–300 g/d, the OR (95 % CI) per SD increment was 0·91 (0·86, 0·96; *P* < 0·001). Panel B. Linear inverse association was observed for vegetable intake (*P*-overall = 0·02, *P*-nonlinearity = 0·64) and the OR (95 % CI) per SD increment of vegetable intake was 0·93 (0·88, 0·98; *P* = 0·007).

although the association was no longer statistically significant after adjusting for vegetables. Nevertheless, dose–response analyses suggested that the association between quantity of fruit intake and cognitive impairment was not entirely linear and the odds appeared to decrease linearly for fruit intake up to about 300 g/d. Consistent with our study, a large cohort study among 27 842 US male health professionals, with an average fruit intake of 1·7 servings/d (about 136 g/d) and more than 20 years of follow-up, also found a weak association between higher quantity in fruit intake and lower odds of poor cognitive function after controlling for vegetable intake[10]. Similar results were also observed in two Chinese studies[35,36]. A study among Chinese population in Hong Kong revealed that the daily fruit consumption of at least two servings (160 g/d) was inversely associated

Table 3. Least-squares means of SM-MMSE score by quartiles of fruit and vegetable (FV) intake (Least-squares mean values and 95 % confidence intervals)

		SM-MMSE score*				
Quartiles	Median intake	Least-squares means	95 % CI	*β*	*P*	*P*-trend†
Quantity of total FV intake, g/d						0·003
Q1	164·98	24·45	24·00, 24·90			
Q2	264·89	24·59	24·14, 25·04	0·14	0·04	
Q3	356·47	24·74	24·28, 25·19	0·29	<0·001	
Q4	520·64	24·65	24·20, 25·11	0·21	0·004	
Quantity of fruit intake, g/d						0·18
Q1	76·30	24·51	24·06, 24·96			
Q2	158·84	24·62	24·16, 25·07	0·11	0·13	
Q3	235·08	24·71	24·26, 25·17	0·20	0·004	
Q4	383·44	24·61	24·16, 25·07	0·10	0·16	
Quantity of vegetable intake, g/d						<0·001
Q1	62·62	24·47	24·02, 24·92			
Q2	92·56	24·57	24·12, 25·02	0·10	0·15	
Q3	119·41	24·71	24·26, 25·17	0·24	<0·001	
Q4	169·11	24·70	24·25, 25·15	0·23	0·002	
Variety score of total FV intake						<0·001
Q1	17·87	24·38	23·94, 24·83			
Q2	22·76	24·73	24·28, 25·19	0·35	<0·001	
Q3	26·31	24·88	24·43, 25·34	0·50	<0·001	
Q4	30·46	24·81	24·36, 25·27	0·43	<0·001	
Variety score of fruit intake						<0·001
Q1	3·69	24·43	23·98, 24·88			
Q2	5·85	24·83	24·38, 25·28	0·40	<0·001	
Q3	7·58	24·72	24·27, 25·18	0·29	<0·001	
Q4	9·76	24·83	24·37, 25·28	0·39	<0·001	
Variety score of vegetable intake						<0·001
Q1	12·94	24·52	24·07, 24·97			
Q2	16·53	24·72	24·27, 25·17	0·20	0·004	
Q3	19·07	24·83	24·37, 25·28	0·31	<0·001	
Q4	21·95	24·75	24·29, 25·20	0·23	0·002	

SM-MMSE, Singapore-modified version of Mini-Mental State Examination.
* Covariates in the general linear models were the same as in the final models of Table 2.
† Linear trend was tested by treating the median values of quartiles as a continuous variable.

Table 4. Joint association of quantities and varieties in fruit and vegetable (FV) intake with cognitive impairment (Odds ratios and 95 % confidence intervals)

	Case/*n*	OR*	95 % CI	*P*
Total FV intake				
Lower variety and quantity†	714/4480	1·00		
Lower variety but higher quantity	560/3888	0·91	0·80, 1·04	0·16
Higher variety but lower quantity	567/3888	0·89	0·78, 1·01	0·07
Higher variety and quantity	556/4481	0·77	0·68, 0·88	<0·001
Fruit intake				
Lower variety and quantity†	751/4537	1·00		
Lower variety but higher quantity	567/3831	0·94	0·82, 1·07	0·32
Higher variety but lower quantity	526/3831	0·89	0·78, 1·01	0·07
Higher variety and quantity	553/4538	0·81	0·71, 0·93	0·002
Vegetable intake				
Lower variety and quantity†	669/4454	1·00		
Lower variety but higher quantity	548/3914	0·97	0·85, 1·11	0·65
Higher variety but lower quantity	607/3914	1·01	0·89, 1·15	0·86
Higher variety and quantity	573/4455	0·87	0·76, 0·99	0·03

* Covariates in the logistic regression models were the same as in the final models of Table 2.
† Median values of varieties and quantities (24.6 scores and 308.4 g/d for total FV intake; 6.7 scores and 194.0 g/d for fruit intake; 17.8 scores and 105.3 g/d for vegetable intake) were used as cut points to define lower or higher intake.

with the risk of dementia[35]. Meanwhile, in another Chinese population cohort with generally low level of fruit intake, the daily consumers had better cognitive function compared with those who seldom ate fruits[36]. Together with these previous studies, our study indicated that increasing the quantity of fruit intake may benefit cognitive function, especially among participants with a low intake in fruits. The inverse association observed in the moderate-glycaemic-index subgroup added evidence for the possible role of insulin sensitivity in the central nervous system in maintaining cognitive function[37].

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To the best of our knowledge, this is the first and largest cohort study that comprehensively assessed the association between varieties of fruits and vegetables and risk of cognitive impairment. The inverse association between total variety and odds of cognitive impairment in our study was consistent with a cross-sectional study in 1412 middle-aged and older Puerto Rican adults, where higher variety of fruits and vegetables was associated with higher MMSE scores and better performance in individual cognitive domains[20]. A wider intake variety in fruits and vegetables could confer additional benefit for cognitive health independent of quantity, because greater variety may provide a better mixture of antioxidant phytochemicals such as phenolic acids, flavonoids and carotenoids, which contribute synergistically to the antioxidant capacity[38]. When we considered fruits and vegetables separately, inverse association was observed for both vegetables and fruits. Notably, our study had thirty-nine items of fruits and vegetables to create a wide variability in variety score. In contrast, a prospective study among 436 community-dwelling older Chinese adults that reported no significant association between vegetable variety and cognitive decline could have been hampered by a small range of up to only five in the variety score[39].

The population in this study had a similar intake of fruit and vegetables with another population-based study in Singapore[40]. We have noted that our study population had a greater intake of fruits but less intake of vegetables compared with the populations in Western countries and other Asian countries[41,42], including China[43]. Nevertheless, the range of intake was still wide enough for us to make broad contrasts (see Table 2).

The strengths in the current study included the large sample size and the long follow-up period covering the early stage of cognitive decline through midlife to late life[44]. Besides, we comprehensively considered the fruit and vegetable intake in both quantity and variety. However, several limitations should be noted. First, dietary intake was only assessed at baseline. Hence, we could not examine subsequent changes in diet. Nevertheless, dietary habits are basically established by midlife, and food patterns have been found to be generally stable in population-based studies, despite expected changes in perceptions of what is considered healthy related to one's disease status over time[45]. In this regard, we have conducted sensitivity analyses by excluding participants who had chronic diseases at baseline and the results did not materially change. Second, the cognitive function was only assessed at the third follow-up visits, and we could not be certain that participants were all cognitively intact at baseline. Nonetheless, since 95 % of this current study population were younger than 65 years of age at baseline and were able to participate in face-to-face interviews using complex questionnaires, the possibility of them having moderate-to-severe cognitive impairment at baseline was small. Besides, cognitive function might be influenced by the medical events just before the third follow-up, such as post-stroke cognitive impairment, which may recover afterwards[46]. Nevertheless, the results did not materially change in the sensitivity analysis that excluded the participants who reported the medical history of stroke at the third follow-up. Third, selection bias was possible because our study only involved a proportion of those recruited at baseline. As shown in our previous analysis, participants who did not attend the third follow-up visits were generally older and more likely to have co-morbidities and unhealthy lifestyles at baseline, and hence at higher risk of cognitive impairment[15]. Meanwhile, they were also more likely to have lower intake levels of fruits and vegetables (see online Supplemental Table 6). Hence, this omission of participants with lower intake of fruits and vegetables, but with higher odds of cognitive impairment could lead to an underestimation of the risk estimates in our study. Finally, residual confounding cannot be fully eliminated in our study, although we have tried our best to adjust for a comprehensive set of confounders that also included multiple dietary variables.

In conclusion, our findings support the public health recommendation in consuming more fruits and vegetables for neurocognitive health in ageing and provide evidence for increasing both the quantity as well as the variety in the types of fruits and vegetables consumed. Further studies are warranted to further identify the subgroups of fruits and vegetables, and the optimal combinations in preventing cognitive impairment.

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There are no conflicts of interest.

Supplementary material

For supplementary material/s referred to in this article, please visit https://doi.org/10.1017/S0007114522000848

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