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Author(s)	Mameno, Tomoaki; Moynihan, Paula; Nakagawa, Takeshi et al.
Citation	Journal of Dentistry. 2024, 145, p. 104991
Version Type	VoR
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### Journal of Dentistry



journal homepage: www.elsevier.com/locate/jdent

# Exploring the association between number of teeth, food intake, and cognitive function: A 9-year longitudinal study

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#### ARTICLE INFO

Keywords: Number of teeth Food intake Cognitive function Older adults Longitudinal study

#### ABSTRACT

*Objectives*: This study aimed to investigate the association between the number of teeth, food intake, and cognitive function in Japanese community-dwelling older adults.

*Methods*: This 9-year longitudinal study included a total of 293 analyzable participants who participated in baseline and follow-up surveys. Dental status (number of teeth and periodontal pocket depth), dietary assessment using the brief-type self-administered diet history questionnaire, cognitive function, and the following confounding factors were evaluated: educational level, financial satisfaction, living situation, smoking and drinking habits, history of chronic diseases, apolipoprotein E-ε4 carrier, body mass index, handgrip strength, instrumental activities of daily living, and depressive symptomatology. The Japanese version of the Montreal Cognitive Assessment was used to evaluate cognitive function. A multinomial logistic regression analysis for the intake level of each food categorized into three groups (low, moderate, high), and a generalized estimating equation (GEE) for cognitive function over nine years were performed.

*Results*: After controlling for confounding factors, the number of teeth was shown to be associated with the intake of green-yellow vegetables and meat. Furthermore, the GEE indicated that the lowest quartile of intake of green-yellow vegetables significantly associated with lower cognitive function (unstandardized regression coefficient [B] = -0.96, 95 % confidence interval [CI]: -1.72 to -0.20), and the lowest quartile of intake of meat significantly associated with lower cognitive function (B = -1.42, 95 % CI: -2.27 to -0.58).

*Conclusions:* The intake of green and yellow vegetables and meat, which is influenced by the number of teeth, was associated with cognitive function in Japanese community-dwelling older adults.

*Clinical Significance:* There are few studies that have examined the association between oral health, food intake, and cognitive function. This 9-year longitudinal study suggests that it is important to maintain natural teeth to enable the functional means to consume green-yellow vegetables and meat, and thereby help maintain cognitive function.

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#### https://doi.org/10.1016/j.jdent.2024.104991

Received 5 December 2023; Received in revised form 27 March 2024; Accepted 5 April 2024 Available online 10 April 2024 0300-5712/© 2024 The Author(s). Published by Elsevier Ltd. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).

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#### 1. Introduction

Dementia is a major global health concern, with around 55 million people currently affected in 2021 [1], and the number expected to reach over 152 million by 2050 [2]. It poses a significant burden on individuals, families, and society, emphasizing the need for preventive measures. The 2020 report of the Lancet Commission for Dementia identified 12 modifiable risk factors (including less education, hypertension, hearing impairment, smoking, obesity, depression, physical inactivity, diabetes, low social contact, excessive alcohol consumption, head injury, and air pollution) and suggested that addressing these factors could potentially prevent around 40 % of dementia cases [3]. Oral health and nutrition, associated with some of these factors, are increasingly gaining attention in geriatric research regarding their relationship with cognitive function.

A meta-analysis of longitudinal studies with an average follow-up of 8.6 years showed that tooth loss was associated with increased risk of cognitive decline and dementia [4]. The proposed mechanisms mainly involve nutrition, inflammation, and neural feedback, with a particular focus on the deficiency of several nutrients, such as vitamin D and iron [4]. Diet has been widely acknowledged as modifiable lifestyle factors affecting the brain pathology [5]. A systematic review has shown an association between the consumption of fruits, vegetables, and legumes and cognitive function in oldest-old adults [6]. Dietary intake has been considered as an intermediate in the pathway between oral health and diet-related chronic diseases. A systematic review reported that tooth loss was associated with the nutritional status of older people [7]. However, the majority of evidence concerning the relationship between diet and tooth loss is of a cross-sectional nature [8]. Additionally, few previous analyses have examined the potential role of food intake as a mediating factor between oral health and cognition, and these have relied on subject-reported assessments of dental status [9]. In other words, the mechanism linking dentist assessed oral health to cognitive function through nutrition intake remains unclear.

This study aims to bridge this research gap by exploring the association between number of teeth, food intake, and cognitive function in older adults. The hypothesis was that having fewer teeth leads to avoidance of neuroprotective foods, which consequently results in cognitive impairment.

#### 2. Methods

#### 2.1. Participants

The study involved a longitudinal analysis of data collected during baseline and follow-up assessments for the "Septuagenarians, Octogenarians, Nonagenarians Investigation with Centenarians" (SONIC) study, a prospective cohort study of health and longevity [10]. Participants in the baseline assessment (Wave 1) were community-dwelling adults aged 69-71 years in 2010-2011 (70-year group), and 79-81 years in 2011-2012 (80-year group) who resided in two main regions of Japan: Itabasi Ward (urban) and Nishitama Country (rural) in Tokyo (Eastern Japan) and Itami City (urban) and Asago City (rural) in Hyogo (Western Japan). The participants were recruited from the resident registration, and they were invited to participate in the venue survey by mail. The three follow-up venue surveys were conducted every three years (Wave 2: 2013-2015, Wave 3: 2016-2018, Wave 4: 2019-2022). Participants who did not join all the follow-up surveys and who had missing data were excluded. The study protocol was approved by the Institutional Review Board of the University (approval number H22-E9, H27-E4). Informed consent was obtained from all participants. This study also followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines [11].

#### 2.2. Data collection

The outcome variable was cognitive function, and the independent variables included dental status (number of teeth and periodontal pocket depth) and dietary intake, which were assessed at each wave. The following confounding factors, which were considered to be relevant to cognitive impairment based on previous studies [6,12-22], were evaluated at baseline: educational level, financial satisfaction, living situation, smoking habits, alcohol drinking habits, history of chronic diseases (hypertension, diabetes, dyslipidemia, stroke, heart disease and cancer), apolipoprotein E (ApoE)- $\epsilon$ 4 carrier, body mass index (BMI), handgrip strength, instrumental activities of daily living (IADL) and geriatric depression scale.

#### 2.3. Dental examination

Registered dentists examined participants for the number of teeth and periodontal pocket depth (PPD). The number of teeth ranges from 0 to 28 excluding the third molar. Dentists measured PPD at six sites (mesiobuccal, midbuccal, distobuccal, mesiolingual, midlingual, and distolingual) for all teeth present using a color-coded probe (CP-12; Hu-Friedy, Chicago, IL, USA). The mean of the maximum PPD per tooth (mean PPD) was used as an indicator of periodontal status [23].

#### 2.4. Dietary assessment

The habitual diet during the preceding month was assessed with a brief self-administered diet history questionnaire (BDHQ) [24–26]. The BDHQ specifically designed for older adults is a validated 10-page questionnaire with a fixed portion format. Using an ad hoc computer algorithm developed for the BDHQ, the daily intake estimates for 58 food, beverage items and for energy were derived. The validity of the BDHQ was established by comparing it with semi-weighed dietary records across a wide range of age groups [24–26]. The dietary outcome variables were energy-adjusted using the density method (that is, amount per 1000 kcal of energy). The 12 food groups evaluated included: grains; potatoes; pulses; green and yellow vegetables; other vegetables; fruits; seafood; meat; eggs; dairy products; table sugar; and confectionery. Details of these food groups can be found in Supplementary Table S1.

#### 2.5. Cognitive function

Cognitive function was measured by the Japanese version of the Montreal Cognitive Assessment (MoCA-J). MoCA-J score ranges from 0 to 30 points, and a higher score reflects higher cognitive function. The MoCA-J showed better reliability and validity in the detection of cognitive decline among community-dwelling older adults than conventional cognitive tests [27,28].

#### 2.6. Medical assessment

Hypertension, diabetes and dyslipidemia were diagnosed from blood pressure actual values, blood test results, and medication status. The diagnostic criteria for these conditions were assessed using the method described by Ryuno et al. [29]. Participants were also interviewed to assess whether they had previously had a stroke, heart disease or cancer. Data for ApoE genotyping were analyzed using a venous blood sample. Participants with at least one  $\varepsilon$ 4 allele were defined as ApoE- $\varepsilon$ 4 carriers [30].

#### 2.7. Evaluation of depression

A 5-item version of the Geriatric Depression Scale (GDS-5) was used to assess depression. Scores ranged from 0 to 5 points, with a higher score reflecting a more depressive state [31].

#### 2.8. Other recorded variables

Participants were interviewed to ascertain their educational level (< 10 years [junior high school or less], 10–12 years [high school], or > 12 years [university or higher]), self-assessed economic satisfaction (low, moderate, high), living situation (with others or living alone), drinking habits (daily alcohol consumption [yes/no]), and smoking habits (smoking one or more cigarettes per day [ves/no]). BMI was calculated from the values of height and weight obtained through body measurements. Handgrip strength was considered as an indication of muscle strength. The test was performed twice with a Smedley hand dynamometer (Model YD-100; Yagami Ltd, Tokyo, Japan) using the dominant hand. The average of the first and second measurements was used for analysis [10]. IADL was assessed using a validated questionnaire [32]. Participants answered "yes" or "no" to five questions about their ability to complete specific activities, such as using public transportation, shopping, food preparation, paying bills, and handling a bank account. Scores ranged from 0 to 5 points, with 1 point for each "yes." Higher scores indicated greater independence.

#### 2.9. Statistical analysis

Baseline characteristics between the dropout and follow-up groups were compared using Mann-Whitney U tests for continuous variables and chi-square tests for categorical variables.

First, the participants were divided into three groups based on the intake of each food at Wave 1. The food intake was categorized as follows: the first quartile was labeled as "low," the fourth quartile as "high," and the second and third quartiles as "moderate." A multinomial logistic analysis was used to estimate the effect of number of teeth on food intake at baseline, adjusting for factors related to food selection: age, sex, educational level, financial satisfaction, living situation, smoking and drinking habits, history of chronic diseases (hypertension, diabetes and dyslipidemia), BMI, IADL and GDS-5 score, and mean PPD. Furthermore,

for the food items that showed an association with the number of teeth, the Friedman test was applied to investigate the overall change in MoCA-J score across four time points (Wave 1 to 4). Bonferroni post hoc Wilcoxon signed-rank tests compared pairs of time points.

Next, a linear regression using generalized estimating equations (GEE) was performed to estimate the effect of selected food intake and number of teeth at baseline on cognitive function at all four waves. GEE is able to take into account correlations between data within the same subject, meaning it is a suitable statistical method for longitudinal analysis. In the GEE model, the following demographic and confounding factors for cognitive function were added as independent variables: age, sex, educational level, financial satisfaction, living situation, smoking habits, drinking habits, history of chronic diseases (hypertension, diabetes, dyslipidemia, stroke, heart disease and cancer), ApoE- $\epsilon$ 4 carrier, BMI, handgrip strength, IADL and GDS-5 score, and elapsed years.

All statistical analyses were performed with SPSS version 28 (IBM Japan, Tokyo, Japan). The level of significance was set at P = 0.05 (two-sided).

#### 3. Results

In total, 4267 residents in the 70-year group and 5378 residents in the 80-year group were identified and sent invitation letters. Of these, 1000 residents in the 70 s cohort and 973 residents in the 80 s cohort participated in the venue survey. The final analysis included 293 participants (81.6 % in the 70-year group) who completed the examinations at follow-ups (Fig. 1).

Table 1 shows the baseline characteristics for the follow-up and dropout groups. There were no significant differences between the groups in sex, financial satisfaction, living situation, smoking habits, history of diseases excluding hypertension, ApoE- $\epsilon$ 4 carrier, mean PPD, food intake (excluding meat), and BMI. However, participants were more likely to be lost to follow-up if they were 80-year group or had a poor educational level, drank alcohol, had hypertension, lower



Fig. 1. Flow chart of the participants.

#### Table 1

Comparison of characteristics between follow-up (n = 293) and dropout groups (n = 916).

Variables		Follow-up	Dropout	<i>P</i> -
		group	group	value
A	70 / 00	000 / 54	046 / 570	-0.01
Age group	/0- / 80-	239 / 54	346 / 570	< 0.01
Sex	male / remale	138 / 155	432 / 484	0.98
Education level	<10y / 10–12y /	70 / 137 /	295 / 367 /	0.02
	>13y	86	254	
Financial	low / moderate /	47 / 170 /	202 / 514 /	0.06
satisfaction	high	76	200	
Living situation	alone / with	47 / 246	165 / 751	0.44
	others			
Smoking habit	yes / no	18 / 275	70 / 856	0.39
Drinking habit	yes / no	119 / 174	304 / 612	0.02
Hypertension	yes / no	184 / 109	698 / 218	< 0.01
Diabetes	yes / no	33 / 260	124 / 792	0.31
Dyslipidemia	yes / no	178 / 115	521 / 395	0.24
Stroke	yes / no	5 / 288	35 / 881	0.08
Heart disease	yes / no	33 / 260	122 / 794	0.36
Cancer	yes / no	32 / 261	99 / 817	0.96
ApoE-e4 carrier	yes / no	44 / 249	119 / 797	0.38
	Median (Q1 - Q3	) Media	n (Q1 - Q3)	P-value
MoCA-L score	24.0 (23.0 - 26.0	) 22.0 (	20.0 - 25.0)	<0.01
Number of teeth	24.0 (25.0 - 20.0	22.0(	20.0 - 25.0) 9.0 - 25.0)	<0.01
Mean periodontal	30(27-36)	31(2	8-37)	0.06
nocket denth	0.0 (2.7 0.0)	0.1 (2	.0 0.7)	0.00
Food intake (g/1000	<b>`</b>			
kcal)	•			
Grains	204 7 (172 3 - 2)	45 1) 207 7	(165.3 - 256.6)	0.60
Potatoes	204.7 (172.3 - 2	207.7	(105.5 - 250.0) 13.8 - 46.4)	0.00
Pulses	35.0 (20.3 - 54.6	352(	21.3 - 53.6)	0.80
Green and vellow	64 5 (44 2 - 89 2	64.6(	43.6 - 90.5)	0.00
vegetables	04.3 (44.2 - 05.2	.) 04.0 (	43.0 - 90.3)	0.90
Other vegetables	100.3 (76.3 - 12)	<b>3</b> .9) 97.3 (	71 - 129 8)	0.58
Fruits	76.3 (44.7 - 115	1) 78.9 (	43.8 - 119.5)	0.69
Seafood	52.9 (35.7 - 72.8	52.8(	33.4 - 73.9)	0.98
Meats	30.5 (21.6 - 40.2	285(	19.4 - 40.5)	0.04
Foos	159(101-275	161(	10.2 - 28.2)	0.80
Dairy products	75 5 (31.0 - 107	1) 775(	30.8 - 111.1	0.43
Table sugar	26(16-40)	27(1	8-40)	0.15
Confectionery	2.0 (1.0 - 4.0)	2.7(1)	12 2 20 0)	0.15
Body mass index	22.1 (12.7 - 30.0	27.7(	20.6 24.5)	0.21
$(l_{1}a/m^2)$	22.4 (20.3 - 24.0	) 22.4(	20.0 - 24.3)	0.05
(Kg/III) Crin strength (kaf)	24.0 (18.5 32.0	) 215(	16 9 29 5)	<0.01
Instrumentel	24.0 (10.3 - 32.0 5 0 (5 0 E 0)	-) 21.3 ( E 0./F	0 5 0)	< 0.01
not unental	3.0 (3.0 - 3.0)	5.0 (5	.0 - 3.0)	0.04
activities of dally				
invite of				
living	10(00.10)	1.0.00	0.00	-0.01

Q1: the first quartile, Q3: the third quartile, ApoE: apolipoprotein E, MoCA-J: Japanese version of the Montreal Cognitive Assessment, GDS-5: A 5-item version of the Geriatric Depression Scale. *P*-values from chi-square tests for categorical variables and Mann–Whitney U test for continuous variables.

cognitive function, a fewer number of teeth, a lower intake of meat, a lower grip strength, a lower IADL score, and a higher GDS-5 score at baseline.

Table 2 summarizes the adjusted odds ratios (ORs) and 95 % confidence intervals (CIs) of the number of teeth for the low and the moderate intake groups of each food group at Wave 1, obtained from multinomial logistic regression analyses with the high intake group as the reference. The detailed results of the analyses of each food type, including the adjusted variables, can be found in Supplementary Tables S2–13. The results showed that individuals in the low intake groups of green and yellow vegetables (OR = 0.94, 95 % CI: 0.89 to 0.99), meat (OR = 0.95, 95 % CI: 0.90 to 0.99) and dairy products (OR = 0.92, 95 % CI: 0.87 to 0.98), and in the moderate intake group of dairy products (OR = 0.94, 95 % CI: 0.89 to 0.99) had significantly fewer teeth compared with those in the high intake groups.

Fig. 2 shows the longitudinal changes in cognitive function over nine years for each group of intake levels of green and yellow vegetables, meat, and dairy products. Overall, a gradual decline in MoCA-J scores

was observed from Wave 1 to 4. The Friedman tests conducted by the intake group indicated that there were differences in the distribution of MoCA-J scores between four time points in the low and high intake groups of green and yellow vegetables (P < 0.01 and P = 0.03), as well as the moderate intake group of meat (P = 0.04). Wilcoxon signed-rank tests conducted subsequently revealed significant differences between W2 and W4 in the low-intake group (P < 0.01) and between W1 and W4 in the high-intake group (P = 0.04) of green and yellow vegetables after Bonferroni's adjustment (Fig. 2-A). There were no significant differences observed in MoCA-J scores at four time points among any of the meat intake groups (Fig. 2-B).

The GEE model examining the association between cognitive function and the selected food groups revealed significant associations with intake of green and yellow vegetables and meat. No significant association was found for intake of dairy products (Supplementary Table S14). The GEE results of the green and yellow vegetables, teeth, and teethadjusted models are presented in Table 3. The green and yellow vegetable model showed a significant association between the low intake group and lower cognitive function (unstandardized regression coefficient [B] = -0.96, 95 % CI: -1.72 to -0.20), after adjusting for confounding factors. Participants with low intake of green and yellow vegetables had a MoCA-J score that was 0.96 points lower compared with the high intake group independent of elapsed years. In this model, participants were more likely to have lower cognitive function if they were in the 80-year group (B = -1.50, 95 % CI: -2.28 to -0.72), had less than 10 years of education (B = -1.06, 95 % CI: -1.85 to -0.27), lower grip strength (B = 0.05, 95 % CI: 0.01 to 0.09), and a more depressive state (B = -0.46, 95 % CI: -0.77 to -0.14). The interaction of green and yellow vegetables intake and elapsed years was not significant. In the teeth model, a significant association was found between the number of teeth and cognitive function (B = 0.05, 95 % CI: 0.01 to 0.09). However, in the teeth-adjusted model that included both the number of teeth and intake of green-yellow vegetables as variables, the significance of green-yellow vegetables remained unchanged, and no significant association was observed with the number of teeth. Table 4 shows the GEE results of meat. The meat model showed a significant association between the low intake group and lower cognitive function (B = -1.42, 95 % CI: -2.27 to -0.58). In the meat model as well, similar to the green and yellow vegetable model, the number of teeth was not shown to be a significant variable in the teeth-adjusted model.

#### 4. Discussion

In this longitudinal study over nine years, the relationship between the number of teeth and food intake, as well as their long-term association with cognitive function in Japanese community-dwelling older adults was studied. The intake of green and yellow vegetables, as well as the intake of meat, which are influenced by the number of teeth, was shown to be associated with cognitive function, after controlling for confounding factors.

There are very few studies that have directly examined the intermediate role of dietary intake between oral health and cognitive function. The elucidation of this pathway was attempted in the past by Kiuchi et al. [9]. The authors conducted a 6-year study with 35,744 Japanese older individuals, assessing the incidence of dementia over three years. As a result, it was concluded that the frequency of vegetable and fruit intake partially mediated the relationship between tooth loss and the development of dementia. While the evidence is supported by data from a large number of participants, it is important to note that the number of teeth was assessed through self-report, and the evaluation of dietary intake only considered the frequency of intake of total vegetable and fruit. The information regarding the intake of vegetables and fruits was not collected through a validated tool, and there was no control for energy intake. This leaves room for further consideration and investigation.

This prospective cohort study had several strengths. Firstly, it

#### Table 2

Adjusted odds ratios of the number of teeth obtained from multinomial logistic regression analyses with the high intake group as the reference, conducted for each food intake group at Wave 1.

Model	Variable	Low				Moderate			
		Adjusted OR*	95 % CI		P-value	Adjusted OR*	95 % CI		P-value
			Lower	Upper			Lower	Upper	
Grains	Number of teeth	0.99	0.94	1.04	0.63	1.01	0.96	1.05	0.80
Potatoes	Number of teeth	1.04	0.99	1.10	0.13	1.02	0.98	1.07	0.32
Pulses	Number of teeth	1.00	0.95	1.05	0.94	1.02	*0.97	1.06	0.43
Green and yellow vegetables	Number of teeth	0.94	0.89	0.99	0.04	0.99	0.94	1.04	0.68
Other vegetables	Number of teeth	1.00	0.95	1.06	0.96	1.00	0.95	1.04	0.84
Fruits	Number of teeth	1.00	0.94	1.06	0.91	0.99	0.95	1.04	0.82
Seafood	Number of teeth	0.99	0.93	1.04	0.62	0.99	0.95	1.04	0.71
Meats	Number of teeth	0.95	0.90	0.99	0.047	0.99	0.95	1.04	0.74
Eggs	Number of teeth	1.00	0.95	1.06	0.91	0.99	0.95	1.04	0.71
Dairy products	Number of teeth	0.92	0.87	0.98	0.01	0.94	0.89	0.99	0.02
Table sugar	Number of teeth	1.05	1.00	1.11	0.06	1.03	0.98	1.07	0.26
Confectionery	Number of teeth	1.05	0.99	1.10	0.09	1.04	1.00	1.08	0.07

OR: odds ratio, CI: confidence interval, ref: reference.

<sup>\*</sup> The adjusted variables were age, sex, educational level, financial satisfaction, living situation, smoking, alcohol drinking habits, history of chronic diseases (hypertension, diabetes and dyslipidemia), BMI, IADL and GDS-5 score, and mean periodontal pocket depth.



**Fig. 2.** Longitudinal changes in cognitive function over a 9-year period for each intake group. MoCA-J: Japanese version of the Montreal Cognitive Assessment, Q1: the first quartile, Q3: the third quartile. \*P < 0.05 after Bonferroni's adjustment.

specifically targeted participants aged 70 and 80 years, which are critical ages for cognitive decline and dementia, and observed changes over nearly a decade. Secondly, data collection was carried out by experts in the relevant fields, and the assessment of dietary intake was performed using validated tool, ensuring high reliability. In this study, third molars were excluded from the evaluation due to reasons such as false periodontal pockets or non-participation in occlusion. Additionally, PPDs were examined by dentists; however, other necessary assessments for diagnosing periodontal disease such as radiographic bone loss and clinical attachment loss levels [33] were not evaluated. It is undesirable

#### Table 3

Results of the generalized estimating equation for green and yellow vegetable intake on cognitive function over a period of nine years.

	Green and yellow vegetables model			Teeth model			Teeth-adjusted model		
	В	95 % CI		В	95 % CI		В	95 % CI	
		Lower	Upper		Lower	Upper		Lower	Upper
Age group, 80- (ref: 70-)	-1.50	-2.28	-0.72	-1.49	-2.38	-0.60	-1.54	-2.39	-0.68
Sex, male (ref: female)	0.29	-0.74	1.33	0.67	-0.42	1.76	0.34	-0.76	1.43
Educational level <10y (ref: >12y)	-1.06	-1.85	-0.27	-1.13	-1.97	-0.30	-0.95	-1.77	-0.12
Educational level 10–12y (ref: >12y)	0.46	-0.16	1.09	0.50	-0.19	1.18	0.57	-0.10	1.24
Financial satisfaction, low (ref: high)	-0.64	-1.54	0.27	-0.69	-1.75	0.36	-0.60	-1.61	0.41
Financial satisfaction, moderate (ref: high)	-0.25	-0.91	0.41	-0.08	-0.77	0.61	-0.06	-0.74	0.61
Living alone, yes (ref: no)	-0.06	-0.86	0.75	-0.01	-0.88	0.86	-0.01	-0.86	0.83
Smoking, yes (ref: no)	-0.12	-0.97	0.73	0.23	-0.78	1.24	0.28	-0.73	1.29
Drinking, yes (ref: no)	-0.54	-1.20	0.12	-0.50	-1.22	0.23	-0.61	-1.31	0.08
Hypertension, yes (ref: no)	-0.26	-0.83	0.31	-0.32	-0.92	0.29	-0.25	-0.85	0.36
Diabetes, yes (ref: no)	-0.37	-1.31	0.57	-0.32	-1.16	0.52	-0.31	-1.12	0.51
Dyslipidemia, yes (ref: no)	0.51	-0.05	1.08	0.81	0.09	1.52	0.71	0.01	1.42
Stroke, yes (ref: no)	-1.63	-3.28	0.02	-1.43	-3.16	0.30	-1.54	-3.05	-0.03
Heart disease, yes (ref: no)	-0.29	-1.19	0.62	0.24	-0.74	1.22	0.22	-0.70	1.14
Cancer, yes (ref: no)	0.39	-0.57	1.35	0.09	-0.92	1.09	0.23	-0.75	1.22
ApoE-ɛ4 carrier, yes (ref: no)	-0.60	-1.30	0.11	-0.21	-0.98	0.57	-0.17	-0.90	0.55
BMI (kg/m2)	-0.04	-0.16	0.07	-0.04	-0.16	0.07	-0.05	-0.16	0.06
Grip strength (kgf)	0.05	0.01	0.09	0.03	-0.02	0.08	0.03	-0.02	0.08
IADL	0.65	-0.28	1.58	0.97	0.02	1.92	0.95	0.09	1.81
GDS-5 score	-0.46	-0.77	-0.14	-0.46	-0.79	-0.13	-0.43	-0.77	-0.09
Elapsed year (per 3 years)	-0.19	-0.30	-0.07	-0.19	-0.31	-0.08	-0.19	-0.31	-0.08
Intake group, low (ref: high)	-0.96	-1.72	-0.20				-0.91	-1.70	-0.11
Intake group, moderate (ref: high)	0.14	-0.53	0.82				0.20	-0.50	0.90
Number of teeth				0.05	0.01	0.09	0.04	-0.01	0.08
Mean periodontal pocket depth				-0.06	-0.41	0.28	-0.05	-0.39	0.29

B: unstandardized regression coefficient, CI: confidence interval, ref: reference, ApoE: apolipoprotein E, BMI: body mass index, IADL: instrumental activities of daily living, GDS-5: a 5-item version of the Geriatric Depression Scale.

Bold values indicate significance at P < 0.05.

#### Table 4

Results of the generalized estimating equation for meat intake on cognitive function over 9 years.

	Meat model			Teeth model			Teeth-adjusted model		
	В	B 95 % CI		В	95 % CI		В	95 % CI	
		Lower	Upper		Lower	Upper		Lower	Upper
Age group, 80- (ref: 70-)	-1.66	-2.50	-0.82	-1.49	-2.38	-0.60	-1.46	-2.33	-0.60
Sex, male (ref: female)	0.54	-0.52	1.61	0.67	-0.42	1.76	0.55	-0.54	1.64
Educational level <10y (ref: >12y)	-1.07	-1.91	-0.23	-1.13	-1.97	-0.30	-0.99	-1.79	-0.19
Educational level 10–12y (ref: >12y)	0.55	-0.13	1.24	0.50	-0.19	1.18	0.62	-0.06	1.30
Financial satisfaction, low (ref: high)	-0.79	-1.82	0.24	-0.69	-1.75	0.36	-0.70	-1.68	0.29
Financial satisfaction, moderate (ref: high)	-0.16	-0.85	0.52	-0.08	-0.77	0.61	-0.08	-0.76	0.61
Living alone, yes (ref: no)	-0.10	-0.98	0.77	-0.01	-0.88	0.86	-0.08	-0.97	0.82
Smoking, yes (ref: no)	-0.10	-0.99	0.79	0.23	-0.78	1.24	0.13	-0.81	1.07
Drinking, yes (ref: no)	-0.50	-1.22	0.22	-0.50	-1.22	0.23	-0.53	-1.23	0.16
Hypertension, yes (ref: no)	-0.37	-0.99	0.24	-0.32	-0.92	0.29	-0.30	-0.92	0.32
Diabetes, yes (ref: no)	-0.21	-1.02	0.59	-0.32	-1.16	0.52	-0.35	-0.96	0.25
Dyslipidemia, yes (ref: no)	0.82	0.09	1.56	0.81	0.09	1.52	0.25	-0.56	1.06
Stroke, yes (ref: no)	-1.47	-3.06	0.12	-1.43	-3.16	0.30	-1.70	-3.65	0.25
Heart disease, yes (ref: no)	-0.36	-1.31	0.59	0.24	-0.74	1.22	-0.10	-1.00	0.79
Cancer, yes (ref: no)	0.15	-0.83	1.12	0.09	-0.92	1.09	0.07	-0.88	1.03
ApoE-e4 carrier, yes (ref: no)	-0.22	-0.97	0.53	-0.21	-0.98	0.57	-0.20	-0.94	0.54
BMI (kg/m2)	-0.07	-0.19	0.04	-0.04	-0.16	0.07	-0.06	-0.17	0.04
Grip strength (kgf)	0.04	-0.01	0.09	0.03	-0.02	0.08	0.04	-0.01	0.09
IADL	1.05	0.08	2.01	0.97	0.02	1.92	0.97	0.01	1.94
GDS-5 score	-0.53	-0.87	-0.20	-0.46	-0.79	-0.13	-0.52	-0.85	-0.18
Elapsed year (per 3 years)	-0.19	-0.31	-0.08	-0.19	-0.31	-0.08	-0.19	-0.31	-0.08
Intake group, low (ref: high)	-1.42	-2.27	-0.58				-1.41	-2.24	-0.57
Intake group, moderate (ref: high)	-0.72	-1.44	0.01				-0.73	-1.44	-0.03
Number of teeth				0.05	0.01	0.09	0.04	-0.01	0.08
Mean periodontal pocket depth				-0.06	-0.41	0.28	-0.14	-0.46	0.18

B: unstandardized regression coefficient, CI: confidence interval, ref: reference, ApoE: apolipoprotein E, BMI: body mass index, IADL: instrumental activities of daily living, GDS-5: a 5-item version of the Geriatric Depression Scale.

Bold values indicate significance at P < 0.05.

to assess periodontal status only with specific thresholds for PPD. Instead, the mean value of PPD across all teeth was used as an indicator of periodontal status [23]. These reliable and objective assessments enabled for various confounding factors related to cognitive decline to be accounted for and a robust investigation into the impact of oral and dietary intake on cognitive function to be conducted.

The current study has shown that the number of teeth is associated with the intake of green and vellow vegetables, meat, and dairy products. Among them, it was shown that low intake of green and yellow vegetables, and low intake of meat were associated with lower cognitive function. Furthermore, the results of the Friedman test revealed significant temporal changes across the four time points in certain groups of green and yellow vegetables and meat. However, the results of the Wilcoxon signed-rank tests indicated that the only group showing a significant decline in MoCA-J scores from W1 was the high-intake group of green and yellow vegetables. This could be associated with the higher cognitive function observed in this group at W1. The lack of a significant decrease observed in the high-intake group of meat, despite having high scores at W1, could be attributed to the potential greater impact of high meat intake on maintaining cognitive function. This notion is further supported by the observation that the absolute value of the B in the GEE model for meat intake was larger than that of green and yellow vegetables model. At the same time, consistent with many other studies [4], the number of teeth was also associated with cognitive function over the 9 years. Furthermore, results from the teeth-adjusted model indicate that green-yellow vegetables and meat intake have a greater impact on cognitive function rather than the number of teeth. Consistent with other reports [34,35], the present findings suggest that green-yellow vegetables may reduce the risk of cognitive impairment and dementia. Green and yellow vegetables are known to contain many bioactive compounds including polyphenolic flavonoids and antioxidants such as vitamin C, vitamin E, and carotenoids, as well as folic acid. These components may contribute to inhibitory effects on cognitive decline. [36–39] Emerging evidence suggests that a diet rich in polyphenolic flavonoids may reduce the risk of chronic degenerative diseases [40–42]. Vitamin C is a potent water-soluble antioxidant that prevents the oxidative process and multiple cohort studies have shown that an increase in vitamin C intake is associated with a reduced risk of incident Alzheimer's disease [37]. Systematic review and meta-analysis suggest a significant association between higher consumption of vitamin E and reduced incidence of Alzheimer's disease [36]. Vitamin E has the potential to reduce oxidative stress and lipid peroxidation, and prevent nerve damage, according to animal studies [43]. However, an appraisal of available evidence syntheses from studies conducted in humans, concluded that it is not possible to draw conclusions on the association between dementia and intake of vitamin E [44]. However, evidence synthesis has shown an association between higher intakes of folate and a reduced risk of Alzheimer's disease, and a recent systematic review has demonstrated that supplementing with folic acid suggests a positive effect in preventing the risk of cognitive impairment [39]. Conversely, consistent results have not been obtained regarding the association between meat intake and cognitive function [45]. Meat contains high levels of saturated fat and cholesterol, which are associated with an increased risk of Alzheimer's disease, including midlife hypertension and hypercholesterolemia [46]. Western diet patterns, such as a high-fat diet with a high glycemic load and high cholesterol, are considered a risk factor for developing Alzheimer's disease [47]. However, the opposite has been demonstrated in the older adults. A cross-sectional study included individuals aged  $\geq$  65 years and revealed that a dietary pattern of high protein intake, including meat, is associated with good cognitive function [48]. Meat, especially lean meat, is rich in protein and essential amino acids which are important nutrients for human health. The systematic review explores the association of meat intake with cognitive function and suggests that meat intake is protective against cognitive disorders in older adults [45]. At the same time, as being associated with cognitive function, green-yellow vegetables and meat are related to oral

health status. A 5-year longitudinal study conducted on Japanese older adults showed that impaired dentition may partly contribute to a decrease in vegetable and meat intake [49]. The present findings are consistent with this study. Impaired dental status can result in avoidance of foods that are considered difficult to chew and consequently a preference for soft and easily chewable foods [50]. On the other hand, the foods such as fish, pulses, and fruits, which have been suggested to be associated with cognitive function [34], did not show any relationship in this study.

The current findings suggest that it is important to maintain natural teeth to enable the functional means to consume green-yellow vegetables and meat, and thereby help maintain cognitive function. The present study is one of the few studies that have demonstrated the role of dietary components as intermediate factors between dental status and cognitive function over the long-term. The current study has some limitations which need to be acknowledged. The study targeted participants who took part in all four surveys conducted every three years, aiming to assess cognitive function with temporal changes rigorously. As a trade-off, the number of participants was limited to 293, excluding 75.8 % of the baseline participants from the analysis. This may have resulted in reduced statistical power, potentially leading to the nondetection of small effect sizes. There may also have been some selection bias; participants were not a representative sample of older Japanese in the general population because the study cohort only included non-institutionalized, community-dwelling older adults. Because the study targeted individuals who were able to participate in the venue surveys over a period of nine years, those with severely impaired cognitive function were unlikely to be included in the analyzable samples. Furthermore, the median number of teeth was 24, suggesting that the oral health of the analyzable participants was relatively good. It is important to note this bias when interpreting the results. In this study, the number of teeth and individual food intake were assessed, which aimed the interpretation of mechanisms and longitudinal changes. However, in this study, the cross-sectional relationship between the number of teeth and food intake was examined. The intermediate factors between the number of teeth and cognitive function were not investigated rigorously. Based on the findings from this study, it is believed that there is a need to examine more complex longitudinal effects, the oral function restored through prosthetic rehabilitation, dietary diversity, and dietary patterns.

#### 5. Conclusions

In conclusion, the intake of green and yellow vegetables, along with the intake of meat, influenced by the number of teeth, was found to be associated with cognitive function in Japanese community-dwelling older adults.

#### CRediT authorship contribution statement

Tomoaki Mameno: Writing - original draft, Investigation, Formal analysis. Paula Moynihan: Writing - review & editing, Supervision, Formal analysis. Takeshi Nakagawa: Writing - review & editing, Investigation, Data curation. Hiroki Inagaki: . Suzuna Akema: Writing - review & editing, Investigation, Data curation. Yuki Murotani: Writing - review & editing, Investigation, Data curation. Satoko Takeuchi: Writing - review & editing, Investigation, Data curation. Ayaka Kimura: Writing - review & editing, Investigation, Data curation. Yoshie Okada: Writing - review & editing, Investigation, Data curation. Yoshitaka Tsujioka: Writing - review & editing, Investigation, Data curation. Kotaro Higashi: Writing - review & editing, Investigation, Data curation. Hiromasa Hagino: Writing - review & editing, Investigation, Data curation. Yusuke Mihara: Writing - review & editing, Supervision. Takayuki Kosaka: Writing - review & editing, Supervision. Toshihito Takahashi: Writing - review & editing, Supervision. Masahiro Wada: Writing - review & editing, Supervision.

Yasuyuki Gondo: Writing – review & editing, Project administration, Methodology, Conceptualization. Kei Kamide: Writing – review & editing, Project administration, Methodology, Conceptualization. Hiroshi Akasaka: Writing – review & editing, Project administration, Methodology, Conceptualization. Mai Kabayama: Writing – review & editing, Project administration, Methodology, Conceptualization. Tatsuro Ishizaki: Writing – review & editing, Project administration, Methodology, Conceptualization. Yukie Masui: Writing – review & editing, Project administration, Methodology, Conceptualization. Kazunori Ikebe: Writing – review & editing, Project administration, Methodology, Conceptualization.

#### Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

Paula Moynihan reports a relationship with GSK Consumer Healthcare that includes: consulting or advisory. Paula Moynihan reports a relationship with Haleon Oral Health Strategic Advisory Council that includes: consulting or advisory. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

#### Acknowledgements

This study was supported by a Grant-in-Aid for Scientific Research (JP15H05025, JP18H02990, JP21H03130 and JP22K100740) from the Japan Society for the Promotion of Science. The funder had no roles in design, methods, data collection, analysis, or preparation of this manuscript.

#### Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jdent.2024.104991.

#### References

- S. Gauthier, P. Rosa-Neto, J.A. Morais, C. Webster, World Alzheimer Report 2021: journey through the diagnosis of dementia, Alzheimer's Disease Int. 2022 (2021) 30.
- [2] E. Nichols, J.D. Steinmetz, S.E. Vollset, K. Fukutaki, J. Chalek, F. Abd-Allah, A. Abdoli, A. Abualhasan, E. Abu-Gharbieh, T.T. Akram, Estimation of the global prevalence of dementia in 2019 and forecasted prevalence in 2050: an analysis for the Global Burden of Disease Study 2019, Lancet Public Health 7 (2) (2022) e105–e125.
- [3] G. Livingston, J. Huntley, A. Sommerlad, D. Ames, C. Ballard, S. Banerjee, C. Brayne, A. Burns, J. Cohen-Mansfield, C. Cooper, S.G. Costafreda, A. Dias, N. Fox, L.N. Gitlin, R. Howard, H.C. Kales, M. Kivimäki, E.B. Larson, A. Ogunniyi, V. Orgeta, K. Ritchie, K. Rockwood, E.L. Sampson, Q. Samus, L.S. Schneider, G. Selbæk, L. Teri, N. Mukadam, Dementia prevention, intervention, and care: 2020 report of the Lancet Commission, Lancet 396 (10248) (2020) 413–446.
- [4] L. Li, Q. Zhang, D. Yang, S. Yang, Y. Zhao, M. Jiang, X. Wang, L. Zhao, Q. Liu, Z. Lu, X. Zhou, Y. Gan, C. Wu, Tooth loss and the risk of cognitive decline and dementia: a meta-analysis of cohort studies, Front. Neurol. 14 (2023) 1103052.
- [5] C.-Q. Chu, L.-I. Yu, G.-y. Qi, Y.-S. Mi, W.-Q. Wu, Y.-k. Lee, Q.-X. Zhai, F.-W. Tian, W. Chen, Can dietary patterns prevent cognitive impairment and reduce Alzheimer's disease risk: exploring the underlying mechanisms of effects, Neurosci. Biobehav. Rev. 135 (2022) 104556.
- [6] K.X. Ye, L. Sun, L. Wang, A.L.Y. Khoo, K.X. Lim, G. Lu, L. Yu, C. Li, A.B. Maier, L. Feng, The role of lifestyle factors in cognitive health and dementia in oldest-old: a systematic review, Neurosci. Biobehav. Rev. 152 (2023) 105286.
- [7] M.P. Toniazzo, P.S. Amorim, F. Muniz, P. Weidlich, Relationship of nutritional status and oral health in elderly: systematic review with meta-analysis, Clin. Nutr. 37 (3) (2018) 824–830.
- [8] P. Gaewkhiew, W. Sabbah, E. Bernabé, Does tooth loss affect dietary intake and nutritional status? A systematic review of longitudinal studies, J. Dent. 67 (2017) 1–8.
- [9] S. Kiuchi, U. Cooray, T. Kusama, T. Yamamoto, H. Abbas, N. Nakazawa, K. Kondo, K. Osaka, J. Aida, Oral status and dementia onset: mediation of nutritional and social factors, J. Dent. Res. 101 (4) (2022) 420–427.
- [10] Y. Gondo, Y. Masui, K. Kamide, K. Ikebe, Y. Arai, T. Ishizaki, SONIC study: a longitudinal cohort study of the older people as part of a centenarian study, in: N.

A. Pachana (Ed.), Encyclopedia of Geropsychology, Springer Singapore, Singapore, 2015, pp. 1–10.

- [11] E. von Elm, D.G. Altman, M. Egger, S.J. Pocock, P.C. Gøtzsche, J. P. Vandenbroucke, The strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies, J. Clin. Epidemiol. 61 (4) (2008) 344–349.
- [12] C. Kilian, S. Klinger, J. Rehm, J. Manthey, Alcohol use, dementia risk, and sex: a systematic review and assessment of alcohol-attributable dementia cases in Europe, BMC. Geriatr. 23 (1) (2023) 246.
- [13] J. Wee, S. Sukudom, S. Bhat, M. Marklund, N.J. Peiris, C.M. Hoyos, S. Patel, S. L. Naismith, G. Dwivedi, A. Misra, The relationship between midlife dyslipidemia and lifetime incidence of dementia: a systematic review and meta-analysis of cohort studies, Alzheimers. Dement. (Amst) 15 (1) (2023) e12395.
- [14] M.A. Beydoun, H.A. Beydoun, A.A. Gamaldo, A. Teel, A.B. Zonderman, Y. Wang, Epidemiologic studies of modifiable factors associated with cognition and dementia: systematic review and meta-analysis, BMC. Public Health 14 (2014) 643.
- [15] R. Desai, A. John, J. Stott, G. Charlesworth, Living alone and risk of dementia: a systematic review and meta-analysis, Ageing Res. Rev. 62 (2020) 101122.
- [16] A.R. Zammit, A. Robitaille, A.M. Piccinin, G. Muniz-Terrera, S.M. Hofer, Associations between aging-related changes in grip strength and cognitive function in older adults: a systematic review, J. Gerontol. a Biol. Sci. Med. Sci. 74 (4) (2019) 519–527.
- [17] K. Jekel, M. Damian, C. Wattmo, L. Hausner, R. Bullock, P.J. Connelly, B. Dubois, M. Eriksdotter, M. Ewers, E. Graessel, M.G. Kramberger, E. Law, P. Mecocci, J. L. Molinuevo, L. Nygård, M.G. Olde-Rikkert, J.M. Orgogozo, F. Pasquier, K. Peres, E. Salmon, S.A. Sikkes, T. Sobow, R. Spiegel, M. Tsolaki, B. Winblad, L. Frölich, Mild cognitive impairment and deficits in instrumental activities of daily living: a systematic review, Alzheimers. Res. Ther. 7 (1) (2015) 17.
- [18] V. Hachinski, K. Einhäupl, D. Ganten, S. Alladi, C. Brayne, B.C.M. Stephan, M. D. Sweeney, B. Zlokovic, Y. Iturria-Medina, C. Iadecola, N. Nishimura, C. B. Schaffer, S.N. Whitehead, S.E. Black, L. Østergaard, J. Wardlaw, S. Greenberg, L. Friberg, B. Norrving, B. Rowe, Y. Joanette, W. Hacke, L. Kuller, M. Dichgans, M. Endres, Z.S. Khachaturian, Preventing dementia by preventing stroke: the Berlin Manifesto, Alzheimers. Dement. 15 (7) (2019) 961–984.
- [19] D. Hughes, C. Judge, R. Murphy, E. Loughlin, M. Costello, W. Whiteley, J. Bosch, M.J. O'Donnell, M. Canavan, Association of blood pressure lowering with incident dementia or cognitive impairment: a systematic review and meta-analysis, JAMa 323 (19) (2020) 1934–1944.
- [20] M.W. Strachan, R.M. Reynolds, R.E. Marioni, J.F. Price, Cognitive function, dementia and type 2 diabetes mellitus in the elderly, Nat. Rev. Endocrinol. 7 (2) (2011) 108–114.
- [21] J.S. Wefel, S.R. Kesler, K.R. Noll, S.B. Schagen, Clinical characteristics, pathophysiology, and management of noncentral nervous system cancer-related cognitive impairment in adults, CA Cancer J. Clin. 65 (2) (2015) 123–138.
- [22] F.J. Wolters, R.A. Segufa, S.K.L. Darweesh, D. Bos, M.A. Ikram, B. Sabayan, A. Hofman, S. Sedaghat, Coronary heart disease, heart failure, and the risk of dementia: a systematic review and meta-analysis, Alzheimers. Dement. 14 (11) (2018) 1493–1504.
- [23] K. Ikebe, Y. Gondo, K. Kamide, Y. Masui, T. Ishizaki, Y. Arai, H. Inagaki, T. Nakagawa, M. Kabayama, H. Ryuno, H. Okubo, H. Takeshita, C. Inomata, Y. Kurushima, Y. Mihara, K. Hatta, M. Fukutake, K. Enoki, T. Ogawa, K.I. Matsuda, K. Sugimoto, R. Oguro, Y. Takami, N. Itoh, Y. Takeya, K. Yamamoto, H. Rakugi, S. Murakami, M. Kitamura, Y. Maeda, Occlusal force is correlated with cognitive function directly as well as indirectly via food intake in community-dwelling older Japanese: from the SONIC study, PLoS. One 13 (2018) e0190741.
- [24] S. Kobayashi, S. Honda, K. Murakami, S. Sasaki, H. Okubo, N. Hirota, A. Notsu, M. Fukui, C. Date, Both comprehensive and brief self-administered diet history questionnaires satisfactorily rank nutrient intakes in Japanese adults, J. Epidemiol. 22 (2) (2012) 151–159.
- [25] S. Kobayashi, K. Murakami, S. Sasaki, H. Okubo, N. Hirota, A. Notsu, M. Fukui, C. Date, Comparison of relative validity of food group intakes estimated by comprehensive and brief-type self-administered diet history questionnaires against 16 d dietary records in Japanese adults, Public Health Nutr. 14 (7) (2011) 1200–1211.
- [26] S. Kobayashi, X. Yuan, S. Sasaki, Y. Osawa, T. Hirata, Y. Abe, M. Takayama, Y. Arai, Y. Masui, T. Ishizaki, Relative validity of brief-type self-administered diet history questionnaire among very old Japanese aged 80 years or older, Public Health Nutr. 22 (2) (2019) 212–222.
- [27] Y. Fujiwara, H. Suzuki, M. Yasunaga, M. Sugiyama, M. Ijuin, N. Sakuma, H. Inagaki, H. Iwasa, C. Ura, N. Yatomi, K. Ishii, A.M. Tokumaru, A. Homma, Z. Nasreddine, S. Shinkai, Brief screening tool for mild cognitive impairment in older Japanese: validation of the Japanese version of the Montreal Cognitive Assessment, Geriatr. Gerontol. Int. 10 (3) (2010) 225–232.
- [28] K. Narazaki, Y. Nofuji, T. Honda, E. Matsuo, K. Yonemoto, S. Kumagai, Normative data for the montreal cognitive assessment in a Japanese community-dwelling older population, Neuroepidemiology. 40 (1) (2013) 23–29.
- [29] H. Ryuno, K. Kamide, Y. Gondo, M. Kabayama, R. Oguro, C. Nakama, S. Yokoyama, M. Nagasawa, S. Maeda-Hirao, Y. Imaizumi, M. Takeya, H. Yamamoto, M. Takeda, Y. Takami, N. Itoh, Y. Takeya, K. Yamamoto, K. Sugimoto, T. Nakagawa, S. Yasumoto, K. Ikebe, H. Inagaki, Y. Masui, M. Takayama, Y. Arai, T. Ishizaki, R. Takahashi, H. Rakugi, Longitudinal association of hypertension and diabetes mellitus with cognitive functioning in a general 70-year-old population: the SONIC study. Hypertens. Res. 40 (7) (2017) 665–670.

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- [30] A. Cedazo-Mínguez, Apolipoprotein E and Alzheimer's disease: molecular mechanisms and therapeutic opportunities, J. Cell Mol. Med. 11 (6) (2007) 1227–1238.
- [31] P. Rinaldi, P. Mecocci, C. Benedetti, S. Ercolani, M. Bregnocchi, G. Menculini, M. Catani, U. Senin, A. Cherubini, Validation of the five-item geriatric depression scale in elderly subjects in three different settings, J. Am. Geriatr. Soc. 51 (5) (2003) 694–698.
- [32] W. Koyano, H. Shibata, K. Nakazato, H. Haga, Y. Suyama, Measurement of competence: reliability and validity of the TMIG Index of Competence, Arch. Gerontol. Geriatr. 13 (2) (1991) 103–116.
- [33] P.N. Papapanou, M. Sanz, N. Buduneli, T. Dietrich, M. Feres, D.H. Fine, T. F. Flemmig, R. Garcia, W.V. Giannobile, F. Graziani, H. Greenwell, D. Herrera, R. T. Kao, M. Kebschull, D.F. Kinane, K.L. Kirkwood, T. Kocher, K.S. Kornman, P. S. Kumar, B.G. Loos, E. Machtei, H. Meng, A. Mombelli, I. Needleman, S. Offenbacher, G.J. Seymour, R. Teles, M.S. Tonetti, Periodontitis: consensus report of workgroup 2 of the 2017 world workshop on the classification of periodontal and peri-implant diseases and conditions, J. Periodontol. 89 (Suppl 1) (2018) S173–S182.
- [34] N. Scarmeas, C.A. Anastasiou, M. Yannakoulia, Nutrition and prevention of cognitive impairment, Lancet Neurol. 17 (11) (2018) 1006–1015.
- [35] X. Jiang, J. Huang, D. Song, R. Deng, J. Wei, Z. Zhang, Increased consumption of fruit and vegetables is related to a reduced risk of cognitive impairment and dementia: meta-analysis, Front. Aging Neurosci. 9 (2017) 18.
- [36] W. Xu, L. Tan, H.F. Wang, T. Jiang, M.S. Tan, L. Tan, Q.F. Zhao, J.Q. Li, J. Wang, J. T. Yu, Meta-analysis of modifiable risk factors for Alzheimer's disease, J. Neurol. Neurosurg. Psychiatry 86 (12) (2015) 1299–1306.
- [37] B.C. da Cunha Germano, L.C.C. de Morais, F. Idalina Neta, A.C.L. Fernandes, F. I. Pinheiro, A.C.M. do Rego, I. Araújo Filho, E.P. de Azevedo, J.R.L. de Paiva Cavalcanti, F.P. Guzen, R.N. Cobucci, Vitamin E and its molecular effects in experimental models of neurodegenerative diseases, Int. J. Mol. Sci. 24 (13) (2023).
- [38] F. Zhou, X. Xie, H. Zhang, T. Liu, Effect of antioxidant intake patterns on risks of dementia and cognitive decline, Eur. Geriatr. Med. 14 (1) (2023) 9–17.
- [39] V. Gil Martínez, A. Avedillo Salas, S. Santander Ballestín, Vitamin supplementation and dementia: a systematic review, Nutrients. 14 (5) (2022).

- [40] N.M. Wedick, A. Pan, A. Cassidy, E.B. Rimm, L. Sampson, B. Rosner, W. Willett, F. B. Hu, Q. Sun, R.M. van Dam, Dietary flavonoid intakes and risk of type 2 diabetes in US men and women, Am. J. Clin. Nutr. 95 (4) (2012) 925–933.
- [41] M. Rossi, C. Bosetti, E. Negri, P. Lagiou, C.La Vecchia, Flavonoids, proanthocyanidins, and cancer risk: a network of case-control studies from Italy, Nutr. Cancer 62 (7) (2010) 871–877.
- [42] A.N. Panche, A.D. Diwan, S.R. Chandra, Flavonoids: an overview, J. Nutr. Sci. 5 (2016) e47.
- [43] I.I. Kruman, T.S. Kumaravel, A. Lohani, W.A. Pedersen, R.G. Cutler, Y. Kruman, N. Haughey, J. Lee, M. Evans, M.P. Mattson, Folic acid deficiency and homocysteine impair DNA repair in hippocampal neurons and sensitize them to amyloid toxicity in experimental models of Alzheimer's disease, J. Neurosci. 22 (5) (2002) 1752–1762.
- [44] Scientific Advisory Committee on Nutrition, SACN statement on diet, cognitive impairment and dementia. GOV.UK. https://www.gov.uk/government/publica tions/sacn-statement-on-diet-cognitive-impairment-and-dementia/, (accessed 30 November 2023).
- [45] H. Zhang, L. Hardie, A.O. Bawajeeh, J. Cade, Meat consumption, cognitive function and disorders: a systematic review with narrative synthesis and meta-analysis, Nutrients. 12 (2020) 1528.
- [46] C. Ballard, S. Gauthier, A. Corbett, C. Brayne, D. Aarsland, E. Jones, Alzheimer's disease, Lancet 377 (2011) 1019–1031.
- [47] I.Xu Lou, K. Ali, Q. Chen, Effect of nutrition in Alzheimer's disease: a systematic review, Front. Neurosci. 17 (2023) 1147177.
- [48] K. Sakurai, E. Okada, S. Anzai, R. Tamura, I. Shiraishi, N. Inamura, S. Kobayashi, M. Sato, T. Matsumoto, K. Kudo, Y. Sugawara, T. Hisatsune, Protein-balanced dietary habits benefit cognitive function in Japanese older adults, Nutrients. 15 (2023) 770.
- [49] M. Iwasaki, A. Yoshihara, H. Ogawa, M. Sato, K. Muramatsu, R. Watanabe, T. Ansai, H. Miyazaki, Longitudinal association of dentition status with dietary intake in Japanese adults aged 75 to 80 years, J. Oral Rehabil. 43 (10) (2016) 737–744.
- [50] S. Watson, L. McGowan, L.A. McCrum, C.R. Cardwell, B. McGuinness, C. Moore, J. V. Woodside, G. McKenna, The impact of dental status on perceived ability to eat certain foods and nutrient intakes in older adults: cross-sectional analysis of the UK National Diet and Nutrition Survey 2008-2014, Int. J. Behav. Nutr. Phys. Act. 16 (1) (2019) 43.