Mushroom Consumption and Incident Dementia in Elderly Japanese: The Ohsaki Cohort 2006 Study

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BACKGROUND: Both *in vivo* and *in vitro* studies have indicated that edible mushrooms may have preventive effects against cognitive impairment. However, few cohort studies have yet examined the relationship between mushroom consumption and incident dementia.

OBJECTIVE: We examined the relationship between mushroom consumption and incident dementia in a population of elderly Japanese subjects.

DESIGN: Prospective cohort study.

SETTING: Ohsaki Cohort 2006 Study.

PARTICIPANTS: 13,230 individuals aged ≥65 years living in Ohsaki City, northeastern Japan.

MEASUREMENTS: Daily mushroom consumption, other lifestyle factors, and dementia incidence.

RESULTS: The 5.7 years incidence of dementia was 8.7%. In comparison with participants who consumed mushrooms <1 time/wk, the multi-adjusted HRs (95% CI) for incident dementia among those did so 1–2 times/week and ≥3 times/week were 0.95 (0.81, 1.10) and 0.81 (0.69, 0.95), respectively (*P*-trend <.01). The inverse association persisted after excluding participants whose dementia event occurred in the first 2 years of follow-up and whose baseline cognitive function was lower. The inverse association did not differ statistically in terms of vegetable consumption (*P*-interaction = .10).

CONCLUSIONS: This cohort study suggests that frequent mushroom consumption is significantly associated with a lower risk of incident dementia, even after adjustment for possible confounding factors. **J Am Geriatr Soc 65:1462–1469, 2017.**

Key words: mushroom; dementia; cohort study; elderly; Japan

As the world's population ages, the number of people with dementia has been increasing,[1] In the absence of curative treatment, a nutritional approach for prevention of dementia has been widely investigated.[2]

In recent years, researchers have begun to pay attention to the health impacts of mushrooms. Several *in vivo*[3,4] and *in vitro*[5] experiments have suggested that mushrooms have beneficial effects on cognitive function. Some animal experiments have revealed that mushrooms can protect cells from oxidative damage[6–8] and inflammation,[9,10] both of which have been implicated in the pathogenesis of dementia.[11,12] Mushrooms have also been shown to have hypolipidemic and antiatherogenic effects,[13,14] playing an indirect role in dementia prevention.

It would therefore be informative to investigate the effects of habitual mushroom intake on cognitive decline or onset of dementia. To date, however, only three epidemiological studies have examined the influence of mushroom consumption on cognition.[15–17] All of them indicated that mushroom consumption was associated with better cognitive performance in terms of perceptual speed, executive function, and memory. However, none of these studies investigated the relationship between mushroom consumption and the risk of incident dementia. In the present study, therefore, we examined this relationship in a population of elderly Japanese subjects.

METHODS

Study Cohort

The design of the Ohsaki Cohort 2006 Study has been described in detail elsewhere.[18] In brief, the source population for the baseline survey comprised 31,694 men and women aged ≥65 years, in Ohsaki City, northeastern Japan, on 1 December 2006.

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The baseline survey was conducted between 1 December and 15 December 2006, and follow-up of the participants was started from 1 April 2007. A questionnaire was distributed by the heads of individual administrative districts to individual households and then collected by mail. In this analysis 23,091 people provided valid responses formed the study cohort (Figure 1). We excluded 6,333 people who did not provide written consent for review of their long-term care insurance (LTCI) information, 2,102 people who had already been certified as having disability by the LTCI before follow-up (1 April 2007), 62 people who had died or moved out of the district during the period of the baseline survey, 192 people whose doctor's opinion paper or cognitive status in the doctor's opinion paper were unavailable and 1,172 persons whose mushroom consumption data were missing. Thus, 13,230 responses were analyzed for the purposes of this study. During the 5.7-year period, only 123 people were lost to follow-up because of migration from the study area, without developing incident dementia, which provided a follow-up rate of 99.1%. Among 65,571 person-years, incident dementia was determined for 1,148 people (8.7%).

Consumption of Mushrooms and Other Foods

We asked about the consumption of mushrooms and other food items using a food-frequency questionnaire (FFQ). The frequency of mushroom consumption was categorized as <1 time/wk, 1–2 times/wk, and ≥3 times/wk.

We conducted a validation study of the FFQ in which 113 respondents provided four 3-day food records within 1 year and subsequently responded to the questionnaire. The Spearman rank correlation coefficient between mushroom consumption according to the questionnaire and that according to the food records was 0.32 for men and 0.55 for women; the correlation between the consumptions measured by the two questionnaires administered 1 year apart was 0.30 for men and 0.33 for women.[19]

Covariates

Body mass index was calculated as the self-reported body weight (kg) divided by the square of the self-reported body height (m).

The K6 was used as an indicator of psychological distress.[20,21] Using six questions, respondents were asked about their mental status over the last month. Total point scores ranged from 0 to 24. Being that a score of 13 is the optimal cut-off point for mental illness in the validation study, we classified individuals with scores of ≥13 as having psychological distress.[21]

The Kihon Checklist was developed by the Ministry of Health, Labor, and Welfare of Japan in order to predict functional decline in community-dwelling elderly. With regard to the motor function score in the Kihon Checklist, respondents were asked about their current motor function

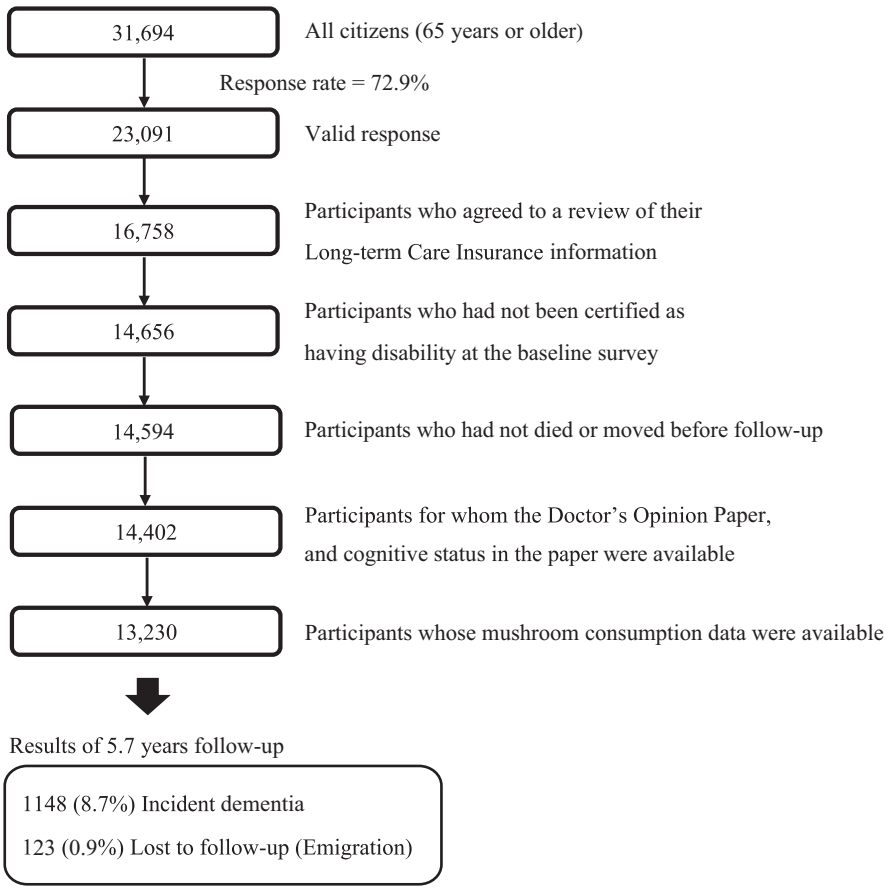

Figure 1. Flow chart of the study participants: the Ohsaki Cohort 2006 Study.

status using five binary questions, yielding total point scores ranging from 0 to 5. As the optimal cut-off point for functional decline suggested in the validation study, we classified individuals with scores of <3 as having better motor function.[22] With regard to the cognitive function score in the Kihon Checklist, respondents were asked about their current cognitive function status using three binary questions yielding total point scores ranging from 0 to 3. The validity of the cognitive function score in the Kihon Checklist had been confirmed in a previous study using the clinical dementia rating (CDR) as a gold standard (sensitivity/specificity: 0.720/0.665 when estimating for a CDR of 1+ (refer to dementia); with all three questions).[23]

Follow-up (Incident Dementia)

The primary outcome was incident dementia, defined as disabling dementia according to the criteria of the long-term care insurance (LTCI) system used in Japan.[24]

The LTCI is a mandatory form of national social insurance to assist daily activity in the disabled elderly.[25–27] Everyone aged ≥40 years pays premiums, and everyone aged ≥65 years is eligible for formal caregiving services under a uniform standard of disability certification. The procedure for disability certification comprises two parts, (1) assessment of the degree of functional disability using a questionnaire developed by the Ministry of Health, Labor, and Welfare, and (2) reference to the doctor's opinion paper prepared by the attending physician.[28] The doctor's opinion paper is a standard form used for assessing patients' chronic medical conditions and functions of daily life.

Disabling dementia was defined as incident functional disability due to dementia according to the LTCI system, the dementia rank II or greater on the Dementia Scale (degree of independence in daily living for elderly with dementia), as entered on the doctor's opinion paper. The Dementia Scale is classified into six ranks (0, I–IV, M; Rank M means that an individual has severe dementia-related behavioral disturbance that requires medical intervention), and a rank exceeding I is usually used as an outcome measure of incident dementia because individuals who have mild or moderate dementia are classified as rank II.[24,29–31] A previous study has shown that the Dementia Scale is negatively correlated with the Mini Mental State Examination score (Spearman rank correlation coefficient = −0.736).[32]

We obtained a dataset that included information on LTCI certification, death, or emigration from Ohsaki City. All data were transferred from the Ohsaki City Government under an agreement related to epidemiologic research and privacy protection.

Ethical Issues

We considered the return of completed questionnaires to imply consent to participate in the study involving the baseline survey data and subsequent follow-up of death and emigration. We also confirmed information regarding LTCI certification status after obtaining written consent along with the questionnaires returned from the subjects at the time of the baseline survey. The Ethics Committee of Tohoku University Graduate School of Medicine (Sendai, Japan) reviewed and approved the study protocol.

Statistical Analysis

We counted the person-years of follow-up for each subject from 1 April 2007 until the date of incident dementia, date of emigration from Ohsaki City, date of death, incident functional disability without dementia, or the end of the study period (30 November 2012), whichever occurred first. In our analysis, deaths without LTCI certification were treated as censored.

The multiple adjusted Cox proportional hazards model was used to calculate the hazard ratios (HRs) and 95% confidence intervals (95% CIs) for incident dementia according mushroom consumption. Dummy variables were created for the mushroom consumption groups, and respondents who consumed mushrooms <1 time/wk (lowest) were defined as a reference category. Multivariate models were adjusted for the following variables. Model 1 was adjusted for age (65–69, 70–74, 75–79, 80–84, or ≥85 years) and gender. To examine whether the association between mushroom consumption and dementia was attributable to a healthy physical status or other lifestyle factors, Model 2 was further adjusted for BMI (in kg/m^2; <18.5, 18.5–25, ≥25, or missing), history of disease (stroke, hypertension, myocardial infarction, diabetes, or hyperlipidemia—yes/no; for each term), education level (age at last school graduation: <16, 16–18, ≥19 years, or missing), smoking (never, former, current, or missing), alcohol drinking (never/former, current, or missing), time spent walking (<1 h/d, ≥1 h/d, or missing) and psychological distress score (<13, ≥13, or missing). In order to adjust for the influence of other dietary factors, model 3 added the consumption volume of specific foods (meat, fish, green and yellow vegetables, and fruits—gender-specific tertile categories, or missing). To test for linear trends, the mushroom consumption categories were entered as a continuous term (scored 1, 2, or 3 instead of <1 time/wk, 1–2 times/wk and ≥3 times/wk, respectively) in the corresponding Cox model.

Considering possible reverse causality, we analyzed whether the association would change if only individuals who had higher cognitive function at the baseline were selected. In this sensitivity analysis, "cognitive function score in the Kihon Checklist = 0 point" was defined as higher cognitive function. Another sensitivity analysis was also conducted by excluding participants whose disability event occurred in the first 2 years of follow-up.

In order to avoid overestimation of the protective effects of mushroom consumption against dementia as far as possible, survival analysis was also conducted using the competing-risk regression model. Competitive events were defined as (1) death, and (2) any other types of disability and death together. For linear trends test, the mushroom consumption categories were entered as a continuous term (scored 1, 2, or 3 instead of <1 time/wk, 1–2 times/wk, and ≥3 times/wk, respectively) in the corresponding competing-risk regression model.

In addition, subgroup analyses were used to investigate whether there was any difference in the relationship between mushroom consumption and incident dementia in

terms of gender. In consideration that frequent mushroom consumption might be along with higher vegetable consumption, subgroup analyses by vegetable consumption volume (<median and ≥median) were also performed. Last, since a higher level of education has been indicated as a protective factor against incident dementia, subgroup analysis by education level (age at last school graduation <16 or ≥16 years) was performed. Meanwhile, a covariate-level-dependent variable was created by forming interaction (cross-product) terms between mushroom consumption and gender, vegetable consumption volume (<median and ≥median), and education level (age at last school graduation <16 or ≥16 years) all variables were categorical, respectively. These interactions were then added as an additional term to the multivariate Cox regression model, separately. We tested whether the effects of mushroom consumption varied according to gender, vegetable consumption volume and education level, and presented the data as the value of *P* for interaction[33] (assuming a null hypothesis that mushroom consumption has no varying effects at different covariate levels).

All data were analyzed using SAS version 9.4 (SAS Inc.). All statistical tests described here were two-sided, and differences at $P < .05$ were accepted as significant.

RESULTS

Baseline Characteristics

The baseline characteristics of the 13,230 participants according to mushroom consumption categories are shown in Table 1. Subjects with a higher mushroom consumption frequency were less likely to be the men, to have an education level of less than 16-year-old when graduated, to be current smokers and alcohol drinkers, and to have psychological distress. Subjects with a lower mushroom consumption frequency were less likely to have a history of hyperlipidemia, to spend 1 hour or more per day walking, and to consume meat, fish, vegetables, and fruits.

Mushroom Consumption and Incident Dementia

The association between mushroom consumption and incident dementia is shown in Table 2. In comparison with participants whose mushroom consumption was <1 time/wk, the incident dementia HR (95% CI) was 0.80 (0.69, 0.92) for participants who consumed mushrooms 1–2 times/wk and 0.63 (0.54, 0.72) for those who consumed mushrooms ≥3 times/wk (*P*-trend <.01 in the crude model). Even after full adjustment for confounding factors, the HR (95% CI) for participants who consumed mushrooms ≥3 times/wk still remained at 0.81 (0.69, 0.95) (*P*-trend <.01 in Model 3).

To examine possible reverse causality for the association between mushroom consumption and incident dementia (Table 3), we analyzed the association after excluding 331 participants who developed incident dementia in the first 2 years of follow-up, but the results for mushroom consumption did not change substantially; the multivariate HR (95% CI) was 1.00 (reference) for <1 time/wk, 0.80 (0.67, 0.95) for 1–2 times/wk, and 0.72 (0.60, 0.87) for ≥3 times/wk (*P*-trend <.01 in Model 3). To consider the

Table 1. Baseline Characteristics of the Participants According to Mushroom Consumption (n = 13,230)

	Mushroom Consumption			
	<1 time/wk	1–2 times/wk	≥3 times/wk	*P*-Value[a]
No. of all participants	3107	4345	5778	
Age (years)	74.2 (6.1)[b]	73.7 (5.9)	73.5 (5.8)	<.01
Gender (male, n (%))	1,735 (55.8)	2,051 (47.2)	2,133 (36.9)	<.01
Body mass index (kg/m^2)	23.6 (3.3)	23.7 (3.4)	23.6 (3.3)	<.01
Past history of (n (%))				
Stroke	90 (2.9)	121 (2.8)	156 (2.7)	.86
Hypertension	1,349 (43.4)	1,888 (43.5)	2,530 (43.8)	.92
Myocardial infarction	187 (6.0)	195 (4.5)	272 (4.7)	<.01
Diabetes	386 (12.4)	498 (11.5)	697 (12.1)	.42
Hyperlipidaemia	173 (5.6)	355 (8.2)	627 (10.9)	<.01
Educational level <16 years (n (%))[c]	1,019 (32.8)	1,253 (28.8)	1,386 (24.0)	<.01
Current smoker (n (%))	1,392 (44.8)	1,623 (37.4)	1,699 (29.4)	<.01
Current alcohol drinker (n (%))	1,592 (51.2)	2,013 (46.3)	2,262 (39.2)	<.01
Psychological distress (n (%))[d]	181 (5.8)	154 (3.5)	180 (3.1)	<.01
Better motor function (n (%))[e]	2,253 (72.5)	3,274 (75.4)	4,350 (75.3)	<.01
Time spent walking ≥1 h/d (n (%))	793 (25.5)	1,157 (26.6)	1,625 (28.1)	.03
Intake of (g/d)				
Meat (beef, pork, ham and chicken)	17.5 (14.1)	20.9 (13.7)	24.6 (16.0)	<.01
Fish	51.4 (32.1)	58.5 (30.2)	69.8 (30.2)	<.01
Green and yellow vegetables	66.9 (43.3)	86.3 (42.6)	115.8 (43.6)	<.01
Fruits	103.3 (86.1)	133.3 (86.0)	169.2 (91.2)	<.01

[a]Obtained using chi-squared test for proportional variables and 1-factor ANOVA for continuous variables.
[b]Mean (SD) (all such values if not specified).
[c]Age at last school graduation <16 years.
[d]Kessler 6-item psychological distress scale score ≥13.
[e]Motor function score of the Kihon Checklist <3.

Table 2. Relationships Between Mushroom Consumption and Incident Dementia (n = 13,230)[a]

	Mushroom Consumption			
	<1 time/wk	1–2 times/wk	≥3 times/wk	*P*-Trend[f]
Person-years	15,056	21,419	29,096	
Incident dementia (%)	11.0	9.0	7.2	
Incidence rate/1,000 person-years	22.7	18.2	14.3	
Crude	1.00	0.80 (0.69, 0.92)[e]	0.63 (0.54, 0.72)	<.01
Model 1[b]	1.00	0.87 (0.75, 1.00)	0.68 (0.59, 0.78)	<.01
Model 2[c]	1.00	0.91 (0.78, 1.05)	0.74 (0.64, 0.86)	<.01
Model 3[d]	1.00	0.95 (0.81, 1.10)	0.81 (0.69, 0.95)	<.01

[a]Analysis by the Cox proportional hazards model.
[b]Model 1 was adjusted for age (65–69, 70–74, 75–79, 80–84, or ≥85 years) and gender.
[c]Model 2 was adjusted as for model 1 plus BMI (<18.5, 18.5–25, ≥25, or missing), history of disease (stroke, hypertension, myocardial infarction, diabetes or hyperlipidemia (yes, no; for each term)), education level (age at last school graduation: <16 years, 16–18 years, ≥19 years, or missing), smoking (never, former, current, or missing), alcohol drinking (never/former, current, or missing), time spent walking (<1 h/d, ≥1 h/d, or missing), psychological distress score (<13, ≥13, or missing).
[d]Model 3 was adjusted as for model 2 plus 4 groups of consumption volume of meat, fish, green and yellow vegetables and fruits (gender-specific tertile categories, or missing).
[e]Adjusted hazard ratios (95% confidence interval) (all such values).
[f]Probability value for trend was computed by entering the categories as a continuous term (score variable: 1, 2 or 3) in the Cox model.

Table 3. Relationships Between Mushroom Consumption and Incident Dementia (Baseline Lower Cognitive Function Excluded, n = 8,191, and 2 Years Dementia Incident Excluded, n = 12,899)[a]

	Mushroom Consumption			
	<1 time/wk	1–2 times/wk	≥3 times/wk	*P* for Trend[f]
Baseline lower cognitive function excluded				
No. of all participants	1,794	2,645	3,752	
Person-years	9,041	13,590	19,509	
Primary outcome events (%)	7.6	5.6	4.3	
Incidence rate/1,000 person-years	15.0	11.0	8.3	
Crude	1.00	0.72 (0.57, 0.91)[e]	0.54 (0.43, 0.68)	<.01
Model 1[b]	1.00	0.81 (0.64, 1.02)	0.60 (0.47, 0.75)	<.01
Model 2[c]	1.00	0.85 (0.67, 1.07)	0.65 (0.52, 0.83)	<.01
Model 3[d]	1.00	0.89 (0.70, 1.13)	0.73 (0.57, 0.95)	.02
2 years dementia incident excluded				
No. of all participants	3,029	4,213	5,657	
Person-years	14,964	21,279	28,972	
Primary outcome events (%)	8.7	6.1	5.2	
Incidence rate/1,000 person-years	17.6	12.1	10.2	
Crude	1.00	0.67 (0.57, 0.80)	0.57 (0.48, 0.67)	<.01
Model 1[b]	1.00	0.73 (0.61, 0.86)	0.60 (0.51, 0.71)	<.01
Model 2[c]	1.00	0.76 (0.64, 0.90)	0.65 (0.55, 0.77)	<.01
Model 3[d]	1.00	0.80 (0.67, 0.95)	0.72 (0.60, 0.87)	<.01

[a]Analysis by Cox proportional hazards model.
[b]Model 1 was adjusted for age (65–69, 70–74, 75–79, 80–84, or ≥85 years) and gender.
[c]Model 2 was adjusted as for model 1 plus BMI (<18.5, 18.5-25, ≥25, or missing), history of disease (stroke, hypertension, myocardial infarction, diabetes or hyperlipidemia (yes, no; for each term)), educational level (age at last school graduation: <16, 16–18, ≥19 years, or missing), smoking (never, former, current, or missing), alcohol drinking (never/former, current, or missing), time spent walking (<1 h/d, ≥1 h/d, or missing), psychological distress score (<13, ≥13, or missing).
[d]Model 3 was adjusted as for model 2 plus 4 groups of consumption volume of meat, fish, green and yellow vegetables and fruits (gender-specific tertile categories, or missing).
[e]Adjusted hazard ratios (95% confidence interval) (all such values).
[f]Probability value for trend was computed by entering the categories as a continuous term (score variable: 1, 2 or 3) in the Cox model.

possibility that cognitive function at the baseline might affect the association between mushroom consumption and incident dementia, we also analyzed the association after selecting 8,191 participants who had better cognitive function (cognitive function score of the Kihon Checklist = 0). However, the results for mushroom consumption did not change substantially; the multivariate HR (95% CI) was 1.00 (reference) for <1 time/wk, 0.89 (0.70, 1.13)

for 1–2 times/week, and 0.73 (0.57, 0.95) for ≥3 times/wk (*P*-trend = .02 in Model 3).

Subgroup Analysis

Sensitivity analysis using subgroups of gender, vegetable consumption volume (<median and ≥median) and education level (age at last school graduation <16 and ≥16 years) (Table S1) were conducted. After adjusting for multivariates, an inverse correlation between mushroom consumption and incident dementia was found only in women (*P* for interaction = .01). This inverse association did not differ significantly between the different volumes of vegetable consumption (*P* for interaction = .10) and the different education levels (*P* for interaction = .63).

DISCUSSION

In this cohort study, we investigated the relationship between mushroom consumption and incident dementia, and observed a significant inverse dose–response association between the two. To our knowledge, this is the first cohort study to have investigated the association between mushroom consumption and incident dementia.

Our results are consistent with previous studies indicating potential benefits of mushroom intake in terms of cognitive function. A randomized double-blind placebo-controlled clinical trial involving 30 subjects with mild cognitive impairment suggested that intake of Yamabushitake mushrooms was associated with significantly increased scores on a cognitive function scale based on the Revised Hasegawa Dementia Scale (HDS-R),[17] and another cross-sectional study suggested that high consumption of mushrooms was associated with better test scores in terms of perceptual speed, executive function, semantic memory, and episodic memory in an elderly population.[15]

Considering the possibility that individuals with weaker cognitive function might have less opportunity to consume mushrooms, we investigated the effects of reverse causality. However, even after excluding individuals who developed incident dementia in the first 2 years of follow-up, the HRs for each category were also almost the same. Additionally, even when we selected only individuals who had better cognitive function at the baseline, the inverse association between mushroom consumption and incident dementia persisted. These findings suggest that the present results are unlikely to be attributable to reverse causality.

In order to eliminate any potential effects of competitive events, we also conducted survival analysis using the competing-risk regression model (Table S2). The significant inverse relationship persisted even when the competing risk of death was considered (*P*-trend <.01 in Model 3). Moreover, the significant inverse relationship also persisted when we considered the competing risk of any other types of disability or death together (*P*-trend <.01 in Model 3).

Even when we performed subgroup analysis by vegetable consumption volume, the results for the relationship between mushroom consumption and incident dementia did not change substantially. Therefore, the association between mushroom consumption and incident dementia seems difficult to explain in terms of vegetable consumption volume.

Our analysis by gender demonstrated a significant inverse dose–response association between mushroom consumption and incident dementia for women, but not for men. This may have been due to a validity difference of mushroom consumption on FFQ between the genders. In our validation study, the Spearman rank correlation coefficient (age- and energy-adjusted and de-attenuated) for mushroom consumption was lower for men than for women (0.32 vs 0.55).[19] If there had been appreciable non-differential misclassification, the present results would have been underestimated.[34] Because the correlations observed here were not particularly high, the use of this FFQ might have attenuated the relationship between mushroom consumption and incident dementia, especially for men. Therefore, the non-significant relationship between mushroom consumption and incident dementia in men might have been explained by non-differential misclassification of mushroom consumption among men.

Others have demonstrated that mushrooms contain various types of natural free radical scavengers, including polysaccharide,[35] polyphenol,[36] vitamins,[37,38] and ergosterol.[39] Therefore, it is plausible that mushrooms could provide beneficial effects by supplying such free-radical scavengers. Previous research has also shown that mushrooms possess anti-oxidant[40–42] and anti-inflammatory[9,43,44] functions, which might have preventive effects against dementia development.

In addition, some studies have also indicated that mushrooms might have protective effects against diseases that increase the risk of dementia, such as atherosclerosis,[45] hypertension,[46] and diabetes,[47] by inhibiting abnormal proliferation of vascular smooth muscle cells,[48] reducing blood fat and retarding atherosclerosis,[13] and ameliorating hyperglycemia and hypercholesterolemia,[49] thus reducing the risk of dementia onset. The present results are consistent with prior evidence suggesting that mushrooms have considerable potential for prevention of dementia.

Our study had a number of strengths: (1) it was a large population-based prospective study involving 13,230 persons; (2) the follow-up rate was almost 100%; (3) many confounding factors were taken into account; and (4) the study subjects lived in an area in which mushrooms are widely consumed.

However, there were also several limitations. First, the causes of dementia were not evaluated, and therefore the mechanism responsible for reduction of incident dementia by mushroom consumption remained unclarified. Second, information on mushroom consumption using the FFQ was obtained only at the baseline, and the study subjects might have changed their mushroom consumption during the course of follow-up. Third, not all potential confounding factors were considered. The baseline characteristics suggested that participants who consumed mushrooms frequently tended to be healthier and have better environmental factors overall (e.g., a lower proportion had a history of hyperlipidemia, were current smokers, or had psychological distress; a higher proportion had better motor function, spent time walking, and consumed fish, green and yellow vegetables, and fruit). Therefore, we could not rule out the possibility that participants with higher mushroom consumption might also have had more favorable potential confounding factors. For example, with

regard to socioeconomic status, previous studies have suggested that education is associated with certain health conditions among the elderly.[50] In the present study, to consider the confounding effect of education, we included education in the multiple-adjustment model and conducted subgroup analysis according to education. As a result, the inverse association between mushroom consumption and incident dementia did not change. Therefore, we assumed that any confounding effect associated with education would have been unable to explain this inverse association totally. However, we might not have eliminated all residual confounding by unmeasured socioeconomic factors such as income.[51] Fourth, we did not attempt to identify the types of mushrooms consumed, and therefore the specific effect of each type remained uncertain.

In conclusion, the present study has shown that mushroom consumption is associated with a decreased risk of incident dementia in Japanese elderly individuals. Our results suggest that habitual mushroom consumption may have a preventive effect against the incident risk of dementia.

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SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article:

Table S1. Relationships between mushroom consumption and incident dementia by gender, vegetable consumption volume, and education level (gender subgroup, n = 13,230; vegetable consumption volume subgroup, n = 11,515; education level subgroup, n = 12,570. Missing data of each subgroup were excluded respectively)[a].

Table S2. Relationships between mushroom consumption and incident dementia (n = 13,230)[a].

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