Original Article

Associations of dietary diversity with allergic diseases in Japanese workers: a cross-sectional study

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Background and Objectives: The aim of this study was to determine the associations of dietary diversity with prevalences of allergic diseases. **Methods and Study Design:** The participants were 1,317 men and women aged 20 to 63 years who were living in Tokushima Prefecture, Japan during the period 2012–2013. We obtained anthropometric data and information on lifestyle characteristics and current medical histories of allergic diseases using a self-administered questionnaire. Dietary intake was assessed using a food frequency questionnaire, and dietary diversity was determined using the Quantitative Index for Dietary Diversity (QUANTIDD). The ORs and 95% CIs for each of the allergic diseases with a 1 standard deviation (SD) increase in the QUANTIDD score were estimated, controlling for age, family history of allergic diseases, education, smoking, drinking, physical activity, energy intake and BMI. **Results:** Higher dietary diversity showed significant inverse dose-response relationships with allergic diseases and allergic rhinitis in women. Multivariate-adjusted ORs (95% CI) for allergic diseases and allergic rhinitis with 1 SD increase in the QUANTIDD score were 0.77 (95% CI: 0.60-0.98, p=0.037) and 0.69 (95% CI: 0.53-0.90, p=0.007), respectively, in women. There were no significant associations between dietary diversity and allergic diseases in men. **Conclusions:** The results indicate that there is an inverse association between higher dietary diversity and allergic rhinitis in Japanese female workers.

Key Words: allergic diseases, allergic rhinitis, dietary diversity, Japanese workers, cross-sectional study

INTRODUCTION

Overeating and an unbalanced diet such as insufficient intake of vegetables have become public health problems in Japan. According to the National Health and Nutrition Survey, intake of healthy food groups (such as fish and shellfish, beans, vegetables and fruits) has been decreasing, especially in young Japanese aged 20-30 years.[1] Dietary guidelines for Japanese recommended eating a variety of foods.[2] Several world dietary guidelines also indicate the importance of eating a variety of foods at all life stage.[3,4]

In the past few decades, the incidence of allergic diseases has been increasing, especially in developed countries.[5-7] A recent study has shown that the increasing incidence of allergic diseases in Asia is related to the changing lifestyle.[8] A survey on the prevalence of allergies and arthritis was carried out in Japan, and it was shown that the prevalence of asthma among adults had consistently increased from 1985 to 2006.[9] The burden of allergic diseases in the world has become a serious problem, and preventive strategies are needed.

Given the potential modulatory effects of nutritional factors on disease, altering dietary habits including intake

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of maternal foods during pregnancy and/or lactation has been considered for preventing allergic diseases.[10-13] Although there have been some epidemiological studies on the associations between dietary diversity and allergic diseases, the results have not been consistent.[14-18] In prospective studies, it has been shown that a higher dietary diversity is associated with lower risks of allergic diseases including allergic dermatitis, asthma and allergic rhinitis in Western children.[14-16] On the other hand, other studies have shown that dietary diversity is not related to allergic dermatitis or atopic hypersensitivity in European infants and young children.[17,18] Those studies were mainly conducted in Western countries and the subjects were only children. The dietary diversity in Western countries may differ from that in Asian countries due to differences in diet, dietary culture and habitual dietary intake. Thus, the associations of dietary diversity with allergic diseases, including allergic rhinitis, atopic dermatitis and asthma, in Japanese adults have not been elucidated. We therefore analyzed the associations of dietary diversity with some allergic diseases in Japanese adults.

METHODS

Study population

This cohort study is a population-based annual examination of a dynamic cohort that was established in Tokushima Prefecture in Japan in 2008, and it is still ongoing. In 2008, the study participants included 821 workers (550 men and 271 women) in Tokushima Prefecture, which is located in Shikoku Island of Japan. The ages of the participants at the first study wave of the study (June 2008-February 2009) were 20-60 years. Workers who were more than 20 years old and were living in Tokushima Prefecture were also newly recruited every year. About double the number of workers were recruited (total number of participants=1,460) from the third-wave survey (June 2010-February 2011). The participants were followed up every year from the first-wave survey and numbers of participants in the follow-up surveys were as follows: second-wave survey (June 2009-February 2010, n=736), third-wave survey (June 2010-February 2011, n=1,460), fourth-wave survey (June 2011-February 2012, n=1,349), fifth-wave survey (June 2012-February 2013, n=1,399), sixth-wave survey (June 2013-February 2014, n=1,432), seventh-wave survey (June 2014-February 2015, n=1,414), eighth-wave survey (June 2015-February 2016, n=1,430), ninth-wave survey (June 2016-February 2017, n=1,455), tenth-wave survey (June 2017-February 2018, n=1,394), and eleventh-wave survey (June 2017-February 2018, n=1,373). For assessment of dietary intake and physical activity, the participants were then followed up with an interval of 5 years from the fifth-wave survey (June 2012-February 2013). In this cross-sectional occupation-based study, data from the fifth-wave survey (June 2012-February 2013) were used. The participants were essentially voluntary participants.

The present study population consisted of 1,399 men and women aged 20-63 years. Participants with missing data for a current medical history of allergic diseases (n=20) including allergic rhinitis, atopic dermatitis and asthma, drinking habits (n=3), education (n=24) and current physical activity (n=7) were excluded. Subjects with a medical history of cancer, heart diseases or stroke (n=16) were also excluded from analysis. Twelve participants whose daily total energy intake was extremely high (mean + 3 standard deviations (SD): 3174.5 kcal/day in men and 2806.7 kcal/day in women) or low (mean – 3 SD: 517.3 kcal/day in men and 499.3 kcal/day in women) were also excluded. Finally, data for the remaining 1,317 participants (972 men and 345 women) were analyzed in this study (Figure 1). The study protocol was approved by the institutional review boards of Tokushima University

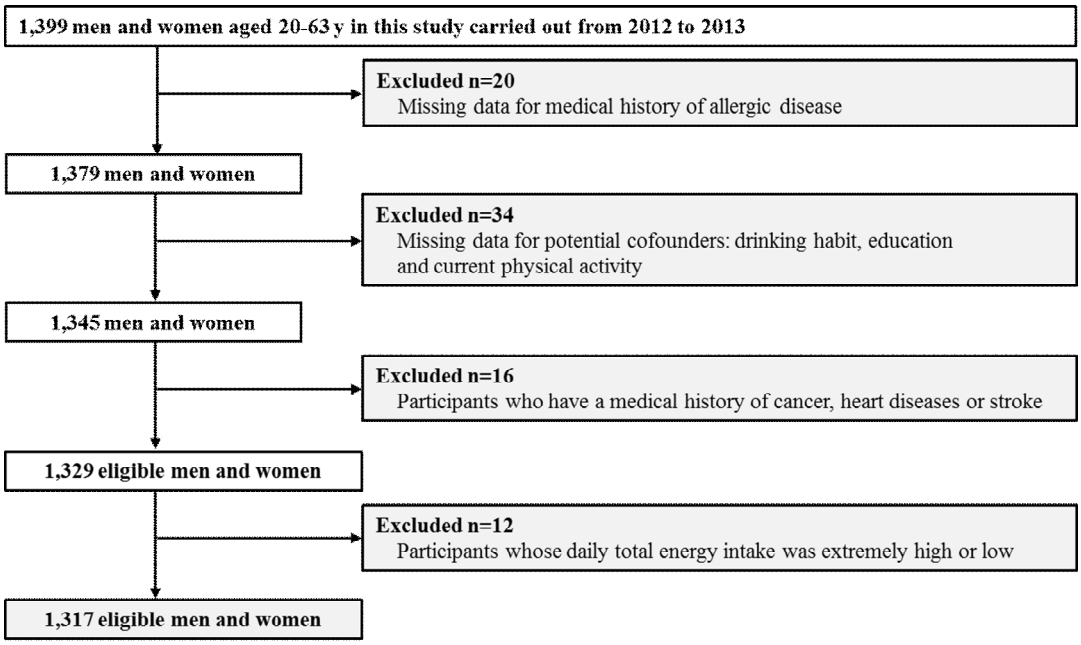

Figure 1. Overview of the participants. Of 1,399 participants aged 20-63 years, we excluded participants for whom some data were missing. Next, we excluded 16 subjects with a medical history of cancer, heart diseases or stroke. We also excluded 12 participants whose daily total energy intake was extremely high or low. Data for the remaining 1,317 participants (972 men and 345 women) were used for analysis in this study.

Hospital (Ethical approval number: 2868).

Assessment of allergic diseases

Allergic diseases were assessed by the question "Have you ever been diagnosed with any allergic diseases by a doctor?" Similar questions were asked for allergic rhinitis, atopic dermatitis and asthma. We defined participants who answered 'Yes' for this question as cases of each allergic disease. We defined participants who is cases of any allergic disease including allergic rhinitis, atopic dermatitis or asthma as 'allergic diseases' in this study. Questions were also given about the age at first diagnosis of each allergic disease and family history of allergic diseases.

Dietary assessment

The participants were requested to complete a questionnaire to obtain data on dietary intake.

Regarding the amounts of intake for food groups and energy, participants were asked about meals taken in the past month using "FFQg ver.2.0" (Kenpakusha Inc.) as a food frequency questionnaire method for determining the frequency and amount of food intake. Food intake was estimated using questionnaires about both the amounts and frequencies of 29 food items and 10 cooked meals. Amounts of food intake were finally calculated for 17 food groups (cereals, potatoes and starches, deep yellow vegetables, mushrooms and other vegetables, seaweed, beans, fish and shellfish, meat, eggs, milk and dairy products, fruits, confectionaries, beverages, sugar and sweeteners, nuts and seeds, fat and oil, and seasonings and spices). The validity of FFQg was verified by Takahashi et al. by comparing food intake amounts using the weighting method for seven consecutive days.[19] The frequency and amount of all foods consumed at each meal were asked (how many times and how much consumed per week). The amount of each food consumed per week was calculated by summing the product of the frequency of intake and the amount consumed at each meal.

Dietary diversity was determined using the Quantitative Index for Dietary Diversity (QUANTIDD) developed by Katanoda et al.[20] QUANTIDD score is calculated by the proportion of foods that contribute to total energy or the amount of foods and the number of food groups using the following formula: QUANTIDD = (1-summation operation prop[j]^2) / (1-1/n), where prop(j) is the proportion of food group(s) j that contributes to total energy or nutrient intake, n is the number of food groups, and j = 1, 2, . ., n. The possible score ranges from 0 to 1. A higher score reflects equal distributions of food groups, and a lower score reflects an unbalanced diet. We calculated the score based on the amounts of 16 food groups excluding beverages.

Dietary patterns were assessed using a correlation matrix for 17 food groups based on principal component analysis. In principal component analysis, the principal components were selected on the basis of eigenvalues (>1.0) and interpretability, and three dietary patterns were identified. Those three principal components explained 39.7% of the total variance (Supplemental Table 1). The first principal component was labeled the healthy dietary pattern because of the higher factor loadings for deep yellow vegetables, mushrooms and other vegetables and beans. The second principal component was labeled the western dietary pattern because of the higher factor loadings for meat, eggs, beverages and seasonings and spices. The third component was labeled snacks because of the higher factor loadings for confectionaries and fat and oil. The three principal component scores were saved for each individual and used for analysis.

Other measurements

The participants were requested not to eat overnight and they underwent a medical health check-up the following day in each worksite. Body height was measured to the nearest 0.1 cm with participants standing without shoes, and body weight was measured to the nearest 0.1 kg with participants wearing lightweight clothing. BMI was calculated by weight (kg) / height (m)^2. Daily values of physical activity (MET-hours/week) were calculated using the International Physical Activity Questionnaire.[21] Data for medical history (binary; yes or no), education level (categorical; elementary, junior high and high schools, tertiary college, career college and junior college, college and graduate school or other), drinking habits (binary; current or former/never) and smoking habits (categorical; current, former or never) were obtained by a self-administered questionnaire. The questionnaire was completed by subjects before the physical examination day, and then it was checked and collected.

Statistical analysis

First, comparisons of the basic and dietary characteristics of the participants by allergic diseases were performed. Continuous variables were expressed as means ± SD, and simple comparisons of the means of data were performed using Student's t-test. Categorical variables were expressed as numbers (percentages), and comparisons of proportions were performed using the chi-square test.

Next, multiple logistic regression analysis was used to estimate the ORs and 95% CIs for medical history of allergic diseases according to a 1 SD increase in QUANTIDD score after controlling for the following variables. The confounding variables were 1) age-adjusted model, age (continuous); 2) Model 1, age-adjusted model + family history of allergic diseases (categorical: yes, no or unknown), smoking habits (binary, current or former/never), drinking habits (binary, current or former/never), physical activity (categorical, yes or no), education level (categorical; elementary and junior high schools, high school and junior college, college and graduate school, other) and BMI (continuous, kg/m^2); and 3) Model 2, Model 1 + energy intake (continuous, kcal/day). In addition, since the associations between dietary diversity and allergic diseases might be confounded by dietary quality such as specific dietary pattern, those associations were further adjusted as follows: 4) Model 3, Model 2 + healthy dietary pattern score (continuous); 5) Model 4, Model 2 + western dietary pattern score (continuous); 6) Model 5, Model 2 + snacks dietary pattern score (continuous).

All statistical analyses were performed separately for both sexes. All statistical tests were based on two-sided probabilities and were performed using SPSS version 18.0J for Windows (SPSS Inc., Japan, Tokyo, Japan).

All p values<0.05 were considered statistically significant.

RESULTS

Characteristics of the participants

The distribution of participants according to the QUANTIDD score is shown in Figure 2. The mean QUANTIDD scores were 0.81±0.087 (minimum-maximum: 0.41-0.95) in men and 0.86±0.056 (minimum-maximum: 0.58-0.96) in women. Table 1 shows the characteristics of participants according to allergic diseases. The proportion of participants with a family history of allergic diseases was higher in participants with allergic diseases than in participants without allergic diseases in both sexes.

Intake of energy and each food group in participants with and those without allergic diseases is shown in Table 2. The amounts of meat intake was greater in participants with allergic diseases than in participants without allergic diseases in women. The amount of fat and oil intake in participants with allergic diseases was greater than that in participants without allergic diseases in both men and women.

Associations of dietary diversity with allergic diseases

Table 3 shows multivariate-adjusted ORs (95% CI) for each of the allergic diseases by increasing 1 SD of the QUANTIDD score.

The score of QUANTIDD showed significant inverse dose-response relationships with allergic diseases and allergic rhinitis. In women, OR (95% CI) for allergic diseases with 1 SD increase in the QUANTIDD score was 0.77 (0.60-0.98; p=0.037) after controlling for age, family medical history of allergic diseases, smoking habits, drinking habits, physical activity, education level, BMI and energy intake (model 2). In addition, OR (95% CI) for allergy rhinitis with 1 SD increase in the QUANTIDD score was 0.69 (0.53-0.90; p=0.007) in women in model 2. Although there was not statistical significance, the QUANTIDD score tended to show an inverse relationship with asthma (OR [95% CI]=0.59 [0.33-1.08], p=0.088 in model 2). The QUANTIDD score in women had no significant association with atopic dermatitis. In men, on the other hand, the QUANTIDD score had no significant association with any of the allergic diseases.

To determine whether the associations between dietary diversity and allergic diseases were confounded by dietary quality such as specific dietary pattern (e.g., healthy dietary pattern, western dietary pattern and/or snacks dietary pattern), those factors were further adjusted (Table 4). After controlling for healthy and/or western dietary pattern scores, although a significant inverse association between QUANTIDD score and allergic rhinitis was maintained, the association between QUANTIDD score and allergic diseases was attenuated in women. However, the other results were essentially the same after adjustment for other dietary patterns.

DISCUSSION

In our study, a higher QUANTIDD score was associated with reduced ORs of allergic diseases, especially allergic rhinitis in women (Table 3). Furthermore, those associations were essentially the same after adjustment for the snacks dietary pattern score (Table 4). However, the associations between QUANTIDD score and allergic diseases were attenuated after controlling for healthy and/or western dietary pattern scores, although the results for allergic rhinitis were essentially the same in women (Table 4). A higher QUANTIDD score was not significantly associated with atopic dermatitis or asthma in women (Tables 3 and 4). In contrast to the results for women, no significant association was found between the QUANTIDD score and each of the allergic diseases in men (Tables 3 and 4).

An inverse association between dietary diversity and allergic rhinitis was shown in this study (Tables 3 and 4), and this result is consistent with the results of a previous study for 3,142 Finnish infants and young children.[14] A previous study in 958 Japanese adults aged over 20 years showed that the prevalence of cedar pollinosis, which is the main symptom of allergic rhinitis, was 39.9%.[22] In that study, it was shown that the incidence of cedar pollinosis until 15 years of age was 5.3% and that almost all of the participants developed allergic rhinitis after adulthood.[22] Therefore, dietary habits in adulthood are more crucial for prevention of the development of allergic rhi-

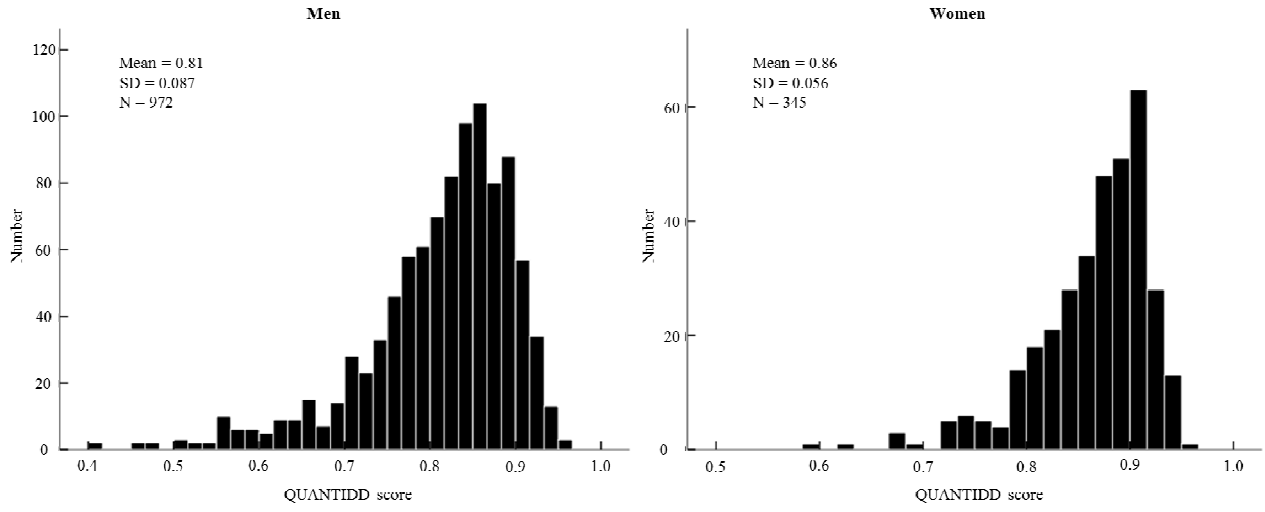

Figure 2. Number of participants (frequency distribution) according to the QUANTIDD score by sex. The mean QUANTIDD scores were 0.81±0.087 (minimum-maximum: 0.41-0.95) in men and 0.86 ± 0.056 (minimum-maximum: 0.58-0.96) in women.

Table 1. Characteristics of participants according to allergic diseases in this study

	Men			Women		
Number of subjects	Without allergic diseases (n=632)	With allergic diseases (n=340)	*p* value	Without allergic diseases (n=184)	With allergic diseases (n=161)	*p* value
Age (years)[†§]	41.5±10.3	40.8±9.3	0.292	39.8±10.3	39.7±9.4	0.970
BMI (kg/m^2)[†§]	23.9±3.5	23.9±3.2	0.905	21.2±3.0	21.2±3.1	0.537
Physical activity (MET-hours/week)[†§]	28.6±49.3	23.5±50.1	0.128	17.2±46.6	20.2±53.9	0.575
Education level[‡¶]			0.573			0.510
Elementary, junior high and high schools	160 (25.3)	80 (23.5)		53 (28.8)	42 (26.1)	
Tertiary college, career college and junior college	130 (20.6)	79 (23.2)		38 (20.7)	44 (27.3)	
College and graduate school	329 (52.1)	177 (52.1)		81 (44.0)	67 (41.6)	
Other	13 (2.1)	4 (1.2)		12 (6.5)	8 (5.0)	
Smoking habits[‡¶]			0.096			0.510
Current	235 (37.2)	106 (31.2)		11 (6.0)	12 (7.5)	
Never	246 (38.9)	155 (45.6)		163 (88.6)	136 (84.5)	
Former	151 (23.9)	79 (23.2)		10 (5.4)	13 (8.1)	
Drinking habits[‡¶]			0.053			0.490
Current	376 (59.5)	221 (65.0)		57 (31.0)	51 (31.7)	
Former / never	256 (40.5)	119 (35.0)		127 (69.0)	110 (68.3)	
Family medical history of allergic diseases[‡¶]	70 (11.1)	119 (35.0)	<0.001	40 (21.7)	74 (46.0)	<0.001

[†]Mean±SD.
[‡]Number (%).
[§]Student's t-test was used to calculate the *p* value.
[¶]The chi-square test or Fisher's exact test was used to calculate the *p* value.

Table 2. Intake of energy and food groups according to allergic diseases in this study[†, ‡]

	Men			Women		
	Without allergic diseases (n=632)	With allergic diseases (n=340)	*p* value	Without allergic diseases (n=184)	With allergic diseases (n=161)	*p* value
Energy intake (kcal/day)	1817±420	1862±412	0.110	1603±337	1675±372	0.062
QUANTIDD score	0.81±0.09	0.82±0.08	0.085	0.87±0.06	0.86 ±0.06	0.695
Cereals (g/day)	400±120	399±109	0.923	315±82.4	331±73.8	0.059
Potatoes and starches (g/day)	19.1±18.4	19.4±18.8	0.815	25.9±21.4	28.1±23.4	0.351
Deep yellow vegetables (g/day)	46.2±32.0	46.5±31.1	0.867	61.9±38.8	55.9±32.5	0.124
Mushrooms and other vegetables (g/day)	77.7±51.2	77.5±46.4	0.944	98.8±58.6	94.9±53.3	0.520
Seaweed (g/day)	2.8±2.5	3.0±2.4	0.215	2.8±2.4	2.8±2.2	0.766
Beans (g/day)	38.6±29.9	41.6±30.7	0.137	37.1±24.9	39.1±31.9	0.510
Fish and shellfish (g/day)	48.6±32.1	50.7±36.1	0.357	45.9±28.3	46.4±29.7	0.877
Meat (g/day)	82.8±43.7	86.5±42.4	0.205	68.5±36.9	81.6±43.0	0.003
Eggs (g/day)	28.5±17.5	29.2±17.9	0.559	25.8±14.3	25.8±15.8	0.993
Milk and dairy products (g/day)	92.7±102	98.1±91.6	0.415	102±81.8	114±100	0.204
Fruits (g/day)	39.2±47.0	39.1±49.7	0.982	62.8±65.9	55.3±55.9	0.260
Confectioneries (g/day)	60.4±44.7	59.8±44.1	0.850	72.2±49.8	72.3±44.6	0.980
Beverages (g/day)	286±230	303±267	0.282	103±125	87.5±115	0.234
Sugar and sweeteners (g/day)	4.6±4.2	4.6±3.8	0.842	6.0±4.2	6.3±4.5	0.584
Nuts and seeds (g/day)	1.6±2.7	1.9±3.5	0.134	1.7±3.2	1.9±3.3	0.693
Fat and oil (g/day)	12.6±7.2	13.6±6.7	0.038	11.9±6.0	13.3±6.8	0.045
Seasonings and spices (g/day)	23.1±10.6	23.9±11.3	0.286	18.7±9.4	19.6±8.5	0.376

[†]Mean±SD

[‡]Student's t-test was used to calculate the *p* value.

Table 3. ORs (95% CI) for each of the allergic diseases according to 1 standard deviation increase in the QUANTIDD score[†¶]

	Men	*p* value	Women	*p* value
Allergic diseases				
Number of cases/subjects	340/972		161/345	
Age-adjusted model	1.13 (0.99, 1.28)	0.078	0.93 (0.75, 1.15)	0.500
Model 1[‡]	1.09 (0.94, 1.26)	0.244	0.88 (0.70, 1.10)	0.273
Model 2[§]	1.06 (0.92, 1.23)	0.406	0.77 (0.60, 0.98)	0.037
Allergy rhinitis				
Number of cases/subjects	283/972		123/345	
Age-adjusted model	1.11 (0.96, 1.27)	0.156	0.88 (0.71, 1.10)	0.255
Model 1[‡]	1.07 (0.92, 1.24)	0.404	0.79 (0.62, 1.00)	0.054
Model 2[§]	1.04 (0.89, 1.22)	0.589	0.69 (0.53, 0.90)	0.007
Atopic dermatitis				
Number of cases/subjects	59/972		37/345	
Age-adjusted model	1.22 (0.92, 1.61)	0.177	0.99 (0.70, 1.39)	0.939
Model 1[‡]	1.19 (0.89, 1.59)	0.242	1.02 (0.70, 1.47)	0.928
Model 2[§]	1.23 (0.90, 1.67)	0.188	0.86 (0.57, 1.29)	0.468
Asthma				
Number of cases/subjects	16/972		13/345	
Age-adjusted model	1.47 (0.81, 2.64)	0.202	0.64 (0.40, 1.03)	0.064
Model 1[‡]	1.50 (0.81, 2.77)	0.197	0.62 (0.37, 1.06)	0.079
Model 2[§]	1.17 (0.62, 2.18)	0.629	0.59 (0.33, 1.08)	0.088

[†]Logistic regression analysis was used to calculate the OR (95% CI).
[‡]Model 1: Adjusted for age (continuous, years), family medical history of allergic diseases (binary, yes or no), smoking habits (binary, current or former/never), drinking habits (binary, current or former/never), physical activity (continuous, MET-hours/week), education level (categorical; elementary, junior high and high schools, tertiary college, career college and junior college, college and graduate school or other) and BMI (continuous, kg/m^2)
[§]Model 2: Adjusted for age, family medical history of allergic diseases, smoking habits, drinking habits, physical activity, education level, BMI and energy intake (continuous, kcal/day)
[¶]1 standard deviations of the QUANTIDD score were 0.087 for men and 0.056 for women.

Table 4. ORs (95% CI) for each of the allergic diseases according to 1 standard deviation increase in the QUANTIDD score after adjustment for dietary patterns [†, ††]

	Men	*p* value	Women	*p* value
Allergic diseases				
Number of cases/subjects	340/972		161/345	
Model 3[‡]	1.09 (0.91, 1.31)	0.330	0.79 (0.59, 1.05)	0.109
Model 4[§]	1.09 (0.94, 1.95)	0.255	0.85 (0.65, 1.11)	0.224
Model 5[¶]	1.08 (0.93, 1.25)	0.335	0.77 (0.60, 0.99)	0.039
Allergy rhinitis				
Number of cases/subjects	283/972		123/345	
Model 3[‡]	1.08 (0.90, 1.31)	0.398	0.67 (0.49, 0.90)	0.009
Model 4[§]	1.07 (0.91, 1.26)	0.436	0.74 (0.56, 0.99)	0.040
Model 5[¶]	1.07 (0.91, 1.25)	0.433	0.70 (0.53, 0.91)	0.008
Atopic dermatitis				
Number of cases/subjects	59/972		37/345	
Model 3[‡]	1.53 (1.05, 2.23)	0.026	0.92 (0.58, 1.47)	0.734
Model 4[§]	1.29 (0.94, 1.78)	0.115	0.92 (0.60, 1.43)	0.726
Model 5[¶]	1.16 (0.85, 1.59)	0.357	0.85 (0.57, 1.27)	0.427
Asthma				
Number of cases/subjects	16/972		13/345	
Model 3[‡]	1.46 (0.67, 3.20)	0.340	0.54 (0.27, 1.10)	0.088
Model 4[§]	1.16 (0.60, 2.26)	0.651	0.57 (0.31, 1.05)	0.071
Model 5[¶]	1.12 (0.59, 2.13)	0.736	0.59 (0.32, 1.08)	0.086

[†]Logistic regression analysis was used to calculate the OR (95% CI).
[‡]Model 3: Adjusted for Model 2 + healthy dietary pattern score (continuous)
[§]Model 4: Adjusted for Model 2 + western dietary pattern score (continuous)
[¶]Model 5: Adjusted for Model 2 + snacks dietary pattern score (continuous)
[††]1 standard deviations of the QUANTIDD score were 0.087 for men and 0.056 for women

nitis than are dietary habits in infants and children. In fact, it has been reported that several dietary patterns affect allergic rhinitis in adults.[23, 24] In a study in the UK in subjects aged 15 to 50 years, it was shown that a dietary pattern with higher intake of vegetables and fruits increased the risk of rhinitis.[23] It has been reported that dietary patterns with higher intake of meat and fish were associated with increased prevalence of asthma and rhinitis including hay fever in Australian adults aged 45 and over.[24] Although these results are for Western people, who have a

different food culture and dietary habits from those of Asians including Japanese, our results also suggest that dietary habits, especially higher dietary diversity, contribute greatly to a reduction in the risk of allergic rhinitis in Japanese adults.

One possible reason for the results obtained in this study is that higher dietary diversity reflects healthy dietary habits. It has been shown that dietary diversity is related to food quality.[25] In the present study, though the results for allergic rhinitis were essentially the same, the association between QUANTIDD score and allergic diseases in women was attenuated after controlling for a healthy dietary pattern score (Table 4). This indicates the possibility that people who have a higher QUANTIDD score consume more healthy foods (e.g., vegetables, fruits, beans and fish) and specific nutrients (e.g., vitamins, dietary fiber, polyphenols and polyunsaturated fatty acid). Actually, both male and female participants who had a higher QUANTIDD score tended to consume more healthy foods (Supplemental Table 3). Intake of lactic acid bacteria,[26] polyphenols,[27] fish oil,[28] vitamin B-6[29] and dietary fiber[30] has been shown to shift the Th1 / Th2 balance to a dominant Th1 response. Dietary habits with higher dietary diversity might shift the Th1 / Th2 balance to Th1 through intake of healthy foods, resulting in a reduction of the prevalence of allergic rhinitis. Another possible reason for the results obtained in this study is that exposure to many kinds of food antigens enhances maturation of the mucosal immune system. In previous studies, exposure to various food antigens was shown to improve the intestinal environment and promote resistance to allergens.[31] Exposure to various dietary antigens by eating many kinds of food may enhance the maturation of the mucosal immune system and reduce the risk of allergic rhinitis. As another possible reason for the results, higher dietary diversity may induce regulatory T cells to inhibit the development of allergic disease. In a prospective study in 1,133 European infants, it was shown that higher food diversity scores were associated with increased gene expression of forkhead box protein 3, which is related to regulatory T cells, and decreased expression of Cε germline transcript, reflecting antibody isotype switching to IgE.[16]

In our study, although higher dietary diversity was associated with reduced ORs of allergic rhinitis, no significant association between dietary diversity and atopic dermatitis or asthma was found in women (Tables 3 and 4). One reason for this result may be that there were differences in the onset times of allergic diseases. It is known that allergic diseases develop mostly in infancy and that their symptoms and causes change with growth. The progression of allergic diseases with growth is called 'allergy march'. Allergy march refers to the progression of allergic diseases from food allergy during infancy to the development of asthma and allergic rhinitis.[32,33] Allergic rhinitis including pollinosis might develop more frequently during adulthood than other allergic diseases such as food allergy or atopic dermatitis based on allergy march. Therefore, allergic rhinitis might be affected more than other allergic diseases by the dietary diversity in adulthood. However, the effects of dietary diversity on allergic diseases have not been fully clarified and further studies are needed.

In this study, the associations between dietary diversity and each of the allergic diseases were different in men and women (Tables 3 and 4). Those results might mean that the effect of dietary diversity on allergic diseases is stronger in women than in men. In this study, the prevalences of allergic diseases were 35.0 % in men and 46.7 % in women. It has been reported that the prevalences of allergic diseases such as allergic rhinitis are lower in men than in women.[34] Another possible reason for the gender difference is the difference in secular change of dietary intake. In our study, the adjusted QUANTIDD decreased significantly from 2010 to 2012 in men but did not change in women (adjusted QUANTIDD scores in 2010, 2011 and 2012: 0.838, 0.820 and 0.812 in men, $p<0.001$; 0.872, 0.872 and 0.866 in women, $p=0.194$) (Supplemental Figure 1).

Our study has some limitations. First, because of the cross-sectional approach, the temporal relationship between dietary diversity and each of the allergic diseases remains obscure. People who have any allergic disease are likely to have had an allergic disease when they were younger such as in early childhood.[35] People who have an allergic disease, especially food allergies, in infancy may have lower dietary diversity because of their limited eatable foods. Therefore, after exclusion of participants who had a medical history of food allergies (case numbers of food allergies: 29 in men and 20 in women), we analyzed the association between QUANTIDD score and allergic diseases. The results obtained after exclusion of those participants were essentially the same as the results shown in Tables 3 and 4 for both sexes. The ORs (95% CIs; *p*-value) for allergic diseases, allergic rhinitis, atopic dermatitis and asthma with 1 SD increase in the QUANTIDD score were 0.72 (0.55-0.93; $p=0.013$), 0.70 (0.53-0.92; $p=0.011$), 0.93 (0.60-1.44; $p=0.729$) and 0.67 (0.37-1.21; $p=0.183$), respectively, in women, though there were no significant associations in men. However, further prospective studies are needed to clarify the effects of dietary diversity on allergic diseases. Second, the sample size of this study, especially for women, was small. Third, the findings might not be generalizable to other populations because the study participants were only Japanese workers. We could not obtain information on the kind of occupation for each of the participants, though the kind of occupation is important information for workers. Fourth, we could not take into consideration the effects of diet restriction to maintain weight and a good figure on eating behavior (e.g. eating a variety of foods) because we could not obtain information on whether participants in this study actually restrict their diet or not. It was shown in a previous study that the percentage of people who underreported their energy intake was higher in people who wanted to reduce their weight than in people who did not want to reduce their weight.[36] In addition, it was also shown that people who were actually trying to lose weight underreported their energy intake.[36] Therefore, it is possible that the relationship between dietary diversity and allergic diseases be distorted if participants actually restricted their diet to maintain weight and a good figure. Consequently, we tried to analyze the associations be-

tween dietary diversity and allergic diseases after controlling for information on whether participants try to maintain an ideal weight or a weight close to the ideal weight. The results were essentially the same after adjustment for information on whether participants try to maintain an ideal weight or a weight close to the ideal weight: ORs (95% CIs; *p*-value) for allergic rhinitis, atopic dermatitis and asthma with 1 SD increase in the QUANTIDD score were 0.71 (0.54-0.92; p=0.011), 0.90 (0.59-1.37; p=0.625) and 0.62 (0.33-1.16; p=0.135), respectively, in women. Fifth, although it is known that allergic diseases, especially atopic dermatitis, develop mostly in infancy, [35] dietary intake was assessed during adulthood. In fact, in our study, 58.6% of the participants with an allergic disease had an allergy onset age of under 20 years, and the mean allergy onset age was 20.1±12.4 years (data not shown). This time lag may have resulted in a random measurement error in exposure variables. However, the effect may be toward an attenuation of the relation. Sixth, information on current medical history of allergic diseases was based on self-reporting, and occult and undiagnosed patients may have been missed. In the case of misclassifications of self-reported information, the effect might also have masked the true effects. In addition, because there were few cases of atopic dermatitis and asthma (prevalence rates: 6.1% and 1.6% in men and 10.7% and 3.8% in women, respectively) in our study, our results for atopic dermatitis and asthma may have been accidentally obtained. Therefore, interpretation of our results for atopic dermatitis and asthma needs to be done carefully. Finally, there may be confounding factors that were not removed completely, though various potentially-important confounders were adjusted in the analysis.

In conclusion, our results indicate the possibility that dietary diversity is inversely associated with allergic diseases, especially allergic rhinitis. Further large-scale prospective studies on the effects of dietary diversity on allergic diseases are needed.

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AUTHOR DISCLOSURES

All authors state that they have no conflicts of interest.

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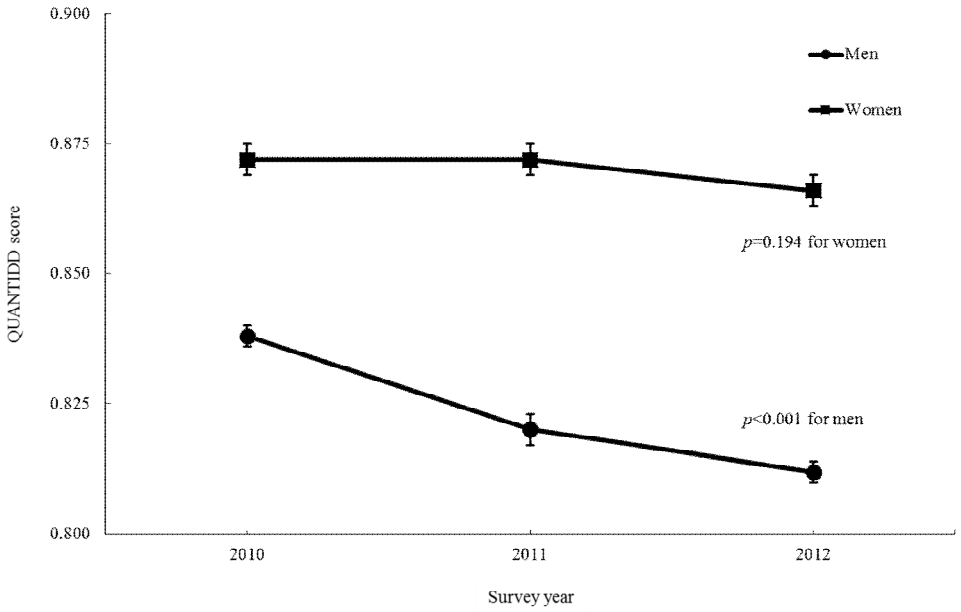

Supplemental figure 1. Data are shown as means ± standard error. Mixed-effects regression models were used for analyses of repeated measures of the QUANTIDD score from 2010 to 2012. Male adjusted QUANTIDD score decreased significantly for three years (cumulative number=3,100, $p<0.001$), but female adjusted QUANTIDD score did not change (cumulative number=1,101, $p=0.194$).

Supplemental table 1. Factor loading matrix for major dietary patterns [†, ‡]

	Dietary pattern		
	Healthy	Western	Snacks
Cereals	0.185	0.442[†]	-0.244
Potatoes and starches	0.587[†]	-0.143	0.197
Deep yellow vegetables	0.710[†]	-0.262	-0.112
Mushrooms and other vegetables	0.742[†]	-0.186	-0.057
Seaweed	0.586[†]	-0.031	-0.246
Beans	0.607[†]	-0.007	-0.335
Fish and shellfish	0.582[†]	0.099	-0.288
Meat	0.351	0.519[†]	0.194
Eggs	0.353	0.418[†]	-0.019
Milk and dairy products	0.288	-0.237	0.243
Fruits	0.514[†]	-0.392	0.080
Confectionaries	0.077	-0.002	0.717[†]
Beverages	-0.119	0.500[†]	0.012
Sugar and sweeteners	0.505[†]	-0.132	0.308
Nuts and seeds	0.333	-0.029	0.141
Fat and oil	0.383	0.412[†]	0.443[†]
Seasonings and spices	0.451[†]	0.466[†]	-0.068
Eigen value	3.8	1.6	1.3
Contribution rate, %	22.4	9.6	7.7
Cumulative contribution rate, %	22.4	32.1	39.7

[†]Value indicates a case in which each factor loading value for each dietary pattern was <-0.40 or >0.40.
[‡]The principal components were selected on the basis of eigenvalues (≥1.0) and interpretability. Principal component scores were saved for each individual.

Supplemental table 2. Characteristics of participants according to tertiles of dietary diversity score in this study by sex

	Men (n=972)					Women (n=345)				
	QUANTIDD score §§					QUANTIDD score §§				
	Tertile 1 (low)	Tertile 2	Tertile 3 (high)	*p* value	*p* for trend	Tertile 1 (low)	Tertile 2	Tertile 3 (high)	*p* value	*p* for trend
number of subjects	324	325	323			115	115	115		
Age (years)†¶	40.0±9.8	41.1±9.6	42.6±10.2	0.005	0.002	37.4±8.9	39.9±9.5	42.0±10.5	0.001	0.002
BMI (kg/m^2)†¶	23.9±3.4	23.9±3.4	23.8±3.3	0.934	0.686	20.9±3.0	21.8±3.2	21.2±3.0	0.061	0.382
Physical activity (MET-hours/week)†, ††	23.4±53.6	26.3±51.1	30.9±43.5	<0.001	<0.001	15.4±30.5	13.6±21.2	26.8±78.0	0.133	0.067
Education level ‡, ‡‡				<0.001	<0.001				0.561	0.357
Elementary, junior high and high schools	95 (29.3)	81 (24.9)	64 (19.8)			29 (25.2)	32 (27.8)	34 (29.6)		
Tertiary college, career college and junior college	82 (25.3)	70 (21.5)	57 (17.6)			30 (26.1)	26 (22.6)	26 (22.6)		
College and graduate school	144 (44.4)	171 (52.6)	191 (59.1)			46 (40.0)	50 (43.5)	52 (45.2)		
Other	3 (0.9)	3 (0.9)	11 (3.4)			10 (8.7)	7 (6.1)	3 (2.6)		
Smoking habits‡, ‡‡				0.006	0.002				0.401	0.149
Current	137 (42.3)	111 (34.2)	93 (28.8)			12 (10.4)	6 (5.2)	5 (4.3)		
Never	115 (35.5)	143 (44.0)	143 (44.3)			96 (83.5)	101 (87.8)	102 (88.7)		
Former	72 (22.2)	71 (21.8)	87 (26.9)			7 (6.1)	8 (7.0)	8 (7.0)		
Drinking habits‡, ‡‡				0.011	0.004				0.041	0.016
Current	178 (54.9)	206 (63.4)	213 (65.9)			29 (25.2)	33 (28.7)	46 (40.0)		
Former / never	146 (45.1)	119 (36.6)	110 (34.1)			86 (74.8)	82 (71.3)	69 (60.0)		
Family medical history of allergic diseases‡, ‡‡				0.598	0.369				0.650	0.679
Yes	61 (18.8)	61 (18.8)	67 (20.7)			33 (28.7)	39 (33.9)	42 (36.5)		

†Mean±SD ‡Number (%) §Median (25%, 75%)
‡Analysis of variance was used to calculate the p value and the Jonckheere-Terpstra test was used to calculate the *p* for trend.
††The Kruskal-Wallis test was used to calculate the p value and the Jonckheere-Terpstra test was used to calculate the *p* for trend.
‡Analysis of variance was used to calculate the p value and the Jonckheere-Terpstra test was used to calculate the *p* for trend.
‡‡The chi-square test was used to calculate the p value and the Mantel-Haenszel test was used to calculate the *p* for trend
§§ QUANTIDD score: T1: 0-0.795, T2: 0.795-0.859, T3: 0.859-1.00 for men, T1: 0-0.853, T2: 0.853-0.898, T3: 0.898-1.00 for women

Supplemental table 3. Energy and food intake according to tertiles of dietary diversity score by sex[†‡]

	Men (n=972)					Women (n=345)				
	QUANTIDD score [§]			*p* value	*p* for trend	QUANTIDD score [§]			*p* value	*p* for trend
	Tertile 1 (low)	Tertile 2	Tertile 3 (high)			Tertile 1 (low)	Tertile 2	Tertile 3 (high)		
number of subjects	324	325	323			115	115	115		
Energy intake (kcal/day)	1723±415	1792±370	1982±423	<0.001	<0.001	1476±299	1633±292	1802±389	<0.001	<0.001
Cereals (g/day)	463±121	387±97.5	347±97.7	<0.001	<0.001	348±76.5	330±64.8	289±82.7	<0.001	<0.001
Potatoes and starches (g/day)	11.8±12.4	17.0±14.4	28.7±22.8	<0.001	<0.001	16.0±14.7	26.5±20.2	38.3±25.1	<0.001	<0.001
Deep yellow vegetables (g/day)	30.7±22.1	43.5±25.8	64.7±35.6	<0.001	<0.001	37.5±26.5	58.6±28.8	81.1±37.8	<0.001	<0.001
Mushrooms and other vegetables (g/day)	49.9±33.5	74.6±42.5	109±52.1	<0.001	<0.001	64.6±39.9	100±51.5	126±57.9	<0.001	<0.001
Seaweed (g/day)	1.9±1.7	2.6±2.1	4.0±2.9	<0.001	<0.001	2.0±1.9	2.8±2.2	3.5±2.6	<0.001	<0.001
Beans (g/day)	26.7±21.1	36.9±26.3	55.4±34.3	<0.001	<0.001	27.1±22.1	38.9±28.9	48.1±26.9	<0.001	<0.001
Fish and shellfish (g/day)	36.1±27.8	47.2±28.4	64.9±37.2	<0.001	<0.001	30.2±23.6	49.6±28.8	58.5±26.9	<0.001	<0.001
Meat (g/day)	71.9±41.2	83.3±43.2	97.0±41.9	<0.001	<0.001	57.9±30.3	77.7±40.7	88.3±43.0	<0.001	<0.001
Eggs (g/day)	24.1±15.8	28.5±16.3	33.6±19.3	<0.001	<0.001	23.0±15.3	26.3±14.4	28.1±15.0	0.035	0.003
Milk and dairy products (g/day)	52.8±78.2	103±105	129±95.4	<0.001	<0.001	91.6±117	111±77.1	119±70.4	0.058	<0.001
Fruits (g/day)	18.5±29.0	33.7±44.0	65.4±54.6	<0.001	<0.001	34.1±37.3	52.8±58.3	90.9±70.3	<0.001	<0.001
Confectioneries (g/day)	49.8±41.2	57.7±40.0	73.0±48.6	<0.001	<0.001	60.5±42.7	69.0±44.0	87.3±51.3	<0.001	<0.001
Beverages (g/day)	292±247	283±246	300±238	0.682	0.315	99.2±132	73.6±98.5	115±126	0.033	0.202
Sugar and sweeteners (g/day)	3.3±3.0	4.2±3.5	6.3±4.9	<0.001	<0.001	4.7±3.6	5.7±4.1	8.0±4.5	<0.001	<0.001
Nuts and seeds (g/day)	1.1±2.4	1.6±2.8	2.4±3.5	<0.001	<0.001	0.8±2.3	1.6±2.6	2.9±4.2	<0.001	<0.001
Fat and oil (g/day)	10.4±5.4	13.0±6.8	15.5±7.8	<0.001	<0.001	10.6±6.3	12.5±5.3	14.6±7.0	<0.001	<0.001

[†]Mean±SD.
[‡]Analysis of variance was used to calculate the p value and the Jonckheere-Terpstra test was used to calculate the *p* for trend.
[§]QUANTIDD score: T1: 0-0.795, T2: 0.795-0.859, T3: 0.859-1.00 for men, T1: 0-0.853, T2: 0.853-0.898, T3: 0.898-1.00 for women.