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Vegetable and fruit intake and risk of type 2 diabetes: Japan Public Health Center-based Prospective Study

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Abstract

Vegetable and fruit intake has been associated with a reduced risk of cancer and CVD, but its relationship to the risk of type 2 diabetes remains unclear. We prospectively examined the association between vegetable and fruit intake and the incidence of type 2 diabetes. Subjects were 21 269 men and 27 168 women aged 45–75 years who participated in the second survey of the Japan Public Health Center-based Prospective Study and had no history of type 2 diabetes or other serious diseases. Intake of vegetables and fruit was estimated using a validated 147-item FFQ. The OR of self-reported, physician-diagnosed type 2 diabetes over 5 years was estimated using multiple logistic regression. A total of 896 newly diagnosed cases of type 2 diabetes were self-reported. Intake of vegetables and fruit combined or fruit only was not associated with a lower risk of type 2 diabetes. However, there was an approximately 20 %, albeit not statistically significant, risk reduction associated with vegetables (men only), green leafy vegetables (men and women) and cruciferous vegetables (men only). Such risk reduction was somewhat greater among obese or smoking men than non-obese or non-smoking men. In conclusion, although a small beneficial effect of vegetables, especially green leafy and cruciferous vegetables, cannot be excluded, vegetable and fruit intake may not be appreciably associated with the risk of type 2 diabetes for Japanese adults.

Key words: Vegetables: Fruit: Type 2 diabetes: Green leafy vegetables

Type 2 diabetes is among the most common chronic diseases in the world, with the estimated prevalence being 2·8 % in 2000 and 4·4 % in 2030[1]. In Japan, the prevalence of diabetes has increased markedly in the last few decades[2]. Dietary factors may play an important role in the development of type 2 diabetes[3]. As vegetables and fruit are rich in antioxidants and Mg, both of which have been associated with a decreased risk of type 2 diabetes[4,5], intake of these foods may prevent type 2 diabetes. Vegetables and fruit are a major source of dietary fibre[6], which has been shown to improve insulin sensitivity and insulin secretion[7]. However, a meta-analysis of prospective studies showed that vegetable and fruit fibre is inconsistently associated with the risk of type 2 diabetes[8]. In two meta-analyses of prospective studies mainly conducted among Western populations, intakes of vegetables and fruit combined, vegetable only, and fruit only were not significantly associated with the risk of type 2 diabetes[4,9]. However, further analysis found a statistically significant 14 % reduction in the risk of developing type 2 diabetes in individuals with a high intake of green leafy vegetables[9], suggesting a possibility that specific groups of vegetables, rather than total vegetables, may protect against the development of type 2 diabetes.

The relationship of vegetable and fruit intake to the risk of type 2 diabetes has received little attention in Asia, where only one Chinese study examined the association in a prospective design[10]. There are differences in types of vegetable consumed between Asian and Western populations[11]. For instance, Asian people consume a large amount of cruciferous vegetables[12], which contain substantial amounts of isothiocyanates, which have antioxidant properties[13]. However, epidemiological evidence regarding cruciferous vegetable intake and the risk of type 2 diabetes is limited and inconsistent[10,14].

Abbreviation: JPHC, Japan Public Health Center-based Prospective.

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In addition, Japanese patients with type 2 diabetes are generally leaner than Western counterparts[15], and Japanese-Americans are known to have lower β-cell function than non-Hispanic whites[16]. Thus, aetiological factors of this disease in Japanese may differ from those in Western populations. Furthermore, most large-scale prospective studies on this issue included women only or men and women combined, and the evidence in men is sparse. Here, we prospectively investigated the risk of type 2 diabetes in relation to vegetable and fruit intake in a large-scale, population-based cohort of Japanese men and women. We also examined the association with specific groups of vegetables and fruits.

Materials and methods

Study design

The Japan Public Health Center-based Prospective (JPHC) Study was established in 1990 for cohort I and in 1993 for cohort II[17]. The study protocol was approved by the institutional review board of the National Cancer Center, Tokyo, Japan. The participants of cohort I included residents aged 40–59 years in five Japanese public health centre areas (Iwate, Akita, Nagano, Okinawa and Tokyo); the participants of cohort II included residents aged 40–69 years in six public health centre areas (Ibaraki, Niigata, Kochi, Nagasaki, Okinawa and Osaka). Although we did not require written informed consent, the study participants were informed of the objectives of the study, and participants who responded to the questionnaire survey were considered to have consented to participate in the survey. A questionnaire survey was conducted at baseline (in 1990 for cohort I and in 1993 for cohort II), at the 5-year follow-up (in 1995 for cohort I and in 1998 for cohort II) and at the 10-year follow-up (in 2000 for cohort I and in 2003 for cohort II). Information on medical histories and health-related lifestyle, smoking, drinking, and dietary habits was examined at each survey. The present study was approved by the Institutional Review Board of the National Cancer Center of Japan.

From the baseline subjects (*n* 140 420), 113 403 subjects responded to the questionnaire survey at baseline. Of these, 89 947 (79·3 %) subjects responded to the 5-year follow-up survey (second survey). Of these subjects, 76 901 (67·8 %) responded to the questionnaire survey at the 10-year (third) survey. We excluded 28 073 subjects who reported a history of type 2 diabetes or severe disease at baseline or the second survey, or kidney disease at baseline survey, and, additionally, missing information for vegetable and fruit intake. We also excluded 391 subjects who reported extreme total energy intakes (outside of the mean ± 3 SD according to sex). Finally, a total of 48 437 subjects (21 269 men and 27 168 women) remained in this analysis.

FFQ

Participants completed a self-administered FFQ at baseline, and at the second and third surveys. We used data that included 147 food and beverage items and nine frequency categories[18] from the second survey as baseline data in the present analysis, because the questionnaire used for the second survey more comprehensively inquired about food intakes than did that used for the baseline survey. At the second survey, the FFQ asked about the usual consumption of sixteen fruit (papaya, mandarin oranges, other oranges, apples, persimmons, strawberries, grapes, melons, watermelon, peaches, pears, kiwifruit, pineapple, bananas, 100 % orange juice and 100 % apple juice) and thirty vegetable (carrots, spinach, pumpkins, cabbage, Chinese cabbage, Chinese radishes, salted pickles of Chinese radishes, salted pickles of green leafy vegetables, pickled plums, pickled Chinese cabbage, pickled cucumbers, pickled eggplant, sweet pepper, tomatoes, Chinese chives, garland chrysanthemums, *komatsuna*, broccoli, onions, cucumbers, bean sprouts, snap beans, lettuce, *chingensai*, leaf mustard, bitter gourds, (Swiss) chard, loofah, mugwort and tomato juice) items commonly consumed in Japan in the past year[18]. The seasonal variation of fruit and vegetable intake was reported. Seasonal coefficients, which were determined based on the intake reported by dietary records by season, were used to calculate the average annual intake of such foods. For most food items, nine response options were available to describe consumption frequency, ranging from rarely (<1 time/month) to ≥7 times/d. A standard portion size was specified for each food, and respondents were asked to denote their usual portion size from three options (≤0·5 times, standard or ≥1·5 times). The daily intake of vegetables and fruit was calculated by multiplying daily consumption frequency by the typical portion size, and expressed as g/d. These individual items were categorised into three main groups of total fruit and vegetables, total vegetables, and total fruits, and into four subgroups of total green and yellow vegetables (spinach, *komatsuna*, Chinese chives, garland chrysanthemums, *chingensai*, leaf mustard, mugwort, (Swiss) chard, broccoli, sweet pepper, snap beans, carrots, tomatoes, pumpkins and tomato juice), green leafy vegetables (spinach, *komatsuna*, Chinese chives, garland chrysanthemums, *chingensai*, leaf mustard, mugwort and (Swiss) chard), cruciferous vegetables (cabbage, Chinese radishes, *komatsuna*, broccoli, Chinese cabbage, *chingensai* and leaf mustard) and citrus fruits (mandarin oranges, other oranges and 100 % orange juice).

Referring to the Standard Tables of Food Composition in Japan[19], dietary intake for energy and selected nutrients was estimated. The validity and reproducibility of the FFQ were examined in a subsample of the participants in the JPHC Study cohort I and cohort II (215 men and women in cohort I and 350 men and women in cohort II for validity, 209 men and women in cohort I and 289 men and women in cohort II for reproducibility). Details of the validation study have been described elsewhere[20–22]. The participants completed both FFQ at a 1-year interval and a total of 28 or 14 d dietary records. For validity of the FFQ, Spearman's correlation coefficients between intake values for vegetables and fruit derived from the FFQ and those derived from dietary records were 0·23–0·47 and 0·23–0·55, respectively, for cohorts I and II[20,21]. With regard to the reproducibility of the FFQ, Spearman's correlation coefficients for the intake of vegetables and fruit derived from the two FFQ administered 1 year apart were 0·53–0·62 and 0·50–0·57, respectively, for cohorts I and II[20,22].

Ascertainment of type 2 diabetes

Type 2 diabetes was ascertained by a self-administered questionnaire. At the third survey, study participants were asked whether they had ever been diagnosed with diabetes, and if so, when the initial diagnosis had been made. Because the 5-year survey was used as baseline in the present study, only participants who were subsequently diagnosed were regarded as incident cases during the follow-up. Details regarding assessment of the validity of self-reported diabetes have been described elsewhere[23]. Previously, we found that 94 % of self-reported diabetes cases were confirmed as such by medical records. We also conducted a cross-sectional survey in 1990 to examine the sensitivity of diagnosed diabetes according to the criteria at that time for a JPHC subpopulation (health check-up participants) whose plasma glucose data were available[23]. The sensitivity and specificity of diagnosed diabetes were 85·5 and 99·7 %, respectively, in men and 79·3 and 99·7 %, respectively, in women.

Statistical analyses

Analyses were performed on men and women, separately. Participants were divided into intake quartiles. Confounding variables considered were as follows: age (years, continuous); study area (eleven areas); BMI (<21, 21–22·9, 23–24·9, 25–26·9 or ≥27 kg/m^2); smoking status (lifetime non-smoker, former smoker, or current smoker with a consumption of either <20 or ≥20 cigarettes/d); alcohol consumption (non-drinker, occasional drinker, or drinker with a consumption of <150, 150–299, 300–499 or ≥450 g ethanol/week for men and <150 or ≥150 g ethanol/week for women); leisure-time activity (<1 time/month, 1–3 times/month or ≥1 time/week); history of hypertension (yes or no); family history of diabetes mellitus (yes or no); coffee consumption (almost never, <1, 1 or ≥2 cups/d); total energy intake (kJ/d, continuous); Ca intake (mg/d, continuous); Mg intake (mg/d, continuous). An indicator variable for missing data was created for each covariate. Trend associations between confounding factors and vegetable or fruit intakes were used by using the Mantel–Haenszel χ^2 test for categorical variables and linear regression analysis for continuous variables.

The association between intakes of vegetables and fruit combined, vegetable, fruit, or specific vegetable or fruit items and diabetes risk was assessed by OR, which were estimated by multiple logistic regression. A 95 % CI of OR was estimated by the Wald method. The first model was adjusted for age and study area, and the second model was further adjusted for BMI, smoking status, alcohol consumption, family history of diabetes mellitus, history of hypertension, leisure-time activity, total energy intake, coffee consumption, and intakes of Ca and Mg. Trend associations were assessed by assigning the ordinal numbers 0–3 to the four categories of each vegetable and/or fruit or specific groups of vegetable or fruit consumption. We also analysed data by BMI (<25 or ≥25 kg/m^2) in both men and women and smoking status (non-smoker or current smoker) in men. An interaction term of dietary intake (continuous) and the above stratifying variables (dichotomous) was created and added to the model to assess statistical interactions. Statistical significance was declared if the two-sided *P*-value was less than 0·05 or if 95 % CI did not include unity. All analyses were performed using SAS software (version 9.2; SAS Institute).

Results

At baseline (at the time of the second survey), both men and women with higher intakes of vegetable and fruit were more likely to be old and less likely to report a smoking habit or alcohol use. They also had higher leisure-time activity, and intakes of energy and micronutrients than those without (Table 1). Only men with higher intakes of vegetables and fruit had higher BMI and intakes of protein and fat than those with lower intakes.

During the 5-year period, 896 participants (530 men and 366 women) were newly diagnosed with type 2 diabetes. There was no statistically significant association with the risk of type 2 diabetes and intakes of vegetables and fruit combined in both men and women (Table 2). We also observed no statistically significant association with intakes of either vegetables or fruit. However, men in the highest quartile of vegetable intake had a 19 % lower odds of developing type 2 diabetes compared with those in the lowest quartile (OR 0·81, 95 % CI 0·59, 1·13).

No statistically significant associations were found between specific groups of vegetable items and the risk of type 2 diabetes (Table 3). However, the risk of type 2 diabetes was 17 % lower among men (OR 0·83, 95 % CI 0·62, 1·12) and 19 % lower among women (OR 0·81, 95 % CI 0·57, 1·16) in the highest quartile of green leafy vegetable intake compared with those in the lowest intake group of each sex. Additionally, men, but not women, in the highest quartile of cruciferous vegetable intake had a 22 % lower odds of developing type 2 diabetes compared with those in the lowest quartile (OR 0·78, 95 % CI 0·58, 1·06).

In stratified analyses by BMI among men, the highest quartile of vegetable intake was associated with a 24 %, albeit not statistically significant, lower odds of type 2 diabetes compared with the lowest quartile in the overweight group (OR 0·76, 95 % CI 0·47, 1·22), whereas a smaller (12 %) risk reduction was observed in the normal-weight group (OR 0·88, 95 % CI 0·55, 1·40, *P* for interaction=0·42). As regards cruciferous vegetable intake, a greater risk reduction was observed in overweight men than those of normal weight. In the analyses by smoking among men, intake of cruciferous vegetables was marginally, inversely associated with the risk of type 2 diabetes in current smokers; the multivariate-adjusted OR of type 2 diabetes for the lowest to the highest quartile category of intake were 1·00 (reference), 0·72 (95 % CI 0·51, 1·02), 0·79 (95 % CI 0·55, 1·12) and 0·64 (95 % CI 0·42, 0·98) (*P* for trend=0·06). In contrast, no such trend association

Table 1. Baseline characteristics of the subjects according to categories of total vegetable and fruit intake
(Mean values and standard deviations)

	Men									Women								
	Quartiles of total vegetable and fruit intake									Quartiles of total vegetable and fruit intake								
	Q1 (low)		Q2		Q3		Q4 (high)			Q1 (low)		Q2		Q3		Q4 (high)		
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	*P* for trend*	Mean	SD	Mean	SD	Mean	SD	Mean	SD	*P* for trend*
n	5317		5317		5318		5317			6793		6791		6792		6792		
Age (years)	49·6	7·5	50·2	7·6	50·8	7·7	51·7	7·5	< 0·0001	50·5	8·1	50·6	7·6	51·0	7·5	51·3	7·3	< 0·0001
BMI (kg/m^2)	23·5	2·9	23·6	2·8	23·6	2·8	23·7	2·8	< 0·0001	23·4	3·2	23·3	3·1	23·3	3·0	23·5	3·0	0·50
Current smoker (%)	53·8		46·8		43·0		39·1		< 0·0001	7·1		4·5		3·6		2·9		< 0·0001
Alcohol consumption ≥ 1 d/week (%)	71·1		69·6		68·3		64·6		< 0·0001	15·3		14·3		12·8		10·9		< 0·0001
Sports ≥ 1 time/week (%)	17·7		22·0		23·3		24·4		< 0·0001	17·6		21·8		23·0		23·7		< 0·0001
History of hypertension (%)	15·5		15·9		17·3		16·5		0·052	17·8		17·1		16·9		17·7		0·81
Family history of diabetes (%)	8·3		8·0		9·0		8·8		0·15	8·5		9·3		9·0		10·0		0·007
Postmenopause (%)										66·9		71·1		73·1		76·5		< 0·0001
Food and nutrient intake																		
Total energy intake (kJ/d)†	443	131	499	135	555	144	661	181	< 0·0001	359	103	424	110	478	119	591	158	< 0·0001
Protein (g/d)†	69	14	73	13	75	13	76	12	< 0·0001	68	11	70	10	70	10	68	9	0·96
Fat (g/d)†	52	17	56	16	57	15	58	14	< 0·0001	57	15	58	12	57	11	54	10	< 0·0001
Carbohydrate (g/d)†	274	51	278	47	284	46	298	47	< 0·0001	250	37	252	33	256	33	288	35	< 0·0001
Ca (mg/d)†	434	228	488	217	525	211	571	201	< 0·0001	506	235	552	209	573	199	585	185	< 0·0001
Mg (mg/d)†	250	47	273	47	289	46	317	51	< 0·0001	246	43	267	42	282	43	302	48	< 0·0001
Coffee consumption ≥ 1 cup/d (%)	31·3		34·9		34·4		32·8		< 0·0001	39·4		38·7		37·2		34·5		< 0·0001

* On the basis of the Mantel–Haenszel χ^2 test for categorical variables and linear regression analysis for continuous variables with assignment of ordinal numbers 0–3 to categories of total vegetable and fruit intake.
† Energy-adjusted intake.

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Table 2. Type 2 diabetes according to quartile categories of total vegetable and/or fruit intakes
(Odds ratios and 95 % confidence intervals)

	Men									Women								
	Quartile category									Quartile category								
	Q1 (low)		Q2		Q3		Q4 (high)		*P* for trend*	Q1 (low)		Q2		Q3		Q4 (high)		*P* for trend*
	OR	95 % CI	OR	95 % CI	OR	95 % CI	OR	95 % CI		OR	95 % CI	OR	95 % CI	OR	95 % CI	OR	95 % CI	
Total vegetable and fruit intake																		
No. of subjects/cases	5317/145		5317/118		5318/146		5317/121			6793/100		6791/89		6792/75		6792/102		
Median (g)	146·0		273·1		414·1		686·8			209·7		365·7		532·9		858·7		
Range (g)	0–212·06		212·11–336·84		336·86–516·96		≥516·97			8·81–290·69		290·70–443·07		443·08–657·47		≥657·5		
Age and area-adjusted OR†	1·00	Ref	0·82	0·64, 1·05	1·01	0·80, 1·28	0·85	0·66, 1·08	0·47	1·00	Ref	0·90	0·67, 1·20	0·75	0·55, 1·01	1·00	0·76, 1·34	0·76
Multivariate-adjusted OR‡	1·00	Ref	0·85	0·66, 1·10	1·08	0·83, 1·40	0·93	0·67, 1·29	0·90	1·00	Ref	0·94	0·69, 1·28	0·79	0·56, 1·11	1·04	0·69, 1·55	0·83
Total vegetable intake																		
No. of subjects/cases	5317/145		5317/134		5318/134		5317/117			6793/96		6790/97		6793/74		6792/99		
Median (g)	75·2		141·7		213·1		355·4			99·5		172·7		252·5		406·9		
Range (g)	0–110·10		110·12–175·00		175·02–266·67		≥266·73			0–137·90		137·95–209·24		209·27–312·17		≥312·20		
Age and area-adjusted OR†	1·00	Ref	0·93	0·73, 1·18	0·93	0·73, 1·18	0·81	0·63, 1·04	0·13	1·00	Ref	1·02	0·77, 1·36	0·76	0·56, 1·03	0·99	0·74, 1·32	0·53
Multivariate-adjusted OR‡	1·00	Ref	0·93	0·73, 1·19	0·92	0·70, 1·20	0·81	0·59, 1·13	0·25	1·00	Ref	1·04	0·77, 1·41	0·76	0·54, 1·08	0·99	0·66, 1·47	0·53
Total fruit intake																		
No. of subjects/cases	5316/146		5319/132		5317/124		5317/128			6792/103		6792/71		6792/92		6792/100		
Median (g)	36·4		113·1		191·6		362·4			74·4		166·3		272·2		487·1		
Range (g)	0–75·51		75·53–146·85		146·86–252·99		≥253·20			0–123·95		123·96–214·66		214·67–353·41		≥353·46		
Age and area-adjusted OR†	1·00	Ref	0·96	0·88, 1·04	1·01	1·00, 1·02	1·02	0·71, 1·46	0·27	1·00	Ref	0·70	0·51, 0·95	0·92	0·68, 1·23	0·99	0·74, 1·33	0·66
Multivariate-adjusted OR‡	1·00	Ref	0·94	0·73, 1·19	0·91	0·70, 1·18	0·94	0·71, 1·26	0·64	1·00	Ref	0·73	0·53, 1·00	0·96	0·70, 1·32	1·04	0·73, 1·48	0·54

Ref, reference.
* Linear trends across quartiles of fruit and vegetable intake were tested by using the median consumption for each quartile as an ordinal variable.
† Adjusted for age and public health centre area.
‡ Additionally adjusted for BMI, smoking status, alcohol consumption, leisure-time activity, history of hypertension, coffee consumption, family history of diabetes, Mg intake, Ca intake and energy intake.

Table 3. Type 2 diabetes according to quartile categories of specific vegetable or fruit intakes

(Odds ratios and 95 % confidence intervals)

	Men									Women								
	Quartile category									Quartile category								
	Q1 (low)		Q2		Q3		Q4 (high)			Q1 (low)		Q2		Q3		Q4 (high)		
	OR	95 % CI	OR	95 % CI	OR	95 % CI	OR	95 % CI	*P* for trend*	OR	95 % CI	OR	95 % CI	OR	95 % CI	OR	95 % CI	*P* for trend*
Total green and yellow vegetables																		
Median (g)	24·7		58·8		94·6		172·4			35·4		70·9		113·2		197·5		
Range (g)	0–41·22		41·23–75·27		75·28–122·62		≥122·63			0–53·72		53·73–89·72		89·73–142·95		≥142·96		
Age and area-adjusted OR†	1·00	Ref	0·81	0·63, 1·04	0·99	0·78, 1·25	0·83	0·65, 1·07	0·38	1·00	Ref	1·04	0·78, 1·37	0·83	0·62, 1·13	0·88	0·66, 1·18	0·21
Multivariate-adjusted OR‡	1·00	Ref	0·82	0·64, 1·06	1·05	0·82, 1·36	0·90	0·66, 1·22	0·91	1·00	Ref	1·06	0·79, 1·42	0·84	0·61, 1·17	0·89	0·61, 1·29	0·32
Green leafy vegetables																		
Median (g)	4·5		11·8		22·7		47·2			7·4		16·7		29·5		57·5		
Range (g)	0–8·17		8·18–16·32		16·33–31·53		≥31·54			0–11·91		11·92–22·49		22·50–39·35		≥39·36		
Age and area-adjusted OR†	1·00	Ref	0·89	0·70, 1·13	0·86	0·68, 1·10	0·79	0·62, 1·02	0·07	1·00	Ref	0·80	0·60, 1·08	0·88	0·66, 1·17	0·82	0·61, 1·10	0·27
Multivariate-adjusted OR‡	1·00	Ref	0·92	0·72, 1·17	0·88	0·68, 1·14	0·83	0·62, 1·12	0·22	1·00	Ref	0·81	0·60, 1·10	0·88	0·65, 1·20	0·81	0·57, 1·16	0·34
Cruciferous vegetables																		
Median (g)	17·6		37·3		60·8		103·9			24·0		47·6		72·5		119·8		
Range (g)	0–27·12		27·13–48·48		48·49–76·55		≥76·58			0–35·59		35·60–59·35		59·36–89·82		≥89·84		
Age and area-adjusted OR†	1·00	Ref	1·01	0·80, 1·28	0·96	0·76, 1·22	0·78	0·61, 1·01	0·06	1·00	Ref	1·06	0·79, 1·43	1·08	0·81, 1·45	1·04	0·78, 1·41	0·76
Multivariate-adjusted OR‡	1·00	Ref	1·02	0·80, 1·30	0·94	0·73, 1·22	0·78	0·58, 1·06	0·12	1·00	Ref	1·09	0·80, 1·48	1·13	0·82, 1·55	1·10	0·77, 1·57	0·57
Citrus fruits																		
Median (g)	7·2		46·5		79·3		165·4			19·1		66·0		114·8		248·9		
Range (g)	0–23·13		23·17–60·03		60·60–108·15		≥108·21			0–47·51		47·61–86·42		86·60–154·07		≥154·56		
Age and area-adjusted OR†	1·00	Ref	1·00	0·79, 1·27	0·81	0·63, 1·04	0·98	0·77, 1·25	0·50	1·00	Ref	0·89	0·66, 1·19	0·88	0·65, 1·19	1·11	0·83, 1·48	0·51
Multivariate-adjusted OR‡	1·00	Ref	1·00	0·79, 1·28	0·85	0·65, 1·10	1·04	0·79, 1·36	0·85	1·00	Ref	0·91	0·67, 1·23	0·92	0·67, 1·27	1·14	0·82, 1·58	0·47

Ref, reference.

* Linear trends across quartiles of fruit and vegetable intake were tested by using the median consumption for each quartile as an ordinal variable.

† Adjusted for age and public health centre area.

‡ Additionally adjusted for BMI, smoking status, alcohol consumption, leisure-time activity, history of hypertension, coffee consumption, family history of diabetes, Mg intake, Ca intake and energy intake.

was observed among non-smoking men; the multivariate-adjusted OR of type 2 diabetes for the lowest to the highest quartile category of intake were 1·00 (reference), 1·49 (95% CI 1·04, 2·13), 1·20 (95% CI 0·81, 1·76) and 1·03 (95% CI 0·66, 1·61) (P for trend=0·81, P for interaction=0·51). There was no differential association of BMI in women.

Discussion

In the present large-scale, population-based, prospective study in Japanese adults, we found no significant association of the intake of vegetables and fruit combined and of either vegetables or fruit with the risk of type 2 diabetes. High consumptions of green leafy vegetables (men and women) and cruciferous vegetables (men) were associated, albeit not statistically significant, with a reduced risk of type 2 diabetes.

The present finding of the null association between total vegetable and fruit intake and type 2 diabetes is consistent with the result of a meta-analysis of four prospective studies among Western populations (pooled hazard ratio 1·00, 95% CI 0·92, 1·09)[9]. Additionally, a meta-analysis of data from five prospective studies including a Chinese one found no clear association with vegetable intake and the risk of type 2 diabetes[9], although a statistically significant inverse association was observed in the Shanghai Women's Health Study. Fruit intake was not associated with the risk of type 2 diabetes in the present study, a finding also consistent with that of the above meta-analysis[9]. Vegetables and fruit are rich in fibre[6]. Several studies have shown that dietary fibre was associated with insulin sensitivity and improved ability to secrete insulin adequately to overcome insulin resistance[7], but recent two meta-analyses of prospective cohort studies did not detect any clear association between vegetable and fruit fibre and the risk of type 2 diabetes[8,24]. Mg, which is also contained in vegetables and fruit, has been associated with a lower risk of type 2 diabetes[5,8]. In the present study population, however, Mg intake was not clearly associated with the risk of type 2 diabetes[25].

Few prospective studies have investigated the risk of type 2 diabetes in association with individual vegetable groups. As regards green leafy vegetables, men and women in the highest quartile of intakes had a 17 and 19%, respectively, lower risk of type 2 diabetes compared with those in the lowest quartile, although the reductions were not statistically significant. Such a modest decrease in risk agrees with the result of a meta-analysis of four prospective studies including the Shanghai Women's Health Study, the Nurses' Health Study, the National Health and Nutrition Examination Survey and the Finnish Mobile Clinic Health Examination Survey[9], in which the risk of type 2 diabetes for the highest category of green leafy vegetable intake was 14% lower compared with that for the lowest category. Green leafy vegetables are rich in phytochemicals such as vitamin C and carotenoids (α-carotene, β-carotene and lutein)[26], which are known for their antioxidant properties, in addition to vitamins A and K, and folate. Antioxidants have been shown to improve insulin sensitivity in several clinical trials[27] and associated with a decreased risk of type 2 diabetes in a meta-analysis of US cohort studies[4]. Anti-diabetic effects of these nutrients might thus explain the protective association between green leafy vegetables and type 2 diabetes.

Cruciferous vegetables contain substantial amounts of glucocinolates, which are hydrolysed to isothiocyanates and indoles[12]. Isothiocyanate is an antioxidant that can attenuate oxidative stress and tissue/cell damage both *in vivo* and *in vitro* experimental studies[13]. In the present study, there was a suggestive inverse association between cruciferous vegetable intake and type 2 diabetes in men, but not in women. Epidemiological evidence on this topic is limited and inconsistent. The Shanghai Women's Health Study showed a significant inverse association between cruciferous vegetable intake and type 2 diabetes[10], whereas the Women's Health Study found no clear association[14]. The inconsistency in results might be ascribed, at least in part, to the difference in the amount of cruciferous vegetable intake[12] and the method of food grouping among studies.

Obesity and smoking are known predictors for the risk of type 2 diabetes[28,29]. In the present study, a suggestive protective association of total and cruciferous vegetable intake with the risk of type 2 diabetes was somewhat stronger among men with BMI $\geq 25\,kg/m^2$ or smoking men compared with those with BMI $< 25\,kg/m^2$ or non-smoking men, respectively. This could be attributed solely to chance, but other explanation is possible. Cigarette smoking is a cause of oxidative stress, which can induce β-cell dysfunction and insulin resistance[27]. In obesity, adipose tissue releases large amounts of NEFA, glycerol, hormones, pro-inflammatory cytokines and other factors that are involved in the development of insulin resistance[30]. Although vegetable intake was not clearly associated with type 2 diabetes among overall subjects in the present and previous studies, it may exert a favourable effect, through its antioxidative properties, on glucose metabolism specifically for persons with increased oxidative stress due to smoking and obesity.

The effect of vegetable intake on glucose metabolism may differ according to cooking method. In the present study population, the major cooking styles of vegetables were stewing (36·3% in men and 42·2% in women, respectively) and stir-frying (41·7% in men and 42·1% in women, respectively), but mainly eating raw vegetable was less common (15·8% in men and 10·4% in women, respectively). However, because we did not ask consumption of vegetables by cooking method, we could not analyse the data in detail. Further studies should address this issue by using a dietary questionnaire that assesses dietary consumption according to cooking method.

The major strengths of the present study included a large number of the participants including both men and women, population-based prospective design, use of a validated FFQ and adjustment for or stratification by potentially important confounding variables. In addition, our dietary questionnaire included many vegetable items, which allowed us to examine the association for specific groups of vegetables. Limitations of the present study also deserve mention. First, subclinical diseases at baseline might have distorted our risk estimate to some extent. Second, because we had no source of information other than questionnaire for the identification of type

2 diabetes, we might have underestimated the incidence of type 2 diabetes. Such underestimation probably did not vary by dietary intake level and thus might not have influenced the risk estimate. However, if the participants with higher vegetable and fruit intake sought medical attention to a greater degree than those with lower vegetable and fruit intake, then type 2 diabetes might have been diagnosed more frequently among those with higher vegetable and fruit intake, which might have attenuated the estimated OR in the present study. Third, the loss-to-follow-up bias is a concern in longitudinal studies. In the present study, participants with the highest level of vegetable and fruit intake (86·8 % in men and 90·0 % in women) were more likely to participate into the follow-up survey than those with the lowest level (80·1 % in men and 83·1 % in women). Given the relatively high follow-up rate, however, we believe that the effect of bias associated with differential follow-up was small, if any. Fourth, the follow-up period was relatively short (5 years). Fifth, the validity of the FFQ for vegetable and fruit intake was moderate at best (r 0·23–0·55). The measurement error in the FFQ might result in biased associations between vegetable and fruit intake and type 2 diabetes towards the null. In the present study, the observed associations would have underestimated the true magnitude of the protective association between vegetable and fruit intake and type 2 diabetes. In addition, dietary intake was assessed at baseline only and may not have represented long-term habitual intake relevant to the development of type 2 diabetes. Repeated assessment of diet over a long period of time before disease onset will probably provide a better estimate of exposure status. Finally, we could not rule out the possibility of unmeasured and residual confounding.

In conclusion, the present study provided no evidence to support a protective role of vegetable and fruit intake against type 2 diabetes in Japanese. A modest reduction in type 2 diabetes risk associated with intakes of green leafy vegetables (men and women) or cruciferous vegetables (men only) deserves further investigation.

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