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Intake of Fruits and Vegetables, and Risk of Endometrial Cancer in Women in the NIH-AARP Diet and Health Study

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Abstract

Fruits and vegetables contain a wide variety of phytochemicals which may have anti-carcinogenic effects. Although the results of case-control studies have suggested a possible protective effect of fruit and vegetable intake on the risk of endometrial carcinoma, few cohort studies have examined this association. We used data from the NIH-AARP Diet and Health Study to assess the association of fruit and vegetable consumption, as well as intake of specific botanical groupings of fruits and vegetables, with endometrial cancer risk among 112,088 women who completed a food-frequency questionnaire at baseline, in 1995–1996. During 8 years of follow-up 1142 incident cases of endometrial cancer were ascertained. Cox proportional hazards models were used to estimate hazard ratios (HR) and 95% confidence intervals (95% CI). After adjustment for covariates, HRs for the highest compared to the lowest quintile of total vegetable and total fruit intake were 1.30 (95% CI 1.04–1.61, P for trend 0.05) and 1.09 (95% CI 0.90–1.33, P for trend 0.55), respectively. No inverse associations were observed for intake of any of 13 botanical groupings of fruits and vegetables. Results from this large prospective study do not support a protective role of a high intake of fruits or vegetables on the risk of endometrial cancer.

Introduction

Endometrial cancer is the fourth most common cancer in women in the United States, accounting an estimated 42,000 new cases and for 8,000 deaths in 2009 (1). Established risk factors for endometrial cancer include obesity and use of unopposed estrogens (2, 3). The association between dietary factors and endometrial cancer risk has also been investigated, particularly consumption of dietary fat, fiber, and fruits and vegetables, but the results have been inconclusive (2). Two recent reviews of the association of fruit and vegetable intake and risk of endometrial cancer have suggested that there may be a modest inverse association between total vegetable, cruciferous vegetable, and total fruit intake (4) or between intake of "non-starchy vegetables" or cruciferous vegetables (5) and risk of endometrial cancer. Such associations could be due to one or more of the many compounds in fruits and vegetables which may inhibit carcinogenesis, including carotenoids, tocopherols, indoles, isothiocyanates, isoflavones, phytosterols, and flavonoids (5–7). However, studies showing inverse association have almost exclusively been case-control studies. Indeed, only two cohort studies have addressed the association between fruit and vegetable intake and endometrial cancer risk, and their results have been null (8, 9). Thus, there is a need for further cohort studies on this topic.

We used data from a large prospective cohort study of endometrial cancer in older women to assess the association of fruit and vegetable intake, as well as intake of specific botanical groups, and risk of endometrial cancer.

Materials and Methods

Study Population

The NIH-AARP Diet and Health Study is a large prospective cohort study of AARP members initiated in 1995–1996. The rationale and design of the study have been described in detail previously (10). In brief, 617,119 AARP members between the ages of 50 and 71 years, residing in six U.S. states and two metropolitan areas covered by population-based cancer registries, responded to self-administered questions covering demographic characteristics, dietary intake, and numerous health-related behaviors. The baseline questionnaire was satisfactorily completed by 567,169 of these respondents, of whom 227,021 were women. After exclusion of duplicates, women who died or moved away before the study start date, or withdrew from the study, 226,733 women were available for analysis. The study was approved by the National Cancer Institute Special Studies Institutional Review Board, and return of the questionnaire signified consent.

Among women with completed questionnaires, we excluded subjects who had questionnaires completed by proxy respondents (N = 1,265), who had had previous cancers (N = 23,343), who were in poor health (N = 3,412) or had end-stage renal disease (N =285), who had prevalent endometrial cancer (N = 57), or who died before study entry (N = 44). In addition, we excluded women who reported having had a hysterectomy (N = 80,445) or with unknown hysterectomy status (N = 2,897), those who reported that their periods stopped due to surgery, chemotherapy, or radiation treatment (N = 1,875), cases with non-epithelial cancers of the uterus (N = 80), 938 women with extreme values for calorie intake, and 3 women who died and 1 woman who moved out of the study area before the start date (scanning of the baseline questionnaire). After these exclusions, the analytic dataset consisted of 112,088 women of whom 1142 were cases.

Assessment of Dietary Intake

The baseline semi-quantitative food-frequency questionnaire asked about participants' usual intake and portion size of 124 food items, including 14 fruit items and 23 vegetable items during the previous year. Participants were asked about their frequency of consumption in 10 preset categories ranging from "never" to "2+ times per day" for solid foods and "never" to "6+ times per day" for beverages. For each line item the respondent could select one of three possible portion size categories. In addition, respondents were asked to record the usual number of servings of vegetables (not including salad or potatoes) and fruit (not including juices) in terms of 9 frequency categories ranging from "less than one per week" to "≥4 per day." The food items, portion sizes, nutrient database, and food servings database were constructed using methods developed by Subar et al. (11) based on national dietary data from the U.S. Department of Agriculture's 1994–1996 Continuing Survey of Food Intakes by Individuals (12). The MyPyramid Equivalents Database (MPED) version 1.0 used a recipe file to disaggregate food mixtures into their component ingredients and assign them to food groups and to calculate cup equivalents for fruits and vegetables. A cup equivalent is defined as 1 cup of raw or cooked vegetable or fruit; 1 cup of vegetable or fruit juice; ½ cup of dried fruit; 2 cups of leafy salad greens (13). White potatoes were excluded from the total vegetable group. Fruits and vegetables were also grouped into botanical families, in which foods are classified according to their phytochemical content and proposed mechanism of action (14). In addition, other groupings of fruits and vegetables (e.g., dark green vegetables, orange vegetables, starchy vegetables, etc.) were also analyzed.

The food frequency questionnaire was validated using two 24-hour recalls in a subset of the cohort (15). Energy-adjusted correlation coefficients for total fruits and vegetables were 0.72 and 0.61 in men and women, respectively.

Ascertainment of Endometrial Cancer

New cases of endometrial cancer occurring in members of the cohort were ascertained by linkage to eight state cancer registries up to December 31, 2003 (22). Surveillance was recently expanded to include 3 additional states (TX, AZ, and NV) to identify cancer diagnoses among cohort members who moved to those states during follow-up. Histology was defined according to the International Classification of Diseases for Oncology codes (3rd edition) (SEER ICD-O-3). A validation study indicated that study procedures identified approximately 90% of all incident cases within the eight registries (16).

Statistical Analysis

Follow-up of the cohort was calculated from the date of date of return of the baseline questionnaire until diagnosis of endometrial cancer, the date of moving out of registry ascertainment area, death, or end of the follow-up period (December 31, 2003). Cox proportional hazards models, with duration of follow-up (person-years) as the underlying metric, were used to estimate hazard ratios (HR) and 95% confidence intervals (95% CI) for the association of fruit and vegetable intake with risk of endometrial. The fruit and vegetable variables were energy-adjusted using the density method, with energy included in the model, because most dietary variables were correlated with total energy intake (17). Quintiles of intake were computed based on the distribution in the total study population, after the exclusions described above. In addition, we categorized fruit and vegetable intake into deciles in order to examine a wider range of intake. In order to adjust for the potential confounding variables, multivariate models included the following variables: age at baseline (continuous), race/ethnicity (white, other), education (high school graduate or less, some college or more), body mass index (<25 kg/m2, 25–29, ≥30, missing), smoking (never, former, current), age at menarche (<13 years, 13–14, ≥15), parity (none, 1, 2, ≥3), use of oral contraceptives (ever, never), use of hormone therapy (ever, never), age at menopause (premenopausal, <45 years, 45–49, ≥55, postmenopausal, unknown age), frequency of vigorous physical activity (never/rarely, >1 time/month but <3 times/week, ≥3 times/week, missing), total fat intake (continuous), and caloric intake (continuous). Tests for trend across ordered categorical variables were calculated using the median value for each category. In addition, we carried out stratified analyses to determine whether fruit and vegetable intake were associated with endometrial cancer in specific subgroups at increased or reduced risk due to established risk factors (age, body mass index, hormone therapy, smoking status, and physical activity).

Because type 1 endometrial cancer (endometrioid adenocarcinoma) appears to differ in terms of etiology and prognosis from type 2 (clear cell and papillary carcinomas) (18–20), we repeated the main analysis restricted to type 1 endometrial cancer, which accounted for 85% of cases (972 cases out of 1,142). We also performed a sensitivity analysis excluding endometrial cancer cases diagnosed within the first 3 years following baseline.

Results

Age at menarche, parity, oral contraceptive use, hormone therapy, and age at menopause varied little by level of total intake of fruits and vegetables (Table 1). Women who were younger, less educated, obese, were current smokers, or never-or-rarely engaged in physical activity tended to consume fewer fruits and vegetables. Total calorie intake was inversely related to fruit and vegetable intake.

In both age-adjusted and multivariable-adjusted models, total combined intake of fruits and vegetables and total vegetable intake were not associated with endometrial cancer (Table 2). In both age-adjusted and multivariable-adjusted models, hazard ratios for quintiles 2–5 of total fruit intake were modestly elevated, with no clear trend (although the test for trend was of borderline statistical significance in the multivariate model). The associations of total fruit intake and total vegetable intake were not affected by mutual adjustment and were only slightly attenuated by the addition of fiber and folate intake to the model (data not shown). Finer adjustment for smoking, including amount smoked and years since quitting, did not alter the hazard ratios for fruit and vegetable intake. The results were not altered when the analysis was restricted to cases of endometrioid adenocarcinoma. Additionally, exclusion of cases diagnosed during the first 3 years of follow-up did not materially affect the results. Examination of deciles of intake fruits and vegetables combined, total fruit, and total vegetables did not show any significant associations or linear trends (hazard ratios for the highest decile [95% confidence interval] relative to the lowest: 1.04 (0.77–1.40); 1.13 (0.83–1.54); 1.12 (0.85–1.48), and the corresponding p-values for linear trend were: 0.32, 0.14, and 0.53, respectively.

Of 13 botanical groupings, relatively greater intake of cruciferous vegetables and of bananas showed modest but significant elevations in risk (Table 3). No other groupings were associated with endometrial cancer. Additional groupings of fruits and vegetables (including citrus + melon + berries; fruit juice; fruit not including juice; other fruit; dark green vegetables; orange vegetables; other vegetables; white potatoes; tomatoes; and starchy vegetables) were not associated with altered risk (data not shown),

In agreement with previous reports, body mass index and hormone therapy were positively associated with endometrial cancer risk, and parity, cigarette smoking, and physical activity showed inverse associations with disease (21, 22). In analyses stratified by age (<60, 60–64, ≥65). body mass index (<25, 25–29, ≥30), hormone therapy (never, former, current), smoking status (never, former, current), and physical activity (never/rarely, ≥1 time/month but <3 times/week, ≥3 times/week), intake of total fruits and vegetables, total fruits, and total vegetables did not show any trends with risk of endometrial cancer (data not shown).

Discussion

In this large prospective cohort study, we found no associations between total fruit and vegetable intake or intake of specific botanical groups and risk of endometrial cancer. Total fruit intake and intake of bananas and cruciferous vegetables showed modest positive associations with disease; however, there was no clear trend over quintiles or deciles. Additionally, analyses stratified by age, body mass index, hormone therapy, smoking status, and physical activity did not reveal any clear associations or trends of total fruit and vegetable intake, total fruit intake, or total vegetable intake with risk of endometrial cancer.

Previous studies that have examined fruit and vegetable intake in relation to endometrial cancer risk have been largely case-control studies (23–39). These studies have varied in sample size, the population studied, the extent of dietary information collected, the type of analysis conducted, the presentation of results, and in their findings. Furthermore, they have presented their results in terms of total intake of fruits and vegetables, intake of specific groups of fruits and vegetables (e.g. cruciferous vegetables; legumes; dark-green, leafy vegetables, etc.), specific fruit and vegetable items, intake of micronutrients (e.g., β-carotene, vitamin C, lycopene, etc.), and food patterns (plant-based pattern; phytoestrogen-rich diet). Nine (23–25, 27, 30/31*, 32–34, 37) of 16 case-control studies provided some

*These two papers provide analyses of the same dataset.

evidence of an inverse association with either fruit or vegetable intake. However, within the nine positive studies, there were inconsistencies in the findings: four (23, 25, 30/31, 34) found significant inverse associations between both fruit and vegetable intake and risk, whereas the remaining five studies (24, 27, 32, 33, 37) reported an inverse association with total vegetable intake but not with total fruit intake.

Two systematic reviews of the evidence (both limited to the case-control studies) found evidence for modest inverse associations with endometrial cancer risk of: 1) total vegetable intake, particularly cruciferous vegetables, and total fruit intake (4) and 2) “non-starchy vegetables” and cruciferous vegetables (5). Both reviews noted the tentativeness of the associations, given the lack of data from cohort studies and the modest magnitude of the inverse associations.

In contrast to findings from some case-control studies, the two published cohort studies (8, 9) have provided no evidence of an association of fruit and vegetable intake with endometrial cancer risk. The study by Terry et al. (8) had a limited number of cases (N = 133) and only presented results for total fruit and vegetable intake combined. They reported finding no clear pattern of risk by levels of combined fruit and vegetable intake, but noted that “the data suggest an increased risk with very low fruit and vegetable intake.” However, there were only 2 cases with “little or no” fruit and vegetable intake, and the pattern of risk for the two intermediate of four consumption levels suggested decreased risk with decreased intake. The second cohort study (9) involved 435 incident cases ascertained in a cohort of 41,000 postmenopausal women who completed a diet and lifestyle questionnaire in 1992–1993 and were followed until 2003. No association with endometrial cancer risk was seen for intake of total fruit, total vegetables, cruciferous vegetables, citrus fruit, high-β-carotene foods, high-lycopene foods, or legumes, whereas intake of high-lutein foods and high-vitamin C foods were modestly but positively associated with endometrial cancer risk.

Our results are consistent with those of the two previous cohort studies and particularly those of the study by McCullough et al. (9). The lack of any suggestion of inverse associations in the prospective studies suggests that recall bias or selection bias may have played a role in the findings of slightly more than half of the case-control studies.

Fruits and vegetables contain a wide variety of biologically active compounds including carotenoids, vitamin C, tocopherols, indoles, isothiocyanates, sulfurofane, isoflavones, phytosterols, and flavonoids (6, 7). These compounds have the potential to affect the initiation and promotion of epithelial cancers through a range of mechanisms, including: quenching of reactive oxygen species by anti-oxidants such as β-carotene, vitamin C, tocopherol, and flavonoids (7, 40); modulation of endogenous antioxidant enzymes such as glutathione S-transferases (7, 40); modulation of drug-metabolizing enzymes including cytochrome P-450 and detoxifying enzymes (40); inhibition of nitrosamine formation (7, 40); shifting of estrogen metabolism toward the 2-hydroxylation pathway, thought to inhibit cell proliferation (7, 40, 41); binding of carcinogens to glucuronates and sulfates enabling their excretion (40, 42); enhancement of cell differentiation (40); induction of apoptosis (40, 43); and stimulation of immune surveillance (7, 39). While animal and cell culture experiments provide support for some of these mechanisms, little is known about the effects of different phytochemicals at doses habitually consumed by humans on specific tissues of interest (7). As suggested by reviews of the association of consumption of fruits and vegetables with cancers at different sites (5, 44), the effects of phytochemicals may differ by site. Furthermore, phytochemicals can activate multiple, overlapping pathways and may have synergistic, additive, or inhibitory effects (7). For example, while isothiocyanates and indoles present in cruciferous vegetables induce conjugating enzymes and would therefore be expected to inhibit carcinogenesis (45), they also may play a role in the activation of carcinogens (46). Finally, fruits and vegetables contain complex mixtures of phytochemicals whose net effects may be the result of opposing influences on endometrial carcinogenesis.

Given the difficulty of extrapolating from experimental studies to humans, prospective epidemiologic studies which characterize habitual dietary intake are crucial for assessing the long-term effects of different types of diet on human health. Although there is a need for further cohort studies on diet and endometrial cancer risk, the lack of any suggestion of a protective effect of consuming a diet high in fruits and vegetables, or high in specific classes of vegetables, suggests that consumption of fruits and vegetables does not reduce the risk of this disease in older women. One important possibility not addressed by this study is that a relatively high intake of fruits and vegetables earlier in life, and particularly in adolescence, may inhibit endometrial carcinogenesis.

Strengths of the present study include its prospective nature, large sample size, classification of botanical groups which may operate through distinct mechanisms, the wide range of intake of fruits and vegetables in this study population, and information on potential confounding factors. A number of limitations should be kept in mind. Dietary assessment using food frequency questionnaires is subject to measurement error which could have affected our results (47, 48). In spite of the fact that intake of fruits and vegetables assessed by FFQ has shown reasonable correlations with consumption estimated by other methods, such as food records and multiple 24-hour recalls, it is still possible that our dietary assessment failed to detect a moderate inverse association with cancer risk. Additionally, dietary intake in this study was assessed only at baseline, and therefore does not reflect changes that may have occurred during the 8 years of follow-up. However, results from two cohort studies suggest that reporting of fruit and vegetable intake remains consistent over a number of years (49, 50). The small number of premenopausal women in the present cohort precluded separate analysis of this group. Finally, information on intake of certain vegetable items which may play a role in inhibiting the development of cancer, including allium (onions and garlic) and fungi, were not available in this study.

In conclusion, this large prospective cohort study found no evidence that intake of all fruits or vegetables, of specific botanical groupings, or of groupings based on appearance (dark green, leafy vegetables; orange vegetables, etc.) is associated with reduced risk of endometrial cancer

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Table 1

Baseline characteristics (proportions and means) of women according to quintiles of total fruit and vegetable intake at baseline, NIH-AARP Diet and Health Study, 1995–1996.[1]

Characteristic	Quintiles of Total Fruit and Vegetable Intake[2]				
	Servings per 1,000 kcal/day				
	<1.6	1.6–<2.1	2.1–<2.7	2.7–<3.4	≥3.4
No. of participants	22,417	22,418	22,418	22,418	22,417
Age (years)					
<55	19.3	16.7	14.9	14.6	13.8
55–59	25.2	23.5	23.1	22.5	22.6
60–64	26.8	27.6	27.4	26.9	27.1
≥65	28.7	32.2	34.7	36.0	36.5
Education					
Less than college graduate	69.5	64.7	62.3	61.0	61.5
College graduate/post-college	27.7	33.0	35.6	36.3	34.7
Missing	2.8	2.3	2.1	2.7	3.8
Race					
White	91.9	92.7	91.7	90.8	86.8
Other	8.1	7.3	8.3	9.2	13.2
Body mass index (kg/m^2)					
<25	44.1	44.8	46.0	48.2	51.3
25–29	30.7	32.3	32.0	31.9	30.8
≥30	25.2	22.9	21.9	19.9	17.9
Age at menarche (years)					
<13	46.7	46.4	47.9	48.3	48.0
13–14	43.6	43.8	43.1	42.4	42.0
≥15	9.8	9.8	9.0	9.3	9.9
Parity					
Nulliparous	18.6	17.8	17.1	17.4	17.1
1	11.5	10.4	10.4	10.3	11.6
2	25.2	25.8	26.5	27.3	27.4

Characteristic	Quintiles of Total Fruit and Vegetable Intake[2]				
	Servings per 1,000 kcal/day				
	<1.6	1.6–<2.1	2.1–<2.7	2.7–<3.4	≥3.4
≥3	44.7	46.0	46.0	45.0	43.8
Oral contraceptive use					
Never	56.7	57.4	58.9	60.0	63.0
Ever	43.3	42.6	41.1	40.0	37.1
Hormone therapy use					
Never	62.1	58.4	58.1	58.7	61.6
Ever	37.9	41.6	41.9	41.3	38.4
Age at menopause (years)					
Premenopausal	8.7	8.7	8.1	8.0	6.9
<45	13.0	10.6	10.2	9.8	10.1
45–49	27.8	26.0	24.5	24.8	24.9
≥55	50.0	54.3	56.8	57.0	57.6
Postmenopausal, unknown age	0.4	0.4	0.5	0.5	0.6
Smoking					
Never	37.3	43.9	46.4	48.6	50.0
Former	35.1	40.2	41.4	41.3	41.5
Current	27.6	16.0	12.3	10.1	8.5
Vigorous physical activity					
Never/rarely	33.5	24.0	19.2	16.3	14.4
≥1 time/month but <3 times/week	38.2	39.3	37.4	34.6	29.9
≥3 times/week	28.3	36.8	43.4	49.1	55.7
Means – delete this section					
Age at baseline	60.9	61.5	61.8	61.9	62.1
Total energy intake, kcal/day	1696	1624	1565	1509	1450
Alcohol, drinks/day	0.80	0.51	0.41	0.34	0.25

[1] Cohort of 112,088 women among whom 1142 endometrial cancer cases were ascertained.

[2] Intake, servings/1,000 kcal/day

Table 2

Age-adjusted and multivariate-adjusted hazard ratios (HR) and 95% confidence intervals (95% CI) for risk of endometrial cancer by quintiles of intake of fruits and vegetables, NIH-AARP Diet and Health Study, 1995–2003.

Intake, servings/1,000 kcal/day	No. cases	Age- adjusted HR	95% CI	MV- adjusted HR*	95% CI
Total fruit and vegetables					
<1.61	198	1.00	reference	1.00	reference
1.61–<2.14	218	1.08	0.89–1.31	1.08	0.89–1.31
2.14–<2.68	271	1.33	1.10–1.59	1.32	1.09–1.60
2.68–<3.42	240	1.17	0.97–1.41	1.24	1.02–1.52
≥3.42	215	1.04	0.86–1.26	1.12	0.90–1.39
P for trend		*0.81*		0.28	
Total fruit					
<0.61	186	1.00	reference	1.00	reference
0.61–<0.97	243	1.27	1.05–1.54	1.28	1.05–1.56
0.97–<1.36	230	1.19	0.98–1.44	1.21	0.99–1.48
1.36–<1.91	252	1.29	1.07–1.56	1.36	1.11–1.67
≥1.91	231	1.18	0.97–1.43	1.30	1.04–1.61
P for trend		*0.26*		0.05	
Total vegetables					
<0.74	207	1.00	reference	1.00	reference
0.74–<1.00	246	1.18	0.98–1.42	1.17	0.97–1.41
1.00–<1.27	226	1.08	0.89–1.30	1.06	0.87–1.28
1.27–<1.67	241	1.15	0.95–1.38	1.16	0.96–1.40
≥1.67	222	1.06	0.88–1.28	1.09	0.90–1.33
P for trend		*0.85*		0.55	

*Adjusted for age at baseline (continuous), race/ethnicity (white, other), education (high school graduate or less, some college or more), age at menarche (<13, 13–14, ≥15), parity (none, 1, 2, ≥3, oral contraceptives (ever, never), hormone therapy (ever, never), age at menopause (premenopausal, <45, 45–49, ≥55, postmenopausal, unknown age), body mass index – kg/m^2 (<25, 25–29, ≥30, missing), smoking (never, former, current), frequency of vigorous physical activity (never/rarely, ≥1 time/month but <3 times/week, ≥3 times/week, missing), total fat intake (continuous), and caloric intake (continuous).

Table 3

Botanical group: intake, servings/1,000 kcal/day	**No. cases**	**Hazard ratio***	**95% CI**
Chenopodiaceae: raw spinach and cooked spinach			
1	239	1.00	(ref.)
2	217	0.95	0.79–1.14
3	236	1.04	0.87–1.25
4	227	1.02	0.85–1.23
5	223	1.02	0.85–1.24
P for trend		*0.69*	
Compositae: lettuce			
1	206	1.00	(ref.)
2	235	1.16	0.96–1.40
3	238	1.16	0.96–1.40
4	246	1.23	1.02–1.48
5	217	1.13	0.93–1.38
P for trend		*0.48*	
Convolvulaceae: sweet potatoes and yams			
1	227	1.00	(ref.)
2	223	0.95	0.79–1.15
3	224	0.95	0.78–1.14
4	228	0.95	0.79–1.15
5	240	1.04	0.87–1.26
P for trend		*0.40*	
Cruciferae: broccoli, cauliflower, Brussels spouts, turnip, cabbage, coleslaw, collard, mustard, kale			
1	210	1.00	(ref.)
2	209	1.01	0.83–1.23
3	245	1.19	0.99–1.44
4	232	1.14	0.94–1.38
5	246	1.22	1.01–1.48
P for trend		*0.03*	
Cucurbitaceae: cantaloupe, watermelon, and honeydew melon			
1	213	1.00	(ref.)
2	223	1.03	0.85–1.25
3	236	1.10	0.91–1.32
4	225	1.01	0.84–1.23
5	245	1.12	0.92–1.35
P for trend		*0.35*	
Gramineae: corn			
1	230	1.00	(ref.)
2	232	1.01	0.84–1.23
3	228	0.97	0.80–1.16
4	225	0.96	0.80–1.16

Botanical group: intake, servings/1,000 kcal/day	No. cases	Hazard ratio*	95% CI
5	227	0.98	0.81–1.18
P for trend		*0.75*	
Leguminosae: dried beans, string beans, and peas			
1	214	1.00	(ref.)
2	222	1.01	0.84–1.22
3	241	1.10	0.91–1.32
4	221	1.01	0.84–1.22
5	244	1.09	0.90–1.31
P for trend		*0.44*	
Musaceae: bananas			
1	199	1.00	(ref.)
2	221	1.05	0.86–1.27
3	210	1.01	0.83–1.23
4	245	1.19	0.98–1.44
5	267	1.30	1.07–1.58
P for trend		*0.002*	
Rosaceae: apples, peach, nectarines, plums, pears, and strawberries			
1	212	1.00	(ref.)
2	215	0.99	0.81–1.20
3	227	1.04	0.86–1.26
4	247	1.16	0.96–1.41
5	241	1.14	0.94–1.39
P for trend		*0.08*	
Rutaceae (citrus): oranges, tangerines, tangelos, and grapefruits			
1	212	1.00	(ref.)
2	206	0.93	0.76–1.12
3	243	1.09	0.90–1.31
4	250	1.14	0.94–1.37
5	231	1.07	0.88–1.30
P for trend		*0.20*	
Solanaceae: tomatoes, peppers			
1	216	1.00	(ref.)
2	239	1.14	0.95–1.38
3	220	1.06	0.88–1.28
4	238	1.13	0.94–1.37
5	229	1.12	0.93–1.36
P for trend		*0.39*	
Umbelliferae: carrots			
1	212	1.00	(ref.)
2	251	1.18	0.98–1.42
3	218	1.01	0.83–1.23
4	230	1.08	0.89–1.31

Botanical group: intake, servings/1,000 kcal/day	No. cases	Hazard ratio*	95% CI
5	231	1.09	0.90–1.32
P for trend		*0.79*	
Vitaceae: grapes			
1	250	1.00	(ref.)
2	211	0.85	0.71–1.02
3	243	0.97	0.81–1.17
4	229	0.92	0.77–1.11
5	209	0.86	0.72–1.04
P for trend		*0.28*	

*Adjusted for age at baseline (continuous), race/ethnicity (white, other), education (high school graduate or less, some college or more), age at menarche (<13, 13–14, ≥15), parity (none, 1, 2, ≥3, oral contraceptives (ever, never), hormone therapy (ever, never), age at menopause (premenopausal, <45, 45–49, ≥55, postmenopausal, unknown age), body mass index – kg/m^2 (<25, 25–29, ≥30, missing), smoking (never, former, current), frequency of vigorous physical activity (never/rarely, ≥1 time/month but <3 times/week, ≥3 times/week, missing), total fat intake (continuous), and caloric intake (continuous).