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Fruit and vegetable intake and gastric cancer risk in a large United States prospective cohort study

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Abstract
Objective Fruit and vegetable intake may protect against gastric cancer incidence. Results from case–control studies have indicated an inverse association, but results from cohort studies are inconsistent.
Methods We prospectively investigated the association in 490,802 participants of the NIH-AARP Diet and Health Study using Cox proportional hazards models adjusted for gastric cancer risk factors. We present hazard ratios (HR) and 95% confidence intervals (CI) per increase of one daily serving per 1,000 calories.
Results During 2,193,751 person years, 394 participants were diagnosed with incident gastric cancer. We observed no significant associations between total fruit and vegetable intake (1.01, 0.95–1.08), fruit intake (1.04, 0.95–1.14), or vegetable intake (0.98, 0.88–1.08) and gastric cancer risk. Results did not vary by sex or anatomic subsite (cardia versus non-cardia). All 13 botanical subgroups examined had no significant associations with either anatomic sub-site.
Conclusion We did not observe significant associations between overall fruit and vegetable intake and gastric cancer risk in this large prospective cohort study.

Keywords Gastric cancer · Fruits · Vegetables · Cohort

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Introduction

Though incidence rates have decreased, gastric cancer remains the second leading cause of cancer related mortality worldwide [1]. Dietary factors, including fruit and vegetable intake, have been hypothesized to protect against gastric cancer incidence. Results from almost 40 case–control studies consistently indicate an inverse association with fruit and vegetables [2]. However, case–control designs can be subject to both recall and selection bias. At least 15 prospective studies have investigated this association. Some prospective studies have shown significant inverse associations with intake of fruits [3–7] or vegetables [4, 8, 9], but most have not found significant associations [2, 10–12].

Gastric cancer has two main anatomic subsites, cardia, and non-cardia. Over the last 30 years, the rates of gastric cardia have increased in the United States by approximately 50%, while the rates of gastric non-cardia have decreased by approximately 25% [13, 14]. The etiologies of tumors at these sites may be distinct [15, 16]. For example, seropositivity for *Helicobacter pylori* was recently shown to be positively associated with non-cardia cancer, yet inversely associated with cardia cancer [16]. However, most previous examinations of fruit and vegetable intake and gastric cancer risk have not distinguished among these sites.

We studied the association between fruit and vegetable intake and risk of gastric cardia and gastric non-cardia in 490,802 participants of the NIH-AARP Diet and Health Study.

Materials and methods

Study participants

A description of the NIH-AARP Diet and Health Study has been published [17]. Study participants were members of AARP, the organization formerly known as the American Association of Retired Persons, who resided in eight states with excellent cancer registries. The study was approved by the Special Studies Institutional Review Board of the U.S. National Cancer Institute (NCI).

We excluded those with cancer at baseline ($n = 51{,}229$), proxy respondents ($n = 15{,}760$), and those with total energy intake or fruit and vegetable intake more than two interquartile ranges from the median ($n = 8{,}616$). The final analytic cohort consisted of 490,802 participants (292,898 men and 197,904 women).

Cohort follow-up and case identification

Follow-up time extended from study baseline (between 1995 and 1996) to diagnosis of head and neck, esophageal, or stomach cancer (diagnosis of one of these cancers would be associated with increased surveillance of the other sites), date of death, end of study (31 December 2000), or the date a participant moved out of the registry ascertainment area.

We identified incident cancer cases by linkage between study participants and the appropriate state cancer registry databases. Gastric cancer cases were defined by anatomic site and histologic code of the International Classification of Disease for Oncology [18], as previously described [19]. Approximately 90% of cancer cases are detected in the cohort by this approach [20]. Cardia tumors ($n = 198$ cases) had site code C16.0 (defined as the cardioesophageal junction, the esophagogastric junction, and the gastroesophageal junction [18]). We classified tumors with site codes C16.1–C16.9 as non-cardia tumors (196 cases). Over 13% of noncardia tumors were an overlapping lesion of the stomach (ICD-O site code C16.8) and 28% were gastric not otherwise specified (ICD-O site code C16.9), raising the possibility that cardia cancers might be present in the noncardia category. However, excluding these 81 participants from the analysis did not appreciably change the risk estimates (data not shown).

Exposure assessment

At baseline in 1995–1996, participants completed a questionnaire that included 124 food items [17]. Participants were asked to report their usual frequency of intake and portion size over the last 12 months, using ten frequency categories ranging from 'never' to 'six+ times per day' for beverages and from 'never' to 'two+ times per day' for solid foods and three categories of portion size. Total fruit and vegetable intake was calculated from individual and mixed foods as pyramid servings, as defined in the US Department of Agriculture's food guide pyramid as previously described [21]. One pyramid serving corresponded to one serving in the US Department of Agriculture's food guide Pyramid—one medium sized fresh fruit, half a cup cut fruit, six oz juice, one cup leafy vegetables, or half a cup other vegetables [22]. The FFQ was validated using two non-consecutive 24-h recalls in 1, 953 participants. For fruit and vegetable intake combined, the energy-adjusted Pearson correlation coefficients between the FFQ and the 24-h recalls were 0.72 and 0.61 for men and women, respectively [23].

We excluded white potatoes from the vegetable group and created quintiles of fruit and vegetable variables. Similar results were observed for variables that included potatoes. We also examined groups based on botanical taxonomy to help identify possible associations according to chemopreventive phytochemicals [24]. We used tertiles for the botanical groups due to the large number of participants who did not regularly consume food items from some of the botanical groups.

Statistical analysis

Analyses were performed with SAS version 8.2. An alpha level of <0.05 was considered statistically significant and all tests were two-sided. Hazard ratios (HR) and 95% confidence intervals (CI) were calculated using Cox proportional hazards regression [25] using follow-up time as the underlying time metric. We tested for and found no deviations from the proportional hazards assumption. Using age as the underlying time metric did not affect results (data not shown).

We adjusted for energy intake using the nutrient density method (per 1,000 calories) and included total energy in the model. Analyzing data using a standard multivariate model that included fruit and vegetable intake (daily servings), total energy, and other covariates yielded similar results (data not shown). All multivariate models were adjusted for sex, age (continuous), body mass index in kg/m^2: <18.5, 18.5– <25, 25– <30, 30– <35, and ≥35, total energy intake (continuous), education (<high school, completion of high school,

some post-high school training, completion of college, and completion of graduate school), alcohol intake (0 drinks/day, $0 < - \leq 1$ drinks/day, $1 < - \leq 3$ drinks/day, and >3 drinks/day), cigarette use (never smokers, former smokers who smoked ≤1 pack/day, former smokers who smoked >1 pack/day, current smokers who smoked ≤1 pack/day, and current smokers who smoked >1 pack/day), usual activity throughout the day (sit all day, sit much of the day/walk some, stand/walk often/no lifting, lift/carry light loads, and carry heavy loads), vigorous physical activity (never, rarely, one to three times/month, one to two times/week, three to four times/week, five or more times per week), and ethnicity (non-Hispanic white, non-Hispanic black, Hispanic, and Asian/Pacific Islander/Native American). Missing values for adjusting covariates were included as dummy variables in the models.

In additional models, fruits and vegetables were mutually adjusted for each other. We conducted linear trend tests across categories of intake by assigning participants the median intake for their categories and entering it as a continuous term in the regression model. We examined possible effect modification by cigarette smoking status (ever/former/never), alcohol use (ever/never or <3 drinks/day/≥3 drinks/day, or body mass index (dichotomous variable split at the median: 26.5) by stratifying the continuous intakes of fruits and vegetables by each variable and calculating *p*-values for statistical interactions using a likelihood ratio test with the appropriate degrees of freedom.

Results

Table 1 describes the baseline characteristics of study participants, stratified by quintile of total fruit and vegetable intake. Study participants in quintile 5 (median of 5.8 daily servings per 1,000 calories) were more often women, college graduates, non-smokers, consumers of <3 alcoholic drinks per day, and completed vigorous physical activity five or more times per week than study participants in quintile 1 (median of 1.5 daily servings per 1,000 calories). Age and body mass index were similar across categories of fruit and vegetable intake.

During 2,193,751 person-years of follow-up (mean = 4.5 years), 394 participants developed gastric cancer. The age and sex adjusted HR (95% CI) associated with each daily serving of total fruit and vegetable intake per 1,000 calories was 0.98 (0.92–1.04). After adjustment for other potential gastric cancer risk factors, including sex, body mass index, education, alcohol intake, cigarette smoking, physical activity, and ethnicity, the risk per daily serving per 1,000 calories was 1.01 (0.95–1.08) (Table 2). We examined fruit and vegetable intake separately in mutually adjusted models, and observed a HR per daily serving per 1,000 calories of fruit of 1.04 (0.95–1.14) and of vegetables (0.98, 0.88–1.08). Results in men and women were similar. We further examined associations with whole fruits and fruit juice. The HR per daily serving per 1,000 calories for fruit juice was 0.97 (0.83–1.13) and for whole fruits was 1.09 (0.97–1.23).

Table 3 presents estimates for fruit and vegetable intake and risk of gastric cancer subtypes (gastric cardia-198 cases and gastric non-cardia-196 cases). There were no statistically significant associations. We also divided fruit and vegetables into categories based on botanical classifications (Table 4). Results were insignificant for all botanical groups examined, though we found a borderline association between Convolvulaceae intake (sweet potatoes and yams) and cancers of the gastric non-cardia (Tertile 3 versus Tertile 1, 0.70, 0.49–1.00). The *p*-for trend across tertiles of Convolvulaceae intake and non-cardia cancer risk was 0.07. We found no association between Convolvulaceae and gastric cardia cancer risk (Tertile 3 versus Tertile 1, 0.85, 0.60–1.20).

Excluding the first two years follow-up did not affect HR estimates (data not shown)

We looked for effect modification by cigarette smoking status, alcohol drinking, and body mass index, but found no significant differences (data not shown).

Discussion

In this large United States cohort, we found no significant associations between fruit and vegetable intake and gastric cancer risk. We observed similar results in men and women. Results for all 13 botanical groups examined were not statistically significant. The borderline significant association between Convolvulaceae intake (sweet potatoes and yams) and gastric non-cardia risk may be a true association or a chance finding due to multiple comparisons. To our knowledge, previous studies have not examined the association of sweet potatoes/yams and gastric cancer risk.

In contrast to the results of this analysis, most previous case–control studies of the association between fruit and vegetable intake and gastric cancer have found an inverse association. A meta-analysis of case control studies found a protective association with vegetables (17 studies: per 100 g/day, OR: 0.78, 95% CI: 0.71–0.86) and fruits (24 studies: per 100 g/day, OR: 0.69, 95% CI: 0.62–0.77) [12]. However, recall bias and selection bias may have affected these studies. Prospective

Table 1 Study characteristics by quintiles of fruit and vegetable intake per 1,000 calories per day

	Quintiles of fruit and vegetable intake									
	*Q*1		*Q*2		*Q*3		*Q*4		*Q*5	
Cohort (Number, %)	98,160	20.0	98,161	20.0	98,160	20.0	98,161	20.0	98,160	20.0
Total fruit and vegetable intake[a] (Median, interquartile range)	1.5	1.2–1.8	2.4	2.2–2.6	3.2	3.0–3.4	4.1	3.8–4.4	5.8	5.2–6.8
Sex (Number, %)										
Male	72,564	24.8	66,681	22.8	59,794	20.4	52,360	17.9	41,499	14.2
Female	25,596	12.9	31,480	15.9	38,366	19.4	45,801	23.1	56,661	28.6
Age (Median, interquartile range)	61.6	56.8–66.0	62.4	57.6–66.5	62.8	57.9–66.7	63	58.1–66.8	63.1	58.2–66.9
BMI, m/kg^2 (Median, interquartile range)	26.6	24.2–29.8	26.6	24.3–29.7	26.5	24.0–29.5	26.3	23.8–29.3	25.8	23.4–28.9
Total daily energy intake (calories) (Median, interquartile range)	1,955	1,447.0–2,600.5	1,802	1,377.5–2,333.9	1,694	1,306.6–2,176.6	1,592	1,231.8–2,046.7	1,445	1,105.0–1,870.4
Education (Number, %)[b]										
Less than high school	7,941	27.3	5,921	20.3	5,207	17.9	5,018	17.2	5,052	17.3
12 years (completed high school)	22,827	23.8	19,259	20.1	18,227	19.0	17,951	18.7	17,605	18.4
Some post-high school training	34,195	21.1	32,565	20.1	32,008	19.7	31,506	19.4	31,934	19.7
Completed college	16,889	18.3	19,487	21.1	19,397	21.0	18,867	20.4	17,803	19.3
Completed graduate school	13,529	14.0	18,421	19.0	20,659	21.3	22,047	22.8	22,235	22.9
Alcohol intake (Number, %)[b]										
Zero drinks/day	22,190	18.9	21,390	18.2	22,045	18.8	23,725	20.2	28,100	23.9
0 < – 1 drinks/day	42,652	16.4	49,926	19.2	53,571	20.6	56,320	21.7	57,509	22.1
1 < – 3 drinks/day	14,960	20.1	17,443	23.4	16,749	22.5	14,555	19.6	10,700	14.4
>3 drinks/day	17,959	48.6	9,071	24.5	5,496	14.9	3,146	8.5	1,306	3.5
Cigarette smoking Status (Number, %)[b]										
Never smoked	24,729	14.2	32,456	18.6	36,076	20.7	39,010	22.4	41,764	24.0
Former	46,465	19.4	49,386	20.6	49,164	20.5	48,320	20.1	46,652	19.4
Current	25,090	36.8	14,670	21.5	11,346	16.7	9148	13.4	7844	11.5
Usual activity throughout the day (Number, %)[b]										
Sit during the day/little walking	9,392	24.2	8,224	21.2	7,579	19.5	7,160	18.5	6,435	16.6
Sit during the day/walk a fair amount	31,793	20.1	32,733	20.7	32,401	20.5	31,556	20.0	29,543	18.7
Stand/walk a lot—no lifting	34,213	18.5	35,845	19.4	36,930	20.0	38,053	20.6	39,707	21.5
Lift/carry light loads, stairs, hills	16,593	19.7	16,469	19.6	16,693	19.9	16,892	20.1	17,372	20.7
Do heavy work/carry loads	4,055	28.9	2,961	21.1	2,508	17.9	2,270	16.2	2,220	15.8
Vigorous physical activity (Number, %)[b]										
Never	6,885	31.6	4,458	20.5	3,860	17.7	3,306	15.2	3,248	14.9
Rarely	18,844	28.3	14,589	21.9	12,690	19.1	10,954	16.5	9,487	14.3
1–3 times/month	16,509	24.8	14,869	22.3	13,127	19.7	11,998	18.0	10,161	15.2
1–2 times/week	21,624	20.5	22,750	21.5	22,036	20.9	20,897	19.8	18,379	17.4
3–4 times/week	19,907	15.2	24,859	18.9	27,379	20.9	29,209	22.3	29,895	22.8
Five or more times/week	13,405	14.3	15,652	16.7	18,164	19.4	20,761	22.2	25,625	27.4

Table 1 continued

	Quintiles of fruit and vegetable intake									
	*Q*1		*Q*2		*Q*3		*Q*4		*Q*5	
Ethnicity (Number, %)[b]										
Non-hispanic white	91,501	20.4	91,368	20.4	90,578	20.2	89,111	19.9	85,920	19.2
Non-Hispanic black	2,900	15.6	2,947	15.8	3,265	17.5	3,922	21.0	5,614	30.1
Hispanic	1,351	14.7	1,461	15.8	1,726	18.7	2,063	22.4	2,619	28.4
Asian/Pacific Islander/ Native American	1,220	15.2	1,313	16.4	1,473	18.4	1,758	22.0	2,239	28.0

[a] Daily servings per 1,000 calories

[b] Categories do not add up to 490,802 persons due to missing data

Table 2 Fruit and vegetable intake and gastric cancer risk overall and stratified by sex

	Total		Men		Women	
Category of intake[a]	Cases	HR[b] (95% CI)	Cases	HR[c] (95% CI)	Cases	HR[c] (95% CI)
Fruit + Vegetables						
Continuous (Daily serving per 1000 calories)		1.01 (0.95–1.08)		1.00 (0.93–1.08)		1.03 (0.92–1.16)
Quintile 1 (1.51)[d]	93	1.00 (ref)	84	1.00 (ref)	9	1.00 (ref)
Quintile 2 (2.41)	83	1.01 (0.74–1.36)	72	1.01 (0.73–1.39)	11	1.06 (0.44–2.57)
Quintile 3 (3.18)	77	1.00 (0.73–1.37)	57	0.91 (0.64–1.29)	20	1.60 (0.72–3.57)
Quintile 4 (4.11)	80	1.12 (0.81–1.53)	61	1.11 (0.79–1.58)	19	1.29 (0.57–2.93)
Quintile 5 (5.81)	61	0.91 (0.64–1.30)	39	0.86 (0.58–1.29)	22	1.19 (0.52–2.70)
p for trend		0.784		0.654		0.856
Fruits[e]						
Continuous		1.04 (0.95–1.14)		0.99 (0.89–1.11)		1.18 (1.00–1.38)
Quintile 1 (0.45)	93	1.00 (ref)	80	1.00 (ref)	13	1.00 (ref)
Quintile 2 (0.98)	93	1.10 (0.53–1.03)	80	1.14 (0.83–1.56)	13	0.91 (0.42–1.97)
Quintile 3 (1.46)	59	0.74 (0.53–1.03)	50	0.78 (0.54–1.13)	9	0.55 (0.23–1.32)
Quintile 4 (2.06)	70	0.91 (0.66–1.27)	52	0.89 (0.61–1.28)	18	0.96 (0.46–2.03)
Quintile 5 (3.20)	79	1.04 (0.75–1.45)	51	0.93 (0.64–1.37)	28	1.30 (0.64–2.64)
p for trend		0.973		0.444		0.172
Vegetables[f]						
Continuous		0.98 (0.88–1.08)		1.01 (0.90–1.14)		0.89 (0.72–1.09)
Quintile 1 (0.71)	85	1.00 (ref)	75	1.00 (ref)	10	1.00 (ref)
Quintile 2 (1.15)	92	1.22 (0.91–1.65)	73	1.16 (0.84–1.60)	19	1.67 (0.77–3.61)
Quintile 3 (1.56)	90	1.28 (0.94–1.73)	67	1.19 (0.85–1.66)	23	1.76 (0.83–3.73)
Quintile 4 (2.08)	69	1.04 (0.94–1.73)	53	1.07 (0.74–1.53)	16	1.03 (0.46–2.30
Quintile 5 (3.15)	58	0.96 (0.68–1.37)	45	1.15 (0.78–1.69)	13	0.64 (0.27–1.49)
p for trend		0.465		0.644		0.022

[a] Fruit and vegetable constituents—Vegetables = spinach, turnip, collard greens, mustard, kale, cole slaw, cabbage, sauerkraut, carrots, string beans, dried beans, peas, corn, broccoli, cauliflower, Brussels sprouts, mixed vegetables, tomatoes, sweet papers, lettuce salad, sweet potatoes, yams, tomato juice, tomato sauce, chili, and salsa; Fruits = apples, apple sauce, pears, bananas, dried fruit excluding apricots, peaches, nectarines, plums, cantaloupe, other melons, strawberries, oranges, tangerines, tangelos, grapefruit, grapes, orange and grapefruit juice, and other fruit juices and drinks. Quintiles of cohort fruit and vegetable intake were created and each contained 20% of the distribution

[b] Adjusted for sex, age at entry into cohort, BMI, total energy, education, alcohol intake, cigarette-smoke-dose, usual activity throughout the day, vigorous physical activity, and ethnicity

[c] Adjusted for age at entry into cohort, BMI, total energy, education, alcohol intake, cigarette-smoke-dose, usual activity throughout the day, vigorous physical activity, and ethnicity

[d] Median intake of those in quintile (daily servings per 1,000 calories)

[e] Additionally adjusted for continuous vegetable intake

[f] Additionally adjusted for continuous fruit intake

Table 3 Fruit and vegetable intake and gastric cancer risk overall and by anatomic subsite

	Cardia		Non-cardia	
Category of intake[a]	Cases	HR[b] (95% CI)	Cases	HR[b] (95% CI)
Fruit + Vegetables				
Continuous (Daily servings per 1000 calories)		0.96 (0.87–1.06)		1.05 (0.97–1.14)
Quintile 1 (1.51)[c]	48	1.00 (ref)	45	1.00 (ref)
Quintile 2 (2.41)	53	1.33 (0.89–1.98)	30	0.70 (0.44–1.11)
Quintile 3 (3.18)	40	1.14 (0.74–1.76)	37	0.88 (0.56–1.37)
Quintile 4 (4.11)	37	1.20 (0.76–1.89)	43	1.03 (0.66–1.61)
Quintile 5 (5.81)	20	0.77 (0.44–1.33)	41	0.97 (0.61–1.54)
p for trend		0.330		0.597
Fruits[d]				
Continuous		0.94 (0.82–1.09)		1.12 (1.00–1.26)
Quintile 1 (0.45)	51	1.00 (ref)	42	1.00 (ref)
Quintile 2 (0.98)	54	1.23 (0.84–1.82)	39	0.95 (0.61–1.48)
Quintile 3 (1.46)	36	0.92 (0.59–1.43)	23	0.57 (0.34–0.95)
Quintile 4 (2.06)	31	0.87 (0.54–1.39)	39	0.95 (0.60–1.50)
Quintile 5 (3.20)	26	0.80 (0.48–1.32)	53	1.22 (0.78–1.91)
p for trend		0.168		0.176
Vegetables[e]				
Continuous		0.98 (0.84–1.14)		0.97 (0.85–1.12)
Quintile 1 (0.71)	44	1.00 (ref)	41	1.00 (ref)
Quintile 2 (1.15)	43	1.15 (0.75–1.75)	49	1.31 (0.86–1.98)
Quintile 3 (1.56)	55	1.63 (1.09–2.45)	35	0.95 (0.60–1.50)
Quintile 4 (2.08)	31	1.03 (0.64–1.66)	38	1.05 (0.67–1.65)
Quintile 5 (3.15)	25	1.03 (0.61–1.72)	33	0.90 (0.58–1.47)
p for trend		0.895		0.399

[a] Fruit and vegetable constituents—Vegetables = spinach, turnip, collard greens, mustard, kale, cole slaw, cabbage, sauerkraut, carrots, string beans, dried beans, peas, corn, broccoli, cauliflower, Brussels sprouts, mixed vegetables, tomatoes, sweet papers, lettuce salad, sweet potatoes, yams, tomato juice, tomato sauce, chili, and salsa; Fruits = apples, apple sauce, pears, bananas, dried fruit excluding apricots, peaches, nectarines, plums, cantaloupe, other melons, strawberries, oranges, tangerines, tangelos, grapefruit, grapes, orange and grapefruit juice, and other fruit juices and drinks. Quintiles of cohort fruit and vegetable intake were created and each contained 20% of the distribution.

[b] Adjusted for sex, age at entry into cohort, BMI, total energy, education, alcohol intake, cigarette-smoke-dose, usual activity throughout the day, vigorous physical activity, and ethnicity

[c] Median intake of those in quintile (daily servings per 1,000 calories)

[d] Additionally adjusted for continuous vegetable intake

[e] Additionally adjusted for continuous fruit intake

examinations of these associations have been less consistent. Some prospective studies observed significant inverse associations with fruits [3–7] or vegetables [4, 8, 9]; most studies reported inverse but non-significant associations [2, 10–12]. The summary estimates from the most recent meta-analysis of cohort studies comparing highest versus lowest consumption category were 0.89 (0.78–1.02) for fruits (13 studies) and 0.98 (0.86–1.13) for vegetables (8 studies) [11]. Our hazard ratios are consistent with these summary estimates (Quintile 5 versus Quintile 1—fruits: 1.04, 0.75–1.45; vegetables: 0.96, 0.68–1.37) and do not exclude the possibility of a modest association between fruit and vegetable intake and gastric cancer risk.

Most case–control studies indicate an inverse association between fruit and vegetable intake and cancers of both the cardia and non-cardia. The summary estimates from a recent meta-analysis of case–control studies comparing the risk of those in the highest category to those in the lowest category of intake showed inverse associations between fruit and vegetable intake and the risk of both cardia (fruit, six studies: 0.58, 0.38–0.89; vegetables, six studies: 0.63, 0.50–0.79) and non-cardia (fruit, six studies: 0.61, 0.44–0.84; vegetables, eight studies: 0.75, 0.59–0.95) gastric cancer [26]. To our knowledge, four previous prospective studies examined the association by anatomic site [5, 7, 10, 27]. One study in China observed a significant inverse association with fruit in

Table 4 Multivariate hazard ratios and 95% confidence intervals for fruit and vegetable botanical groups and gastric cancer

Botanical group	Tertile	Tertile median[a]	Cardia Cases	Non-cardia HR[b] (95% CI)	Cases	HR[b] (95% CI)
Chenopodiaceae: raw spinach and cooked spinach	*Q*1	0	85	1.00 (ref)	67	1.00 (ref)
	*Q*2	0.18	42	0.55 (0.38–0.80)	56	0.87 (0.61–1.25)
	*Q*3	0.96	71	1.12 (0.81–1.55)	73	1.13 (0.80–1.60)
Compositae: lettuce	*Q*1	0.03	79	1.00 (ref)	77	1.00 (ref)
	*Q*2	0.16	75	1.12 (0.81–1.54)	59	0.93 (0.66–1.31)
	*Q*3	0.54	44	0.77 (0.53–1.13)	60	1.03 (0.72–1.46)
Convolvulaceae: sweet potatoes and yams	*Q*1	0	85	1.00 (ref)	75	1.00 (ref)
	*Q*2	0.02	56	0.75 (0.54–1.06)	64	0.83 (0.59–1.16)
	*Q*3	0.06	57	0.85 (0.60–1.20)	57	0.70 (0.49–1.00)
Cruciferae: broccoli, cauliflower, brussels sprouts, turnip, cabbage, coleslaw, collard, mustard, and kale	*Q*1	0.06	87	1.00 (ref)	68	1.00 (ref)
	*Q*2	0.18	57	0.80 (0.57–1.12)	68	1.14 (0.81–1.60)
	*Q*3	0.46	54	0.95 (0.67–1.35)	60	1.03 (0.72–1.48)
Cucurbitaceae: cantaloupe, watermelon, and honeydew melon	*Q*1	0.01	73	1.00 (ref)	67	1.00 (ref)
	*Q*2	0.04	71	1.10 (0.79–1.53)	57	0.92 (0.64–1.31)
	*Q*3	0.17	54	0.98 (0.69–1.41)	72	1.19 (0.85–1.68)
Gramineae: corn	*Q*1	0.01	65	1.00 (ref)	71	1.00 (ref)
	*Q*2	0.05	61	0.97 (0.69–1.38)	59	0.91 (0.64–1.28)
	*Q*3	0.13	72	1.21 (0.86–1.71)	66	1.05 (0.75–1.47)
Leguminosae: dried beans, string beans, and peas	*Q*1	0.12	71	1.00 (ref)	66	1.00 (ref)
	*Q*2	0.28	63	0.95 (0.68–1.34)	61	0.95 (0.67–1.34)
	*Q*3	0.59	64	1.08 (0.76–1.52)	69	1.03 (0.73–1.45)
Musaceae: bananas	*Q*1	0.02	74	1.00 (ref)	60	1.00 (ref)
	*Q*2	0.16	79	1.20 (0.87–1.65)	70	1.18 (0.83–1.67)
	*Q*3	0.45	45	0.73 (0.50–1.06)	66	1.01 (0.71–1.46)
Rosaceae: apples, peach, nectarines, plums, pears, and strawberries	*Q*1	0.06	76	1.00 (ref)	68	1.00 (ref)
	*Q*2	0.22	64	1.05 (0.75–1.47)	59	0.93 (0.65–1.32)
	*Q*3	0.63	58	1.12 (0.78–1.60)	69	1.07 (0.75–1.52)
Rutaceae (citrus): oranges, tangerines, tangelos, and grapefruits	*Q*1	0.08	83	1.00 (ref)	56	1.00 (ref)
	*Q*2	0.46	55	0.73 (0.52–1.03)	62	1.15 (0.80–1.67)
	*Q*3	1.12	60	0.88 (0.62–1.23)	78	1.36 (0.96–1.94)
Solanaceae: tomatoes, peppers	*Q*1	0.11	75	1.00 (ref)	62	1.00 (ref)
	*Q*2	0.24	64	0.93 (0.67–1.31)	71	1.32 (0.93–1.86)
	*Q*3	0.51	59	0.93 (0.65–1.31)	63	1.19 (0.83–1.70)
Umbelliferae: carrots	*Q*1	0.01	83	1.00 (ref)	64	1.00 (ref)
	*Q*2	0.04	71	1.00 (0.73–1.38)	71	1.27 (0.90–1.79)
	*Q*3	0.18	44	0.79 (0.54–1.15)	61	1.18 (0.82–1.70)
Vitaceae: grapes	*Q*1	0	79	1.00 (ref)	68	1.00 (ref)
	*Q*2	0.03	63	0.90 (0.64–1.24)	59	0.95 (0.67–1.35)
	*Q*3	0.14	56	0.92 (0.65–1.31)	69	1.09 (0.78–1.54)

[a] Median intake of those in tertile (daily servings per 1,000 calories)

[b] Adjusted for sex, age at entry into cohort, BMI, education, alcohol intake, cigarette-smoke-dose, vigorous physical activity, usual activity throughout the day, ethnicity, and total energy

All p for trends across tertiles were >0.05

cardia but not non-cardia gastric cancer [7]. A study of Finnish smokers, though, observed a significant inverse association with fruit intake and non-cardia but not cardia gastric cancer [5]. Results from the EPIC cohort study [10] and the Japan Public Health Center-based prospective study [27], like our study, did not observe significant inverse associations with either cardia or non-cardia gastric cancer. We did not observe significant associations with either anatomic site, but our results do not exclude the possibility of a modest inverse association.

Our study had several strengths, including its prospective design, large study size, wide range of fruit and vegetable intake, and adjustment for most gastric cancer risk factors. We lacked information on *Helicobacter pylori* (Hp) infection, an important gastric cancer risk factor. However, Hp was not found to modify the association with fruit and vegetable intake in the EPIC cohort study [10], and did not confound or modify the association in two case–control studies [28, 29]. We did not observe an association with either cardia or non-cardia cancer, which may have distinct associations with Hp [16]. We did not collect nonsteroidal anti-inflammatory drug use for all subjects and therefore we could not adjust for NSAID use in this analysis. We also assessed fruit and vegetable intake at a single time point using a food frequency questionnaire. Food frequency questionnaires are subject to measurement error [30] which could potentially obscure a true yet modest association between gastric cancer risk and fruit and vegetable intake and result in the observed null findings.

In summary, we found no association between total fruit and vegetable intake and gastric cancer risk in our large prospective cohort study.

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