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Association of *Helicobacter pylori* infection and diet on the risk of gastric cancer: a case–control study in Hawaii

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Abstract

Objective—The risk factors most strongly associated with gastric cancer are the gastric bacteria *Helicobacter pylori* and diet. Utilizing data from a case–control study among residents in Hawaii, we examined the association of diet, presence of *H. pylori*, and non-cardia gastric cancer risk. Methods Serum taken at diagnosis for cases (n = 212) and at interview for controls (n = 336) was assayed for IgG antibodies to *H. pylori* group antigens and to a recombinant fragment of the cytotoxin-associated antigen A (CagA) protein, and subjects completed food frequency questionnaires. Risk measures were calculated using logistic regression. The likelihood ratio test was used to assess interactions.

Results—Inverse associations were found between gastric cancer risk and increasing intake of several micronutrients and vegetables among all individuals. For *H. pylori*/CagA-positive subjects, significant trends were present for total, green, and yellow vegetables, while a significant trend was present only for yellow vegetables among *H. pylori*/CagA-negative individuals. For intestinal gastric cancer, there was a suggestion that intake of vegetables, especially cruciferous vegetables, had a stronger protective effect for the *H. pylori*/CagA-positive group. Conclusions Diet may play a greater role in the etiology of non-cardia gastric cancer among individuals with evidence of *H. pylori* infection than among those without.

Keywords

Helicobacter pylori; Diet; Gastric cancer

Introduction

While the incidence of gastric cancer has been on the decline for the past 30 years, it remains the fourth most commonly diagnosed cancer worldwide and the second most common cause

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of death from cancer [1,2]. The map of stomach cancer incidence reveals an interesting pattern with highest rates in East Asia, Eastern Europe, and parts of South America, and lowest rates in North America, Northern Europe, South and Southeast Asia, and Africa [3]. Migration studies show a consistent decline in gastric cancer incidence within two generations when individuals migrate from a high-risk country to a low-risk country, particularly among Asian migrants to the United States, highlighting the importance of environmental factors [4].

Gastric cancer is generally categorized by anatomic subsite as either in the cardia of the stomach, including the cardioesophageal junction, or more distally (non-cardia), including the corpus and the antrum. Cardia and non-cardia gastric cancers appear to have different etiologies; although the incidence of cardia cancers may have increased somewhat in recent years, non-cardia cancers still constitute the majority (estimated at 65–90%) of gastric cancers worldwide [5].

In epidemiologic studies, the risk factor most strongly associated with non-cardia gastric cancer is the gastric bacteria *Helicobacter pylori*. For example, a 2001 analysis of 12 nested case–control studies found a greater than doubling of risk of gastric cancer for those testing positive for *H. pylori* [6], and a more recent study found an odds ratio (OR) of 7.9 (95% CI: 3.0–20.9) for the association of *H. pylori* and non-cardia gastric cancer [7]. Additionally, a prospective study of 1,526 Japanese patients with ulcers, gastric hyperplasia, or non-ulcer dyspepsia at enrollment, and followed for a mean of 8 years, found that none of the patients who were *H. pylori*-negative progressed to cancer, while 36 (3%) of those testing positive for *H. pylori* did [8]. In 1994, the International Agency for Research on Cancer classified *H. pylori* as a class 1 carcinogen [9].

Recent reviews of both cohort and case–control studies have examined the relationship between gastric cancer and diet. They have concluded that gastric cancer appears strongly associated with low intakes of both vegetables and fruit, and high intakes of salt, salt-preserved food, and processed meat [5,10,11]. It has been hypothesized that the benefit of high fruit and vegetable intake is related to the presence of the antioxidants carotenoids, vitamin C, and vitamin E, which are believed to prevent the formation of nitrosamines and neutralize the action of preformed nitrosamides, thereby reducing tumor formation [12-14]. On the other hand, excess salt may destroy the mucosal barrier, causing gastritis, and potentially aiding in the colonization of *H. pylori* [12,15-18].

Eight case–control [19-26] and three cohort studies [27-29] have specifically examined whether an interaction between *H. pylori* and diet might affect gastric cancer risk; 9 [19-22, 24-27,29] of the 11 found evidence supportive of an interaction, but only two found significant interaction terms—one for intake of smoked-salted meat and fermented pork fat [26] and the other for a high-salt “preference” [21].

In earlier analyses of a gastric cancer case–control study among residents of Hawaii, we reported an inverse association with consumption of vegetables and a positive association with consumption of processed meats and bacon [30], as well as a strong positive association of *H. pylori* or cytotoxin-associated antigen A (CagA) seropositivity with the risk of non-cardia tumors [31]. In this analysis, we examined the possibility of an interaction between diet and *H. pylori*, on the risk of non-cardia gastric cancer in this same study.

Materials and methods

The study population and data collection methods have been described in detail elsewhere [30,31]; a brief description follows.

Study population

Cases in this study included patients diagnosed with gastric cancer at eight major hospitals on the Hawaiian island of Oahu, between September 1993 and April 1999, and identified by the Hawaii Tumor Registry, a member of the US National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) program [32]. Cases were required to be residents of Oahu and in one of the following six ethnic groups: Caucasian, Chinese, Filipino, Japanese, Korean, or Native Hawaiian (including part Hawaiian); the patients ranged from 26 to 79 years old.

Of the 299 patients identified with gastric carcinoma who had a serum sample obtained at the time of diagnosis available for study, 276 had *H. pylori*/CagA tests performed (due to limited amounts of sera, the other 23 only had serum pepsinogen tests performed). Of these 276 cases, 33 were excluded as they were determined to have cardia gastric cancer (defined by whether the cardioesophageal junction was involved), and 31 were excluded as they were missing dietary data, leaving 212 cases for this study.

Potential controls were identified from lists of Oahu residents who were interviewed by the Health Surveillance Program of the Hawaii Department of Health, which conducts an annual 1% random sample of all households in the state [33]. The Health Care Financing Administration (now the Centers for Medicare and Medicaid Services), estimated to service 95% of individuals aged 65 years and older in the United States [34], was used to identify further eligible controls over 65 years old.

The population-based controls were frequency matched to the case patients on the basis of sex, ethnicity, and age (within 5 years). Of the 446 controls who completed interviews, 336 (75%) provided blood samples, 84 (19%) refused, and 26 (6%) provided other reasons for not donating blood samples.

Questionnaire data collection

Questionnaires consisting of a detailed food frequency section, and questions on education, smoking history, alcohol intake, medical history, medication use (including aspirin and other non-steroidal anti-inflammatory drugs), and a family history of cancer were administered by trained interviewers at the home of the subjects. The dietary method used in this study has previously been validated in our population [35]. For each food item (of the over 250 food items or food groups included in the questionnaire), eight frequency categories were included, together with three choices of portion size. Cases were asked about their usual diet during the year prior to diagnosis (on average, cases were interviewed within 4.2 months of diagnosis), while controls were asked about their usual diet during the year before the interview.

For each subject, daily intake in grams was computed for each food item and food group (e.g., processed meats), with the food group intake computed by summing the grams across relevant food items and the appropriate portions in mixed dishes. We computed individual nutrient intakes by using food composition data that were based on the US Department of Agriculture's Handbook No. 8 [36] and complemented with other sources [37-40]. The computation of micronutrients in this study did not include vitamin and mineral supplements. Food consumption data for non-starch polysaccharides (NSP) were obtained from values published by Englyst et al. [41].

Nutrients, foods, and food groups that had previously been associated with gastric cancer risk in this population [30] were chosen for these analyses. These included the nutrients NSP, β-carotene, vitamin A, vitamin C, vitamin E, and folate. The foods and food groups selected were: total vegetables, green vegetables, yellow vegetables, cruciferous vegetables, processed meats, and bacon.

Pathologic classification

The hematoxylin-eosin-stained slides used for this study were classified based on Lauren's histologic classifications of: intestinal, diffuse, and mixed/other [42].

Serologic methods

Following exactly the protocol described in other studies [43,44], assays for serum IgG antibodies to *H. pylori* group antigens and to a recombinant fragment of the CagA protein were performed on all cases and controls. Some strains of *H. pylori* also inject a bacterial protein, CagA protein, into host cells, altering host cell physiology and impacting the adaptive immune response in a manner favorable to chronic *H. pylori* infection [45,46]. Testing for *H. pylori* can be falsely negative in that some individuals with CagA+ *H. pylori* strains may have antibody levels below the cutoff value and thus be incorrectly classified as *H. pylori* seronegative [47]. Thus in our original analyses, to reduce the possibility of obtaining false negatives, we classified any subject as exposed if they were seropositive for either *H. pylori* or CagA. Laboratory personnel, blinded to the status of the study subjects, performed all assays at least in duplicate.

Statistical analysis

In order to estimate the association of exposures of interest and gastric cancer stratified by *H. pylori* or CagA status, we used unconditional logistic regression models to compute ORs and 95% CIs. All models were adjusted for the variables used in the original frequency match: age (as a continuous variable), ethnicity, and sex. Log calories were included in the logistic regression when a food or nutrient was the exposure of interest. Additional adjustment variables included non-dietary variables found to be associated with risk of gastric cancer, including pack-years for cigarette smoking, high-school education (yes versus no), history of gastric ulcer (yes versus no), NSAID use (at least twice a week for 3 months or longer versus less frequently), and family history of gastric cancer (yes versus no). Dietary exposures were categorized into tertiles based on the control distributions and were modeled with dummy variables. Linear trend in the logit of risk was tested by modeling the dietary exposure as a trend variable assigned the median value of the appropriate tertile. The likelihood ratio test was used to examine interactions among the dietary variables as trends and *H. pylori*/CagA status in relation to gastric cancer risk. Trends were also modeled as continuous log values, and similar results were found (data not shown). Sex-specific tertiles and models were performed initially, but resulted in very similar findings. Therefore, models combining men and women, using common tertiles, are shown here.

Results

Study population

As shown in Table 1, there are generally similar distributions of cases and controls by sex, age, and ethnicity, even after the original frequency matching was broken by the inclusion of only individuals with *H. pylori*/CagA and diet data. Table 2 shows the ORs for gastric cancer associated with selected non-dietary variables, by *H. pylori*/CagA status. For both seropositive and seronegative subjects, a history of gastric ulcer and a family history of gastric cancer are positively associated with risk of gastric cancer, while use of NSAIDs is inversely associated with risk. Additionally, associations are seen with cigarette smoking and an increase in risk and a high-school education and a decrease in risk, although the associations are stronger for seropositive than seronegative subjects. For both groups of subjects, alcohol use and a history of duodenal ulcer are not associated with gastric cancer risk.

Dietary results

In general, trends of decreasing risk of non-cardia gastric cancer with increasing consumption of all nutrients examined are seen for all individuals, regardless of *H. pylori*/CagA status. No interactions were found among *H. pylori*/CagA status and nutrient intake in relation to gastric cancer risk in men and women (Table 3).

In Table 4, significant inverse trends were present for total, green, and yellow vegetables among *H. pylori*/CagA-positive individuals, but only for yellow vegetables among *H. pylori*/CagA-negative individuals. Additionally, there is a suggestion of a decreasing risk with increasing intake of cruciferous vegetables among *H. pylori*/CagA-positive individuals, but no suggestion of such a trend with cruciferous vegetables is seen among *H. pylori*/CagA-negative individuals (*p* for interaction = 0.12).

The results also suggest an increase in risk for *H. pylori*/ CagA-positive individuals who are in the second and third tertiles of processed meat intake (OR = 2.7, 95% CI: 1.4–5.2; and OR = 2.0, 95% CI: 1.0–4.0, respectively), while there is no suggestion of a change in risk for *H. pylori*/CagA-negative individuals. For bacon, specifically, there is a suggestion of an association of increasing risk of gastric cancer with increasing intake for all individuals, although again the trend is significant for *H. pylori*/CagA-positive individuals only.

We then sought to stratify by histologic type. It is hypothesized that the intestinal type of gastric cancer has more of an environmental etiology while the diffuse type of gastric cancer is more genetically determined [5], although both are associated with *H. pylori* positivity [5,6,31]. For intestinal-type gastric cancers, findings for the associations with nutrients do not change (data not shown). For the food groups, however, the inverse associations with all vegetable groups are now stronger among the *H. pylori*/CagA-positive individuals, and for cruciferous vegetables the discrepancy between the seropositive and seronegative groups is especially magnified in association with the intestinal-type gastric cancers (*p* for interaction = 0.04) (Table 5). Unfortunately, we are not able to perform these same analyses stratified by *H. pylori*/CagA-status for diffuse-type gastric cancer cases, as of our 48 diffuse-type cases, only seven were *H. pylori*/CagA-negative.

Discussion

This study found that diet appears to influence the risk of gastric cancer in both seropositive and seronegative groups, while also suggesting that there is a stronger inverse effect of greater intake of vegetables among *H. pylori*-positive individuals. Similar to three of the five prior studies that examined the potential benefits of nutrients and/or fruits and vegetables and gastric cancer risk, this study had findings of a significant inverse association among *H. pylori*-positive individuals, but the power to detect a significant interaction term was hampered by low numbers of *H. pylori*-negative cases [19,20,25]. The other two reports did not have any evidence for an interaction or variation by *H. pylori*-status [23,28]. Exposure to antioxidants from fruits and vegetables may protect the epithelium from *H. pylori*-induced inflammatory responses, and also interfere with the development of carcinogenic N-nitroso compounds [48].

The findings in our sub-analysis by histologic type show that vegetable intake, and particularly cruciferous vegetable intake, might be associated with a reduced risk of non-cardia intestinal-type gastric cancer among those individuals who are *H. pylori*/CagA-positive but not be protective for those who are *H. pylori*/CagA-negative. The stronger finding for cruciferous vegetables may relate to the specific anticarcinogenic properties of brassica vegetables. In their review of the literature, Talalay and Fahey [49] present evidence indicating that cruciferous vegetables are rich in phytochemicals called glucosinolates, and that glucosinolates are converted to isothiocyanates by plant myrosinase and gastrointestinal microbiota. A likely

mechanism for an anticarcinogenic effect of isothiocyanates is by modulating the activity of enzymes involved in the metabolism of carcinogens, especially the induction of phase 2 detoxification enzymes [49]. There is growing evidence for an important function of phase 2 enzymes in susceptibility to carcinogens, with their induction diminishing such susceptibility [49]. Thus, the phase 2 enzymes induced by the glucosinolates from cruciferous vegetables may be involved in offsetting the harmful effects from *H. pylori*.

However another possibility for our finding may be related to the way cruciferous vegetables (especially cabbage) are eaten in our population—for example, in mixed dishes for which other aspects of the meal could be creating the effect. Additionally, the role of chance in a particular type of vegetable exhibiting a stronger association, given the multiple numbers of associations we examined, cannot be ruled out.

Other limitations relate to the case-control design of this study. While the serum to measure *H. pylori* status was taken preoperatively, there still can be inaccuracies with measurement taken at time of diagnosis, as it has been shown in endoscopic studies that as gastric damage progresses, the presence of *H. pylori* diminishes [50,51]. This misclassification would bias our results toward the null hypothesis of no association, weakening our findings. Similarly, diet was assessed by a food frequency questionnaire administered after diagnosis, and there is the possibility that our findings were affected by recall bias, which in this instance would result in a less conservative estimate, strengthening the associations found. However, our findings that the association in trends between intake of specific foods and food groups and gastric cancer risk appeared to vary by *H. pylori* serologic status, which would generally be unknown to the subjects prior to our testing, suggest that the recall bias in this study is minimal.

A strength of this study was our ability to focus on homogeneous case groups, thereby increasing the sensitivity of the study. Unlike six of the 11 studies examining the possible modification of the diet-gastric cancer association by *H. pylori* status, we were able to limit our analyses to non-cardia gastric cancer cases only, as cardia gastric cancer displays different epidemiologic patterns [52]. And, like only half of the previous studies, our relatively large number of *H. pylori*-negative cases ($n = 52$) allowed us to stratify by histologic type.

Our results indicate that the importance of diet, especially intake of vegetables, in the etiology of non-cardia gastric cancer may vary by the *H. pylori* status of the individual. The implications of these findings are twofold. First, they suggest that the results of previous studies of diet and gastric cancer that were not able to stratify by *H. pylori* status may have been attenuated toward the null hypothesis of no association, and that future studies of diet and gastric cancer will benefit from distinguishing cases as either *H. pylori*-positive or negative. Second, this finding suggests that there are possibly at least two pathways to non-cardia gastric cancer, especially of the intestinal-type. Diet may play a greater role in the etiology of gastric cancer among individuals with *H. pylori* than among those without evidence of *H. pylori* infection.

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Table 1

Characteristics of cases and controls

Characteristics	Cases (*n* = 212)		Controls (*n* = 336)	
	No.	%	No.	%
Sex				
Men	128	60.4	228	67.9
Women	84	39.6	108	32.1
Age (years)				
<65	46	21.7	78	23.2
65–74	82	38.7	119	35.4
75–84	61	28.7	106	31.6
>85	23	10.9	33	9.8
Ethnicity				
Japanese	128	60.4	185	55.1
Hawaiian	33	15.6	56	16.7
Caucasian	18	8.5	37	11.0
Filipino	15	7.1	30	8.9
Korean	11	5.2	12	3.6
Chinese	7	3.3	16	4.8

Table 2

Odds ratios[a] for gastric cancer by selected non-dietary variables, by *Helicobacter pylori* status

	***H. pylori*+ and/or CagA+**					***H. pylori*− and CagA−**				
	Cases (*n* = 160)		**Controls (*n* = 164)**		**Odds ratio (95% CI)**	**Cases (*n* = 52)**		**Controls (*n* = 172)**		**Odds ratio (95% CI)**
	No.	**%**	**No.**	**%**		**No.**	**%**	**No.**	**%**	
Cigarette smoking[b]										
Never	59	38.1	78	47.6	1.0	18	36.0	90	52.3	1.0
0.1–15.5 pack per years	22	14.2	29	17.7	1.0 (0.5–1.9)	9	18.0	28	16.3	1.7 (0.7–4.5)
15.5–38.25 pack per years	27	17.4	32	19.5	1.3 (0.7–2.5)	14	28.0	23	13.4	3.5 (1.4–8.5)
>38.25 pack per years	47	30.3	25	15.2	3.2 (1.7–6.2)	9	18.0	31	18.0	1.4 (0.5–3.8)
p-value for trend					0.0004					0.21
Ever drank alcohol[c]										
No	76	47.5	80	48.8	1.0	26	50.0	80	46.5	1.0
Yes	84	52.5	84	51.2	1.3 (0.8–2.1)	26	50.0	92	53.5	1.1 (0.5–2.3)
High-school education										
No	62	38.8	49	29.9	1.0	18	34.6	39	22.7	1.0
Yes	98	61.3	115	70.1	0.5 (0.3–0.9)	34	65.4	133	77.3	0.7 (0.3–1.6)
NSAID use[d]										
No	133	83.1	110	67.1	1.0	43	82.7	117	68.0	1.0
Yes	27	16.9	54	32.9	0.4 (0.2–0.7)	9	17.3	55	32.0	0.4 (0.2–0.9)
History of duodenal ulcer										
No	150	93.8	155	94.5	1.0	52	100.0	165	96.5	1.0
Yes	10	6.3	9	5.5	1.2 (0.5–3.1)	0	0.0	6	3.5	0.0 (0.0–2.8)
History of gastric ulcer										
No	131	82.4	153	93.3	1.0	43	82.7	162	94.7	1.0
Yes	28	17.6	11	6.7	3.1 (1.5–6.7)	9	17.3	9	5.3	4.0 (1.4–11.2)
Parent or sibling with gastric cancer										
No	120	75.0	142	86.6	1.0	39	75.0	149	86.6	1.0
1 relative	32	20.0	21	12.8	1.9 (1.0–3.5)	11	21.2	22	12.8	1.8 (0.8–4.2)

	H. pylori+ and/or CagA+					*H. pylori*− and CagA−				
	Cases (*n* = 160)		Controls (*n* = 164)		Odds ratio (95% CI)	Cases (*n* = 52)		Controls (*n* = 172)		Odds ratio (95% CI)
	No.	%	No.	%		No.	%	No.	%	
2+ relatives	8	5.0	1	0.6	8.6 (1.1–70.5)	2	3.9	1	0.6	7.4 (0.6–86.6)
p-value for trend					0.004					0.04

[a] Adjusted for sex, age, and ethnicity

[b] Missing data on number of pack years for two *H. pylori*− and *CagA*− cases

[c] Alcohol use on a regular basis for at least once a week for 6 months or more

[d] Non-steroidal drug anti-inflammatory use for a least twice a week for 3 months or longer

Table 3

Adjusted ORs[a] (95% CIs) for gastric cancer by tertile of nutrient intake,[b] by *H. pylori* status

Nutrient	Tertile	*H. pylori*+ and/or CagA+ (160 cases, 164 controls)	*H. pylori*− and CagA− (52 cases, 172 controls)	*p* for interaction
Total NSP[c]	T_1	1.0 (reference)	1.0 (reference)	
	T_2	0.6 (0.3–1.1)	0.4 (0.2–0.8)	
	T_3	0.4 (0.2–0.8)	0.3 (0.1–0.6)	
	p for trend	0.01	0.004	0.39
β-carotene	T_1	1.0 (reference)	1.0 (reference)	
	T_2	0.6 (0.3–1.1)	0.3 (0.1–0.6)	
	T_3	0.3 (0.2–0.7)	0.3 (0.1–0.8)	
	p for trend	0.002	0.01	0.84
Vitamin A	T_1	1.0 (reference)	1.0 (reference)	
	T_2	0.3 (0.2–0.7)	0.3 (0.1–0.7)	
	T_3	0.3 (0.2–0.6)	0.4 (0.2–1.0)	
	p for trend	0.001	0.09	0.56
Vitamin C	T_1	1.0 (reference)	1.0 (reference)	
	T_2	0.6 (0.3–1.0)	0.8 (0.3–1.7)	
	T_3	0.5 (0.2–0.9)	0.5 (0.2–1.2)	
	p for trend	0.03	0.13	0.90
Vitamin E	T_1	1.0 (reference)	1.0 (reference)	
	T_2	0.3 (0.1–0.5)	0.6 (0.2–1.3)	
	T_3	0.4 (0.2–0.9)	0.3 (0.1–0.8)	
	p for trend	0.09	0.02	0.46
Folate	T_1	1.0 (reference)	1.0 (reference)	
	T_2	0.6 (0.3–1.2)	0.5 (0.2–1.2)	
	T_3	0.3 (0.2–0.7)	0.5 (0.2–1.2)	
	p for trend	0.002	0.13	0.45

[a] Adjusted for age, sex, ethnicity, cigarette smoking status, education, NSAID use, family history of cancer, and total calories

[b] The range for the second tertile for daily nutrient intake were as follows: total non-starch polysaccharide, 12.0–17.9 g; *β*-carotene, 2,783–4,706 μg; vitamin A, 871–1,363 RE; vitamin C, 124–207 mg; vitamin E, 7.4–10.6 mg; folate 240–349 μg

[c] NSP, non-starch polysaccharide

Table 4

Adjusted ORs[a] (95% CIs) for gastric cancer by tertile of intake of food or food groups,[b] by *H. pylori* status

Foods or food groups	Tertile	*H. pylori*+ and/or CagA+ (160 cases, 164 controls)	*H. pylori*− and CagA− (52 cases, 172 controls)	*p* for interaction
Total vegetables	T_1	1.0 (reference)	1.0 (reference)	
	T_2	0.4 (0.2–0.8)	0.3 (0.1–0.8)	
	T_3	0.4 (0.2–0.8)	0.5 (0.2–1.2)	
	p for trend	0.02	0.23	0.52
Green vegetables	T_1	1.0 (reference)	1.0 (reference)	
	T_2	0.4 (0.2–0.8)	0.7 (0.3–1.7)	
	T_3	0.4 (0.2–0.7)	0.6 (0.3–1.4)	
	p for trend	0.01	0.27	0.41
Yellow vegetables	T_1	1.0 (reference)	1.0 (reference)	
	T_2	1.1 (0.6–2.0)	0.4 (0.2–0.8)	
	T_3	0.3 (0.2–0.7)	0.4 (0.2–0.8)	
	p for trend	0.001	0.03	0.78
Cruciferous vegetables	T_1	1.0 (reference)	1.0 (reference)	
	T_2	0.7 (0.4–1.4)	0.8 (0.3–2.0)	
	T_3	0.6 (0.3–1.2)	1.3 (0.6–3.0)	
	p for trend	0.19	0.38	0.12
Processed meats	T_1	1.0 (reference)	1.0 (reference)	
	T_2	2.7 (1.4–5.2)	1.0 (0.4–2.2)	
	T_3	2.0 (1.0–4.0)	0.8 (0.3–2.0)	
	p for trend	0.16	0.65	0.20
Bacon	T_1	1.0 (reference)	1.0 (reference)	
	T_2	0.8 (0.4–1.4)	0.9 (0.4–2.2)	
	T_3	1.7 (0.9–3.1)	1.4 (0.6–3.3)	
	p for trend	0.02	0.26	0.60

[a] Adjusted for age, sex, ethnicity, cigarette smoking status, education, NSAID use, family history of cancer, and total calories

[b] The range for the second tertile for daily food intake (g) was as follows: processed meats, 8.7–25.4; bacon, 0.005–1.1; total vegetables, 241.5–374.6; green vegetables, 80.1–142.9; yellow vegetables, 14.0–31.1; cruciferous vegetables, 26.8–54.1

Table 5

Adjusted ORs[a] (95% confidence intervals) for INTESTINAL gastric cancer by tertile of intake of food or food groups,[b] by *H. pylori* status

Foods or food groups	Tertile	*H. pylori*+ and/or CagA+ (109 cases, 164 controls)	*H. pylori*− and CagA− (40 cases, 172 controls)	*p* for interaction
Total vegetables	T_1	1.0 (reference)	1.0 (reference)	
	T_2	0.4 (0.2–0.8)	0.4 (0.2–1.2)	
	T_3	0.3 (0.2–0.7)	0.7 (0.3–1.7)	
	p for trend	0.01	0.63	0.17
Green vegetables	T_1	1.0 (reference)	1.0 (reference)	
	T_2	0.4 (0.2–0.9)	1.1 (0.4–2.6)	
	T_3	0.3 (0.2–0.7)	0.9 (0.3–2.4)	
	p for trend	0.01	0.83	0.12
Yellow vegetables	T_1	1.0 (reference)	1.0 (reference)	
	T_2	1.1 (0.6–2.2)	0.3 (0.1–0.9)	
	T_3	0.2 (0.1–0.5)	0.4 (0.1–0.9)	
	p for trend	0.0002	0.04	0.50
Cruciferous vegetables	T_1	1.0 (reference)	1.0 (reference)	
	T_2	0.7 (0.3–1.3)	0.7 (0.2–2.0)	
	T_3	0.6 (0.3–1.1)	1.6 (0.6–3.9)	
	p for trend	0.12	0.17	0.04
Processed meats	T_1	1.0 (reference)	1.0 (reference)	
	T_2	2.5 (1.2–5.3)	1.0 (0.4–2.6)	
	T_3	2.0 (0.9–4.1)	0.9 (0.3–2.5)	
	p for trend	0.22	0.89	0.37
Bacon	T_1	1.0 (reference)	1.0 (reference)	
	T_2	0.7 (0.3–1.4)	0.6 (0.2–1.7)	
	T_3	1.7 (0.9–3.2)	1.2 (0.5–2.8)	
	p for trend	0.02	0.39	0.49

[a] Adjusted for age, sex, ethnicity, cigarette smoking status, education, NSAID use, family history of cancer, and total calories

[b] The range for the second tertile for daily food intake (g) was as follows: processed meats, 8.7–25.4; bacon, 0.005–1.1; total vegetables, 241.5–374.6; dark green vegetables, 25.0–51.9; light green vegetables, 52.0–92.0; yellow vegetables, 14.0–31.1; cruciferous vegetables, 26.8–54.1