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To investigate the role of a wide range of foods and beverages on the risk of stomach cancer, we analyzed data from a case-control study carried out in Italy between 1997 and 2007 on 230 subjects with incident histologically confirmed stomach cancer (143 men and 87 women, age range 22–80 yr) and 547 controls (286 men and 261 women, age range 22–80 yr) admitted to hospital for acute, non-neoplastic diseases. Odds ratios (OR) of stomach cancer and their corresponding 95% confidence intervals (CI) were estimated using unconditional multiple logistic regression models, adjusted for age, sex, energy intake, and other selected variables. A direct association with stomach cancer risk was observed for cereals (OR = 2.07, 95% CI = 1.01–4.24, for the highest compared to the lowest quintile of intake, *P* for trend = 0.03), soups (OR = 1.94, 95% CI = 1.10–3.42, *P* for trend = 0.05), and potatoes (OR = 2.04, 95% CI = 1.05–3.98, *P* for trend = 0.04). Conversely, inverse trends in risk were observed with vegetables (OR = 0.47, 95% CI = 0.27–0.81, *P* for trend = 0.01) and fruit intake (OR = 0.53, 95% CI = 0.30–0.93, *P* for trend = 0.08). The results of this study confirm a protective role of vegetables and fruit against stomach cancer and suggest a detrimental effect of (refined) cereals on this neoplasm.

INTRODUCTION

Gastric cancer has been steadily declining for more than 50 yr, but remains the third most common cause of cancer death in Italy after lung and colorectal cancer in both sexes combined (1). *Helicobacter pylori* (*H. pylori*) infection, tobacco smoking, obesity, unfavorable socioeconomic conditions, family history, but also selected aspects of diet and nutrition (such as poor food preservation and salt consumption) have been associated to the risk of gastric cancer (2–5).

With reference to specific foods and food groups, an expert panel of the World Cancer Research Fund and American Institute for Cancer Research concluded that "a diet rich in non-starchy and allium vegetables and fruit probably decreased the risk of stomach cancer" (6). The evidence of a favorable role of fruit and vegetables on stomach cancer risk is, however, more consistently reported in case-control studies, whereas it is less supported by cohort studies (6–9). Among more recent studies, the Sweden Mammography Cohort and the Cohort of Swedish Man conducted on 139 incident cases of gastric cancer reported that vegetables were inversely related to gastric cancer risk but showed no significant association for fruit (10), whereas in the European Prospective Investigation into Cancer and Nutrition study conducted on 330 gastric cancer cases (11) and in the National Institute of Health and American Association of Retired Persons Diet and Health study from United States on 394 cases (12), no significant associations were observed for both fruit and vegetables.

The evidence regarding cereal products and stomach cancer is conflicting. A direct association with cereals in general has been observed in several case-control and cohort studies (13–17), although not in all (17–20). Moreover, results for specific cereal products (i.e., rice, bread, pasta) are less consistent, and wholegrain cereals (17,21) and cereal fibers (22) have been inversely related to gastric cancer risk.

Consumption of meat and fish has not been related with stomach cancer risk (13,14,16,17,23,24). However, there has been a suggestion of a direct association with cured or processed meat (6,18,23,25).

With respect to beverages, coffee and black tea have not been consistently related to stomach cancer risk (14,15,17,24), whereas high consumption of green tea has been suggested to decrease the risk, although the evidence is still inconclusive (17,24,26,27). No relation has emerged in most studies with alcohol consumption (14,17,24,28–30).

We analyzed the role of a wide range of foods and beverages on the risk of stomach cancer using data from a case-control study conducted in Northern Italy in which dietary habits have

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been recorded using a validated food-frequency questionnaire (FFQ) (31,32).

MATERIAL AND METHODS

A case-control study of stomach cancer was conducted between 1997 and 2007 in the province of Milan, Italy. Cases were 230 patients (143 male and 87 female) under age 80 yr (median age 63 yr, range = 22–80 yr) admitted to major teaching and general hospitals in the study area with incident, histologically confirmed stomach cancer (International Classification of Diseases–9, 151.0–151.9), diagnosed no longer than 1 yr before the interview and with no previous diagnosis of cancer. Most cases were from fundus/corpus (about 50%) or pilorus (about 40%). Controls were 547 patients (286 male and 261 female) under age 80 yr (median age 63 yr, range = 22–80 yr), frequency matched to cases by age and sex (with a ratio of 2:1 for men and of 3:1 for women) and admitted to the same hospitals as cases for a wide spectrum of acute, nonneoplastic conditions, unrelated to known or potential risk factors for stomach cancer or long-term diet modification. Of controls, 20% were admitted for traumatic orthopedic disorders, mostly fractures and sprains; 23% for other orthopedic disorders such as low back pain and disc disorders; 22% for acute surgical conditions; and 35% for miscellaneous other illnesses including eye, nose, ear, skin, or dental disorders. Less than 5% of cases and controls approached refused to be interviewed.

For both cases and controls, data were collected during their hospital stay by trained interviewers using a structured questionnaire. This included information on sociodemographic characteristics, anthropometric measures, selected lifestyle habits including tobacco smoking and alcohol consumption, a personal medical history, and family history of cancer.

A FFQ was used to assess subjects' habitual diet during the 2 yr before diagnosis or hospital admission (for controls). The FFQ included 78 foods and beverages as well as a range of recipes, including the most common ones in the Italian diet, grouped into 6 sections: milk and hot beverages, bread and cereal dishes (first courses), meat and other main dishes (second courses), vegetables (side dishes), fruit, sweets and desserts, and soft drinks. Another section dealt with alcoholic beverages. Subjects were asked to indicate the average weekly frequency of consumption for each dietary item; intakes lower than once a wk but at least once a mo were coded as 0.5 per wk. For a few vegetables and fruits, seasonal consumption and the corresponding duration was elicited. At the end of each section, one or two open questions were used to include other foods eaten at least once per wk. To estimate total energy intake, an Italian food composition database was used, integrated with other sources when needed (33,34). The FFQ was satisfactorily valid (31) and reproducibile (32), with Spearman correlation coefficients between .60 and .80 for most items.

As previously described (35), food and beverage items were categorized in 16 groups: milk and yoghurt, coffee and tea, cereals, soups, eggs, poultry, red meat, processed meat, cheese, pulses, vegetables, potatoes, fruit, desserts, sugars, and alcohol. The weekly intake for each group was obtained by summing up the intake of the food items included in each food group and was then distributed into approximate quintiles among controls (quartiles or tertiles for a few food groups not frequently consumed).

Odds ratios (OR) of stomach cancer and their corresponding 95% confidence intervals (CI) were estimated using unconditional multiple logistic regression models (36). All models included terms for age (5-yr groups), sex, education (<7, 7–11, ≥ 12 yr), year of interview, body mass index (BMI; <20, 20–<25, 25–<30, and ≥ 30 kg/m^2), tobacco smoking (never, ex-smokers, current smokers of <15 or ≥ 15 cigarettes per day), family history of stomach cancer in first-degree relatives (yes, no), and total energy intake (quintiles on the distribution of controls) (36,37). The OR estimates were not meaningfully modified after further allowance in the models for aspirin use or occupation as indicator of socioeconomic growth. Tests for trend were based on the likelihood-ratio test between models with and without a linear term for each food group. To test for interaction, the difference in $-2 \times \log(\text{likelihood})$ of the models with and without interaction terms were compared with the χ^2 distribution with 1 *df*.

RESULTS

Table 1 shows the distribution of 230 stomach cancer cases and 547 controls according sex, age, and other selected variables. By design, the proportion of women was higher in controls than in cases, and cases and controls had similar age distributions. Cases were more frequently current and ex-smokers, reported more frequently a history of stomach cancer in first-degree relatives, and had higher total caloric intake than controls. No association was observed with education and BMI. Table 2 gives the cutoff points for quintiles of selected food groups and beverages and the distribution of cases and controls across subsequent quintiles.

Table 3 gives the corresponding multivariate ORs of stomach cancer. A direct association was observed for cereals (OR = 2.07, 95% CI = 1.01–4.24 for the highest compared to the lowest quintile of intake, *P* for trend = 0.03), soups (OR = 1.94, 95% CI = 1.10–3.42, *P* for trend = 0.05), and potatoes (OR = 2.04, 95% CI = 1.05–3.98, *P* for trend = 0.04). Conversely, inverse trends in risk were observed for vegetables (OR = 0.47, 95% CI = 0.27–0.81, *P* for trend = 0.01), and fruit (OR = 0.53, 95% CI = 0.30–0.93, *P* for trend = 0.08). Intake of milk and yoghurt, coffee and tea, eggs, poultry, red meat, processed meat, cheese, pulses, desserts, sugars, and alcohol were unrelated to stomach cancer risk. With respect to individual food items among cereals, the strongest positive association was found for bread (OR = 2.45, 95% CI = 1.23–4.89, *P* for trend = 0.02); whereas among fruit, the strongest inverse association was found for non-citrus fruit (OR = 0.44, 95% CI = 0.25–0.78, *P* for trend = 0.01).

TABLE 1
Distribution of 230 Cases of Stomach Cancer and 547 Controls According to Age, Education, and other Selected Variables, Italy, 1997–2007

	Cases		Controls	
Characteristic	No.	%	No.	%
Sex				
Men	143	62.2	286	52.3
Women	87	37.8	261	47.7
Age (yr)				
<50	39	17.0	97	17.7
50–60	58	25.2	137	25.1
60–70	86	37.4	202	36.9
≥70	47	20.4	111	20.3
Education (yr)[a]				
<7	95	41.8	236	43.5
7–11	86	37.9	174	32.0
≥12	46	20.3	133	24.5
Body mass index (kg/m^2)[a]				
<20	12	5.3	33	6.1
20–<25	106	46.9	215	39.4
25–<30	82	36.3	223	40.9
≥30	26	11.5	74	13.6
Smoking status[a]				
Never smokers	96	41.9	261	47.8
Ex-smokers	75	32.8	167	30.6
Current smokers				
<15 cigarettes/day	25	10.9	49	9.0
≥15 cigarettes/day	33	14.4	69	12.6
Family history of stomach cancer[b]				
No	200	87.0	516	94.3
Yes	30	13.0	31	5.7
Total energy intake (kcal/day)				
<1,569	21	9.1	109	19.9
1,567–<1,916	38	16.5	109	19.9
1,916–<2,230	54	23.5	110	20.1
2,230–<2,602	55	23.9	109	19.9
≥2,602	62	27.0	110	20.1

[a]The sum does not add up to the total because of some missing values.
[b]In first-degree relatives.

Selected food groups found to be significantly associated to the risk of stomach cancer (i.e., cereals, vegetables, and fruit) were further examined in strata of sex, age (<65 and ≥65 yr), education (<7 and ≥7 yr), BMI (<25 and ≥25 kg/m^2), and tobacco smoking (never smokers and smokers; Table 4). No significant heterogeneity in risk estimates across strata of various covariates emerged for any of the food groups considered.

DISCUSSION

The results of this study provide additional evidence on a favorable role of vegetables and fruit against stomach cancer and suggest a detrimental effect of cereals on this neoplasm.

The inverse relation between vegetables and fruit consumption and stomach cancer risk is consistent with the findings of most previous case-control studies (6–8,10). The inverse association with vegetables and fruit consumption has been less consistently reported in cohort studies (6–12). The different results between case-control and cohort studies may be due to recall bias in retrospective studies. However, the association may have been underestimated in prospective studies because of the combined effect of imprecise dietary measurement, the limited variability of dietary intakes within each cohort, and the changes in diet between data collection and disease occurrence (7,9).

Vegetables and fruit are rich in several micronutrients, such as carotenoids, vitamins C and E, and other food compounds; fibers, flavonoids, and plant sterols, which display variable mechanisms of action including antioxidant effects, binding, and dilution of carcinogens in the digestive tract (38,39). In particular, carotenoids and vitamin C have been inversely related to stomach cancer risk (17), although the evidence is less consistent than that for vegetables and fruit. It is still unclear whether the combined effect of several concurrent mechanisms explains the favorable effect of vegetables and fruit on stomach cancer. Moreover, a frequent consumption of vegetables and fruit may be a nonspecific indicator of a more affluent and better-planned diet.

In our study, an increased risk of stomach cancer was found for increasing consumption of cereals (particularly bread), soups (including cereals based ones), and potatoes. Desserts and sugars were also directly, although not significantly, associated to stomach cancer risk. Other studies have suggested an increased risk of gastric cancer with higher consumption of cereal-based products (13–17), although a few have reported no association (17,21). The relation between cereal products and gastric cancer risk may depend on the degree to which these products are refined. Whole-grain cereals (17,21) and cereals fiber (22) have been, in fact, associated to a reduced risk of stomach cancer. Cereals consumed in Italy are mostly refined, leading to a higher ratio between starch and fiber intake than in other populations. The high glycemic index of these cereals, and their involvement in hyperinsulinemia and insulin-like growth factors, may thus explain the positive association with stomach cancer risk (40,41).

As in most previous investigations, we did not find any association with consumption of meat, fish, and other protein-rich foods (13,14,16,17,20,24). We found, however, no-significant inverse association with processed meat, which is in contrast to what has been reported by other studies (18,19,23,42), possibly reflecting the composition of processed meat in Italy, some of which (e.g., raw ham) are not indicators of a poorer diet.

Our study confirms that coffee (17,24) and black tea (17) are unrelated to stomach cancer risk.

TABLE 2
Distribution of 230 Cases of Stomach Cancer and 547 Controls According the Intake of Selected Food Groups and Beverages, Italy, 1997–2007

	Quintiles of Intake				
Food Group (Servings/Wk)	1	2	3	4	5
Milk and yoghurt					
Upper limit	0.5	4.5	7	9	24
Cases:controls	52:115	36:104	58:143	32:81	53:104
Coffee and tea					
Upper limit	7.5	14	21	28	60
Cases:controls	41:108	45:114	62:148	47:97	35:80
Cereals					
Upper limit	15.8	20.8	24.8	31.3	64.3
Cases:controls	21:104	39:110	48:109	54:109	68:115
Soups					
Upper limit	1	2	3.5	5	10
Cases:controls	32:115	41:107	59:111	47:114	51:100
Eggs					
Upper limit	0.5	1.5	6		
Cases:controls	69:189	65:152	96:206		
Poultry					
Upper limit	0.5	2	2	5	
Cases:controls	31:105	87:151	71:177	41:114	
Red meat					
Upper limit	1.5	2.5	3.5	4.8	11.8
Cases:controls	33:104	32:100	36:112	60:111	69:120
Processed meat					
Upper limit	1.5	2	2.5	4.5	15
Cases:controls	48:98	32:92	30:58	76:183	44:116
Cheese					
Upper limit	1.8	3.0	3.8	5.1	10.7
Cases:controls	30:107	45:110	51:108	48:112	56:110
Pulses					
Upper limit	0	0.5	7		
Cases:controls	56:151	61:138	113:258		
Vegetables					
Upper limit	5.4	7.7	10.5	13.7	33.2
Cases:controls	59:108	47:108	53:111	37:109	34:111
Potatoes					
Upper limit	0	0.5	1	1.5	8
Cases:controls	15:71	24:60	63:173	35:65	93:178
Fruit					
Upper limit	8.7	13.6	17.4	24.5	55.3
Cases:controls	54:111	45:107	39:109	58:110	34:110
Desserts					
Upper limit	0.7	2.3	5.4	8.4	28
Cases:controls	26:105	45:111	54:108	47:115	58:108
Sugars					
Upper limit	6.5	16	27.5	42.6	134
Cases:controls	30:103	43:114	37:101	59:118	61:111
Alcohol[a]					
Upper limit	0.5	6.5	13	20	80
Cases:controls	52:148	38:95	29:81	53:119	56:104

[a]The sum does not add up to the total because of some missing values.

TABLE 3
Odds Ratios (OR) and Corresponding 95% Confidence Intervals (CI) According to the Intake of Selected Food Groups and Beverages Among 230 Stomach Cancer Cases and 547 Controls, Italy, 1997–2007[a]

	Quintiles of Intake					
Food Group	1[b]	2	3	4	5	χ^2 *P* Value
Milk and yoghurt						
OR	1	0.77	0.81	0.88	1.06	0.14
(95% CI)		(0.45–1.33)	(0.50–1.30)	(0.50–1.54)	(0.64–1.78)	0.71
Coffee and tea						
OR	1	1.02	0.96	1.06	0.91	0.03
(95% CI)		(0.60–1.74)	(0.58–1.57)	(0.61–1.83)	(0.50–1.67)	0.85
Cereals						
OR	1	1.29	1.57	1.69	2.07	4.57
(95% CI)		(0.66–2.52)	(0.81–3.07)	(0.86–3.35)	(1.01–4.24)	0.03
Soups						
OR	1	1.50	2.14	1.50	1.94	3.88
(95% CI)		(0.85–2.64)	(1.25–3.68)	(0.86–2.61)	(1.10–3.42)	0.05
Eggs						
OR	1	0.99	1.15			0.51
(95% CI)		(0.64–1.52)	(0.77–1.70)			0.48
Poultry						
OR	1	1.94	1.45	1.32		0.03
(95% CI)		(1.16–3.27)	(0.86–2.44)	(0.74–2.37)		0.87
Red meat						
OR	1	0.78	0.83	1.32	1.22	2.45
(95% CI)		(0.43–1.42)	(0.47–1.50)	(0.75–2.30)	(0.70–2.15)	0.12
Processed meat						
OR	1	0.67	0.93	0.77	0.60	2.27
(95% CI)		(0.38–1.18)	(0.51–1.71)	(0.48–1.23)	(0.35–1.02)	0.13
Cheese						
OR	1	1.38	1.43	1.22	1.63	1.57
(95% CI)		(0.79–2.41)	(0.82–2.49)	(0.70–2.15)	(0.92–2.90)	0.21
Pulses						
OR	1	1.14	1.09			0.10
(95% CI)		(0.71–1.83)	(0.72–1.65)			0.75
Vegetables						
OR	1	0.73	0.80	0.55	0.47	7.85
(95% CI)		(0.44–1.21)	(0.49–1.32)	(0.32–0.96)	(0.27–0.81)	0.01
Potatoes						
OR	1	1.98	1.46	2.33	2.04	4.05
(95% CI)		(0.91–4.28)	(0.75–2.85)	(1.10–4.94)	(1.05–3.98)	0.04
Fruit						
OR	1	0.79	0.73	0.89	0.53	3.02
(95% CI)		(0.47–1.33)	(0.43–1.23)	(0.53–1.48)	(0.30–0.93)	0.08
Desserts						
OR	1	1.57	1.80	1.22	1.57	0.52
(95% CI)		(0.88–2.81)	(1.00–3.25)	(0.67–2.22)	(0.86–2.88)	0.47
Sugars						
OR	1	1.33	1.11	1.45	1.60	2.42
(95% CI)		(0.75–2.36)	(0.61–2.01)	(0.82–2.55)	(0.90–2.85)	0.12
Alcohol						
OR	1	1.02	0.82	0.91	1.02	0.01
(95% CI)		(0.60–1.72)	(0.45–1.47)	(0.53–1.56)	(0.57–1.83)	0.92

[a]ORs are estimates from unconditional logistic regression models adjusted for sex, age, education, year of interview, body mass index, tobacco smoking, family history of stomach cancer, and total energy intake.
[b]Reference category.

TABLE 4
Odds Ratios[a] (OR) and Corresponding 95% Confidence Intervals (CI) for an Intake Increase of 1 Daily Serving of Selected Food Groups in Strata of Covariates Among 230 Stomach Cancer Cases and 547 Controls, Italy, 1997–2007

		OR (95% CI)									
		Sex		Age (yr)		Education (yr)		Body Mass Index (kg/m^2)		Smoking	
Food Group	Overall	Men	Women	<65	≥65	<7	≥7	<25	≥25	Never Smokers	Smokers
Cereals	1.13	1.18	1.06	1.12	1.15	1.21	1.07	1.20	1.16	1.07	1.19
	(1.00–1.29)	(1.01–1.39)	(0.89–1.27)	(0.94–1.32)	(0.98–1.35)	(1.02–1.43)	(0.91–1.26)	(0.94–1.30)	(0.99–1.37)	(0.90–1.26)	(1.02–1.41)
Vegetables	0.69	0.78	0.55	0.67	0.71	0.59	0.73	0.56	0.86	0.53	0.80
	(0.53–0.88)	(0.57–1.05)	(0.36–0.84)	(0.49–0.93)	(0.49–1.02)	(0.39–0.90)	(0.54–0.99)	(0.39–0.80)	(0.61–1.22)	(0.35–0.81)	(0.59–1.08)
Fruit	0.86	0.89	0.83	0.79	0.97	0.75	0.93	0.79	0.92	0.84	0.87
	(0.75–0.98)	(0.75–1.05)	(0.67–1.02)	(0.66–0.94)	(0.79–1.17)	(0.60–0.93)	(0.79–1.10)	(0.65–0.97)	(0.77–1.10)	(0.69–1.03)	(0.73–1.04)

[a]ORs are estimates from unconditional logistic regression adjusted for sex, age, education, year of interview, body mass index, smoking status, family history of stomach cancer, and total energy intake. Continuous OR for an increment equal to 1 daily serving.

Similarly, we did not observe any association with alcohol consumption, consistent with the results of other studies (14,16,17,24,28–30).

Among the limitations of our investigation is the fact that no information on *H. pylori* was available in our study. Although the prevalence of *H. pylori* infection is declining (43), it was relatively high (about 45%) in Italy in the mid 1990s, it increased with age, and was more frequent in men than women (44). Thus, a large proportion of the population studied is likely to be *H. pylori* positive. However, case-control studies have limited ability to measure *H. pylori* because blood samples obtained at stomach cancer diagnosis are of a low value.

Case-control studies are susceptible to selection and information bias. To minimize any possible recall bias due to the onset or treatment of the disease, we investigated dietary habits in the 2 yr prior to interview. Moreover, bias in the recall of food intake by cases should be limited given the limited knowledge and attention paid in the population to specific relations between diet and stomach cancer. The use of hospital controls may be criticized because their dietary habits may differ from those of the general population (36). However, given the same interview setting, information provided by hospital controls should have a good comparability with that from cases. Moreover, separate comparisons of cases with controls from major diagnosis categories (traumas, other orthopedic, surgical, and miscellaneous other conditions) gave comparable results. Other aspects that support the validity of our investigation are the comparable catchment areas of cases and controls; the high response rate of study participants; and the use of a valid, reproducible, and detailed FFQ allowing us to estimate, and hence adjust for, total energy intake (37).

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