Dietary Factors and Risk of Colon Cancer in Shanghai, China

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Abstract

Colon cancer incidence rates have risen sharply in Shanghai, China, since the early 1970s, and diet may have contributed to the rising incidence. To clarify the role of dietary factors for colon cancer in Shanghai, we analyzed data from a population-based case-control study of 931 cases (462 males and 469 females) and 1552 controls (851 males and 701 females) ages 30–74 years in Shanghai, China, from 1990–1993. Subjects were interviewed in person for a detailed history of dietary practices and food preferences by using a food-frequency questionnaire. Colon cancer risk was estimated by odds ratios (ORs) and 95% confidence intervals (CIs), adjusting for age, total energy, and other confounding factors. Risk for the highest *versus* the lowest quartile of intake was elevated for red meat (OR, 1.5; 95% CI, 1.0–2.1 for men and OR, 1.5; 95% CI, 1.0–2.2 for women), fish (OR, 1.7; 95% CI, 1.2–2.4 for men and OR, 1.2; 95% CI, 0.8–1.7 for women), and eggs (OR, 1.4; 95% CI, 1.0–1.9 for men and OR, 1.3; 95% CI, 0.9–1.9 for women), but was reduced for fresh fruit (OR, 0.7; 95% CI, 0.5–1.0 for men and OR, 0.6, 0.4–0.9 for women). High intake of preserved foods, whether animal or plant source, was associated with an excess risk of colon cancer (OR, 2.0; 95% CI, 1.5–2.9 for men and OR, 2.7; 95% CI, 1.9–3.8 for women). For dietary nutrients, risk generally declined with greater consumption of fiber and micronutrients common in fruit and vegetables, including vitamin C, carotene, and vitamin E. Intake of macronutrients in general was not significantly related to risk. Our findings suggest that diets high in fruit and antioxidant vitamins that are common in plant foods reduce the risk of colon cancer, whereas diets high in red meat, eggs, and preserved foods increase the risk.

Introduction

Colon cancer is generally less common in Asia, Africa, and Latin America than in North America, Western Europe, and Australia (1), but incidence is increasing in previously low-risk areas (2–4). In Shanghai, China, the age-adjusted incidence rate of colon cancer has increased about 100%, or 4% per year between 1972–1977 and 1990–1994 (3, 5). The increase has occurred in both men (from 6 to 13 per 100,000 person-years) and women (from 6 to 11 per 100,000 person-years) and cannot be fully explained by ascertainment criteria or the increased use of screening procedures (3).

The variation in colon cancer incidence and mortality found geographically (6), among migrants (7), and by socioeconomic status (8) suggests that diet may play a major etiological role. A number of analytic epidemiological studies have reported that the risk of developing colon cancer is influenced by the intake of red meat (9), fat (10), dietary fiber (11), and vegetables and fruit (12), but the evidence is not entirely consistent. Most of the reports have come from Western countries, whereas the role of diet in relation to colon cancer risk in comparatively low-incidence areas has received only limited attention.

The living standard among Shanghai residents, including the availability of a variety of foods, has improved markedly since the early 1970s (13). The consumption of animal foods increased 50–160% in China during 1954–1979 (14) and tended to be higher in Shanghai than in China overall (15). The adoption of Westernized diets and lifestyle may have contributed to the rapid rise in colon cancer incidence. To identify dietary risk factors for colon cancer in Shanghai, we examined colon cancer data as part of a case-control study of four gastrointestinal sites (colon, rectum, pancreas, and esophagus).

Materials and Methods

Study Population. A population-based, multicancer case-control study was conducted in Shanghai, China, between October 1, 1990, and June 30, 1993. Detailed methods have been reported elsewhere (16, 17). Briefly, eligible cases were residents of urban Shanghai, ages 30–74 years, newly diagnosed with colon cancer. The study area refers to 10 districts that comprise 6.8 million residents and is covered by the population-based Shanghai Cancer Registry. A rapid reporting system of incident cases was established for the study.

A total of 931 colon cancer patients (462 males and 469 females) were interviewed, yielding a participation rate of 92%. All of the cases were confirmed by either histopathology (95%) or other methods including surgical examination, computed tomography scan/ultrasound, or X-ray (5%). Excluded from the study were 59 colon cancer patients who died before participation, 14 who moved away, and 7 who refused the interview.

Controls were randomly selected from residents of urban Shanghai and frequency-matched to the expected age (5-year category) and sex distribution of the four gastrointestinal cancers combined in the overall study. Personal identification cards from the Shanghai Resident Registry were used to select con-

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trols. The cards contained information on name, address, date of birth, gender, and other demographic factors. Two random numbers (a four-digit number for locating a drawer and a three-digit number for locating a personal identification card within the drawer) were generated to select each control. For each control chosen, an alternate control subject was also selected. If the first control could not be interviewed, the alternate was enrolled in the study. A total of 1552 controls were interviewed, yielding a participation rate of 84.5%. Of these, 240 (15%) were alternates.

Data Collection. Study participants were interviewed in person by trained interviewers, using a structured questionnaire to obtain information on demographic and residential characteristics, height and weight, diet, cigarette smoking, alcohol and other beverage consumption, physical activity, medical history, family history of cancer, and lifetime occupational history. Dietary intake included 86 food items commonly consumed in Shanghai during the late 1980s. The questionnaire design was adapted from Block's food frequency questionnaire (18). Subjects were asked to report the usual frequency and amount (in liangs, as the common unit of weight in China, 1 liang = 50 g) of consumption for each food item 5 years before diagnosis for cases and 5 years before the date of interview for controls. Information on eating preferences (saltiness, temperature), preference for selected cooking methods (deep fried, smoked, grilled, cured foods) and other dietary habits (eating punctually, speed) was also obtained. The use of vitamin supplements was uncommon and, therefore, not ascertained in this study.

Data Analysis. The monthly intake of individual nutrients from foods were computed using Chinese food composition tables (19). The total dietary intake of each nutrient was calculated by summing up the amount of intake across all of the food items, which was individually estimated by multiplying the nutrient content with the reported frequency and the amount of intake for each food item. Because a large number of vegetables and fruit in China were available only seasonally, the average monthly intake of those foods was calculated by weighting the length of time that the food was available each year. Related food items were combined into food groups according to their dietary similarities (Appendix A).

Nondietary variables of interest were categorized into standard strata. Adjustment for physical activity levels was based on an index of low, medium, and high activities of usual occupation estimated by an industrial hygienist (20, 21). Further adjustment for an index of lifetime cumulative hours spent on moderate activities (*e.g.*, cleaning the house and climbing stairs) and heavy activities (*e.g.*, heavy lifting and jogging) did not alter risk estimates appreciably and, therefore, was not included in the final model.

Dietary variables were categorized into four levels of frequency of consumption based on quartile (or tertiles when appropriate) distribution among controls, separately for men and women (see Appendix B for cut points for food items and food groups, Appendix C for cut points for preserved foods, and Appendix D for nutrient quartiles). Energy adjustment procedures included standard and energy-partition methods (22). The Mantel-Haenszel stratified estimation method and unconditional logistic regression were used to adjust for the possible effect of confounding factors and to derive adjusted ORs[2] and 95% CIs (23), with the lowest intake category representing the reference category. Forward stepwise logistic regression with $P = 0.15$ as entry criterion and $P = 0.2$ as staying criterion was used to select potential confounders for the basic model. Each parameter measuring nutrients and food groups that were associated with the risk of colon cancer in age- and energy-adjusted analyses was then independently forced into the basic model to yield the full model. Tests for trend across the quartiles were performed through logistic regression by assigning scores of 1–4 to the first to fourth quartiles, respectively. All of the analyses were conducted separately for men and women. All of the ORs were adjusted for age, total energy intake, education, body mass index, monthly family per capita income, and occupational physical activity. The ORs did not change substantially when dietary factors that were not highly correlated were modeled together (*e.g.*, vegetables and preserved foods, fruit and preserved foods, vegetables and preserved vegetables, preserved vegetables and preserved animal foods, vitamin C and vitamin E, or fruit and red meat).

[2] The abbreviations used are: OR, odds ratio; CI, confidence interval.

Results

Table 1 presents demographic characteristics of study subjects and the distribution of selected colon cancer risk factors. Cases and controls were similar with respect to age, marital status, alcohol use, tea consumption, smoking history, and family history of large bowel cancer. However, in comparison with controls, cases are more likely to have higher education, family income, and body mass index, and lower occupational physical activity level.

An elevated risk of colon cancer was generally linked to high intake of animal foods, including red meats, poultry, fish, and eggs (Table 2). Among men, risk for the highest quartile relative to the lowest quartile of intake of these foods ranged from 1.4 for eggs to 1.7 for fish. Among women, the corresponding risks tended to be lower than those for men, ranging from no association with poultry to an OR of 1.5 for fresh red meat. There was no association with dairy products in either men or women.

The consumption of fresh fruit was inversely associated with the risk of colon cancer (Table 2). Among men, ORs decreased from 1.0 (95% CI, 0.7–1.3) in the second quartile of intake to 0.9 (95% CI, 0.7–1.3) and 0.7 (95% CI, 0.5–1.0) in the third and fourth quartiles, respectively. Corresponding ORs for women were 0.8 (95% CI, 0.6–1.1), 0.8 (95% CI, 0.6–1.2), and 0.6 (95% CI, 0.4–0.9). There was a suggestive trend toward a decreased risk of colon cancer with greater consumption of vegetables in men. The inverse associations were similar for all types of vegetables, including dark green leafy, carotene-rich, cruciferous, and allium vegetables. No association with vegetable intake was found among women. Soy foods were not related to risk in either men or women.

The risk of colon cancer increased significantly with increasing consumption of preserved foods in both sexes (Table 3). Among men, the ORs increased from 1.2 (95% CI, 0.8–1.7) in the second quartile of intake to 1.4 (95% CI, 1.0–2.0) and 2.0 (95% CI, 1.5–2.9) in the third and fourth quartiles, respectively. Corresponding ORs for females were 1.2 (95% CI, 0.8–1.7), 1.4 (95% CI, 1.0–2.0), and 2.7 (95% CI, 1.9–3.8). The overall association with preserved foods was more pronounced for preserved vegetables than for animal foods. Risk was not confined to any specific type of preserved animal or plant foods and was unrelated to the degree of doneness or intake level of deep-fried or grilled foods (data not shown).

Colon cancer risk was generally not related to the con-

Table 1 Distribution of demographic characteristics of colon cancer cases and controls by sex

Characteristics	Males				Females			
	Controls		Cases		Controls		Cases	
	n	(%)	*n*	(%)	*n*	(%)	*n*	(%)
Total[a]	851		462		701		469	
Age (years)								
30–49	130	(15)	75	(16)	108	(15)	90	(19)
50–59	182	(21)	95	(21)	194	(28)	94	(20)
60–64	195	(23)	108	(23)	147	(21)	105	(22)
65–69	183	(22)	100	(22)	136	(19)	97	(21)
70–74	161	(19)	84	(18)	116	(17)	83	(18)
Education (years)								
0–6	313	(37)	144	(32)	399	(58)	260	(57)
7–12	400	(48)	234	(51)	248	(36)	163	(36)
≥13	122	(15)	78	(17)	42	(6)	34	(7)
Monthly income/person (yuan)								
<30	250	(30)	99	(21)	251	(36)	118	(25)
30–49	303	(36)	159	(34)	242	(35)	161	(34)
50+	294	(35)	203	(44)	203	(29)	189	(40)
Marital status								
Married	769	(90)	427	(92)	543	(77)	372	(79)
Others	82	(10)	35	(8)	158	(23)	97	(21)
Body mass index								
Males								
≤19.4	216	(26)	106	(23)				
19.5–20.6	220	(26)	96	(21)				
20.7–22.4	195	(23)	110	(24)				
≥22.5	216	(26)	149	(32)				
Females								
≤19.4					171	(25)	106	(23)
19.5–21.3					177	(25)	115	(25)
21.4–23.1					174	(25)	105	(23)
≥23.2					173	(25)	139	(30)
Alcohol use								
No	462	(54)	248	(54)	659	(94)	448	(96)
Yes	389	(46)	214	(46)	42	(6)	21	(4)
Tea drinking								
No	302	(35)	176	(38)	529	(75)	369	(79)
Yes	549	(65)	286	(62)	172	(25)	100	(21)
Cigarette smoking								
Never	289	(34)	176	(38)	613	(87)	429	(91)
Ever	562	(66)	286	(62)	88	(13)	40	(9)
Occupational physical activity								
Low	312	(37)	179	(39)	210	(30)	158	(34)
Medium	337	(40)	209	(45)	411	(59)	279	(60)
High	199	(23)	74	(16)	80	(11)	31	(7)
Family history of large bowel cancer								
No	842	(99)	456	(99)	689	(98)	461	(98)
Yes	9	(1)	6	(1)	12	(2)	8	(2)

[a] The numbers do not always add up to the appropriate total because of missing data.

sumption of total energy or macronutrients, including various carbohydrate, protein, and fat components, among men and women in this study (Table 4). A few significant associations were observed, although not consistently, in both men and women, including the reduction in risk with increasing consumption of total energy among women and of total protein among men, and an elevated risk with an increasing intake of animal fat among women. In addition, no association was observed with the fraction of calories from fat, protein, or carbohydrate (data not shown).

The risk of colon cancer declined with the greater consumption of fiber and micronutrients that were common in plant foods, including vitamin C, carotene, and vitamin E (Table 4). At the highest quartiles of consumption, risks were reduced by 50–60% among men and by 30–40% among women. The only exception was a lack of association with vitamin E among women. The risk among men and women increased with an increasing intake of vitamin A, but this association was no longer significant after an adjustment for meat consumption (animal sources of preformed vitamin A), which suggests that other components in meat, rather than vitamin A itself, may be important risk determinants. Except for fiber from rice, which was universally consumed in Shanghai, inverse associations were generally observed for various fibers from other foods. Whereas risk reduction associated with fibers from fruit and vegetables was strong and consistent among both men and women, the inverse associations with fiber from wheat was confined to women, and the inverse associations with fiber from beans/peas was confined to men (data not shown).

Table 2 ORs of colon cancer and 95% CIs according to the level of intake of selected food groups and food items (servings per month) by sex, Shanghai, China, 1990–1993

Food group/item	Quartile (Q), OR (95% CI)[a]				*P* trend
	Q1 (low)	Q2	Q3	Q4 (high)	
Fresh red meats					
Male (M)	1.0 (referent)	1.2 (0.8–1.6)	1.3 (0.9–1.8)	1.5 (1.0–2.1)	0.03
Female (F)	1.0 (referent)	1.3 (0.9–1.8)	1.0 (0.7–1.4)	1.5 (1.0–2.2)	0.08
Poultry					
M	1.0 (referent)	1.3 (0.9–1.9)	1.3 (0.9–1.9)	1.5 (1.1–2.2)	0.03
F	1.0 (referent)	1.0 (0.7–1.4)	1.0 (0.7–1.4)	0.8 (0.5–1.1)	0.2
Fish					
M	1.0 (referent)	1.4 (1.0–2.0)	1.9 (1.3–2.7)	1.7 (1.2–2.4)	<0.01
F	1.0 (referent)	1.0 (0.7–1.4)	1.4 (1.0–2.0)	1.2 (0.8–1.7)	0.2
Eggs					
M	1.0 (referent)	1.1 (0.8–1.6)	1.4 (1.0–2.0)	1.4 (1.0–1.9)	0.03
F	1.0 (referent)	1.2 (0.8–1.7)	1.3 (0.9–1.9)	1.3 (0.9–1.9)	0.1
Dairy					
M	1.0 (referent)	1.2 (0.8–1.6)	1.0 (0.7–1.3)	0.9 (0.7–1.3)	0.5
F	1.0 (referent)	0.9 (0.6–1.3)	1.2 (0.8–1.6)	1.0 (0.7–1.4)	0.9
All fruits					
M	1.0 (referent)	1.0 (0.7–1.3)	0.9 (0.7–1.3)	0.7 (0.5–1.0)	0.06
F	1.0 (referent)	0.8 (0.6–1.1)	0.8 (0.6–1.2)	0.6 (0.4–0.9)	0.02
All vegetables					
M	1.0 (referent)	1.0 (0.7–1.3)	0.7 (0.5–1.0)	0.8 (0.5–1.1)	0.04
F	1.0 (referent)	1.4 (1.0–2.0)	1.1 (0.8–1.6)	1.0 (0.7–1.5)	0.5
Dark green leafy vegetables					
M	1.0 (referent)	0.9 (0.6–1.2)	0.8 (0.6–1.2)	0.7 (0.5–1.0)	0.07
F	1.0 (referent)	1.0 (0.7–1.5)	1.1 (0.8–1.5)	0.9 (0.6–1.2)	0.5
Carotene-rich vegetables					
M	1.0 (referent)	1.2 (0.9–1.6)	0.8 (0.6–1.1)	0.8 (0.6–1.1)	0.06
F	1.0 (referent)	1.1 (0.7–1.5)	0.9 (0.6–1.3)	0.8 (0.6–1.2)	0.2
Vitamin C-rich vegetables					
M	1.0 (referent)	0.9 (0.7–1.3)	0.9 (0.7–1.3)	0.7 (0.5–1.0)	0.08
F	1.0 (referent)	0.8 (0.6–1.2)	1.1 (0.8–1.5)	1.0 (0.7–1.4)	0.7
Cruciferous vegetables					
M	1.0 (referent)	0.8 (0.6–1.2)	0.8 (0.6–1.2)	0.7 (0.5–1.0)	0.07
F	1.0 (referent)	1.2 (0.8–1.7)	1.5 (1.0–2.1)	1.2 (0.8–1.7)	0.3
Allium vegetables					
M	1.0 (referent)	0.8 (0.6–1.2)	0.9 (0.7–1.3)	0.8 (0.6–1.1)	0.3
F	1.0 (referent)	1.4 (1.0–2.0)	1.4 (1.0–2.0)	1.1 (0.7–1.5)	0.8
Soy foods					
M	1.0 (referent)	1.1 (0.8–1.5)	1.1 (0.8–1.5)	0.9 (0.6–1.3)	0.6
F	1.0 (referent)	1.0 (0.7–1.4)	1.0 (0.7–1.4)	0.8 (0.6–1.2)	0.2

[a] Adjusted for age (30–49, 50–59, 60–64, 65–69, 70–74), total energy (quartile), education (three levels), body mass index (quartile), income (three levels), and occupational physical activity (three levels).

Discussion

In this population-based case-control study in Shanghai, China, the risk of colon cancer was elevated among those with a high intake of fresh animal foods, including red meats, poultry, fish, and eggs, but was reduced with a high intake of fresh fruit. Risk also increased significantly with increasing consumption of preserved plant and animal foods. For dietary nutrients, colon cancer risk was inversely associated with the intake of micronutrients that were common in plant foods, including vitamin C, carotene, and vitamin E. We found no suggestion that the consumption of total fat, unsaturated fat, saturated fat, or carbohydrates was associated with excess risk in either men or women.

The high intake of animal foods, low physical activity level, and obesity have been linked to colon cancer risks in Western populations (12) and in China (20, 24, 25). In Shanghai, a recent study (26) correlated increases in fat, poultry, and pork consumption with the rising incidence of colorectal cancer. In China, whereas the intake of meat increased more than 340% between 1960 and 1990 (27), physical activity levels have declined in urban populations (28) and have been accompanied by substantial increases in the prevalence of obesity (29). These patterns suggest that the adoption of an increasingly westernized lifestyle and dietary practices among Shanghai residents may play an important role in the upward colon cancer trends.

Of particular interest is the finding of a 2–3-fold increase in colon cancer risk with the consumption of preserved foods. A high consumption of smoked or salted fish (30, 31), salt-preserved vegetables (32), cured meat (31), and processed meats (9, 10, 33) have been linked in some studies to an increased risk of colorectal cancer. The mechanism is unclear, but preserved foods contain *N*-nitrosodimethylamine and other volatile N-nitroso compounds (34) that show mutagenicity (35, 36) and carcinogenicity in laboratory animals (37, 38). Although there is no clear evidence that nitrosamines are involved in the development of colon cancer in humans, the role of the endogenous formation of the N-nitroso compounds or the metabolic activity of intestinal bacteria in colon cancer remains to be determined. In our

Table 3 ORs of colon cancer and 95% CIs according to the level of intake of preserved foods (servings per month) by sex, Shanghai, China, 1990–1993

Dietary factors	Quartile (Q), OR (95% CI)[a]				*P* trend
	Q1 (low)	Q2	Q3	Q4 (high)	
Preserved foods					
Male (M)	1.0 (referent)	1.2 (0.8–1.7)	1.4 (1.0–2.0)	2.0 (1.5–2.9)	<0.01
Female (F)	1.0 (referent)	1.2 (0.8–1.7)	1.4 (1.0–2.0)	2.7 (1.9–3.8)	<0.01
Preserved vegetables					
M	1.0 (referent)	1.2 (0.9–1.8)	1.6 (1.2–2.3)	2.0 (1.4–2.9)	<0.01
F	1.0 (referent)	1.2 (0.8–1.8)	1.4 (1.0–2.1)	2.6 (1.8–3.7)	<0.01
Preserved animal foods					
M	1.0 (referent)	1.1 (0.8–1.5)	1.3 (0.9–1.8)	1.4 (1.0–2.0)	0.02
F	1.0 (referent)	1.1 (0.7–1.5)	1.6 (1.1–2.2)	1.6 (1.1–2.3)	<0.01
Salted fish					
M	1.0 (referent)	1.5 (1.1–1.9)	1.6 (1.2–2.2)		<0.01
F	1.0 (referent)	1.3 (1.0–1.8)	1.4 (1.1–1.9)		<0.01

[a] Adjusted for age (30–49, 50–59, 60–64, 65–69, 70–74), total energy (quartile), education (three levels), body mass index (quartile), income (three levels), and occupational physical activity (three levels).

Table 4 ORs of colon cancer and 95% CIs according to the level of intake of selected nutrients per day by sex, Shanghai, China, 1990–1993

Food group/item	Quartile (Q), OR (95% CI)[a]				*P* trend
	Q1 (low)	Q2	Q3	Q4 (high)	
Total energy intake, kcal/day					
Male (M)	1.0 (referent)	1.0 (0.7–1.4)	1.0 (0.7–1.4)	1.0 (0.7–1.4)	0.9
Female (F)	1.0 (referent)	0.9 (0.6–1.2)	0.9 (0.6–1.2)	0.7 (0.5–1.0)	0.04
Total protein, g/day					
M	1.0 (referent)	0.8 (0.6–1.2)	0.6 (0.4–0.9)	0.5 (0.3–0.8)	0.01
F	1.0 (referent)	1.0 (0.7–1.5)	0.9 (0.6–1.5)	1.2 (0.7–2.2)	0.7
Animal protein, g/day					
M	1.0 (referent)	1.0 (0.7–1.4)	1.0 (0.7–1.5)	1.3 (0.9–1.9)	0.1
F	1.0 (referent)	1.2 (0.8–1.7)	1.3 (0.9–1.9)	1.2 (0.8–1.8)	0.4
Total fat, g/day					
M	1.0 (referent)	1.0 (0.7–1.4)	0.8 (0.6–1.2)	1.1 (0.8–1.7)	0.7
F	1.0 (referent)	1.2 (0.9–1.8)	1.3 (0.9–1.9)	1.2 (0.8–1.8)	0.4
Animal fat, g/day					
M	1.0 (referent)	1.0 (0.7–1.5)	1.0 (0.7–1.5)	1.2 (0.8–1.7)	0.4
F	1.0 (referent)	1.1 (0.8–1.6)	1.3 (0.9–1.8)	1.4 (1.0–2.1)	0.08
Unsaturated fat, g/day					
M	1.0 (referent)	0.9 (0.7–1.3)	0.8 (0.5–1.1)	1.2 (0.8–1.7)	0.6
F	1.0 (referent)	1.3 (0.9–1.9)	1.3 (0.9–1.9)	1.3 (0.8–1.9)	0.4
Saturated fat, g/day					
M	1.0 (referent)	1.2 (0.8–1.6)	0.8 (0.6–1.2)	1.2 (0.8–1.8)	0.7
F	1.0 (referent)	0.9 (0.6–1.3)	1.0 (0.7–1.5)	1.1 (0.7–1.7)	0.5
Carbohydrate, g/day					
M	1.0 (referent)	1.1 (0.8–1.6)	1.2 (0.7–1.9)	0.8 (0.4–1.3)	0.4
F	1.0 (referent)	0.7 (0.5–1.1)	0.6 (0.3–1.0)	0.9 (0.4–1.7)	0.5
Fiber, g/day					
M	1.0 (referent)	0.7 (0.5–1.0)	0.6 (0.4–0.9)	0.5 (0.3–0.7)	<0.01
F	1.0 (referent)	0.8 (0.6–1.1)	0.8 (0.5–1.2)	0.6 (0.4–1.0)	0.04
Vitamin C, mg/day					
M	1.0 (referent)	0.7 (0.5–0.9)	0.6 (0.4–0.8)	0.4 (0.3–0.6)	<0.01
F	1.0 (referent)	1.0 (0.7–1.5)	0.9 (0.6–1.3)	0.7 (0.5–1.1)	0.1
Carotene, mg/day					
M	1.0 (referent)	0.8 (0.6–1.2)	0.6 (0.5–0.9)	0.5 (0.3–0.7)	<0.01
F	1.0 (referent)	0.7 (0.5–0.9)	0.8 (0.5–1.1)	0.6 (0.4–0.9)	0.02
Vitamin E, TE[b]/day					
M	1.0 (referent)	0.7 (0.5–1.0)	0.6 (0.4–0.9)	0.5 (0.4–0.8)	<0.01
F	1.0 (referent)	1.6 (1.1–2.2)	1.3 (0.9–1.9)	1.0 (0.7–1.6)	0.8
Vitamin A, RE/day					
M	1.0 (referent)	0.9 (0.6–1.3)	1.2 (0.8–1.7)	1.4 (1.0–1.9)	0.04
F	1.0 (referent)	1.3 (0.9–1.9)	1.4 (1.0–2.0)	1.4 (1.0–2.1)	0.06

[a] Adjusted for age (30–49, 50–59, 60–64, 65–69, 70–74), total energy (quartile), education (three levels), body mass index (quartile), income (three levels), and occupational physical activity (three levels).
[b] TE, milligram of α-tocopherol (1 TE = 1.5 IU); RE, retinol equivalent.

study, the positive association was somewhat stronger for preserved vegetables than for preserved animal products. Unlike preserved vegetables, preserved animal foods are relatively expensive specialty items in China, and past consumption levels were probably lower than levels for preserved vegetables. Because consumption of preserved foods likely has declined after the popularization of refrigerators in China since the 1980s, its impact on the rising colon cancer trends appears small.

Consistent with several (24, 39–43) but not all (44, 45) studies in Chinese and Western populations, we found a reduced risk of colon cancer associated with a high intake of fruit, but only a weak association with the intake of vegetables that was limited to men only. The mechanisms for the protective effect of fruit and vegetables are not clear; but antioxidants (*e.g.,* carotene, vitamin C, and vitamin E), fiber, and other constituents (*e.g.,* protease inhibitors, phytoestrogens) have been shown to possess cancer-inhibiting effects in experimental studies (46). Antioxidants may decrease risk by quenching free radicals and reducing oxidative damage to DNA (47), whereas vitamins C and E may block the endogenous formation of N-nitroso compounds (48). The inverse associations that we observed with carotene, vitamin C, and vitamin E are consistent with the antioxidant hypothesis.

Colon cancer risk was reduced with the increasing consumption of fiber in our study, mainly through the intake of fruit and vegetables. Dietary fiber may lower colon cancer risk by affecting the metabolic activity of colonic microflora and secondary bile acids (49, 50). However, our findings of much stronger and more consistent inverse associations with fibers from fruit and vegetables than with fibers from other plant foods suggest that other constituents with anticarcinogenic properties in fruit and vegetables, and not just fiber *per se*, have contributed to the reduction in colon cancer risk.

We found no evidence of any substantial effect of total energy, fat, or protein intake on risk of colon cancer in the present study. These results are consistent with findings from some previous studies (9, 39, 51, 52), but not all (24, 53). However, the estimated fat intakes in our study subjects are low when compared with those in Western studies (10, 24, 54) that have related high-fat intake to colon cancer. In the United States, over 40% of calories is derived from dietary fat (55), *versus* an average of 22% of calories from fat among our study subjects. In addition, the risk of colorectal cancer and adenomas has been related to the intake of heterocyclic amines and polycyclic aromatic hydrocarbons (56, 57), generated by cooking meat at high temperatures, but we found no association with frequent consumption of deep-fried/grilled foods or degree of doneness, a crude surrogate measure of these pyrolysis carcinogens. It is noteworthy, however, that the number of our study subjects who often consumed deep-fried or grilled foods was relatively small.

Consideration must be given to the potential limitations in the present study that may have influenced the observed associations. First, because we analyzed the associations between colon cancer and approximately 90 food items, some of the significant findings may be attributable to chance alone. However, the consistent findings between men and women for preserved vegetables, preserved animal foods, fruit, and antioxidant vitamins argue against multiple comparison as an explanation for these associations. Second, we were not able to integrate vitamin supplement use into our estimates of nutrient intake, but supplements were rarely used in this study population. Third, some random misclassification of diet is likely, but nondifferential misclassification generally tends to bias the risk estimates toward the null. Fourth, gastrointestinal and other symptoms in the period before the diagnosis of colon cancer may alter the dietary pattern of a patient, which may influence recall and the reporting of usual diet 5 years before diagnosis. We were unable to address these issues because of the retrospective design, but such recall bias has not been shown to be a source of error in previous epidemiological studies of diet and cancer (58, 59). Finally, we did not collect information on the use of nonsteroidal anti-inflammatory drugs (NSAIDs), a protective factor for colon cancer (60). The use of aspirin for the prevention of cardiovascular disease, a common practice in the United States, was not common in China. In addition, the effect of further adjustment for any additional variable in our final model tended to be small or none.

In summary, our large population-based case-control study of colon cancer in Shanghai provides further evidence that diets high in fresh fruit and antioxidant vitamins commonly found in plant foods reduce the risk of colon cancer, whereas diets high in animal foods such as red meat increase the risk. Excess risks were also linked to frequent consumption of preserved animal and plant foods in both sexes. The increasing food availability and westernization of the diet in urban China should provide further opportunities to investigate the dietary and nutritional determinants underlying the upward trends in colon cancer.

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Appendices

Appendix A

Table A1 Composition of food groups

Food group or item	Composition
Preserved vegetables	Salted, moldy, dried vegetables; salted vegetables, hot pickled mustard stem, fermented bean curd
Preserved animal foods	Sausages, salted egg, preserved limed duck eggs, salted pork, salted fish
Fresh red meats	Pork chops, pork spareribs, pork feet, fresh pork (fat), fresh pork (lean), fresh pork (fat and lean), pork liver, other organ meats, beef and mutton
Poultry	Chicken, duck
Fish	Salt water fish (*e.g.*, hairtail, yellow croaker), fresh water fish (*e.g.*, silver carp, golden carp), eel
Eggs	Fresh poultry eggs, salted eggs, limed duck eggs
All vegetables	Shanghai bok choy, spinach, cabbage, Chinese cabbage, cauliflower, celery, bean sprouts, eggplant, wild rice stem, pea pods, green peas, green bean, green broad beans, celtuce, potato, white gourd, cucumber, carrot, dried mushrooms, fresh mushrooms, red and green pepper, tomato, bamboo shoot, lotus root, luffa or sponge gourd, garlic, onion, Chinese chives, spring onion, corn, garlic stalks, ginger, kelp and seaweeds
Dark green leafy vegetables	Spinach, Chinese chives, spring onion
Cruciferous vegetables	Shanghai bok choy, cabbage, Chinese cabbage, cauliflower
Soy foods	Bean curd, soybean milk, textured soybean products
All fruits	Apples, pears, oranges/tangerines, bananas, grapes

Appendix B

Table B1 Cutpoints for quartiles (Q1, Q2, Q3, Q4) of frequency of consumption of food groups and food items per month by sex

Food group/item	Quartile (times per week)			
	Q1 (low)	Q2	Q3	Q4 (high)
Fresh red meats				
Male (M)	≤13.7	13.8–22.5	22.6–37.7	≥37.8
Female (F)	≤10.7	10.7–19.8	19.9–33.1	≥33.1
Poultry				
M	≤0.5	0.6–1.3	1.4–2.8	≥2.9
F	≤0.5	0.6–1.1	1.2–2.0	≥2.1
Fish				
M	≤2.6	2.7–5.0	5.1–9.3	≥9.4
F	≤2.9	3.0–5.4	5.5–10.9	≥11.0
Eggs				
M	≤7.4	7.5–13.9	14.0–22.3	≥22.4
F	≤6.5	6.6–13.8	13.9–22.4	≥22.5
Dairy				
M	≤0.1	0.2–0.7	0.8–12.5	≥12.6
F	≤0.1	0.2–0.4	0.5–10.6	≥10.7
All fruits				
M	≤1.7	1.8–5.7	5.8–14.6	≥14.7
F	≤2.1	2.2–7.1	7.2–16.4	≥16.5
All vegetables				
M	≤68.6	68.7–92.0	92.1–122.1	≥122.2
F	≤66.7	66.8–91.9	92.0–118.5	≥118.6
Dark green leafy vegetables				
M	≤2.3	2.4–4.6	4.7–10.4	≥10.5
F	≤2.3	2.4–4.1	4.2–10.1	≥10.2
Carotene-rich vegetables				
M	≤2.5	2.6–5.4	5.5–11.2	≥11.3
F	≤2.2	2.3–4.7	4.8–11.1	≥11.2
Vitamin C-rich vegetables				
M	≤3.8	3.9–6.8	6.9–9.9	≥10.0
F	≤3.7	3.8–6.5	6.6–10.1	≥10.2
Cruciferous vegetables				
M	≤15.0	15.1–22.3	22.4–25.3	≥25.4
F	≤15.7	15.8–22.4	22.5–25.7	≥25.8
Allium vegetables				
M	≤1.5	1.6–4.4	4.5–14.6	≥14.7
F	≤0.5	0.6–2.4	2.5–10.2	≥10.3
Soy foods				
M	≤8.0	8.1–13.1	13.2–25.7	≥25.8
F	≤7.0	7.1–12.9	13.0–22.4	≥22.5

Appendix C

Table C1 Cutpoints for quartiles (Q1, Q2, Q3, Q4) of frequency of consumption of preserved foods per month by sex

Dietary factors	Quartile (times per week)			
	Q1 (low)	Q2	Q3	Q4 (high)
Preserved foods				
Male (M)	≤5.7	5.8–11.0	11.1–22.3	≥22.4
Female (F)	≤5.4	5.5–11.1	11.2–21.5	≥21.6
Preserved vegetables				
M	≤2.3	2.4–6.3	6.4–13.9	≥14.0
F	≤2.8	2.9–6.4	6.5–13.1	≥13.2
Preserved animal foods				
M	≤1.6	1.7–2.8	2.9–7.2	≥7.3
F	≤1.3	1.4–2.8	2.9–7.2	≥7.3
Salted fish				
M	0	0.1–0.3	≥0.4	
F	0	0.1–0.3	≥0.4	

Appendix D

Table D1 Cutpoints for quartiles (Q1, Q2, Q3, Q4) of nutrient intake per day by sex

Nutrient (unit)	Quartile			
	Q1 (low)	Q2	Q3	Q4 (high)
Total energy, kcal				
Male (M)	≤2157.7	2157.8–2540.3	2540.4–2931.4	≥2931.5
Female (F)	≤1777.4	1777.5–2097.2	2097.3–2442.1	≥2442.2
Total protein, g				
M	≤60.9	61.0–73.7	73.8–92.4	≥92.5
F	≤49.5	49.6–60.9	61.0–74.3	≥74.4
Animal protein, g				
M	≤10.7	10.8–17.3	17.4–25.3	≥25.4
F	≤7.7	7.8–14.4	14.5–22.0	≥22.1
Total fat, g				
M	≤45.6	45.7–58.0	58.1–73.4	≥73.5
F	≤38.4	38.5–48.4	48.5–61.0	≥61.1
Animal fat, g				
M	≤10.3	10.4–17.1	17.2–28.2	≥28.3
F	≤7.1	7.2–12.3	12.4–18.7	≥18.8
Unsaturated fat, g				
M	≤33.4	33.5–41.8	41.9–52.0	≥52.1
F	≤28.7	28.8–36.1	36.2–44.2	≥44.3
Saturated fat, g				
M	≤11.2	11.3–15.4	15.5–20.4	≥20.5
F	≤9.1	9.2–12.1	12.2–16.0	≥16.1
Carbohydrate, g				
M	≤358.4	358.5–412.4	412.5–498.0	≥498.1
F	≤284.1	284.2–354.3	354.4–404.0	≥404.1
Fiber, g				
M	≤7.0	7.1–9.0	9.1–12.3	≥12.4
F	≤6.0	6.1–7.7	7.8–10.4	≥10.5
Vitamin C, mg				
M	≤29.8	29.9–41.6	41.7–56.9	≥57.0
F	≤28.9	29.0–41.2	41.3–54.3	≥54.4
Carotene, mg				
M	≤447.3	447.4–676.3	676.4–1040.2	≥1040.3
F	≤465.9	466.0–638.1	638.2–1039.2	≥1039.3
Vitamin E, TE[a]				
M	≤26.1	26.2–31.8	31.9–40.8	≥40.9
F	≤24.1	24.2–29.1	29.2–37.1	≥37.2
Vitamin A, RE				
M	≤176.0	176.1–269.1	269.2–402.8	≥402.9
F	≤163.7	163.8–242.0	242.0–366.5	≥366.6

[a] TE, milligram of α-tocopherol (1 TE = 1.5 IU); RE, retinal equivalent.

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