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# Animal Origin Foods and Colorectal Cancer Risk: A Report From the Shanghai Women's Health Study

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# Animal Origin Foods and Colorectal Cancer Risk: A Report From the Shanghai Women's Health Study

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**The association of animal-origin food consumption and cooking patterns with colorectal cancer (CRC) risk was evaluated in a cohort of 73,224 participants of the Shanghai Women's Health Study. After a mean follow-up time of 7.4 yr, 394 incident cases of CRC (colon = 236; rectal = 158) were diagnosed. Overall, no association was found between the risk of CRC and intake of total meat and total fish. Eel ($P_{\text{trend}} = 0.01$), shrimp ($P_{\text{trend}} = 0.06$), and shellfish ($P_{\text{trend}} = 0.04$) consumption were positively associated with CRC risk. High egg intake and high intake of total cholesterol were also related to risk of CRC (RR for the highest vs. lowest quintiles of intake were 1.4 (95% CI = 1.1–2.0) for eggs and 1.6 (95% CI = 1.1–2.3) for cholesterol). Milk intake was inversely associated with the risk of colon cancer ($P_{\text{trend}} = 0.05$). Common Chinese cooking practices except the smoking method of cooking were not related to CRC risk. The latter was positively associated with colon cancer (RR = 1.4 for ever vs. never, 95% CI = 1.1–1.9). A possible role of cholesterol and environmental pollution in the etiology of CRC was suggested.**

## INTRODUCTION

Colorectal cancer is one of the most common cancers in industrialized countries. Although the highest incidence rates have been observed in North America, Western Europe, Australia, and New Zealand (1,2), incidence and mortality rates have been rising rapidly in some low-incidence countries including China (3) and Japan (4). According to incidence data from the population-based cancer registry in Shanghai, China, age-adjusted colorectal cancer incidence rates increased more than 50%, from 14 to 22 per 100,000 among men and from 12 to 19 per 100,000 among women, between 1972 and 1994 (3).

In a landmark report published in 2007, the American Institute for Cancer Research classified red meat as a probable risk factor and processed meat and highly cooked meat as "possible" risk factors for colorectal cancer (5). Epidemiological reports on meat consumption and colorectal cancer risk, however, have not been consistent. A meta-analysis that examined 34 case-control and 14 cohort studies published between 1973 and 1999 (6) suggested that high consumption of red meat and processed meat is associated with increased risk of colorectal cancer, although total meat consumption was unrelated to risk. Since the meta-analysis report, 13 cohort (7–19) and 9 case-control studies (20–28) have evaluated the association. Only 5 cohort (7–11) and 5 case-control studies (20–24) showed a positive association with consumption of one or more types of red meat. Another meta-analysis (29), which included only prospective studies published from 1966 through 2006, also suggested that red/processed meat consumption is associated with an increased risk of colorectal cancer. The association between fish intake and colorectal cancer is not consistent. Fish intake was not associated with colorectal cancer in the most recently published prospective studies (9,10,14,30), whereas reports from the European Prospective Investigation into Cancer and Nutrition (EPIC) (7) and the Cancer Prevention Study II (CPS II) (8) have indicated an inverse association. To date, although many cohort studies have evaluated the effect of animal-origin food intake on colorectal cancer, most have been conducted in the United States or Europe. The most recent cohort studies conducted in

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Japan did not find any association between red/processed meat or fish intake and colorectal cancer (12,13,30).

Consumption patterns of animal-origin foods in Asia, including amount, frequency, and cooking methods, differ substantially from that in Western countries. In Asian countries, including China, the frequency and absolute amount of meat consumed as well as the use of high-temperature cooking methods (related to heterocyclic amine levels in cooked meat) is much lower than in Western countries. In this report, we describe the association of animal-origin food consumption and cooking methods with colorectal cancer using data from a population-based cohort study, the Shanghai Women's Health Study (SWHS).

## MATERIALS AND METHODS

### Subjects

The SWHS, initiated in March 1997, is a population-based prospective cohort study of approximately 75,000 women who were 40 to 70 yr of age at recruitment and lived in 7 urban communities of Shanghai, China. The study was approved by the relevant institutional review boards for human research, and the detailed methodology has been published elsewhere (31). Briefly, between 1997 and 2000, 74,942 women of age 40 to 70 yr were recruited from 81,170 eligible women with a participation rate of 92.7%. All subjects were interviewed in person by trained interviewers using a structured questionnaire, and written, informed consent was obtained prior to interview. The questionnaire included questions on sociodemographic factors, diet and lifestyle habits, menstrual and reproductive history, hormone use, and medical history. Anthropometric measurements, including current weight, height, and circumferences of the waist and hips, were also taken.

### Dietary Assessment

A validated, quantitative food-frequency questionnaire (FFQ) was used to assess usual dietary intake at the baseline survey and again at the first follow-up survey conducted 2 to 3 yr after the baseline survey (31,32). During the in-person interviews, each participant was first asked how often, on average, during the past 12 mo she had consumed a specific food or food group (the possible responses were daily, weekly, monthly, yearly, or never) followed by a question on the amount consumed in grams per unit of time. The participant was also asked about the cooking methods she used (deep frying, stir frying, or roasting) to prepare meats and fish and how frequently she used each cooking method to prepare these foods. Information on consumption of preserved foods, including smoked meat/bacon and salted meat, fish, and eggs, was also collected. The FFQ was validated against the averages of multiple 24-h dietary recalls. The correlation coefficients between the intake derived from the FFQ and the average intake derived from multiple 24-h recalls were 0.52, 0.48, 0.50, and 0.58 for red meat, poultry, fish, and eggs, respectively. The correlation coefficient between the 2 FFQs administered 2 yr apart were 0.48 to 0.51 for macronutrients and 0.47, 0.49, 0.49, and 0.57 for red meat, poultry, fish, and eggs, respectively (32). The FFQ included 19 food items/groups of animal origin. Total fat, including saturated, monounsaturated, and polyunsaturated fatty acids, and total cholesterol intake was calculated as the sum of contributions from all foods based on the Chinese Food Composition Tables (33).

### Ascertainment of Colorectal Cancer Cases

The cohort is followed by a combination of active surveys conducted every 2 yr and periodic linkage of the study population to cancer case data collected by the population-based Shanghai Cancer Registry and death certificates collected by the Shanghai Municipal Center for Disease Control and Prevention. Every 2 yr, all cohort members are interviewed to record details of their interim health history including cancer, cardiovascular disease, stroke, and other chronic diseases. The response rates for first (2000–2002), second (2002–2004), and third (2004–2007) in-person follow-up surveys were 99.8%, 98.7%, and 96.7%, respectively. Annual record linkage of cohort members with the cancer registry and death certificate registry is conducted to assure a timely and complete ascertainment of new cancer cases and deceased subjects in the study cohort. All possible matches are checked manually and verified through home visits. Copies of medical charts from the diagnostic hospital are obtained to verify the diagnosis and collect detailed information on the pathology characteristics of the tumor. Diagnosis was based on pathological evidence for 93.7% of colorectal cancer cases in this study.

### Statistical Analysis

For this study, we excluded women with a history of cancer ($n = 1{,}576$) at baseline, women with extreme total energy intake ($<500$ or $\geq 3{,}500$ kcal/day; $n = 124$), women lacking detailed information on cancer ($n = 10$), and women who were lost to follow-up ($n = 8$) shortly after recruitment, resulting in a total of 73,224 women for the present study. Person years of follow-up were calculated for each participant from the date of the baseline interview to the date of cancer diagnosis, death, or date of last follow-up, whichever came first. The date of last follow-up was defined as December 31, 2005 for study participants whose last in-person contact was before December 31, 2005, 6 mo prior to the most recent record linkage, in order to allow for delay in records processing.

Dietary information collected in the baseline survey was used for the initial analysis. To improve the dietary assessment (34), we also used the cumulative average diet reported on the baseline and first follow-up FFQs in the analysis for women who did not report any cancer, diabetes, myocardial infarction or stroke, or did not report any of these conditions until the first follow-up survey. For women who reported any of these conditions, including colorectal cancer between the baseline and first follow-up

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TABLE 1
Age-adjusted relative risk (95% confidence intervals) for colorectal cancer and trend of selected participant characteristics

| Characteristic | Person Years | Colorectal Cancer ($n = 394$) | | | Colon ($n = 236$) | | | Rectal ($n = 158$) | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | N | RR (95% CI) | $P_{Trend}$ | N | RR (95% CI) | $P_{Trend}$ | N | RR (95% CI) | $P_{Trend}$ |
| Age | | | | | | | | | | |
| <45 | 153,780 | 37 | Reference | | 14 | Reference | | 23 | Reference | |
| 45–54 | 189,113 | 67 | 1.3 (0.7–2.5) | | 38 | 1.4 (0.5–3.7) | | 29 | 1.3 (0.6–2.9) | |
| 55–64 | 124,403 | 156 | 2.4 (1.0–6.2) | | 101 | 2.2 (0.6–8.3) | | 55 | 2.9 (0.7–11.3) | |
| ≥65 | 72,860 | 134 | 3.8 (1.4–10.4) | 0.002 | 83 | 3.3 (0.8–13.5) | 0.026 | 51 | 4.8 (1.1–21.7) | 0.035 |
| Education | | | | | | | | | | |
| <Elementary | 112,838 | 164 | Reference | | 102 | Reference | | 62 | Reference | |
| Middle | 200,499 | 108 | 1.1 (0.8–1.5) | | 63 | 1.2 (0.8–1.7) | | 45 | 1.0 (0.6–1.5) | |
| High | 151,690 | 81 | 1.0 (0.7–1.4) | | 47 | 1.1 (0.7–1.6) | | 34 | 0.9 (0.6–1.5) | |
| College+ | 75,035 | 41 | 0.8 (0.6–1.2) | 0.24 | 24 | 0.8 (0.5–1.3) | 0.45 | 17 | 0.8 (0.4–1.4) | 0.35 |
| Income | | | | | | | | | | |
| Low | 147,022 | 151 | Reference | | 97 | Reference | | 54 | Reference | |
| Middle | 209,024 | 151 | 0.9 (0.7–1.2) | | 82 | 0.8 (0.6–1.1) | | 69 | 1.1 (0.8–1.6) | |
| High | 183,981 | 92 | 0.8 (0.6–1.1) | 0.16 | 57 | 0.9 (0.6–1.2) | 0.26 | 35 | 0.8 (0.5–1.3) | 0.41 |
| Married | | | | | | | | | | |
| Married | 481,070 | 316 | Reference | | 191 | Reference | | 125 | Reference | |
| Single | 59,085 | 78 | 1.3 (1.0–1.7) | 0.04 | 45 | 1.2 (0.9–1.7) | 0.30 | 33 | 1.5 (1.0–2.2) | 0.05 |
| Regular exercise | | | | | | | | | | |
| Never | 352,065 | 216 | Reference | | 123 | Reference | | 93 | Reference | |
| <5.5 (MET/h/wk) | 68,738 | 40 | 0.7 (0.5–1.0) | | 26 | 0.8 (0.5–1.2) | | 14 | 0.7 (0.4–1.1) | |
| 5.5–13.6 | 61,006 | 63 | 1.0 (0.8–1.4) | | 39 | 1.1 (0.7–1.5) | | 24 | 1.0 (0.6–1.6) | |
| ≥13.6 | 58,345 | 75 | 1.1 (0.9–1.5) | 0.42 | 48 | 1.2 (0.8–1.7) | 0.38 | 27 | 1.1 (0.7–1.7) | 0.86 |
| Body mass index (kg/m$^2$) | | | | | | | | | | |
| Quartile 1 (<21.6) | 135,169 | 72 | Reference | | 44 | Reference | | 28 | Reference | |
| Quartile 2 (21.6–23.6) | 136,712 | 86 | 1.1 (0.8–1.5) | | 47 | 0.9 (0.6–1.4) | | 39 | 1.3 (0.8–2.1) | |
| Quartile 3 (23.7–26.0) | 134,598 | 118 | 1.3 (1.0–1.7) | | 79 | 1.4 (0.9–2.0) | | 39 | 1.2 (0.7–1.9) | |
| Quartile 4 (≥26.1) | 133,675 | 118 | 1.1 (0.8–1.5) | 0.50 | 66 | 0.9 (0.6–1.3) | 0.98 | 52 | 1.4 (0.9–2.2) | 0.27 |
| Waist-to-hip ratio | | | | | | | | | | |
| Quartile 1 (<0.774) | 135,855 | 66 | Reference | | 37 | Reference | | 29 | Reference | |
| Quartile 2 (0.774–0.806) | 134,719 | 87 | 1.2 (0.8–1.6) | | 54 | 1.2 (0.8–1.9) | | 33 | 1.0 (0.6–1.7) | |
| Quartile 3 (0.807–0.843) | 135,321 | 102 | 1.1 (0.8–1.6) | | 66 | 1.2 (0.8–1.9) | | 36 | 1.0 (0.6–1.7) | |
| Quartile 4 (≥0.844) | 134,259 | 139 | 1.2 (0.9–1.6) | 0.27 | 79 | 1.1 (0.8–1.7) | 0.78 | 60 | 1.4 (0.9–2.2) | 0.17 |
| Family history of CRC | | | | | | | | | | |
| No | 528,033 | 384 | Reference | | 232 | Reference | 0.68 | 152 | Reference | |
| Yes | 12,122 | 10 | 1.2 (0.7–2.3) | 0.54 | 4 | 0.8 (0.3–2.2) | | 6 | 1.8 (0.8–4.1) | 0.15 |
| Tea consumption | | | | | | | | | | |
| No | 376,816 | 312 | Reference | | 184 | Reference | | 128 | Reference | |
| Yes | 163,339 | 82 | 0.8 (0.6–1.0) | 0.03 | 52 | 0.8 (0.6–1.2) | 0.27 | 30 | 0.7 (0.4–1.0) | 0.03 |
| Total energy intake | | | | | | | | | | |
| Quartile 1 (<1,407) | 133,283 | 111 | Reference | | 63 | Reference | | 48 | Reference | |
| Quartile 2 (<1,610) | 135,389 | 81 | 0.8 (0.6–1.1) | | 53 | 1.0 (0.7–1.4) | | 28 | 0.7 (0.4–1.0) | |
| Quartile 3 (<1,844) | 135,503 | 94 | 1.0 (0.8–1.3) | | 50 | 1.0 (0.7–1.4) | | 44 | 1.1 (0.7–1.6) | |
| Quartile 4 (≥1,844) | 135,980 | 108 | 1.2 (0.9–1.6) | 0.08 | 70 | 1.4 (1.0–2.0) | 0.06 | 38 | 1.0 (0.6–1.5) | 0.69 |

*(Continued on next page)*

TABLE 1
Age-adjusted relative risk (95% confidence intervals) for colorectal cancer and trend of selected participant characteristics *(Continued)*

| Characteristic | Person Years | Colorectal Cancer ($n = 394$) N | RR (95% CI) | $P_{Trend}$ | Colon ($n = 236$) N | RR (95% CI) | $P_{Trend}$ | Rectal ($n = 158$) N | RR (95% CI) | $P_{Trend}$ |
|---|---|---|---|---|---|---|---|---|---|---|
| Vegetable and fruit intake[b] | | | | | | | | | | |
| Quartile 1 (<325) | 133,940 | 114 | Reference | | 68 | Reference | | 46 | Reference | |
| Quartile 2 (<476) | 135,103 | 93 | 1.0 (0.8–1.3) | | 50 | 0.9 (0.6–1.3) | | 43 | 1.1 (0.7–1.7) | |
| Quartile 3 (<663) | 135,817 | 96 | 1.1 (0.9–1.5) | | 61 | 1.2 (0.9–1.0) | | 35 | 1.0 (0.6–1.6) | |
| Quartile 4 (≥663) | 135,295 | 91 | 1.2 (0.9–1.6) | 0.25 | 57 | 1.3 (0.8–1.9) | 0.14 | 34 | 1.0 (0.6–1.7) | 0.99 |

[a]Abbreviations are as follows: RR, relative risk; CI, confidence interval; MET, metabolic equivalent; CRC, colorectal cancer.
[b]Adjusted for age and total energy intake.

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survey, and for women with only one dietary assessment, only information from the baseline FFQ was used.

Study participants were classified into 5 categories according to quintile distributions of whole cohort for all types of animal-origin foods and fat intake, with the exception of shellfish, which was classified into tertiles. Based on the distribution of subjects by each cooking method, we derived 3 categories for frequency of consumption for each method (roasted, deep fried, and stir fried) used to cook meat or fish, 3 categories for salted meat, and 2 categories for smoked meat/bacon and salted fish. The lowest frequency category served as the reference group. Relative risks (RRs) and 95% confidence intervals (CIs) associated with animal-origin food intake and cooking methods were estimated using Cox proportional hazards regression modeling (35). Cancer incidence rates were modeled as a function of age (36). Covariates included in the model were age, education, income, season of recruitment, tea consumption, nonsteroidal anti-inflammatory drug (NSAID) use, total energy intake, and fiber intake. Tests of linear trend were estimated by modeling each animal-origin food and fat/cholesterol intake as continuous variables. All statistical tests were based on two-sided probability. Statistical analyses were carried out using SAS version 9.1 (SAS Institute, Cary, NC).

## RESULTS

Over a mean follow-up of 7.4 yr (540,156 person years) of the cohort women, 394 incident cases of colorectal cancer (colon = 236 and rectal = 158) were identified (Table 1). The mean age at diagnosis of colorectal cancer was 58.9 yr (±8.39 yr). Education, income, body mass index (BMI), waist-to-hip ratio (WHR), regular exercise (MET/h/wk), family history of colorectal cancer, and total intake of fruits and vegetables were not significantly associated with colorectal cancer risk. On the other hand, single women and women who never drank tea had a higher risk of rectal cancer than married women or ever tea drinkers. There was an association of borderline significance between increased risk of colon cancer and the highest quintile of total energy intake compared to the lowest quintile. Very few women in this cohort were regular alcohol drinkers (1.9%), cigarette smokers (2.4%), or hormone replacement therapy users (3.9%) (33); these variables were not adjusted for in multivariate analyses.

Total meat intake was not associated with the risk of colorectal cancer ($P_{\text{trend}} = 0.30$) nor was red meat ($P_{\text{trend}} = 0.53$) or poultry intake ($P_{\text{trend}} = 0.23$; Table 2). Analyses stratified by colon and rectal cancer showed similar results. Neither marine nor fresh-water fish intake was related to the risk of colorectal cancer. Eel ($P_{\text{trend}} = 0.01$), shrimp ($P_{\text{trend}} = 0.06$), and shellfish ($P_{\text{trend}} = 0.04$) intake, on the other hand, were significantly associated with an increased risk of colon cancer. Women in the highest quintile of egg intake had a higher risk of colorectal cancer compared to women in the lowest quintile, but the test for trend was not significant. Milk intake was inversely associated with the risk of colon cancer ($P_{\text{trend}} = 0.05$) but was unrelated to the risk of rectal cancer.

Neither total fat intake nor subtypes of fat intake, including saturated, monounsaturated, and polyunsaturated fatty acids, were associated with the risk of colorectal cancer (Table 3). However, women in the highest quintile of cholesterol intake had an increased risk of colorectal cancer, although the risk estimate was only statistically significant for colon cancer (RR = 1.6 for colorectal cancer, 95% CI = 1.1–2.3; RR = 1.7 for colon cancer, 95% CI = 1.1–2.7; and RR = 1.5 for rectal cancer, 95% CI = 0.8–2.6).

In this population, 72.9% of women reported using the deep-frying method of cooking, 98.7% reported stir frying, 69.4% reported roasting, 37.2% reported smoking, 81.4% reported salting meat, and 38.0% reported salting fish. The only cooking method associated with the risk of colon cancer was smoking (RR = 1.4 for ever vs. never, 95% CI = 1.1–1.9; Table 4). Other cooking methods, including deep frying, stir frying, roasting, and salting, were not related to the risk of colorectal cancer. No significant interaction between cooking methods and meat intake was observed.

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TABLE 2
Relative risk (RR) of colorectal cancer in relation to animal food intake (g/day)[a]

| | Colorectal Cancer | | | | | | Colon Cancer | | | | | | Rectal Cancer | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Food | $Q_1$ | $Q_2$ | $Q_3$ | $Q_4$ | $Q_5$ | $P_{Trend}$ | $Q_1$ | $Q_2$ | $Q_3$ | $Q_4$ | $Q_5$ | $P_{Trend}$ | $Q_1$ | $Q_2$ | $Q_3$ | $Q_4$ | $Q_5$ | $P_{Trend}$ |
| Total meat | | | | | | | | | | | | | | | | | | |
| Intake[b] | <33 | <49 | <65 | <89 | ≥89 | | | | | | | | | | | | | |
| Person years | 106,299 | 107,607 | 108,563 | 108,684 | 109,001 | | | | | | | | | | | | | |
| Cases | 106 | 82 | 61 | 79 | 66 | | 64 | 48 | 34 | 45 | 45 | | 42 | 34 | 27 | 34 | 21 | |
| RR (95% CI) | Ref | 0.9 | 0.8 | 1.1 | 0.9 (0.7–1.4) | 0.30 | Ref | 0.9 | 0.7 | 1.1 | 1.1 (0.7–1.8) | 0.15 | Ref | 1.0 | 0.8 | 1.1 | 0.7 (0.4–1.3) | 0.88 |
| Red meat | | | | | | | | | | | | | | | | | | |
| Intake[b] | <24 | <36 | <49 | <67 | ≥67 | | | | | | | | | | | | | |
| Person years | 106,383 | 107,803 | 108,157 | 108,710 | 109,103 | | | | | | | | | | | | | |
| Cases | 108 | 80 | 65 | 79 | 62 | | 63 | 49 | 40 | 43 | 41 | | 45 | 31 | 25 | 36 | 21 | |
| RR | Ref | 0.9 | 0.7 | 1.0 | 0.8 (0.6–1.1) | 0.53 | Ref | 0.9 | 0.8 | 0.9 | 0.9 (0.6–1.5) | 0.31 | Ref | 0.8 | 0.7 | 1.0 | 0.6 (0.3–1.1) | 0.79 |
| Poultry | | | | | | | | | | | | | | | | | | |
| Intake[b] | <4 | <10 | <14 | <24 | ≥24 | | | | | | | | | | | | | |
| Person years | 106,231 | 107,036 | 109,968 | 108,384 | 108,534 | | | | | | | | | | | | | |
| Cases | 92 | 83 | 75 | 69 | 75 | | 57 | 47 | 42 | 45 | 45 | | 35 | 36 | 33 | 24 | 30 | |
| RR (95% CI) | Ref | 1.0 | 1.0 | 1.0 | 1.2 (0.9–1.7) | 0.23 | Ref | 1.0 | 0.9 | 1.1 | 1.2 (0.8–1.8) | 0.15 | Ref | 1.2 | 1.2 | 0.9 | 1.3 (0.7–2.1) | 0.90 |
| Total fish | | | | | | | | | | | | | | | | | | |
| Intake[b] | <20 | <33 | <49 | <74 | ≥74 | | | | | | | | | | | | | |
| Person years | 106,583 | 108,434 | 108,685 | 108,512 | 107,941 | | | | | | | | | | | | | |
| Cases | 88 | 83 | 71 | 83 | 69 | | 56 | 49 | 36 | 51 | 44 | | 32 | 34 | 35 | 32 | 25 | |
| RR | Ref | 1.2 | 1.2 | 1.5 | 1.3 (0.9–1.9) | 0.21 | Ref | 1.1 | 1.0 | 1.4 | 1.4 (0.9–2.1) | 0.39 | Ref | 1.3 | 1.5 | 1.5 | 1.3 (0.7–2.4) | 0.35 |
| Marine fish | | | | | | | | | | | | | | | | | | |
| Intake[b] | <4 | <10 | <17 | <32 | ≥32 | | | | | | | | | | | | | |
| Person years | 102,517 | 112,342 | 108,957 | 105,674 | 110,665 | | | | | | | | | | | | | |
| Cases | 113 | 64 | 64 | 82 | 71 | | 76 | 34 | 36 | 52 | 38 | | 37 | 30 | 28 | 30 | 32 | |
| RR | Ref | 0.7 | 0.8 | 1.1 | 1.0 (0.7–1.4) | 0.34 | Ref | 0.5 | 0.7 | 1.1 | 0.8 (0.5–1.2) | 0.59 | Ref | 0.9 | 1.0 | 1.2 | 1.4 (0.8–2.3) | 0.39 |
| Fresh water fish | | | | | | | | | | | | | | | | | | |
| Intake[b] | <4 | <10 | <15 | <26 | ≥26 | | | | | | | | | | | | | |
| Person years | 110,314 | 113,998 | 96,933 | 108,847 | 110,063 | | | | | | | | | | | | | |
| Cases | 94 | 85 | 58 | 83 | 74 | | 61 | 52 | 32 | 45 | 46 | | 33 | 33 | 26 | 38 | 28 | |
| RR | Ref | 1.0 | 0.8 | 1.0 | 0.9 (0.6–1.2) | 0.67 | Ref | 0.9 | 0.7 | 0.8 | 0.8 (0.5–1.2) | 0.55 | Ref | 1.0 | 1.0 | 1.4 | 1.0 (0.6–1.7) | 0.95 |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Eel | | | | | | | | | | | | | | | | | | |
| Intake[b] | 0 | <0.3 | <1.4 | <3.5 | ≥3.5 | | | | | | | | | | | | | |
| Person years | 162,308 | 51,351 | 103,906 | 122,316 | 100,274 | | | | | | | | | | | | | |
| Cases | 136 | 39 | 87 | 74 | 58 | | 88 | 23 | 47 | 39 | 39 | | 48 | 16 | 40 | 35 | 19 | |
| RR (95% CI) | Ref | 1.1 | 1.4 | 1.2 | 1.3 (0.9–1.7) | 0.01 | Ref | 1.0 | 1.2 | 1.0 | 1.4 (0.9–2.1) | 0.05 | Ref | 1.3 | 1.7 | 1.5 | 1.1 (0.6–1.9) | 0.03 |
| Shrimp | | | | | | | | | | | | | | | | | | |
| Intake[b] | <2.4 | <4.8 | <8.6 | <14.6 | ≥14.6 | | | | | | | | | | | | | |
| Person years | 115,327 | 86,739 | 119,995 | 117,351 | 100,743 | | | | | | | | | | | | | |
| Cases | 104 | 52 | 99 | 68 | 71 | | 65 | 29 | 53 | 44 | 45 | | 39 | 23 | 46 | 24 | 26 | |
| RR (95% CI) | Ref | 0.9 | 1.3 | 1.0 | 1.3 (1.0–1.9) | 0.06 | Ref | 0.8 | 1.1 | 1.1 | 1.4 (0.9–2.1) | 0.04 | Ref | 1.0 | 1.6 | 0.9 | 1.3 (0.7–2.2) | 0.64 |
| Shellfish | | | | | | | | | | | | | | | | | | |
| Intake[b] | 0 | <0.6 | ≥0.6 | | | | | | | | | | | | | | | |
| Person years | 201,839 | 127,854 | 201,461 | | | | | | | | | | | | | | | |
| Cases | 169 | 89 | 136 | | | | 99 | 54 | 83 | | | | 70 | 35 | 53 | | | |
| RR (95% CI) | Ref | 1.1 | 1.3 (1.0–1.6) | | | 0.04 | Ref | 1.2 | 1.4 (1.0–1.9) | | | 0.03 | Ref | 1.0 | 1.1 (0.8–1.6) | | | 0.52 |
| Eggs | | | | | | | | | | | | | | | | | | |
| Intake[b] | <12 | <22 | <31 | <44 | ≥44 | | | | | | | | | | | | | |
| Person years | 94,771 | 113,056 | 98,813 | 94,986 | 138,529 | | | | | | | | | | | | | |
| Cases | 73 | 90 | 73 | 49 | 109 | | 41 | 59 | 49 | 24 | 63 | | 32 | 31 | 24 | 25 | 26 | |
| RR (95% CI) | Ref | 1.3 | 1.3 | 1.0 | 1.4 (1.1–2.0) | 0.57 | Ref | 1.5 | 1.5 | 0.8 | 1.5 (1.0–2.3) | 0.57 | Ref | 1.0 | 0.9 | 1.1 | 1.4 (0.9–2.2) | 0.85 |
| Milk | | | | | | | | | | | | | | | | | | |
| Intake[b] | 0 | <20 | <100 | <200 | ≥200 | | | | | | | | | | | | | |
| Person years | 142,414 | 71,622 | 120,600 | 165,661 | 39,856 | | | | | | | | | | | | | |
| Cases | 146 | 51 | 81 | 92 | 24 | | 92 | 31 | 50 | 48 | 15 | | 54 | 20 | 31 | 44 | 9 | |
| RR (95% CI) | Ref | 0.8 | 0.9 | 0.7 | 0.8 (0.5–1.2) | 0.09 | Ref | 0.7 | 0.9 | 0.6 | 0.8 (0.4–1.3) | 0.05 | Ref | 0.8 | 0.9 | 0.9 | 0.8 (0.4–1.7) | 0.80 |

[a]RR is adjusted for age, education, income, survey season, tea consumption, nonsteroidal anti-inflammatory drug use, energy intake, and fiber intake.
[b]Range of fat intake (g/day). Abbreviations are as follows: Q, quintile; CI, confidence interval.

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TABLE 3

Relative risk (RR) of colorectal cancer in relation to fat intake (g/day)[a]

| | Colorectal Cancer | | | | | | Colon Cancer | | | | | | Rectal Cancer | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Food | $Q_1$ | $Q_2$ | $Q_3$ | $Q_4$ | $Q_5$ | $P_{Trend}$ | $Q_1$ | $Q_2$ | $Q_3$ | $Q_4$ | $Q_5$ | $P_{Trend}$ | $Q_1$ | $Q_2$ | $Q_3$ | $Q_4$ | $Q_5$ | $P_{Trend}$ |
| Total fat | | | | | | | | | | | | | | | | | | |
| Intake[b] | <20 | <26 | <31 | <38 | ≥38 | | | | | | | | | | | | | |
| Person years | 106,681 | 108,018 | 108,335 | 108,738 | 108,384 | | | | | | | | | | | | | |
| Cases | 103 | 85 | 69 | 52 | 85 | | 60 | 56 | 33 | 29 | 58 | | 43 | 29 | 36 | 23 | 27 | |
| RR (95% CI) | Ref | 1.0 | 0.9 | 0.7 | 1.1 (0.7–1.7) | 0.82 | Ref | 1.1 | 0.7 | 0.7 | 1.4 (0.8–2.3) | 0.84 | Ref | 0.8 | 1.0 | 0.7 | 0.8 (0.4–1.5) | 0.53 |
| Saturated fatty acid | | | | | | | | | | | | | | | | | | |
| Intake[b] | <5.6 | <7.5 | <9.2 | <11 | ≥11 | | | | | | | | | | | | | |
| Person years | 106,587 | 108,132 | 108,405 | 108,633 | 108,399 | | | | | | | | | | | | | |
| Cases | 109 | 82 | 65 | 56 | 82 | | 65 | 50 | 37 | 29 | 55 | | 44 | 32 | 28 | 27 | 27 | |
| RR (95% CI) | Ref | 0.9 | 0.8 | 0.7 | 1.1(0.7–1.6) | 0.95 | Ref | 0.9 | 0.8 | 0.6 | 1.2 (0.8–2.1) | 0.86 | Ref | 0.8 | 0.8 | 0.8 | 0.8 (0.4–1.5) | 0.74 |
| Monounsaturated fatty acid | | | | | | | | | | | | | | | | | | |
| Intake[b] | <8.3 | <11 | <13 | <17 | ≥17 | | | | | | | | | | | | | |
| Person years | 106,501 | 108,105 | 108,516 | 108,579 | 108,453 | | | | | | | | | | | | | |
| Cases | 108 | 74 | 78 | 63 | 71 | | 65 | 41 | 46 | 37 | 47 | | 43 | 33 | 32 | 26 | 24 | |
| RR (95% CI) | Ref | 0.8 | 0.9 | 0.8 | 0.9 (0.6–1.3) | 0.73 | Ref | 0.8 | 0.9 | 0.8 | 1.0 (0.6–1.7) | 0.48 | Ref | 0.9 | 0.9 | 0.8 | 0.7 (0.4–1.3) | 0.74 |
| Polyunsaturated fatty acid | | | | | | | | | | | | | | | | | | |
| Intake[b] | <5.3 | <6.7 | <8.1 | <10 | ≥10 | | | | | | | | | | | | | |
| Person years | 106,989 | 108,197 | 108,502 | 108,274 | 108,193 | | | | | | | | | | | | | |
| Cases | 89 | 85 | 61 | 79 | 80 | | 48 | 51 | 33 | 49 | 55 | | 41 | 34 | 28 | 30 | 25 | |
| RR (95% CI) | Ref | 1.0 | 0.7 | 0.9 | 0.8 (0.5–1.3) | 0.75 | Ref | 1.2 | 0.8 | 1.2 | 1.2 (0.7–2.1) | 0.65 | Ref | 0.8 | 0.7 | 0.7 | 0.5(0.3–0.9) | 0.27 |
| Cholesterol[c] | | | | | | | | | | | | | | | | | | |
| Intake[b] | <180 | <256 | <330 | <410 | ≥410 | | | | | | | | | | | | | |
| Person years | 106,370 | 108,100 | 108,341 | 108,748 | 108,595 | | | | | | | | | | | | | |
| Cases | 91 | 69 | 92 | 63 | 79 | | 55 | 41 | 60 | 30 | 50 | | 36 | 28 | 32 | 33 | 29 | |
| RR (95% CI) | Ref | 1.0 | 1.5 | 1.1 | 1.6 (1.1–2.3) | 0.09 | Ref | 1.0 | 1.6 | 0.9 | 1.7 (1.1–2.7) | 0.15 | Ref | 1.0 | 1.3 | 1.5 | 1.5 (0.8–2.6) | 0.35 |

[a]RR is adjusted for age, education, income, survey season, tea consumption, nonsteroidal anti-inflammatory drug use, energy intake, and fiber intake. Abbreviations are as follows: Q, quintile, CI, confidence interval.

[b]Range of fat intake (mg/day).

[c]See Appendix 1, which presents the concentration of cholesterol for each animal-origin food in the food frequency questionnaire.

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TABLE 4
Relative risk (RR) of colorectal cancer in relation to animal food cooking method[a]

| | | Colorectal Cancer | | | Colon Cancer | | | Rectal Cancer | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Cooking methods (%)[b] | Person Years | N | RR (95%CI) | $P_{\text{Trend}}$ | N | RR (95%CI) | $P_{\text{Trend}}$ | N | RR (95%CI) | $P_{\text{Trend}}$ |
| Deep fried (72.9%) | | | | | | | | | | |
| Never | 144,682 | 112 | Reference | | 62 | Reference | | 50 | Reference | |
| <1 time/mo | 153,579 | 123 | 1.2 (0.9–1.5) | | 80 | 1.4 (1.0–1.9) | | 43 | 0.9 (0.6–1.4) | |
| ≥1 time/mo | 241,876 | 159 | 1.1 (0.9–1.4) | 0.54 | 94 | 1.2 (0.9–1.7) | 0.39 | 65 | 1.0 (0.7–1.4) | 0.94 |
| Stir fried (98.7%) | | | | | | | | | | |
| <1–2 times/month | 11,949 | 88 | Reference | | 50 | Reference | | 38 | Reference | |
| <3–4 times/month | 203,937 | 144 | 0.9 (0.7–1.1) | | 91 | 1.0 (0.7–1.4) | | 52 | 0.7 (0.5–1.1) | |
| ≥1 time/week | 245,846 | 162 | 0.9 (0.7–1.2) | 0.57 | 95 | 1.0 (0.7–1.4) | 0.80 | 67 | 0.8 (0.6–1.3) | 0.57 |
| Roasted (69.4%) | | | | | | | | | | |
| Never | 166,287 | 120 | Reference | | 71 | Reference | | 49 | Reference | |
| <1 time/month | 191,342 | 144 | 1.1 (0.9–1.4) | | 85 | 1.1 (0.8–1.5) | | 59 | 1.1 (0.8–1.6) | |
| ≥1 time/month | 182,526 | 130 | 1.2 (0.9–1.5) | 0.17 | 80 | 1.2 (0.9–1.7) | 0.20 | 50 | 1.1 (0.8–1.7) | 0.56 |
| Smoked (37.2%) | | | | | | | | | | |
| Never | 339,209 | 266 | Reference | | 149 | Reference | | 117 | Reference | |
| Ever | 200,946 | 128 | 1.1 (0.9–1.4) | 0.32 | 87 | 1.4 (1.1–1.9) | 0.01 | 41 | 0.8 (0.5–1.1) | 0.16 |
| Salted meat (81.4%) | | | | | | | | | | |
| Never | 99,998 | 93 | Reference | | 55 | Reference | | 38 | Reference | |
| <1 time/month | 321,042 | 209 | 0.9 (0.7–1.1) | | 123 | 0.9 (0.7–1.2) | | 86 | 0.7 (0.6–1.3) | |
| ≥1 time/month | 119,115 | 92 | 1.1 (0.8–1.4) | 0.77 | 58 | 1.1 (0.8–1.6) | 0.51 | 34 | 0.9 (0.6–1.5) | 0.73 |
| Salted fish (38.0%) | | | | | | | | | | |
| Ever | 207,431 | 139 | 0.9 (0.7–1.1) | 0.39 | 81 | 0.9 (0.7–1.1) | 0.32 | 58 | 1.0 (0.7–1.4) | 0.89 |
| Never | 332,717 | 255 | Reference | | 155 | Reference | | 100 | Reference | |

[a]Abbreviation is as follows: CI, confidence interval. RR is adjusted for age, education, income, survey season, tea consumption, and energy intake.

[b]Percentage of women who had used each of the cooking methods in the cohort.

## DISCUSSION

In this large-scale, population-based cohort study conducted among Chinese women in Shanghai, we found no evidence of an association between meat or fat consumption, including any of their subtypes, and colorectal cancer incidence. We also found no apparent association of total fish consumption with colorectal cancer, although intake of cholesterol-rich fish, including eel, shrimp, and shellfish, was related to a higher risk of colon cancer. In addition, we found that colon cancer risk was positively associated with high intake of eggs and cholesterol. Traditional Chinese cooking methods were unrelated to the risk of colorectal cancer with the exception of use of smoking as a cooking method, which was related to increased risk of colon cancer.

Meat consumption has long been suspected as an important risk factor for colorectal cancer. This hypothesis was initially based on migrant studies, secular trends of cancer incidence within countries, and international correlations between per capita food disappearance data and incidence rates for the disease (37). The geographic distribution of colorectal cancer follows the division between Westernized vs. developing countries, and incidence rates are increasing in countries adopting Western-style dietary habits (38). Mortality from colon cancer has rapidly increased in the past few decades in Japan, and the increase has generally been ascribed to the Westernization of the diet, characterized by high intake of fat and meat (39). Two recent population-based cohort studies conducted in Japan (12,13), however, failed to find a positive association between meat intake and incidence of colorectal cancer. The incidence of colorectal cancer in Shanghai has also been increasing during the last two decades (3). We found no apparent evidence of a positive association between total meat intake and colorectal cancer risk in this population, similar to results from Japanese studies (12,13). The lack of an overall association between total meat intake and colorectal cancer has also been reported in several cohort studies conducted in European and North American countries (6,12–19). However, a number of other studies have reported positive associations ranging from 80 to 120 g/day for the highest quintile of meat intake (6–11). The median of raw red meat intake among women in Shanghai is 42.3 g/day (1.5 oz/day), which is much lower than the 100 g or less per day (3.5 oz/day) of raw red meat recommended by the World Cancer Research Fund/American Institute for Cancer Research

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(WCRF/AICR) (5). The average amount of red meat intake for women in countries that participated in the European Prospective Investigation into Cancer and Nutrition (EPIC) study ranged from 34.6 g/day (1.2 oz/day, Greece) to 81.2 g/day (2.9 oz/day, Netherlands), and the mode was 71.3 g/day (2.5 oz/day) (7). In further analyses, the proportional hazard ratios (HR) were 1.03 (95% CI = 0.73–1.47) for red meat intake of ≥80 g/day, 1.29 (95% CI = 0.88–1.89) for ≥90 g/day, and with 100 g/day as the reference, the HR was 1.67 (95% CI = 1.11–2.52) for ≥100 g/day. Thus, lack of an association between total meat intake and CRC risk in our study population may be explained by an overall low level of meat consumption.

Several prospective studies have reported an inverse association between colon cancer risk and high intake of poultry and fish (7,8,11,40–42). However, other studies have found that poultry and fish intake were either not associated with risk (9,10,14,17,19,43–45) or were related to increased risk (18,46,47). In our study, poultry and total fish intake, including marine and fresh-water fish, was unrelated to the risk of colorectal cancer, comparable to results from a study in Japan (30) in which fish intake was high. However, in our study, intakes of eel, shrimp, and shellfish, all of which have a relatively high level of cholesterol compared to other types of fish, were associated with an increased the risk of colorectal cancer, although some of the associations were only marginally significant. The inconsistency between our findings and results from previous studies that have found a protective effect of fish intake on CRC (7,8,11,40–42) could be attributed to the effect of water pollution. Nakata et al. (48) reported a high concentration of DDT in spiny-head croaker, trident goby, and pike eel collected from Hangzhou Bay, south of Shanghai. Fish, particularly shellfish raised in industrial areas such as Shanghai, may have a high level of methyl mercury, polychlorinated dibenzo-p-dioxins and dibenzofurans, organochlorine residues, and other chemicals, some of which have been shown to be mutagens or animal carcinogens (49). A few epidemiological studies have also suggested some of these chemicals may be related to colorectal cancer (50,51). Given that the fish intake of women in this population (50.6 g/day) is about 1.5 times higher than that of women in European countries (average 32.8 g/day) (7) and that the amount of fresh-water fish production has increased continuously, whereas salt water fish production has decreased in the population of Shanghai since 1990 (52), the effect of long-term consumption of fish, particularly shellfish, on health needs to be further evaluated.

On the other hand, eel, shrimp, and shellfish are rich in cholesterol. We found that high intake of eggs, another cholesterol-rich food, and total dietary cholesterol, were positively associated with CRC risk. A combined analysis of 13 case-control studies showed a significant association between dietary cholesterol intake and cancer risk (53), although prospective studies have, in general, reported null results (19,38,40,41). However, a recent prospective study, with a considerably longer follow-up period (up to 32 yr) than other prospective studies, suggested that high dietary intake of cholesterol was associated with increased risk of colorectal cancer (18). Cholesterol acts as a cocarcinogen in the development of colorectal cancer in animal studies (54). Several other mechanisms have also been proposed to explain the effect of dietary cholesterol in modifying the carcinogenic process, which include the effect of the bacterial products of cholesterol and bile acid (55).

Several studies have suggested that milk consumption may be related to a reduced risk of colorectal cancer (19,56). The main hypothesis underlying a possible protective effect of dairy products relates to their calcium content and to a lesser extent vitamin D, conjugated linoleic acid, sphingolipids, butyric acid, and fermentation products. As summarized in a review, cohort studies have quite consistently found a protective effect of total dairy products and milk intake, whereas findings of case-control studies were not very supportive (56). Milk is the predominant dairy product consumed in Shanghai. However, the level of milk intake in our study was much lower (70 g/day) than in other cohort studies (range: 120–800 g/day). We found suggestive evidence of an inverse association between milk intake and colorectal cancer.

It has been shown that heterocyclic amines (HCAs) and polycyclic aromatic hydrocarbons (PAHs) can be activated in vivo by metabolic enzymes to exert their carcinogenic effect (57,58). Although an earlier epidemiological study showed that consumption of well-done and/or very well-done red meat and meat cooked using high temperature methods, such as roasting and possibly deep-frying, were related to an increased risk of colorectal cancer (58), we found little evidence of a relationship between cooking methods and risk of cancer. In addition to low consumption of meat, it is noteworthy that roasting and deep-frying are not common cooking methods in our study population. Although we found an increased risk of colon cancer with ever use of smoking as a cooking method, the frequency of using this method is low; only 9% of women reported having used smoking more than once per month, which prohibited a more detailed analysis.

Our study has several strengths. Dietary information was collected by in-person interview using a validated FFQ. The high participation rates for both baseline recruitment and cohort follow-ups minimized selection bias. The two FFQs, assessed 2 to 3 yr apart, improved the dietary assessment. The extensive information on lifestyle factors allowed for comprehensive evaluation and adjustment for potential confounders. The study, however, is limited by its relatively short follow-up time. It is possible that the dietary intake of participants who were diagnosed with colorectal cancer shortly after recruitment may have been affected by preclinical symptoms. However, excluding the first 2 yr of observations and colorectal cancer patients from the analyses did not substantially alter the association between animal-origin food and colorectal cancer. Multiple comparisons and the relatively low amount of consumption of eel, shrimp, and shellfish increase the possibility that our findings are due to chance. We could not examine the interactive effect of cooking methods and meat/fish intake for colon or rectal cancer separately due to a lack of statistical power. Continuing to follow this cohort for exposure updates, as is planned for the study, would yield more conclusive results.

In summary, in this large, population-based cohort study, we did not find an overall association between total consumption of animal origin food and risk of CRC. However, we did observe a positive association between CRC and consumption of eel, shrimp, shellfish, and eggs as well as the smoking method of cooking. More research is needed to investigate the role of cholesterol and environmental pollution in the etiology of CRC.

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APPENDIX 1
Concentration of cholesterol for animal-origin foods in the FFQ[a]

| Animal Origin Food | Concentration of Cholesterol (mg/100 g) |
|---|---|
| Pork chops | 112.2 |
| Pork ribs | 105.1 |
| Pig's feet | 115.2 |
| Fresh pork (fat) | 109.0 |
| Fresh pork (lean) | 81.0 |
| Fresh pork (mixture) | 80.0 |
| Pig liver, cow liver, sheep liver | 285.1 |
| Animal parts (heart, brain, tongue, tripe, intestine) | 147.6 |
| Beef, lamb | 70.4 |
| Chicken eggs, duck eggs | 507.8 |
| Chicken | 70.0 |
| Duck, goose | 60.5 |
| Marine fish | 55.5 |
| Fresh water fish | 62.1 |
| Rice field eel or river eel | 97.3 |
| Shrimp, crab, etc. | 111.7 |
| Shellfish (conch, etc.) | 61.2 |
| Fresh milk | 15 |
| Powdered milk | 110 |

[a] Abbreviation is as follows: FFQ, food frequency questionnaire.

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