12-2002

Food groups and the risk of colorectal carcinoma in an Asian population

Adeline SEOW

Stella QUAH

Denis NYAM

Paulin Tay STRAUGHAN
Singapore Management University, paulints@smu.edu.sg

Terrence CHUA

See next page for additional authors

DOI: https://doi.org/10.1002/cncr.10971

Citation

SEOW, Adeline, QUAH, Stella, NYAM, Denis, STRAUGHAN, Paulin Tay, CHUA, Terrence, & AW, Tar-Choon.(2002). Food groups and the risk of colorectal carcinoma in an Asian population. *Cancer, 95(11)*, 2390-2396.
Available at: https://ink.library.smu.edu.sg/soss_research/2204

Author
Adeline SEOW, Stella QUAH, Denis NYAM, Paulin Tay STRAUGHAN, Terrence CHUA, and Tar-Choon AW

Published in Cancer, 2002 December, Volume 95, Issue 11, Pages 2390-2396
http://doi.org/10.1002/cncr.10971

Food Groups and the Risk of Colorectal Carcinoma in an Asian Population

Adeline Seow, M.D.[1]
Stella R. Quah, Ph.D.[3]
Denis Nyam[2]
Paulin T. Straughan, Ph.D.[3]
Terrence Chua[4]
Tar-Choon Aw[5]

[1] Department of Community, Occupational, and Family Medicine, National University of Singapore, Singapore.

[2] Department of Colorectal Surgery, Singapore General Hospital, Singapore.

[3] Department of Sociology, National University of Singapore, Singapore.

[4] National Heart Center, Singapore.

[5] Department of Pathology, National University of Singapore, Singapore.

Supported by a National University of Singapore research grant (R111-000-004-112).

The authors express their appreciation to the Singapore General Hospital (SGH) and the SGH Department of Colorectal Surgery for their assistance in recruitment of patients for the study. They are grateful to all persons who consented to be interviewed and who shared their information.

Denis Nyam is currently at Mount Elizabeth Medical Center, 3 Mount Elizabeth, No. 14-02, Singapore 228510.

Address for reprints: Adeline Seow, M.D., Department of Community, Occupational, and Family Medicine, National University of Singapore, 16 Medical Drive, Singapore 117597; Fax: 011-65-67791489, E-mail cofseowa@nus.edu.sg

Received October 31, 2001; revision received April 17, 2002; accepted June 25, 2002.

BACKGROUND. Singapore Chinese have experienced a rapid transition toward a pattern of disease in which lifestyle-related, chronic, degenerative diseases are major public health concerns. The rates of colorectal carcinoma have increased 2-fold over the last 3 decades. It has long been known that dietary factors play a role in the risk of this disease, although studies in Asian populations, with their unique dietary intake, have been few.

METHODS. The authors conducted a population-based case-control study that included 121 Chinese patients with colorectal carcinoma and 222 healthy control participants who provided information on usual intake of major food groups in the preceding 3 years, physical activity, family history of colorectal carcinoma, and demographic variables through an in-person questionnaire.

RESULTS. High intake of red meat, but not other meats, indicated a predisposition to risk of colorectal carcinoma (adjusted odds ratio [OR] for the highest tertile vs. the lowest tertile, 2.2; 95% confidence interval [95%CI], 1.1–4.2). A low vegetable intake also was associated with a higher risk, and the combined effect appeared to be additive. Those in the highest tertile of meat intake and the lowest quartile of vegetable intake had an OR of 2.6 (95%CI, 1.0–6.7). The authors observed a slight, albeit nonsignificant, positive association with foods high in refined sugars. There was no association observed with fruit or soy-legume intake in this study. Among nondietary variables, a family history of colorectal carcinoma conferred a significant increase in risk (OR, 6.7; 95% CI 2.4–18.7).

CONCLUSIONS. Meat intake and vegetable intake were associated significantly with risk of colorectal carcinoma in this Asian population, and further studies on the effects of changes in these specific types of food may shed light on how best to reduce the rapid increase in rates in similar populations. ***Cancer*** **2002;95:2390–6.**

DOI 10.1002/cncr.10971

KEYWORDS: case-control study, colorectal carcinoma, diet, population-based, red meat.

Colorectal carcinoma is the most commonly diagnosed malignancy in Singapore, an island state in Southeast Asia with a population of 3 million. The country has undergone rapid industrialization over the past several decades, and this has brought with it changes in dietary habits[1] and a more sedentary lifestyle.[2] Colon carcinoma rates increased significantly between 1968 and 1997, from 10.4 to 20.9 per 100,000 males and from 9.0 to 17.9 per 100,000 females.[3,4] Similar increases have been noted for rectal carcinoma.

Ethnic Chinese constitute 77% of the Singapore population and account for 91% of all patients who are diagnosed with colorectal carcinoma in Singapore.[4] The wide variation in rates between countries and the evidence from migrant studies point to the importance of environmental factors, particularly diet, in the causation of this disease. In the context of worldwide colorectal carcinoma incidence, Singapore's rates rapidly are approaching the rates seen in developed countries and are among the highest in Asia (between two times and nine times higher than the rates in China).[5,6]

Studies on dietary risk factors for colon carcinoma have been consistent in demonstrating a positive association with the consumption of meat, particularly red meat, and an inverse association with vegetable consumption.[7] Despite rising affluence and the gradual adoption of a Western-style diet, many Singapore Chinese have retained their traditional methods of cooking and food preferences. The distribution of meat types, vegetables, and animal proteins versus plant proteins in the local diet still differ significantly from the West. For example, this population has a high consumption of cruciferous vegetables and soy foods.[8,9] The meats that are eaten most commonly are pork and fish rather than beef (unpublished data). In addition, as more countries experience a similar increase in the incidence of lifestyle-related chronic diseases, such as carcinoma, a study of dietary effects on colorectal carcinoma in a rapidly developing Asian population may shed light on the most important preventive measures that may have an impact on the rise in incidence of this disease among these populations.

MATERIALS AND METHODS

Methodology

The case population included Chinese patients with incident colorectal carcinoma, both male and female, who were admitted to Singapore General Hospital (SGH) between October, 1999 and May, 2000. Due to the small size of the country, there are no geographic boundaries that limit catchment areas for healthcare institutions. Public hospitals account for 80% of hospital care, and patients attending SGH, the largest public hospital, are likely to be representative of patients with colorectal carcinoma in the country. The research staff identified eligible patients, explained the purpose of the study, and invited them to participate. Patients were interviewed after they signed an informed-consent form.

The control population included a probability sample of adults from the Singapore population using two-stage, disproportionate, stratified, random sampling. The sample was drawn from the 1996 Singapore Parliamentary Electoral Register, which covered the 24 constituencies in the country. We stratified constituencies based on population size in the first stage of the sampling, so that the largest constituencies would not be overrepresented in the final sample. Using a table of random numbers, two constituencies were drawn from the first category (comprising the smallest constituencies), and one constituency was drawn from each of the other three categories. In the second stage of the sampling, a separate sample of equal size was drawn systematically from the three major ethnic groups (Chinese, Malay, and Indian) residing in the selected constituencies. Addresses on the list that were found to be vacant or demolished or for which the occupant could not be contacted after three visits were considered ineligible. The current analysis was restricted to Chinese respondents only. Like the patient population, all participants provided informed consent for the study before the interview.

Data Collection

Personal interviews were conducted with each respondent following a structured questionnaire. The questionnaire was translated into three languages (English, Malay, and Mandarin), and interviews were conducted in the respondent's dominant language. The interviews took place in the participants' homes for 99% of the control group. Ninety percent of patients were interviewed at the hospital, and the remaining 10% of patients were interviewed at home.

The questionnaire elicited information on demographic variables, family history of colorectal carcinoma, smoking history, and physical activity in addition to other factors. Usual physical activity was assessed with a modified version of the Behavioral Risk Factor Surveillance System questionnaire[10] by self-reported number of hours, both occupational and recreational, spent on vigorous, moderate, and light activity and hours spent sitting and sleeping daily. For this analysis, the total number of hours spent weekly in either moderate activity or vigorous activity was entered as a covariate.

For the diet section of the questionnaire, respondents were asked to indicate their usual frequency of intake *over the last 3 years* of a list of food groups (see Table 1). For each food group, the questionnaire included examples of common local foods. Respondents were asked to select the option that best denoted their frequency of intake from a list of six options ranging from *not at all*, to *less than once a month*, to *daily*. They were then asked to indicate the usual portion size as a multiple (0.5, 1.0, 1.5, 2.0, etc.) of a standard portion that was illustrated on a card, which the interviewers carried with them. In the data analysis, each frequency option was multiplied by a standardized factor to obtain the frequency per year and then multiplied further by the portion size to obtain portions per year.

TABLE 1
Food Groups in the Questionnaire

Food group	Examples
Red meat	Pork, beef, lamb, and mutton
Other meat	Chicken
Fish and shellfish	Fish, prawns, and squid
Soy and legumes	Yong tau foo, taupok, and taukwa
Cruciferous vegetables	Pak choy, choy sum, kai lan, cabbage, broccoli, and cauliflower
All vegetables	All cruciferous vegetables, kangkong, spinach, cucumber, all beans, all peas, corn, carrots, tomatoes, bitter gourd, and bean sprouts
Foods high in refined sugar/ sweet desserts	Sweet drinks, chocolates, and other candies; traditional sweet desserts
All fruit	Includes fresh fruit juices
Rice, bread, and noodles	Includes rice porridge and mixed noodle dishes

We categorized respondents further according to their intake of each food group using cut-off points based on tertiles, the median, or the 25th percentile, according to the distribution of intake in the study population. For heavily skewed distributions, the median or 25th percentile was used.

Statistical Analysis

The statistical analysis was performed using SPSS software (version 10.0 for Windows; SPSS, Chicago, IL). Odds ratios (ORs) and 95% confidence intervals (95%CIs) were computed using unconditional logistic regression analysis with potential confounders entered into the model as bivariates. Covariates were identified as potential confounders if it was known empirically or shown in the univariate analysis that they were associated with a risk of colorectal carcinoma. All *P* values quoted are two-sided.

RESULTS

Overall, 95% of the patient population (cases) and 75.5% of the control population (controls) agreed to participate. A further 0.4% of control questionnaires were incomplete. In total, questionnaire data were available for 126 Chinese patients with colorectal carcinoma and 310 respondents in the control group who also were Chinese. There was a difference in age distribution: A significantly larger proportion of the control group (27.5%) was age < 40 years compared with the patient group (3.2%). To enhance the comparability of cases and controls, the analysis was restricted to the 121 patients with colorectal carcinoma and the 222 controls who were age ≥ 40 years at the time of the interview.

The mean age at the time patients were diagnosed with colorectal carcinoma was 65 years. Of the 121 patients, information on tumor site was available for 103 patients (85.1%). The majority of patients (80 patients; 77.7%) had tumors on the left side, 22 patients (21.4%) had tumors on the right side, and 1 patient had tumors in both the transverse colon and the sigmoid colon at diagnosis. Staging information was available for 103 patients (85.1%), with the following stage distribution: 16.8% of patients had Duke Stage A disease, 24.8% of patients had Duke Stage B disease, 35.6% of patients had Duke Stage C disease, and 22.7% of patients had Duke Stage D disease.

TABLE 2
Demographic Characteristics of Patients with Colorectal Carcinoma and Population Control Participants

Characteristic	Patients with colorectal carcinoma (*n* = 121 patients)	Control participants (*n* = 222 participants)
Age (yrs)		
Mean	64.9	56.9
SD	10.1	12.2
Education level (yrs)		
Mean	4.9	6.7
SD	4.8	4.8
Gender: No. (%)		
Male	56 (46.3)	89 (40.1)
Female	65 (53.7)	133 (59.9)
Current residence: No. (%)		
1–2 room flat, shop house, etc.	6 (5.0)	17 (7.7)
3–5 room flat	85 (71.4)	133 (60.2)
Executive, private, or landed property	28 (23.5)	71 (32.1)
Family history of colorectal carcinoma (first degree relative) No. (%)		
Yes	12 (9.9)	5 (2.3)
No	109 (90.1)	217 (97.7)
Smoked at least 100 cigarettes in lifetime: No. (%)		
Yes	47 (38.8)	61 (27.5)
No	74 (61.2)	161 (72.5)
Usual hours of physical activity (moderate/vigorous) per week		
Mean	30.2	35.4
SD	19.3	19.4

SD: standard deviation.

Table 2 shows the basic sociodemographic characteristics of the study group. On average, the patients were older and had fewer years of education compared with the control group. The gender distribution was similar between the patient group and the control group. Both groups had a comparable distribution of housing types, an approximate indicator of socioeconomic status.

It is noteworthy that the proportion of patients with a first-degree relative who was diagnosed with colorectal carcinoma was 9.9% compared with 2.3% among the control group. The age-adjusted OR for the risk of colorectal carcinoma associated with this family history was 6.7 (95%CI, 2.4–18.7), indicating a significantly elevated risk.

Respondents with a positive smoking history comprised 38.8% of the patient group and 27.5% of the control group. The age-adjusted OR for smoking was 1.5 (95%CI, 0.9–2.5).

We compared the patient group and the control group with respect to the number of hours spent in moderate or vigorous activity per week over the past year. The mean number of hours for the patient group was lower compared with the control group ($P < 0.05$). Because the patients were interviewed very close to the time of their initial diagnosis of colorectal carcinoma, this was meant to measure prediagnostic activity, although the possibility that early preclinical effects of the disease may have reduced the activity of these patients should be considered.

Table 3 shows the ORs for colorectal carcinoma by food group. Dietary intake of red meat showed a significant, positive association with the risk of colorectal carcinoma. Persons in the highest tertile of intake had a two-fold risk compared with the lowest tertile after adjustment for age, gender, education, family history, smoking history, and physical activity (P for trend < 0.05). There was no correlation between the risk of colorectal carcinoma and the intake of other meat or of fish and/or shellfish.

Because more than 67% of respondents reported consuming vegetables (both cruciferous and all vegetables) daily, a cut-off point at the 25th percentile was used to categorize study participants into a low-intake group (< 25th percentile) and high-intake group. Higher total vegetable intake significantly lowered risk (adjusted OR, 0.6; 95%CI, 0.3–1.0). Conversely, we did not observe a lowering of risk with higher cruciferous vegetable intake when this group was considered on its own.

The intake of fruit and fruit juices did not show an association with colorectal carcinoma risk in this analysis. There was also no correlation with tertiles of soy-legume intake. Foods high in refined sugars included sweet beverages and sweet desserts (Table 1) and the risk associated with the highest tertile of intake was 1.6 (95%CI, 0.9–2.9), which was attenuated to 1.4 (95%CI, 0.8–2.7) after further adjustment for potential confounders.

Although no attempt was made to measure total energy intake in this study, we elicited intake of rice, bread, and noodles, which are the main staple foods consumed in this population and form the major source of energy. We did not find a material difference in the risk estimates after adjusting for intake of these foods.

The effects of red meat intake and vegetable intake were considered in combination (Table 4). A significant, positive association was observed in respondents in the highest tertile of red meat intake if they also reported a lower total vegetable intake (OR, 2.6;

TABLE 3
Food Group Intake and Risk of Colorectal Carcinoma among Singapore Chinese (*n* = 343 participants)

Food group intake (portions per yr)	No. of cases/ controls	Adjusted OR (95%CI)[a]	Adjusted OR (95%CI)[b]
Meat			
Red meat			
< 39	20/58	1.0[c]	1.0[c]
39–< 117	34/76	1.2 (0.6–2.4)	1.1 (0.5–2.2)
≥ 117	66/82	2.3 (1.2–4.4)	2.2 (1.1–4.2)
Other meat (excluding fish and shellfish)			
< 78	43/74	1.0	1.0
78–< 234	40/74	1.0 (0.6–1.8)	1.0 (0.6–1.8)
≥ 234	38/67	1.2 (0.7–2.1)	1.2 (0.7–2.1)
Fish and shellfish			
< 234	37/72	1.0	1.0
≥ 234	83/142	1.3 (0.8–2.2)	1.3 (0.8–2.2)
Soy and legumes			
< 78	25/55	1.0	1.0
78–< 234	36/59	1.4 (0.7–2.8)	1.4 (0.7–2.9)
≥ 234	59/99	1.3 (0.7–2.4)	1.3 (0.7–2.4)
Vegetables			
All vegetables			
≤ 78	47/49	1.0	1.0
> 78	74/162	0.5 (0.3–0.9)[d]	0.6 (0.3–1.0)[d]
Cruciferous vegetables			
≤ 234	31/60	1.0	1.0
> 234	90/154	1.2 (0.7–2.1)	1.3 (0.7–2.3)
Tomatoes			
< 24	27/49	1.0	1.0
24–< 78	22/29	1.3 (0.6–2.9)	1.3 (0.6–3.0)
≥ 78	71/136	1.0 (0.5–1.7)	1.0 (0.5–1.7)
All fruit and juices			
< 234	41/67	1.0	1.0
234–< 365	24/37	1.6 (0.8–3.2)	1.6 (0.8–3.3)
≥ 365	53/109	1.1 (0.6–1.9)	1.2 (0.7–2.2)
Foods high in refined sugars			
< 6	34/60	1.0	1.0
6–< 108	39/87	1.0 (0.5–1.9)	1.0 (0.5–1.9)
≥ 108	44/64	1.6 (0.9–2.9)	1.4 (0.8–2.7)

OR: odds ratio; 95%CI: 95% confidence interval.
[a] Adjusted for age and family history of colorectal carcinoma.
[b] Adjusted for age, family history of colorectal carcinoma, gender, smoking history (ever smoked or never smoked), years of formal education, and usual number of hours of moderate/vigorous exercise per week.
[c] P value for trend < 0.05.
[d] $P < 0.05$.

TABLE 4
Odds Ratios and 95% Confidence Intervals for the Combined Effect of Red Meat and Vegetable Intake on the Risk of Colorectal Carcinoma

All vegetable intake (portions per year)	Red meat intake (portions per year in tertiles)		
	<39	39–< 117	≥ 117
High (> 78)			
OR[a]	1.0 (ref)	0.7	1.9
95%CI	—	0.3–1.8	0.8–4.4
Cases/controls	15/46	18/57	40/59
Low (≤ 78)			
OR[a]	0.9	1.8	2.6
95%CI	0.2–3.8	0.6–5.0	1.0–6.7
Cases/controls	5/9	16/18	26/22

OR: odds ratio; ref: reference group; 95%CI: 95% confidence interval.
[a] Adjusted for age, gender, family history of colorectal carcinoma, smoking history (ever, never), years of formal education, and usual number of hours of moderate/vigorous exercise per week.

95%CI, 1.0–6.7). For respondents with a similar red meat intake, the risk was slightly lower if vegetable intake was higher (OR, 1.9; 95%CI, 0.9–4.4).

DISCUSSION

In summary, our results among Chinese in this population-based case-control study were consistent with previous studies in other populations showing that high red meat intake and low vegetable intake confer a significantly elevated risk of colorectal carcinoma. We did not observe any effect with intake of other meats, nor did we see an association with fruit intake.

Although, by considering dietary factors in terms of food groups rather than individual foods or nutrients, it is not possible to attribute effects to specific factors or mechanisms, it has the advantage that it can be translated directly to public health recommendations. Conversely, the potential limitations of this study and their bearing on the results should be borne in mind. Like all questionnaire-based studies, deficiencies in recall on the part of the interviewee may have resulted in nondifferential misclassification of respondents with respect to food intake. This is a conservative bias and may explain why we did not observe associations with foods like cruciferous vegetables that have been shown fairly consistently in other studies. Due to the retrospective nature of the current study, some inaccuracies in recall that may have occurred to different extents between the patient group and the control group may have led to recall bias, for example, in the estimation of diet or physical activity in the past. Because we did not have a measure of total energy, we were unable to examine the effect of an overall reduction in dietary intake among patients compared with controls. However, among the major findings, it is not likely that increased intake of red meat among patients can be attributed to this bias. Finally, the questionnaire was not designed to discriminate among persons with high intake (more than once per day) of a particular food group; thus, the exposure of persons in this category may be underestimated. In the analysis, the use of tertiles or other relevant categorizations of intake minimized bias due to this, but it also limited our ability to examine the effect of very common foods (e.g., vegetables) in greater detail.

Dietary intake of red meat (primarily beef) intake in Western populations has been related to the risk of colorectal carcinoma in many (but not all) studies,[11–14] and this appears to be independent of its contribution to total fat or protein content.[15] In some studies, a correlation with total meat or white meat also has been observed,[7,11] and others also found a correlation with well-done meat,[16,17] supporting the view that mutagens formed during high temperature meat cooking, such as carcinogenic heterocyclic amines, may be a plausible mechanism by which risk can be increased. The red meat consumed in this population is primarily pork. Although there have been reports of increased risk with processed pork[18,19] when it is examined separately from fresh meat, the current study did not collect information on this group of foods.

Vegetable intake may protect against carcinogenesis through its antioxidant content or through components like isothiocyanates, protease inhibiters, or fiber, which decreases transit time, lowers pH, and results in the formation of short-chain fatty acids.[20] Their protective effect in colon carcinoma has been demonstrated in many[18,21–23] (but not all,[24]) studies. In their review of the epidemiologic evidence, Steinmetz and Potter[25] pointed out that, among specific categories of vegetables, cruciferous vegetables have been most consistently associated with a protective effect. A previous case-control study in Singapore[26] also found a risk reduction of 50% in the upper tertile, relative to the lowest tertile, for both cruciferous vegetables and total vegetables, and the lack of effect in the current study is somewhat surprising and is not explained easily. One possible explanation is that the current study lacked information on genetic factors that influence susceptibility, such as factors relating to metabolic enzymes, which other studies have shown can modify the effect of isothiocyanates in cruciferae on the risk of developing malignant disease.[8]

Several studies have reported a positive correlation with obesity or total energy intake and an inverse correlation with physical activity.[7,27] These factors promote a hyperinsulinaemic state, which, in turn, increases the bioactivity of insulin-like growth factor 1 (IGF-1). Both insulin and IGF-1 stimulate cell proliferation and inhibit apoptosis, and it is believed that both are involved in the mechanism by which a positive energy balance increases the risk of developing various malignancies.[28] In support of this hypothesis, it was found that levels of IGF-1 and its binding protein predicted the risk of colorectal carcinoma in prospective studies in the United States.[29,30] Also in line with this hypothesis are previous findings of a positive association between sucrose-rich foods or a high glycemic index with the risk of colorectal carcinoma.[31,32] In the current study, there was the suggestion of a positive correlation, although it was not significant, with foods that are high in simple sugars.

We did not find an association with soy-legume intake despite the known anticarcinogenic properties of these foods[33] and the wide range of intake in this population.[9] Studies in a low-risk population have reported an interaction between red meat and legume intake such that a high meat:legume ratio confers a higher risk.[11] We also examined the ratio of legume to red meat intake in this study and did not find a significant association. Possibly, part of the previously observed effect may have been due to the high fiber content in other legumes, such as beans, peas, and lentils. One possible explanation for the lack of observed effect in this population is that soy foods, which are lower in fiber compared with other legumes,[34] are a major source of legumes among Chinese.

The results of the current study demonstrated that, in this Asian population, the risk of colorectal carcinoma is associated positively with intake of red meat, specifically when combined with a low vegetable intake, in common with risk factors that are identified most commonly among Western populations. Our results suggest that further studies on the impact of specific changes in dietary patterns in these groups are important to prevent the continued increase in the incidence of colorectal carcinoma in Asian populations.

REFERENCES

1. Lee HP, Gourley L. Food availability in Singapore from 1961 to 1983; implications for health research. *Food Nutr Bull.* 1987;8:50–54.
2. Epidemiology and Disease Control Department, Ministry of Health, Singapore. National health survey 1998. Singapore: Ministry of Health, 1999.
3. Chia KS, Lee HP, Seow A, Shanmugaratnam KS. Trends in cancer incidence in Singapore 1968–1992. Report no. 4. Singapore: Singapore Cancer Registry, 1996.
4. Chia KS, Seow A, Lee HP, Shanmugaratnam KS. Cancer incidence in Singapore 1993–1997. Report no. 5. Singapore: Singapore Cancer Registry, 2000.
5. Parkin DM, Muir CS, Whelan, SL, Gao YT, Ferlay J, Powell J, editors. Cancer incidence in five continents,. vol VI. IARC Scientific Publication No. 120. Lyon, IARC, 1992.
6. Flood DM, Weiss NS, Cook LS, Emerson JC, Schwartz SM, Potter JD. Colorectal cancer incidence in Asian migrants to the United States and their descendants. *Cancer Causes Control.* 2000;11:403–411.
7. Potter JD. Nutrition and colorectal cancer. *Cancer Causes Control.* 1996;7:127–146.
8. Seow A, Shi CY, Chung FL, et al. Urinary total isothiocyanate (ITC) in a population-based sample of middle-aged and older Chinese in Singapore: relationship with dietary total ITC and glutathione S-transferase M1/T1/P1 genotypes. *Cancer Epidemiol Biomarkers Prev.* 1998;7:775–781.
9. Seow A, Shi CY, Franke AA, Hankin JH, Lee HP, Yu MC. Isoflavonoid levels in spot urine are associated with frequency of dietary soy intake in a population-based sample of middle-aged and older Chinese in Singapore. *Cancer Epidemiol Biomarkers Prev.* 1998;7:135–140.
10. U.S. Department of Health and Human Services. Behavioral risk factor surveillance system. Atlanta: Centers for Disease Control and Prevention, 1996.
11. Singh PN, Fraser GE. Dietary risk factors for colon cancer in a low-risk population. *Am J Epidemiol.* 1998;148:761–774.
12. Franceschi S, Favero A, La Vecchia C, et al. Food groups and risk of colorectal cancer in Italy. *Int J Cancer.* 1997;72:56–61.
13. Isovich JM, L'Abbe KA, Castelleto R, et al. Colon cancer in Argentina: I: risk from intake of dietary items. *Int J Cancer.* 1992;51:851–857.
14. Thun MJ, Calle EE, Namboodiri MM, et al. Risk factors for fatal colon cancer in a large prospective study. *J Natl Cancer Inst.* 1992;84:1491–1500.
15. Giovannuci E, Rimm EB, Stampfer MJ, et al. Intake of fat, meat, and fiber in relation to risk of colon cancer in men. *Cancer Res.* 1994;54:2390–2397.
16. Gerhardsson de Verdier M, Hagman U, Peters RK, Steineck G, Overvik E. Meat, cooking methods and colorectal cancer: a case-referent study in Stockholm. *Int J Cancer.* 1991;49: 520–525.
17. Lang NP, Butler MA, Massengill J, et al. Rapid metabolic phenotypes for acetyltransferase and cytochrome P4501A2 and putative exposure to food-borne heterocyclic amines increase the risk for colorectal cancer or polyps. *Cancer Epidemiol Biomarkers Prev.* 1994;3:675–682.
18. Levi F, Pasche C, La Vecchia C, Lucchini F, Franceschi S. Food groups and colorectal cancer risk. *Br J Cancer.* 1999; 79:1283–1287.
19. Kampman E, Slattery ML, Bigler J, et al. Meat consumption, genetic susceptibility, and colon cancer risk: a United States multicenter case-control study. *Cancer Epidemiol Biomarkers Prev.* 1999;8:15–24.
20. Fuchs CS, Giovannucci EL, Colditz GA, et al. Dietary fiber and the risk of colorectal cancer and adenoma among women. *N Engl J Med.* 1999;340:169–176.
21. Slattery ML, Potter JD, Coates A, et al. Plant foods and colon cancer: an assessment of specific foods and their related nutrients (United States). *Cancer Causes Control.* 1997;8: 575–590.
22. Kampman E, Verhoeven D, Sloots L, van't Veer P. Vegetable and animal products as determinants of colon cancer risk in Dutch men and women. *Cancer Causes Control.* 1995;6:225–234.

23. Verhoeven DTH, Goldbohm RA, van Pappel G, Verhagen H, van den Brandt PA. Epidemiological studies on brassica vegetables and cancer risk. *Cancer Epidemiol Biomarkers Prev.* 1996;5:733–748.
24. Michels KB, Giovannucci E, Joshipura KJ, et al. Prospective study of fruit and vegetable consumption and incidence of colon and rectal cancers. *J Natl Cancer Inst.* 2000;92:1740–1752.
25. Steinmetz KA, Potter JD. Vegetables, fruit, and cancer. I. Epidemiology. *Cancer Causes Control.* 1991;2:325–357.
26. Lee HP, Gourley L, Duffy SW, Esteve J, Lee J, Day NE. Colorectal cancer and diet in an Asian population—a case-control study among Singapore Chinese. *Int J Cancer.* 1989; 43:1007–1016.
27. McTiernan A, Ulrich C, Slate S, Potter J. Physical activity and cancer etiology: associations and mechanisms. *Cancer Causes Control.* 1998;9:487–509.
28. Kaaks R, Lukanova A. Energy balance and cancer: the role of insulin and insulin-like growth factor-I. *Proc Nutr Soc.* 2001; 60:91–106.
29. Ma J, Pollak MN, Giovannucci E, et al. Prospective study of colorectal cancer risk in men and plasma levels of insulin-like growth factor (IGF)-1 and IGF-binding protein-3. *J Natl Cancer Inst.* 1999;91:620–625.
30. Kaaks R, Toniolo P, Akhmedkhanov A, et al. Serum C-peptide, insulin-like growth factor (IGF)-I, IGF-binding proteins, and colorectal cancer risk in women. *J Natl Cancer Inst.* 2000;92:1592–1600.
31. Slattery ML, Benson J, Berry TD, et al. Dietary sugar and colon cancer. *Cancer Epidemiol Biomarkers Prev.* 1997;6: 677–685.
32. Bostick RM, Potter JD, Kushi LH, et al. Sugar, meat and fat intake and non-dietary risk factors for colon cancer incidence in Iowa women (United States). *Cancer Causes Control.* 1994;5:38–52.
33. Messina M, Persky V, Setchell KDR, Barnes S. Soy intake and cancer risk: a review of in vitro and in vivo data. *Nutr Cancer.* 1994;21:113–131.
34. Ang CYW. Health implication of Asian diets and supplements. In: Ang CYW, Liu K, Huang YW, editors. Asian foods: science and technology. Philadelphia: Technomic Publishing Company, Inc., 1999:487–530.