Tea Consumption and Ovarian Cancer Risk: A Case-Control Study in China[1]

Min Zhang, Colin W. Binns, and Andy H. Lee[2]

School of Public Health, Curtin University of Technology, Perth, WA 6845
Australia

Abstract

To investigate whether tea consumption has an etiological association with ovarian cancer, a case-control study was conducted in China during 1999–2000. The cases were 254 patients with histologically confirmed epithelial ovarian cancer. The 652 controls comprised 340 hospital visitors, 261 non-neoplasm hospital outpatients, and 51 women recruited from the community. Information on the frequency, type, and duration of tea consumption was collected by personal interview using a validated questionnaire. The risk of ovarian cancer for tea consumption was assessed using adjusted odds ratios based on multivariate logistic regression analysis, accounting for confounding demographic, lifestyle, and familial factors including hormonal status and family ovarian cancer. The ovarian cancer risk declined with increasing frequency and duration of overall tea consumption. The adjusted odds ratio was 0.39 for those drinking tea daily and 0.23 for those drinking tea for >30 years, compared with nontea drinkers. The dose response relationships were significant, and the inverse association with ovarian cancer was observed for green tea consumption. We concluded that increasing frequency and duration of tea drinking, especially green tea, can reduce the risk of ovarian cancer. However, the protective effects of black tea and Oolong tea need to be additionally investigated.

Introduction

Ovarian cancer is the seventh most common cancer in women and the leading cause of death among gynecological cancers (1). Its incidence varies considerably between countries. Compared with other countries, China has a relatively low incidence of ~5/100,000 females, which is about one-fourth the incidence in northern European countries (2). The lack of screening tests for early detection and limited treatment options for this malignancy means that the survival rate remains disappointingly low. Five-year survival rates are <30% of all of the women

diagnosed with ovarian cancer (3). Therefore, primary prevention has been a major focus of research. However, little is known concerning the etiological factors of the malignancy (3). Most of the known risk factors are related to parity (4, 5) and family history of ovarian cancer (6, 7). Identification of common exposures associated with ovarian cancer may provide a viable method for prevention.

Tea is a natural beverage widely consumed around the world. As a potential antitumor agent, tea has been examined in several *in vivo* and *in vitro* studies (8, 9). The tumor-inhibitory effect of tea has been demonstrated in experimental animals (9). However, epidemiological studies on the relation between tea consumption and cancer risk have been inconsistent (10), particularly for ovarian caner (8, 9, 11). This may be partly because of differences in habit, type, and duration of tea drinking in different study populations, or failure to control for potential confounding factors (11, 12). We are unable to find any literature that documented the association between the type and/or duration of tea consumption and ovarian cancer.

Tea drinking varies greatly around the world. There are tea-drinking practices specific to the southeastern region of China. In view of the variation in ovarian cancer incidence and the different tea consumption patterns and habits, a case-control study was conducted in China to ascertain the relationship between tea consumption and ovarian cancer.

Materials and Methods

Study Design and Participants. A case-control design was used to investigate the association between tea consumption and ovarian cancer. Recruitment of cases focused on epithelial ovarian cancer that accounts for >90% of all of the ovarian malignancies (13). Two hundred and fifty five hospital patients with epithelial carcinoma of the ovary were identified in Hangzhou, China, between July 1999 and June 2000. To ascertain cases, all of the relevant hospital and laboratory pathology reports were reviewed. Pathological diagnoses were based on the International Histological Classification of Ovarian Tumors recommended by the Fédération Internationale des Gynaecologistes et Obstetristes (13, 14). With the exception of 1 patient lost after discharge, all of the eligible cases were recruited during the period of data collection. Inclusion criteria for cases were defined to be women <75 years of age, who were residents (at least 10 years living in Zhejiang province) diagnosed with epithelial ovarian cancer and confirmed histopathologically within the past 3 years. Most patients were identified in the Women's Hospital, School of Medicine, Zhejiang University (168 cases, 66%) and Zhejiang Cancer Hospital (53 cases, 21%). The remaining 13% were identified in 9 other general hospitals, but their pathological diagnoses had been reviewed and confirmed by pathologists of the former 2 hospitals. There was no significant difference in pathological diagnosis (serous cell *versus* other types) between the 2 teaching hospitals and the 9 community hospitals. Both Women's Hospital and Zhejiang

Table 1 Distribution of diagnosis and recruitment of cases	
	Frequency (%)
Pathological diagnosis of epithelial ovarian cancer	
Serous cystadnocarcinoma	106 (41.7)
Mucinous cystadnocarcinoma	35 (13.8)
Endometrioid cystadnocarcinoma	21 (8.3)
Mixed epithelial cystadnocarcinoma	7 (2.8)
Undifferentiated carcinoma	36 (14.2)
Borderline malignancy	40 (15.7)
Clear cell carcinoma	5 (2.0)
Transitional cell carcinoma	2 (0.8)
Malignant Brenner's tumor	2 (0.8)
Months between diagnosis and interview	
1–12	191 (75.2)
13–24	34 (13.4)
25–36	29 (11.4)
Type of interview	
In person	241 (95)
Next of kin	13 (5)
Place of interview	
Hospital	226 (89)
Home	25 (10)
Work place	3 (1)

Cancer Hospital are public teaching hospitals with >500 beds and receive patients from all over the province. In 1999, there were ~12,000 inpatients with 8,000 operations performed and 450,000 outpatients at the Women's Hospital (15). All of the hospitals are located in Hangzhou, the capital city of Zhejiang province. Most of the cases (75.2%) were recent patients interviewed within 12 months from diagnosis. Details of cases recruited are provided in Table 1.

During the same period 652 controls were recruited and interviewed. Controls were not to have a neoplasm, bilateral oophorectomy, hormone related conditions, nor to have been on long-term modifications of diet for medical reasons. Women recruited for controls were matched with cases by age and geographical area. A total of 601 women were recruited in the Women's Hospital. This hospital-based control sample consisted of 340 hospital visitors (15 women declined to be interviewed, nonresponse rate 4.4%) and 261 outpatients (nonresponse rate 1.2%). The hospital visitors were recruited while they visited their relatives or friends having deliveries, when they came for their own family planning, or when they came for a routine medical examination. All of the outpatients were recruited after they had consulted their doctors and their diagnoses were confirmed as minor gynecological diseases (84.7% had vulvitis, vaginitis, or cervicitis, 6.5% diagnosed with urethritis, and 5.7% had menopausal symptoms).

To control for bias in selecting the hospital controls, consulting rooms for outpatients and ward numbers for healthy women were chosen using random numbers. If no suitable subjects were found in the chosen room/ward, the adjacent room/ward was used instead. This systematic selection process was adopted throughout the entire recruitment period. Another sample of 51 community women was recruited from nine different districts of Hangzhou (nonresponse rate 7.8%). The project was approved by the Chinese hospital authorities and the Human Research Ethics Committee of the researchers' institution.

Questionnaire and Interview. A structured questionnaire, available from the authors on request, was used to collect the required information on tea consumption, demographic characteristics, personal habits, usual diet, and factors relevant to hormonal status. The questionnaire was modified from the Hawaii Cancer Research Survey (16). The components relating to habitual diet in the questionnaire were adapted from a Food Frequency Questionnaire (17) used for studying cancers of the esophagus, pancreas, and stomach in Shanghai (<200 km from Hangzhou), to ensure cultural relevance in southeast China. Additional lifestyle questions were taken from the Australian Health Survey 1995 (18) and the United States food survey 1992 (19). The questionnaire was translated into Chinese and checked (back translated) by three professional Chinese translators.

Tea consumption over the past years was evaluated by several methods. Participants were first classified as either "never" or "ever" tea drinkers. Information was then sought from all of the ever-drinkers on their usual consumption pattern, types of tea, years of tea drinking, and average frequency for each type of tea (number of cups brewed from each new batch of tea). Green tea was defined as the nonoxidized/nonfermented product, such as "Long Jing" tea. Black tea was specified as the oxidized/fermented product, such as "Lipton" tea, whereas Oolong tea was a partially oxidized/fermented product (8). The color of a brew of tea was used to identify tea types for those few participants who could not differentiate the kind of tea they drank. Green tea appears light green in color, whereas black tea shows a dark color after being brewed in hot water. Because the tea intake among the study population varied from never to four or more times a day, the frequency of habitual tea consumption was categorized as follows: never or seldom, once a month, two to three times a month, once a week, two to three times a week, four to six times a week, once a day, two to three times a day, and more than or equal to four times a day.

Tea consumption was measured using a standard container (350-ml tea cup) during the interviews. The use of teapots and small cups in other parts of China is not popular among Zhejiang residents (whose average cup size being 300–350 ml). The common method is to brew dry tea leaves in a cup using hot water without milk and sugar. The amount of dry tea leaves used depends on individual preference, but usually varies between 2 and 4 grams. Each new batch of tea is typically brewed once or twice for personal consumption. Therefore, it is appropriate to quantify tea consumption by counting the number of cups brewed from each new batch of tea. For infrequent tea drinkers and those reported drinking less than one cup at a time, their actual tea consumption was recorded instead.

Data were collected by face-to-face interview after obtaining the consent of the participant. All of the interviews were conducted in the native Hangzhou dialect by the first author. Habitual tea drinking was assessed before a "reference date," defined as 5 years before the diagnosis (cases) or interview (controls). Frequencies and quantities of tea consumed were estimated by the participants without any attempt to recall what they exactly consumed at that time. Each interview usually took between 40 and 50 min. For the cases, 226 women (89%) were either inpatients or at hospitals for follow-up treatment, 25 women (10%) were interviewed at their homes, whereas 3 women (1%) completed their interviews at their work places. The 51 community women were interviewed at their homes, community areas near their homes, or their work places.

The validity and reliability of the questionnaire was evaluated in a preliminary study. To assess its feasibility, face, and content validity, the questionnaire was pretested on 51 Chinese women who had migrated recently from southeastern China to Australia. The subjects in this pilot trial were recruited by quota and snowball strategies. Essentially the same questionnaire was

administered in both Australia and China, although feedback from the pretest of the 51 women had led to some minor modifications of the initial questionnaire, which measured their tea consumption and habitual diet back in China. The internal reliability and reproducibility of the questionnaire were then assessed by a test-retest conducted in Hangzhou, confirming that it was an appropriate instrument to measure the required information for adult Chinese women (20).

Statistical Analysis. All of the data were checked for completeness at the end of each interview. The data were coded and analyzed using the SPSS package (21). To assess the differences between the control groups, tea consumption, demographic, lifestyle, physical activity, and dietary variables were initially compared between the two hospital control groups, and then compared between hospital and community controls. The consistency of findings among the three groups would suggest that hospital bias was minimal. To assess potential survival bias, data for the 127 patients (interviewed within 3 months from diagnosis) and data for all of the cases (interviewed within 3 years from diagnosis) were also analyzed separately.

Demographic characteristics and potential risk factors between cases and controls were compared by t test for continuous variables and χ^2 test for categorical variables. To facilitate analysis, data on tea consumption frequency were reclassified as never or seldom (reference group representing the nontea drinkers), at most once a week (but at least once a month), two to six times a week, and at least once a day. The duration of tea drinking was also categorized into four consumption levels (0, <15 years, 15–30 years, and >30 years). A χ^2 test was performed to determine any association between overall tea consumption and common risk factors. Unlike green tea, black tea and Oolong tea were not commonly consumed by Zhejiang residents. Only two hospital controls reported drinking both Oolong tea and black tea. To assess the effects of different types of tea, three categories of tea drinking, "green tea only," "black or Oolong tea" and "green and black tea," were considered in separate models.

Univariate analysis was undertaken to screen potentially significant variables for subsequent multivariate analysis. ORs[3] of ovarian cancer for tea consumption variables and associated 95% CIs were computed, using unconditional multivariate logistic regression models, adjusting for age at interview, education, living area, BMI (5 existence ago), family income (yuan per month), alcohol consumption, coffee drinking, tobacco smoking, marital and menopause status, parity (full-term pregnancy), tubal ligation, oral contraceptive use, physical activity, and family history of ovarian cancer. These variables were included in the multivariate models because they were either established risk factors of ovarian cancer (1, 3–7) or significant confounders with tea consumption from the univariate analysis. Each ordinal quantity of tea consumption was subjected to a linear trend test. Finally, model adequacy was assessed using the Hosmer and Lemeshow goodness-of-fit statistic.

Results

There were no significant differences between the two hospital control groups in terms of tea consumption variables and other variables relevant to the outcome of this study (except that hospital visitors consumed more dairy products but less vegetable oil than outpatients). There were also no differences in

demographic and tea consumption variables between hospital controls and community controls (except that the community controls consumed slightly less pickled vegetables, less animal oil and cereals, but more dairy products and vegetable oil than hospital controls). Therefore, data from all three of the control groups were combined to form a single control group in subsequent analyses. Results from the 127 recent patients (interviewed within 3 months from diagnosis) and all of the cases (interviewed within 3 years from diagnosis) were also similar, suggesting survival bias was minimal. Therefore, we report the combined results of all of the cases below.

Table 2 contrasts the sample characteristics of women with and without ovarian cancer. There were no differences between cases and controls in mean age at interview, locality (urban or rural areas), education, BMI (5 years ago), alcohol and coffee consumption, tobacco smoking, menopause status, and tubal ligation. Compared with controls, patients with epithelial ovarian cancer tended to have less physical activity and less oral contraceptive use, but higher family income and lower parities. More of them were unmarried, had apparent family susceptibility, and consumed less tea. In particular, 44.5% of the cases were classified as nontea drinkers compared with 25.5% of the controls.

The distributions of overall tea consumption by potential confounding variables were next considered. For the cases, only alcohol consumption was significantly associated with tea consumption. However, for the controls, there were positive associations between tea consumption and age at interview, and coffee and alcohol consumption. Therefore, these variables were included in the multivariate logistic regression models.

Table 3 gives the crude ORs and adjusted ORs of ovarian cancer for the four levels of overall tea consumption, years of tea drinking, green tea only, black or Oolong tea, and green and black tea drinking. The risk of ovarian cancer appears to decline with increasing consumption level and years of tea drinking. The adjusted OR was 0.39 for those drinking tea daily and 0.23 for those who drank >30 years, compared with never or seldom tea-drinkers. The corresponding linear trend was also significant. When different types of tea were considered, the inverse association was observed across all levels of green tea drinking, with a significant dose-response relationship. However, the reduced risk of ovarian cancer was only evident for daily drinking of black or Oolong tea, and green and black tea. Finally, the Hosmer and Lemeshow goodness-of-fit statistic ranged between 2.72 ($P = 0.95$) and 14 ($P = 0.08$), indicating no lack of fit for the logistic regression models.

It is also interesting to report that serous cell ovarian cancer appeared to have a stronger inverse association with tea consumption. The adjusted ORs were 0.32 (95% CI, 0.18–0.54) for those drinking tea daily and 0.12 (95% CI, 0.05–0.31) for those drinking tea >30 years compared with nontea drinkers. The adjusted OR was 0.34 (95% CI, 0.19–0.59) for drinking green tea at least once a day. For brevity, the full set of results for serous cell type is not presented but available from the authors on request.

Discussion

A new finding from this study was that green tea drinking, and increased frequency and duration of tea consumption, can reduce the risk of epithelial ovarian cancer, especially for serous cell type. This provides additional evidence to a 9-year follow-up study in Japan, in which green tea consumption was found to be associated with a slowdown in cancer mortality and a later onset of cancer in all of the sites (22). Although epide-

---

[3] The abbreviations used are: OR, odds ratio; CI, confidence interval; BMI, body mass index.

	Cases (n = 254)		Controls (n = 652)		P
Table 2 Selected characteristics of participants with and without ovarian cancer					
	No.	(%)	No.	(%)	
Age at interview (years): mean (SD)	47.5 (12.6)		48.0 (10.2)		
≤34[a]	42	16.5	63	9.7	
35–49	100	39.4	285	43.7	
50–64	86	33.9	265	40.6	
≥65	26	10.3	39	6.0	
Area of resident					
Urban[a]	148	58.3	354	54.3	
Rural	106	41.7	298	45.7	
Income in 1998 (year/month)					<0.01
≤1000[a]	193	76.0	571	87.6	
1001–2000	50	19.7	69	10.6	
≥2001	11	4.3	12	1.8	
Education					
None[a]	44	17.3	133	20.4	
Primary	73	28.7	216	33.1	
Secondary	95	37.5	230	35.3	
Tertiary	42	16.5	73	11.2	
BMI (5 years ago, kg/m^2)					
≤18.5[a]	16	6.3	58	8.9	
18.5–24.5	190	74.8	496	76.1	
≥25	48	18.9	98	15.0	
Vigorous activity					<0.01
Never (0 h/week)[a]	202	79.5	456	69.9	
Ever (>1 h/week)	52	20.5	196	30.1	
Overall tea consumption					<0.01
Never[a]	113	44.5	166	25.5	
Ever	141	55.5	486	74.5	
Alcohol consumption[b]					
Never[a]	197	77.6	452	69.5	
Ever	57	22.4	198	30.5	
Coffee consumption[b]					
Never[a]	247	97.2	629	96.8	
Ever	7	2.8	21	3.2	
Tobacco smoking					
Never[a]	249	98.0	634	97.2	
Ever	5	2.0	18	2.8	
Marital status					<0.01
Never married[a]	7	2.8	8	1.2	
Married	231	90.9	610	93.6	
Widowed, divorced, separated	16	6.3	34	5.2	
Menopause status[b]					
No[a]	150	59.1	394	60.6	
Yes	104	40.9	256	39.4	
No. of delivery of full-term pregnancy[b]					<0.05
0[a]	35	13.8	42	6.5	
1	86	33.9	220	33.8	
2	77	30.3	233	35.8	
≥3	56	22.0	155	23.8	
Oral contraceptive use[b]					<0.01
Never[a]	198	78.0	416	64.0	
Ever	56	22.0	234	36.0	
Tubal ligation[b]					
No[a]	184	72.4	447	68.8	
Yes	70	27.6	203	31.2	
Ovarian cancer in first degree relatives[b]					<0.01
No[a]	248	97.6	649	99.8	
Yes	6	2.4	1	0.2	

[a] Reference category.
[b] Data missing for two controls.

miological evidence was available from other studies on digestive and urinary tract organs, breast, and skin cancers (11, 12, 23–25), the inverse relationship has not been established for ovarian cancer (9, 11, 26).

As a possible cancer preventive agent, green tea has been the subject of considerable interest over the past 10 years. Laboratory studies on tea have revealed consistent inhibitory effects against carcinogenesis in a variety of organs in rodents. Both green tea and black tea are known to contain polyphenols and other antioxidant compounds, which may be anticarcino-

Table 3 Crude and adjusted ORs[a] (95% CI) of epithelial ovarian cancer for tea drinking[b]

	No. of cases	No. of controls	Crude OR	95% CI	Adjusted OR	95% CI
Years of tea drinking						
0	113	166	1.0		1.0	
<15	77	222	0.51	0.36–0.73	0.47	0.32–0.70
15–30	42	144	0.43	0.28–0.65	0.43	0.28–0.68
>30	22	120	0.27	0.16–0.45	0.23	0.13–0.41
χ^2 for trend[c]				36.10[d]		35.71[d]
Overall tea consumption						
Never or seldom	113	166	1.0		1.0	
At most once a week	34	103	0.49	0.31–0.77	0.44	0.27–0.72
2–6 times a week	27	105	0.38	0.23–0.61	0.37	0.22–0.63
At least once a day	80	278	0.42	0.30–0.60	0.39	0.27–0.57
χ^2 for trend[c]				30.73[d]		30.06[d]
Green tea only						
Never or seldom	113	166	1.0		1.0	
At most once a week	25	75	0.49	0.29–0.82	0.42	0.24–0.73
2–6 times a week	23	85	0.40	0.24–0.67	0.40	0.23–0.70
At least once a day	76	243	0.46	0.32–0.65	0.43	0.30–0.63
χ^2 for trend[c]				32.79[d]		31.78[d]
Black or Oolong tea						
Never or seldom	113	166	1.0		1.0	
At most once a week	5	12	0.61	0.21–1.79	0.98	0.32–3.01
2–6 times a week	1	13	0.11	0.02–0.88	0.13	0.02–1.04
At least once a day	1	14	0.11	0.01–0.81	0.06	0.01–0.50
χ^2 for trend[c]				36.43[d]		39.68[d]
Green and black tea						
Never or seldom	113	166	1.0		1.0	
At most once a week	4	16	0.37	0.12–1.13	0.26	0.07–0.96
2–6 times a week	3	7	0.63	0.16–2.49	0.44	0.08–2.39
At least once a day	3	21	0.21	0.06–0.72	0.25	0.07–0.87
χ^2 for trend[c]				33.78[d]		32.07[d]

[a] Estimates from multivariate logistic regression models included terms for age at interview (in years; continuous), education (none, primary, secondary, tertiary), living area (urban, rural), BMI (5 years ago; continuous), tobacco smoking (never, ever), alcohol consumption (never, ever), coffee drinking (never, ever), family income (*yuan* per month; ≤1000, 1001–2000, ≥2001), marital status (never married, married, widowed or divorced or separated), menopause status (no, yes), parity (full-term pregnancy; continuous), tubal ligation (no, yes), oral contraceptive use (no, yes), physical activity (never, ever), and family history of ovarian cancer (no, yes).
[b] Never or seldom, or zero is the reference category.
[c] Ordinal quantity of tea drinking was tested for linear trend.
[d] $P < 0.001$.

genic, whereas extracts of tea have blocked nitrosamine-induced cancer in experimental animals (27–30). Despite such clear indications from laboratory studies, the association between tea drinking and human ovarian cancer was inconclusive (10). Such inconsistency may be attributed to differences in tea types and duration of habitual tea consumption in various study populations or because of a lack of control for confounding factors (11, 12). A lack of detailed and specific information on tea consumption also limited the conclusion drawn by previous studies.

The present study investigates the relation between tea consumption and ovarian cancer by assessing the type and duration of tea consumption. There are several advantages of this approach. Green tea is a local product of Zhejiang province and is the main type of tea consumed in southeast China. For our sample, >90% of tea drinkers reported consuming green tea. There is also little variation in the method of tea preparation by Zhejiang residents. The measurement of tea consumption was also based on the standard adopted by other studies. The first two cups brewed from each new batch contain almost equal amounts of epigallocatechin gallate (the main active constituent of tea polyphenols), but its level can be substantially decreased in the third cup (22). It has been reported that 69–85% of the total antioxidant in tea leave could enter liquid tea within 5 min of brewing. Additional antioxidants become soluble with a second brewing for an additional 5 min (31).

Moreover, drinking tea slowly has been suggested as an effective way of delivering tea catechin (32). Although tea polyphenols can be distributed from the digestive tract to various organs including the ovary in animal experiments (33), only hot but not iced black tea consumption was associated with a significantly lower risk of skin cancer (12), suggesting that the protective effects of tea can be influenced by the method of preparation.

Geologic and botanic evidence suggested that the tea plant was originated from China (30). Tea leaves are primarily manufactured as green, black, or Oolong tea in China. It has been observed that both green tea and black tea are effective antioxidants (34, 35). Previous evidence also revealed that the tumor-inhibitory effect of tea may depend on its intake level. However, the protective effect of black tea or Oolong tea consumption needs to be additionally investigated because of the fewer participants that drank black or Oolong tea in our study.

Several strengths and limitations should be considered when interpreting the findings. A major feature of this study is that extensive information was obtained on tea consumption and personal habits, as well as diet, lifestyle, and factors relevant to hormonal status. A validated and reliable instrument specifically for Chinese women was used to collect the required information. Test-retest results, conducted in Hangzhou, confirmed the reproducibility of the questionnaire. The intraclass correlation coefficient was 0.83 for tea consumption.

Our case-control study might introduce certain biases. Firstly, the association between tea consumption and ovarian cancer has not been firmly established at the time of interview; therefore, information bias concerning personal habits thus appears unlikely. All of the interviews were conducted by a single investigator (first author) to avoid intra-interview bias. Although tea consumption can be recalled by the participants with reasonable accuracy, misclassification of its exposure level may still exist. However, such random errors are unlikely to influence the observed association between tea drinking and ovarian cancer. The recall between cases and controls may differ because of variations in the perceived reference frame or in subject motivation. Cases were more likely to sustain recall bias, because the onset of the disease might change their personal habits or at least the recall of their habits. Therefore, a fixed recall period (5 years before diagnosis for cases and 5 years before interview for controls) was adopted to avoid possible exposure change relating to case disease status.

Selection bias appeared to be minimal in view of the low refusal rate and the recruitment procedure used. Although the study attracted participation from most (99.6%) ovarian patients, it was possible a few cases had been omitted and not interviewed. But this was unlikely, because hospital records were reviewed daily and all of the new cases have been accounted for during the data collection period. Survival bias was also found to be minimal in this study. For the hospital control sample, it is possible that their reported tea consumption may not be representative of the Zhejiang female population. Consequently, another sample of community women was recruited whose tea consumption level was found to be similar to the hospital-based controls.

In conclusion, our study of Chinese women suggests that, by increasing the frequency and duration of tea consumption, especially the drinking of green tea, contributes to a decline in ovarian cancer risk. This finding is well supported by the tumor-inhibitory effects of tea and tea polyphenols demonstrated in animal studies, and other *in vitro* and *in vivo* experiments.

References

1. Kristensen, G. B., and Trope, C. Epithelial ovarian carcinoma. Lancet, *349:* 113–117, 1997.

2. Jin, F., Shu, X. O., Devesa, S. S., Zheng, W., Blot W. T., and Gao, Y. T. Incidence trends for cancers of the breast, ovary, and corpus uteri in urban Shanghai, 1972–89. Cancer Causes Control, *4:* 355–360, 1993.

3. World Cancer Res. Fund in association with American Institute for Cancer Research (eds.), Food, Nutrition and the Prevention of Cancer: a Global Perspective, pp. 288–293. Washington: World Cancer Res. Fund/American Institute for Cancer Research, 1997.

4. Byers, T., Marshall, J., Graham, S., Mettlin, C., and Swanson, M. A case-control study of dietary and nondietary factors in ovarian cancer. J. Natl. Cancer Inst., *71:* 681–686, 1983.

5. Whittemore, A. S. Characteristics relating to ovarian cancer risk: implications for prevention and detection. Gynecol. Oncol., *55:* S15–S19, 1994.

6. Kerber, R. A., and Slattery, M. L. The impact of family history on ovarian cancer risk. The Utah Population Database. Arch. Intern. Med., *155:* 905–912, 1995.

7. Ford, D., and Easton, D. F. The genetics of breast and ovarian cancer. Br. J. Cancer, *72:* 805–812, 1995.

8. IARC. Coffee, tea, mate, methylxanthines and methylglyoxal. Working Group on the Evaluation of Carcinogenic Risks to Humans. Lyon, 27 February to 6 March 1990. IARC Monogr. Eval. Carcinog. Risks Hum., *51:* 1–513, 1991.

9. Yang, C. S., and Wang, Z. Y. Tea and cancer. J. Natl. Cancer Inst., *85:* 1038–1049, 1993.

10. Blot, W. J., Chow, W. H., and McLaughlin, J. K. Tea and caner: a review of the epidemiological evidence. Eur. J. Cancer Prev., *5:* 425–438, 1996.

11. Zheng, W., Doyle, T. J., Kushi, L. H., Sellers, T. A., Hong, C. P., and Folsom, A. R. Tea consumption and cancer incidence in a prospective cohort study of postmenopausal women. Am. J. Epidemiol., *144:* 175–182, 1996.

12. Hakim, I. A., Harris, R. B., and Weisgerber, U. M. Tea intake and squamous cell carcinoma of the skin: influence of type of tea beverages. Cancer Epidemiol. Biomark. Prev., *9:* 727–731, 2000.

13. Cotran, R. S., Kumar, V., and Collins, T. (eds). Robbins Pathologic Basis of Disease, p. 1067. Philadelphia: W. B. Saunders Company, 1999.

14. Underwood, J. C. E. (ed). Ovarian Neoplasms. General and Systematic Pathology, pp. 512–513. Sydney: Churchill Livingstone, 2000.

15. Xie, X. Annual Report of Women's Hospital, School of Medicine, Zhejiang University. Hangzhou: Women's Hospital, School of Medicine, Zhejiang University, 2000.

16. Thompson, F. E., and Byers, T. Dietary assessment resource manual. J. Nutr., *124:* 2245S–2317S, 1994.

17. Ji, B. T., Chow, W. H., Yang, G., Mclaughlin, J. K., Zheng, W., Shu, X. O., Jin, F., Gao, R. N., Gao, Y. T., and Fraumeni, J. J. F. Dietary Habits and stomach cancer in Shanghai, China. Int. J. Cancer, *76:* 659–664, 1998.

18. Australian Bureau of Statistics. National Health Survey 1995: Summary of Results. Canberra, Australia: Australian Bureau of Statistics, 1995.

19. National Information Services. Food Questionnaire. National Information Services (NIS), Washington, DC, 1992.

20. Zhang, M., Binns, C. W., and Lee, A. H. Dietary patterns and nutrient intake of adult women in south-east China: a nutrition study in Zhejiang province. Asia Pacific J. Clin. Nutr., *11:* 13–21, 2002.

21. SPSS Incorporation. SPSS for Windows, Release 10, Chicago, IL, 2000.

22. Nakachi, K., Imai, K., and Suga, K. Epidemiological evidence for prevention of cancer and cardiovascular disease by drinking green tea. *In*: H. Ohigashi, T. Osawa, S. Watanabe, and T. Yoshikawa (eds.). Food Factors for Cancer Prevention, pp. 105–108. Tokyo: Springer-Verlag, 1997.

23. Gao, Y. T., McLaughlin, J. K., Blot, W. J., Ji, B. T., Dai, Q., and Fraumeni, J. F., Jr. Reduced risk of esophageal cancer associated with green tea consumption. J. Natl. Cancer Inst., *86:* 855–858, 1994.

24. Yu, G. P., and Hsieh, C. C. Risk factors for stomach cancer: a population-based case-control study in Shanghai. Cancer Causes Control, *2:* 169–174, 1991.

25. Nakachi, K., Suemasu, K., Suga, K., Takeo, T., Imai, K., and Higashi, Y. Influence of drinking green tea on breast cancer malignancy among Japanese patients. Jpn. J. Cancer Res., *89:* 254–261, 1998.

26. Kuper, H., Titus-Ernstoff, L., Harlow, B. L., and Cramer, D. W. Population based study of coffee, alcohol and tobacco use and risk of ovarian cancer. Int. J. Cancer, *88:* 313–318, 2000.

27. Xu, G. P., Song, P. J., and Reed, P. I. Effects of fruit juices, processed vegetable juice, orange peel and green tea on endogenous formation of *N*-Nitrosoproline in subjects from a high-risk area for gastric cancer in Moping County, China. Eur. J. Cancer Prev., *2:* 327–335, 1993.

28. Sugiyama, T., and Sadzuka, Y. Enhancing effects of green tea components on the antitumor activity of adriamycin against M5076 ovarian sarcoma. Cancer Lett., *133:* 19–26, 1998.

29. Suganuma, M., Okabe, S., Kai, Y., Sueoka, N., Sueoka, E., and Fujiki, H. Synergistic effects of (-) – Epigallocatechin gallate with (-) – epicatechin, sulindac, or tamoxifen on cancer-preventive activity in the human lung cancer cell line PC-9. Cancer Res., *59:* 44–47, 1999.

30. Fujiki, H., Suganuma, M., Okabe, S., Sueoka, E., Suga, K., Imai, K., and Nakachi, K. A new concept of tumor promotion by tumor necrosis factor-α, and cancer preventive agents (-) – Epigallocatechin gallate and green tea – a review. Cancer Detect. Prev., *24:* 91–99, 2000.

31. Phipps, R. P. The second international scientific symposium on tea and human health. September 14th, 1998. Nutrition, *15:* 968–971, 1999.

32. Yang, C. S., Lee, M. J., and Chen, L. Human salivary tea catechin levels and catechin esterase activities: implication in human cancer prevention studies. Cancer Epidemiol. Biomark. Prev., *8:* 83–89, 1999.

33. Suganuma, M., Okabe, S., Oniyama, M., Tada, Y., Ito, H., and Fujiki, H. Wide distribution of [^{3}H] (-) – epigallocatechin gallate, a cancer preventive tea polyphenol, in mouse tissue. Carcinogenesis (Lond.), *10:* 1771–1776, 1998.

34. Lu, Y. P., Lou, Y. R., Lin, Y., Shih, W. J., Huang, M. T., Yang, C. S., and Conney, A. H. Inhibitory effects of orally administered green tea, black tea, and caffeine on skin carcinogenesis in mice previously treated with ultraviolet B light (high-risk mice): relationship to decreased tissue fat. Cancer Res., *61:* 5002–5009, 2001.

35. Yang, C. S., Maliakal, P., and Meng, X. Inhibition of carcinogenesis by tea. Annu. Rev. Pharmacol. Toxicol., *42:* 25–54, 2002.

Tea Consumption and Ovarian Cancer Risk: A Case-Control Study in China

Min Zhang, Colin W. Binns and Andy H. Lee

Updated version	Access the most recent version of this article at: http://cebp.aacrjournals.org/content/11/8/713

Cited articles	This article cites 24 articles, 4 of which you can access for free at: http://cebp.aacrjournals.org/content/11/8/713.full#ref-list-1
Citing articles	This article has been cited by 6 HighWire-hosted articles. Access the articles at: http://cebp.aacrjournals.org/content/11/8/713.full#related-urls

E-mail alerts	Sign up to receive free email-alerts related to this article or journal.
Reprints and Subscriptions	To order reprints of this article or to subscribe to the journal, contact the AACR Publications Department at pubs@aacr.org.
Permissions	To request permission to re-use all or part of this article, use this link http://cebp.aacrjournals.org/content/11/8/713. Click on "Request Permissions" which will take you to the Copyright Clearance Center's (CCC) Rightslink site.