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Fruit and vegetable consumption associated with reduced risk of epithelial ovarian cancer in southern Chinese women

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Research Highlights

- First report on fruit and vegetable intake and ovarian cancer in southern China.
- High fruit and vegetable consumption appears protective against ovarian cancer.
- Intakes of nutrients derived from fruits and vegetables are inversely associated with the ovarian cancer risk.

ABSTRACT

Objective: To investigate the association between fruit and vegetable consumption and the risk of epithelial ovarian cancer in southern Chinese women.

Methods: A case-control study was undertaken in Guangzhou, Guangdong Province, between 2006 and 2008. Participants were 500 incident ovarian cancer patients and 500 hospital-based controls. Information on habitual fruit and vegetable consumption was obtained by face-to-face interview using a validated and reliable food frequency questionnaire. Unconditional logistic regression analyses were performed to assess the association between fruit and vegetable intakes and the ovarian cancer risk.

Results: The mean fruit and vegetable daily intakes of ovarian cancer patients (324.2 g (SD 161.9) and 582.7 g (SD 250.2)) were significantly lower ($p < 0.001$) than those of controls (477.3 g (SD 362.1) and 983.3 g (SD 739.9)). The adjusted odds ratios were 0.30 (95% confidence interval (CI) 0.21 to 0.44) and 0.07 (95% CI 0.04 to 0.12) for more than 490 g of fruits and 970 g of vegetables per day, relative to at most 320 g and 690 g per day, respectively. With the exception of lycopene, substantial risk reductions were evident for a variety of nutrients derived from fruits and vegetables.

Conclusion: Consumption of fruits and vegetables was inversely associated with the incidence of epithelial ovarian cancer in southern Chinese women.

Word count: 212

Keywords: China; Fruit; Vegetables; Nutrients; Ovarian cancer

INTRODUCTION

Ovarian cancer is the second most common gynaecological malignancy and the seventh leading cause of cancer-related deaths among women worldwide [1]. In 2008, approximately 225,000 new cases of ovarian cancer and 140,000 related deaths were reported [1]. Ovarian cancer is usually diagnosed at an advanced stage and has a five-year survival rate of only 25–30% [2]. Exploring ways to prevent this disease is therefore important. Besides genetic, familial and reproductive factors, physical activity and body size are known to be related with the development of ovarian cancer for Chinese women [3-6].

Fruits and vegetables are rich in cancer-preventive agents, such as carotenoids, vitamins, folate, dietary fibre and certain minerals [7]. A number of studies, mostly from Europe and North America, have investigated the effect of fruit and vegetable consumption on the ovarian cancer risk. While some case-control studies [8-10] and prospective cohort studies [11,12] observed inverse associations, others reported no associations between intakes of fruit and/or vegetable and ovarian cancer risk [13,14].

Few epidemiologic studies of ovarian cancer have been conducted among Chinese women in relation to their intake of fruits and vegetables. Despite apparent risk reductions at high levels of intake were found in women residing in Hangzhou, China [15], another study in Taiwan provided inconclusive evidence [16]. The present study aimed to investigate the association between fruit and vegetable consumption and the risk of ovarian cancer in southern Chinese women.

METHODS

Study design and subjects

A hospital-based case-control study of epithelial ovarian cancer was conducted in Guangzhou, southern China, between August 2006 and July 2008 [4]. Details of the methodology have been reported elsewhere [17]. Subjects were recruited from four public hospitals, namely, The Overseas Hospital (affiliated with Jinan University), Zhujiang Hospital, General Hospital of Guangzhou Military Command, and Second Affiliated Hospital of Zhongshan University. Eligibility criteria were age 75 years or less and residence in metropolitan Guangzhou for at least the past 10 years.

Medical records and pathology reports were reviewed to identify newly diagnosed patients (within the past 12 months). Pathological diagnoses were based on the International Histological Classification of Ovarian Tumors [18]. Patients without histopathologically confirmed invasive and borderline malignant epithelial ovarian cancer and those who had self-reported memory problems affecting their recall of past events were excluded. Of the total 504 patients identified, 500 consented to participate.

Controls were recruited from inpatients at the same hospitals from Ophthalmology, Orthopaedics, Respiratory Diseases, Gastroenterology and Physiotherapy departments. Exclusion criteria for controls were previous diagnosis of malignant disease; history of bilateral oophorectomy; having self-reported memory problems; on long-term medical diet; in addition to non-residency and age above 75 years. Whenever more controls were available than could be interviewed, the final selection was made using random numbers. Of the 512 eligible controls recruited to frequency matched with cases by age (± 5 years), 500 women agreed to take part in the study. There were no significant differences in age, education level and marital status between participants and non-participants.

The study was approved by the participating hospitals and the Human Research Ethics Committee of Curtin University (number HR 78/2006). Written informed consent was obtained from all participants. They were assured of the right to withdraw any time without prejudice.

Data collection

All participants were interviewed by trained interviewers in either Mandarin or Cantonese, usually in the presence of their next-of-kin to help the recall of dietary habits. The structured questionnaire used composed of questions on demographic characteristics, anthropometry, reproductive history, hormonal status, past and family medical history and lifestyle, including diet. Current weight, weight five years before the interview and height were used to calculate body mass index (BMI) at both times. In addition, participants estimated their average time engaged in various physical activities. Total physical activity was quantified in terms of metabolic equivalent tasks (MET)-hours per week [4].

A 125-item semi-quantitative food frequency questionnaire including commonly consumed fruits and vegetables, developed and tested for the southern Chinese population, was used to collect dietary information and alcohol consumption [19,20]. Frequency and amount of intake were recorded in detail. The reference recall period for dietary variables was five years before diagnosis for cases and five years before interview for controls. The energy content of each food or beverage item was obtained from the Chinese Food Composition Tables to estimate total energy intake (kcal) [21].

Statistical analysis

Descriptive statistics were used to summarize the sample characteristics. Unconditional logistic regression analyses were performed to ascertain the effects of fruit and vegetable intakes on the epithelial ovarian cancer risk. Total vegetable intake was defined as the sum of daily consumption of green leafy vegetables (spinach, water spinach, watercress), cruciferous vegetables (Chinese cabbage, cabbage mustard, flowering stalk, cole, cabbage, cauliflower, radish), yellow orange vegetables (tomato, carrot, sweat potatoes), allium vegetables (leek, green onion, garlic, onion) and other vegetables (bean spout, celery, caraway, balsam pear, zucchini, cucumber, green capsicum, bamboo shoot, potato, ginger). Total fruit intake was defined as the sum of daily consumption of yellow orange fruits (guava, orange, mandarin orange, peach, mango, watermelon) and other fruits (apple, banana, pear, lichee, grape, longan).

The main nutrients contained in fruits and vegetables, except carotenoids, were next identified and estimated using the Chinese Food Composition Tables [21]. The nutrient database of the USA Department of Agriculture [22] was used for the conversion to carotenoids. Effects of the selected nutrients were then assessed by separate logistic regression models.

For each exposure variable of interest, the tertiles of consumption among controls were obtained, with the lowest level being the reference category. In addition to reporting crude and adjusted odds ratios (OR) and corresponding 95% confidence intervals (CI), dose-response relationships were assessed by tests for linear trend with the exposure variable being continuous. Confounding variables included in the logistic regression models were age at interview (years, continuous), education level (none or primary, secondary, vocational or tertiary), BMI (5 years ago, kg/m^2, continuous), physical activity (MET-hours/week, continuous), fresh meat consumption (g/day, continuous), seafood consumption (g/day, continuous), total energy intake (kcal/day, continuous), parity (continuous), oral contraceptive use (never, ever), menopausal status (pre, post), tubal ligation (no, yes), history of hormone replacement therapy (no, yes), smoking status (never, past, current), alcohol drinking (no, yes), and family history of ovarian or breast cancer in first-degree relatives (no, yes). Participants who consumed at least 500 ml of alcoholic beverages per week were classified as 'yes', otherwise they were referred to as 'no'. These variables were either established or plausible risk factors from the literature. Sensitivity of the analyses to histologic subtypes of epithelial ovarian tumours, and energy-adjustment for nutrients based on the regression residuals method [23], were also conducted. All statistical analyses were performed using the SPSS package version 20.0 (SPSS Inc. 2012).

RESULTS

Half of the 500 epithelial ovarian cancer patients were histologically diagnosed as serous carcinoma, while mucinous tumours comprised 16% of the cases. Other histologic subtypes included borderline malignancy (13.1%), undifferentiated carcinoma (11.8%), endometrioid cystadenocarcinoma (3.8%), mixed epithelial cystadenocarcinoma (2.6%), clear cell carcinoma (1.4%), transitional cell carcinoma (0.8%) and malignant Brenner's tumour (0.6%).

Table 1 summarizes characteristics of the sample by case-control status. The average age of participants was 59.4 (SD 6.1) years. They were predominantly post-menopausal (95.2%). Most of them had attained secondary school education or above (59.9%), never had a tubal ligation (64.9%), were non-smokers (96.6%) and seldom drank alcoholic beverages (72.4%). Women with ovarian cancer tended to have less oral contraceptive use and lower parities, higher mean BMI, consume significantly less seafood and were less physically active than their control counterparts.

In relation to fruit and vegetable consumption, patients with ovarian cancer consumed significantly less fruit (324.2 (SD 161.9) g/day), vegetable (582.7 (SD 250.2) g/day) and their subgroups than women without the disease (477.3 (SD 362.1) and 983.3 (SD 739.9) g/day). Table 2 shows that apparent reductions in risk of ovarian cancer were observed at high intakes of total fruits and total vegetables, after accounting for the effects of potential confounders. The adjusted OR were 0.30 (95% CI 0.21 to 0.44) and 0.07 (95% CI 0.04 to 0.12) for women consuming more than 490 g of fruits and 970 g of vegetables per day, relative to those with daily consumption at most 320 g and 690 g, respectively.

Compared to controls, the ovarian cancer patients had significantly lower intakes of all selected dietary nutrients derived from fruits and vegetables (results available upon request). Table 3 presents the corresponding multivariate logistic regression results. With the exception of lycopene, high intakes of these nutrients were associated with reduced risk of ovarian cancer.

Table 4 shows the logistic regression results of total fruit and total vegetable consumption for all, serous and mucinous ovarian tumours. Analyses were not performed for other histologic subtypes due to the low number of cases available. Similar to all cases, inverse associations with fruit and vegetable consumptions were found for serous and mucinous ovarian tumours. In addition, tests for trend were all significant, suggesting inverse linear dose-response relationships.

Finally, Table 5 provides the logistic regression results of selected nutrients derived from fruits and vegetables for all, serous and mucinous ovarian tumours. Other than lycopene, apparent risk reductions could be achieved by high intakes of these nutrients, again with significant linear trends, which support the results based on the consumption of fruits and vegetables. The regression residuals method for adjustment of total energy intake produced similar results which were omitted for brevity.

DISCUSSION

This case-control study of southern Chinese women suggested a protective role for fruit and vegetable consumption against epithelial ovarian cancer, with supportive evidence from the corresponding intake of selected dietary nutrients. Our results are consistent with a previous hospital-based case-control study conducted in Hangzhou, China [15]. Another hospital-based case-control study from Shandong Province, China, similarly reported the potential preventive effect of a “high vegetable and fruit diet” [24]. In contrast, no association was found between ovarian cancer risk and fruit intake for women from a hospital-based case-control study in Taiwan [16].

It is noteworthy that the intakes of all fruit and vegetable subgroups were inversely related to the ovarian cancer risk in the present study, suggesting that diverse compounds or nutrients contained in fruits and vegetables might be responsible for the beneficial effect. A range of mechanisms have been proposed through which such nutrients affect the cancer risk. For instance, dietary fibre may influence ovarian carcinogenesis by reducing the bioavailability of steroid hormones via changes in bacterial macroflora, lowering serum levels and availability of oestrogens, and increasing protection of lignans or other phytoestrogens [25]. Sufficient dietary folate may inhibit carcinogenesis due to its role in the one-carbon metabolism pathway, which is important for DNA synthesis, methylation and repair [26]. The antioxidant effects of vitamin C, vitamin E and carotenoids may protect ovarian cells against oxidative damage and impede malignant transformation [27]. Calcium, on the other hand, can minimize the absorption and reduce the serum level of specific fatty acids, thereby reducing the risk of ovarian cancer [28].

Dietary lycopene derived from fruit and vegetables was the only nutrient that exhibited no association with the ovarian cancer. Since carotenoids were not available from the Chinese Food Composition tables, data from the USDA nutrients database were substituted instead. The lack of information on lycopene for some commonly consumed fruit items (e.g. guava) might contribute to the observed null association in the study.

In this study, a standardized identification procedure was implemented that ensured ascertainment of cases was maximized and complete. To avoid misclassification of the case-control status, we recruited only incident patients who had been histopathologically diagnosed with epithelial ovarian cancer within the past 12 months and subsequently confirmed with pathology. All controls were carefully screened. A high response rate (98%) added weight to the conclusions. Habitual food consumption was measured using a validated and reliable questionnaire specifically developed for the southern Chinese population, with information on frequency and quantity of intake recorded in detail. To determine the effect of fruit and vegetable consumption, information on other exposures and confounding factors such as tobacco smoking, alcohol drinking and physical activity was also collected. It is possible that some ovarian cancer cases might have modified their dietary habits since the onset of the disease. To avoid reverse causation, the reference period for habitual fruit and vegetable consumption was set at five years before diagnosis for cases and five years before interview for controls. Moreover, no participant reported any changes in eating habits for medical reasons within the past five years.

Several other issues and limitations should be taken into account. A major limitation was the retrospective case-control study design so that any cause-effect relationship between fruit and vegetable consumption and ovarian cancer risk could not be established. In addition, the use of hospital-based controls may lead to selection bias if their characteristics are different from those of the general population [29]; yet community-based controls are difficult to recruit in China due to large number of refusals. The use of four hospitals reduced sampling bias, and as they serve the entire catchment region, the participants could be considered as representative of the target population. Although the recall of regular fruit and vegetable consumption should not be affected by the case-control status, dietary assessment was made based on self-report, which probably introduced some recall error in the participant response. Face-to-face interviews were thus conducted in the presence of next-of-kin to help improve the accuracy of their answers. Information bias and recall bias were unlikely because all participants were blind to the study hypothesis. Finally, using proxy values from the USDA nutrients database might lead to underestimation of certain carotenoid intakes, especially since some fruits and vegetables commonly consumed in southern China were not covered by the database. Nevertheless, it should not bias the results as the same estimation procedure was applied to both case and control groups.

CONCLUSION

Inverse associations were found between epithelial ovarian cancer risk and habitual consumption of fruits and vegetables in southern Chinese women, together with significant dose-response relationships observed for selected dietary nutrients derived from fruits and vegetables. While further prospective cohort studies are required to confirm the effect of long term consumption, it is appropriate to recommend consuming a diverse variety of fruits and vegetables for the prevention of ovarian cancer.

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Conflict of interest statement

The authors declare that there are no conflicts of interest.

Word Count: 2412

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TABLE LEGEND

Table 1. Characteristics of participants by case-control status in southern China.

Table 2. Crude and adjusted odds ratios (95% confidence intervals) of epithelial ovarian cancer risk for fruit and vegetable consumption in southern China.

Table 3. Crude and adjusted odds ratios (95% confidence intervals) of epithelial ovarian cancer risk for intake of selected nutrients derived from fruits and vegetables in southern China.

Table 4. Adjusted odds ratios (95% confidence intervals) of risk of all, serous and mucinous ovarian tumours for fruit and vegetable consumption in southern China.

Table 5. Adjusted odds ratios (95% confidence intervals) of risk of all, serous and mucinous ovarian tumours for intake of selected nutrients derived from fruits and vegetables in southern China.

Table 1. Characteristics of participants by case-control status in southern China.

Variable	Cases n (%)	Controls n (%)	p[a]
Marital status			0.83
Never married	7 (1.4%)	8 (1.6%)	
Married	449 (89.8%)	443 (88.6%)	
Widowed or divorced or separated	44 (8.8%)	49 (9.8%)	
Education level			0.90
None or primary	204 (40.8%)	197 (39.4%)	
Secondary	171 (34.2%)	175 (35.0%)	
Vocational or tertiary	125 (25.0%)	128 (25.6%)	
Parity			< 0.01
0	8 (1.6%)	14 (2.8%)	
1	172 (34.4%)	143 (28.6%)	
2	219 (43.8%)	176 (35.2%)	
≥ 3	101 (20.2%)	167 (33.4%)	
Oral contraceptive use			< 0.01
Never	417 (83.4%)	380 (76.0%)	
Ever	83 (16.6%)	120 (24.0%)	
Menopausal status			0.24
Pre	28 (5.6%)	20 (4.0%)	
Post	472 (94.4%)	480 (96.0%)	
Tubal ligation			0.95
No	325 (65.0%)	324 (64.8%)	
Yes	175 (35.0%)	176 (35.2%)	
Hormone replacement therapy			1.00
No	493 (98.6%)	493 (98.6%)	
Yes	7 (1.4%)	7 (1.4%)	
Smoking status			0.37
Never	481 (96.2%)	485 (97.0%)	
Past	14 (2.8%)	8 (1.6%)	

Current	5 (1.0%)	7 (1.4%)	
Alcohol drinking			0.16
No	352 (70.4%)	372 (74.4%)	
Yes	148 (29.6%)	128 (25.6%)	
Family history of ovarian or breast cancer in first-degree relatives			0.39
No	480 (96.0%)	485 (97.0%)	
Yes	20 (4.0%)	15 (3.0%)	
	mean (SD)	mean (SD)	
Age at interview (years)	59.1 (5.7)	59.7 (6.5)	0.10
Body mass index (5 years ago, kg/m^2)	21.7 (2.5)	21.1 (2.3)	< 0.01
Physical activity (MET-hours/week)	16.2 (14.1)	18.8 (13.0)	< 0.01
Fresh meat consumption (g/day)	288 (157.9)	285 (166.9)	0.74
Seafood consumption (g/day)	122 (74.0)	141 (136.6)	< 0.01
Vegetable consumption (g/day)	582.7 (250.2)	983.3 (739.9)	< 0.001
Fruit consumption (g/day)	324.2 (161.9)	477.3 (362.1)	< 0.001

[a] Chi-square or t-test for difference between cases and controls

Table 2. Crude and adjusted odds ratios (95% confidence intervals) of epithelial ovarian cancer risk for fruit and vegetable consumption in southern China.

Daily intake (g)	**Cases** n (%)	**Controls** n (%)	**Crude OR**[a] (95% CI)	**Adjusted OR**[b] (95% CI)	**p**[b]
Total vegetables					< 0.001
≤ 690	392 (78.4%)	165 (33.0%)	1	1	
691 – 970	78 (15.6%)	168 (33.6%)	0.20 (0.14, 0.28)	0.17 (0.12, 0.24)	
> 970	30 (6.0%)	167 (33.4%)	0.08 (0.05, 0.13)	0.07 (0.04, 0.12)	
Total fruits					< 0.001
≤ 320	287 (57.4%)	170 (34.0%)	1	1	
321 – 490	144 (28.8%)	167 (33.4%)	0.53 (0.39, 0.71)	0.49 (0.36, 0.67)	
> 490	69 (13.8%)	163 (32.6%)	0.31 (0.22, 0.44)	0.30 (0.21, 0.44)	

[a] From separate logistic regression models adjusting for age at interview (years, continuous) and total energy intake (kcal/day, continuous).

[b] From separate logistic regression models adjusting for age at interview (years, continuous), education level (none or primary, secondary, vocational or tertiary), body mass index (5 years ago, kg/m^2, continuous), physical activity (MET-hours/week, continuous), fresh meat consumption (g/day, continuous), seafood consumption (g/day, continuous), total energy intake (kcal/day, continuous), parity (continuous), oral contraceptive use (never, ever), menopausal status (pre, post), tubal ligation (no, yes), hormone replacement therapy (no, yes), smoking status (never, past, current), alcohol drinking (no, yes), and family history of ovarian or breast cancer in first-degree relatives (no, yes).

Table 3. Crude and adjusted odds ratios (95% confidence intervals) of epithelial ovarian cancer risk for intake of selected nutrients derived from fruits and vegetables in southern China.

Daily intake	**Cases** n (%)	**Controls** n (%)	**Crude OR**[a] (95% CI)	**Adjusted OR**[b] (95% CI)	**p**[b]
Dietary fibre (g)					< 0.001
< 13.0	357 (71.4%)	165 (33.0%)	1	1	
13.0 – 17.7	108 (21.6%)	166 (33.2%)	0.31 (0.23, 0.43)	0.28 (0.20, 0.38)	
> 17.7	35 (7.0%)	169 (33.8%)	0.11 (0.07, 0.17)	0.11 (0.07, 0.17)	
Vitamin C (mg)					< 0.001
< 285.0	382 (76.4%)	165 (33.0%)	1	1	
285.0 – 390.0	85 (17.0%)	169 (33.8%)	0.22 (0.16, 0.31)	0.21 (0.15, 0.29)	
> 390.0	33 (6.6%)	166 (33.2%)	0.10 (0.06, 0.15)	0.09 (0.06, 0.15)	
Vitamin E (mg)					< 0.001
< 7.3	361 (72.2%)	168 (33.6%)	1	1	
7.3 – 10.8	98 (19.6%)	166 (33.2%)	0.29 (0.21, 0.39)	0.25 (0.18, 0.36)	
> 10.8	41 (8.2%)	166 (33.2%)	0.13 (0.09, 0.20)	0.13 (0.08, 0.20)	
Niacin (mg)					< 0.001
< 6.5	389 (77.8%)	165 (33.0%)	1	1	
6.5 – 8.6	74 (14.8%)	168 (33.6%)	0.19 (0.14, 0.27)	0.16 (0.12, 0.23)	
> 8.6	37 (7.4%)	167 (33.4%)	0.11 (0.07, 0.17)	0.10 (0.06, 0.16)	
Folate (μg)					< 0.001
< 112.3	370 (74.0%)	169 (33.8%)	1	1	

112.3 – 160.0	72 (14.4%)	164 (32.8%)	0.21 (0.15, 0.29)	0.19 (0.14, 0.28)	
> 160.0	58 (11.6%)	167 (33.4%)	0.19 (0.13, 0.27)	0.18 (0.12, 0.26)	
α-carotene (μg)					0.001
< 28.2	228 (45.6%)	167 (33.4%)	1	1	
28.2 – 56.5	152 (30.4%)	164 (32.8%)	0.69 (0.51, 0.93)	0.78 (0.56, 1.07)	
> 56.5	120 (24.0%)	169 (33.8%)	0.56 (0.41, 0.77)	0.53 (0.37, 0.74)	
β-carotene (μg)					< 0.001
< 1203	250 (50.0%)	166 (33.2%)	1	1	
1203 – 2728	180 (36.0%)	169 (33.8%)	0.73 (0.55, 0.98)	0.70 (0.52, 0.95)	
> 2728	70 (14.0%)	165 (33.0%)	0.33 (0.23, 0.47)	0.28 (0.19, 0.41)	
β-cryptoxanthin (μg)					< 0.001
< 133.5	243 (48.6%)	166 (33.2%)	1	1	
133.5 – 256.0	144 (28.8%)	167 (33.4%)	0.63 (0.46, 0.85)	0.61 (0.44, 0.84)	
> 256.0	113 (22.6%)	167 (33.4%)	0.51 (0.73, 0.70)	0.45 (0.32, 0.64)	
lutein + zeaxamthin (μg)					< 0.001
< 160.0	243 (48.6%)	170 (34.0%)	1	1	
160.0 – 250.0	144 (28.8%)	165 (33.0%)	0.58 (0.43, 0.77)	0.55 (0.40, 0.75)	
> 250.0	113 (22.6%)	165 (33.0%)	0.23 (0.16, 0.34)	0.22 (0.15, 0.32)	
lycopene (μg)					0.289
< 405.0	166 (33.2%)	161 (32.2%)	1	1	
405.0 – 811.0	167 (33.4%)	168 (33.6%)	0.87	0.77	

			(0.64, 1.19)	(0.55, 1.07)	
> 811.0	167 (33.4%)	171 (34.2%)	1.03 (0.76, 1.41)	0.91 (0.64, 1.28)	
Potassium (mg)					< 0.001
< 631.0	334 (66.8%)	166 (33.2%)	1	1	
631.0 – 874.0	109 (21.8%)	168 (33.6%)	0.33 (0.24, 0.44)	0.30 (0.22, 0.42)	
> 874.0	57 (11.4%)	166 (33.2%)	0.21 (0.15, 0.30)	0.19 (0.13, 0.29)	
Magnesium (mg)					< 0.001
< 71.3	341 (68.2%)	167 (33.4%)	1	1	
71.3 – 99.3	107 (21.4%)	166 (33.2%)	0.32 (0.23, 0.43)	0.30 (0.22, 0.42)	
> 99.3	52 (10.4%)	167 (33.4%)	0.19 (0.13, 0.28)	0.18 (0.12, 0.27)	
Calcium (mg)					< 0.001
< 182.0	372 (74.4%)	168 (33.6%)	1	1	
182.0 – 256.0	86 (17.2%)	167 (33.4%)	0.25 (0.18, 0.34)	0.23 (0.17, 0.33)	
> 256.0	42 (8.4%)	165 (33.0%)	0.13 (0.09, 0.20)	0.13 (0.08, 0.19)	
Iron (mg)					< 0.001
< 4.60	376 (75.2%)	168 (33.6%)	1	1	
4.60 – 6.23	79 (15.8%)	166 (33.2%)	0.22 (0.16, 0.30)	0.20 (0.14, 0.28)	
> 6.23	45 (9.0%)	166 (33.2%)	0.14 (0.10, 0.21)	0.14 (0.09, 0.21)	

[a] From separate logistic regression models adjusting for age at interview (years, continuous) and total energy intake (kcal/day, continuous).

[b] From separate logistic regression models adjusting for age at interview (years, continuous), education level (none or primary, secondary, vocational or tertiary), body mass index (5 years

ago, kg/m^2, continuous), physical activity (MET-hours/week, continuous), fresh meat consumption (g/day, continuous), seafood consumption (g/day, continuous), total energy intake (kcal/day, continuous), parity (continuous), oral contraceptive use (never, ever), menopausal status (pre, post), tubal ligation (no, yes), hormone replacement therapy (no, yes), smoking status (never, past, current), alcohol drinking (no, yes), and family history of ovarian or breast cancer in first-degree relatives (no, yes).

Table 4. Adjusted odds ratios (95% confidence intervals) of risk of all, serous and mucinous ovarian tumours for fruit and vegetable consumption in southern China.

	Cases						**Controls**
	All (n = 500)		**Serous** (n = 250)		**Mucinous** (n = 80)		(n = 500)
Daily intake (g)	n (%)	Adjusted OR[a] (95% CI)	n (%)	Adjusted OR[a] (95% CI)	n (%)	Adjusted OR[a] (95% CI)	n (%)
Total vegetables		p[b] < 0.001		p[b] < 0.001		p[b] < 0.001	
≤ 690	392 (78.4%)	1	199 (79.6%)	1	65 (81.3%)	1	165 (33.0%)
691 – 970	78 (15.6%)	0.17 (0.12, 0.24)	41 (16.4%)	0.18 (0.12, 0.28)	10 (12.5%)	0.12 (0.06, 0.25)	168 (33.6%)
> 970	30 (6.0%)	0.07 (0.04, 0.12)	10 (4.0%)	0.05 (0.02, 0.10)	5 (6.3%)	0.07 (0.02, 0.19)	167 (33.4%)
Total fruits		p[b] < 0.001		p[b] < 0.001		p[b] = 0.001	
≤ 320	287 (57.4%)	1	147 (58.8%)	1	41 (51.3%)	1	170 (34.0%)
321 – 490	144 (28.8%)	0.49 (0.36, 0.67)	74 (29.6%)	0.49 (0.33, 0.72)	30 (37.5%)	0.69 (0.39, 1.22)	167 (33.4%)
> 490	69 (13.8%)	0.30 (0.21, 0.44)	29 (11.6%)	0.25 (0.15, 0.41)	9 (11.3%)	0.26 (0.12, 0.57)	163 (32.6%)

[a] From separate logistic regression models adjusting for age at interview (years, continuous), education level (none or primary, secondary, vocational or tertiary), body mass index (5 years ago, kg/m^2, continuous), physical activity (MET-hours/week, continuous), fresh meat consumption (g/day, continuous), seafood consumption (g/day, continuous), total energy intake (kcal/day, continuous), parity (continuous), oral contraceptive use (never, ever), menopausal status (pre, post), tubal ligation (no, yes), hormone replacement therapy (no, yes),

smoking status (never, past, current), alcohol drinking (no, yes), and family history of ovarian or breast cancer in first-degree relatives (no, yes).

[b] Test for linear trend with exposure variable being continuous (g/day).

Table 5. Adjusted odds ratios (95% confidence intervals) of risk of all, serous and mucinous ovarian tumours for intake of selected nutrients derived from fruits and vegetables in southern China.

	Cases						**Controls**
	All (n = 500)		**Serous** (n = 250)		**Mucinous** (n = 80)		(n = 500)
Daily intake	n (%)	Adjusted OR[a] (95% CI)	n (%)	Adjusted OR[a] (95% CI)	n (%)	Adjusted OR[a] (95% CI)	n (%)
Dietary fibre (g)		$p^b < 0.001$		$p^b < 0.001$		$p^b < 0.001$	
< 13.0	357 (71.4%)	1	182 (72.8%)	1	57 (71.3%)	1	165 (33.0%)
13.0 – 17.7	108 (21.6%)	0.28 (0.20, 0.38)	55 (22.0%)	0.29 (0.20, 0.44)	21 (26.3%)	0.33 (0.18, 0.59)	166 (33.2%)
> 17.7	35 (7.0%)	0.11 (0.07, 0.17)	13 (5.2%)	0.08 (0.04, 0.15)	2 (2.5%)	0.04 (0.01, 0.16)	169 (33.8%)
Vitamin C (mg)		$p^b < 0.001$		$p^b < 0.001$		$p^b < 0.001$	
< 285.0	382 (76.4%)	1	194 (77.6%)	1	63 (78.8%)	1	165 (33.0%)
285.0 – 390.0	85 (17.0%)	0.21 (0.15, 0.29)	44 (17.6%)	0.22 (0.14, 0.33)	11 (13.8%)	0.15 (0.07, 0.31)	169 (33.8%)
> 390.0	33 (6.6%)	0.09 (0.06, 0.15)	12 (4.8%)	0.07 (0.04, 0.14)	6 (7.5%)	0.11 (0.04, 0.26)	166 (33.2%)
Vitamin E (mg)		$p^b < 0.001$		$p^b < 0.001$		$p^b < 0.001$	
< 7.3	361 (72.2%)	1	181 (72.4%)	1	58 (72.5%)	1	168 (33.6%)
7.3 – 10.8	98 (19.6%)	0.25 (0.18, 0.36)	55 (22.0%)	0.28 (0.19, 0.42)	16 (20.0%)	0.24 (0.12, 0.45)	166 (33.2%)
> 10.8	41	0.13	14	0.09	6	0.11	166

	(8.2%)	(0.08, 0.20)	(5.6%)	(0.05, 0.17)	(7.5%)	(0.04, 0.27)	(33.2%)
Niacin (mg)		$p^b < 0.001$		$p^b < 0.001$		$p^b < 0.001$	
< 6.5	389 (77.8%)	1	197 (78.8%)	1	65 (81.3%)	1	165 (33.0%)
6.5 – 8.6	74 (14.8%)	0.16 (0.12, 0.23)	40 (16.0%)	0.18 (0.12, 0.28)	11 (13.8%)	0.15 (0.07, 0.30)	168 (33.6%)
> 8.6	37 (7.4%)	0.10 (0.06, 0.16)	13 (5.2%)	0.07 (0.04, 0.13)	4 (5.0%)	0.06 (0.02, 0.17)	167 (33.4%)
Folate (µg)		$p^b < 0.001$		$p^b < 0.001$		$p^b < 0.001$	
< 112.3	370 (74.0%)	1	180 (72.0%)	1	64 (80.0%)	1	169 (33.8%)
112.3 – 160.0	72 (14.4%)	0.19 (0.14, 0.28)	36 (14.4%)	0.20 (0.13, 0.32)	12 (15.0%)	0.18 (0.09, 0.36)	164 (32.8%)
> 160.0	58 (11.6%)	0.18 (0.12, 0.26)	34 (13.6%)	0.21 (0.13, 0.34)	4 (5.0%)	0.06 (0.02, 0.19)	167 (33.4%)
α-carotene (µg)		$p^b < 0.001$		$p^b = 0.001$		$p^b = 0.091$	
< 28.2	228 (45.6%)	1	111 (44.4%)	1	37 (46.3%)	1	167 (33.4%)
28.2 – 56.5	152 (30.4%)	0.78 (0.56, 1.07)	79 (31.6%)	0.88 (0.59, 1.32)	24 (30.0%)	0.73 (0.40, 1.35)	164 (32.8%)
> 56.5	120 (24.0%)	0.53 (0.37, 0.74)	60 (24.0%)	0.56 (0.36, 0.85)	19 (23.8%)	0.51 (0.27, 0.97)	169 (33.8%)
β-carotene (µg)		$p^b < 0.001$		$p^b < 0.001$		$p^b < 0.001$	
< 1203	250 (50.0%)	1	130 (52.0%)	1	43 (53.8%)	1	166 (33.2%)
1203 – 2728	180 (36.0%)	0.70 (0.52, 0.95)	85 (34.0%)	0.68 (0.47, 0.99)	25 (31.3%)	0.52 (0.29, 0.91)	169 (33.8%)
> 2728	70 (14.0%)	0.28 (0.19, 0.41)	35 (14.0%)	0.29 (0.18, 0.47)	12 (15.0%)	0.26 (0.12, 0.53)	165 (33.0%)

β-crypto-xanthin (μg)		$p^b < 0.001$		$p^b < 0.001$		$p^b = 0.041$	
< 133.5	243 (48.6%)	1	125 (50.0%)	1	33 (41.3%)	1	166 (33.2%)
133.5 – 256.0	144 (28.8%)	0.61 (0.44, 0.84)	68 (27.2%)	0.59 (0.39, 0.87)	29 (36.3%)	0.88 (0.49, 1.59)	167 (33.4%)
> 256.0	113 (22.6%)	0.45 (0.32, 0.64)	57 (22.8%)	0.44 (0.29, 0.67)	18 (22.5%)	0.52 (0.27, 1.02)	167 (33.4%)
lutein + zeaxamthin (μg)		$p^b < 0.001$		$p^b < 0.001$		$p^b < 0.001$	
< 160.0	243 (48.6%)	1	145 (58.0%)	1	42 (52.5%)	1	170 (34.0%)
160.0 – 250.0	144 (28.8%)	0.55 (0.40, 0.75)	79 (31.6%)	0.58 (0.40, 0.85)	31 (38.8%)	0.68 (0.39, 1.19)	165 (33.0%)
> 250.0	113 (22.6%)	0.22 (0.15, 0.32)	26 (10.4%)	0.21 (0.12, 0.35)	7 (8.8%)	0.18 (0.07, 0.43)	165 (33.0%)
lycopene (μg)		$p^b = 0.002$		$p^b = 0.002$		$p^b = 0.476$	
< 405.0	166 (33.2%)	1	84 (33.6%)	1	27 (33.8%)	1	161 (32.2%)
405.0 – 811.0	167 (33.4%)	0.77 (0.55, 1.07)	87 (34.8%)	0.76 (0.51, 1.15)	26 (32.5%)	0.73 (0.39, 1.38)	168 (33.6%)
> 811.0	167 (33.4%)	0.91 (0.64, 1.28)	79 (31.6%)	0.82 (0.54, 1.26)	27 (33.8%)	1.05 (0.55, 2.00)	171 (34.2%)
Potassium (mg)		$p^b < 0.001$		$p^b < 0.001$		$p^b < 0.001$	
< 631.0	334 (66.8%)	1	168 (67.2%)	1	52 (65.0%)	1	166 (33.2%)
631.0 – 874.0	109 (21.8%)	0.30 (0.22, 0.42)	54 (21.6%)	0.31 (0.20, 0.46)	20 (25.0%)	0.34 (0.19, 0.62)	168 (33.6%)
> 874.0	57 (11.4%)	0.19 (0.13, 0.29)	28 (11.2%)	0.19 (0.12, 0.32)	8 (10.0%)	0.18 (0.08, 0.40)	166 (33.2%)

Magnesium (mg)		$p^b < 0.001$		$p^b < 0.001$		$p^b < 0.001$	
< 71.3	341 (68.2%)	1	171 (68.4%)	1	57 (71.3%)	1	167 (33.4%)
71.3 – 99.3	107 (21.4%)	0.30 (0.22, 0.42)	52 (20.8%)	0.30 (0.20, 0.45)	18 (22.5%)	0.30 (0.17, 0.55)	166 (33.2%)
> 99.3	52 (10.4%)	0.18 (0.12, 0.27)	27 (10.8%)	0.20 (0.12, 0.33)	5 (6.3%)	0.10 (0.04, 0.26)	167 (33.4%)
Calcium (mg)		$p^b < 0.001$		$p^b < 0.001$		$p^b < 0.001$	
< 182.0	372 (74.4%)	1	185 (74.0%)	1	64 (80.0%)	1	168 (33.6%)
182.0 – 256.0	86 (17.2%)	0.23 (0.17, 0.33)	41 (16.4%)	0.24 (0.15, 0.36)	12 (15.0%)	0.18 (0.09, 0.37)	167 (33.4%)
> 256.0	42 (8.4%)	0.13 (0.08, 0.19)	24 (9.6%)	0.15 (0.09, 0.25)	4 (5.0%)	0.06 (0.02, 0.19)	165 (33.0%)
Iron (mg)		$p^b < 0.001$		$p^b < 0.001$		$p^b < 0.001$	
< 4.60	376 (75.2%)	1	188 (75.2%)	1	66 (82.5%)	1	168 (33.6%)
4.60 – 6.23	79 (15.8%)	0.20 (0.14, 0.28)	37 (14.8%)	0.18 (0.12, 0.28)	11 (13.8%)	0.14 (0.07, 0.29)	166 (33.2%)
> 6.23	45 (9.0%)	0.14 (0.09, 0.21)	25 (10.0%)	0.16 (0.10, 0.27)	3 (3.8%)	0.05 (0.02, 0.18)	166 (33.2%)

[a] From separate logistic regression models adjusting for age at interview (years, continuous), education level (none or primary, secondary, vocational or tertiary), body mass index (5 years ago, kg/m^2, continuous), physical activity (MET-hours/week, continuous), fresh meat consumption (g/day, continuous), seafood consumption (g/day, continuous), total energy intake (kcal/day, continuous), parity (continuous), oral contraceptive use (never, ever), menopausal status (pre, post), tubal ligation (no, yes), hormone replacement therapy (no, yes),

smoking status (never, past, current), alcohol drinking (no, yes), and family history of ovarian or breast cancer in first-degree relatives (no, yes).

[b] Test for linear trend with exposure variable being continuous.