


ORIGINAL ARTICLE

Peanut consumption associated with a reduced risk of esophageal squamous cell carcinoma: A case-control study in a high-risk area in China

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Keywords

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Abstract

Background: Esophageal cancer (EC) is ranked as the top 10th malignancy in China; however, an association between peanut consumption and EC risk has not yet been identified. This study explored the protective effects of peanut consumption against the risk of developing esophageal squamous cell carcinoma (ESCC) in a high-risk area.

Methods: A case-control design was applied, with frequency matching by age and gender. A logistic regression model was used to estimate odds ratios (OR) and 95% confidence intervals (CI). Two hundred and twenty-two cases and 222 controls were recruited from Yanting County from 2011 to 2012.

Results: Peanut consumption 1–3 times per week reduced cancer risk by 38% (OR 0.62, 95% CI 0.34–1.13), while consumption ≥ 4 times per week reduced the risk by 70% (OR 0.31, 95% CI 0.16–0.59). A significant association was observed among individuals with negative family EC history (OR 0.25, 95% CI 0.12–0.49).

Conclusion: Peanut consumption may act as a protector against the occurrence of ESCC in high-risk areas, thus production and consumption should be promoted in high-risk areas in order to reduce the ESCC burden.

Introduction

China has the highest esophageal cancer (EC) burden, accounting for nearly 50% of new cases and specific deaths worldwide in 2012.¹ From 2003, EC incidence and mortality have been declining in China.² In cancer registration areas, the age-standardized incidence rate decreased from 39.5/100 000 in 1989 to 23.0/100 000 in 2008, with an average annual percentage change of -3.3% (95% confidence interval [CI] -2.8% – -3.7%).² Many factors have contributed to the reduction in EC incidence, such as improvements in economic status, screening, and dietary intervention. However, EC populations in high-risk areas

still suffer from esophageal squamous cell carcinoma (ESCC), the main pathological type of EC in China.³ Exploring the significant factors of ESCC risk may assist vulnerable people in high-risk areas.

Peanut consumption is associated with decreased overall and cardiovascular disease-specific mortality in individuals from low social economic status groups in China.⁴ Previous studies have reported the protective effects of peanut consumption against cancer risk. In the Nurses' Health Study, women consuming nuts ≥ 2 /week had a 13% lower risk of developing colorectal cancer compared to those who rarely consumed any form of nuts; however, the association was not statistically significant (relative risk [RR] 0.87, 95% CI

0.72–1.05; P for trend = 0.06).⁵ Consumption ≥ 2 /week was related to a significantly lower risk of developing pancreatic cancer (RR 0.65, 95% CI 0.47–0.92; P for trend = 0.007).⁵ Among Japanese women, peanut consumption was shown to reduce the risk of developing endometrial adenocarcinoma by 52%.⁶ Even in benign breast disease in women, consumption of peanut oil during pre-adolescence and adolescence was associated with a 50% lower risk.⁷ Increasing peanut consumption has been associated with a reduced risk of obesity, type II diabetes and some cancers. However, the association between peanut consumption and ESCC risk is unknown. Peanuts are generally affordable to Chinese people and there are a number of areas within China that produce peanuts. Sichuan Province is one of the top 10 peanut production areas, with annual production of 0.6 million tons in 2010.⁸ Yanting is a high-risk area for ESCC in Sichuan province, with an annual rate five times higher than the national average. This study examines the association of peanut consumption with ESCC risk in a high-risk population in Yanting County.

Methods

Study design

A case-control design was applied in this study. Controls were frequency-matched with ESCC cases by age and gender.

Study population

Incident cases (i.e. the interval between diagnosis and interview was < 3 months) aged 40–69 years and pathologically diagnosed with primary ESCC between 2011 and 2012 were recruited from Yanting Cancer Hospital. Individuals with no diagnosis of cancer who participated in an EC screening program for local Yanting people aged 40–69 between 2011 and 2012 were defined as controls. The participation rate of controls was $> 95\%$. The cases and controls were frequency-matched by gender and five-year age intervals. Endoscopy with iodine staining was used to detect precancerous lesions.⁹

Item definition

Dietary factors including frequencies of consumption of peanuts, preserved vegetables, fruits, fresh vegetables, and corn were collected during the interview. In Yanting, preserving vegetables is a common process. Vegetables are boiled and kept in a sealed container to ferment for about two weeks. Body mass index (BMI) was estimated by dividing weight in kilograms by current height in squared meters. “Ever smoker” was defined as smoking $>$

100 cigarettes or equivalent use of a pipe over a lifetime.¹⁰ “Ever alcohol drinkers” were defined as individuals who consumed alcohol at least once per month.¹¹ Family EC history was considered as EC occurrence in first-degree genetic relatives (parents, siblings and offspring).

Data collection

Two health workers from Yanting Cancer Hospital attended workshop training on data collection. Interviewers collected socioeconomic, dietary, and other lifestyle data using a Modified Food frequency questionnaire.¹² The collected data reflected the habits of the previous year. Options for consumption frequency included: < 1 /month, 1–3 times/month, 1–3 times/week, 4–6 times/week, 1/day and ≥ 2 /day.¹² The repeatability and validity of the modified questionnaire were tested among the rural population.¹² The same staff conducted data collection among cases and controls. The study subjects were blinded to the study hypotheses.

This study was conducted according to the guidelines laid down in the Declaration of Helsinki. The Ethical Committee of Shijitan Hospital, Capital Medical University approved all procedures involving human subjects and written informed consent was obtained from all participants.

Statistical analysis

SPSS version 17.0 (SPSS Inc., Chicago, IL, USA) was used to analyze the data. Missing data was not included in the analysis. Differences in age and BMI between the groups were estimated using t -tests. Gender, smoking status, alcohol consumption status, family EC history, and frequency of fresh vegetables and corn consumption were analyzed by chi-square test. Education level, and frequencies of fruit, preserved vegetables, and peanut consumption were determined between the two groups using a Cochran–Armitage test. Odds ratios (ORs) and 95% confidence intervals of peanut consumption between ESCC cases and controls were estimated by unconditional logistic regression, with further adjustments for age, gender, family EC history, education level, BMI, smoking, alcohol consumption, and fruit and preserved vegetable consumption. The P for trend was estimated by treating categorical variables as continuous variables in the logistic model. Sensitivity analyses were processed using stratifications of age, gender, and family cancer history. All tests were two-sided, with a significance level of 0.05.

Results

In total, 222 cases and 222 matched controls were enrolled in the study. There were no significant differences in age,

gender, BMI, education level, smoking or alcohol consumption between the groups ($P > 0.05$) (Table 1). However, ESCC cases were 20.8% more likely to have a positive family EC history than control subjects ($P < 0.05$).

Participants with ESCC were less likely to consume peanuts, with 21.6% of cases consuming peanuts ≥ 4 times/week compared to 42.2% of controls ($P < 0.001$) (Table 2). ESCC patients were more likely to consume preserved vegetables, with 35.7% of cases and 10.0% of controls consuming preserved vegetables ≥ 4 times/week ($P < 0.001$). Fifteen percent of cases compared to 31% of controls consumed fruit ≥ 1 /week and the difference was significant ($P < 0.001$). Frequencies of fresh vegetables and corn consumption were similar between the two groups ($P > 0.05$). The crude OR of ESCC patients who drank tea was 0.73 (95% CI 0.60–0.90) for ESCC.

After further adjustments, the consumption of peanuts 1–3/week reduced the OR of ESCC to 0.62 (95%CI 0.34–1.13), while consumption ≥ 4 /week reduced the risk to 0.31 (OR 0.31, 95% CI 0.16–0.59) (Table 3). Preserved vegetable consumption ≥ 4 /week increased the risk 5.69-fold. Consuming fruit ≥ 1 /week and drinking tea were associated with 53% (OR 0.53, 95% CI 0.33–0.97) and 42% reduced risks of developing ESCC ($P < 0.05$), respectively, but a positive family history of EC increased the risk 4.55-fold ($P < 0.05$).

In stratified analyses, the beneficial effects of peanut consumption observed were significant, regardless of age or gender (Table 4). In individuals without family EC

history, peanut consumption frequency of ≥ 4 /week was associated with a 75% reduced risk of developing ESCC (OR 0.25, 95% CI 0.12–0.49).

Discussion

Peanut intake has beneficial effects on overall mortality, cardiovascular disease, and obesity reduction.^{4,13,14} The Nurses' Health Study reported that the multivariate RR for type 2 diabetes was 0.79 (95% CI 0.68–0.91; P for trend < 0.001) in women consuming peanut butter ≥ 5 /week compared to those who never/almost never ate peanut butter.¹⁵ In this population-based case-control study, peanut consumption ≥ 4 /week was associated with an OR for developing ESCC of 0.31. The inverse association was consistent within strata defined by age and gender.

Preserved vegetable consumption was related to a higher risk of developing ESCC, which was consistent with the results of previous studies.¹⁶ Our results indicated that fruit consumption had a protective effect against developing ESCC, consistent with the results of previous studies.¹⁷ A European prospective investigation into cancer and nutrition found that drinking tea was related to a reduced risk of developing ESCC,¹⁸ and this protective association was consistent with the results of a systematic review (OR 0.46–0.64).¹⁹ The association between peanut consumption and ESCC risk has not been comprehensively investigated; however, high nut consumption has been associated with a lower risk of developing ESCC.²⁰ Nut consumption has also been linked to lower risk in other cancer sites. The Nurses' Health Study reported that women who consumed nuts ≥ 2 /week had a lower risk of developing pancreatic cancer (RR 0.68, 95% CI 0.48–0.95).²¹ The frequency of nut consumption has also been reported to be associated with a lower risk of developing colorectal cancer (RR 0.87, 95% CI 0.72–1.05).⁵ Among Taiwanese women, frequent peanut consumption was reported to reduce the RR of colorectal cancer to 0.42 (95% CI 0.21–0.84).²² Higher peanut consumption has also been associated with a lower risk of developing endometrial adenocarcinoma (OR 0.48, 95% CI 0.27–0.86) in Japanese women.⁶ Young women consuming peanuts or peanut products face a lower risk of benign breast disease (OR 0.56, 95% CI 0.35–0.87), and a significant protective effect was even observed in girls with a positive family history of breast cancer.⁷

Peanuts and peanut products are sources of beta-sitosterol, which has anticancer properties.²³ Diet-derived beta-sitosterol intake is significantly associated with a lower risk of developing ESCC.²⁴ However, if all diet intakes were adjusted, the association between beta-sitosterol and cancer risk was no longer significant, indicating that the anti-

Table 1 General characteristics between ESCC cases and controls

Characteristic	Control	ESCC	<i>P</i>
Age (mean \pm SD)	59.5 \pm 5.29	58.7 \pm 5.78	0.161
Gender			—
Male	146 (65.8)	146 (65.8)	
Female	76 (34.2)	76 (34.2)	
BMI (mean \pm SD)	22.4 \pm 3.28	22.7 \pm 3.18	0.295
Education level†			0.76
< Primary school	83 (40.1)	83 (38.1)	
Primary school	73 (35.3)	83 (38.1)	
Junior high school	46 (22.2)	42 (19.3)	
> Junior high school	5 (2.4)	10 (4.6)	
Smoking			0.364
Never	108 (48.6)	98 (44.3)	
Current/ever	114 (51.4)	123 (55.7)	
Alcohol consumption			0.885
Never	106 (47.7)	104 (47.1)	
Current/ever	116 (52.3)	117 (52.9)	
Family history of EC			< 0.001
No	192 (88.1)	148 (67.3)	
Yes	26 (11.9)	72 (32.7)	

†Cochran–Armitage test. BMI, body mass index; EC, esophageal cancer; ESCC, esophageal squamous cell carcinoma; SD, standard deviation.

Table 2 Frequency of consumption between ESCC cases and controls

Food type	Control	ESCC	<i>P</i>	Crude OR	95% CI
Peanuts†			< 0.001		
< 1/week	39 (17.9)	80 (36.0)		1.00	
< 4/weeks	87 (39.9)	94 (42.3)		0.53	0.33–0.85
≥ 4/weeks	92 (42.2)	48 (21.6)		0.25	0.15–0.43
Preserved vegetables†			< 0.001		
< 1/month	86 (38.9)	59 (26.7)		1.00	
< 1/week	37 (16.7)	18 (8.1)		0.71	0.37–1.36
< 4/weeks	76 (34.4)	65 (29.4)		1.25	0.78–1.99
≥ 4/weeks	22 (10.0)	79 (35.7)		5.23	2.94–9.32
Fruit†			< 0.001		
< 1/month	98 (44.7)	125 (56.6)		1.00	
< 1/week	53 (24.2)	62 (28.1)		0.92	0.58–1.44
≥ 1/week	68 (31.1)	34 (15.4)		0.39	0.24–0.64
Fresh vegetables			0.086		
< 2/days	111 (50.2)	129 (58.4)		1.00	
≥ 2/week	110 (49.8)	92 (41.6)		0.72	0.49–1.05
Corn			0.131		
< 1/day	24 (10.9)	15 (6.8)		1.00	
≥ 1/day	197 (89.1)	206 (93.2)		1.67	0.85–3.28
Tea			0.002		
No	73 (32.9)	104(47.5)		1.00	
Yes	149 (67.1)	115(52.5)		0.73	0.60–0.90

†Cochran–Armitage test. CI, confidence interval; ESCC, esophageal squamous cell carcinoma; OR, odds ratio.

Table 3 Multivariate analysis between factors and ESCC†

Food type	OR _{adjusted}	95% CI	<i>P</i>	<i>P</i> for trend
Peanuts				< 0.001
< 1/week	1.00			
1–3/weeks	0.62	0.34, 1.13	0.116	
≥ 4/weeks	0.31	0.16, 0.59	<0.001	
Preserved vegetables				< 0.001
< 1/month	1.00			
1–3/months	0.83	0.38, 1.80	0.633	
1–3/weeks	1.36	0.78, 2.36	0.279	
≥ 4/weeks	5.69	2.75, 11.81	< 0.001	
Fruit				0.049
< 1/month	1.00			
1–3/months	0.98	0.57, 1.69	0.946	
≥ 1/week	0.53	0.28, 0.97	0.040	
Tea				
No	1.00			
Yes	0.58	0.33, 1.00	0.049	
Family history of EC				
No	1.00			
Yes	4.54	2.40, 8.59	< 0.001	

†Further adjusted by age, gender, smoking, alcohol consumption, and education level. CI, confidence interval; EC, esophageal cancer; ESCC, esophageal squamous cell carcinoma; OR, odds ratio.

cancer benefits were derived from food intake. As previously reported, beta-sitosterol can reduce cyclin B1 and cdc2 levels and increase p21waf1/cip1 in malignant cell lines.²⁵ In addition, resveratrol is a natural phytoalexin in peanuts and peanut products.²⁶ Resveratrol supplementation has proven effective for preventing esophagitis initiation and carcinogenic progression to esophageal adenocarcinoma in male Sprague Dawley rats.²⁷ Resveratrol suppressed esophageal adenocarcinoma cell line proliferation and the underlying mechanisms included the reduction of p27Kip1, a cyclin-dependent kinase inhibitor, decrease of 26S proteasome activity, and increased levels of SPK2 of p27Kip1-E3 ubiquitin ligase.²⁸ Resveratrol also induced ESCC cell apoptosis and the cytotoxicity was promoted from resveratrol-causing autophagy in the cancer cells.²⁹ Peanuts also contain other nutrients and bioactive compounds, such as vitamins (e.g. folate, niacin, vitamin E) and phytochemicals (e.g. carotenoids, and flavonoids) with antioxidant, anti-inflammatory, and anticancer properties.³⁰ Vitamin E and beta-carotene were reported to produce a protective effect against ESCC in a young Chinese population.³¹

An association between peanut consumption and ESCC risk has not been well established. Our results provide population-based case-control data indicating a significant protective effect. Beta-sitosterol and resveratrol are candidate components, extending the anti-carcinogenic

Table 4 Subgroup analyses of association between peanut consumption and ESCC†

Age	Peanut	N (ESCC/control)	Adjusted OR	95% CI	
< 60	< 1/week	35/19	1		
	1–3/weeks	46/42	0.67	0.29, 1.55	
	≥ 4/weeks	25/41	0.32	0.12, 0.81	
≥ 60	< 1/week	45/20	1		
	< 4/weeks	48/45	0.47	0.21, 1.05	
	≥ 4/weeks	23/51	0.23	0.09, 0.55	
Gender	Male	< 1/week	41/23	1	
		1–3/weeks	71/60	0.81	0.40, 1.65
		≥ 4/weeks	34/61	0.37	0.17, 0.80
	Female	< 1/week	39/16	1	
		1–3/weeks	23/27	0.23	0.07, 0.76
		≥ 4/weeks	14/31	0.14	0.04, 0.53
Family EC history	Yes	< 1/week	22/7	1	
		1–3/weeks	28/10	0.79	0.16, 3.95
		≥ 4/weeks	22/8	0.52	0.09, 2.88
	No	< 1/week	57/32	1	
		1–3/weeks	65/76	0.58	0.31, 1.08
		≥ 4/weeks	26/81	0.25	0.12, 0.49

†Adjusted for age; gender; family EC history; education level; BMI; smoking; and alcohol, fruit, and preserved vegetable consumption. CI, confidence interval; EC, esophageal cancer; ESCC, esophageal squamous cell carcinoma; OR, odds ratio.

features of peanuts. This does not rule out the role of other components, such as folic acid, calcium, dietary fiber, protease inhibitors, oligosaccharides, saponins, and isoflavones in protecting against ESCC. However, peanut or peanut product consumption was related to a 3.0-fold increased risk of hepatocellular carcinoma, and in Henan, China, the risk increased 13.6-fold.^{32,33} Aflatoxin contamination was detected in 23–80% of Chinese peanuts or peanut products, and the higher risk findings in these studies were attributed such contamination.^{34,35} Humid storage of peanuts induces aflatoxin contamination and the null genotype of metabolizing aflatoxin enzyme contributes to a higher risk of developing hepatocellular carcinoma.³² Appropriate storage and non-contaminated peanut consumption needs to be promoted.

Sichuan Province produces a high quantity of peanuts in China. From 1990 to 2013 in Sichuan Province, annual peanut production increased from 0.2 million to 0.7 million tons and ESCC incidence decreased from 147/10⁵ to 80/10⁵. An inverse linear regression was observed between annual peanut production and ESCC rate, with a correlation coefficient of -1.25 ($P < 0.001$). The coefficient of determination (R^2) was 0.8. The inverse correlation between annual peanut production and ESCC incidence indicates the potential benefits of peanut consumption. Peanuts are common and easy to access in China, thus

peanuts provide the potential to act as an anticancer food in vulnerable populations.

Yanting Cancer Hospital is the only cancer specialist hospital in Yanting County and maintains cancer and all-cause death registries. The cancer registry program covers all villages, consisting of a three-level network (village, town, and county). Village physicians report diagnosed cases to township physicians who then report to physicians at Yanting Cancer Hospital. The EC screening program conducted since 2006 includes local Yanting residents aged 40–69. Endoscopies are processed with iodine staining to detect precancerous lesions. Positive cases detected by endoscopy are then assigned to biopsy for histological tests. The screening program has had a positive participation rate.

This observational study was limited by its retrospective design, which cannot match the power of a prospective design. Selection and recall bias may have occurred. In addition, the use of cases from only one hospital may have introduced selection bias; however, Yanting Cancer Hospital is the only cancer-specific hospital in Yanting County and most ESCC patients access health services at this hospital. The selection of controls from the screening participants cannot represent the overall population of Yanting County. It is possible that the cases were more likely to believe they had consumed fewer peanuts or peanut products than the controls and this was the reason for their developing cancer. Another limitation of the study was the focus on individual diet rather than dietary pattern. This study investigated the intake frequency but not the amount; it was difficult to classify the intake amount. Finally, smoking and alcohol consumption were assessed using a dichotomous category, which was inadequate for this analysis.

Peanut consumption has a protective effect against ESCC in high-risk populations. The anti-carcinogenic property of peanuts warrants further investigation. Peanut production and consumption should be promoted in high-risk areas in order to reduce the ESCC burden.

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Disclosure

No authors report any conflict of interest.

References

- 1 Ferlay J, Soerjomataram I, Ervik M *et al.* *GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11*. IARC, Lyon 2013. [Cited 11 Jul 2015.] Available from URL: <http://globocan.iarc.fr>.
- 2 Zhao J, He YT, Zheng RS, Zhang SW, Chen WQ. Analysis of esophageal cancer time trends in China, 1989-2008. *Asian Pac J Cancer Prev* 2012; **13**: 4613-7.
- 3 He J, Zhao P, Chen W. *Chinese Cancer Registry Annual Report 2011*. Military Medical Science Press, Beijing 2011.
- 4 Luu HN, Blot WJ, Xiang YB *et al.* Prospective evaluation of the association of nut/peanut consumption with total and cause-specific mortality. *JAMA Intern Med* 2015; **175**: 755-66.
- 5 Yang M, Hu FB, Giovannucci EL *et al.* Nut consumption and risk of colorectal cancer in women. *Eur J Clin Nutr* 2016; **70**: 333-7.
- 6 Takayama S, Monma Y, Tsubota-Utsugi M *et al.* Food intake and the risk of endometrial endometrioid adenocarcinoma in Japanese women. *Nutr Cancer* 2013; **65**: 954-60.
- 7 Berkey CS, Willett WC, Tamimi RM, Rosner B, Frazier AL, Colditz GA. Vegetable protein and vegetable fat intakes in pre-adolescent and adolescent girls, and risk for benign breast disease in young women. *Breast Cancer Res Treat* 2013; **141**: 299-306.
- 8 Liu X, Teng C, Yang H *et al.* *Sichuan Statistical Yearbook 2012*. China Statistics Press, Beijing 2012.
- 9 Disease Prevention and Control Bureau, Ministry of Health, Expert Committee of Cancer Early Detection and Treatment. *Guidelines of Cancer Early Detection and Treatment*. People's Medical Publishing House, Beijing 2011.
- 10 Pandeya N, Williams GM, Sadhegi S, Green AC, Webb PM, Whiteman DC. Associations of duration, intensity, and quantity of smoking with adenocarcinoma and squamous cell carcinoma of the esophagus. *Am J Epidemiol* 2008; **168**: 105-14.
- 11 Pandeya N, Williams G, Green AC, Webb PM, Whiteman DC, Australian Cancer Study. Alcohol consumption and the risks of adenocarcinoma and squamous cell carcinoma of the esophagus. *Gastroenterology* 2009; **136**: 1215-24, e1-2.
- 12 Liu X, Wang X, Lin S, Song Q, Lao X, Yu IT. Reproducibility and validity of a food frequency questionnaire for assessing dietary consumption via the dietary pattern method in a Chinese rural population. *PLoS One* 2015; **10**: e0134627.
- 13 Bes-Rastrollo M, Wedick NM, Martinez-Gonzalez MA, Li TY, Sampson L, Hu FB. Prospective study of nut consumption, long-term weight change, and obesity risk in women. *Am J Clin Nutr* 2009; **89**: 1913-9.
- 14 Li TY, Brennan AM, Wedick NM, Mantzoros C, Rifai N, Hu FB. Regular consumption of nuts is associated with a lower risk of cardiovascular disease in women with type 2 diabetes. *J Nutr* 2009; **139**: 1333-8.
- 15 Jiang R, Manson JE, Stampfer MJ, Liu S, Willett WC, Hu FB. Nut and peanut butter consumption and risk of type 2 diabetes in women. *JAMA* 2002; **288**: 2554-60.
- 16 Song QK, Zhao L, Li J *et al.* Adverse effects of preserved vegetables on squamous cell carcinoma of esophagus and precancer lesions in a high risk area. *Asian Pac J Cancer Prev* 2013; **14**: 659-63.
- 17 Jeurink SM, Büchner FL, Bueno-de-Mesquita HB *et al.* Variety in vegetable and fruit consumption and the risk of gastric and esophageal cancer in the European Prospective Investigation into Cancer and Nutrition. *Int J Cancer* 2012; **131**: E963-73.
- 18 Zamora-Ros R, Luján-Barroso L, Bueno-de-Mesquita HB *et al.* Tea and coffee consumption and risk of esophageal cancer: The European prospective investigation into cancer and nutrition study. *Int J Cancer* 2014; **135**: 1470-9.
- 19 Zheng JS, Yang J, Fu YQ, Huang T, Huang YJ, Li D. Effects of green tea, black tea, and coffee consumption on the risk of esophageal cancer: A systematic review and meta-analysis of observational studies. *Nutr Cancer* 2013; **65**: 1-16.
- 20 Hajizadeh B, Rashidkhani B, Rad AH, Moasheri SM, Saboori H. Dietary patterns and risk of oesophageal squamous cell carcinoma: A case-control study. *Public Health Nutr* 2010; **13**: 1107-12.
- 21 Bao Y, Hu FB, Giovannucci EL *et al.* Nut consumption and risk of pancreatic cancer in women. *Br J Cancer* 2013; **109**: 2911-6.
- 22 Yeh CC, You SL, Chen CJ, Sung FC. Peanut consumption and reduced risk of colorectal cancer in women: A prospective study in Taiwan. *World J Gastroenterol* 2006; **12**: 222-7.
- 23 Awad AB, Chan KC, Downie AC, Fink CS. Peanuts as a source of beta-sitosterol, a sterol with anticancer properties. *Nutr Cancer* 2000; **36**: 238-41.
- 24 De Stefani E, Brennan P, Boffetta P, Ronco AL, Mendilaharsu M, Deneo-Pellegrini H. Vegetables, fruits, related dietary antioxidants, and risk of squamous cell carcinoma of the esophagus: A case-control study in Uruguay. *Nutr Cancer* 2000; **38**: 23-9.
- 25 Han C, Ding H, Casto B, Stoner GD, D'Ambrosio SM. Inhibition of the growth of premalignant and malignant human oral cell lines by extracts and components of black raspberries. *Nutr Cancer* 2005; **51**: 207-17.
- 26 Ibern-Gómez M, Roig-Pérez S, Lamuela-Raventós RM, de la Torre-Boronat MC. Resveratrol and piceid levels in natural and blended peanut butters. *J Agric Food Chem* 2000; **48**: 6352-4.
- 27 Woodall CE, Li Y, Liu QH, Wo J, Martin RC. Chemoprevention of metaplasia initiation and carcinogenic progression to esophageal adenocarcinoma by resveratrol supplementation. *Anticancer Drugs* 2009; **20**: 437-43.
- 28 Fan GH, Wang ZM, Yang X *et al.* Resveratrol inhibits oesophageal adenocarcinoma cell proliferation via AMP-

- activated protein kinase signaling. *Asian Pac J Cancer Prev* 2014; **15**: 677–82.
- 29 Tang Q, Li G, Wei X *et al.* Resveratrol-induced apoptosis is enhanced by inhibition of autophagy in esophageal squamous cell carcinoma. *Cancer Lett* 2013; **336**: 325–37.
- 30 González CA, Salas-Salvadó J. The potential of nuts in the prevention of cancer. (Published erratum appears in *Br J Nutr* 2008; 99: 447–8). *Br J Nutr* 2006; **96** (Suppl 2): S87–94.
- 31 Qiao YL, Dawsey SM, Kamangar F *et al.* Total and cancer mortality after supplementation with vitamins and minerals: Follow-up of the Linxian General Population Nutrition Intervention Trial. (Published erratum appears in *J Natl Cancer Inst* 2010; 102: 140). *J Natl Cancer Inst* 2009; **101**: 507–18.
- 32 Omer RE, Verhoef L, van't Veer P *et al.* Peanut butter intake, GSTM1 genotype and hepatocellular carcinoma: A case-control study in Sudan. *Cancer Causes Control* 2001; **12**: 23–32.
- 33 Zhang JY, Wang X, Han SG, Zhuang H. A case-control study of risk factors for hepatocellular carcinoma in Henan, China. *Am J Trop Med Hyg* 1998; **59**: 947–51.
- 34 Li FQ, Li YW, Wang YR, Luo XY. Natural occurrence of aflatoxins in Chinese peanut butter and sesame paste. *J Agric Food Chem* 2009; **57**: 3519–24.
- 35 Wang J, Liu XM. Contamination of aflatoxins in different kinds of foods in China. *Biomed Environ Sci* 2007; **20**: 483–7.