Fruit and vegetable consumption and risk of esophageal cancer:

A case-control study in northwest China

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ABSTRACT

The north-western region of China carries a big burden of esophageal cancer with incidence above the national average. This study ascertained the association between fruit and vegetable consumption and the risk of esophageal cancer in this remote part of China. A case-control study was undertaken in Urumqi and Shihezi, Xinjiang Uyghur Autonomous Region of China, between 2008 and 2009. Participants were 359 incident esophageal cancer patients and 380 hospital-based controls. Information on habitual fruit and vegetable consumption was obtained by face-to-face interview using a validated semi-quantitative food frequency questionnaire. Unconditional logistic regression analyses were performed to assess the strength of the associations. The esophageal cancer patients consumed significantly less fruits (mean 364.3, SD 497.4 g) and vegetables (mean 711.4, SD 727.9 g) daily than their counterparts without the disease (mean 496.5, SD 634.4 g and mean 894.5, SD 746.1 g, respectively). The adjusted odds ratios were 0.48 (95% confidence interval 0.33 to 0.71) and 0.46 (95% confidence interval 0.32 to 0.68) for consuming at least 515 g of fruits and 940 g of vegetables per day, respectively, relative to at most 170 g and 520 g. With respect to nutrients contained in fruits and vegetables, intakes of vitamin C, vitamin E, β-cryptoxanthin, potassium and magnesium at high levels also reduced the esophageal cancer risk. In conclusion, inverse associations were evident between consumption of fruits and vegetables and the risk of esophageal cancer for adults residing in northwest China.

Keywords: fruit, vegetable, nutrients, esophageal cancer, China

INTRODUCTION

Esophageal cancer is the eighth most common malignancy and the sixth leading cause of cancer-related deaths worldwide. In 2008, more than 480,000 new cases of esophageal cancer and approximately 407,000 related deaths were reported.[1] Esophageal cancer is typically diagnosed at an advanced stage. It has a poor prognosis with five-year survival rate less than 20%.[2] Therefore, primary prevention of this major disease of the esophagus is important.

Fruits and vegetables are rich in anticancer agents, such as vitamins, folate, carotenoids and certain minerals.[3] Previous studies have generally demonstrated fruits and vegetables can inhibit the development of esophageal cancer,[4-6] but the findings remained inconsistent.[7,8] Similarly, conflicting results have been reported in the Chinese population, especially with respect to vegetable consumption. A recent case-control study, conducted in Shanxi Province of north-central China, attributed the observed reduced risk of esophageal cancer to regular intake of fruits and vegetables.[9] However, a prospective cohort study in Shanghai found little association between the esophageal cancer risk and vegetable consumption, which could be due to the loss of protective components during high-heat stir-frying.[10]

Xinjiang Uyghur Autonomous Region, located in the northwest of China, is one of the areas constituting the so-called 'Asian Esophageal Cancer Belt'.[11] According to a survey conducted in Xinjiang between 2005 and 2008, the incidence of esophageal cancer was

30.2 per 100,000, much higher than the national average during the same period.[12] In view

of the conflicting epidemiological evidence, the present study aimed to ascertain the

association between fruit and vegetable consumption and the risk of esophageal cancer

among adults residing in this remote region of China.

MATERIALS AND METHODS

Study design and participants

A hospital-based case-control study of esophageal cancer was conducted in Urumqi and

Shihezi, Xinjiang Uyghur Autonomous Region of China, between January 2008 and

December 2009. Participants were recruited from the Xinjiang Tumour Hospital, Shihezi

People's Hospital, Kuitong Hospital and No. 1 Affiliated Hospital of Shihezi University.

Medical records and pathology reports were checked to identify newly diagnosed

patients (within the past 12 months). Pathological diagnoses were based on the World

Health Organization's Classification of Tumours of the Digestive System.[13] Patients

without histopathological confirmation were excluded. Of the total 364 incident patients

identified, 359 consented to participate.

Meanwhile, controls were recruited among inpatients at the same hospitals from the

departments of Ophthalmology, Orthopaedic, Respiratory Disease and Physiotherapy.

Exclusion criteria for controls were previous diagnosis of any malignant disease, on long-

term medical diet, and self-reported memory problems assessed by asking whether they

could recall previous day events. Whenever more controls were available than could be interviewed, the final selection was made using random numbers. Of the 400 eligible controls recruited to frequency matched with cases by gender and age (within 5 years), 380 eventually gave their consent to be interviewed (response rate 95%). There were no significant differences in age, gender and demographics between participants and non-participants in both case and control groups.

The study protocol was approved by the participating hospitals and the Human Research Ethics Committee of Curtin University (approval number HR 56/2006), and conformed to the provisions of the Declaration of Helsinki. Written informed consent was obtained from all participants, who were assured of confidentiality of the information provided and their right to withdraw at any time without prejudice

Data collection

All participants were interviewed face-to-face by trained nursing staff, usually in the presence of their next-of-kin to help the recall of past events. A structured questionnaire was administered to collect information on demographic characteristics, anthropometry, past and family medical history, as well as lifestyle such as cigarette smoking and alcohol drinking. Information on diet was solicited using a validated 137-item semi-quantitative food frequency questionnaire, which included commonly consumed fruits and vegetables in northwest China. Frequency and amount of intake were recorded in detail. The reference

recall period for dietary variables was set at 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.[14] We then estimated each participant's total energy intake (kcal/day) by summing the energy content across individual items consumed.

Total vegetable intake was defined as the sum of daily consumption of green leafy vegetables (spinach, lettuce, celtuce leaf, pea shoot), cruciferous vegetables (broccoli, cole, cabbage, Chinese cabbage, cauliflower, white radish), yellow orange vegetables (tomato, carrot, sweat potatoes, red chilli), allium vegetables (leek, onion, scallion, garlic bolt, garlic) and other vegetables (celery, eggplant, cucumber, zucchini, lotus root, potato, Chinese yam, lentil, snow pea, snap bean , long bean, mung bean sprout, green capsicum, celtuce stem, bitter gourd, wax gourd, bamboo shoot). Preserved (salted/pickled) vegetables, typically consumed in small amounts, were excluded in the total fresh vegetable intake. Total fruit intake was defined as the sum of daily consumption of yellow orange fruits (banana, orange, peach, persimmon, watermelon, strawberry, pineapple, hawthorn fruit, fresh date) and other fruits (apple, pear, grape, dew melon).

Statistical analysis

Descriptive statistics were used to summarize the sample characteristics. Unconditional logistic regression analyses were performed to assess the effects of fruit and vegetable

consumption on the esophageal cancer risk. Both crude and adjusted odds ratios (OR) and corresponding 95% confidence intervals (CI) were computed.

The main nutrients contained in fruits and vegetables, except carotenoids, were identified and estimated using the Chinese Food Composition Tables.[14] The nutrient database of the USA Department of Agriculture[15] was used for the calculation of carotenoids. Effects of the selected nutrients were then ascertained by separate logistic regression models.

For each exposure variable of interest, the categorical cutoff points were derived from the tertiles of consumption corresponding to the control distribution, with the lowest level being the reference category. Confounding variables included in the logistic regression models were age (years), gender, education level (none/primary, secondary, tertiary), body mass index (5 years ago, kg/m^2), total energy intake (kcal/day), smoking status (never, ever), alcohol drinking (never/seldom, often) and family history of cancer in first-degree relatives (no, yes). These variables were either established or plausible risk factors of esophageal cancer from the literature. All statistical analyses were undertaken using the SPSS package version 20.

RESULTS

Table 1 presents characteristics of the sample by case-control status. The participants were on average 61 (SD 11.4) years old with mean body mass index 24.1 (SD 3.7) kg/m^2. The

majority (72%) of them were male. Approximately half the participants were smokers and regularly drank alcoholic beverages. Compared to the controls, patients with esophageal cancer tended to belong to the ethnic minority group (p = 0.001), have lower education level (p < 0.001) but a family history of esophageal cancer (p < 0.001).

Table 2 compares the mean daily consumptions of fruits and vegetables between case and control groups. Patients with esophageal cancer consumed significantly less total fruits (mean 364.3, SD 497.4 g) and total vegetables (mean 711.4, SD 727.9 g) per day than adults without the disease (mean 496.5, SD 634.4 g and mean 894.5, SD 746.1 g, respectively), according to both t tests and Mann-Whitney tests. Table 3 shows the daily intake of selected nutrients derived from fruits and vegetables. Compared to controls, the esophageal cancer patients reported significantly lower intakes of vitamin C, vitamin E, niacin, folate, β-cryptoxanthin, potassium, magnesium and calcium. Further subgroup analysis by ethnicity (Han versus Uyghur minority people) produced similar results which were omitted for brevity.

Table 4 gives the results of logistic regression analyses for fruit, vegetable and their subgroups. Over 50% reductions in esophageal cancer risk were observed for the highest levels of total fruit and total vegetable intake; the adjusted OR being 0.48 (95% CI 0.33 to 0.71) and 0.46 (95% CI 0.32 to 0.68) for consuming at least 515 g of fruit and 940 g of vegetable, respectively, relative to at most 170 g and 520 g. With the exception of green

leafy vegetable, increased consumption at each subgroup was apparently associated with a reduced risk of esophageal cancer.

Finally, Table 5 summarises the logistic regression results for selected nutrients contained in fruits and vegetables. Inverse associations were found between the incidence of esophageal cancer and intakes of Vitamin C, Vitamin E, β-cryptoxanthin, potassium and magnesium, together with significant dose-response relationships (results omitted for brevity).

DISCUSSION

This case-control study in north-western China suggested a protective role for fruits vegetables against esophageal cancer development, with supportive evidence from the corresponding dietary nutrients. Compared with previous research for the Chinese population, our findings are consistent with a hospital-based case-control study in Shanxi Province[9] and two other case-control studies conducted in Taiwan,[16, 17] though somewhat different from a prospective cohort study undertaken in Shanghai, which found little association between vegetable intake and the esophageal cancer risk.[10]

Besides total fruit and total vegetable, the consumptions of most subgroups were shown to be similarly beneficial in the present study, suggesting that many components or nutrients contained in fruits and vegetables might be responsible for their preventive effect. Vitamin C and vitamin E, acting as scavengers of reactive oxygen species, may protect

esophageal cells against oxidative damage and DNA destruction.[18] Moreover, vitamin C is important in impeding the endogenous synthesis of N-nitroso compounds, which are potential carcinogens for the esophagus.[19] In addition, carotenoids from fruits and vegetables have been implicated in cancer prevention because of their strong antioxidant activity, inhibition of proliferation and induction of detoxifying enzymes.[20]

Similar to a previous study in the USA,[21] among the carotenoids considered, only β-cryptoxanthin emerged to exhibit an inverse association with esophageal cancer. On the other hand, both magnesium and potassium are essential minerals for normal cellular function. Dietary magnesium may inhibit carcinogenesis due to its stabilizing effect on DNA and regulatory role in cell cycle control and apoptosis,[22] whereas experimental studies are needed to understand the biological mechanism concerning the anticancer properties of potassium.

In this study, a standardised identification procedure had been implemented that ensured the ascertainment of cases was maximised and complete. To avoid misclassification of the case-control status, only incident patients were recruited, who had been diagnosed with esophageal cancer within the past 12 months and subsequently confirmed with pathology. All controls were carefully screened. Dietary intake was measured using a validated food frequency questionnaire, 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 family history of cancer was also collected. It was possible that some esophageal cancer patients might have modified their dietary behaviours since the onset of the disease. Therefore, the reference period for habitual fruit and vegetable consumption was set at five years ago to avoid reverse causation.

Several biases and limitations should be taken into consideration. A major limitation concerns the retrospective cross-sectional nature of the case-control design so that a cause-effect relationship between fruit and vegetable consumption and esophageal cancer risk could not be established. Nevertheless, the use of four hospitals reduced sampling bias, and as they serve the entire catchment region, our participants could be considered as representative of the target population of Xinjiang Province. Although the recall of habitual food 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 response of participants. Face-to-face interviews were thus conducted in the presence of next-of-kin to help improve the accuracy of their answers. Furthermore, 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, since several common fruits and vegetables in northwest China were not covered by the database. Nevertheless, it should not bias the results because the same estimation procedure was consistently applied to both case and control groups.

In conclusion, habitual consumption of fruits and vegetables appeared to be inversely associated with the risk of esophageal cancer for adults in northwest China, together with supportive evidence from the corresponding dietary nutrients. While population-based prospective cohort studies are required to confirm the effect of long term consumption, it is still appropriate to recommend consuming a wide variety of fruits and vegetables for the prevention of this major disease.

ACKNOWLEDGEMENTS

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

Variable	Cases	Controls	p†
	n (%)	n (%)	
Gender			0.623
Male	260 (72.4%)	269 (70.8%)	
Female	99 (27.6%)	111 (29.2%)	
Ethnic group			0.001
Han	270 (75.2%)	322 (84.7%)	
Minority	89 (24.8%)	58 (15.3%)	
Education level			< 0.001
None/primary	183 (51.0%)	136 (35.8%)	
Secondary	140 (39.0%)	191 (50.3%)	
Tertiary	36 (10.0%)	53 (13.9%)	
Smoking status			0.188
Never	164 (45.7%)	192 (50.5%)	
Ever	195 (54.3%)	188 (49.5%)	
Alcohol drinking			0.216
Never/seldom	193 (53.8%)	187 (49.2%)	
Often	166 (46.2%)	193 (50.8%)	

Family history of cancer in first-degree relatives			< 0.001
No	306 (85.2%)	356 (93.7%)	
Yes	53 (14.8%)	24 (6.3%)	
Age at interview (years)‡	61.4 (11.0)	60.6 (11.8)	0.338
Body mass index (5 years ago, kg/m^2)‡	24.3 (3.8)	24.0 (3.6)	0.181
Total energy intake (kcal/day)‡	4310 (2681)	4709 (2716)	0.047

† Chi-square or t-test for difference between cases and controls

‡ Mean (SD)

Table 2. Comparison of fruit and vegetable consumption between case and control

groups in northwest China

Daily intake (g)	Cases	Controls	p†
	Mean (SD)	Mean (SD)	
Total vegetables	711.4 (727.9)	894.5 (746.1)	0.001
Green leafy vegetables	52.6 (81.1)	66.6 (107.2)	0.045
Cruciferous vegetables	127.5 (137.2)	173.1 (155.1)	< 0.001
Yellow orange vegetables	138.0 (179.0)	160.5 (223.2)	0.133
Allium vegetables	92.2 (125.5)	103.5 (126.0)	0.222
Other vegetables	301.0 (394.3)	390.8 (381.6)	0.002
Total fruits	364.3 (497.4)	496.5 (634.4)	0.002
Yellow orange fruits	206.0 (336.4)	279.6 (373.1)	0.005
Other fruits	158.2 (212.9)	216.9 (303.9)	0.002

† t-test for mean difference between cases and controls

Table 3. Comparison of selected nutrients intake between case and control groups in

northwest China

Daily intake	Cases	Controls	p†
	Mean (SD)	Mean (SD)	
Vitamin C (mg)	246.44 (270.73)	307.63 (269.58)	0.002
Vitamin E (mg)	7.53 (7.38)	9.41 (8.05)	0.001
Niacin (mg)	8.65 (10.05)	10.45 (13.13)	0.037
Folate (μg)	193.98 (217.69)	229.65 (245.90)	0.037
α-carotene (μg)	1231.88 (2168.69)	1270.55 (2063.44)	0.804
β-carotene (μg)	8555.94 (8826.91)	9708.97 (9600.59)	0.089
β-cryptoxanthin (μg)	151.05 (234.22)	198.39 (255.85)	0.009
Lutein + zeaxanthin (μg)	5532.47 (7801.07)	6023.88 (8642.76)	0.418
Lycopene (μg)	2958.95 (4923.37)	3690.19 (7226.65)	0.110
Potassium (mg)	1561.87 (1458.18)	1962.73 (1729.65)	0.001
Magnesium (mg)	178.01 (180.09)	218.14 (189.43)	0.003
Calcium (mg)	374.87 (391.32)	438.40 (396.63)	0.029
Iron (mg)	10.40 (12.94)	11.76 (10.76)	0.119

† t-test for mean difference between cases and controls

Table 4. Crude and adjusted odds ratio (95% confidence interval) of esophageal cancer

risk for fruit and vegetable consumption among adults in northwest China

Daily intake (g)	Cases n (%)	Controls n (%)	Crude OR (95% CI)	Adjusted OR † (95% CI)	p†
Total vegetables					< 0.001
< 520	190 (52.9%)	127 (33.4%)	1.00	1.00	
520 – 940	89 (24.8%)	129 (33.9%)	0.46 (0.33, 0.66)	0.49 (0.34, 0.70)	
> 940	80 (22.3%)	124 (32.6%)	0.43 (0.30, 0.62)	0.46 (0.32, 0.68)	
Green leafy vegetables					0.997
< 14	119 (33.1%)	127 (33.4%)	1.00	1.00	
14 – 50	126 (35.1%)	128 (33.7%)	1.05 (0.74, 1.49)	0.99 (0.69, 1.42)	

> 50	114	125	0.97	1.00	
	(31.8%)	(32.9%)	(0.68, 1.39)	(0.69, 1.45)	
Cruciferous vegetables					< 0.001
< 81	163	129	1.00	1.00	
	(45.4%)	(33.9%)			
81 – 200	133	128	0.82	0.84	
	(37.0%)	(33.7%)	(0.59, 1.15)	(0.59, 1.19)	
> 200	63	123	0.41	0.43	
	(17.5%)	(32.4%)	(0.28, 0.59)	(0.29, 0.64)	
Yellow orange vegetables					0.038
< 62	127	130	1.00	1.00	
	(35.4%)	(34.2%)			
62 – 155	142	124	1.17	1.22	
	(39.6%)	(32.6%)	(0.83, 1.65)	(0.86, 1.74)	
> 155	90	126	0.73	0.74	
	(25.1%)	(33.2%)	(0.51, 1.05)	(0.50, 1.09)	
Allium vegetables					0.015

< 35	123	132	1.00	1.00	
	(34.3%)	(34.7%)			
35 – 111	153	123	1.34	1.26	
	(42.6%)	(32.4%)	(0.95, 1.88)	(0.89, 1.80)	
> 111	83	125	0.71	0.72	
	(23.1%)	(32.9%)	(0.49, 1.03)	(0.49, 1.07)	
Other vegetables					< 0.001
< 205	190	127	1.00	1.00	
	(52.9%)	(33.4%)			
205 – 420	96	128	0.50	0.54	
	(26.7%)	(33.7%)	(0.35, 0.71)	(0.38, 0.78)	
> 420	73	125	0.39	0.40	
	(20.3%)	(32.9%)	(0.27, 0.56)	(0.27, 0.59)	
Total fruits					0.001
< 170	168	126	1.00	1.00	
	(46.8%)	(33.2%)			
170 – 515	116	131	0.66	0.71	
	(32.3%)	(34.5%)	(0.47, 0.93)	(0.50, 1.02)	
> 515	75	123	0.46	0.48	
	(20.9%)	(32.4%)	(0.32, 0.66)	(0.33, 0.71)	

Yellow orange fruits					< 0.001
< 90	178 (49.6%)	128 (33.7%)	1.00	1.00	
90 – 272	104 (29.0%)	127 (33.4%)	0.59 (0.42, 0.83)	0.59 (0.41, 0.85)	
> 272	77 (21.4%)	125 (32.9%)	0.44 (0.31, 0.64)	0.47 (0.32, 0.69)	
Other fruits					0.015
< 66	156 (43.5%)	127 (33.4%)	1.00	1.00	
66 – 207	121 (33.7%)	126 (33.2%)	0.78 (0.56, 1.10)	0.84 (0.59, 1.19)	
> 207	82 (22.8%)	127 (33.4%)	0.53 (0.37, 0.76)	0.57 (0.39, 0.84)	

† From separate logistic regression models adjusting for age (years), gender, education level (none/primary, secondary, tertiary), body mass index (5 years ago, kg/m^2), total energy intake (kcal/day), smoking status (never, ever), alcohol drinking (never/seldom, often) and family history of cancer in first-degree relatives (no, yes).

OR, odds ration; CI, confidence interval.

Table 5. Crude and adjusted odds ratio (95% confidence interval) of esophageal cancer

risk for intake of selected nutrients among adults in northwest China

Daily intake	Cases	Controls	Crude OR	Adjusted OR†	p†
	n (%)	n (%)	(95% CI)	(95% CI)	
Vitamin C (mg)					0.001
< 168.0	174	126	1.00	1.00	
	(48.5%)	(33.2%)			
168.0 – 310.0	100	127	0.57	0.58	
	(27.8%)	(33.4%)	(0.40, 0.81)	(0.41, 0.83)	
> 310.0	85	127	0.49	0.54	
	(23.7%)	(33.4%)	(0.34, 0.69)	(0.37, 0.79)	
Vitamin E (mg)					0.010
< 5.3	171	129	1.00	1.00	
	(47.6%)	(34.0%)			
5.3 – 9.8	103	124	0.63	0.66	
	(28.7%)	(32.6%)	(0.44, 0.89)	(0.46, 0.94)	
> 9.8	85	127	0.51	0.58	
	(23.7%)	(33.4%)	(0.35, 0.72)	(0.40, 0.85)	
Niacin (mg)					0.110

< 4.7	158	130	1.00	1.00	
	(44.0%)	(34.2%)			
4.7 – 9.9	104	123	0.70	0.73	
	(29.0%)	(32.4%)	(0.49, 0.99)	(0.51, 1.05)	
> 9.9	97	127	0.63	0.70	
	(27.0%)	(33.4%)	(0.44, 0.89)	(0.48, 1.03)	
Folate (μg)					0.302
< 104.5	142	127	1.00	1.00	
	(39.6%)	(33.4%)			
104.5 – 204.5	108	126	0.77	0.75	
	(30.1%)	(33.2%)	(0.54, 1.09)	(0.52, 1.08)	
> 204.5	109	127	0.77	0.87	
	(30.4%)	(33.4%)	(0.54, 1.09)	(0.60, 1.27)	
α-carotene (μg)					0.623
< 270.0	126	127	1.00	1.00	
	(35.1%)	(33.4%)			
270.0 – 1114.0	127	126	1.02	1.02	
	(35.4%)	(33.2%)	(0.72, 1.44)	(0.71, 1.46)	
> 1114.0	106	127	0.84	0.86	
	(29.5%)	(33.4%)	(0.59, 1.20)	(0.59, 1.25)	
β-carotene (μg)					0.944

< 4530.0	124	127	1.00	1.00
	(34.5%)	(33.4%)		
4530.0 – 9800.0	129	126	1.05	1.02
	(35.9%)	(33.2%)	(0.74, 1.49)	(0.71, 1.47)
> 9800.0	106	127	0.86	0.96
	(29.5%)	(33.4%)	(0.60, 1.22)	(0.65, 1.40)

β-cryptoxanthin

(μg)   0.003

< 65.0	170	128	1.00	1.00
	(47.4%)	(33.7%)		
65.0 – 180.0	106	125	0.64	0.64
	(29.5%)	(32.9%)	(0.45, 0.90)	(0.45, 0.92)
> 180.0	83	127	0.49	0.54
	(23.1%)	(33.4%)	(0.34, 0.71)	(0.37, 0.79)

Lutein +

zeaxanthin (μg)   0.082

< 2174.0	133	128	1.00	1.00
	(37.0%)	(33.7%)		
2174.0 – 4965.0	99	126	0.76	0.71
	(27.6%)	(33.2%)	(0.53, 1.08)	(0.49, 1.03)

> 4965.0	127	126	0.97	1.06	
	(35.4%)	(33.2%)	(0.69, 1.37)	(0.74, 1.53)	
Lycopene (µg)					0.083
< 1100.00	144	124	1.00	1.00	
	(40.4%)	(32.9%)			
1100.0 – 3280.0	111	123	0.78	0.75	
	(31.2%)	(32.6%)	(0.55, 1.10)	(0.52, 1.08)	
> 3280.0	101	130	0.67	0.67	
	(28.4%)	(34.5%)	(0.47, 0.95)	(0.46, 0.97)	
Potassium (mg)					0.001
< 1200.0	195	147	1.00	1.00	
	(54.3%)	(38.7%)			
1200.0 – 2290.0	91	119	0.58	0.58	
	(25.3%)	(31.3%)	(0.41, 0.82)	(0.41, 0.84)	
> 2290.0	73	114	0.48	0.54	
	(20.3%)	(30.0%)	(0.34, 0.690	(0.37, 0.80)	
Magnesium (mg)					0.008
< 117.0	166	128	1.00	1.00	
	(46.2%)	(33.7%)			
117.0 – 220.0	106	125	0.65	0.64	
	(29.5%)	(32.9%)	(0.46, 0.93)	(0.45, 0.92)	

> 220.0	87	127	0.53	0.58	
	(24.2%)	(33.4%)	(0.37, 0.76)	(0.40, 0.85)	
Calcium (mg)					0.138
< 260.0	173	149	1.00	1.00	
	(48.2%)	(39.2%)			
260.0 – 470.0	97	114	0.73	0.72	
	(27.0%)	(30.0%)	(0.52, 1.04)	(0.50, 1.03)	
> 470.0	89	117	0.66	0.75	
	(24.8%)	(30.8%)	(0.46, 0.93)	(0.52, 1.10)	
Iron (mg)					0.113
< 6.8	172	145	1.00	1.00	
	(47.9%)	(38.2%)			
6.8 – 13.5	102	121	0.71	0.74	
	(28.4%)	(31.8%)	(0.50, 1.00)	(0.52, 1.06)	
> 13.5	85	114	0.63	0.70	
	(23.7%)	(30.0%)	(0.44, 0.90)	(0.48, 1.02)	

† From separate logistic regression models adjusting for age (years), gender, education level (none/primary, secondary, tertiary), body mass index (5 years ago, kg/m^2), total energy intake (kcal/day), smoking status (never, ever), alcohol drinking (never/seldom, often) and family history of cancer in first-degree relatives (no, yes).

OR, odds ration; CI, confidence interval.