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A Case-control Study of Oral Cancer in Beijing, People's Republic of China. Associations with Nutrient Intakes, Foods and Food Groups

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A case-control study of oral cancer was conducted in Beijing, People's Republic of China to examine the association between dietary nutrient intake and risk of oral cancer, both in terms of estimated intake of nutrients and micro-nutrients, and in terms of specific foods and food groups. The study was hospital-based and controls were hospital in-patients matched for age and sex with the cases. The response rate for cases and controls was 100% and 404 case/control pairs were interviewed. The results suggest that increased protein and fat intake are related to a decreased risk of oral cancer. Carbohydrate intake, however, showed a moderate increased risk for oral cancer. Total carotene intake and carotene intake from fruits and vegetables are inversely associated with risk of oral cancer. A similar pattern was observed for dietary vitamin C intake. Dietary fibre derived from fruits and vegetables showed a strong negative association with oral cancer risk, but fibre derived from other sources did not exhibit any protective effect. At the level of foods and food groups, increased consumption of fresh meat, chicken and liver was significantly associated with a reduction in oral cancer risk: the tests for trend were all statistically significant at the $P < 0.01$ level. Consumption of common carp, hairtail, shrimp and lobster were also associated with decreased risk. Risk was found to increase with increasing consumption of millet and corn bread ($P < 0.01$) but to decrease with increasing consumption of rice ($P < 0.01$). Increased consumption of grapes, bananas, oranges, tangerines, peaches and pears were associated with reduced risk. No association was found with intake of tea or the reported temperature at which it was consumed. These results support the independent role of dietary nutrients in oral cancer.

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INTRODUCTION

THE INCIDENCE and mortality rates of oral cancer are rising in many parts of the world including among young men in western Europe [1]. This is a reversal of the trend witnessed in the first half of this century when oral cancer declined in most of these countries by up to 10-fold [2]. Although there have been relatively few epidemiological studies of oral cancer, a number of risk factors have been identified. There is a strong association, consistently demonstrated by a large number of epidemiological studies, between oral cancer risk and increasing levels of cigarette smoking [3] and alcohol consumption [4]. The effect of both factors is strong and independent and there has frequently been a multiplicative effect found between both exposures in increasing the risk of oral cancer [5]. Alcohol and tobacco have long been recognised as being determinants of oral cancer risk [6] although changing patterns in their use do not appear to explain the current increases in oral cancer being seen in many countries.

Several epidemiological studies have demonstrated that nutritional factors could be important determinants of oral cancer risk [7]. Initially, iron deficiency and primary sideropenic anaemia (the Plummer–Vinson or Paterson–Kelly syndrome) were associated with an increased risk of oral cancer and these observations were partially confirmed by studies in Sweden [8] where this syndrome was particularly common. Upper alimentary tract changes were also seen in patients with pellagra, a disease due to a complex dietary deficiency of niacin and several other micronutrients which was common in parts of the U.S.A. and northern Italy earlier this century.

In the developed countries, such diseases resulting from gross dietary deficiencies are now rare. However, following on

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from these observations interest arose in investigating other dietary factors in the aetiology of oral cancer. Recent studies have shown decreased risks of oral cancer with increasing consumption of vitamin A and C, fresh fruit and vegetables [9]. These findings have been translated into chemoprevention trials where there is now some evidence that retinoids can reduce the occurrence of oral malignancy in patients with oral leukoplakia [10].

In order to investigate further the association between the risk of oral cancer and nutritional factors it was decided to conduct a study in the developing world where some levels of dietary intake more extreme than in western countries could be found. A hospital based case-control study was conducted in Beijing to evaluate the role of dietary habits and nutritional factors as well as other risk factors including tobacco smoking, alcohol beverage consumption, dental health and oral hygiene in the aetiology of oral cancer. The results reported here only deal with nutritional factors.

MATERIALS AND METHODS

Study population

A full description of the study design has been given in detail elsewhere [11]. Briefly, cases consisted of all male and female incident oral cancer patients admitted in any one of seven hospitals that treat oral cancer in Beijing. A total of 404 histologically confirmed oral cancer patients (ICD-9 codes 141, 143–145) [12] were interviewed between 1 May 1989 and 24 December 1989. Cases had an age range between 18 and 80 years at the time of diagnosis. One control was selected for each case matched on referral pattern, sex and age within 5 years. Controls were randomly chosen from the patients whose current hospitalisations were for minor conditions diagnosed within 1 year (and believed not to be associated with the exposures of interest) and included minor surgery (e.g. haemorrhoids, strangulated hernia, etc.), ophthalmic and ear conditions, low back pain and urinary tract infection.

A standard structured questionnaire was used to obtain information on use of tobacco, alcohol, occupational and environmental exposures and dietary intake in study subjects. The dietary section of the questionnaire consisted of 63 food items which represent major sources of energy and nutrient intake, both macro-nutrients and important micro-nutrients, for Chinese populations. This questionnaire was modified from a validated local questionnaire developed by the Chinese Institute of Nutrition [13]. In keeping with the results obtained from validation studies in western countries [14], it was found that inclusion of quantitation of the estimates of consumption (i.e. portion size) had little discriminant value. The nutrients estimated in this case-control study had similar concordance from the results of the study which validated the food-frequency questionnaire.

Dietary practices were assessed in terms of the usual frequency of intake of a number of selected food items. Cases and controls were asked to report their usual frequency of eating each of the food items which were expressed as a particular amount or units typically eaten by this population. Because the Chinese diet, particularly in terms of consumption of animal sources and cereal foods, has been changing rapidly during the past 10 years, information regarding dietary history for meat, fish, dairy products, rice and cereals were requested for two time periods: dietary history before 1976 and a second period approximately 1 year before the onset of cancer symptoms (cases) or interview (controls). Also because the dietary pattern for consumption of fruits and vegetables is quite different between the harvest season and the off-season

Table 1. Quetelet Index and risk of oral cancer

	Quetelet Index				Two tailed *P*-value for trend
	14–20	21–22	23–25	26–28	
Cases	126	107	108	63	
Controls	88	91	121	104	
ORa	1.00	0.82	0.62	0.42	
95% CI		0.55–1.24	0.42–0.92	0.27–0.65	
ORb	1.00	0.62	0.50	0.42	
95% CI		0.38–1.00	0.30–0.84	0.25–0.71	0.001
ORc	1.00	0.61	0.48	0.40	
95% CI		0.37–0.99	0.28–0.80	0.23–0.69	0.001

ORa: Crude ORs from frequency distribution.
ORb: By conditional logistic regression adjusting for tobacco smoking, alcohol drinking, education level, inadequate dentition, sex and age.
ORc: Controlled for all the potential confounding variables for ORb plus total energy intake.

Table 2. Total daily energy intake and risk of oral cancer

	Total Energy Intake (kJ)				Two tailed *P*-value for trend
	1 (low)	2	3	4 (high)	
Cases	97	98	109	100	
Controls	105	105	92	102	
ORa	1.00	1.01	1.28	1.06	
95% CI		0.67–1.52	0.85–1.93	0.70–1.60	
ORb	1.00	1.20	1.45	1.23	
95% CI		0.72–2.02	0.86–2.44	0.69–2.20	0.58
ORc	1.00	1.37	1.46	1.39	
95% CI		0.80–2.34	0.86–2.48	0.77–2.51	0.53

ORa: Crude ORs from frequency distribution.
ORb: By conditional logistic regression adjusting for tobacco smoking, alcohol drinking, education level, inadequate dentition, sex and age.
ORc: Controlled for all the potential confounding variables for ORb plus Quetelet Index.

Table 3. Daily macronutrient intake and risk of oral cancer

Variable	Frequency	OR*	95% CI
Protein	1 (low)	1.00	
	2	1.04	0.61–1.78
	3	0.85	0.47–1.53
	4 (high)	0.67	0.35–1.28
Fat	1 (low)	1.00	
	2	0.88	0.51–1.52
	3	0.79	0.43–1.43
	4 (high)	0.56	0.31–1.01
Carbohydrate	1 (low)	1.00	
	2	1.30	0.75–2.25
	3	1.62	0.89–2.93
	4 (high)	2.05	1.10–3.82

*By conditional logistic regression adjusting for tobacco smoking, alcohol drinking, inadequate dentition, Quetelet Index, years of education, sex and age (adjusting for total energy intake is explained in Materials and Methods).

in this population, the usual consumption for two seasons for fruits, vegetables and other foods which might have varying seasonal patterns were requested.

Interviews were conducted in person by one of two trained retired nurses. Both the interviewers and interviewee had no knowledge of the study hypotheses.

The frequency and quantities usually consumed for each food item were used to develop nutrient indices. Total daily macro- and micro-nutrient intakes were obtained by first multiplying the report frequency of consumption of the specified quantity of each food by the nutrient contents of that quantity of the food, then summing for all the foods consumed. The nutrient value for the specified quantity of each food was obtained from Chinese Food Content Tables [15]. Seasonal variation of consuming vegetables and fruits was taken into account by calculating average daily nutrient intakes. However, no vitamin supplements were included in the calculation of the nutrient indices in this study.

The statistical model used to assess the effect of calorie-providing nutrient intakes was suggested by Willett and Stampfer [16]. In this model, calculated macronutrient intakes were adjusted by taking the residual from a linear, least-square regression model in which total energy intake was the independent variable and protein (or fat, or carbohydrate as appropriate) was the dependent variable. When the impact of micronutrient intakes was considered, each micronutrient was adjusted by adding total caloric intake in the model. For each macro- or micro-nutrient index, quartiles of consumption were produced by dividing the frequency distribution of the entire study group at the 25th, 50th and 75th percentiles.

The exposure odds ratio (OR) was used to estimate the relative risk of oral cancer associated with each risk factor. Crude OR (ORc) were calculated by using the Mantel and Haenszel method [17]. Conditional logistic regression analysis [18] was used to control for potential confounding factors and to obtain adjusted OR (ORa). 95% confidence intervals (CI) were used for estimating the precision of the point estimates. In the text, OR and CI are given to one decimal place but to two places in the tables. Formal statistial testing for trend for macro-or micro-nutrient intake was performed by treating each variable in the model as a continuous variable rather than several indicator variables. The ratio of the estimated

Table 4. Daily dietary intake of vitamin A, carotene and vitamin C and risk of oral cancer

Variable	Case	Control	ORc	ORa*	95% CI	P†
Vitamin A (IU)						
<189	110	76	1.00			
189–458	108	110	0.68	0.70	0.37–1.33	
459–1026	94	115	0.56	0.72	0.43–1.21	
1027–7420	92	103	0.62	0.64	0.35–1.16	0.24
Total carotene (IU)						
<2054	138	80	1.00	1.00		
2054–2652	88	93	0.55	0.47	0.28–0.81	
2653–3485	96	125	0.45	0.64	0.37–1.09	
3486–10855	82	106	0.45	0.51	0.27–0.96	0.08
From vegetables (IU)						
<2054	112	68	1.00	1.00		
2054–2652	107	112	0.58	0.41	0.24–0.69	
2653–3485	89	115	0.47	0.54	0.32–0.93	
3486–10855	86	109	0.48	0.52	0.28–0.98	0.05
From fruits (IU)						
<109	139	76	1.00	1.00		
109–175	102	93	0.60	0.66	0.40–1.10	
176–257	80	108	0.41	0.50	0.29–0.86	
258–948	83	117	0.39	0.58	0.33–1.02	0.27
Total vitamin C (mg)						
<117	122	73	1.00	1.00		
117–151	103	107	0.58	0.68	0.41–1.14	
152–198	90	110	0.49	0.60	0.35–1.02	
199–889	89	114	0.47	0.46	0.25–0.86	0.16
From vegetables (mg)						
<52	125	77	1.00	1.00		
52–70	94	108	0.54	0.46	0.27–0.77	
71–100	88	112	0.48	0.57	0.34–0.97	
101–654	97	107	0.56	0.52	0.28–0.97	0.08
From fruits (mg)						
<47	135	80	1.00	1.00		
47–58	94	97	0.57	0.59	0.37–0.94	
59–74	88	116	0.45	0.60	0.35–1.02	
75–119	87	111	0.46	0.55	0.30–0.99	0.11

*By conditional logistic regression adjusting for tobacco smoking, alcohol drinking, inadequate dentition, Quetelet Index, total energy intake, years of education, sex and age.

†Two-sided *P* values for linear trend test by conditional logistic regression analysis adjusting for all the confounding variables as for ORa.

coefficient to its standard error obtained from the model was used to make statistical inference based upon 2-sided alternative hypothesis at the 5% level.

RESULTS

Table 1 present the results for Quetelet Index and the risk of oral cancer. A strong negative association was present in the data. Those with a higher Quetelet Index showed a sizeably lower risk. The pattern persisted following adjustment for smoking, alcohol drinking, inadequate dentition and other major confounding factors. Controlling for total energy intake did not change the ORs materially.

Nutrients and micro-nutrients

The effects for total energy and total nutrient intakes on the risk of oral cancer were compared for two time periods: 1 year before the diagnosis of the disease and before 1976. Analysis of the data from both time periods produced similar results, and therefore, only the results for total calories and nutrient intake before 1976 are presented here. Table 2 considers the impact of total caloric intake on the risk of oral cancer. The crude OR are almost equal to one. Controlling for major confounding factors slightly elevated these OR above one for the higher intake group, but none of the OR are statistically significant, and the results were almost the same when Quetelet Index was taken into consideration.

Table 3 describes the association between macronutrient intakes and the risk of oral cancer. It can be seen from the results that protein and fat intake are related inversely with oral cancer risk: a marginal statistically significant inverse association was noticed for fat intake at the highest intake level. However, carbohydrate intake showed a moderate increased risk for oral cancer. The OR is statistically significant at the highest intake of carbohydrate.

Table 5. Daily dietary fibre intake and risk of oral cancer

Variable	Case	Control	ORc	ORa*	95% CI	P†
Total fibre (g)	140	69	1.00	1.00		
39–	91	104	0.43	0.41	0.24–0.70	
49–	87	124	0.35	0.34	0.19–0.63	
61–	86	107	0.40	0.38	0.19–0.74	0.04
From vegetables (g)						
<15	140	73	1.00	1.00		
15–	106	97	0.57	0.53	0.32–0.88	
21–	79	118	0.35	0.38	0.21–0.67	
28–	79	116	0.36	0.40	0.22–0.74	0.01
From fruits (g)						
<12	118	71	1.00	1.00		
12–	111	106	0.63	0.65	0.38–1.12	
15–	86	112	0.46	0.47	0.27–0.82	
18–	89	115	0.47	0.50	0.26–0.95	0.06
Other sources (g)						
<12	121	119	1.00	1.00		
12–	109	123	0.87	0.86	0.48–1.54	
15–	85	101	0.83	0.69	0.36–1.33	
18–	89	61	1.43	1.28	0.58–2.83	0.48

*By conditional logistic regression adjusting for tobacco smoking, alcohol drinking, inadequate dentition, Quetelet Index, total energy intake, years of education, sex and age.
†Two-sided *P* values for linear trend test by conditional logistic regression analysis adjusting for all the confounding variables as for ORa.

Table 6. The risk of oral cancer associated with daily intake of calcium, phosphorous and iron

Variable	Case	Control	ORc	ORa*	95% CI	P†
Calcium (mg)						
<593	140	129	1.00	1.00		
593–774	137	132	0.96	0.87	0.52–1.47	
>774	127	143	0.82	0.77	0.40–1.46	0.27
Phosphorous (mg)						
<1801	141	127	1.00	1.00		
1802–2439	133	137	0.87	0.89	0.55–1.44	
<2439	130	140	0.84	0.69	0.32–1.46	0.13
Iron (mg)						
<31	162	126	1.00	1.00		
31–	125	134	0.73	0.71	0.42–1.18	
41–	117	144	0.63	0.65	0.37–1.14	0.34

*By conditional logistic regression adjusting for tobacco smoking, alcohol drinking, inadequate dentition, Quetelet Index, total energy intake, years of education, sex and age.
†Two-sided *P* values for linear trend test by conditional logistic regression analysis adjusting for all the confounding variables as for ORa.

Table 4 considers dietary vitamin A, carotene, vitamin C intake and risk of oral cancer. Dietary vitamin A intake showed a negative association with the risk of oral cancer. However, none of the OR are statistically significant at the 5% significance level. Total carotene intake and carotene intake from fruits and vegetables are inversely associated with risk of oral cancer. A similar pattern was noticed for dietary vitamin C intake. When vitamin A, carotene, and vitamin C were entered simultaneously into the model adjusted for total energy intake, Quetelet Index and other major confounders, the OR related to vitamin C and carotene remained essentially unchanged. However, the association with vitamin A intake was further diminished.

Even though dietary fibre derived from fruits and vegetables showed a strong negative association with risk of oral cancer as presented in Table 5, fibre derived from other sources did not exhibit any such protective effect.

Table 6 considers dietary intake of calcium, phosphorous, iron and risk of oral cancer with both crude and adjusted OR. Even though calcium and phosphorous intake showed negligible risk alterations for both crude and adjusted OR, iron intake, is however, associated with an apparent risk reduction with an OR for the highest intake category which is of borderline significance.

Data relating dietary thiamine, riboflavin and niacin intake with the risk of oral cancer are presented in Table 7. The crude OR for thiamine and niacin are almost equal to one. Controlling for major confounders depressed the OR, but none of them are statistically significant. Riboflavin intake showed a protective effect with a statistically significant OR in the middle intake category and a marginal significant OR for the highest intake group or the adjusted OR.

Foods and food groups

Table 8 gives the frequency distribution, crude and adjusted OR for 33 food items consumed by the cases and controls before 1976. As the Table suggests increased consumption of fresh meat, chicken and liver (mainly of pig liver) are statistically significantly associated with a reduction of oral cancer risk. Two tailed *P*-values for trend are 0.004, 0.001 and 0.002 for consumption of fresh meat, chicken and liver, respectively. The dose–response relationships were maintained after controlling for the effect of major potential confounders. No increased risk was found for consumption of bacon or salted meat. In fact, sausage intake showed a negative association with oral cancer risk.

Consumption of common carp, hairtail and shrimp was associated with risk reduction for oral cancer, but no association was found with consumption of other fish.

Risk of oral cancer associated with cereal intake showed a quite different pattern. Rice intake showed a statistically significant reduction with oral cancer risk. The association persisted after adjusting for the major confounding factors. The trend test was highly significant ($P<0.001$). More cases than controls reported a high consumption of millet and corn bread or corn cakes. The highest intake group showed 2.7 times the risk of the lowest intake group for both products. Tests for trend for consuming both products were statistically significant. A non-statistically significant reduction of risk was found for consumption of bread, and a non-statistically significant increase risk for sorghum consumption.

Neither type of tea drinking exhibited an obvious association with oral cancer risk. Orange juice and other types of fruit juice have an apparent negative association with the risk of oral cancer: the OR, however, are not statistically significant. Drinking milk showed a moderate inverse association with oral cancer risk with a marginally significant OR of 0.5 (0.2–1.0) for consumption once or more per day compared with the lowest intake group.

We also analysed the association between the risk of oral cancer and the same food items presented in Table 8, but consumed one year before the diagnosis. The overall pattern is similar to the results in Table 8 suggesting a negative association with increasing intake of fresh meat, liver, fresh egg, common carp, shrimp, rice and bread, and an increased risk of oral cancer associated with increasing intake of millet and cornbread or cake.

Table 9 presents the results for consumption of fruits and vegetables during the harvest season. More controls than cases reported a higher consumption for most of the fruits presented in Table 9, except for apricots and plums. Consumption of grapes, bananas, oranges and tangerines, peaches and pears was associated with a statistically significant inverse association with oral cancer risk. Apple consumption showed a negative association of borderline significance with the risk of oral cancer. No increased risk was noticeable for consumption of any fruit.

Table 7. The risk of oral cancer associated with daily intake of thiamine, riboflavin and niacin from food

Variable	Case	Control	ORc	ORa*	95% CI	P†
Thiamine (mg)						
<3.38	126	137	1.00	1.00		
3.38–4.39	148	146	1.10	1.03	0.48–2.21	
>4.39	130	121	1.17	0.74	0.25–2.18	0.16
Riboflavin (mg)						
<0.92	172	150	1.00	1.00		
0.92–1.18	126	145	0.76	0.53	0.31–0.92	
>1.18	106	109	0.85	0.62	0.32–1.22	0.13
Niacin (mg)						
<20	150	150	1.00	1.00		
20–25	117	126	0.93	0.68	0.32–1.43	
>25	137	128	1.07	0.60	0.21–1.73	0.05

*By conditional logistic regression adjusting for tobacco smoking, alcohol drinking, inadequate dentition, Quetelet Index, total energy intake, years of education, sex and age.
†Two-sided *P* values for linear trend test by conditional logistic regression analysis adjusting for all the confounding variables as for ORa.

Table 8. The risk of oral cancer associated with specific foods. Consumption before 1976

Food (amount)	Frequency	Case	Control	ORc	RRa*	95% CI
Meats						
Beef (100 g)	<1/month	302	292	1.00		
	1–2/month	51	65	0.76	0.54	0.31–0.93
	>3/month	51	47	1.05	0.82	0.46–1.46
Pork (100 g)	<1/month	72	40	1.00		
	1–2/month	69	55	0.70	0.65	0.33–1.28
	3–4/month	129	138	0.52	0.53	0.30–0.95
	2–3/week	85	103	0.46	0.39	0.21–0.74
	⩾4/week	49	68	0.40	0.32	0.15–0.70
Lamb (100 g)	<1/month	318	326	1.00		
	1–2/month	47	41	1.18	1.03	0. 57–1.86
	⩾3/month	39	37	1.08	0.88	0.48–1.62
Chicken (100 g)	<1/month	293	270	1.00		
	1–2/month	84	94	0.82	0.64	0.39–1.04
	⩾3/month	27	40	0.62	0.38	0.19–0.78
Duck (100 g)	<1/month	378	376	1.00		
	⩾1/month	26	28	0.92	0.93	0.38–2.29
Salted meat (100 g)	<1/month	384	388	1.00		
	⩾1/month	20	16	1.26	1.22	0.43–3.44
Sausage (50 g)	<1/month	315	289	1.00		
	1–2/month	65	82	0.73	0.58	0.35–0.95
	⩾3/month	24	33	0.67	0.55	0.26–1.17
Liver (50 g)	<1/month	337	315	1.00		
	1–2/month	51	70	0.68	0.53	0.30–0.93
	⩾3/month	16	19	0.79	0.34	0.14–0.86
Eggs						
Fresh egg (2)	⩽2/month	127	103	1.00		
	3–4/month	129	144	0.67	0.84	0.54–1.31
	2–3/week	70	87	0.60	0.70	0.41–1.18
	⩾4/week	68	70	0.73	0.68	0.35–1.32
Salted egg (2)	<1/month	344	341	1.00		
	1–2/month	42	40	1.04	1.21	0.64–2.28
	⩾3/month	18	23	0.78	0.69	0.24–1.79
Fish						
Common carp (50 g)	<1/month	337	326	1.00		
	1–2/month	50	50	0.97	0.78	0.41–1.48
	⩾3/month	17	28	0.59	0.30	0.13–0.67
Crucian carp (50 g)	<1/month	355	353	1.00		
	1–2/month	31	32	0.96	0.91	0.45–1.84
Hairtail (50 g)	<1/month	272	221	1.00		
	1–2/month	91	123	0.60	0.56	0.37–0.86
	⩾3/month	41	60	0.56	0.48	0.25–0.91
Squid (50 g)	>1/month	385	383	1.00		
	⩾1/month	19	21	0.90	0.93	0.34–2.56
Shrimp (50 g)	<1/month	339	320	1.00		
	>1/month	65	84	0.73	0.54	0.33–0.90
Crab (50 g)	<1/month	375	375	1.00		
	⩾1/month	29	29	1.00	1.08	0.46–2. 54
Grains						
Rice (200 g)	<2/month	103	53	1.00		
	3–4/month	96	106	0.47	0.57	0.32–1.02
	2–6/week	96	100	0.49	0.48	0.27–0.87
	⩾1/day	109	145	0.39	0.40	0.21–0.76
Millet (200 g)	<1/month	155	178	1.00		
	1–2/month	118	132	1.03	1.11	0.70–1.77
	3–4/month	69	60	1.32	1.38	0.81–2.33
	⩾2/week	62	34	2.09	2.71	1.42–5.16
Steambread (200 g)	<1/week	86	81	1.00		
	2–3/week	86	105	0.77	0.92	0.53–1.60
	4–5/week	65	62	0.99	1.21	0.66–2.20
	6/week	50	47	1.00	1.26	0.64–2.47
	⩾1/day	117	109	1.01	1.25	0.67–2.32
Bundump (200 g)	<1/month	48	45	1.00		
	1–2/month	119	94	1.19	1.15	0.62–2.15
	3–4/month	178	199	0.84	0.69	0.38–1.25
	⩾2/week	59	66	0.84	0.81	0.37–1.75

Table 8. Continued.

Food (amount)	Frequency	Case	Control	ORc	RRa*	95% CI
Pancake (200 g)	<1/month	100	91	1.00		
	1–2/month	121	142	0.78	1.01	0.63–1.63
	3–4/month	122	122	0.91	1.21	0.74–1.97
	⩾2/week	61	49	1.13	1.43	0.78–2.65
Noodles (100 g)	⩽2/month	52	52	1.00		
	3–4/month	113	122	0.93	1.06	0.61–1.85
	2–3/week	149	157	0.95	1.11	0.64–1.94
	⩾4/week	90	73	1.23	1.36	0.73–2.56
Bread (100 g)	<1/month	347	331	1.00		
	⩾1/month	57	73	0.74	0.62	0.36–1.10
Fried dumplings	<1/month	322	330	1.00		
	1–2/month	45	51	0.90	0.90	0.48–1.66
	>3/month	37	23	1.65	1.76	0.83–3.74
Corn bread or cake	⩽2/month	96	122	1.00		
	3–4/month	84	97	1.10	1.33	0.79–2.25
	2–3/week	107	106	1.28	1.38	0.81–2.35
	⩾4/week	117	79	1.53	2.66	1.54–4.61
Sorghum	<1/month	340	370	1.00		
	1–2/month	30	15	2.18	1.89	0.88–4.07
	⩾3/month	34	19	1.95	1.65	0.78–3.46
Beverages						
Black tea (1 cup)	<1/month	380	388	1.00		
	>1/month	24	16	1.53	1.24	0.42–3.63
Green tea (1 cup)	<1/month	374	374	1.00		
	⩾1/month	30	30	1.00	0.85	0.32–2.31
Jasmine tea (1 cup)	⩽2/month	209	205	1.00		
	⩽6/week	28	31	0.89	1.14	0.56–2.30
Fruit juice (1 cup)	<1/month	368	358	1.00		
	⩾1/month	36	46	0.76	0.66	0.33–1.31
Orange juice	<1/month	345	326	1.00		
	1–2/month	23	28	0.78	0.97	0.46–2.02
	>3/month	36	50	0.68	0.82	0.49–1.48
Malted milk (1 cup)	<1/month	365	365	1.00		
	>1/month	39	39	1.00	1.32	0.64–2.71
Milk (250 cc)	<1/month	320	303	1.00		
	⩽4/month	25	28	0.85	1.23	0.63–2.40
	⩽6/week	17	21	0.77	0.89	0.37–2.12
	>1/day	42	52	0.76	0.48	0.23–1. 01

*By conditional logistic regression adjusting for tobacco smoking, alcohol drinking, inadequate dentition, years of education, Quetelet Index, sex and age.

Increased intake of tomatoes, mushrooms, sweet peppers, celery, cauliflower and winter squash are associated with a lower risk of oral cancer. However, an elevated risk was apparent for increased consumption of lentils, Chinese cabbage and pickled vegetables although none of the OR are statistically significant.

The association between oral cancer risk and the same fruit and vegetable items presented in Table 9 but for off-season consumption has also been examined. The frequency of eating most of the fruits and vegetables showed a greatly reduced pattern of intake compared with the frequency of consumption in the harvest season. However, a statistically significant inverse association was found for consumption of oranges, tangerines and apples which could be purchased from the market all year around. A strong negative association was maintained for consumption of tomatoes and cucumber which could be obtained from the market during the off-season although at a relatively high price. The inverse association was also apparent for celery, winter squash and sweet pepper consumption. An increased risk with increasing consumption of Chinese cabbage, hot pepper and pickled vegetables was found, and consumption of pickled vegetables was statistically significantly associated with the risk of oral cancer.

The possible associations between risk of oral cancer and method of food preparation, usual type of fat and number of condiments used for cooking, temperatures of beverages consumed were also examined but none of the factors presented itself as a noteworthy risk factor for oral cancer.

DISCUSSION

The results of this study are compatible with most previous studies which suggest a strong protective effect of carotenoids, vitamin C and fibre intake on the risk of oral cancer [19–21]. However, the results of this study demonstrate some important differences from other studies. It was found that vitamin C and carotene derived from vegetables as well as from fruits are both protective: the reduced risk was not only found for vitamin C derived only from fruits as another recent study has suggested [21]. In a recent study, Marshall *et al.* [22] found that retinoids, riboflavin and calcium intake were associated with an increased risk of oral cancer, and that increased intake

Table 9. The risk of oral cancer associated with specific foods for in season consumption 10 years prior to diagnosis/interview

Food (amount)	Frequency	Case	Control	ORc	ORa*	95% CI
Fruits						
Grapes (200 g)	<1/month	216	160	1.00		
	1–2/month	72	92	0.58	0.63	0.38–1.04
	3–4/month	78	81	0.71	0.86	0.53–1.41
	⩾2/week	38	71	0.40	0.42	0.24–0.73
Banana (2)	<1/month	202	144	1.00		
	1–2/month	79	89	0.63	0.72	0.44–1.18
	3–4/month	76	104	0.50	0.50	0.31–0.81
	⩾2/week	47	67	0.50	0.43	0.24–0.77
Peach (2)	<1/month	163	97	1.00		
	1–2/month	85	90	0.56	0.45	0.27–0.75
	3–4/month	82	104	0.47	0.61	0.37–0.99
	⩾2/week	74	113	0.39	0.37	0.22–0.61
Apricots or plums (2)	<1/month	348	340	1.00		
	1–2/month	49	50	0.96	0.92	0.52–1.63
	⩾3/month	17	14	1.19	0.97	0.40–2.39
Oranges or tangerines (1)	<1/month	158	84	1.00		
	1–2/month	91	85	0.58	0.51	0.30–0.86
	3–4/month	82	109	0.41	0.34	0.20–0.59
	2–3/week	42	84	0.27	0.25	0.14–0.44
	⩾4/week	34	42	0.44	0.36	0.18–0.72
Apple (1)	⩽2/month	108	78	1.00		
	3–4/month	76	73	0.75	0.56	0.32–0.99
	2–3/week	95	76	0.90	0.94	0.56–1. 57
	4–5/week	66	103	0.46	0.40	0.23–0.69
	⩾6/week	59	74	0.58	0.62	0.34–1.12
Pear (1)	<1/month	164	109	1.00		
	1–2/month	118	110	0.71	0.68	0.44–1.08
	3–4 /month	74	97	0.51	0.43	0.26–0.74
	⩾2/week	48	88	0.36	0.27	0.15–0.49
Watermelon (2 slices)	<1/month	26	20	1.00		
	1–4/month	68	47	1.11	1.26	0.53–2.98
	2–3/week	71	63	0.87	0.75	0.32–1.78
	4–5/week	75	64	0.90	1.17	0.49–2.78
	6/week	61	87	0.54	0.52	0.23–1.18
	⩾1/day	103	123	0.64	0.55	0.24–1.29
Dates (50 g)	<1/month	252	236	1.00		
	1–2/month	89	111	0.75	0.74	0.47–1.15
	⩾3/month	63	57	1. 04	0.83	0.52–1.34
Vegetables						
Spinach (100 g)	⩽2/month	43	30	1.00		
	3–4/month	54	65	0.58	0.60	0.28–1.27
	2–3/week	160	184	0.61	0.56	0.30–1.06
	4–5/week	118	196	0.86	0.88	0.45–1.73
	⩾6/week	29	29	0.70	0.59	0.24–1.47
Carrots (100 g)	<1/month	123	110	1.00		
	1–2/month	77	87	0.79	0.93	0.56–1.56
	3–4/month	96	80	1.07	1.16	0.69–1.97
	2–3/week	82	100	0.73	0.54	0.30–0.96
	⩾4/week	26	27	0.86	0.74	0.32–1.76
Chinese cabbage (100 g)	<4/month	56	65	1.00		
	2–3/week	107	110	1.13	0.85	0.43–1.66
	4–5/week	134	143	1.09	0.84	0.40–1.75
	⩾6/week	107	86	1.44	1.45	0.63–3.31
Potato (100 g)	<1/month	67	58	1.00		
	1–2/month	93	101	0.80	0.76	0.42–1.38
	3–4/month	104	117	0.77	0.88	0.51–1.52
	2–3/week	66	77	0.74	0.57	0.30–1.10
	⩾4/week	74	51	1.26	1.07	0.55–2.08
Cauliflower (100 g)	<1/month	167	87	1.00		
	1–2/month	84	93	0.47	0.46	0.27–0.77
	3–4/month	115	157	0.38	0.37	0.23–0.60
	⩾2/week	38	67	0.30	0.24	0.13–0.45
Cabbage (100 g)	<2/month	125	78	1.00		
	3–4/month	131	139	0.59	0.77	0.48–1.24
	2–3/week	110	149	0.46	0.49	0.29–0.81
	⩾4/week	38	38	0.62	0.77	0.37–1.58

Table 9. Continued.

Food (amount)	Frequency	Case	Control	ORc	ORa*	95% CI95% CI
Celery (100 g)	⩽2/month	139	87	1.00		
	3–4/month	143	142	0.63	0.93	0.58–1.48
	2–3/week	111	148	0.47	0.60	0.37–0.96
	⩾4/week	11	27	0.25	0.30	0.12–0.75
Lentils (100 g)	⩽4/month	49	41	1.00		
	2–3/week	133	151	1.05	0.83	0.45–1.53
	4–5/week	167	171	1.17	1.12	0.60–2.08
	⩾6/week	55	41	1.60	1.82	0.83–3.99
Fennel (50 g)	<1/month	187	151	1.00		
	1–2/month	112	147	0.62	0.68	0.44–1.05
	⩾3/month	105	106	0.80	0.95	0.61–1.48
Winter squash (100 g)	<1/month	156	83	1.00		
	1–2/month	60	58	0.55	0.58	0.32–1.05
	3–4/month	111	150	0.39	0.32	0.19–0.52
	⩾2/week	77	113	0.36	0.30	0.18–0.52
Cucumber (100 g)	<4/month	67	44	1.00		
	2–3/week	103	111	0.61	0.61	0.34–1.11
	4–5/week	156	174	0.59	0.59	0.34–1.00
	>6/week	78	75	0.68	0.70	0.38–1.28
Pumpkin (100 g)	<1/month	210	208	1.00		
	1–2/month	95	115	0.82	0.79	0.51–1.22
	⩾3/month	99	81	1.21	1.27	0.81–1.99
Eggplant (100 g)	⩽4/month	102	91	1.00		
	2–3/week	184	191	0.86	0.74	0.46–1.18
	⩾4/week	118	122	0.86	0.77	0.46–1.27
Tomato (2)	⩽3/week	116	82	1.00		
	4–5/week	150	140	0.76	0.80	0.49–1.30
	6/week	86	113	0.54	0.52	0.31–0.88
	⩾1/day	52	69	0.53	0.49	0.26–0.94
Mushroom (50 g)	<1/month	218	164	1.00		
	1–2/month	122	132	0.70	0.82	0.54–1.24
	⩾3/month	64	108	0.45	0.46	0.29–0.74
Chinese chive (25 g)	<1/month	58	59	1.00		
	1–2/month	132	127	1.06	1.02	0.59–1.77
	3–4/month	142	140	1.03	1.19	0.69–2.04
	⩾2/week	72	78	0.94	0.96	0.52–1.78
Lotus (100 g)	<1/month	302	267	1.00		
	1–2/month	71	102	0.62	0.60	0.38–0.94
	⩾3/month	31	35	0.78	0.82	0.40–1.66
Sweet pepper (2)	<1/month	103	61	1.00		
	1–22/month	70	57	0.73	0.91	0.49–1.67
	3–4/month	127	139	0.54	0.70	0.41–1.17
	⩾2/week	104	147	0.42	0.55	0.32–0.93
Hot pepper (2)	<1/month	233	231	1.00		
	1–2/month	62	77	0.80	0.81	0.50–1.33
	3–4/month	50	47	1.05	1.16	0.65–2.05
	⩾2/week	59	49	1.19	1.03	0.59–1.80
Pickled vegetable (50 g)	<1/month	68	72	1.00		
	1–2/month	97	115	0.89	0.70	0.40–1.22
	3–4/month	106	117	0.96	0.89	0.51–1.55
	2–3/week	82	66	1.32	1.36	0.74–2.53
	⩾4/week	51	34	1.59	1.73	0.79–3.77
Seaweed (50 g)	<1/month	293	287	1.00		
	1–2/month	76	81	0.92	0.90	0.55–1.48
	⩾3/month	35	36	0.95	0.82	0.42–1.59

*By conditional logistic regression adjusting for tobacco smoking, alcohol drinking, inadequate dentition, years of education, Quetelet Index, sex and age.

of thiamine, niacin and dietary fibre were significantly protective and, further, that phosphorous and iron intake had almost no impact on oral cancer risk. The results from our study, however, suggest a weaker risk reduction associated with increasing riboflavin and iron intake, and a strong protective effect for dietary fibre intake from fruit and vegetable sources. However, this study does not support an increased risk of oral cancer associated with increasing intake of calcium, retinoid and riboflavin or a protective effect for thiamine and niacin.

Higher Quetelet Index was found to be associated with a lower risk of oral cancer in this study. Adjustment for total energy intake as well as other major confounders further

increased this observed inverse association. Similar results were also reported by some other studies [21, 22].

The results of the study are also consistent with the hypothesis generated from recent studies that increased vegetable and/or fruit consumption might be associated with a reduction in the risk of oral cancer. Winn *et al.* [23] found both fruit and vegetable consumption to be associated with a reduced risk of oral cancer among women in the U.S.A. The effect persisted after adjusting for tobacco and alcohol drinking. McLaughlin *et al.* [21] reported an inverse association between fruit intake and risk of oral cancer, but could find no similar association with vegetable consumption. In a recent case-control study from Brazil, Franco *et al.* [24] found a significant protective effect for increased consumption of carotene-rich vegetables and citrus fruits, but not for green vegetables in general.

It is interesting to note in this study that higher consumption of meat, protein and rice are associated with significant risk reductions of oral cancer, and a reported high consumption of millet, corn bread and sorghum are related to an increased risk in this population. Increased oesophageal cancer rates have been associated with consumption of millet and wheat as reported by a recent ecological study conducted in China which involved 65 Chinese countries [25]. This result is in broad agreement with the observation that during the time period of both the studies in question, individuals in China consumed more meat, protein and rice in this area and generally enjoyed a higher living standard than those who had millet, corn and sorghum as their staple foods. Therefore, it could be hypothesised that multiple, complex dietary deficiencies could be involved in the aetiology of oral cancer in this population. Similar findings have emerged from studies conducted in northern Italy [26].

There are several advantages of the study described here. Principally, incident rather than prevalent cases and controls were used for this study, which would help to reduce the possible information bias resulting from biased recall due to the different disease status of the cases and controls. The fact that total energy intake showed a slightly elevated risk supports the hypothesis that cases did not tend to systematically under-report their overall food intake than controls. Secondly, the use of both hospital cases and controls should increase the comparability of the data derived by interviewing cases and controls. The comparability of the data quality is just as important as other factors which might affect the validity of the study. If hospitalisation had any effect on recalling past dietary intake, by keeping both interviewers and interviewees from knowing the current hypothesis of interest, then this bias should be in the same direction for both cases and controls, and therefore, the possible bias should tend to reduce the observed OR, not exaggerate them. Third, the basic unawareness of the Chinese population regarding any association between dietary habits, nutritional factors and the risk of oral cancer should further serve to reduce any bias resulting from differential recall of dietary intake of specific food items of the cases and controls. Even though several studies relating diet and cancer risk have been conducted, the awareness of the study results for the population in general is very limited.

However, caution should be taken when interpreting the results from this study as with any retrospective study of diet and cancer. Even though several studies have lent some confidence to epidemiological methods of assessing diet and nutrition [27–31], the reliability, validity and consequently the measurement error depend on the memory of the subjects, the willingness of the cases and controls to cooperate with the interviewer and the dedication of the interviewers as well as the interviewees [32]. Recall of past dietary intake might be affected by dietary stability, frequency of use, vegetarian status, education level and current food intake [33–35]. However, every step has been taken to minimise this potential source of bias in this study. It must also be borne in mind that the control group were also hospital patients which may have served to bias some of the risks observed towards unity, e.g. cigarette smoking.

In conclusion, the findings from this case-control study of oral cancer conducted in China support the role of certain nutritional factors and dietary habits in the aetiology of oral cancer. Several recent studies from China also indicate the importance of diet and nutrition in the genesis of oesophageal [25] and nasopharyngeal cancer [36, 37]. Considering the results from this study and other studies, an integrated approach towards oral cancer prevention should take into consideration the dietary practices prevalent in the population.

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