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Dietary patterns and risk of oesophageal cancers: a population-based case–control study

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Abstract

Epidemiological studies investigating the association between dietary intake and oesophageal cancer have mostly focused on nutrients and food groups instead of dietary patterns. We conducted a population-based case–control study, which included 365 oesophageal adenocarcinoma (OAC), 426 oesophagogastric junction adenocarcinoma (OGJAC) and 303 oesophageal squamous cell carcinoma (OSCC) cases, with frequency matched on age, sex and geographical location to 1580 controls. Data on demographic, lifestyle and dietary factors were collected using self-administered questionnaires. We used principal component analysis to derive three dietary patterns: 'meat and fat', 'pasta and pizza' and 'fruit and vegetable', and unconditional logistic regression models to estimate risks of OAC, OGJAC and OSCC associated with quartiles (Q) of dietary pattern scores. A high score on the meat-and-fat pattern was associated with increased risk of all three cancers: multivariable-adjusted OR 2·12 (95 % CI 1·30, 3·46) for OAC; 1·88 (95 % CI 1·21, 2·94) for OGJAC; 2·84 (95 % CI 1·67, 4·83) for OSCC (P-trend < 0·01 for all three cancers). A high score on the pasta-and-pizza pattern was inversely associated with OSCC risk (OR 0·58, 95 % CI 0·36, 0·96, P for trend = 0·009); and a high score on the fruit-and-vegetable pattern was associated with a borderline significant decreased risk of OGJAC (OR for Q4 *v.* Q1 0·66, 95 % CI 0·42, 1·04, P = 0·07) and significantly decreased risk of OSCC (OR 0·41, 95 % CI 0·24, 0·70, P for trend = 0·002). High-fat dairy foods appeared to play a dominant role in the association between the meat-and-fat pattern and risk of OAC and OGJAC. Further investigation in prospective studies is needed to confirm these findings.

Key words: **Dietary patterns: Oesophageal cancer: Case–control studies: Principal component analysis**

Oesophageal cancer is the eighth most frequently diagnosed cancer and the sixth leading cause of cancer death worldwide, with an estimated 482 000 new cases and 407 000 deaths in 2008[1,2]. There are two histological types: adenocarcinoma which can occur in the oesophagus (OAC) or the oesophagogastric junction (OGJAC) and oesophageal squamous cell carcinoma (OSCC). The incidence of OAC has been increasing in Western countries[3] including Australia[4,5], with recent figures showing positive annual percentage changes of 4·2 and 4·3 % in the incidence of OAC for men and women, respectively, in the two decades before 2005 in New South Wales, Australia[6]. These rapid changes in incidence prompted the present study.

Diet is a modifiable risk factor that may influence risk of cancers of the oesophagus[7–9]. The majority of epidemiological studies investigating the association between diet and cancer of the oesophagus have focused on individual nutrients[10–15], individual foods or food groups[10,15–23]; however, because of inconsistency among the results, the evidence for a role of diet in the aetiology of oesophageal cancer is not conclusive. Dietary pattern analysis has emerged in recent years as a way to shed more light on the role of diet in modifying disease risk. Unlike the individual nutrient or food group approach, the dietary pattern approach allows the study of foods as they are actually consumed, thus capturing the inter-correlations between foods and nutrients[24].

Abbreviations: OAC, oesophageal adenocarcinoma; OGJAC, oesophagogastric junction adenocarcinoma; OSCC, oesophageal squamous cell carcinoma; Q, quartile.

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Few epidemiological studies have specifically investigated the association between dietary patterns and risk of OSCC[25–28], and only two have investigated OAC[25,29]. These previous studies have been relatively small in size (185 and 124 OAC cases), and results have been inconsistent. For example, while two studies[28,30] found an increased risk between a 'Western' or 'meat and fat' dietary pattern and the risk of OSCC, another reported a non-significantly decreased risk[25]. To further investigate the role of dietary patterns in OAC risk, we have used the information reported on a validated FFQ from a population-based case–control study to identify common food consumption patterns in Australia, and to relate these patterns to the risk of OAC, OGJAC and OSCC.

Materials and methods

Study design and participants

We used data from a nationwide case–control study of oesophageal cancer conducted in Australia, the details of which have been described elsewhere[31]. In summary, eligible case patients were people aged 18–79 years with a histologically confirmed primary invasive cancer of the oesophagus or oesophagogastric junction diagnosed between 1 July 2002 (1 July 2001, in Queensland) and 30 June 2005, in the mainland states of Australia. Patients were recruited through the major treatment centres and state-based cancer registries. A total of 1577 patients with oesophageal cancer were invited to participate in the study, of whom 1102 patients (858 through clinics and 244 through cancer registries) returned a completed questionnaire (70 % of those invited; 35 % of all patients diagnosed with incident oesophageal cancer during the study period). Details of the histological type and anatomical site of each tumour were abstracted from diagnostic pathology reports by medically qualified investigators. Tumour site was classified according to the WHO classification such that adenocarcinomas that straddled the junction of the oesophagus and stomach were called tumours of the oesophagogastric junction regardless of where the bulk of the tumour lay (OGJAC, ICD-O code 8140/3), while those located entirely above the oesophagogastric junction were considered oesophageal carcinomas[32]. Eight case patients were deemed ineligible on pathology review and excluded from the analysis, leaving 365 OAC, 426 OGJAC and 303 OSCC patients.

Potential controls were selected at random from the Australian Electoral Roll and frequency matched to the case series by age (5-year age groups), sex and state of residence. We aimed for similar numbers of male cases and controls in each stratum of age and state; female controls were intentionally oversampled at all ages to accommodate their simultaneous enrolment in a parallel study of ovarian cancer[33]. Of the 3258 potentially eligible control participants who were contacted and invited to participate, 216 were excluded (sixteen deceased, sixty-one were too ill, ninety-eight were unable to read or write in English and forty-one were unwilling to participate in the study). Of the 3042 remaining controls, 1580 returned the completed questionnaires (51 % of all potentially eligible controls contacted).

All study participants provided informed written consent. The study was approved by the human research ethics committees of the Queensland Institute of Medical Research and all participating institutions.

Exclusions and final sample size

Of the 1094 cases and 1580 controls who returned the main risk factor questionnaire, 199 participants (152 cases and 47 controls) had no opportunity to complete an FFQ because the nutrition component of the study commenced 6 months after the main study. A further thirty-five cases and five controls omitted responses to 10 % or more of FFQ items, while twenty-seven cases and twenty-one controls had implausible total energy intakes (<3360 or >21 000 kJ for men and <2940 or >16 800 kJ for women). The present analysis included 1507 (98 %) controls and 880 (93 %) cases: 299 with OAC, 336 with OGJAC and 245 with OSCC.

Non-dietary data

Data were collected via a self-administered questionnaire. Information was collected on age, education, smoking history, total lifetime alcohol consumption, use of aspirin or other non-steroidal anti-inflammatory drugs during the past 5 years, height and weight 1 year ago (1 year before diagnosis for cases), frequency of symptoms of gastro-oesophageal reflux, defined as the presence of heartburn ('a burning pain behind the breastbone after eating') or acid reflux ('a sour taste from acid or bile rising up into the mouth or throat') 10 years before diagnosis, and physical activity.

Dietary data and food grouping

Dietary data were obtained using a 139-item semi-quantitative FFQ, modified from the instrument developed by Willett *et al.*[34], and shown to be valid against weighed food records[35–37] and serum biomarkers[38], and reproducible[39] for use in Australia. Respondents recalled how often, on average, they consumed a standard serving size of a specific food item in the previous year (for controls) or in the year before their diagnosis (for cases) for 135 food items. Information on four additional items including the quantity of sugar habitually added to food or beverages and the discretionary use of fat as assessed by the frequency with which visible fat from meat, foods fried at home and fried take-away foods were consumed were obtained. We calculated daily food intake in g by multiplying the frequency of consumption per d by the standard serving size of each food as specified in the FFQ. The foods items were grouped into forty-four predefined food groups based on the similarity of nutrient profiles or culinary usage.

Dietary pattern derivation

Principal component analysis is a data reduction technique that reduces the number of observed variables by creating a small number of factors that account for much of the variance in the food groups[40,41]. We used the PROC FACTOR command in SAS (statistical software version 9.1; SAS Institute, Inc., Cary, NC, USA) to derive dietary patterns using the correlation matrix of the forty-four food groups among the combined group of cases and controls (Table S1, supplementary material for this article can be found at http://www.journals.cambridge.org/bjn). We considered eigenvalues > 1, screeplots and interpretability when determining the number of factors to be retained. The preliminary analysis yielded thirteen factors with eigenvalues > 1, which together accounted for 53 % of the variance in the forty-four food groups. However, based on the point at which the screeplot of eigenvalues levelled off, we retained three factors that explained 25 % of the total variance in the diet. To facilitate interpretability, the three factors were rotated using varimax rotation to obtain three dietary patterns that were orthogonal and uncorrelated with each other. Factor loadings were calculated for each food group and dietary pattern (Table 1). A positive loading for a food group indicates a direct association with the dietary pattern while a negative loading indicates that the food group contributes inversely to the dietary

Table 1. Factor loadings* for the relationship between food groups and factors representing dietary patterns in oesophageal cancer cases and controls

	Meat and fat	Pasta and pizza	Fruit and vegetable
Processed meat	0·67	–	–
Potato (high fat)	0·57	–	–
Discretionary fat	0·53	–	–
Red meat	0·50	–	–
High-fat dairy	0·48	–	–
White bread	0·48	–	–
Poultry (high fat)	0·46	–	–
Sweet snacks	0·46	–	–
Fat spread	0·43	−0·22	–
Ketchup/tomato sauce	0·40	–	–
Sweet drinks	0·39	–	–
Beer	0·36	–	−0·22
Savoury snacks	0·36	0·35	–
Low-fat dairy	−0·33	0·21	0·20
Eggs	0·31	–	0·21
Whole-meal bread	−0·30	0·24	0·34
Herbal and green tea	−0·29	0·34	–
Cream soup	0·25	–	0·23
Rice (brown)	−0·24	0·27	0·22
Pizza	0·23	0·52	–
Other fruits†	−0·22	–	0·64
Poultry (low fat)	−0·20	0·26	0·21
Legumes	–	0·28	0·31
Spirits	–	0·31	–
Wine	–	0·55	–
Other vegetables‡	–	–	0·59
Pasta	–	0·67	–
Pasta sauce (tomato-based)	–	0·64	–
Olives or pickled vegetables	–	0·49	–
Rice (white)	–	0·49	–
Salad dressing	–	0·45	0·26
Cereal products	–	0·44	0·26
Oily fish	–	0·34	0·35
Nuts	–	0·31	0·27
Green leafy vegetables	–	0·30	0·51
Other fish or seafood	–	0·29	0·29
Coffee	–	0·28	–
Fruit or vegetable juices	–	0·27	–
Fruits containing high vitamin C or A	–	–	0·60
Red or yellow vegetables	–	–	0·66
Cruciferous vegetables	–	–	0·54
Potato (low fat)	–	–	0·41
Breakfast cereal	–	–	0·39
Tea (black)	–	–	0·32
Vegemite§	–	–	0·21
Cumulative variance explained	11·7	8·2	5·5

* With orthogonal rotation, the factor loading scores are identical to the correlation coefficients; factor loadings with absolute values < 0·20 are not shown for clarity.
† Fruits other than those containing high levels of vitamin A or C.
‡ Vegetables other than red/yellow, leafy green or cruciferous vegetables.
§ An Australian spread made from yeast extract.

pattern. For each dietary pattern, a score was calculated for cases and controls by summing up the intake of each food group (in g) weighted by the factor loading of the food groups (Σ((food group$_i$ g/d) $\times$ (food group$_i$ factor loading)), where i = food group from 1 to 44)[42]. Factor scores for each pattern were then categorised into quartiles using the distribution of the population controls, for further analyses.

Statistical analysis

We used the χ^2 test to check for differences in proportions, and ANOVA to check for differences in the distribution of continuous variables across categories of potential risk factors. Unconditional logistic regression was used to calculate OR and 95 % CI as estimates of the relative risks of OAC, OGJAC and OSCC associated with quartiles of dietary pattern scores. We assessed linear trends by ranking factor scores from 1 to 4 (lowest to highest quartile) and modelling this as a continuous variable. We simultaneously adjusted for the potential confounding effects of factors shown to be associated with> oesophageal cancer in our previous studies[31,43,44]. These include age (years); sex (male, female); BMI 1 year previously (<25, 25·0–29·9, ≥30·0 kg/m^2); education (high school only, technical college or diploma, university); frequency of heartburn or acid reflux symptoms in the 10 years before diagnosis (never, <monthly, <weekly, >weekly, daily); pack-years of smoking (0, 1–14·9, 15–29·9, ≥30); average lifetime alcohol intake (never, <1–6, 7–20, ≥21 drinks/week); non-steroidal anti-inflammatory drugs use during the past 5 years (never, occasionally, less than weekly, at least weekly) and total energy intake (kJ; log-transformed). Further adjustment for state of residence and physical activity did not alter the effect estimates for the dietary patterns; hence these variables were not included in the final models.

Results

The three retained factors were labelled ‘meat and fat’, ‘pasta and pizza’ and ‘fruit and vegetable’ patterns, on the basis of the food groups with the highest factor loadings (Table 1). The meat-and-fat pattern was characterised by high positive loadings for processed meat, high-fat potato, discretionary fat, red meat, high-fat dairy, poultry with skin on, white bread, sweet snacks and fat spreads; and very low factor loadings for fruits, vegetables and fish. The pasta-and-pizza pattern featured high positive loadings for pasta, tomato-based pasta sauce, wine, pizza, olives or pickled vegetables, white rice and cereal products; and very low intakes of processed meat, high-fat potato, discretionary fat, red meat, and high-fat dairy. The fruit-and-vegetable pattern was characterised by high positive loadings for all types of fruits and vegetables, low-fat potatoes, breakfast cereals and wholemeal bread; and low factor loadings for processed meat, high-fat potato, discretionary fat, red meat, high-fat dairy and alcoholic beverages. Together, the three dietary patterns explained 25·4 % of the total variance in dietary intake (11·7 % for the meat-and-fat, 8·2 % for the pasta-and-pizza and 5·5 % for the fruit-and-vegetable patterns). Among control participants, intake of foods with positive factor loadings increased, and that of foods with negative factor loadings decreased monotonically with increasing dietary pattern score. Mean intake of foods with low factor loadings did not differ significantly across quartiles of dietary pattern scores (Table S2, supplementary material for this article can be found at http://www.journals.cambridge.org/bjn).

In general, cases were more likely to be older (≥50 years) and to be heavy smokers (≥30 pack-years) than controls. OAC and OGJAC cases were more likely to be male, obese and to experience symptoms of reflux (>1/month) than OSCC cases and controls, while OSCC cases were more likely to be heavy alcohol consumers (≥21 standard drinks/week) than OAC and OGJAC cases and controls (Table 2). In comparison with controls in the first quartile of the meat-and-fat dietary pattern, those in the fourth quartile were more likely to be male, more likely to be overweight or obese, more likely to smoke heavily (≥30 pack-years) or drink heavily (≥21 standard drinks/week). In contrast, compared with controls in the first quartile of the pasta-and-pizza pattern, those in the fourth quartile were younger, more likely to be female, more likely to have a university education, but less likely to smoke heavily. Compared with controls in the first quartile of the fruit-and-vegetable pattern, those in the fourth quartile were older, more likely to be females and less likely to smoke or drink heavily (Table 3).

A high score on the meat-and-fat dietary pattern was associated with increased risk of all three oesophageal cancers (OR 2·12, 95 % CI 1·30, 3·46, P for trend = 0·002 for OAC; OR 1·88, 95 % CI 1·21, 2·94, P for trend = 0·002 for OGJAC; OR 2·84, 95 % CI 1·67, 4·83, P for trend < 0·0001 for OSCC; Table 4). A high score on the pasta-and-pizza pattern was associated with a decreased risk of OSCC only (OR 0·58, 95 % CI 0·36, 0·96, P-trend = 0·009), while high scores on the fruit-and-vegetable pattern were associated with a borderline significant decreased risk of OGJAC (OR 0·66, 95 % CI 0·41, 1·04) and a significantly decreased risk of OSCC (OR 0·41, 95 % CI 0·24, 0·70, P for trend = 0·002). We found no association between the pasta-and-pizza or the fruit-and-vegetable dietary patterns and risk of OAC (Table 4).

We then considered whether the observed associations with the dietary patterns could be explained by individual food groups that contributed strongly to that pattern. For each pattern, we selected food groups with a loading ≥0·45 (or ≤ − 0·45) and added these one at a time to the model with the dietary pattern variable. Intake of high-fat dairy foods, a major contributor to the meat-and-fat pattern, was significantly associated with increased risk of both OAC and OGJAC. When we included both intake of high-fat dairy foods and the meat-and-fat dietary pattern score in the same model, the association between the meat-and-fat pattern and OAC was attenuated (the OR for quartile (Q) 4 v. Q1 fell from 2·12 to 1·69, 95 % CI 1·00, 2·86) and weaker than that for high-fat dairy foods (OR 2·46, 95 % CI 1·54, 3·94). A similar effect was seen for OGJAC where, in the joint model, there was a strong association with high-fat dairy foods (OR for Q4 v. Q1 = 1·83, 95 % CI 1·17, 2·86) and the association with the meat-and-fat pattern was weakened and non-significant

Table 2. Characteristics of cases and controls
(Numbers and percentages)

Characteristic	Controls (*n* 1507)	OAC (*n* 299)	OGJAC (*n* 336)	OSCC (*n* 245)	*P**
Age group (%)					
< 50 years	17·8	8·4	8·9	6·9	
50–59 years	26·1	27·1	28·8	24·1	
60–69 years	33·6	35·8	33·5	34·7	
≥ 70 years	22·5	28·8	28·8	34·3	< 0·0001
Sex (%)					
Male	66·1	90·6	85·8	60·0	
Female	33·9	9·4	14·2	40·0	< 0·0001
BMI (%)					
< 25 kg/m^2	36·2	20·5	27·4	55·6	
25–29·9 kg/m^2	42·9	42·7	38·9	29·9	
≥ 30 kg/m^2	20·9	36·9	33·7	14·5	0·64
Education (%)					
High school only	40·9	46·5	37·7	57·1	
Technical/diploma	43·6	47·2	51·6	34·3	
University	15·5	6·4	10·7	8·6	< 0·0001
Heartburn or acid reflux symptoms in previous 10 years (%)					
Never	43·1	21·8	28·9	45·9	
< 1/month	30·5	13·4	16·1	12·8	
1/month to < 1/week	14·5	22·5	22·6	13·2	
Daily	11·9	42·3	32·4	28·1	< 0·0001
Pack-years of smoking (%)					
Never smokers	44·7	25·1	24·3	23·1	
0–15	25·2	20·1	19·9	19·8	
15–29	13·2	19·1	22·3	20·2	
≥ 30	16·9	35·8	33·5	34·0	< 0·0001
Alcohol intake, lifetime mean standard drinks per week (%)					
Non-drinkers	10·7	6·4	9·2	12·7	
< 1–6	38·0	27·5	29·7	26·6	
7–20	32·0	36·6	33·5	20·9	
≥ 21	19·3	29·5	27·6	39·8	< 0·0001
Non-steroidal anti-inflammatory drug use (%)					
Never	43·7	46·3	47·6	51·5	
< 1/month	31·4	26·0	28·7	27·4	
< 1/week	9·7	8·8	9·3	7·9	
Weekly or more	15·2	18·9	14·4	13·4	0·08
Physical activity level (%)					
Low	19·3	23·8	21·7	29·5	
Moderate	41·0	36·6	37·7	30·7	
High	39·7	39·6	40·6	39·8	0·09

OAC, oesophageal adenocarcinoma; OGJAC, oesophagogastric junction adenocarcinoma; OSCC, oesophageal squamous cell carcinoma.
* From χ^2 test (sex) or χ^2 test for trend.

(the OR for Q4 *v*. Q1 fell from 1·88 to 1·54, 95 % CI 0·95, 2·48). None of the other high-loading food groups appreciably altered the association with the meat-and-fat pattern when included in the model. This suggests that the observed associations with the meat-and-fat pattern were due largely to the intake of high-fat dairy foods and perhaps not a true effect of the overall dietary pattern.

In contrast, while several food groups from each of the dietary patterns were significantly associated with OSCC risk, none appeared to account for a major portion of the associations between the dietary patterns and OSCC suggesting that these were true pattern effects.

When dietary patterns were derived separately for males and females, we observed factor loadings similar to those reported for the total population. We also found no evidence that the observed associations with dietary patterns were modified by BMI, reflux or smoking (data not shown).

Discussion

We identified three dietary patterns in this population-based case–control study, and together they explained 25 % of the variance in dietary intake as measured by an FFQ. The ‘meat and fat’ and ‘fruit and vegetable’ patterns were similar to those found previously in studies of ovarian cancer[45], and skin cancer[46] using a similar FFQ in an Australian population. Although it had a high positive factor loading for wine and a moderate positive factor loading for spirits, the ‘pasta and pizza’ pattern we observed differed from the ‘alcohol’ or ‘drinker’ dietary patterns described in other studies. Unlike the ‘alcohol’ and ‘drinker’ patterns, this pattern was not characterised by high positive factor loadings on beer, eggs, processed meat, red meat or discretionary fat; instead, it featured moderate loadings on oily fish, nuts, green leafy vegetables, non-oily fish and seafood.

Overall, our results showed that participants with high scores on the meat-and-fat dietary pattern had an almost

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Table 3. Characteristics of 1507 control participants according to quartiles (Q) of dietary pattern score
(Numbers, percentages, mean values and standard deviations)

		Meat-and-fat pattern					Pasta-and-pizza pattern					Fruit-and-vegetable pattern				
Characteristics of study controls	*n*	Q1	Q2	Q3	Q4	*P**	Q1	Q2	Q3	Q4	*P**	Q1	Q2	Q3	Q4	*P**
Age (years)	1507															
Mean		61	61	60	59	0·02	66	63	59	55	< 0·0001	56	60	61	64	< 0·0001
SD		12	11	12	12		9	10	11	12		12	11	11	10	
Sex (%)																
Female	996	49·4	33·7	29·7	15·6	< 0·0001	24·1	38·5	35·9	35·6	0·008	21·5	29·3	36·3	48·1	< 0·0001
Male	511	50·6	66·3	70·3	84·4		75·9	61·5	64·1	64·4		78·5	70·7	63·7	51·9	
BMI (%)																
< 25 kg/m^2	541	43·6	35·6	30·5	32·9		37·1	31·5	37·7	38·2		39·1	33·5	34·8	37·5	
25–29·9 kg/m^2	642	39·5	45·9	43·7	43·0	< 0·0001	42·4	43·3	42·2	43·8	0·15	40·5	45·3	44·2	41·6	0·80
≥ 30 kg/m^2	312	17·0	18·5	25·8	24·1		20·6	25·2	20·1	18·0		20·4	21·2	20·9	20·9	
Education (%)																
High school only	616	40·6	37·6	42·2	44·4		57·4	47·3	36·9	26·3		41·4	36·0	42·8	43·4	
Technical college	657	39·9	46·2	45·3	43·4	0·02	39·8	42·9	48·2	42·7	< 0·0001	42·8	47·4	42·0	42·0	0·28
University	234	19·5	16·3	12·5	12·1		2·9	9·8	14·8	31·0		15·8	16·6	15·1	14·6	
Heartburn or acid reflux symptoms in previous 10 years (%)																
Never	649	46·7	41·6	40·3	43·1	0·006	43·8	43·4	43·0	42·2	0·03	47·0	39·6	42·0	43·9	0·08
< 1/month	460	33·3	33·0	26·1	28·1		24·4	27·3	32·4	36·3		30·1	33·2	33·9	24·7	
1/month to < 1/week	218	10·2	14·1	18·9	16·0		16·4	18·3	12·1	11·9		13·3	15·0	12·3	17·3	
Daily	180	9·8	11·2	14·7	12·9		15·4	10·9	12·6	9·6		9·7	12·2	11·8	14·1	
Pack-years of smoking (%)																
Never smokers	673	50·1	45·7	41·4	38·9	< 0·0001	43·2	46·5	44·7	44·2	< 0·0001	36·2	39·4	51·7	51·1	< 0·0001
≤ 15	380	26·5	25·6	26·7	20·8		18·8	19·7	25·9	34·4		24·3	31·1	22·7	22·6	
15–29	199	10·9	15·3	11·4	16·0		11·1	15·3	13·8	12·4		15·5	12·2	11·5	13·8	
≥ 30	255	12·5	13·4	20·6	24·3		26·9	18·6	15·6	9·1		24·0	17·4	14·1	12·5	
Alcohol intake, lifetime mean standard drinks per week (%)†																
Non-drinkers	161	13·6	12·2	9·2	5·9	< 0·0001	19·4	35·5	24·7	20·4	< 0·0001	6·9	6·7	11·2	17·8	< 0·0001
< 1–6	573	43·8	39·7	36·7	28·5		14·5	44·0	24·9	16·7		31·2	37·1	40·0	43·6	
7–20	482	28·6	33·7	31·7	35·1		8·5	39·7	33·4	18·3		35·4	35·8	31·3	25·5	
≥ 21	291	14·1	14·4	22·5	30·6		2·6	33·2	42·5	21·7		26·5	20·5	17·5	13·0	
Non-steroidal anti-inflammatory drug use (%)																
Never	657	46·7	43·5	43·6	39·7	0·04	48·3	46·2	42·8	39·0	0·61	45·4	41·5	43·7	44·5	0·04
Occasionally	472	29·6	33·2	32·5	30·3		25·4	29·9	34·8	34·2		33·7	32·1	31·7	28·3	
< weekly	145	9·8	8·7	9·2	11·5		7·1	6·9	11·1	12·7		10·6	12·7	8·9	6·4	
At least weekly	228	13·9	14·7	14·7	18·5		19·2	17·0	11·3	14·1		10·3	13·7	15·7	20·8	
Energy intake (kJ)	1507															
Mean		8130	8769	9551	11 389	< 0·0001	8845	9094	9069	9941	< 0·0001	7589	8531	9458	11 453	< 0·0001
SD		2427	2404	2335	2616		2706	2793	2442	2709		2241	2128	2187	2582	

* From χ^2 test for trend (BMI, heartburn, smoking, alcohol, non-steroidal anti-inflammatory drugs use) or heterogeneity (sex, education) or ANOVA (age, energy intake).
† One standard drink = 10 g ethanol.

Table 4. Associations between dietary patterns and risk of oesophageal cancers

(Numbers, percentages, odds ratios and 95 % confidence intervals)

	Controls		OAC				OGJAC				OSCC			
Dietary pattern	*n*	%	*n*	%	OR	95 % CI*	*n*	%	OR	95 % CI*	*n*	%	OR	95 % CI*
Meat and fat														
Q1	434	29·1	42	14·6	1·00		55	16·9	1·00		53	23·6	1·00	
Q2	414	27·8	59	20·5	1·14	0·72, 1·80	63	19·4	0·94	0·62, 1·42	48	21·3	1·15	0·73, 1·82
Q3	357	24·0	80	27·8	1·25	0·79, 1·98	91	28·0	1·27	0·84, 1·91	55	24·4	1·64	1·03, 2·63
Q4	285	49·4	107	37·2	2·12	1·30, 3·46	116	35·7	1·88	1·21, 2·94	69	30·7	2·84	1·67, 4·83
P for trend			0·002				0·002				0·0001			
Pasta and pizza														
Q1	320	21·5	86	29·9	1·00		91	28·0	1·00		83	36·9	1·00	
Q2	363	24·4	73	25·4	0·99	0·67, 1·47	79	24·3	0·87	0·60, 1·26	61	27·1	0·72	0·48, 1·09
Q3	392	26·3	77	26·7	1·00	0·67, 1·50	72	22·2	0·77	0·52, 1·13	41	18·2	0·52	0·33, 0·83
Q4	415	27·6	52	18·1	0·72	0·45, 1·15	83	25·5	1·01	0·67, 1·52	40	17·8	0·58	0·36, 0·96
P for trend			0·25				0·82				0·009			
Fruit and vegetable†														
Q1	355	23·8	60	20·8	1·00		83	25·5	1·00		82	36·4	1·00	
Q2	382	25·6	81	28·1	1·26	0·84, 1·91	76	23·4	0·78	0·53, 1·14	47	20·9	0·57	0·37, 0·89
Q3	381	25·6	68	23·6	1·10	0·70, 1·74	89	27·4	0·92	0·62, 1·37	44	19·6	0·51	0·31, 0·83
Q4	372	25·0	79	27·4	1·29	0·77, 2·14	77	23·7	0·66	0·42, 1·04	52	23·1	0·41	0·24, 0·70
P for trend			0·49				0·16				0·002			

OAC, oesophageal adenocarcinoma; OGJAC, oesophagogastric junction adenocarcinoma; OSCC, oesophageal squamous cell carcinoma; Q, quartiles.

* OR adjusted for age (years); sex; education (school only, technical college or diploma, university); BMI 1 year ago (<25, 25·0–29·9, ≥30·0 kg/m^2); frequency of heartburn or acid reflux 10 years before diagnosis/recruitment (never, <monthly, <weekly, >weekly, daily); pack-years of smoking (0, 1–14·9, 15–29·9, ≥30); non-steroidal anti-inflammatory drugs use (never, occasionally, less than weekly, at least weekly); and total energy (kJ, log transformed).

† Additionally adjusted for lifetime alcohol intake (never, <1–6, 7–20, ≥21 drinks/week). The 'meat and fat' and 'pasta and pizza' patterns were not adjusted for alcohol as alcoholic drinks were high loading components of these patterns; however, additional adjustment for alcohol intake did not alter the results.

2-fold increased risks of OAC and OGJAC, and an almost 3-fold increased risk of OSCC. Participants with high scores on the pasta-and-pizza pattern had a 42 % decreased risk of OSCC, while those with high scores on the fruit-and-vegetable pattern had a borderline significant 34 % decreased risk of OGJAC and a significant 59 % decreased risk of OSCC.

Our finding of a positive association between the meat-and-fat pattern and OAC and OGJAC risks is consistent with the findings of a population-based case–control study from Sweden, where the authors reported a positive association between a high score on a 'Western' dietary pattern, similar to our 'meat and fat' dietary pattern, and risks of gastric cardia adenocarcinoma and OAC[25]. Our finding that this association was driven in part by consumption of high-fat dairy foods is consistent with reports from two population-based case–control studies in which positive associations were found between a high-fat dairy food group[23], or a high-milk dietary pattern[29] and risk of OAC. An inverse association between total intake of dairy products and risk of OAC has been reported however[29] and in our data, the low-fat dairy food group had a negative factor loading (−0·33) in relation to the meat-and-fat pattern, suggesting that participants whose diet followed the meat-and-fat dietary pattern were less likely to consume foods from the low-fat dairy food group. Taken together, it is therefore possible that the fat component of the high-fat dairy food group may be most important in contributing to increased OAC risk.

Our finding of a positive association between the meat-and-fat pattern and OSCC is consistent with findings from other case–control studies from Sweden[25], Uruguay[27] and Iran[28]. One mechanism postulated to explain this association is that processed meat contains high levels of nitrites and *N*-nitroso compounds which might exert a carcinogenic effect[11].

The inverse association we observed between the pasta-and-pizza dietary pattern and risk of OSCC warrants further exploration, given that this factor had a strong positive loading with wine, and the known strong links between alcohol intake and risk of OSCC. It is, however, consistent with our previous study that found a decreased OSCC risk among those with low to moderate intake of alcohol from wine (≤90 g/week)[43]. In the present analyses, the mean intake of alcohol from wine across all quartiles of the pasta-and-pizza pattern (8·8, 23·2, 45·5, 76·1 g/week) was below this level, indicating that this dietary pattern was characterised by modest wine consumption. In addition to wine, the pasta-and-pizza pattern featured moderate intakes of other foods such as green leafy vegetables, fruit and vegetable juices, nuts, legumes, oily fish and whole grains that contain micronutrients with known antioxidant and anticarcinogenic properties including flavonoids, folates, phytosterols, vitamins A, C, E and dietary fibre. Thus, several aspects of the pasta-and-pizza dietary pattern are similar to the 'Mediterranean diet' which has been shown to be associated with decreased risk of cancers of the upper aerodigestive tract[47].

Our finding of an inverse association between the fruit-and-vegetable dietary pattern and risk of OSCC is consistent with the findings of case–control studies from Uruguay[26,27] and Iran[28]. A Swedish study also found an inverse but non-significant association with a 'healthy' dietary pattern with components similar to our fruit-and-vegetable pattern[25]. The World Cancer Research Fund report states that there is evidence to support that fruits probably protect against oesophageal cancer[1]. A population-based case–control study[23], and a prospective study[21] reported inverse association between non-citrus fruits[23] or fruits in the Rosaceae botanical group[21]and decreased OSCC risk. The component of non-citrus fruits and fruits in the Rosaceae family from both studies are similar to 'other' fruits (fruits other than those containing high levels of vitamin C or A) in our study.

The strengths of our present study include its relatively large sample size, the population-based design and our ability to control for a large number of potentially important confounders. Also, ours is one of the few studies to investigate the association between dietary patterns and the three types of oesophageal cancer in the same study. A limitation is the low participation rate among controls and cases. Detailed information on the characteristics of non-participants are not available because of Australian privacy laws; nevertheless, comparison of our study control data to data from the Australian National Health Survey, a representative survey of the Australian adult population conducted in 2004 with a reported 90 % response rate[48], showed similar distributions of key characteristics including educational level, BMI and smoking (ever/never)[49]. The strong influence of current diet on recall of past diet raises concerns regarding the possibility of recall bias among cases if their diet changed as a result of their diagnosis, or because they experienced symptoms as a result of the presence of subclinical disease before diagnosis. To minimise this, study participants were asked to report recent changes to their diet in the last year or two. Exclusion of individuals who reported having changed their diet did not alter our findings. Another limitation is the use of FFQ, an instrument prone to measurement error in collecting dietary data; however, the FFQ from which the dietary patterns were derived has shown reasonably good validity when compared with weighed food records[36,37] and serum biomarkers[38]; and any non-differential measurement error is likely to have attenuated the associations that we have observed, thus strengthening the results of our present study. Finally, it is possible that our results could be biased if the association between dietary patterns and oesophageal cancer differs by tumour grade, a strong predictor of survival, and hence study participation. However, we found no evidence that the reported associations differed by tumour grade.

In conclusion, we have shown that a 'meat and fat' dietary pattern was associated with increased risks of OAC, OGJAC and OSCC, a 'pasta and pizza' pattern was inversely associated with OSCC risk, while a 'fruit and vegetable' pattern was associated with a decreased risk of OSCC and possibly OGJAC but not OAC. However, high-fat dairy foods appear to play a major role in the association between the meat-and-fat dietary pattern and oesophageal cancer. Further analyses using data from prospective studies would be valuable to confirm the role of dietary patterns in oesophageal cancer risk.

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The Australian Cancer Study

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