Original article

Annals of Oncology 14: 162–167, 2003
DOI: 10.1093/annonc/mdg032

Fibre intake and laryngeal cancer risk

C. Pelucchi[1]*, R. Talamini[2], F. Levi[3], C. Bosetti[1], C. La Vecchia[1,4], E. Negri[1], M. Parpinel[2] & S. Franceschi[5]

[1]*Istituto di Ricerche Farmacologiche 'Mario Negri', Milan;* [2]*Servizio di Epidemiologia, Centro di Riferimento Oncologico, Aviano, Italy;* [3]*Registre Vaudois des Tumeurs, Institut Universitaire de Médecine Sociale et Préventive, Lausanne, Switzerland;* [4]*Istituto di Statistica Medica e Biometria, Università degli Studi di Milano, Milan, Italy;* [5]*International Agency for Research on Cancer, Lyon, France*

Received 6 May 2002; revised 7 August 2002; accepted 10 September 2002

Background: Consumption of vegetables, fruit and whole grain cereals has been inversely related to laryngeal cancer risk. Among the potential protective agents found in these foods, information on dietary fibres and laryngeal cancer risk are scanty.

Patients and methods: A multi-centric, hospital-based case–control study was conducted on 527 patients with squamous-cell carcinoma of the larynx and 1297 non-neoplastic controls. Cases and controls, frequency matched by age, sex and study centre, were interviewed using a validated food frequency questionnaire.

Results: Compared with the lowest quintile of fibre intake, the odds ratios (ORs) for the highest quintile were 0.3 [95% confidence interval (CI) 0.2–0.4] for total fibre, 0.3 (95% CI 0.2–0.5) for soluble non-cellulose polysaccharides (NCP) and for total insoluble fibre, including cellulose (OR = 0.3, 95% CI 0.2–0.4) and insoluble NCP (OR = 0.4, 95% CI 0.3–0.7). The ORs were 0.2 (95% CI 0.1–0.4) for fibre from vegetables, 0.5 (95% CI 0.3–0.7) from fruit and 1.1 (95% CI 0.6–1.9) from grains. The inverse association observed was similar among different subsites of laryngeal cancer, and consistent across strata of various covariates.

Conclusions: This study found a strong inverse association between fibre intake and laryngeal cancer risk, which points to fibre as one of the beneficial components of vegetables and fruit.

Key words: case–control study, diet, risk factors, fibre, laryngeal cancer, subsite

Introduction

Several studies have found an inverse association between consumption of fruit and vegetables and the risk of laryngeal cancer [1–3]. A multi-centric study on 1147 male cases and 3057 controls conducted in south-western Europe found odds ratios (OR) for low fruit intake of 1.8 and 1.4 for epilaryngeal and endolaryngeal cancer, respectively, while for low vegetable intake the OR was 1.6 for both subsites [2]. A case–control study from Uruguay found an OR of 0.4 for high consumption of plant foods [4].

Whole grain cereals were also inversely related to laryngeal cancer risk in two case–control studies from Italy (OR = 0.2) [5] and Switzerland (OR = 0.7) [6], while refined grain cereals were directly related to laryngeal cancer risk, the OR being 4.0 in Switzerland and 1.6 in Italy for the combination of cancers of the oral cavity, pharynx, oesophagus and larynx [6, 7]. A Norwegian cohort study of the upper aerogastric tract cancers on 10 960 men reported an OR of 0.2 for high consumption of bread [8].

Among potential anticarcinogens that are found in fruit, vegetables and whole grains [9, 10], various studies have considered carotenoids, vitamins C and E [1, 2, 11, 12], while available information on dietary fibre and laryngeal cancer risk is scanty. No consistent association was found in a study from western New York based on 250 male cases and 250 controls [12]. In the above-mentioned multi-centric study from south-western Europe, fibre intake was significantly lower in cases than in controls, but adjusted ORs were not given [2]. No study analysed the relation between fibre intake and different subsites of laryngeal cancer and, more importantly, no information is available on various types of fibres.

Thus, we considered the relation between intake of various types of fibres, as well as their food source, and risk of laryngeal cancer, also by subsite, in a case–control study conducted in Italy and Switzerland.

Patients and methods

A multi-centric, hospital-based case–control study on laryngeal cancer was conducted from January 1992 to December 2000 in Italy and Switzerland.

Cases were 527 patients (478 men, 49 women), aged 30–79 years (median age 61) with incident, histologically-confirmed squamous-cell carcinoma of the larynx, including 271 cancers of the glottis (International Classification of Diseases (ICD-IX) [13]: 161.0), 117 of the supraglottis (ICD-IX: 161.1), four of the subglottis (ICD-IX: 161.2), five of the laryngeal cartilages (ICD-IX: 161.3), 19 other specified (ICD-IX: 161.8) and 111 unspecified cancers of the larynx (ICD-IX: 161.9). The cases were admitted to the major teaching and general hospitals in two areas of northern Italy, the greater Milan area and the province of Pordenone, and in the Swiss Canton of Vaud.

**Correspondence to:* Dr Claudio Pelucchi, Istituto di Ricerche Farmacologiche 'Mario Negri', Via Eritrea, 62-20157, Milan, Italy.
Tel: +39-02-390141; Fax: +39-02-33200231;
E-mail: pelucchi@marionegri.it

Controls were 1297 subjects (1052 men, 245 women), aged 31–79 years (median age 61) admitted to the same network of hospitals as cases for acute, non-neoplastic conditions unrelated to smoking, alcohol drinking and long-term modifications of diet. Thirty-two per cent of controls were admitted for non-traumatic orthopaedic disorders, such as low back and disc disorders, 26% for traumas, mostly sprains and fractures, 23% for acute surgical conditions and 20% for other diseases, such as eye, ear, nose, skin and dental conditions. Controls were frequency matched with cases by 5-year age group, sex and study centre. To compensate for the rarity of laryngeal cancer in women, a control-to-case ratio of 5 was chosen for females, as compared with 2 for males. A low proportion of the subjects approached refused the interview (about 5% for both cases and controls).

The same structured questionnaire was used in all study centres. It was administered by centrally trained interviewers during the subjects' hospital stay, and included information on socio-demographic characteristics, lifelong smoking and alcohol drinking habits, physical activity, anthropometrical measures at various ages, a problem-oriented medical history and history of cancer in first-degree relatives.

An interviewer-administered food frequency questionnaire (FFQ) was developed to assess the usual diet during the 2 years preceding the diagnosis (for cases) or the hospital admission (for controls), and in order to estimate the intake of total energy as well as that of selected nutrients. The questionnaire included 78 foods, food groups or dishes divided into six sections: (i) bread, cereals, first courses; (ii) second courses (i.e. meat, fish and other main dishes); (iii) side dishes (i.e. vegetables); (iv) fruits; (v) sweets, desserts and soft drinks; (vi) milk, hot beverages and sweeteners.

For a few vegetables and fruits, seasonal consumption and the corresponding duration were elicited. At the end of each section, one or two open questions were used to include foods that were not included in the questionnaire, but eaten at least once per week. There were a few differences in the dietary items listed in the Italian and Swiss versions of the questionnaire, to account for different eating and drinking patterns. To compute energy and nutrient intake, Italian food composition databases were used and integrated with other sources when needed [14]. The FFQ was satisfactorily reproducible [15] and valid [16].

Dietary fibre intake was derived using the Englyst procedure [17, 18], that measures fibre as non-starch polysaccharides. A value was obtained for total fibre, soluble and insoluble fibre. A modification of the method allows cellulose to be measured separately from insoluble non-cellulose polysaccharides (NCP). Values for lignin, a minor component of the human diet, were provided separately. We did not include resistant starch in the computation of total fibre, because the amount depends on how each food is processed and consumed [19], and related food composition tables were not available. Fibre intake was also divided according to the food from which it originated, i.e. vegetables, fruit or cereals.

Data analysis

Odds ratios (OR), and corresponding 95% confidence intervals (CI), for laryngeal cancer were estimated using multiple logistic regression models [20] conditioned on age (<50, 50–54, 55–59, 60–64, 65–69, ≥70 years), sex and study centre, and including terms for education (<7, 7–11, ≥12 years), body mass index (BMI, in quartiles) in the year before the diagnosis or interview (for controls), tobacco smoking (never, ex-, current smokers of <15, 15–24, ≥25 cigarettes/day), alcohol drinking (<2, 2–3, 4–7, ≥8 drinks/day) and energy intake (excluding energy from alcohol drinking, in quintiles). Further adjustments were performed, and results did not differ even when terms were included in the models for the number of cigarettes/day, duration of the habit and the age smoking was commenced.

Results

Table 1 shows the distribution of the matching variables, age, sex and study centre, and the distribution and ORs of the main covariates of interest. An increased risk of laryngeal cancer was observed for the highest level of education (OR = 1.5, 95% CI 1.0–2.2). Only 3.6% of cases were never smokers, compared with 37.3% of controls, and the OR rose to over 40 for the highest tobacco smoking level. For heavy alcohol drinkers the OR was 5.8 (95% CI 3.8–8.9) as compared with non-drinkers and light drinkers.

Table 2 gives the ORs and their 95% CI for the intake of various types of dietary fibres and for the food sources of total fibre. Compared with the lowest quintile of intake, all types of fibres were inversely associated with risk of laryngeal cancer, with a significant trend in risk (P <0.0001). The OR for the highest quintile of intake was 0.3 (95% CI 0.2–0.4) for total fibre; it was also 0.3 (95% CI 0.2–0.5) for both soluble fibre and total insoluble fibre.

With regard to the food source, fibre from vegetables (OR = 0.2, 95% CI 0.1–0.4) and from fruit (OR = 0.5, 95% CI 0.3–0.7) showed an inverse relation with risk of laryngeal cancer. On the other hand, fibre from grain was unrelated to risk (OR = 1.1, 95% CI 0.6–1.9).

Table 3 gives the ORs for total fibre intake according to strata of various covariates. No significant heterogeneity was reported across strata, even if fibre intake appeared to have a greater protective effect in subjects <60 years of age than in subjects ≥60 years of age, and in those with an average daily energy intake above the median value (2630 kcal/day) compared with subjects with energy intake below the median. The inverse relationships were consistent for men and women, despite the low absolute numbers in women.

Table 4 shows the distribution of cases and controls, and the ORs separately for subsites of laryngeal cancer. Comparing with the lowest quintile of total fibre intake, the OR for the highest quintile was 0.3 for those with glottic cancer, 0.3 for those with supraglottic cancer and 0.2 for those with other or unspecified laryngeal cancers.

Discussion

This study found a consistent inverse relationship between intake of dietary fibres and laryngeal cancer risk. Such a relationship was observed for various types of fibres (i.e. soluble, insoluble, lignin) deriving from vegetables and fruit, but not from grain.

The apparent protection conferred by total fibre intake was consistent across strata of age, sex, tobacco smoking, alcohol drinking, energy intake and BMI. For subjects <60 years of age and for energy intake over the median value the protection appeared to be somewhat stronger, but the heterogeneity tests were non-significant. In the two major subsites of laryngeal cancer, i.e. cancers of the supraglottis, including epiglottis, false cords and laryngeal ventricles, and of the glottis, including true vocal cord [21], the multivariate ORs for total fibre intake were similar. Therefore dietary fibre seems to act in the same way on the extrinsic and intrinsic larynx.

Table 1. Distribution of 527 cases of laryngeal cancer and 1297 controls according to selected covariates (Italy and Switzerland, 1992–2000)

	Cases	%	Controls	%	OR[a]	95% CI
Age (years)						
<50	59	11.2	133	10.2	–	–
50–54	74	14.0	188	14.5	–	–
55–59	97	18.4	259	20.0	–	–
60–64	113	21.4	266	20.5	–	–
65–69	105	19.9	264	20.3	–	–
≥70	79	15.0	187	14.4	–	–
Sex						
Male	478	90.7	1052	81.1	–	–
Female	49	9.3	245	18.9	–	–
Centre						
Milan	44	8.4	154	11.9	–	–
Pordenone	416	78.9	934	72.0	–	–
Switzerland	67	12.7	209	16.1	–	–
Education (years)[b]						
<7	289	54.8	652	50.3	1[c]	–
7–11	137	26.0	400	30.9	0.9	0.7–1.3
≥12	101	19.2	244	18.8	1.5	1.0–2.2
Tobacco smoking[b] (cigarettes/day)						
Never	19	3.6	485	37.3	1[c]	–
<15	58	11.1	146	11.3	9.3	5.2–16.4
15–24	187	35.6	142	10.9	29.5	17.0–51.1
≥25	102	19.4	63	4.9	40.8	22.0–75.8
Ex	159	30.3	460	35.6	7.5	4.4–12.9
Alcohol drinking[b] (drinks/day)						
<2	58	11.1	428	33.0	1[c]	–
From 2 to <4	76	14.5	347	26.8	1.3	0.8–1.9
From 4 to <8	176	33.6	362	27.9	2.6	1.8–3.9
≥8	214	40.8	159	12.3	5.8	3.8–8.9

[a]Estimates from logistic regression conditioned on age, sex and study centre, and adjusted for tobacco smoking, alcohol consumption and non-alcohol energy intake.
[b]The sum does not add up to the total because of missing values.
[c]Reference category.

Dietary fibre could protect against cancer through various plausible biological mechanisms [22]. Fibre may reduce glycaemic load [23] and improve insulin sensitivity, favourably influencing insulin-like growth factor I (IGF-1), which is a promoter of the process of carcinogenesis at various sites [24]. A possible explanation for the lack of protection of grain fibre on laryngeal cancer risk could be that it comes mostly from refined cereal, highly consumed in the population studied. Refined cereals are low in dietary fibre (particularly in insoluble fibre) [10] and could be directly related to risk of cancer, as reported in previous studies [6, 7], because of the potential promotional action of starch [25] that may overwhelm any possible protective action of fibre.

Other studies on dietary fibre conducted in the same population have found decreased risk of cancers of the upper digestive tract [26], colorectum [27, 28], ovary [29] and a moderate reduction in breast cancer risk [30]. In three of these studies [27, 29, 30] the protection deriving from cellulose and soluble NCPs was apparently stronger than that from insoluble NCPs and lignin. On the other hand, in this study no clear difference between various types of fibres was visible, and the issue still remains open.

Various models were fitted to understand whether the results found should be attributed to intake of fibre alone, to other nutrients contained in plant foods or to vegetable and fruit whole consumption. It was, however, difficult to infer from these models, due to the colinearity between these variables and hence to possible over adjustments. Total fibre intake was, in fact, directly correlated with fruit ($\rho = 0.69$) and vegetable intake ($\rho = 0.40$), vitamin C ($\rho = 0.65$) and β-carotene ($\rho = 0.59$). The OR for the

Table 2. Odds ratios[a,b] (OR) and 95% confidence intervals (CI) of laryngeal cancer according to the intake of various types of fibre (Italy and Switzerland, 1992–2000)

Type of fibre	Quintile of intake[c]				Trend, χ^2 (*P* value)
	Q2	Q3	Q4	Q5	
Total (Englyst) fibre	(12.0)	(15.2)	(17.7)	(21.7)	
OR	0.6	0.3	0.3	0.3	33.0 (<0.0001)
95% CI	0.4–0.9	0.2–0.5	0.2–0.5	0.2–0.4	
Soluble NCP[d]	(5.8)	(7.3)	(8.6)	(10.3)	
OR	0.6	0.4	0.3	0.3	30.0 (<0.0001)
95% CI	0.4–0.9	0.3–0.7	0.2–0.5	0.2–0.5	
Total insoluble fibre	(6.2)	(7.8)	(9.2)	(11.3)	
OR	0.6	0.4	0.3	0.3	27.4 (<0.0001)
95% CI	0.4–0.8	0.2–0.6	0.2–0.5	0.2–0.5	
Cellulose	(3.1)	(4.0)	(4.7)	(5.8)	
OR	0.6	0.3	0.3	0.3	40.3 (<0.0001)
95% CI	0.4–0.9	0.2–0.5	0.2–0.5	0.2–0.4	
Insoluble NCP[d]	(3.0)	(3.7)	(4.5)	(5.4)	
OR	0.5	0.4	0.3	0.4	18.3 (<0.0001)
95% CI	0.4–0.8	0.2–0.6	0.2–0.4	0.3–0.7	
Lignin	(1.1)	(1.4)	(1.7)	(2.1)	
OR	0.7	0.6	0.4	0.3	20.0 (<0.0001)
95% CI	0.4–1.0	0.4–1.0	0.3–0.7	0.2–0.6	
Vegetable fibre	(4.2)	(5.3)	(6.4)	(7.9)	
OR	0.6	0.5	0.3	0.2	47.5 (<0.0001)
95% CI	0.4–0.9	0.3–0.7	0.2–0.5	0.1–0.4	
Fruit fibre	(2.8)	(4.5)	(5.9)	(8.1)	
OR	0.5	0.4	0.4	0.5	16.9 (<0.0001)
95% CI	0.4–0.7	0.3–0.7	0.3–0.6	0.3–0.7	
Grain fibre	(3.1)	(4.1)	(5.1)	(6.7)	
OR	1.1	1.1	1.1	1.1	0.02 (0.89)
95% CI	0.7–1.8	0.7–1.8	0.6–1.8	0.6–1.9	

[a]Estimates from logistic regression conditioned on age, sex and study centre. All types and sources of fibre are adjusted for education, body mass index, tobacco smoking, alcohol consumption and non-alcohol energy intake.
[b]Quintiles are computed on the distribution of controls. In parentheses, the lower cut-off point of the quintile (in g/day) is given.
[c]The reference category is the first (lowest) quintile.
[d]NCP, non-cellulose polysaccharides.

highest quintile of total fibre was 0.3 (95% CI 0.2–0.6) after adjusting for vegetable and fruit intake (besides other variables), 0.5 (95% CI 0.3–0.8) after adjusting for β-carotene and 0.4 (95% CI 0.2–0.8) for vitamin C, suggesting that there is a protective effect of dietary fibre by itself. The possibility that high fibre intake, and consequently high consumption of fruit, vegetables and/or whole grain cereals, could have acted indirectly by substituting meat, fish and refined grains was also considered, but further adjustment for these variables did not substantially modify the ORs.

Among possible biases of this study are the selection of hospital controls, whose dietary habits may differ from those of the general population. However, we carefully excluded from the comparison group any diagnosis that might have involved long-term modifications of diet, or that could be related to alcohol consumption or smoking habit. To reduce the possibility of recall bias due to dietary modifications after cancer onset, we asked for food consumption in the 2 years before diagnosis. We also performed separate analysis among control groups by main diagnostic categories, and the results were reassuring. The strengths of the study are the satisfactory reproducibility and validity of the FFQ, the comparable catchment areas of cases and controls, the high participation rate of the subjects approached, and the possibility to control, together with major risk factors such as social

Table 3. Odds ratios[a,b] (OR) and 95% confidence intervals (CI) of laryngeal cancer according to total fibre intake, in separate strata of covariates (Italy and Switzerland, 1992–2000)

Strata	Quintile of intake[c]				Trend, χ^2 (*P* value)
	Q2	Q3	Q4	Q5	
Age (years)					
<60	0.5 (0.3–0.9)	0.3 (0.1–0.6)	0.2 (0.1–0.3)	0.2 (0.1–0.3)	29.1 (<0.0001)
≥60	0.6 (0.3–1.0)	0.4 (0.2–0.6)	0.5 (0.3–0.9)	0.3 (0.2–0.7)	9.5 (0.002)
Sex					
Male	0.6 (0.4–0.9)	0.4 (0.2–0.6)	0.3 (0.2–0.5)	0.3 (0.1–0.4)	31.9 (<0.0001)
Female	0.5 (0.1–3.0)	0.1 (0.01–0.5)	0.5 (0.1–3.3)	0.2 (0.02–1.6)	0.7 (0.40)
Smoking status					
Never/ex ≥5 years	0.6 (0.3–1.1)	0.6 (0.3–1.1)	0.3 (0.1–0.7)	0.3 (0.2–0.7)	9.5 (0.002)
Current/ex <5 years	0.6 (0.4–1.0)	0.2 (0.1–0.4)	0.3 (0.2–0.5)	0.2 (0.1–0.5)	23.2 (<0.0001)
Alcohol consumption (drinks/day)					
<4	0.7 (0.4–1.5)	0.3 (0.1–0.6)	0.3 (0.1–0.7)	0.2 (0.1–0.5)	15.4 (<0.0001)
≥4	0.5 (0.3–0.9)	0.4 (0.2–0.7)	0.3 (0.1–0.5)	0.3 (0.2–0.6)	18.4 (<0.0001)
Non-alcohol energy intake (kcal/day)					
<2630	0.7 (0.4–1.3)	0.2 (0.1–0.5)	0.4 (0.2–0.9)	0.5 (0.2–1.2)	9.9 (0.0016)
≥2630	0.4 (0.2–0.9)	0.4 (0.2–0.7)	0.3 (0.1–0.5)	0.2 (0.1–0.4)	19.8 (<0.0001)
BMI (kg/m^2)					
<26.1	0.5 (0.3–0.8)	0.4 (0.2–0.7)	0.2 (0.1–0.5)	0.2 (0.1–0.4)	21.3 (<0.0001)
≥26.1	0.6 (0.3–1.1)	0.3 (0.1–0.6)	0.3 (0.2–0.7)	0.3 (0.2–0.7)	10.6 (0.0011)

[a]Estimates from logistic regression conditioned on age, sex and study centre, and adjusted for education, body mass index (BMI), tobacco smoking, alcohol consumption and non-alcohol energy intake.
[b]Quintiles are computed on the distribution of controls.
[c]The reference category is the first (lowest) quintile.

Table 4. Odds ratios[a] (OR) and 95% confidence intervals (CI) of laryngeal cancer according to total fibre intake, by subsite (Italy and Switzerland, 1992–2000)

Subsite[b]	Quintile of intake					Trend, χ^2 (*P* value)
	Q1	Q2	Q3	Q4	Q5	
Number of cases						
Glottis	72	66	45	43	45	
Supraglottis	31	32	15	19	20	
Other/unspecified	47	32	24	22	14	
Number of controls	260	259	259	260	259	
OR						
Glottis	1[c]	0.6	0.3	0.3	0.3	22.5 (<0.0001)
95% CI	–	0.4–1.0	0.2–0.6	0.2–0.5	0.1–0.5	
Supraglottis	1[c]	0.7	0.3	0.3	0.3	10.6 (0.0011)
95% CI	–	0.3–1.5	0.1–0.7	0.1–0.7	0.1–0.7	
Other/unspecified	1[c]	0.5	0.4	0.3	0.2	15.6 (<0.0001)
95% CI	–	0.2–0.9	0.2–0.7	0.1–0.6	0.1–0.4	

[a]Estimates from logistic regression conditioned on age, sex and study centre, and adjusted for education, body mass index, tobacco smoking, alcohol consumption and non-alcohol energy intake.
[b]Subsites were elicited using the International Classification of Diseases (ICD-IX): 161.0, glottic cancer; 161.1, supraglottic cancer; 161.2–161.9, other/unspecified laryngeal cancer.
[c]Reference category.

class indicators, tobacco and alcohol consumption, for other nutrients and energy intake too.

In conclusion, this study supports the hypothesis that fibre may be one explanation for the marked protection conferred by high fruit and vegetable intake against laryngeal cancer risk. It also suggests that this potentially favourable role of dietary fibre might be similar among the different subsites of laryngeal cancer.

Acknowledgements

This work was conducted with the contribution of the Italian Association for Cancer Research, Milan, the Italian and Swiss Leagues against Cancer and the Swiss Foundation for Research Against Cancer, Bern. The authors would like to thank Mrs C. Pasche and F. Lucchini for data collection and validation, and Mrs I. Garimoldi for editorial assistance.

References

1. Riboli E, Kaaks R, Esteve J. Nutrition and laryngeal cancer. Cancer Causes Control 1996; 7: 147–156.
2. Esteve J, Riboli E, Pequignot G et al. Diet and cancers of the larynx and hypopharynx: the IARC multi-center study in southwestern Europe. Cancer Causes Control 1996; 7: 240–252.
3. La Vecchia C, Tavani A. Fruit and vegetables, and human cancer. Eur J Cancer Prev 1998; 7: 3–8.
4. De Stefani E, Boffetta P, Oreggia F et al. Plant foods and risk of laryngeal cancer: a case–control study in Uruguay. Int J Cancer 2000; 87: 129–132.
5. Chatenoud L, Tavani A, La Vecchia C et al. Whole grain food intake and cancer risk. Int J Cancer 1998; 77: 24–28.
6. Levi F, Pasche C, Lucchini F et al. Refined and whole grain cereals and the risk of oral, oesophageal and laryngeal cancer. Eur J Clin Nutr 2000; 54: 487–489.
7. Chatenoud L, La Vecchia C, Franceschi S et al. Refined-cereal intake and risk of selected cancers in Italy. Am J Clin Nutr 1999; 70: 1107–1110.
8. Kjaerheim K, Gaard M, Andersen A. The role of alcohol, tobacco, and dietary factors in upper aerogastric tract cancers: a prospective study of 10 900 Norwegian men. Cancer Causes Control 1998; 9: 99–108.
9. Steinmetz KA, Potter JD. Vegetables, fruit, and cancer. II. Mechanisms. Cancer Causes Control 1991; 2: 427–442.
10. Slavin JL, Martini MC, Jacobs DR Jr, Marquart L. Plausible mechanisms for the protectiveness of whole grains. Am J Clin Nutr 1999; 70: 459S–463S.
11. Nomura AM, Ziegler RG, Stemmermann GN et al. Serum micronutrients and upper aerodigestive tract cancer. Cancer Epidemiol Biomarkers Prev 1997; 6: 407–412.
12. Freudenheim JL, Graham S, Byers TE et al. Diet, smoking, and alcohol in cancer of the larynx: a case–control study. Nutr Cancer 1992; 17: 33–45.
13. World Health Organization. International Classification of Diseases, 9th edition. Geneva: WHO 1977.
14. Salvini S, Parpinel MT, Gnagnarella P et al. Banca dati di composizione degli alimenti per studi epidemiologici in Italia. Milan: European Institute of Oncology 1998.
15. Franceschi S, Barbone F, Negri E et al. Reproducibility of an Italian food frequency questionnaire for cancer studies: results for specific nutrients. Ann Epidemiol 1995; 5: 69–75.
16. Decarli A, Franceschi S, Ferraroni M et al. Validation of a food frequency questionnaire to assess dietary intakes in cancer studies in Italy: studies for specific nutrients. Ann Epidemiol 1996; 6: 110–118.
17. Englyst HN, Bingham SA, Runswick SA et al. Dietary fibre (non-starch polysaccharides) in fruit, vegetables and nuts. J Hum Nutr Diet 1988; 1: 247–286.
18. Englyst HN, Bingham SA, Runswick SA et al. Dietary fibre (non-starch polysaccharides) in cereal products. J Hum Nutr Diet 1989; 2: 253–271.
19. Cummings JH, Englyst HN. Gastrointestinal effects of food carbohydrate. Am J Clin Nutr 1995; 61: 938S–945S.
20. Breslow NE, Day NE. Statistical Methods in Cancer Research. The Analysis of Case–control Studies, Vol. 1. IARC Scientific Publications No. 32. Lyon: IARC 1980.
21. Austin DF, Reynolds P. Laryngeal cancer. In Schottenfeld D, Fraumeni JF Jr (eds): Cancer Epidemiology and Prevention, 2nd edition. New York: Oxford University Press 1996; 619–636.
22. Ferguson LR, Chavan RR, Harris PJ. Changing concepts of dietary fiber: implications for carcinogenesis. Nutr Cancer 2001; 39: 155–169.
23. Franceschi S, Dal Maso L, Augustin L et al. Dietary glycaemic load and colorectal cancer risk. Ann Oncol 2001; 12: 173–178.
24. Yu H, Rohan T. Role of the insulin-like growth factor family in cancer development and progression. J Natl Cancer Inst 2000; 92: 1472–1489.
25. Giovannucci E. Insulin and colon cancer. Cancer Causes Control 1995; 6: 164–179.
26. Soler M, Bosetti C, Franceschi S et al. Fiber intake and the risk of oral, pharyngeal and esophageal cancer. Int J Cancer 2001; 91: 283–287.
27. Negri E, Franceschi S, Parpinel M, La Vecchia C. Fiber intake and risk of colorectal cancer. Cancer Epidemiol Biomarkers Prev 1998; 7: 667–671.
28. Levi F, Pasche C, Lucchini F, La Vecchia C. Dietary fiber and the risk of colorectal cancer. Eur J Cancer 2001; 37: 2091–2096.
29. Pelucchi C, La Vecchia C, Chatenoud L et al. Dietary fibres and ovarian cancer risk. Eur J Cancer 2001; 37: 2235–2239.
30. La Vecchia C, Ferraroni M, Franceschi S et al. Fibers and breast cancer risk. Nutr Cancer 1997; 28: 264–269.