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Diet and cancer in Mediterranean countries: carbohydrates and fats

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Abstract

Objective: Several aspects of the diet characteristic of the Mediterranean countries are considered favourable not only on cardiovascular disease, but also on cancer risk. We considered some aspects of the Mediterranean diet (including, in particular, the consumption of olive oil and carbohydrates) on cancer risk.
Design, Setting and Subjects: Data were derived from a series of case-control studies, conducted in Italy since the early 1990s, on over 10 000 cases of thirteen cancer sites and over 17 000 controls.
Results: Olive oil, and other mono- and unsaturated fats, appear to be favourable indicators of breast, ovarian, colorectal, but mostly of upper aero-digestive tract cancers. Whole grain foods are also related to reduced risk of upper aero-digestive tract and various other cancers. In contrast, refined grain intake and, consequently, glycaemic index and glycaemic load were associated to increased risk for several cancer sites. Fish, and hence a diet rich in *n*-3 polyunsaturated fatty acids, tended to be another favourable diet indicator, while frequent red meat intake was directly related to some common neoplasms. An *a priori* defined Mediterranean diet score was inversely related to upper digestive and respiratory tract cancers.
Conclusions: These data provide additional evidence that major characteristics of the Mediterranean diet favourably affect cancer risk.

Keywords
Cancer
Diet
Epidemiological studies
Risk factors
Dietary fat
Dietary carbohydrate

The Mediterranean diet includes a complex of dietary patterns with different components in various regions of the Mediterranean, but is generally characterised by frequent consumption of fruit, vegetables, carbohydrates, pulses and fish, low consumption of meat and cheese, and (as a major common characteristic) abundant use of olive oil for seasoning. The Mediterranean diet has been proposed as a plausible explanation for the longevity of populations from most European countries bounded by the Mediterranean Sea[1,2].

Several peculiar aspects of the Mediterranean diet – as well as the Mediterranean diet-related lifestyle as a whole – have been related to a reduced risk not only of cardiovascular disease, but also of cancer[3–5]. It has been suggested that up to 25 % of colorectal, 15 % of breast and 10 % of prostate, pancreas and endometrial cancers could be prevented by adhering to a Mediterranean diet[6].

In the present paper, we review the main findings relating some aspects of the Mediterranean diet (including, in particular, the consumption of olive oil and carbohydrates) to cancer risk using data from an integrated series of multicentric case-control studies conducted in Italy between 1991 and 2007. These include about 10 000 subjects with various common cancers, including 749 oral and pharyngeal, 395 esophageal, 230 gastric, 1225 colon, 728 rectal, 527 laryngeal, 2569 breast, 454 endometrial, 1031 ovarian, 1294 prostate, 767 renal cell cancers and a sum of over 17 000 hospital controls. For all these studies, data collected was based on a reproducible and valid food frequency questionnaire (FFQ)[7,8].

Olive oil

Olive oil – the major common characteristic of diet in various parts of the Mediterranean – is a major source of monounsaturated fats in Mediterranean countries, but also an important source of several micronutrients and food components. It appears to be a favourable indicator of the risk of various common cancers, although the evidence is still open to evaluation.

In our network of case-control studies from Italy, where the subjects' usual diet was investigated through a validated FFQ, including specific questions aimed at assessing added fat intake patterns, we considered the association of olive oil with breast, ovarian, colorectal and upper digestive and respiratory tract cancers.

With reference to breast cancer, after allowance for demographic and reproductive risk factors, energy intake and, mutually, other types of fats, the continuous odds

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ratio (OR) for a unit increase intake of olive oil was 0·89 (95% confidence interval (CI) 0·81, 0·99)[9]. This is consistent with results from animal data, ecologic studies and other epidemiological studies conducted in Greece and Spain[10], which indicate that there is an inverse relation of breast cancer risk with intake of olive oil, but not of butter or margarine.

With reference to ovarian cancer, after allowance for study centre, year at interview, age, education, parity, oral contraceptive use and total energy intake, a reduced risk was observed for high intake of olive oil (OR = 0·68 for the highest quintile of intake compared to the lowest one)[11]. No significant associations were observed for mixed seed oils, butter and margarine. Thus, this large case-control investigation on diet and ovarian cancer conducted on a population with appreciable heterogeneity of fat intake provided a suggestion for a favourable effect of olive oil, which was only partly accounted for by vegetable intake.

For colorectal cancer risk, the OR for subsequent tertiles of olive oil intake, compared with the lowest one, were 0·87 and 0·83 when colorectal carcinoma was analysed as a whole, 0·82 and 0·81 for colon cancer and 0·96 and 0·88 for rectal cancer[12]. Seasoning fats did not appear to increase the risk of colorectal carcinoma, and there was little evidence for a differential effect by fat type. If such a differential effect exists, it could favour olive oil. Likewise, our results did not indicate a relevant role of fried foods on colorectal cancer risk in Italy, and suggested a possible favourable effect of (fried) olive oil on colon cancer risk[13].

The most consistent evidence of a favourable role of olive oil came for upper digestive and respiratory tract cancers. With reference to oral and pharyngeal cancer, high intake of olive oil was associated with significantly lowered risk (OR = 0·4 for the highest *v.* the lowest quintile of intake) (Table 1)[14]. The beneficial effect of olive oil was attenuated by the introduction of vegetable consumption in the model. Mixed seed oils and margarine were not related to cancer risk, whereas a strong positive association emerged for butter (OR = 2·3). Fat intake patterns exerted a stronger influence on the risk of cancer of the oral cavity and pharynx than on colorectal cancer or breast cancer in companion Italian studies.

Table 1 Odds ratios (OR) and corresponding 95% confidence intervals (CI) of upper aero-digestive tract cancers according to intake quintile of olive oil and other added fats[14–16]

	Intake quintile				
		3		5	
	1*	OR	95% CI	OR	95% CI
Oral and pharyngeal cancer					
Olive oil	1	0·7	0·5, 1·1	0·4	0·3, 0·7
Mixed seed oils	1	1·0	0·7, 1·4	1·1	0·7, 1·7
Butter	1	1·3	0·8, 1·9	2·3	1·6, 3·5
Oesophageal cancer					
Olive oil	1	0·3	0·2, 0·6	0·3	0·1, 0·5
Mixed seed oils	1	0·8	0·5, 1·3	0·4	0·2, 0·8
Butter	1	1·7	1·0, 3·0	2·2	1·3, 3·7
Laryngeal cancer					
Olive oil	1	0·8	0·5, 1·2	0·4	0·3, 0·7
Mixed seed oils	1	1·8	1·1, 2·9	2·2	1·3, 3·5
Butter	1	1·0	0·6, 1·5	0·9	0·6, 1·4

*Reference category.

Likewise, in a case-control study of oesophageal cancer, olive oil intake showed a significant reduction of risk (OR = 0·3), while butter consumption was directly associated with oesophageal cancer risk (OR = 2·2) (Table 1)[15]. No significant associations emerged with consumption of specific seed oils, mixed seed oils or margarine. The introduction into the model of total vegetable consumption slightly reduced the association with olive oil, which remained, however, statistically significant.

In an analysis of the role of various seasoning fats in relation to laryngeal cancer risk, a significant reduction of cancer risk was observed for olive oil (OR = 0·4) and specific seed oils (OR = 0·6), while mixed seed oils were directly associated with laryngeal cancer risk (OR = 2·2) (Table 1)[16]. No significant associations emerged for consumption of butter and margarine.

In conclusion, large multricentric Italian studies showed that olive oil is a favourable indicator of breast, ovarian, colorectal, but mostly of upper digestive and respiratory tract cancers. For these neoplasms, the relative risk difference between extreme levels of olive oil *v.* butter consumption reached a factor 4 to 5, pointing to olive oil as a relevant factor of Mediterranean diet on cancer risk.

The beneficial effect of olive oil could be explained by antioxidant properties, due both to oleic acid itself and to the presence of other antioxidants, such as vitamin E and polyphenols[17]. It is, however, possible that the observed associations with olive oil are not due to its specific components, but to the fact that higher consumption of olive oil is an indicator of healthier dietary habits, with a more frequent consumption of vegetables, and possibly of other beneficial lifestyle factors.

Cereals and fibres

In previous studies from northern Italy, refined grain intake was associated with an increased risk of stomach, colorectal, upper aero-digestive tract and thyroid cancers[18], while frequent consumption of whole grains significantly decreased the risk of most cancers analysed, including those of the upper aero-digestive tract, stomach, colorectum, liver, breast, ovary, bladder and kidney[19].

With reference to our data, the OR of colon and rectal cancers were below unity for high intakes of most types of dietary fibres, and no appreciable differences emerged between the two sites[20]. A strong protective effect of

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Table 2 Odds ratios (OR) and corresponding 95 % confidence intervals (CI) of various common cancers according to quantile of glycaemic load[31–36,38,39]

	Glycaemic load quantile								
		2		3		4		5	
Cancer	1*	OR	95 % CI	OR	95 % CI	OR	95 % CI	OR	95 % CI
Upper aero-digestive tract	1	1·2	0·9, 1·8	1·1	0·7, 1·6	1·6	1·0, 2·5	1·8	1·1, 2·9
Stomach	1	1·4	1·1, 1·9	1·6	1·2, 2·2	1·9	1·5, 2·6		–
Colorectum	1	1·2	1·0, 1·5	1·1	0·9, 1·4	1·5	1·2, 1·8	1·8	1·5, 2·2
Breast	1	1·1	0·9, 1·3	1·2	1·0, 1·4	1·3	1·1, 1·6	1·3	1·1, 1·6
Ovary	1	1·4	1·1, 1·8	1·5	1·2, 2·0	1·7	1·3, 2·1		–
Endometrium	1	1·5	1·0, 2·4	1·5	0·9, 2·3	1·5	0·9, 2·3	2·7	1·8, 4·2
Prostate	1	0·9	0·7, 1·2	1·0	0·7, 1·3	1·2	0·9, 1·6	1·4	1·0, 1·9
Thyroid	1	1·8	1·3, 2·5	2·2	1·5, 3·2		–		–

*Reference category.

various types of dietary fibres was also found for upper aero-digestive tract neoplasms (OR were 0·4 for oral/pharyngeal and esophageal and 0·3 for laryngeal cancer)[21,22]. A moderate inverse association between selected fibres, particularly cellulose and soluble non-cellulose polysaccharides, was found for hormone-related cancers, i.e. breast, ovary and prostate[23–25], while no overall association was found for renal cell cancer[26].

Thus, in this Italian population, high frequency of consumption of whole grains is an indicator of reduced cancer risk, whereas high intake of refined grains is directly associated with cancer.

Dietary fibres may act on cancer risk by reducing glycaemic load (GL) and improving insulin sensitivity, favourably influencing insulin-like growth factor 1 (IGF-1), i.e. a promoter of the process of carcinogenesis at various sites[27], and by other mechanisms specific to each site. For example, fibres might protect from colorectal cancer by increasing stool bulk, thus reducing transit time and contact of carcinogens with the colonic mucosa, and by preventing the conversion of primary to secondary bile acids[28]. Also, it was suggested that fibres might influence the levels and availability of estrogens and other steroid hormones in breast carcinogenesis.

In conclusion, whole grain foods – that have a higher content of dietary fibres – should replace refined cereal foods. This is of specific relevance in countries like Italy, where white bread and pasta are major components of the diet.

Glycaemic index and glycaemic load

The roles of refined and whole grain foods and of dietary fibres on cancer are connected to their dietary glycaemic index (GI) (an indicator of the rate of adsorption of carbohydrates and, hence, a measure of insulin demand) – and GL (which combines the quality as well as the quantity of carbohydrate consumed). GI, and in particular GL, have been suggested to be relevant factors in the aetiology of several chronic diseases, including cancers[29,30]. This points to a potential role of insulin and, hence, IGF in cancer promotion.

Several investigations from our network of case-control studies have considered the relation between GI and GL and cancer risk, providing a large amount of data from a population with frequent consumption of carbohydrates (Table 2). The OR of upper aero-digestive tract neoplasms for the highest as compared to the lowest level of dietary GI and GL were 1·5 and 1·8, respectively[31]. The associations were similar for all cancer sites considered, including those of the oral cavity/pharynx, oesophagus and larynx.

With reference to digestive tract cancers, there was a direct association between dietary GL and gastric cancer (OR = 1·9), but no consistent pattern of risk was found with GI[32]. An increased risk of colorectal cancer emerged for high GI (OR = 1·7) and GL (OR = 1·8) after allowance for several covariates, including dietary fibres[33]. The OR were higher for colon than rectal cancer.

Considering female hormone-related neoplasms, direct associations with breast, ovarian and endometrial cancers were found in our studies for both GI (OR between 1·4 and 2·1) and GL (OR between 1·3 and 2·7)[34–36]. The associations were observed in pre- and postmenopausal women, and were consistent across strata of major covariates identified. Furthermore, a prospective investigation conducted in northern Italy between 1987 and 1992, including 289 women with breast cancer found increased risks for women with high dietary GI (relative risk (RR) = 1·57 for the highest *v.* lowest quintile) and GL (RR = 2·53)[37]. Therefore, these studies support the hypothesis of a possible role of hyperinsulinaemia/insulin resistance in selected female cancers.

With reference to the study of prostate cancer, the OR were 1·23, 1·24, 1·47 and 1·57 for increasing levels of GI as compared to the lowest quintile[38]. The corresponding values for GL were 0·91, 1·00, 1·20 and 1·41. Also, GI and GL appeared to have a similar influence at different stages of the disease, measured by the Gleason score.

High dietary levels of GI and GL were associated with thyroid cancer, too[39]. Compared with the lowest tertile, the OR in subsequent tertiles were 1·68 and 1·73 for GI, and 1·76 and 2·17 for GL.

Meat and fish

The traditional Mediterranean diet included a limited intake of red meat that has been associated to increased risks of colorectal and other cancers[6]. In our integrated series of studies from Italy, the multivariate OR for the highest *v.* lowest level of red meat intake were 1·2 for cancer of the oral cavity/pharynx[14], 1·9 for oesophagus[15], 1·2 for stomach[40], 1·1 for colorectum[41], 2·1 for liver[42], 3·1 for larynx[43], 1·1 for breast[44], 1·8 for endometrium, 1·5 for ovary[45], 1·0 for prostate[46] and 0·8 for renal cell cancer[47]. This and previous reports[48] point to red meat as another important factor (after vegetables and fruits) in the nutritional aetiology of selected human cancers.

Fish intake (a major source of *n*-3 polyunsaturated fatty acids, PUFA) has been shown to be a favourable indicator for several common cancers[49]. In our datasets, the continuous OR for an increase of 1 g/week of *n*-3 PUFA were below unity for all cancers considered, except prostate: 0·7 for oral/pharyngeal and oesophageal cancer, and 0·9 for colon, rectal, breast and ovarian cancer[50]. Together with the favourable effect of fish and *n*-3 PUFA intake on the cardiovascular system[51,52], the results from these data indicate that fish is a preferable substitute for meat intake in the Mediterranean diet.

A Mediterranean diet score

In a prospective investigation conducted in Greece including more than 22 000 adults, adherence to the Mediterranean diet was assessed using a ten-point scale[4]. The present study found that a higher degree of adherence to the Mediterranean diet was associated with a reduction in total mortality and mortality from cancer (OR = 0·76 for a two-point increment in the Mediterranean-diet score).

We applied a similar score to define a dietary pattern reflecting favourable aspects of diet in our Italian data. This simple and intuitive score summarised eight of the major characteristics of the Mediterranean diet, i.e. high consumption of cereals, legumes, fruit, vegetables, low consumption of meat, milk and dairy products, high monounsaturated/saturated fat ratio and moderate alcohol intake[3]. The relation between this *a priori* defined nutritional pattern and the risk of cancers of the upper aero-digestive tract has been evaluated. For all cancers considered, a significant reduced risk was found for increasing levels of the Mediterranean score: the multivariate OR for subjects with ≥6 Mediterranean characteristics, compared with those with <3, were 0·40 for oral and pharyngeal, 0·26 for oesophageal and 0·23 for laryngeal cancer.

Conclusions

Findings from our network of case-control studies, together with other reports from Mediterranean and non-Mediterranean countries[4,6,53], provide additional evidence that a number of peculiar characteristics of the Mediterranean diet favourably affect cancer risk. In particular, olive oil appears to have a beneficial effect on cancer risk as compared to butter and other added fats. Moreover, whole grain carbohydrates, which have a higher content of dietary fibres and lower GI, should be preferred to refined ones, for the prevention of several common cancers. A low-risk diet for cancer would also imply reducing red meat and increasing consumption of fish. Recent surveys in Italy also indicated that overweight and obesity have not been rising over the last two decades as in the USA and several European countries[54]. The impact on body weight is therefore an additional favourable effect of the Mediterranean diet, not only for its implication on cardiovascular diseases, but also on cancer risk[55,56].

These data supporting the Mediterranean diet and its favourable effects on cancer are of particular importance at a public health level, given the tendency towards globalisation of diet in most areas of the world.

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References

1. Trichopoulou A, Kouris-Blazos A, Wahlqvist ML, Gnardellis C, Lagiou P, Polychronopoulos E, Vassilakou T, Lipworth L & Trichopoulos D (1995) Diet and overall survival in elderly people. *BMJ* **311**, 1457–1460.
2. WHO (2007) *World Health Statistics 2007*. Geneva: World Health Organization.
3. Bosetti C, Gallus S, Trichopoulou A, Talamini R, Franceschi S, Negri E & La Vecchia C (2003) Influence of the Mediterranean diet on the risk of cancers of the upper aerodigestive tract. *Cancer Epidemiol Biomarkers Prev* **12**, 1091–1094.
4. Trichopoulou A, Costacou T, Bamia C & Trichopoulos D (2003) Adherence to a Mediterranean diet and survival in a Greek population. *N Engl J Med* **348**, 2599–2608.
5. La Vecchia C & Bosetti C (2006) Diet and cancer risk in Mediterranean countries: open issues. *Public Health Nutr* **9**, 1077–1082.

6. Trichopoulou A, Lagiou P, Kuper H & Trichopoulos D (2000) Cancer and Mediterranean dietary traditions. *Cancer Epidemiol Biomarkers Prev* **9**, 869–873.
7. Decarli A, Franceschi S, Ferraroni M, Gnagnarella P, Parpinel MT, La Vecchia C, Negri E, Salvini S, Falcini F & Giacosa A (1996) Validation of a food-frequency questionnaire to assess dietary intakes in cancer studies in Italy. Results for specific nutrients. *Ann Epidemiol* **6**, 110–118.
8. Franceschi S, Barbone F, Negri E *et al.* (1993) Reproducibility of an Italian food frequency questionnaire for cancer studies: results for specific food items. *Eur J Cancer* **29A**, 2298–2305.
9. La Vecchia C, Negri E, Franceschi S, Decarli A, Giacosa A & Lipworth L (1995) Olive oil, other dietary fats, and the risk of breast cancer (Italy). *Cancer Causes Control* **6**, 545–550.
10. Lipworth L, Martinez ME, Angell J, Hsieh CC & Trichopoulos D (1997) Olive oil and human cancer: an assessment of the evidence. *Prev Med* **26**, 181–190.
11. Bosetti C, Negri E, Franceschi S, Talamini R, Montella M, Conti E, Lagiou P, Parazzini F & La Vecchia C (2002) Olive oil, seed oils and other added fats in relation to ovarian cancer (Italy). *Cancer Causes Control* **13**, 465–470.
12. Braga C, La Vecchia C, Franceschi S, Negri E, Parpinel M, Decarli A, Giacosa A & Trichopoulos D (1998) Olive oil, other seasoning fats, and the risk of colorectal carcinoma. *Cancer* **82**, 448–453.
13. Galeone C, Talamini R, Levi F, Pelucchi C, Negri E, Giacosa A, Montella M, Franceschi S & La Vecchia C (2007) Fried foods, olive oil and colorectal cancer. *Ann Oncol* **18**, 36–39.
14. Franceschi S, Favero A, Conti E, Talamini R, Volpe R, Negri E, Barzan L & La Vecchia C (1999) Food groups, oils and butter, and cancer of the oral cavity and pharynx. *Br J Cancer* **80**, 614–620.
15. Bosetti C, La Vecchia C, Talamini R, Simonato L, Zambon P, Negri E, Trichopoulos D, Lagiou P, Bardini R & Franceschi S (2000) Food groups and risk of squamous cell esophageal cancer in northern Italy. *Int J Cancer* **87**, 289–294.
16. Bosetti C, La Vecchia C, Talamini R, Negri E, Levi F, Dal Maso L & Franceschi S (2002) Food groups and laryngeal cancer risk: a case-control study from Italy and Switzerland. *Int J Cancer* **100**, 355–360.
17. Owen RW, Giacosa A, Hull WE, Haubner R, Wurtele G, Spiegelhalder B & Bartsch H (2000) Olive-oil consumption and health: the possible role of antioxidants. *Lancet Oncol* **1**, 107–112.
18. Chatenoud L, La Vecchia C, Franceschi S, Tavani A, Jacobs DR Jr, Parpinel MT, Soler M & Negri E (1999) Refined-cereal intake and risk of selected cancers in Italy. *Am J Clin Nutr* **70**, 1107–1110.
19. Chatenoud L, Tavani A, La Vecchia C, Jacobs DR Jr, Negri E, Levi F & Franceschi S (1998) Whole grain food intake and cancer risk. *Int J Cancer* **77**, 24–28.
20. Negri E, Franceschi S, Parpinel M & La Vecchia C (1998) Fiber intake and risk of colorectal cancer. *Cancer Epidemiol Biomarkers Prev* **7**, 667–671.
21. Pelucchi C, Talamini R, Levi F, Bosetti C, La Vecchia C, Negri E, Parpinel M & Franceschi S (2003) Fibre intake and laryngeal cancer risk. *Ann Oncol* **14**, 162–167.
22. Soler M, Bosetti C, Franceschi S, Negri E, Zambon P, Talamini R, Conti E & La Vecchia C (2001) Fiber intake and the risk of oral, pharyngeal and esophageal cancer. *Int J Cancer* **91**, 283–287.
23. La Vecchia C, Ferraroni M, Franceschi S, Mezzetti M, Decarli A & Negri E (1997) Fibers and breast cancer risk. *Nutr Cancer* **28**, 264–269.
24. Pelucchi C, Talamini R, Galeone C, Negri E, Franceschi S, Dal Maso L, Montella M, Conti E & La Vecchia C (2004) Fibre intake and prostate cancer risk. *Int J Cancer* **109**, 278–280.
25. Pelucchi C, La Vecchia C, Chatenoud L, Negri E, Conti E, Montella M, Calza S, Dal Maso L & Franceschi S (2001) Dietary fibres and ovarian cancer risk. *Eur J Cancer* **37**, 2235–2239.
26. Galeone C, Pelucchi C, Talamini R, Negri E, Montella M, Ramazzotti V, Zucchetto A, Dal Maso L, Franceschi S & La Vecchia C (2007) Fibre intake and renal cell carcinoma: a case-control study from Italy. *Int J Cancer* **121**, 1869–1872.
27. Yu H & Rohan T (2000) Role of the insulin-like growth factor family in cancer development and progression. *J Natl Cancer Inst* **92**, 1472–1489.
28. Bingham SA (1990) Mechanisms and experimental and epidemiological evidence relating dietary fibre (non-starch polysaccharides) and starch to protection against large bowel cancer. *Proc Nutr Soc* **49**, 153–171.
29. Barclay AW, Petocz P, McMillan-Price J, Flood VM, Prvan T, Mitchell P & Brand-Miller JC (2008) Glycemic index, glycemic load, and chronic disease risk – a meta-analysis of observational studies. *Am J Clin Nutr* **87**, 627–637.
30. Jenkins DJ, Kendall CW, Augustin LS, Franceschi S, Hamidi M, Marchie A, Jenkins AL & Axelsen M (2002) Glycemic index: overview of implications in health and disease. *Am J Clin Nutr* **76**, 266S–273S.
31. Augustin LS, Gallus S, Franceschi S, Negri E, Jenkins DJ, Kendall CW, Dal Maso L, Talamini R & La Vecchia C (2003) Glycemic index and load and risk of upper aero-digestive tract neoplasms (Italy). *Cancer Causes Control* **14**, 657–662.
32. Augustin LS, Gallus S, Negri E & La Vecchia C (2004) Glycemic index, glycemic load and risk of gastric cancer. *Ann Oncol* **15**, 581–584.
33. Franceschi S, Dal Maso L, Augustin L, Negri E, Parpinel M, Boyle P, Jenkins DJ & La Vecchia C (2001) Dietary glycemic load and colorectal cancer risk. *Ann Oncol* **12**, 173–178.
34. Augustin LS, Dal Maso L, La Vecchia C, Parpinel M, Negri E, Vaccarella S, Kendall CW, Jenkins DJ & Franceschi S (2001) Dietary glycemic index and glycemic load, and breast cancer risk: a case-control study. *Ann Oncol* **12**, 1533–1538.
35. Augustin LS, Gallus S, Bosetti C, Levi F, Negri E, Franceschi S, Dal Maso L, Jenkins DJ, Kendall CW & La Vecchia C (2003) Glycemic index and glycemic load in endometrial cancer. *Int J Cancer* **105**, 404–407.
36. Augustin LS, Polesel J, Bosetti C *et al.* (2003) Dietary glycemic index, glycemic load and ovarian cancer risk: a case-control study in Italy. *Ann Oncol* **14**, 78–84.
37. Sieri S, Pala V, Brighenti F *et al.* (2007) Dietary glycemic index, glycemic load, and the risk of breast cancer in an Italian prospective cohort study. *Am J Clin Nutr* **86**, 1160–1166.
38. Augustin LS, Galeone C, Dal Maso L *et al.* (2004) Glycemic index, glycemic load and risk of prostate cancer. *Int J Cancer* **112**, 446–450.
39. Randi G, Ferraroni M, Talamini R, Garavello W, Deandrea S, Decarli A, Franceschi S & La Vecchia C (2008) Glycemic index, glycemic load and thyroid cancer risk. *Ann Oncol* **19**, 380–383.
40. Lucenteforte E, Scita V, Bosetti C, Negri E & La Vecchia C (2008) Food groups and alcoholic beverages and the risk of stomach cancer: a case-control study in Italy. *Nutr Cancer* **60**, 577–584.
41. Franceschi S, Favero A, La Vecchia C, Negri E, Conti E, Montella M, Giacosa A, Nanni O & Decarli A (1997) Food groups and risk of colorectal cancer in Italy. *Int J Cancer* **72**, 56–61.
42. Talamini R, Polesel J, Montella M, Dal Maso L, Crispo A, Tommasi LG, Izzo F, Crovatto M, La Vecchia C & Franceschi S (2006) Food groups and risk of hepatocellular carcinoma:

a multicenter case-control study in Italy. *Int J Cancer* **119**, 2916–2921.
43. Bosetti C, Negri E, Kolonel L *et al.* (2002) A pooled analysis of case-control studies of thyroid cancer. VII. Cruciferous and other vegetables (International). *Cancer Causes Control* **13**, 765–775.
44. Franceschi S, Favero A, La Vecchia C, Negri E, Dal Maso L, Salvini S, Decarli A & Giacosa A (1995) Influence of food groups and food diversity on breast cancer risk in Italy. *Int J Cancer* **63**, 785–789.
45. Bosetti C, Negri E, Franceschi S, Pelucchi C, Talamini R, Montella M, Conti E & La Vecchia C (2001) Diet and ovarian cancer risk: a case-control study in Italy. *Int J Cancer* **93**, 911–915.
46. Bosetti C, Micelotta S, Dal Maso L, Talamini R, Montella M, Negri E, Conti E, Franceschi S & La Vecchia C (2004) Food groups and risk of prostate cancer in Italy. *Int J Cancer* **110**, 424–428.
47. Bravi F, Bosetti C, Scotti L, Talamini R, Montella M, Ramazzotti V, Negri E, Franceschi S & La Vecchia C (2007) Food groups and renal cell carcinoma: a case-control study from Italy. *Int J Cancer* **120**, 681–685.
48. Tavani A, La Vecchia C, Gallus S, Lagiou P, Trichopoulos D, Levi F & Negri E (2000) Red meat intake and cancer risk: a study in Italy. *Int J Cancer* **86**, 425–428.
49. Fernandez E, Chatenoud L, La Vecchia C, Negri E & Franceschi S (1999) Fish consumption and cancer risk. *Am J Clin Nutr* **70**, 85–90.
50. Tavani A, Pelucchi C, Negri E, Bertuzzi M & La Vecchia C (2001) *n*-3 Polyunsaturated fatty acids, fish, and non-fatal acute myocardial infarction. *Circulation* **104**, 2269–2272.
51. Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto miocardico (1999) Dietary supplementation with *n*-3 polyunsaturated fatty acids and vitamin E after myocardial infarction: results of the GISSI-Prevenzione trial. *Lancet* **354**, 447–455.
52. Marckmann P & Gronbaek M (1999) Fish consumption and coronary heart disease mortality. A systematic review of prospective cohort studies. *Eur J Clin Nutr* **53**, 585–590.
53. Mitrou PN, Kipnis V, Thiébaut AC *et al.* (2007) Mediterranean dietary pattern and prediction of all-cause mortality in a US population: results from the NIH-AARP Diet and Health Study. *Arch Intern Med* **167**, 2461–2468.
54. Gallus S, Colombo P, Scarpino V, Zuccaro P, Negri E, Apolone G & La Vecchia C (2006) Overweight and obesity in Italian adults 2004, and an overview of trends since 1983. *Eur J Clin Nutr* **60**, 1174–1179.
55. Calle EE, Rodriguez C, Walker-Thurmond K & Thun MJ (2003) Overweight, obesity, and mortality from cancer in a prospectively studied cohort of US adults. *N Engl J Med* **348**, 1625–1638.
56. Reeves GK, Pirie K, Beral V, Green J, Spencer E & Bull D (2007) Cancer incidence and mortality in relation to body mass index in the Million Women Study cohort study. *BMJ* **335**, 1134–1138.