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Fruit and vegetables and cancer risk: a review of southern European studies☆

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Abstract

High intakes of fruit and vegetables may reduce the risk of cancer at several sites. Evidence has been derived mainly from case–control studies. We reviewed the relationship between consumption of vegetables and fruit and the risk of several common cancers in a network of Italian and Swiss case–control studies including over 10 000 cases of fourteen different cancers and about 17 000 controls. Data were suggestive of a protective role of vegetable intake on the risk of several common epithelial cancers. OR for the highest compared with the lowest levels of consumption ranged from 0·2 (larynx, oral cavity and pharynx) to 0·9 (prostate). Inverse associations were found for both raw and cooked vegetables, although for upper digestive tract cancers the former were somewhat stronger. Similar inverse associations were found for cruciferous vegetables. Frequent consumption of allium vegetables was also associated with reduced risk of several cancers. Fruit was a favourable correlate of the risk of several cancers, particularly of the upper digestive tract, with associations generally weaker than those reported for vegetables. A reduced risk of cancers of the digestive tract and larynx was found for high consumption of citrus fruit. Suggestive protections against several forms of cancer, mainly digestive tract cancers, were found for high consumption of apples and tomatoes. High intakes of fibres, flavonoids and proanthocyanidins were inversely related to various forms of cancer. In conclusion, data from our series of case–control studies suggested a favourable role of high intakes of fruit and vegetables in the risk of many common cancers, particularly of the digestive tract. This adds evidence to the indication that aspects of the Mediterranean diet may have a favourable impact not only on CVD, but also on several common (epithelial) cancers, particularly of the digestive tract.

Key words: Cancer risk: Diet: Fruit: Vegetables

The Mediterranean diet is a collection of eating patterns with different components, traditionally followed by populations from countries bordering the Mediterranean Sea, and is generally characterised by frequent consumption of fruit, vegetables, complex carbohydrates, pulses and fish; low consumption of meat and cheese; low-to-moderate amount of wine intake during meals; and use of olive oil for seasoning (as a major common characteristic). This dietary pattern has been suggested as a possible explanation for the longevity of populations from countries in the Mediterranean regions, and for the relatively low occurrence of CHD in such areas[1,2].

The Mediterranean diet as a whole and some of its aspects have been inversely related to the risk of cancer[3–8]. In particular, high intakes of fruit and vegetables have been related to a reduced risk of cancer at several sites, with associations stronger for cancers of digestive and respiratory tracts and somewhat

Abbreviations: FRAP, ferric reducing–antioxidant power; TEAC, Trolox equivalent antioxidant capacity; TRAP, total radical-trapping antioxidant parameter.

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weaker for hormone-related cancers. However, most of the epidemiological evidence supporting a favourable role of vegetables and fruit is derived from case–control studies, whereas evidence from cohort studies is less convincing[9].

In the present review, we discuss and summarise the main findings on the relationship between vegetable and fruit consumption and cancer risk from an integrated series of multi-centric case–control studies conducted in Italy and Switzerland.

Methods

Since the early 1990s, a series of case–control studies of various neoplasms were conducted in Italy and Switzerland. These included 768 cases of oral and pharyngeal cancer[10], 198 cases of nasopharyngeal cancer[11], 304 cases of oesophageal cancer[12], 230 cases of stomach cancer[13], 1953 cases of colorectal cancer[14], 185 cases of liver cancer[15], 326 cases of pancreatic cancer[16], 527 cases of laryngeal cancer[17], 2569 cases of breast cancer[18], 454 cases of endometrial cancer[19], 1031 cases of ovarian cancer[20], 1294 cases of prostate cancer[21] and 767 cases of kidney cancer[22], 190 cases of non-Hodgkin's lymphomas[23] (Table 1); and a total of over 17 000 controls. Cases were individuals admitted to major teaching and general hospitals with incident, histologically confirmed cancers. Controls were patients with no history of cancer, admitted to the same hospitals for acute non-neoplastic condition, unrelated to known risk factors for the corresponding cancer site or dietary modification. The study protocols were revised and approved by the ethical committees of the hospitals involved, according to the regulations at the time of study conduction. All participants gave informed consent.

Trained personnel interviewed cases and controls during their hospital stay using a structured questionnaire, including information on sociodemographic characteristics, anthropometric measures, lifestyle habits (e.g. tobacco smoking and alcohol drinking), dietary habits, personal medical history, family history of cancer, and, for women, menstrual and reproductive factors, use of oral contraceptives and hormone replacement therapy. The usual diet of the subjects 2 years before diagnosis (or hospital admission, for controls) was investigated using a reproducible and valid FFQ[24,25], including seventy-eight food items and beverages. Subjects were asked to indicate the average weekly frequency of consumption for each dietary item, and the seasonal consumption for a few vegetables and fruit, with the corresponding duration.

OR, and the corresponding 95 % CI, for quintiles (computed among controls) of vegetable or fruit intake were estimated by multiple logistic regression models. For nasopharyngeal and liver cancers and non-Hodgkin's lymphomas, subjects were grouped according to quartiles of intake. Although models were derived independently for each cancer site, according to their potential confounding factors, all of them included terms for age, sex (when appropriate), study centre or area of residence, education and energy intake. Models for liver and breast cancers were also adjusted for alcohol drinking; models for stomach cancer were adjusted for tobacco smoking; and models for cancers of oral cavity and pharynx, nasopharynx, oesophagus, pancreas, larynx and kidney were adjusted for both alcohol drinking and tobacco smoking. Allowance for BMI or physical activity was performed for cancers of oral cavity and pharynx, pancreas, kidney and colorectum. A term for hepatitis was included in the models for liver cancer (B and/or C viruses) and non-Hodgkin's lymphomas (C virus). Concerning female hormone-related cancers, OR for breast cancer were also adjusted for parity,

Table 1. Data on selected cancers for the highest *v.* the lowest levels of consumption of cruciferous and allium vegetables in Italy and Switzerland, 1991–2009

(Odds ratios, and 95 % confidence intervals)

		Cruciferous vegetables (≥1 *v.* <1 portion/week)		Allium vegetables: Onion (≥7 *v.* 0 portions/week)		Allium vegetables: Garlic (high *v.* no or low use*)	
Cancer sites	*n*	OR	95 % CI	OR	95 % CI	OR	95 % CI
Oral cavity and pharynx	768	0·83	0·70, 0·98	0·16	0·06, 0·46	0·61	0·44, 0·85
Nasopharynx	198	–		–		–	
Oesophagus	304	0·72	0·52, 0·99	0·12	0·02, 0·58	0·43	0·28, 0·67
Stomach†	230	0·90	0·61, 1·30	0·59	0·25, 1·41	0·69	0·41, 1·15
Colorectum	1953	0·83	0·74, 0·94	0·44	0·28, 0·67	0·74	0·63, 0·86
Liver	185	0·72	0·47, 1·11	–		–	
Pancreas	326	0·90	0·63, 1·30	–		–	
Larynx	527	0·84	0·67, 1·05	0·17	0·05, 0·61	0·56	0·38, 0·82
Breast	2569	0·83	0·74, 0·94	0·75	0·50, 1·12	0·90	0·77, 1·05
Endometrium†	454	0·93	0·68, 1·27	0·40	0·22, 0·72	0·62	0·42, 0·92
Ovary	1031	0·91	0·76, 1·11	0·27	0·08, 0·85	0·78	0·62, 0·98
Prostate	1294	0·87	0·70, 1·09	0·29	0·07, 1·03	0·81	0·64, 1·00
Kidney	767	0·68	0·54, 0·84	0·62	0·18, 2·10	0·69	0·53, 0·92
Non-Hodgkin's lymphomas	190	–		–		–	

* Qualitative variable scored as 1 for 'non-use or low use', 2 for 'intermediate use', and 3 for 'high use'.
† For endometrial and stomach cancer only, the OR is for consuming ≥2 *v.* 0 portions/week of onion.

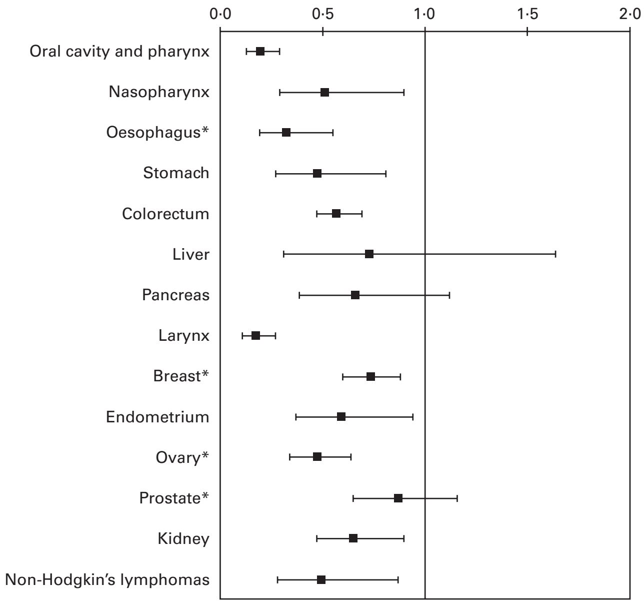

Fig. 1. OR and 95 % CI of selected cancers for the highest quintile *v.* the lowest quintile of vegetable consumption for all cancer sites, except for nasopharyngeal and liver cancers, and non-Hodgkin's lymphomas (quartiles). Italy and Switzerland, 1991–2009. *Raw vegetables.

those for ovarian cancer were adjusted for parity and oral contraceptive use, and those for endometrial cancer were adjusted for parity, oral contraceptive use, hormone replacement therapy, age at menarche, menopausal status and history of diabetes.

In the present review, we also provided results on selected vegetables or fruit of specific interest, i.e. those that are cheap and easy to store and transport, and thus the most frequently consumed.

Vegetables

The present data supported a protective role of high intake of vegetables in the risk of several common epithelial cancers (Fig. 1). In particular, the OR for the highest compared with the lowest levels of vegetable intake were 0·19 (95 % CI 0·13, 0·29) for oral and pharyngeal cancer, 0·51 (95 % CI 0·29, 0·90) for nasopharyngeal cancer, 0·32 (95 % CI 0·19, 0·55) for oesophageal cancer, 0·47 (95 % CI 0·27, 0·81) for stomach cancer, 0·57 (95 % CI 0·47, 0·69) for colorectal cancer, 0·72 (95 % CI 0·31, 1·64) for liver cancer, 0·66 (95 % CI 0·39, 1·12) for pancreatic cancer and 0·17 (95 % CI 0·11, 0·27) for laryngeal cancer. Among hormone-related cancers, breast, endometrial and ovarian cancers were inversely related to vegetable consumption, with OR of 0·73 (95 % CI 0·60, 0·88), 0·59 (95 % CI 0·37, 0·94) and 0·47 (95 % CI 0·34, 0·64), respectively, whereas the estimate for prostate cancer was below unity (i.e. 0·87), but not significant. A favourable role of vegetable intake was also observed for kidney cancer (OR 0·65, 95 % CI 0·47, 0·90), as well as for non-Hodgkin's lymphomas (OR 0·49, 95 % CI 0·28, 0·87).

Cooking food may destroy selected nutrients and enzymes, alter the structure and thus digestibility of the food, and create by-products. However, for some foods and food components (e.g. lycopene), cooking not only kills potentially harmful organisms, but also actually improves the bioavailability of certain nutrients and digestibility. Findings from our case–control studies supported inverse relationships between consumption of both raw and cooked vegetables and the risk of cancers, with the exception of breast cancer, for which an inverse association was found essentially for raw vegetables. In general, these relationships appeared somewhat stronger for raw than cooked vegetables for upper digestive tract cancers. OR for the highest *v.* the lowest intakes (generally quintiles) of raw and cooked vegetables were respectively, 0·25 and 0·50 for oral and pharyngeal cancer[10], 0·54 and 0·67 for nasopharyngeal cancer[11], 0·32 and 0·79 for oesophageal cancer[12], 0·59 and 0·57 for colorectal cancer[14], 0·77 and 0·57 for pancreatic cancer[16], 0·22 and 0·32 for laryngeal cancer[17], 0·73 and 0·96 for breast cancer[18], 0·47 and 0·65 for ovarian cancer[20], 0·87 and 0·74 for prostate cancer[21], and 0·74 and 0·68 for kidney cancer[22].

Cruciferous vegetables (cabbages, cauliflowers, broccoli, brussels sprouts and turnip greens) are important sources of sulphur-containing compounds (glucosinolates), whose major breakdown products (isothiocyanates and indoles) have anti-carcinogenic properties in *in vitro* and animal studies[26]. Our data showed significantly reduced OR for regular (≥1 portion/week) compared with no/occasional intake for cancers of the oral cavity and pharynx, oesophagus, colorectum, breast and kidney (Table 1)[26].

Frequent consumption of allium vegetables, particularly onion, represents a peculiar feature of the Mediterranean diet. Garlic and onion are a source of several organosulphur compounds in addition to amino acids, vitamins and micronutrients, and have anti-inflammatory, anti-thrombotic,

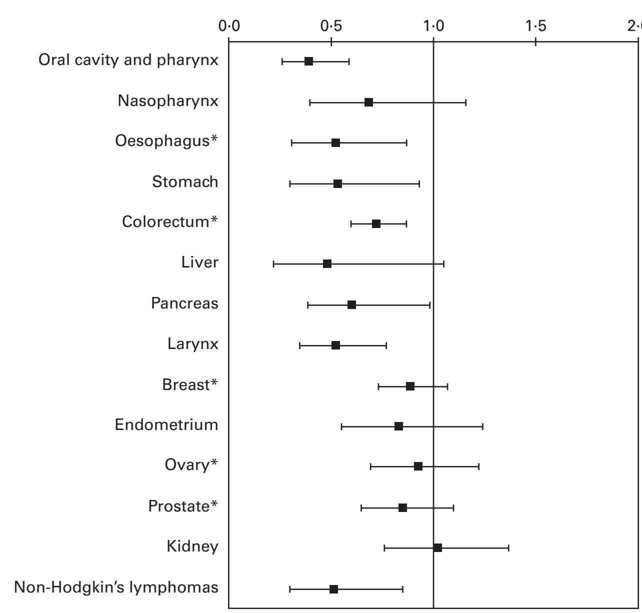

Fig. 2. OR and 95 % CI of selected cancers for the highest quintile *v.* the lowest quintile of fruit consumption for all cancer sites, except for nasopharyngeal and liver cancers, and non-Hodgkin's lymphomas (quartiles). Italy and Switzerland, 1991–2009. *Non-citrus fruits.

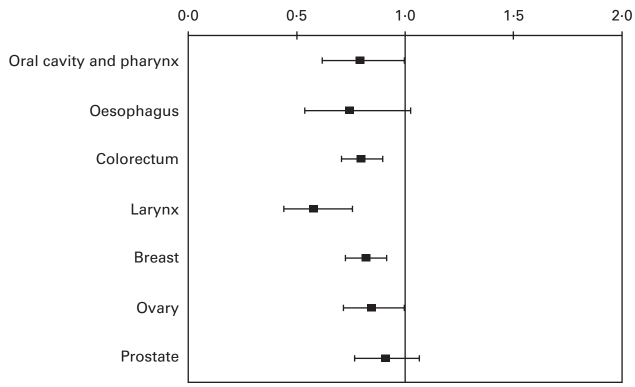

Fig. 3. OR and 95 % CI of selected cancers for consumption of ≥1 *v.* <1 apple/d. Italy, 1991–2002.

cholesterol-lowering and antioxidant effects[27,28]. Data from the present series of case–control studies support a favourable role of allium vegetable intake in cancer risk in Italy and Switzerland (Table 1). In particular, a significantly decreased risk for high intakes of onion and garlic was found for cancers of oral cavity and pharynx, oesophagus, colorectum, larynx, endometrium, ovary and kidney (only garlic)[27–29].

Fruit

Fruit was a favourable correlate of the risk of several cancers, particularly of the digestive tract; however, associations were generally weaker than for vegetables. The OR for the highest compared with the lowest levels of intake were 0·39 (95 % CI 0·26, 0·59) for oral and pharyngeal cancer, 0·52 (95 % CI 0·31, 0·87) for oesophageal cancer, 0·53 (95 % CI 0·30, 0·93) for stomach cancer, 0·72 (95 % CI 0·60, 0·87) for colorectal cancer, 0·60 (95 % CI 0·39, 0·98) for pancreatic cancer and 0·52 (95 % CI 0·35, 0·77) for laryngeal cancer (Fig. 2). A strong association with fruit was also found for non-Hodgkin's lymphomas (OR 0·51, 95 % CI 0·30, 0·85). The OR for liver cancer was around 0·5; however, it did not reach statistical significance. No appreciable association was observed for hormone-related and kidney cancers, with OR ranging from 0·83 (endometrial cancer) to 1·02 (kidney cancer).

A reduced risk of cancers of the digestive tract and larynx was observed in our data for increasing intakes of citrus fruit, rich in vitamin C, flavanones and other compounds with antioxidant, anti-mutagenic and anti-proliferative properties[30]. Compared with subjects consuming less than 1 portion of citrus fruit per week, the OR for those consuming 4 or more portions per week were 0·47 (95 % CI 0·36, 0·61) for oral cavity and pharyngeal cancer, 0·42 (95 % CI 0·25, 0·70) for oesophageal cancer, 0·69 (95 % CI 0·52, 0·92) for stomach cancer, 0·82 (95 % CI 0·72, 0·93) for colorectal cancer and 0·55 (95 % CI 0·37, 0·83) for laryngeal cancer. For other neoplasms, including cancers of breast, ovary, endometrium, prostate and kidney, no evidence of a beneficial effect of citrus fruit was found[30].

Apples contain several phytochemicals, including flavonoids and phenolic acids, and, when compared with other fruits, they had the second highest level of antioxidant activity (after cranberries) and phenolic compounds, and the highest level of free phenolic compounds[31]. Subjects eating at least one apple a day had a reduced risk of cancers of oral cavity and pharynx (OR 0·79, 95 % CI 0·62, 1·00), colorectum (OR 0·80, 95 % CI 0·71, 0·90), larynx (OR 0·58, 95 % CI 0·44, 0·76), breast (OR 0·82, 95 % CI 0·73, 0·92) and ovary (OR 0·85, 95 % CI 0·72, 1·00). OR for oesophageal and prostate cancers were 0·75 (95 % CI 0·54, 1·03) and 0·91 (95 % CI 0·77, 1·07), respectively (Fig. 3)[31].

Tomatoes are a typical aspect of the Italian diet and, in general, of the Mediterranean diet, and are the main source of lycopene, a carotenoid with strong antioxidant properties that is not converted to vitamin A[32]. Compared with the lowest quintile of tomato intake, the OR of colorectal cancer for the highest quintile was 0·8 (95 % CI 0·6, 0·9)[32]. We estimated an OR of 0·65 (95 % CI 0·4, 1·0) for cancer of oral cavity, pharynx and oesophagus, and one of 0·43 (95 % CI 0·3, 0·6) for cancer of the stomach, for the highest compared with the lowest quartile of intake[33].

Fibres, flavonoids and proanthocyanidins

With regard to specific components of vegetables and fruit, dietary fibre intake was inversely associated with most cancers considered, particularly with those of the digestive tract (Fig. 4). The OR for an increment of intake equal to the difference between the 80th and 20th percentile were 0·51 (95 % CI 0·40,

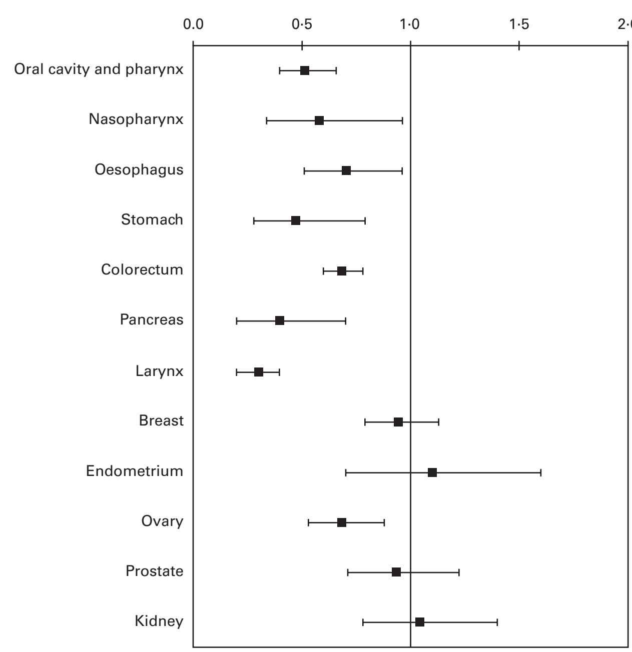

Fig. 4. OR and 95 % CI of selected cancers for fibre consumption. Italy and Switzerland, 1991–2009. Comparisons: difference between 80th and 20th percentile of the control distribution for oral and pharyngeal, oesophageal and colorectal cancer; 4th *v.* 1st quartile of consumption for nasopharyngeal cancer; 5th *v.* 1st quintile of consumption for other cancer sites.

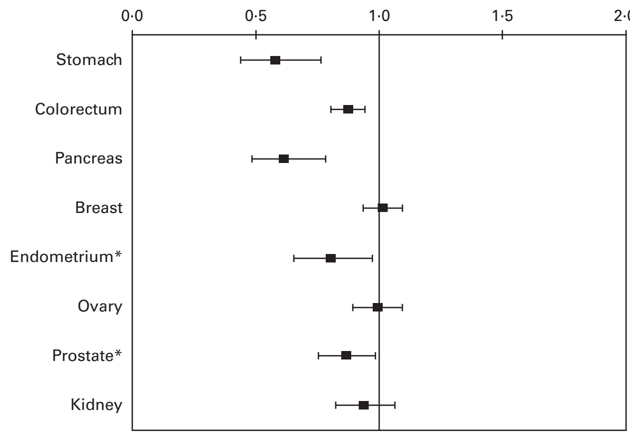

Fig. 5. OR for an increment of proanthocyanidins with ≥3 mers intake equal to the difference between the 80th and 20th percentile. Italy and Switzerland, 1991–2009.*Monomers and dimers.

0·66) for oral and pharyngeal cancer, 0·70 (95 % CI 0·51, 0·96) for oesophageal cancer and 0·68 (95 % CI 0·60, 0·78) for colorectal cancer. The OR for the highest *v.* the lowest categories of intake were 0·58 (95 % CI 0·34, 0·96) for nasopharyngeal cancer, 0·47 (95 % CI 0·28, 0·79) for stomach cancer, 0·4 (95 % CI 0·2, 0·7) for pancreatic cancer, 0·3 (95 % CI 0·2, 0·4) for laryngeal cancer and 0·68 (95 % CI 0·53, 0·88) for ovarian cancer. Conversely, a lack of association was observed for cancers of breast, endometrium, prostate and kidney[34–44].

Results on flavonoids from the present series of Italian and Swiss case–control studies showed a significant protective role of flavanones on upper aero-digestive tract cancers (OR for the highest *v.* the lowest quintiles of intake 0·51, 95 % CI 0·37, 0·71 for oral cavity and pharyngeal cancer; 0·38, 95 % CI 0·23, 0·66 for oesophageal cancer; 0·60, 95 % CI 0·41, 0·89 for laryngeal cancer), flavonols (OR 0·64, 95 % CI 0·54, 0·77) and anthocyanidins (OR 0·67, 95 % CI 0·54, 0·82) on colorectal cancer, flavonols (OR 0·80, 95 % CI 0·66, 0·98) and flavones (OR 0·81, 95 % CI 0·66, 0·98) on breast cancer, and flavonols (OR 0·63, 95 % CI 0·47, 0·84) and isoflavones (OR 0·51, 95 % CI 0·37, 0·69) on ovarian cancer[45,46]. Specific results on proanthocyanidins are shown in Fig. 5. Significant inverse associations were found for cancers of the stomach, colorectum, pancreas, endometrium and prostate, with OR for an increment of intake equal to the difference between the 20th and the 80th percentile of 0·58 (95 % CI 0·44, 0·77) for stomach cancer[47], 0·88 (95 % CI 0·81, 0·95) for colorectal cancer[48], 0·62 (95 % CI 0·49, 0·79) for pancreatic cancer[49], 0·81 for endometrial cancer (95 % CI 0·66, 0·98)[50] and 0·87 (95 % CI 0·76, 0·99) for prostate cancer (unpublished results).

Discussion

Data from this integrated network of studies support a favourable role of vegetable intake on the risk of several common cancers, particularly of the digestive tract. Fruit intake was inversely related to the risk of digestive tract cancers as well, with associations generally less stronger than those for vegetable intake.

Potential limitations include selection and information bias. However, participation of cases and controls was high and similar, and attention was paid in excluding from the control group subjects who were admitted for any condition that might have affected dietary habits. Furthermore, cases and controls came from comparable catchment areas and were interviewed by the same trained personnel in a hospital setting[51]. Among the strengths are the large sample size, the use of a reproducible and valid FFQ[24,25], and the ability to adjust for a number of potential confounding factors for the cancers investigated, as well as energy intake.

In terms of population-attributable risks, 20–60 % of digestive tract cancers in Italy could be attributable to low consumption of vegetables and fruit. In particular, the risks attributable to low consumption of vegetables and fruit in men and women were 25 and 17 % for oral and pharyngeal cancer, 40 and 29 % for oesophageal cancer, and 18 and 15 % for laryngeal cancer, respectively[52]. In both sexes combined, the attributable risks were 60 % for stomach cancer and 43 % for colorectal cancer. For breast cancer, the attributable risk was 21 %[52].

The favourable effect of vegetables and fruit against most forms of cancers has been related to several of their constituents, in the absence, however, of a clear understanding on which of these may be the key relevant ones. Indeed, vegetables and fruit are sources of a wide variety of micronutrients and other bioactive compounds, including carotenoids, folate, vitamins C, D and E as well as vitamin B_6, flavonoids, dietary fibre and selenium. These may act against cancer through their antioxidant activities, free radical-trapping capacity, modulation of detoxification enzymes, anti-mutagenic and anti-proliferative properties, stimulation of the immune system, as well as modulation of hormone concentration and hormone metabolism[53]. Ascorbic acid, carotenoids and other antioxidant vitamins were inversely related to upper digestive and respiratory tract neoplasms[9,54]. Likewise, lycopene was inversely related to several digestive tract neoplasms, and carotenoids, vitamin E and calcium showed an inverse relationship with breast cancer[9,54]. However, despite the promising results of several dietary vitamins and food components on cancer risk from epidemiological studies, trials usually failed to show a protective effect of vitamin supplementation on cancer risk[55].

Interestingly, a varied diet including several different types of fruit and vegetables was protective against several cancers in our data[56–60]. Different fruits and vegetables contain many different bioactive compounds, and these may exert synergistic interaction. It is, therefore, possible that a combination of plant-based bioactive components has a favourable role in cancer risk.

Given the high correlation between several micronutrients, it is difficult to disentangle their role and detect which specific component or group of components is responsible for a protective role against cancer. Since several antioxidants may influence cancer risk and act to prevent carcinogenesis, examining overall antioxidant exposure rather than individual antioxidants has recently been proposed. Inverse relationships of the Non-Enzymatic Antioxidant Capacity

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(NEAC) from diet, measured in terms of ferric reducing–antioxidant power (FRAP), Trolox equivalent antioxidant capacity (TEAC) and total radical-trapping antioxidant parameter (TRAP), were reported in our studies for colorectal and stomach cancer[61]. The OR of colorectal cancer for the highest *v.* the lowest quintiles were 0·68 (95 % CI 0·57, 0·82) for FRAP, 0·69 (95 % CI 0·57, 0·83) for TEAC and 0·69 (95 % CI 0·57, 0·83) for TRAP[61]. The corresponding OR for stomach cancer were 0·54 (95 % CI 0·33, 0·88) for FRAP, 0·67 (95 % CI 0·42, 1·07) for TEAC and 0·57 (95 % CI 0·39, 0·90) for TRAP, respectively (submitted).

The beneficial effect of high intakes of vegetables and fruit in these studies may be also due, at least in part, to the fact that their high consumption often accompanies lower intakes of foods that may be positively related to the risk of cancer. They may, therefore, represent a general indicator of healthy dietary and lifestyle habits. Indeed, high intakes of fruit and vegetables are key features of the Mediterranean diet[62], which has been inversely related to overall mortality as well as to specific health outcomes including CVD and cerebrovascular diseases, as well as cancer[1,2,6,8].

A beneficial role of vegetable and fruit consumption in the risk of cancer has been reported either from a number of case–control studies[63–65] or from some large cohort investigations[66–72]. However, also a number of prospective studies, which generally have a higher level of evidence than case–control studies, have reported null associations, casting some doubts about the possible benefits of high vegetable and fruit consumption[73–77]. Findings from the European Prospective Investigation into Cancer and Nutrition (EPIC) study, across ten countries, have supported significant inverse associations between fruit consumption and upper aero-digestive tract cancers (mouth, pharynx, larynx and oesophagus) and lung cancer (in smokers), as well as between fruit and vegetable consumptions and colorectal cancer. For the other cancer sites considered (i.e. stomach, pancreas, breast, cervix, prostate, bladder and lymphoma), no significant association was reported for both fruit and vegetables consumption[78]. The combined analysis of two major US cohorts, the Nurses' Health Study and the Health Professionals' Follow-up Study (HPFS), indicated no relevant role of fruit and vegetable intake on overall cancer incidence[75] as well as on colon and rectal cancer[76], but suggested possible inverse associations with kidney cancer[71], premenopausal breast cancer[79] and lung cancer in women but not in men[80]. Prospective data from the Netherlands Cohort Study on Diet and Cancer have shown a favourable role of vegetable and fruit intake in colorectal[81] and lung cancers[82], and no significant association with pancreatic[77], ovarian[83], kidney[84] and breast cancers[85]. Moreover, high intake of fruit, but not vegetables, reduced urothelial cancer risk[86], and intakes of specific groups of vegetables (e.g. raw vegetables) and fruits (e.g. citrus fruits) were inversely related to subtypes of oesophageal and stomach cancers[87]. The Pooling Project of prospective Studies of Diet and Cancer, an international consortium of prospective cohort studies[88], found no association between fruit and vegetable consumption and the risk of breast cancer overall (but an inverse association for oestrogen receptor-negative breast tumours; twenty cohorts/24 690 cases)[89], pancreatic cancer (fourteen cohorts/2212 cases)[90], colon cancer overall (but an inverse association for distal colon cancer; fourteen cohorts/5838 cases)[91] and ovarian cancer (twelve cohorts/2130 cases)[92]; a modest inverse association with lung cancer (eight cohorts/3206 cases)[93]; and a significant inverse association with kidney cancer (thirteen cohorts/1474 cases)[94].

In conclusion, our findings, as well as those from other studies conducted in Mediterranean countries[95,96], indicate a large favourable effect of vegetable and fruit intake on the risk of several cancer sites, and this may well be due to the relative abundance of vegetables and fruit in the Mediterranean diet.

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None of the authors has any conflicts of interest to declare.

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