FULL PAPER

BJC

British Journal of Cancer (2013) 109, 1360–1366 | doi: 10.1038/bjc.2013.345

Keywords: case–control; Mediterranean diet; pancreatic cancer; risk factor

The role of Mediterranean diet on the risk of pancreatic cancer

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Background: The Mediterranean diet has been shown to have a beneficial role on various neoplasms, but data are scanty on pancreatic cancer.

Methods: We analysed data from two case–control studies conducted in Italy between 1983 and 2008, including 362 and 326 pancreatic cancer cases and 1552 and 652 hospital-controls, respectively. A Mediterranean Diet Score (MDS) summarising major characteristics of the Mediterranean diet was used in the two studies separately and overall. Two further scores of adherence to the Mediterranean diet were applied in the second study only, the Mediterranean Dietary Pattern Adherence Index (MDP) and the Mediterranean Adequacy Index (MAI).

Results: Odds ratios (ORs) for increasing levels of the scores (i.e., increasing adherence) were estimated using multiple logistic regression models. Odds ratio for a MDS score $\geqslant 6$ compared with <3 was 0.57 (95% confidence interval (CI) 0.34–0.95) in the first study, 0.51 (95% CI 0.29–0.92) in the second study, and 0.48 (95% CI 0.35–0.67) overall. A trend of decreasing risk was observed also for the MDP and MAI the ORs for the highest *vs* the lowest quintile being 0.44 (95% CI 0.27–0.73) for MDP and 0.68 (95% CI 0.42–1.11) for the MAI. The results were consistent across strata of age, sex, education, body mass index, alcohol drinking, tobacco smoking, and diabetes.

Conclusion: Our study provides evidence that *a priori*-defined scores measuring adherence to the Mediterranean diet are favourably associated with pancreatic cancer risk.

The Mediterranean diet typical of southern European countries has different variants but it is generally characterised by some common features, that is, abundant consumption of plant foods, fresh and varied fruit, high consumption of cereals, frequent consumption of fish, olive oil as the main seasoning fat, moderate consumption of wine mainly during meals, and relatively low intake of meat and dairy products (Trichopoulou and Lagiou, 1997). Several epidemiological studies have indicated that adherence to the Mediterranean dietary pattern has a beneficial role on cardiovascular diseases (Panagiotakos *et al*, 2002; Sofi *et al*, 2010; Dilis *et al*, 2012; Misirli *et al*, 2012) and overall mortality (Trichopoulou *et al*, 1995, 2003; Knoops *et al*, 2004; Trichopoulou *et al*, 2005; Mitrou *et al*, 2007; Sofi *et al*, 2010). In particular, for coronary heart diseases, no particular food has been implicated as causal, but the evidence for a favourable role of the Mediterranean dietary pattern is convincing (Mente *et al*, 2009). More recently, other studies suggested that the Mediterranean diet has a favourable impact on common cancers as well (Trichopoulou *et al*, 2000; Bosetti *et al*, 2003; Pelucchi *et al*,

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Received 26 March 2013; revised 7 June 2013; accepted 11 June 2013; published online 8 August 2013

2009; Buckland *et al*, 2010; Verberne *et al*, 2010; Couto *et al*, 2011; Bamia *et al*, 2013; Buckland *et al*, 2013; Giacosa *et al*, 2013).

Adherence to a Mediterranean diet pattern may also have a beneficial role on pancreatic cancer, although only a few studies have evaluated such an association. The US prospective National Institutes of Health-AARP Diet and Health study, including a total of 450 416 participants and 1057 pancreatic cancer cases, reported a relative risk (RR) of 0.92 (95% confidence interval (CI) 0.81–1.05) for high (5–8 points) *vs* low (0–4 points) no-alcohol Mediterranean dietary score. The risk reduction comparing the most extreme categories of the dietary score (7–8 points *vs* 0–1) was 27%, although it was not significant ($P=0.06$) (Jiao *et al*, 2009). In a cohort study from Sweden on 77 151 participants and including 92 pancreatic cancer cases, the Mediterranean diet score (MDS) was significantly inversely related to pancreatic cancer risk (RR $=0.82$, 95% CI 0.72–0.94) (Tognon *et al*, 2012). The adherence to various aspects of the Mediterranean diet, however, is likely to be much lower in those countries than in Italy.

We have therefore evaluated the hypothesis that the Mediterranean diet has a beneficial role on the risk of pancreatic cancer using data from two Italian case–control studies (Turati *et al*, 2011). To measure the adherence to the Mediterranean diet, we used three different *a priori*-defined scores proposed in the literature to combine various foods/food groups, and adopted in various other epidemiological studies (Bach *et al*, 2006). This is an alternative approach to that used in one of the Italian studies (Bosetti *et al*, 2013), where nutrient-based dietary patterns were identified using an exploratory *a posteriori* approach, built on the specific dietary data under consideration.

MATERIALS AND METHODS

We analysed data from two hospital-based case–control studies of pancreatic cancer conducted in Italy. Briefly, the first one was conducted between 1983 and 1992 in the province of Milan on 362 incident cases of pancreatic cancer (229 men, 133 women, median age 60 years, range 18–86) and 1552 controls (1114 men, 411 women, median age 56 years, range 18–84) (La Vecchia *et al*, 1990); the second study was conducted between 1992 and 2008 in the provinces of Milan and Pordenone (northern Italy) on 326 incident cases (174 men, 152 women, median age 62 years, range 34–80) and 652 controls (348 men, 304 women, median age 62 years, range 34–80), frequency-matched to cases by age, sex, and study centre (ratio 2 : 1) (Polesel *et al*, 2010). In both studies, controls were subjects admitted to the same network of hospitals as cases for a wide spectrum of acute, non-neoplastic conditions. Overall, 30% were admitted for traumas, 21% for non-traumatic orthopaedic disorders, 33% for acute surgical conditions, and 16% for miscellaneous other illnesses, including eye, ear, nose, throat, skin, or dental disorders. Less than 5% of cases and controls approached for interview refused to participate.

Cases and controls were personally interviewed by centrally trained interviewers using similar structured questionnaires, including information on socio-demographic characteristics, anthropometric measures (including self-reported weight and height), tobacco smoking, alcohol drinking, other lifestyle habits, and personal medical history of selected diseases. In the first study, subjects' usual diet before cancer diagnosis or hospital admission (for controls) was investigated using a simplified dietary section, including weekly frequency of consumption of 14 selected indicator foods. Subjective scores (low, medium, and high) were used to obtain information on (whole grain) cereals and seasoning fats intake (butter, margarine, and olive oil). In the second study, subjects' usual diet during the 2 years before cancer diagnosis or hospital admission (for controls) was assessed through a validated and reproducible food frequency questionnaire (Franceschi *et al*, 1993; Decarli *et al*, 1996), including 78 foods and beverages, as well as a range of recipes, that is, the most common ones in the Italian diet, grouped into seven sections: (i) bread and cereal dishes (first courses); (ii) meat and other main dishes (second courses); (iii) vegetables (side dishes); (iv) fruit; (v) sweets, desserts, and soft drinks; (vi) milk and hot beverages; and (vii) alcoholic beverages. Subjects were asked to indicate the average weekly frequency of consumption of each dietary item; occasional intake (lower than once a week, but at least once a month) was coded as 0.5 per week. An Italian food composition database, integrated with other sources, was used to estimate nutrient and total energy intake in this study (Salvini *et al*, 1998; Gnagnarella *et al*, 2004).

In both studies, we defined an *a priori* score (the MDS) on the basis of nine (eight for the first study) characteristics of the traditional Mediterranean diet, as suggested by Trichopoulou *et al* (1995) (Supplementary Table): high consumption of cereals, fruit, vegetables, legumes (for the second study only), and fish; high monounsaturated/saturated fat ratio; low consumption of milk and dairy products, and meat and meat products; and moderate alcohol intake. The cut points for the items considered were set to study- and sex-specific median values among controls. For each subject, one point was attributed for the presence of each characteristic; for alcohol, one point was attributed to moderate drinkers (consumption over 0 and below the median), and none to non or heavy drinkers (consumption above the median). We then summed up the points for all the nine (or eight in the first study) items to calculate the MDS, which thus ranged between zero (no adherence) and nine (or eight) (maximum adherence).

Two further scores of adherence to the Mediterranean diet were applied in the second study only, the Mediterranean Dietary Pattern Adherence Index (MDP) and the Mediterranean Adequacy Index (MAI). The MDP was calculated by summing up the standardised residuals of the regression of cereals, fruit, vegetables, legumes, moderate alcohol, monounsaturated to saturated fat ratio on total calories, and subtracting those of milk and meat. The MDP was then expressed as a percentage of adherence using the range of the values in the sample, and assumed values between 0% (low adherence) and 100% (maximum adherence) (Sanchez-Villegas *et al*, 2002). Mediterranean Adequacy Index was calculated by dividing the sum of the intake of seleted typical Mediterranean foods (i.e., bread, cereals, fruit, vegetables, legumes, potatoes, fish, red wine, and vegetable oils) as a percentage of total energy by the sum of the intake of non-typical Mediterranean foods (i.e., milk, cheese, meat, eggs, animal fats and margarines, sweet beverages, cakes, pies and cookies, and sugar) again as the percentage of total energy (Alberti-Fidanza and Fidanza, 2004). In our population, this score ranged between 0.33 and 14.18. The MDP score had a possitive correlation with the MDS (Pearson correlation coefficient $=0.59$), while the correlation coefficient was 0.29 between the MAI and the MDS.

We estimated odds ratios (ORs) and the corresponding 95% CI of pancreatic cancer for categories of the three scores by unconditional multiple logistic regression models (Breslow and Day, 1980), including terms for age (5-year groups), sex, centre, calendar year at diagnosis, years of education (<7, 7–11, and $\geqslant 12$), body mass index (BMI, <25, 25–29.9, and $\geqslant 30\,\mathrm{kg\,m^{-2}}$), tobacco consumption (never, ex-smoker, and current smoker of <15 and $\geqslant 15$ cigarettes per day), history of diabetes (no and yes), and total energy intake (quintiles, available for the second study only). Overall risk estimates for the two studies combined were further adjusted by study. We also computed continuous ORs, for an increment of one unit for MDS and MAI, and of 10 units for the MDP.

To investigate whether the associations with the three dietary scores was homogeneous across strata of selected covariates, we conducted analyses stratified by sex, age, education, BMI, tobacco smoking, alcohol consumption, and history of diabetes. Heterogeneity across strata was tested by likelihood ratio tests and resulting χ^2 statistics.

RESULTS

Table 1 shows the distribution of pancreatic cancer cases and corresponding controls by selected covariates. As compared with controls, cases were more frequently of female sex, were somewhat older, had a lower BMI, were more frequently heavy smoker, and reported more frequently a history of diabetes. No difference was observed with reference to education and alcohol drinking.

Table 1. Distribution of 688 pancreatic cancer cases and 2204 controls according to centre, sex, age, and selected other variables. Italy, 1983–2008

	Cases		Controls	
	No.	%	No.	%
Centre/study				
Milan (first study)	362	52.6	1552	70.4
Pordenone (second study)	175	25.4	350	15.9
Milan (second study)	151	22.0	302	13.7
Sex				
Men	403	58.6	1489	67.6
Women	285	41.2	715	32.4
Age (years)				
<50	92	13.4	519	23.6
50–59	208	30.2	678	30.8
60–69	247	35.9	686	31.1
⩾70	141	20.5	321	14.6
Education (years)[a]				
<7	358	52.2	1087	49.4
7–11	181	26.4	646	29.3
⩾12	147	21.4	469	21.3
Body mass index (kg m^{-2})[a]				
<20	90	13.2	122	5.6
20–24.9	316	46.2	952	43.4
25–29.9	212	31.0	884	40.3
⩾30	66	9.7	234	10.7
Tobacco smoking [a]				
Never smoker	274	39.9	913	41.5
Ex-smoker	173	25.2	521	23.7
Current smoker				
1–19 Cigarettes per day	89	13.0	357	16.2
⩾20 Cigarettes per day	150	21.9	410	18.6
Alcohol drinking (drinks per day)[a]				
<8	257	37.4	804	36.6
8–14	123	17.9	403	18.3
15–21	63	9.2	240	10.9
⩾22	244	35.5	752	34.2
Diabetes				
No	585	85.0	2078	94.3
Yes	103	15.0	126	5.7

[a]The sum does not add up to the total because of some missing values.

The distribution of pancreatic cancer cases and controls, and the corresponding ORs according to the MDS (separately for the two studies and overall) are given in Table 2. A significant reduced risk of pancreatic cancer was found for increasing levels of the MDS: the ORs for subjects with six or more Mediterranean characteristics, compared with those with less than three characteristics, were 0.57 (95% CI 0.34–0.95) in the first study, 0.51 (95% CI 0.29–0.92) in the second study, and 0.48 (95% CI 0.35–0.67) overall. The continuous ORs for a unit increment of the MDS were 0.88 (95% CI 0.81–0.95) in the first study, 0.89 (95% CI 0.81–0.99) in the second study, and 0.85 (95% CI 0.80–0.91) overall. In sensitivity analyses, the overall continuous OR was 0.84 (95% CI 0.79–0.90) after excluding milk from the MDS, 0.83 (95% CI 0.78–0.88) after excluding cereals, 0.86 (95% CI 0.81–0.92) after excluding fruit, 0.84 (95% CI 0.79–0.90) after excluding vegetables, 0.87 (95% CI 0.82–0.93) after excluding meat, 0.85 (95% CI 0.79–0.90) after excluding fish, 0.85 (95% CI 0.80–0.91) after excluding alcohol, and 0.83 (95% CI 0.78–0.89) after excluding monounsaturated to saturated fat ratio.

The association for a continuous increment of the MDS was consistent across strata of age, BMI, alcohol drinking, and tobacco smoking (Table 3). The inverse relation with pancreatic cancer was stronger in subjects with a lower level of education as compared with those with a higher level (OR = 0.79 and 0.91, respectively, P for heterogeneity between strata = 0.0095) and in those with no history of diabetes as compared with those with a history of diabetes (OR = 0.84 and 0.99, respectively, P for heterogeneity between strata = 0.01).

Table 4 shows the distribution of pancreatic cancer cases and controls and corresponding ORs according to the MDP and MAI. A trend of decreasing risk was observed for both scores, with ORs comparing the highest *vs* the lowest quintile of 0.44 (95% CI 0.27–0.72) for the MDP and of 0.68 (95% CI 0.42–1.11) for MAI. The ORs were 0.79 (95% CI 0.69–0.90) for a 10-unit increment of the MDP and 0.82 (95% CI 0.69–0.98) for a 1-unit increment of the MAI. The results for the MDP and MAI were consistent across strata of age, sex, education, BMI, alcohol drinking, tobacco smoking, and diabetes (data not shown).

DISCUSSION

Our study provides evidence that *a priori*-defined scores that include several aspects of the Mediterranean diet are favourably associated with pancreatic cancer risk. Such beneficial role is not meaningfully modified by allowance for known risk factors for this neoplasm, such as BMI, tobacco, alcohol, and diabetes. Moreover, as reported in two other studies that analysed pancreatic cancer risk in relation to Mediterranean diet scores (Jiao *et al*, 2009; Tognon *et al*, 2012), the inverse association was consistent in the two sexes.

Among specific components of the Mediterranean diet, vegetables and fruits have been reported to reduce the risk of pancreatic cancer in a few studies, possibly on account of their high content in vitamin C, folate, and phenolic compounds (Larsson *et al*, 2006; World Cancer Research Fund and American Institute for Cancer Research, 2007; Nothlings *et al*, 2007b; Hart *et al*, 2008; Bae *et al*, 2009; Rossi *et al*, 2012). However, the evidence is not consistent and a recent report of the World Cancer Research Association has judged the evidence for fruit and vegetables on pancreatic cancer 'limited–not conclusive' (Koushik *et al*, 2012; World Cancer Research Fund and American Institute for Cancer Research, 2012).

Table 2. Odds ratios[a] and 95% CI for pancreatic cancer according to the MDS[b] among 688 pancreatic cancer cases and 2204 controls. Italy, 1983–2008

	First study (1983–1992)					Second study (1992–2008)					Overall				
	Cases		Controls			Cases		Controls			Cases		Controls		
MDS[d]	*N*	%	*N*	%	OR[a] (95% CI)	*N*	%	*N*	%	OR[a] (95% CI)	*N*	%	*N*	%	OR[a,c] (95% CI)
<3	110	30.5	380	24.8	1[d]	36	11.0	50	7.7	1[d]	146	21.3	430	19.7	1[d]
3	110	30.5	360	23.5	1.18 (0.85–1.62)	50	15.3	94	14.4	0.69 (0.37–1.29)	160	23.3	454	20.8	0.93 (0.71–1.23)
4	76	21.1	359	23.4	0.81 (0.58–1.15)	72	22.1	151	23.2	0.62 (0.35–1.12)	148	21.5	510	23.3	0.66 (0.50–0.88)
5	42	11.6	263	17.2	0.60 (0.40–0.91)	81	24.9	156	23.9	0.68 (0.38–1.23)	123	17.9	419	19.2	0.57 (0.42–0.77)
⩾6	23	6.4	171	11.2	0.57 (0.34–0.95)	87	26.7	201	30.8	0.51 (0.29–0.92)	110	16.0	372	17.0	0.48 (0.35–0.67)
P-value for trend					0.0009					0.048					<0.0001
OR[e]					0.88 (0.81–0.95)					0.89 (0.81–0.99)					0.85 (0.80–0.91)

Abbreviations: CI = confidence interval; MDS = Mediterranean Diet Score; OR = odds ratio.
[a]Estimates from unconditional logistic regression models adjusted for centre, age, sex, year of interview, education, body mass index, tobacco smoking, alcohol consumption, history of diabetes, and total energy intake (second study only).
[b]The sum does not add up to the total because of some missing values.
[c]Estimates further adjusted for study.
[d]Reference category.
[e]Estimate for an increment of one unit.

Table 3. Odds ratios and 95% CI for pancreatic cancer according to the MDS in strata of selected covariates among 688 pancreatic cancer cases and 2204 controls. Italy, 1983–2008

	Cases/controls	OR[a] (95% CI)
Age (years)		
<60	300/1197	0.85 (0.77–0.93)
⩾60	388/1007	0.86 (0.79–0.93)
Sex		
Men	403/1489	0.84 (0.78–0.91)
Women	285/715	0.87 (0.79–0.97)
Education (years)		
<7	358/1087	0.79 (0.72–0.87)[b]
⩾7	328/1115	0.91 (0.84–0.99)[b]
Body mass index (kg m^{-2})		
<25	406/1074	0.89 (0.82–0.96)
⩾25	278/1118	0.82 (0.75–0.91)
Alcohol drinking (drinks per week)		
1–14	380/1207	0.82 (0.75–0.89)
⩾15	307/992	0.89 (0.81–0.98)
Tobacco smoking		
Never smoker	274/913	0.86 (0.78–0.95)
Ex-smoker	173/521	0.83 (0.73–0.94)
Current smoker	239/767	0.86 (0.77–0.95)
History of diabetes		
No	585/2078	0.84 (0.79–0.89)[b]
Yes	103/126	0.99 (0.81–1.23)[b]

Abbreviations: CI = confidence interval; OR = odds ratio.
[a]Estimates from unconditional logistic regression models adjusted for centre, age, sex, year of interview, education, body mass index, tobacco smoking, alcohol consumption, history of diabetes, total energy intake (second study only) and study. OR for an increment of one unit.
[b]*P*-value for heterogeneity across strata <0.05.

Table 4. Odds ratios and 95% CI for pancreatic cancer according to the MDP and MAI among 326 pancreatic cancer cases and 652 controls. Italy, 1992–2008

	Cases		Controls		
	N	%	N	%	OR[a] (95% CI)
MDP					
<48.7	85	26.1	111	17.0	1[b]
48.7–54.1	67	20.6	129	19.8	0.71 (0.45–1.12)
54.2–59.1	67	20.6	127	19.5	0.71 (0.44–1.13)
59.2–65.4	59	18.1	138	21.2	0.68 (0.42–1.08)
⩾65.5	48	14.7	147	22.5	0.44 (0.27–0.73)
P-value for trend					0.003
OR[c]					0.79 (0.69–0.90)
MAI					
<1.23	76	23.5	119	18.3	1[b]
1.23–1.60	73	23.5	122	18.7	1.04 (0.65–1.64)
1.61–2.95	54	16.7	141	21.7	0.60 (0.37–0.97)
1.96–2.47	66	20.4	129	19.8	0.83 (0.52–1.33)
⩾2.48	55	17.0	140	21.5	0.68 (0.42–1.11)
P-value for trend					0.073
OR[d]					0.82 (0.69–0.98)

Abbreviations: CI = confidence interval; MAI = Mediterranean Adequacy Index; MDP = Mediterranean Dietary Pattern Adherence Index; OR = odds ratio.
[a]Estimates from unconditional logistic regression models adjusted for centre, age, sex, year of interview, education, body mass index, tobacco smoking, alcohol consumption, history of diabetes, and total energy intake.
[b]Reference category.
[c]Estimate for an increment of 10 units.
[d]Estimate for an increment of one unit.

Olive oil, the most commonly used seasoning fat and the main source of monounsaturated fatty acid in Mediterranean countries, has also been reported to be a favourable indicator of various common cancers (Pelucchi *et al*, 2011), although data on pancreatic cancer are scanty (La Vecchia and Negri, 1997). A possible beneficial role of olive oil on cancer has been explained in terms of its strong antioxidant properties, owing to the specific fatty acid composition, as well as to the presence of various nutrients, such as vitamin E and polyphenols (Owen *et al*, 2000; Pelucchi *et al*, 2011). However, olive oil may simply be an indicator of a healthier diet, richer in vegetables and other plant foods.

Refined cereals (such as bread, pasta, or rice), frequently consumed in Italy, have been hypothesised to increase pancreatic cancer risk, through mechanisms involving insulin, insulin resistance, and insulin-like growth factors, and this is reflected in the estimates above unity for cereals in the present study (Polesel *et al*, 2010; Rossi *et al*, 2010). However, most epidemiological data do not indicate that a high intake of carbohydrates has a detrimental role on pancreatic cancer (World Cancer Research Fund and American Institute for Cancer Research, 2007; Nothlings *et al*, 2007a; Hart *et al*, 2008; Aune *et al*, 2012).

A direct association between pancreatic cancer and meat, particularly red meat, has been reported in several epidemiological studies (Stolzenberg-Solomon *et al*, 2007; World Cancer Research Fund and American Institute for Cancer Research, 2007; Zheng and Lee, 2009; Polesel *et al*, 2010; Anderson *et al*, 2012; Larsson and Wolk, 2012). Thus, the limited intake of (red) meat is another characteristic of the Mediterranean diet, which favourably influences pancreatic cancer risk. The association with red meat has been attributed to heterocyclic amines, polycyclic aromatic hydrocarbons, and nitrosamines produced in meat cooking, though the interpretation remains open to discussion (Tavani *et al*, 2000; Risch, 2003; Anderson *et al*, 2005).

The limited intake of animal foods and fats from animal sources, which characterises the Mediterranean diet, may also contribute to its favourable role in pancreatic cancer, although the evidence of the role of animal foods other than meat, including milk and dairy products, eggs, and fish, and of (saturated) fats on this nepolasm, is limited and inconsistent (World Cancer Research Fund and American Institute for Cancer Research, 2007; Hart *et al*, 2008).

Finally, heavy – but not low/moderate – alcohol intake has been associated with an increased pancreatic cancer risk (Tramacere *et al*, 2010; Genkinger *et al*, 2011; Lucenteforte *et al*, 2012). Thus, the regular but moderate consumption of wine mainly during meals, characteristic of the Mediterranean diet, is not an unfavourable indicator of pancreatic cancer.

More than on single dietary aspects, however, the interest of this study has to be related to the strong inverse relationship between pancreatic cancer and the combination of various food items into *a priori*-defined scores that take into consideration the synergistic effects or interactions of foods and nutrients characteristic of the Mediterranean diet. Thus, the combination of the favourable fatty acid profile, high fibre content, antioxidants and phytochemicals typical of the Mediterranean diet, and their synergistic effect appear to have a beneficial role on pancreatic, as on other cancers (Trichopoulou *et al*, 2000; Bosetti *et al*, 2003; Pelucchi *et al*, 2009; Buckland *et al*, 2010; Verberne *et al*, 2010; Couto *et al*, 2011; Buckland *et al*, 2013; Giacosa *et al*, 2013).

With reference to possible sources of bias inherent to case–control studies, in order to reduce any potential information bias, the questionnaires were administered to both cases and controls by the same interviewers, under similar condition. Dietary habits of hospital-controls may be different from those of the general population, but we paid attention to exclude from the control group all diagnoses associated with long-term dietary modifications. Potential recall bias should be limited, given the limited appreciation by the Italian population of a link between diet and pancreatic cancer risk at the time of interview. To reduce any possible dietary modification bias due to the recent cancer diagnosis, we asked for habitual dietary habits before cancer diagnosis, although diet could have changed before owing to subclinical disease. Among the limitations of the study is the short dietary questionnaire of the first study. However, the consistency of the results in the two studies, conducted in different calendar periods and using different dietary questionnaires gives further support to the finding of a beneficial role of the Mediterranean diet on pancreatic cancer. Among the strengths of the study are the relatively large sample size, the almost complete participation of cases and controls, the comparable catchment areas of study subjects, and the accurate control for major recognised risk factors for pancreatic cancer. As other healthy behaviours may be associated with a better diet, unaccounted confounding could partly explain the observed inverse association. The major strength of the study is the application of *a priori* and independently developed Mediterranean scores to a population with a considerable variability with respect to these scores, while other studies on the issue were conducted in non-Mediterranean populations. The comparability of the results obtained from a simple intuitive score (MDS) adopted in various previous epidemiological studies and from two other more complex *a priori* scores (MDP and MAI) proposed to evaluate the adherence to the Mediterranean diet also supports our findings of a beneficial role of the Mediterranean diet on pancreatic cancer.

ACKNOWLEDGEMENTS

This work was conducted with the contribution of the Italian Association for Cancer Research (Grant N. 10068). FT was supported by a fellowship from the Italian Foundation for Cancer Research (FIRC). The authors thank Mrs Ivana Garimoldi for editorial assistance.

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Supplementary Information accompanies this paper on British Journal of Cancer website (http://www.nature.com/bjc)