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ORIGINAL CONTRIBUTION

Dietary patterns and the adenoma-carcinoma sequence of colorectal cancer

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Summary *Background* Food components of a diet are highly related, so that building up dietary patterns may help understand the relationship between chronic diseases and diet, and identify high risk groups that need preventive advice. *Aim* The aim of this study was to determine dietary patterns associated with the colorectal adenoma-carcinoma pathway. *Methods* We performed a two-step analysis using first principal component analysis to select the most appropriate food groups, then a hierarchical agglomerative clustering method, in order to determine dietary patterns in 1372 subjects included in a case-control study. Patients with hyperplastic polyps (n = 103), adenomas < 10 mm, (n = 154) or larger adenomas (n = 208) were then compared with polyp-free controls (n = 426), and colorectal cancer cases (n = 171) compared with population controls (n = 309) using unconditional logistic regression adjusted on age and gender. *Results* Cluster analysis determined five food patterns. Cluster 1 identified a low-energy diet; cluster 2 a high-starch, high-fat, and low-fruit diet; cluster 3 a high-processed meat, -energy, -alcohol, and -starchy foods diet; cluster 4 a high-fish, -cereals, -honey, -olive oil, -fruit and -vegetables diet; and cluster 5 a high-flour, -sugar, -chocolate, -animal fats, and -eggs diet. Logistic regression identified cluster 1 as significantly associated with risk of small adenomas (OR = 1.7; 95 % confidence interval 1.0–2.7), large adenomas (OR = 1.9; 1.2–3.0) and cancers (OR = 1.7; 1.1–2.8) compared with cluster 2. Cluster 4 diet was inversely associated with risk of small adenomas (OR = 0.4; 0.2–1.0). There was no relationship between patterns and risk of hyperplastic polyps. Multiple adjustment decreased the strength of the relationships with cluster 1, which remained significantly associated with adenomas, but not cancer. *Conclusion* A low-energy diet appeared as protective all along the adenoma-carcinoma sequence, contrary to a high-energy, high-processed meat and -animal fat diet.

Key words colorectal neoplasms – adenomatous polyps – food habits – diet – case-control

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Introduction

Although the association between diet and colorectal tumours has been widely described, results usually concern individual foods or nutrients [1]. However, foods or nutrients tend to be closely correlated so that it is not always easy to determine precisely the relative importance of each factor. Attempts have been made over the recent years to investigate broader dietary patterns in order to identify groups at risk for a given disease [2–4], or to identify a protective diet. A recent study in Greece described a significant reduction in mortality both from cardiovascular disease and from cancer in subjects with a typical Mediterranean diet [5]. Several methods are available to identify dietary patterns [6]. Principal com-

European Journal of Nutrition (2005) Vol. 44, Number 5

ponent analysis, followed by a calculation of scores, has been largely used [2–4]. Subjects are then classified according to a categorisation of the scores into tertiles or quintiles. Other methods use cluster analyses, such as hierarchical classification or the κ-means method, to distinguish separate groups with specific dietary profiles. Whatever the method, studies in Western countries have often identified a 'Western' diet as a diet at risk of major diseases such as cancer [7] or cardiovascular disease [8]. On the other hand, a 'prudent' diet, associated with a low risk of disease, identified subjects who followed dietary recommendations [8]. In Western countries, most colorectal cancers arise from the so-called adenoma-carcinoma pathway, i. e. small adenoma formation, adenoma growth, and cancer. As most prevention strategies are focused on the adenoma, it seems important to identify patterns of diet related to both cancer and precancerous lesions. Thus, we attempted to identify dietary patterns associated with risk of colorectal adenomas and cancers within a well-defined French area, using cluster analysis with hierarchical classification.

Subjects and methods

Study population

A case-control study was set up in the Côte d'Or area (Burgundy, France) in order to investigate environmental and familial risk factors in relation to the colorectal adenoma-carcinoma sequence. Details of the study population and design have already been presented [9]. Briefly, subjects eligible for the study were residents of the Côte d'Or area, aged 30–79. The study was designed as two parallel case-control studies, one aimed at investigating risk factors for adenomas and hyperplastic polyps, the other studying risk factors related to colorectal cancers. All adenoma cases, subjects with hyperplastic polyps and the polyp-free control group (n = 426) were recruited from all gastroenterologists of the area: 208 patients with at least one adenoma ≥10 mm in diameter, 154 patients with only small adenomas, and 103 subjects with only hyperplastic polyps. Subjects with a previous history of colorectal tumour were excluded, as this might have led them to modify their dietary habits. Recruitment was obtained from all endoscopy lists of all gastroenterologists of the area. We selected only colonoscopies that reached at least the junction between the sigmoid and the descending colon; when incomplete, most colonoscopies were completed by a double contrast barium enema. The second case-control study involved 171 patients with a histologically proven colorectal carcinoma diagnosed for the first time and recruited through all gastroenterologists and surgeons of the area, with the help of the local registry of digestive cancers. They were compared with 309 population controls, obtained through the INSEE (National institute for statistics and economic studies) as a random sample of the general population, with sex and age distributions similar to the cancer cases. Adenomas, hyperplastic polyps and cancers were classified according to the WHO classification [10].

Data

A 2-h detailed quantitative food history questionnaire about the subjects' diets during the year prior to diagnosis was designed for the study and validated on 40 healthy middle-age volunteers using a 2-week diary record [11]. Specially trained dieticians who also coded the data administered the questionnaire at the subjects' homes. For mixed dishes, recipes were obtained, and a program transformed them into 159 simple foods.

Statistical analysis

Factor analysis

Principal component analyses were performed to describe the structure of the data. We used the correlation matrix in order to standardise the consumed amounts. In order to select the most informative food groups, we performed several principal component analyses successively, and selected, for each possibility of grouping variables, the one that provided the highest proportion of explained variance. This process led us to select 54 food groups for determining food patterns. We used the screeplot of the factors with decreasing eigenvalues, in order to keep only the most informative factors. The shape of the diagram identified a difference in the explained variance after the first 13 factors, which accounted for 40 % of the total variance. Thus, we used these first 13 factors to perform the hierarchical classification.

Cluster analysis [12, 13]

Cluster analysis enabled us to divide the study population into a limited number of maximally differing clusters. We used the hierarchical agglomerative clustering method, with Ward's minimum variance method and squared Euclidean distance. The hierarchical agglomerative clustering method consists of merging the two closest individuals or clusters to form a new cluster that replaces them and iterating the process with the new group until complete regrouping, and provides a dendrogram or classification tree. The Ward's minimum variance method minimised the within-cluster sum of squares at each step of the algorithm. We used the dendrogram to determine the number of clusters, with a maximum proportion of variance accounted for by the clusters and large enough groups to be further studied.

We calculated the squared multiple correlation R^2, which is the proportion of variance accounted for by the clusters. For each cluster, in order to classify foods according to their contribution in defining the cluster, we calculated test values. They represent the number of standard deviations of a normal distribution, and absolute values above 1.96 correspond to a significant difference at the 5 % level [14].

Analysis of clusters in relation to risk of colorectal tumours

In order to study the relationship between food patterns and the adenoma-carcinoma sequence, the cancer group was compared with the population control group, whereas each polyp group (small adenomas, large adenomas and hyperplastic polyps) was compared with the polyp-free control group.

Odds ratios associated with the selected patterns were calculated with an unconditional logistic regression controlling for age and sex. In a second step, we performed additional adjustment on tobacco, alcohol, body mass index, energy and exercise. The statistical significance of each studied variable was tested by the maximum likelihood method.

All calculations were performed using the SAS© software package (8th version).

Results

Dietary patterns

We identified five clusters. Test values, and the cluster and general mean and standard deviations, corresponding to the most determinant food groups for each cluster are presented in Table 1. Test values above 1.96 (or below –1.96) indicate that the corresponding food is consumed statistically significantly more (or less) in the cluster than in the whole studied population. Cluster 1 included 531 subjects. It was characterised by a diet with specifically low intake of high-fat processed meat, eggs, bread, starchy foods, wine, pork, beef and fats, and a high consumption of coffee. It was taken as the reference category in logistic regression analyses. Cluster 2 included 419 subjects with a high intake of bread, pork, oils other than olive oil, wine, starchy foods, and high-fat processed meat. Cluster 3 included 184 subjects who preferably consumed foods with a high energy density such as high-fat delicatessen, beer or wine, starchy foods, bread, saturated margarine, pulses and high-alcohol drinks. Cluster 4 included 125 subjects with a high intake of wholemeal cereal products, fish, honey, chicory drink, olive oil, vegetables and fruit. Cluster 5 included 113 subjects who preferably consumed foods made of flour and sugar, chocolate, animal fats and eggs.

Associations between patterns and socio-demographic characteristics are described in Table 2. The reference pattern (cluster 1) was characterised by a high proportion of women, of subjects with a low education level, and of urban-living subjects, and by a low proportion of men eating while watching television, and a low alcohol intake. Cluster 2 included a relatively high proportion of men, of subjects with a low education level, of rural-living subjects, of subjects eating while watching television, and a high consumption of alcohol and tobacco. Cluster 3 was quite similar to cluster 2, except for a very high proportion of men, and the highest level of physical activity. Cluster 4 was quite the opposite of the two previously described patterns. It included a high proportion of women, subjects with the highest education level, the highest proportion of urban-living subjects, and the lowest proportion of women eating while watching television. Cluster 5 had no significant characteristics.

Risks associated with dietary patterns

When comparing cancer patients with population controls, cluster 2 was associated with a significant risk of cancer as compared with cluster 1 (OR = 1.7; 95 % confidence interval 1.1–2.8). No other pattern was significantly associated with risk, although the odds ratio associated with cluster 5 was 2.0 (0.9–4.6), close to statistical significance.

The risk of small or large adenomas was also associated with cluster 2, the odds ratios being respectively 1.7 (1.0–2.7) and 1.9 (1.2–3.0). There was also an inverse association between risk of small adenomas and cluster 4 (OR = 0.4; 0.2–1.0).

Risk of hyperplastic polyps was not associated with any dietary pattern.

In the multiple adjusted models, including age, gender, body mass index, exercise, energy intake, tobacco and alcohol, most effects were reduced. The significant association between adenomas and cluster 2 remained, while the inverse association with cluster 4 was of the same magnitude, but became borderline significant. No association with cancer remained significant. The factors mostly responsible for decreasing the effects were energy and exercise for cancers, and tobacco for adenomas.

Discussion

The main finding of our study is the identification of a cluster at high risk of small and large colorectal adenomas, as well as of cancer, but not of hyperplastic polyps, thus suggesting a real specificity towards neoplasm.

Several methods are available to identify dietary patterns associated with a given disease. Most studies rely

European Journal of Nutrition (2005) Vol. 44, Number 5

Table 1 Description of the five selected clusters: test value*, mean and standard deviation for each cluster compared with the whole studied population for the most informative food groups

Food groups	Test value*	Mean (g/day)		Standard deviation	
		Cluster	General	Cluster	General
Cluster 1 (n = 531)					
Coffee	2.76	79.06	64.44	175.58	155.80
Flour (white)	–8.55	13.91	18.36	9.87	15.30
Pulses	–8.76	4.31	8.29	7.52	13.37
Pork	–9.27	12.81	17.73	11.33	15.62
Beef	–9.43	30.25	39.81	20.19	29.82
Sugar	–9.53	18.35	24.66	14.58	19.46
Vegetable oils**	–9.78	11.75	15.24	8.20	10.49
Animal fats	–10.11	18.14	24.68	12.87	19.03
Wine	–10.37	114.70	245.06	199.70	369.75
Rice, pasta and potatoes	–10.41	121.59	148.70	59.51	76.65
Bread	–10.80	93.17	126.46	61.87	90.73
Eggs	–10.86	24.50	32.61	15.36	21.97
High-fat processed meat	–13.59	9.62	18.20	9.27	18.58
Cluster 2 (n = 419)					
Bread	7.53	154.31	126.46	83.42	90.73
Pork	6.63	21.95	17.73	15.68	15.62
Vegetable oils**	6.06	17.83	15.24	11.19	10.49
Wine	5.96	334.83	245.06	405.65	369.75
Rice, pasta and potatoes	5.87	167.02	148.70	71.38	76.65
High-fat processed meat	5.65	22.48	18.20	16.33	18.58
Fruit	–3.19	230.40	249.05	125.10	143.67
Sugar-free cereals	–3.32	0.14	1.03	1.36	6.58
Coffee	–4.13	38.24	64.44	102.05	155.80
Wholemeal cereal products	–4.60	0.95	5.94	7.38	26.66
Yoghurt	–6.78	29.06	48.97	50.22	72.10
Cluster 3 (n = 184)					
High-fat processed meat	13.92	35.96	18.20	26.23	18.58
Beer	12.67	153.78	37.81	304.27	133.38
Rice, pasta and potatoes	12.36	213.71	148.70	94.63	76.65
Wine	12.26	556.20	245.06	531.93	369.75
Hard margerine	12.05	7.72	3.45	9.07	5.17
Bread	11.50	198.04	126.46	113.99	90.73
Pulses	10.66	18.07	8.29	23.52	13.37
High-alcohol drinks	9.80	11.89	4.19	22.98	11.44
Sugar	9.63	37.52	24.66	21.77	19.46
Fruit	–3.39	215.64	249.05	152.18	143.67
Mineral water	–3.41	140.78	256.06	378.69	493.09
Honey	–3.73	1.18	3.10	4.05	7.51
Coffee	–4.79	13.21	64.44	68.42	155.80
Cluster 4 (n = 125)					
Sugar-free cereals	12.82	8.22	1.03	17.69	6.58
Fish	11.68	48.96	26.23	37.72	22.82
Chicory drink	10.33	1.29	0.16	3.80	1.28
Wholemeal cereal products	10.21	29.15	5.94	51.15	26.66
Honey	9.91	9.45	3.10	13.74	7.51
Olive oil	9.62	4.16	1.11	6.54	3.72
Coffee	9.51	190.79	64.44	248.92	155.80
Fruit	9.20	361.79	249.05	166.03	143.67
Vegetables	6.35	223.77	173.38	97.93	93.06
High-fat processed meat	–5.24	9.89	18.20	10.37	18.58
Pork	–5.66	10.20	17.73	10.62	15.62
Bread	–7.28	70.13	126.46	68.58	90.73
Rice, pasta and potatoes	–7.39	100.41	148.70	48.59	76.65

Table 1 *Continued*

Food groups	Cluster 5 (n = 113)				
	Test value*	Mean (g/day)		Standard deviation	
		Cluster	General	Cluster	General
Flour (white)	12.22	35.21	18.36	25.48	15.30
Sugar	11.88	45.50	24.66	27.88	19.46
Chocolate	11.18	24.45	8.74	27.82	15.59
Animal fats	9.28	40.59	24.68	22.75	19.03
Eggs	8.92	50.28	32.61	25.44	21.97
Jam and marmelade	8.58	27.64	12.13	34.94	20.05
Wine	–2.47	162.83	245.06	227.06	369.75
Cruciferous vegetables	–2.49	21.23	25.07	11.91	17.05

* Test values represent the number of standard deviations of a normal distribution, so that absolute values above 1.96 correspond to a significant difference at the 5 % level [14]; ** all oils except olive oil

Table 2 Description of dietary patterns by gender

		Cluster 1	Cluster 2	Cluster 3	Cluster 4	Cluster 5	P value
Gender N (%)	Men	160 (30.1)	297 (70.9)	164 (89.1)	38 (30.4)	65 (57.5)	< 0.001
	Women	371 (69.9)	122 (29.1)	20 (10.9)	87 (69.6)	48 (42.5)	
Education level (% with school to age 18 or over)	Men	12.5	12.5	12.2	47.4	24.6	< 0.001
	Women	8.9	6.6	10.0	26.4	16.7	< 0.001
% living in urban setting	Men	74.4	59.9	58.9	81.6	75.4	< 0.001
	Women	68.6	67.2	65.0	90.8	83.3	< 0.001
% eating often or always in front of television	Men	33.1	40.0	46.4	34.2	38.5	0.17
	Women	34.2	38.5	40.0	19.5	39.6	0.04
Energy (Kcal/d)	Men	1838 ± 400	2407 ± 487	3033 ± 753	2361 ± 571	3286 ± 747	< 0.001
Mean ± SD	Women	1660 ± 388	2153 ± 458	2559 ± 681	2039 ± 639	2363 ± 662	< 0.001
Alcohol (g/day)	Men	24.0 ± 23.7	41.9 ± 36.8	64.7 ± 48.9	29.3 ± 31.7	27.5 ± 25.2	< 0.001
Mean ± SD	Women	5.6 ± 9.3	8.5 ± 11.6	13.7 ± 19.1	4.3 ± 7.8	4.2 ± 5.9	< 0.001
Smoking (pack-years)	Men	19.2 ± 18.7	20.1 ± 19.3	25.5 ± 20.1	13.0 ± 15.7	15.5 ± 17.4	< 0.001
Mean ± SD	Women	1.3 ± 6.6	3.0 ± 11.5	3.3 ± 6.8	3.3 ± 8.1	3.1 ± 8.9	0.09
BMI as % ≥ 25 kg/m^2	Men	45.6	53.9	57.3	42.1	46.2	0.13
	Women	31.3	33.6	20.0	18.4	33.3	0.10
Physical activity (% low)	Men	17.0	11.3	8.0	13.2	20.3	0.001
	Women	27.4	30.8	42.1	26.4	27.7	0.72

on principal component analysis, and identify main trends in dietary habits. A scoring system is applied to each individual who, thus, participates more or less in each determined pattern. On the other hand, cluster analysis is aimed at identifying subjects with similar behaviour, as different as possible from those of the other clusters. All these techniques are mainly descriptive and exploratory and, therefore, have their own limitations, related to the choices made along the classification process. The main advantage of the hierarchical classification that we used is that it provides straightforward grouping of individuals with meaningful description of dietary habits, and identifies groups that should specifically benefit from dietary advice and screening measures. Most studies provide names for the observed dietary patterns, but these can easily be misleading as they rarely correspond exactly to similarly named patterns in other countries [2, 3, 7]. As an example, our high risk cluster, cluster 2, could be named Western, as it involved a preferential intake of many foods often associated with a Western pattern, such as white bread, pork and processed meat, potatoes, rice and pasta, while fruit, wholemeal grains and yoghurt were little consumed. However, in a prospective study of Swedish women [2], the Western diet, defined by preferential intakes of processed and red meats, sodas and sweets, refined breads and potatoes, and high-fat dairy products (thus, a mixture of our cluster 2 and cluster 5) was not significantly associated with an increased risk of colorectal cancer. In a large US case-control study [3], the Western profile was defined both in men and in women as high levels of red meat, processed meat, refined grains and sugar-containing foods, and low levels of vegetables and fresh fruit. High scores for the Western diet were signif-

Table 3 Relationship between clusters and risk of colorectal tumours (odds ratios and 95% confidence interval)

	Cluster 1	Cluster 2	Cluster 3	Cluster 4	Cluster 5
Cancers vs. population controls					
n cases/controls	52/132	69/93	25/46	13/22	12/16
Non-adjusted[a]	1.0	1.7* (1.1–2.8)	1.3 (0.7–2.4)	1.6 (0.7–3.4)	2.0 (0.9–4.6)
Adjusted[a]	1.0	1.5 (0.9–2.5)	1.0 (0.5–2.2)	1.4 (0.6–3.1)	1.5 (0.6–3.8)
All adenomas vs. polyp-free controls					
Non-adjusted[a]	1.0	1.7** (1.2–2.5)	1.1 (0.7–1.9)	0.7 (0.4–1.2)	0.7 (0.4–1.2)
Adjusted[a]	1.0	1.5* (1.0–2.2)	0.9 (0.5–1.5)	0.7 (0.4–1.2)	0.7 (0.4–1.2)
Large adenomas vs. polyp-free controls					
n cases/controls	72/180	78/95	30/46	16/54	12/52
Non-adjusted[a]	1.0	1.9** (1.2–3.0)	1.3 (0.7–2.4)	0.9 (0.5–1.8)	0.6 (0.3–1.3)
Adjusted[a]	1.0	1.6* (1.0–2.5)	0.9 (0.5–1.7)	0.9 (0.5–1.8)	0.6 (0.3–1.3)
Small adenomas vs. polyp-free controls					
n cases/controls	60/180	57/95	17/46	7/54	13/52
Non-adjusted[a]	1.0	1.7* (1.0–2.7)	1.0 (0.5–1.9)	0.4* (0.2–1.0)	0.8 (0.4–1.5)
Adjusted[a]	1.0	1.5* (1.0–2.5)	0.9 (0.5–1.9)	0.4 (0.2–1.0)	0.7 (0.4–1.5)
Hyperplastic polyps vs. polyp-free controls					
n cases/controls	35/180	27/95	20/46	13/54	8/52
Non-adjusted[a]	1.0	1.3 (0.7–2.3)	1.7 (0.8–3.4)	1.3 (0.6–2.6)	0.7 (0.3–1.6)
Adjusted[a]	1.0	1.1 (0.6–2.0)	1.3 (0.6–2.8)	1.4 (0.7–2.8)	0.7 (0.3–1.6)

[a] Non-adjusted: adjusted only on age and gender; Adjusted: adjusted on age, gender, energy, body mass index, exercise, tobacco and alcohol
* $p < 0.05$; ** $p < 0.01$

icantly associated with an increased risk of colon cancer. In the Nurses' Health Study [7], the Western diet consisted of high intakes of refined grains, processed and red meat, desserts, high-fat dairy products and French fries. Thus, people who consume the most important quantities of foods associated with a high risk of colorectal tumours, such as refined cereal products [15, 16] and processed meat [17], are also those with the lowest intake in foods associated with a decreased risk such as vegetables and fruit [18]. This could explain why it is often difficult to disentangle the various factors, and why studies may be controversial on some dietary factors [19–21]. Our high-risk pattern was quite close to cluster 3, which was characterised by a preference for foods with a high-energy content and a low micronutrient content. However, the latter was not associated with any type of tumour, although it included people with a higher energy intake, more alcohol and more smoking, but also with a higher level of exercise in men. This emphasises the fact that dietary factors which help identify specific patterns may not be the only explanation for observed effects within a group. Other factors such as education, lifestyle related to place of residence, and eating while watching the television also play a role.

The most important characteristics of our low-risk diet, cluster 1, were a low intake of 'unhealthy foods' such as starchy foods, white bread, high-fat processed meat, animal fats and sugar rather than a high intake of 'healthy foods'. This diet, which was quite consistently associated with the lowest risk of colorectal tumours, was almost the opposite of our high-risk diet. Our low-risk pattern could also be called a low-energy pattern, which could explain why adjusting on energy decreased the observed difference between the low- and high-risk clusters. The other characteristic of our low-risk diet was unexpectedly a high coffee intake, although the association was not very strong. Coffee has been inversely associated with risk of colorectal cancer in several studies, especially case-control studies [22], and an effect via a modification in cholesterol excretion was suggested. However, most cohort studies failed to find an association with coffee [23], an explanation could be that other features of the pattern rather than coffee itself could be of importance.

Surprisingly, there was little beneficial effect of the diet rich in fruit, vegetables and olive oil (cluster 4), although such a diet is usually associated with a lower risk of chronic diseases, and especially of colorectal cancer. In our study, this diet was only inversely associated with risk of small adenomas. Although it could be considered as a local version of a Mediterranean diet, it may include too low quantities of the foods or nutrients that characterise a true Mediterranean diet. A study of mortality in Greece has observed that the quality of adherence to a Mediterranean diet was strongly associated with the beneficial effect in terms of reduction of mortality [5]. In that study, median intake of olive oil was about 40 g/day, whereas our cluster consumed a mean 4.2 g/day. As olive oil has been suggested to be a major reason for the protective effect of the Mediterranean

diet both in epidemiological and in experimental studies [24], this might explain the lack of association between our Mediterranean pattern and late events of colorectal carcinogenesis. Other hypotheses on the relationship between diet and colorectal tumours have involved refined carbohydrates and sugars via their effect on insulin and IGF-1 [25, 26]. However, we did not observe any association between cluster 5, with a high sweets and cakes intake, and any step of the adenoma-carcinoma sequence. It could be a problem of power because of the small sample size of this cluster, as we observed a 2.0 odds ratio for the risk of cancer, which was on the verge of statistical significance. However, for adenomas, associations tended to be negative, suggesting that such a diet may be only related to the late events of carcinogenesis.

A limitation of our study is that we had a relatively limited sample size. However, we paid special attention to the quality of our dietary data, using a lengthy interview with specially trained dieticians, and helping subjects to remember their diet by going through the different meals [11]. We think that this procedure might reduce misclassification bias of dietary intake and, thus, partly overcome the size problem. However, only positive findings must be highlighted, whereas we cannot discard the effects of the patterns with small sample sizes. Another aspect which needs discussion is the decreased association between patterns and colorectal tumours when adjusting on several risk factors, especially energy. We think that this explains rather than reduces the importance of our findings. The fact that adjustment on energy makes the comparison between cancer cases and controls non-significant suggests that our high-risk diet, cluster 2, is mostly associated with cancer because of its high-energy component.

In conclusion, our data support a protective effect of a low-energy diet, and a deleterious effect of a Western-like diet, all along the adenoma-carcinoma sequence.

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