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# A case-control study of gastric cancer and nutritional factors in Marseille, France

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**Abstract.** A case-control study was conducted in Marseille (France) to investigate the relationship between usual diet and risk of gastric cancer. Patients with histologically confirmed gastric adenocarcinoma were identified in 8 major centres for gastric surgery. Controls were selected in specialized medical centres from patients undergoing functional reeducation for injuries or trauma, according to the age and sex distributions of the cases. The study involved 92 cases and 128 controls who were interviewed with a dietary history questionnaire on their usual diet during the year preceding first symptoms for cases, or preceding interview for controls. Odds ratios for specific foods were calculated after adjustment for age, sex, occupation and energy intake. A reduced risk was observed for consumption of raw vegetables (OR2: 0.55; OR3: 0.41 for the second and third tertiles, respectively), fresh fruit (OR2: 0.63; OR3: 0.50), vegetable oil (OR2: 0.60; OR3: 0.52), pasta and rice (OR2: 1.06; OR3: 0.50) whereas consumption of cakes and pastries (OR2: 1.02; OR3: 2.96), sugar and confectionery (OR2: 0.96; OR3: 1.68) was associated with an increased risk. An increased risk was found for intake of saturated fat (OR2: 1.49; OR3: 1.67), simple sugars (OR2: 1.18; OR3: 1.78) and calcium (OR2: 1.84; OR3: 2.57). A decreased risk was observed with intake of fiber (OR2: 0.49; OR3: 0.59), fibre from vegetables and fruit (OR2: 0.83; OR3: 0.53) and iron (OR2: 0.70; OR3: 0.41).

**Key words:** Dietary factors, Gastric cancer

## Introduction

The most striking feature of gastric cancer patterns is undoubtedly the worldwide decline in both incidence and mortality since the 1930s. The highest incidence rates have been reported in Asia (particularly Japan), in Latin America (Chile, Costa Rica) and in eastern Europe, whereas lower rates have been recorded in western Europe and North America [33]. In France, cancer of the stomach was for a long time the most common cancer. However, as in nearly all countries of the world, a decreasing trend has been observed: the annual variation in mortality over the period 1950–1985 was about –4.5% for women and –3.6% for men. It was the first cause of mortality from a specific cancer site in 1950 and the fifth in 1985 [17].

The decline in gastric cancer remains largely unexplained, and the aetiological factors have not been clearly identified. Various factors, such as changes in classification, detection, diagnosis or treatment could partly explain the observed temporal and geographic patterns, but studies of migrants suggest that environmental agents may be involved. Recent reviews concerning risk factors for gastric cancer conclude that environmental agents, especially diet, are of major importance [2, 12, 18]. Furthermore, a human model of gastric carcinogenesis has recently been developed, based on a multistage process in which dietary constituents act on the mucosa at various stages, leading from superficial gastritis to carcinoma, and the role of N-nitroso compounds has been emphasized [8].

Substantial research has been developed worldwide to investigate the relation between gastric cancer and usual diet, mainly through case-control studies. However, as far as we know, the present investigation is the first to be carried out in France. The aims were on one hand to test in a French population the hypotheses provided by previous studies regarding risk related to specific foods and nutrients (in particular: fruit, vegetables, smoked and salted foods), and on the other hand to evaluate the role in the etiology of gastric cancer of nitrites, nitrates and nitrosamines in foods. In this paper, we report the results of the analyses on consumption of foods and nutrients; results concerning nitroso-compounds are reported in a companion paper [28].

## Materials and methods

The investigation was conducted in the urban area of Marseille between March 1985 and December 1988. Incident cases of gastric cancer were identified in the departments of gastroenterological surgery of 8 major clinics and hospitals in Marseille. Patients were interviewed during their first hospitalization for gastric cancer and, in most cases, before surgical treatment. Diagnosis was usually based on radiological or endoscopic examinations and anatamopathological reports. Only cases with histologically confirmed gastric adenocarcinoma were included. This excluded a priori cases with non-operable cancers and those treated by endoscopic excision in non-surgical departments.

Controls were selected in two specialized medical centres from patients undergoing functional reeducation for trauma or injuries which reduced their mobility. They were matched to cases by group matching based on age- and sex-distribution of cases; the group matching procedure, instead of one-to-one matching, explains why the number of cases is not the same as that of controls. Controls who had had accidents possibly related to excessive alcohol intake were not eligible. All subjects with a previous history of tumours of the digestive tract or gastroenteric diseases were excluded as were subjects whose diet had recently been restricted for medical reasons (such as diabetes or nephropathy).

Cases and controls were all interviewed in hospital by the same trained nutritionist with the full cooperation of the responsible clinicians, and none of the eligible subjects refused to participate.

A detailed, structured questionnaire designed for previous studies on diet and colorectal cancer and polyps [23, 24] was used to obtain demographic data and information on socio-economic status, residence, occupation, medical history and occurrence of cancer among relatives. Dietary patterns were assessed following the dietary history questionnaire developed by the French National Institute of Health and Medical Research (INSERM) [27] and used in previous French and European studies [31]. The interviewer was trained by the INSERM Unit which developed the questionnaire. Before working on this study, she had the experience of conducting about 600 interviews in our previous studies on colorectal cancers and polyps. The diet questionnaire was adapted from the original one to include details on smoked, cured and salted foods and on different varieties of vegetables. The questionnaire was composed of 5 sections according to the usual French eating habits: breakfast, lunch, dinner and snacks between meals. Subjects were asked to describe their usual diet during the year preceding the interview or the first symptoms of the disease. They were invited to estimate the weekly frequency of the consumption of each food item and to describe the usual portion size. Food items seldom consumed (i.e. less than 0.5 times a week) were not recorded. Seasonal aspects of consumption of vegetables and fruit were assessed on the basis of their average intake during the relevant period of the year. The portion sizes estimated by the subjects were transcribed into weight (grams) by the interviewer. The composition of the food groups and subgroups is given in Table 1. In general, the interview took between 35 and 45 minutes.

Quantative estimates of calories and nutrients in each food were based on *ad hoc* food tables derived from French and English tables [25, 26, 29, 30] and previously developed for the needs of local studies on diet and cancer [23, 24].

Statistical analysis was performed by means of the SAS and GLIM packages. For descriptive analysis on qualitative variables, cases and controls were compared through Pearson's chi-square. Means, medians and percentiles were computed for quantitative variables. Means between cases and controls were compared through Student's t-test after checking for normality of the distributions. For variables not normally distributed, cases and controls were compared using the non-parametric Wilcoxon test. Odds ratios (ORs) were estimated by unconditional logistic regression [4]. All models fitted were adjusted for age at four levels ($\leqslant 55$; 56 to 65; 66 to 75; $\geqslant 76$), sex, occupation as indicator of socio-economic status (i.e. present occupation of the subject or of the husband for women at home, or past occupation for retired people, categorized into 5 levels) (see Table 2). Statistical adjustment for total energy intake (including energy from alcohol) was made using the method proposed by Willett & Stampfer [37].

Residuals were computed from regression models with total calorie intake (as the independent variable) and absolute food or nutrient intake in grams per day (as the dependent variable). Residuals for each given food or nutrient as well as total calorie intake were included as independent variables in the logistic models fitted to calculate the odds ratios for a given food or nutrient. ORs for specific foods were estimated for 3 levels of consumption based on tertile distribution. Ninety-five percent confidence intervals (95% CI) were computed for ORs based on the standard deviation of the corresponding logistic $\beta$. Chi-squares for linear trend were calculated, residuals being considered as continuous variables (absolute levels).

## Results

The present analyses are based on 92 cases (59 men and 33 women) and 128 controls (74 men and 54

**Table 1.** Food groups

| Food groups | Description |
|---|---|
| Total dairy products | Total milk, hard cheese, soft cheese, yoghurt, cream cheese |
| Total milk | Whole milk, skim milk, half-cream milk |
| Hard cheese | All types |
| Soft cheesee | All types |
| Yoghurt | All types |
| Total meat products | Meat, poultry, offal, ham, salami, other 'charcuterie' |
| Meat | Beef, horse, pork, mutton, veal |
| Poultry | All types |
| Offal | All types |
| Ham | All types |
| Salami | All types |
| Other 'charcuterie' | |
| Fish | Fresh fish |
| Eggs | |
| Butter and cream | All types |
| Oil | All types |
| Total flour products | Bread and flour products, cakes and pastries, pasta and rice |
| Bread and flour products | White bread, wholemeal bread, toasted bread, rusks |
| Cakes and Pastries | Cake, croissants, fine pastries |
| Pasta and rice | All types |
| Total fresh fruit | Citrus fruit, other fresh fruit |
| Citrus fruit | All types |
| Non-citrus fruit | |
| Total vegetables | All types except dried vegetables and potatoes |
| Raw vegetables* | Tomato, radishes, lettuce, cucumber, celery |
| Cooked vegetables* | Courgette, beetroot, cauliflower, green beans, peas, cabbages, spinach, egg-plant, leek, Swiss chard, mushrooms |
| Raw or cooked vegetables* | Carrots, onion, endive |
| Potatoes | All types |
| Dried vegetables | All types |
| Sugar and confectionery | Sugar, honey, jam, jelly, chocolate, sweets |

* On the assumption that certain vegetables are usually consumed raw, others cooked, and some either cooked or raw.

women). The distributions of cases and controls according to age and main non-dietary variables of potential interest are reported in Table 2. The male-to-female sex ratio was 1.8. Since social class is associated with both incidence of gastric cancer and dietary habits, occupation was included as an indicator of socio-economic status in all the logistic regression models. More cases than controls were, or had been, manual workers or office clerks, while more controls than cases belonged to the higher occupational categories (directors, managers, professional white collar). More cases (7.6%) than controls (2.3%) reported that one of their parents had suffered from gastric cancer, but this difference was not statistically significant.

No material differences in smoking or drinking habits were observed between cases and controls. The risk for current smokers of more than one pack of cigarettes per day relative to non-smokers was 1.01 (95% CI: 0.55–1.84). The risk for current consumption of 50 ml of alcohol or more per day was 1.11 (95% CI: 0.54–2.30). There were no significant differences between cases and controls regarding the age at which they started drinking alcohol (age 20.7 and 21.9 for cases and controls, respectively) nor for duration of their drinking habit (36.1 and 37.3 years for cases and controls, respectively).

Mean, median, 25th and 75th percentiles of food and nutrient intake for cases and controls are shown in Appendices 1 and 2. Consumption of fresh fruit (especially citrus fruit) and vegetables (especially raw vegetables) was statistically significantly higher among controls. Cases reported significantly higher consumption of dairy products (especially hard cheese), total flour products (especially cakes and pastries), and sugar and confectionery. Intake of protein, animal protein, fat, saturated fat, carbohydrates, calcium, vitamin $B_2$ and vitamin D were significantly higher for cases than for controls. Intake of phosphorus was significantly lower for cases than for controls.

**Table 2.** Distribution of gastric cancer cases and controls according to age and selected variables

| | | | Cases (n = 92) | Controls (n = 128) | |
|---|---|---|---|---|---|
| | | | N (%) | N (%) | *p* |
| Age (years) | | Mean ± SD | 66.6 ± 10.4 | 66.5 ± 9.8 | NS |
| | | ≤55 | 14 (15.2) | 18 (14.1) | |
| | | 56–65 | 23 (25.0) | 35 (27.3) | |
| | | 66–75 | 35 (38.1) | 53 (41.4) | |
| | | ≥76 | 20 (21.7) | 22 (17.2) | NS |
| Usual weight (kg) | | Mean ± SD | 68.6 ± 13.6 | 68.6 ± 12.2 | NS |
| Height (cm) | | Mean ± SD | 165.2 ± 8.8 | 165.5 ± 7.5 | NS |
| Marital status | | Married, widowed | 78 (84.8) | 109 (85.1) | |
| | | Divorced, separated | 6 (6.5) | 7 (5.5) | |
| | | Single | 2 (2.2) | 8 (6.3) | |
| | | Unknown | 6 (6.5) | 4 (3.1) | NS[a] |
| Nationality | | French | 90 (97.8) | 128 (100) | |
| | | Italian and Portuguese | 2 (2.2) | 0 (0.0) | NS[b] |
| Occupation[c] | 2/3 | Directors, managers | 14 (15.6) | 24 (18.9) | |
| | 4 | Professional white collar | 9 (10.0) | 22 (17.3) | |
| | 5 | Office employees | 18 (20.0) | 15 (11.8) | NS |
| | 6 | Blue collar | 38 (42.2) | 49 (38.6) | |
| | 1/7/8 | Farmers, servants, army, police | 11 (12.2) | 17 (13.4) | |
| | | Unknown | 2 | 1 | |
| Mother or father had gastric cancer: | | | | | |
| | | Yes | 7 (7.6) | 3 (2.3) | |
| | | No | 85 (92.4) | 125 (97.7) | NS |

NS: not significant.
[a] Given the small numbers, chi-square has been computed for groups 'married/widowed', 'divorced/separated', 'single/unknown'.
[b] Given the small numbers, chi-square has been computed for groups 'French' and 'Italian/Portuguese'.
[c] Job category of French National Institute of Statistics and Economic Studies (INSEE).

**Table 3.** Odds ratios (OR)[a] for gastric cancer associated with consumption of specific foods

| | $OR_1$ | $OR_2$ (95% CI) | $OR_3$ (95% CI) | *p*-value for trend[b] |
|---|---|---|---|---|
| Total dairy products | 1.0 | 1.10 (0.53–2.30) | 1.80 (0.89–3.66) | 0.01 |
| Milk (all types) | 1.0 | 1.53 (0.73–3.19) | 1.57 (0.75–3.29) | 0.02 |
| Hard cheese | 1.0 | 1.09 (0.52–2.26) | 1.48 (0.74–2.96) | 0.36 |
| Soft cheese | 1.0 | 0.64 (0.31–1.30) | 0.92 (0.47–1.80) | 0.90 |
| Yoghurt | 1.0 | 0.86 (0.40–1.88) | 0.75 (0.37–1.54) | 0.87 |
| Total meat products | 1.0 | 0.90 (0.44–1.83) | 0.61 (0.29–1.29) | 0.27 |
| Meat | 1.0 | 0.92 (0.47–1.80) | 0.57 (0.28–1.19) | 0.28 |

**Table 3** (continued)

| | $OR_1$ | $OR_2$ (95% CI) | $OR_3$ (95% CI) | *p*-value for trend[b] |
|---|---|---|---|---|
| Poultry | 1.0 | 0.84 (0.38–1.83) | 0.69 (0.34–1.36) | 0.27 |
| Offal | 1.0 | 3.18 (1.24–8.14) | 2.22 (0.99–4.96) | 0.49 |
| Ham | 1.0 | 1.64 (0.78–3.45) | 1.59 (0.77–3.29) | 0.29 |
| Salami | 1.0 | 1.14 (0.50–2.61) | 1.02 (0.50–2.09) | 0.45 |
| Other 'charcuterie' | 1.0 | 0.92 (0.31–2.75) | 0.90 (0.45–1.82) | 0.35 |
| Fish | 1.0 | 0.73 (0.33–1.60) | 0.97 (0.48–1.96) | 0.90 |
| Eggs | 1.0 | 0.98 (0.48–2.02) | 0.84 (0.42–1.68) | 0.09 |
| Butter and cream | 1.0 | 1.31 (0.64–2.71) | 1.44 (0.71–2.93) | 0.18 |
| Vegetable oil | 1.0 | 0.60 (0.30–1.19) | 0.52 (0.25–1.10) | 0.02 |
| Total flour products | 1.0 | 1.16 (0.56–2.40) | 1.08 (0.53–2.22) | 0.48 |
| Bread and flour products | 1.0 | 0.76 (0.37–1.55) | 0.70 (0.34–1.43) | 0.12 |
| Cakes and pastries | 1.0 | 1.02 (0.46–2.30) | 2.96 (1.42–6.19) | 0.03 |
| Pasta and rice | 1.0 | 1.06 (0.53–2.15) | 0.50 (0.24–1.04) | 0.01 |
| Total fresh fruit | 1.0 | 0.63 (0.31–1.25) | 0.50 (0.25–1.03) | 0.02 |
| Citrus fruit | 1.0 | 0.78 (0.36–1.70) | 0.57 (0.26–1.25) | 0.17 |
| Non-citrus fruit | 1.0 | 0.54 (0.27–1.10) | 0.63 (0.31–1.26) | 0.03 |
| Total vegetables | 1.0 | 0.90 (0.43–1.86) | 0.77 (0.37–1.60) | 0.68 |
| Raw vegetables | 1.0 | 0.55 (0.27–1.10) | 0.41 (0.19–0.88) | 0.02 |
| Cooked vegetables | 1.0 | 0.60 (0.28–1.26) | 1.06 (0.53–2.13) | 0.51 |
| Raw or cooked vegetables[c] | 1.0 | 0.68 (0.33–1.42) | 0.95 (0.46–1.96) | 0.53 |
| Potatoes | 1.0 | 1.46 (0.71–3.02) | 1.47 (0.72–2.98) | 0.58 |
| Dried vegetables | 1.0 | 0.56 (0.16–2.02) | 0.80 (0.39–1.67) | 0.97 |
| Sugar and confectionery | 1.0 | 0.96 (0.46–2.04) | 1.68 (0.84–3.33) | 0.03 |

[a] ORs were adjusted for age, sex, occupation and total energy intake as indicated in the text.
[b] Linear trend test based on regression residuals as a continuous variable.
[c] Vegetables consumed either raw or cooked.

Table 3 provides the ORs and 95% CI for 3 levels of consumption of selected foods after adjustment for age, sex, occupation and total energy intake, and the associate $p$-value of the test for trend. A significant increased risk was found for consumption of dairy products (OR2: 1.10; OR3: 1.80), milk (OR2: 1.53; OR3: 1.57), cakes and pastries (OR2: 1.02; OR3: 2.96), sugar and confectionery (OR2: 0.96; OR3: 1.68). A decreased risk was found for consumption of vegetable oil (OR1: 0.60; OR3: 0.52), pasta and rice (OR2: 1.06; OR3: 0.50) total fresh fruit (OR2: 0.63; OR3: 0.50), non-citrus fruit (OR2: 0.54; OR3 0.63), raw vegetables (OR2: 0.55; OR3: 0.41). A non significant reduction in risk was observed for high consumption of citrus fruit (OR2: 0.78; OR3: 0.57). Neither vegetables consumed either raw or cooked, cooked vegetables, vegetables as a whole, potatoes, dried vegetables, meat, fish, other foods of animal origin nor bread and flour products showed any relation with gastric cancer. When specific vegetables were considered separately, a decreased risk was associated with radishes and tomatoes (raw) and green peas and cabbage (cooked). However, increased intake of green beans and swiss chard was associated with an increased risk (data not shown).

Table 4 shows the ORs in relation to tertile of nutrient intake. A significantly increased risk was found for intake of saturated fat (OR2: 1.49; OR3: 1.67), simple sugars (OR2: 1.18; OR3: 1.78) and calcium (OR2: 1.84; OR3: 2.57). A decreasing risk was observed with intake of fibre (OR2: 0.49; OR3: 0.59), fibre from vegetables and fruit (OR2: 0.83; OR3: 0.53), and iron (OR2: 0.70; OR3: 0.41). The decrease in risk was almost significant for vitamin C intake (OR2: 0.49; OR3: 0.43). Other nutrients, minerals and vitamins were not related to gastric cancer.

## Discussion

The findings presented in this paper provide confirmation that a diet rich in fresh fruit and raw vegetables is related to a lower risk of gastric cancer. In addition we found that high consumption of vegetable oil, pasta and rice was associated with a reduced risk. On the other hand, cakes and pastries, sugar and confectionery, and milk showed a positive association with gastric cancer in this data set. As far as nutrients are concerned, our results indicated that saturated fat, simple sugars and calcium were associated with an increased risk, while fibre, fibre from vegetables and fruit, and iron were associated with a reduction in the risk of gastric cancer. A similar but less pronounced association was seen for vitamin C intake.

As in every case-control study with hospital controls, selection bias may have occurred. However, the participation rate was 100% among eligible subjects, as nobody refused to be interviewed. Cases and controls were comparable for all the demographic and socio-economic characteristics considered in the study (Table 2).

Potential misclassification of subjects for both disease diagnosis and exposure should be carefully considered. While misclassification of cancer diagnosis seems improbable since only histologically confirmed cases were included, it is well known that usual diet is quite difficult to estimate and can only be measured with some degree of approximation. Since cases and controls were interviewed in different centres, the interviewer was aware of the subjects' status. The diet history questionnaire used here, however, is particularly detailed and covers extensively the variety of foods typical of the Mediterranean diet. It had been previously administered in several European case-control studies [23, 24, 31, 35, 36], and the original questionnaire had been evaluated for validity and repeatability in French populations [27]. Only incident cases were included and most of them were interviewed when gastric cancer was already suspected but before gastric surgery (i.e. before the formal diagnosis was known). Potential recall bias should therefore be minimal. Furthermore, the interviews were administered and coded by a single trained nutritionist, used to the dietary history method, in order to ensure a certain homogeneity in data collection between cases and controls.

**Table 4.** Odds ratios (OR)[a] for gastric cancer associated with nutrient intake

| | $OR_1$ | $OR_2$ (95% CI) | $OR_3$ (95% CI) | $p$-value for trend[b] |
|---|---|---|---|---|
| Protein | 1.0 | 0.67 (0.34–1.34) | 0.47 (0.23–0.94) | 0.90 |
| Animal protein | 1.0 | 0.77 (0.37–1.57) | 0.99 (0.49–1.99) | 0.54 |
| Vegetable protein | 1.0 | 0.56 (0.27–1.17) | 0.87 (0.44–1.75) | 0.21 |

**Table 4** (continued)

| | $OR_1$ | $OR_2$ (95% CI) | $OR_3$ (95% CI) | *p*-value for trend[b] |
|---|---|---|---|---|
| Fat | 1.0 | 1.13 (0.54–2.37) | 1.53 (0.75–3.11) | 0.42 |
| Saturated fat | 1.0 | 1.49 (0.71–3.11) | 1.67 (0.82–3.40) | 0.05 |
| Monounsaturated fat | 1.0 | 0.74 (0.35–1.55) | 1.01 (0.51–2.01) | 0.67 |
| Polyunsaturated fat | 1.0 | 0.82 (0.41–1.64) | 0.82 (0.39–1.73) | 0.77 |
| Carbohydrates | 1.0 | 0.86 (0.39–1.90) | 1.20 (0.59–2.42) | 0.77 |
| Simple sugars | 1.0 | 1.18 (0.56–2.48) | 1.78 (0.88–3.60) | 0.02 |
| Complex carbohydrates | 1.0 | 0.65 (0.31–1.36) | 0.82 (0.41–1.67) | 0.22 |
| Fibre | 1.0 | 0.49 (0.24–0.99) | 0.59 (0.29–1.21) | 0.05 |
| Fibre from vegetables and fruit | 1.0 | 0.83 (0.43–1.63) | 0.53 (0.26–1.11) | 0.05 |
| Fibre from other foods | 1.0 | 0.94 (0.47–1.89) | 0.74 (0.36–1.55) | 0.16 |
| Calcium | 1.0 | 1.84 (0.56–2.48) | 2.57 (0.88–3.60) | 0.04 |
| Phosphorus | 1.0 | 1.83 (0.86–3.87) | 1.55 (0.75–3.18) | 0.78 |
| Potassium | 1.0 | 0.83 (0.41–1.68) | 0.72 (0.36–1.43) | 0.45 |
| Iron | 1.0 | 0.70 (0.35–1.40) | 0.41 (0.19–0.89) | 0.02 |
| Magnesium | 1.0 | 0.68 (0.34–1.37) | 0.87 (0.44–1.73) | 0.52 |
| Vitamin C | 1.0 | 0.49 (0.25–0.94) | 0.43 (0.20–0.94) | 0.06 |
| Vitamin C from vegetables and fruit | 1.0 | 0.67 (0.34–1.34) | 0.47 (0.23–0.94) | 0.22 |
| Vitamin C from other foods | 1.0 | 0.48 (0.24–0.99) | 0.63 (0.32–1.25) | 0.07 |
| Vitamin $B_1$ | 1.0 | 0.91 (0.46–1.80) | 0.53 (0.25–1.11) | 0.07 |
| Vitamin $B_2$ | 1.0 | 1.02 (0.49–2.11) | 1.55 (0.78–3.08) | 0.13 |
| Vitamin $B_6$ | 1.0 | 0.79 (0.40–1.57) | 0.63 (0.31–1.29) | 0.34 |
| Vitamin A | 1.0 | 1.11 (0.55–2.24) | 1.47 (0.72–2.99) | 0.11 |
| Vitamin D | 1.0 | 1.19 (0.58–2.44) | 1.20 (0.60–2.37) | 0.61 |
| Vitamin E | 1.0 | 0.53 (0.26–1.08) | 0.44 (0.21–0.96) | 0.71 |

[a] ORs were adjusted for age, sex, occupation and total energy intake as indicated in the text.
[b] Linear trend test based on regression residuals included in the model as a continuous variable.

Overall, our results are in agreement with previous findings. Several studies have found a significantly lower risk associated with intake of vegetables as a whole [1, 8, 10, 11, 19, 22, 32]. A protective effect has been reported for raw vegetables or salads [2, 7, 15, 16, 34]. Our findings are in line with those of Buiatti et al. [5] whose investigation was able to distinguish between cooked and raw vegetables and showed a decreased risk only for the latter, whereas Tuyns et al. [36] found a protective effect with regard to consumption of both cooked and raw vegetables. A strong inverse significant association between gastric cancer risk and fresh fruit was detected in our study, which is in agreement with the results reported by most of the studies mentioned above as well as by Jedrychowski et al. [20] and Kono et al. [21]. In our study, the protection from non-citrus fruit was statistically significant, while protection from citrus fruit, for which the OR estimates were very similar, was not statistically significant. However, citrus fruit represented only 10% of total fruit, and the lack of statistical significance may simply be due to limited statistical power. The protective effect associated with vegetables and fruit may be related to antioxidant agents, vitamin C in particular, but the mechanism is still unclear. It has been postulated that vitamin C, which is ingested together with nitrate and nitrite through vegetables, may inhibit nitrosation and endogenous formation of nitrosamines, potential carcinogens to the stomach [13]. We reported a protective effect of vitamin C (although not statistically significant) in line with previous investigations [1, 3, 6, 9, 14]. On the other hand, the protective effect of vegetables and fruit could be at least partly explained by their fibre content. In our study, a significant negative association with gastric cancer was found for fibre intake (especially fibre from vegetables and fruit) which has also been reported by Risch et al. [32] and González et al. [14].

Regarding fat we found contrasting associations for vegetable oil (mainly olive and seed oils) among foods, and saturated fat among nutrients. An increased risk for saturated fat was previously reported in a study in Italy [6] while Graham et al. [16] reported an increased risk with total fat.

We also found a significant positive association with dairy products, total milk and, as a consequence, calcium. A possible explanation is that milk and dairy products have traditionally been recommended against gastric pain, and higher consumption among cases may reflect recent changes in diet.

In addition, we observed a significant positive link between gastric cancer and cakes and pastries, and a negative one for pasta and rice. Other authors have found significantly increased risks for cakes and pastries [9, 36], pasta or rice [22, 34, 36] or potatoes [15, 19]. Finally, we identified a significantly higher risk associated with the intake of sugar and confectionery, which is in line with the results of other studies [22, 36]. It is unclear whether these results point to a real biological effect or whether they reflect mainly an indication of food habits, but they seem to suggest that the association is positive for consumption of foods rich in simple sugars and negative for starchy foods. This hypothesis seems to be confirmed by our analysis at the nutrient level, which showed an increased risk related to simple sugars and a decreased risk for fibres, in agreement with the results of a Canadian study [32].

Although there is growing evidence that *Helicobacter pylori* infection of the gastric mucosa increases the risk of gastric cancer, the present study was not designed to investigate the aetiological role of *H. pylori*. However, it would undoubtedly be of interest to plan new studies to investigate the effect of diet in relation to the presence or absence of *H. pylori* infection.

In conclusion, we reported results from the first case-control study on diet and gastric cancer in a French population and, despite the relatively limited size of the study population, we reached conclusions which are very similar to those of previous studies conducted in developed countries, which point to the protective role of fruits and vegetables against gastric cancer. While the biochemical mechanisms underlying these associations are not fully understood, the consistency of this finding justifies recent public health recommendations aimed at increasing fruit and vegetable consumption, particularly among those populations where it is traditionally low.

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**Appendix 1**: Means, medians, 25th and 75th percentiles of daily food consumption of gastric cancer cases and controls (g/day)

| | Cases | | | | Controls | | | |
|---|---|---|---|---|---|---|---|---|
| | Mean ± SD | Percentile distribution | | | Mean ± SD | Percentile distribution | | |
| | | 25% | Median | 75% | | 25% | Median | 75% |
| Total dairy products* | 246 ± 170 | 140 | 229 | 290 | 187 ± 105 | 94 | 190 | 268 |
| Milk (all types) | 125 ± 138 | 29 | 100 | 179 | 89 ± 90 | 0 | 68 | 150 |
| Hard cheese* | 33 ± 23 | 17 | 33 | 46 | 26 ± 21 | 11 | 23 | 39 |
| Soft cheese | 33 ± 33 | 11 | 34 | 46 | 30 ± 22 | 17 | 29 | 40 |
| Yoghurt | 42 ± 69 | 0 | 0 | 54 | 39 ± 53 | 0 | 18 | 63 |
| Total meat products | 149 ± 64 | 114 | 137 | 177 | 148 ± 51 | 109 | 144 | 189 |
| Meat | 97 ± 51 | 64 | 86 | 125 | 98 ± 41 | 69 | 86 | 120 |
| Poultry | 22 ± 17 | 17 | 21 | 30 | 24 ± 16 | 17 | 21 | 39 |
| Offal | 5 ± 8 | 0 | 0 | 11 | 4 ± 8 | 0 | 0 | 0 |
| Ham | 10 ± 11 | 0 | 7 | 14 | 9 ± 10 | 0 | 7 | 14 |
| Salami | 7 ± 11 | 0 | 0 | 14 | 6 ± 8 | 0 | 0 | 11 |
| Other 'charcuterie' | 7 ± 12 | 0 | 0 | 13 | 7 ± 13 | 0 | 0 | 14 |
| Fish | 29 ± 20 | 17 | 21 | 43 | 29 ± 23 | 21 | 21 | 43 |
| Eggs | 18 ± 12 | 14 | 14 | 29 | 20 ± 16 | 14 | 14 | 29 |
| Butter and cream | 15 ± 10 | 9 | 13 | 19 | 13 ± 7 | 8 | 11 | 18 |
| Vegetable oil | 26 ± 9 | 20 | 26 | 31 | 27 ± 8 | 21 | 27 | 33 |
| Total flour products* | 210 ± 95 | 137 | 189 | 257 | 191 ± 106 | 118 | 169 | 241 |
| Bread and flour | 134 ± 79 | 80 | 105 | 200 | 133 ± 88 | 80 | 100 | 200 |
| Cakes and pastries* | 48 ± 48 | 14 | 38 | 69 | 29 ± 42 | 0 | 21 | 43 |
| Pasta and rice | 28 ± 15 | 17 | 24 | 40 | 30 ± 18 | 17 | 23 | 40 |
| Total fresh fruit* | 220 ± 142 | 107 | 254 | 300 | 248 ± 105 | 171 | 257 | 300 |
| Citrus* | 21 ± 34 | 0 | 0 | 43 | 28 ± 33 | 0 | 21 | 43 |
| Non-citrus* | 199 ± 128 | 86 | 216 | 300 | 220 ± 94 | 150 | 236 | 300 |
| Total vegetables* | 267 ± 92 | 199 | 261 | 325 | 273 ± 73 | 229 | 276 | 326 |
| Raw* | 75 ± 35 | 49 | 77 | 100 | 86 ± 35 | 64 | 86 | 114 |
| Cooked | 131 ± 54 | 90 | 126 | 167 | 126 ± 40 | 100 | 124 | 151 |
| Raw or cooked[a] | 61 ± 28 | 43 | 57 | 79 | 61 ± 23 | 43 | 64 | 79 |
| Potatoes | 94 ± 40 | 64 | 100 | 111 | 86 ± 43 | 57 | 80 | 109 |
| Dried vegetables | 2 ± 4 | 0 | 0 | 4 | 2 ± 3 | 0 | 0 | 4 |
| Sugar and confectionery | 33 ± 26 | 12 | 30 | 49 | 23 ± 19 | 9 | 20 | 35 |

* $p \leq 0.05$ for 2-sided t-test of differences between cases and controls (normality of the distribution was checked and, when necessary Wilcoxon sum-rank test was performed).
[a] Vegetables consumed either raw or cooked.

**Appendix 2**: Means, medians, 25th and 75th percentiles of daily food consumption of gastric cancer cases and controls

| | Cases | | | | Controls | | | |
|---|---|---|---|---|---|---|---|---|
| | Mean ± SD | Percentile distribution | | | Mean ± SD | Percentile distribution | | |
| | | 25% | Median | 75% | | 25% | Median | 75% |
| Protein (g)* | 81 ± 19 | 67 | 80 | 90 | 75 ± 18 | 63 | 74 | 85 |
| Animal (g)* | 58 ± 14 | 49 | 57 | 66 | 53 ± 13 | 45 | 52 | 62 |
| Vegetable (g)* | 23 ± 7 | 17 | 22 | 28 | 22 ± 8 | 17 | 20 | 26 |
| Fat (g)* | 95 ± 24 | 78 | 91 | 109 | 87 ± 22 | 71 | 84 | 98 |
| Saturated (g)* | 39 ± 11 | 33 | 38 | 45 | 34 ± 9 | 29 | 34 | 34 |
| Mono-unsaturated (g) | 40 ± 11 | 32 | 38 | 47 | 38 ± 11 | 30 | 37 | 45 |
| Poly-unsaturated (g) | 9 ± 6 | 6 | 7 | 10 | 9 ± 5 | 6 | 7 | 9 |

**Appendix 2** (continued)

| | Cases | | | | Controls | | | |
|---|---|---|---|---|---|---|---|---|
| | Mean ± SD | Percentile distribution | | | Mean ± SD | Percentile distribution | | |
| | | 25% | Median | 75% | | 25% | Median | 75% |
| Carbohydrates (g)* | 224 ± 67 | 170 | 217 | 276 | 205 ± 67 | 159 | 196 | 242 |
| Simple sugars (g)* | 31 ± 21 | 14 | 30 | 45 | 22 ± 16 | 10 | 21 | 31 |
| Complex carbohydrates (g) | 193 ± 57 | 152 | 185 | 219 | 184 ± 64 | 144 | 168 | 212 |
| Fibre (g) | 24 ± 7 | 19 | 24 | 29 | 24 ± 7 | 19 | 22 | 27 |
| from vegetables and fruit (g) | 6 ± 2 | 5 | 6 | 7 | 7 ± 2 | 6 | 6 | 8 |
| from other foods (g) | 18 ± 6 | 13 | 17 | 22 | 17 ± 6 | 13 | 15 | 20 |
| Calcium (mg)* | 901 ± 274 | 742 | 875 | 1031 | 772 ± 243 | 601 | 770 | 906 |
| Phosphorus (mg)* | 1231 ± 258 | 1050 | 1217 | 1384 | 1144 ± 263 | 966 | 1121 | 1264 |
| Potassium (mg) | 2769 ± 612 | 2396 | 2724 | 3075 | 2720 ± 510 | 2379 | 2733 | 3023 |
| Iron (mg) | 12 ± 3 | 10 | 12 | 14 | 12 ± 3 | 10 | 12 | 14 |
| Magnesium (mg) | 220 ± 49 | 184 | 208 | 253 | 210 ± 49 | 179 | 206 | 234 |
| Vitamin C (mg) | 93 ± 38 | 63 | 94 | 116 | 99 ± 30 | 84 | 100 | 119 |
| from vegetables & fruit (mg) | 43 ± 20 | 27 | 38 | 54 | 46 ± 19 | 32 | 44 | 59 |
| from other foods (mg) | 51 ± 24 | 30 | 54 | 68 | 53 ± 18 | 42 | 56 | 67 |
| Vitamin $B_1$ (mg) | 1.2 ± 0.3 | 1.0 | 1.1 | 1.3 | 1.1 ± 0.2 | 0.9 | 1.1 | 1.3 |
| Vitamin $B_2$ (mg)* | 1.5 ± 0.4 | 1.2 | 1.5 | 1.8 | 1.4 ± 0.3 | 1.2 | 1.4 | 1.6 |
| Vitamin $B_6$ | 1.1 ± 0.3 | 1.0 | 1.1 | 1.3 | 1.1 ± 0.2 | 0.9 | 1.1 | 1.2 |
| Vitamin A (μg) | 1167 ± 405 | 915 | 1127 | 1379 | 1083 ± 316 | 871 | 1050 | 1237 |
| Vitamin D (mg)* | 1.4 ± 1.0 | 1.0 | 1.2 | 1.5 | 1.2 ± 0.8 | 0.8 | 1.0 | 1.4 |
| Vitamin E (IU) | 5.7 ± 4.0 | 4.0 | 4.5 | 5.7 | 6.0 ± 3.7 | 4.1 | 4.8 | 5.8 |

* $p \leq 0.05$ for 2-sided t-test for differences between cases and controls. (Normality of distribution was checked and, when necessary, the Wilcoxon rank test was performed.)

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