# Foods, nutrients and prostate cancer: a case-control study in Uruguay 

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#### Abstract

Summary A case-control study of diet and prostate cancer was conducted in Montevideo, Uruguay involving 175 cases and 233 controls. When the highest quartile of intake was compared with the lowest, positive findings were obtained for red meat intake (OR $2.0,95 \% \mathrm{Cl}$ $1.1-3.8$ ), desserts (OR $1.8,95 \% \mathrm{Cl} 0.9-3.3$ ), total energy (OR 1.9, $95 \% \mathrm{Cl} 1.0-3.4$ ) and total fat intake (OR $1.8,95 \% \mathrm{Cl} 0.9-3.4$ ). On the other hand, vegetables and fruits (OR $0.5,95 \% \mathrm{Cl} 0.3-0.9$ ), vitamin C (OR $0.4,95 \% 0.2-0.8$ ) and vitamin E (OR $0.6,95 \% \mathrm{Cl} 0.3-1.1$ ) were associated with reduced risks of prostate cancer. Possible mechanisms are discussed.


Prostate cancer is the second commonest malignancy among Uruguayan men, with an age-adjusted incidence rate of 32.6 per 100000 (Parkin et al, 1997). According to a previous study (De Stefani et al, 1994), the mortality rate for prostate cancer has increased by $77 \%$ in the period between 1953 and 1991. Also, migrants from Spain and Italy have increased their risk of prostate cancer after arrival in Uruguay, suggesting the importance of environmental factors (De Stefani et al, 1990).

In the only previous analytic study conducted in Uruguay (De Stefani et al, 1995), diet was assessed by food groups; both red meat and dairy foods were associated with an increased risk of prostate cancer. Also, fruit intake was associated with a risk increase of $70 \%$ (De Stefani et al, 1995). Since these estimates were not energy-adjusted some uncertainty remains about its validity. Therefore, we have decided to carry out a new case-control study on dietary factors and prostate cancer, based on a more detailed food-frequency questionnaire.

## SUBJECTS AND METHODS

Selection of cases. In the period 1994-1997, all incident- and histologically verified prostatic adenocarcinomas occurring in men in the age range 40-89 years, admitted to the four major hospitals in Montevideo, were considered eligible for this study. Of 190 cases identified, 15 patients refused interview, leaving 175 cases of prostate carcinomas (response rate $92.1 \%$ ). The stage distribution was as follows: localized $25 \%$, regional $72 \%$ and disseminated $3 \%$. There were no cases with latent carcinomas, and, therefore, this series is representative of a series of mainly advanced prostate tumours. The stage distribution of our series was compared with the figures drawn from the National Cancer Registry. According to this source, $70 \%$ of prostate cancers were

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locally advanced (regional) or disseminated at the time of the diagnosis. These figures reflect the fact that there are no mass screening programmes for prostate cancer in Uruguay.

## Controls selection

In the same period, all patients admitted to the same hospitals as the cases with conditions unrelated to diet were considered eligible as controls if below age 90. A total of 240 patients were hospitalmatched to the cases; from this initial number seven patients refused interview, leaving a total of 233 controls (response rate $97.1 \%$ ). The distribution of controls by disease category was as follows: eye disorders ( 87 patients, $37.3 \%$ ), abdominal hernia ( 56 patients, $24.0 \%$ ), acute appendicitis ( 25 patients, $10.7 \%$ ), fractures and trauma ( 23 patients, $9.9 \%$ ), hydatid cyst ( 15 patients, $6.4 \%$ ), skin diseases ( 14 patients, $6.1 \%$ ) and varicose veins (13 patients, 5.6\%).

## Questionnaire

Both cases and controls were specifically called up to the hospital for a face-to-face interview after diagnosis or treatment. The mean time since admission for cases was 62 days, and for controls was 50 days. Both cases and controls completed a detailed questionnaire which covered sociodemographic variables, anthropometric variables, occupational exposures, family history of cancer, tobacco history, alcohol consumption and diet. The foodfrequency questionnaire included 64 food items, representative of usual diet of the Uruguayan population. This food-frequency questionnaire was not previously validated but was studied regarding its reproducibility. The Pearson correlation coefficients ranged from 0.30 for calcium to 0.79 for total carbohydrate intake. For each food, a commonly used unit or portion size was specified, and participants were asked how often, on average, over the past year or the year prior to onset of symptoms, they had consumed that amount of each food. The responses were open-ended allowing each food to be treated as a continuous variable (Willett, 1990). Responses were converted to times per year, multiplying by the appropriate time units. We consider that this type of recording
food consumption reflects the true consumption more accurately, instead of forcing responses into pre-existing categories. The following food groups were analysed in this study:
1.Red meat, i.e. beef and lamb
2. White meat, i.e. poultry and fish
3.Processed meat, i.e. sausage, bacon, salami, saucisson, mortadella, ham and salted meat
4.Offal, i.e. tripe, kidney and liver
5.Total meat, i.e. the sum of the previous items
6.Dairy foods, i.e. cheese, butter, whole milk and ice cream
7. Desserts, i.e. rice pudding, custard, cake, marmalade and jam
8. Eggs, i.e. poached, boiled and fried eggs
9. Grains, i.e. rice, polenta, pasta, bread and croissants
10.Tubers, i.e. potato and sweet potato
11. Legumes, i.e. kidney beans and lentils
12. Vegetables and fruits, i.e. carrot, tomato, lettuce, onion, garlic, swiss chard, spinach, cabbage, cauliflower, winter squash, zucchini, red pepper, orange, orange juice, apple, peach, pear, grapes, figs, banana and fruit cocktail.

Nutrient indices were derived from local food tables (Mazzei and Puchulu, 1996). Since values for beta-carotene and other carotenoids are not available in Uruguay, the estimates of Mangels et al were used (1993).

Table 1 Distribution of cases and controls by selected variables

| Variable: Category | Cases | Controls |
| :--- | ---: | ---: |
| Hospital |  |  |
| Cancer Institute | $50(28.6)$ | $65(27.9)$ |
| Pasteur | $29(16.6)$ | $105(46.3)$ |
| University | $77(44.0)$ | $25(10.7)$ |
| Maciel | $19(10.8)$ |  |
| Age (years) |  | $3(1.3)$ |
| 40-49 | $2(1.1)$ | $22(9.4)$ |
| 50-59 | $7(4.0)$ | $83(35.6)$ |
| 60-69 | $54(30.9)$ | $103(44.2)$ |
| 70-79 | $87(49.5)$ | $22(9.4)$ |
| 80-89 | $25(14.3)$ | $122(52.4)$ |
| Residence |  | $111(47.6)$ |
| Montevideo | $85(48.6)$ | $178(76.4)$ |
| Other counties | $90(51.4)$ | $55(23.6)$ |
| Urban/rural status |  |  |
| Urban | $118(67.4)$ | $70(30.0)$ |
| Rural | $57(32.6)$ | $73(31.3)$ |
| Education (years) | $58(33.1)$ | $90(38.6)$ |
| 0-2 | $67(38.3)$ |  |
| 3-5 | $50(28.6)$ | $233(99.6)$ |
| 6+ |  | $73(31.3)$ |
| Monthly income | $7(4.0)$ | $69(29.6)$ |
| (US dollars) | $175(100)$ | $91(39.1)$ |
| <157 |  |  |
| 158+ | $48(27.4)$ |  |
| Unknown | $49(28.0)$ |  |
| Family history |  |  |
| of prostate cancer |  |  |
| No |  |  |
| Yes |  |  |
| Number of patients |  |  |
|  |  |  |

## Statistical analysis

Crude and adjusted odds ratios (OR) and the corresponding 95\% confidence intervals (CI) were calculated by multiple logistic regression (Breslow and Day, 1980). In all models, potential confounders were included. These were: age (continuous), residence (Montevideo vs other counties), urban/rural status (urban vs rural), family history of prostate cancer (no vs yes), body mass index (continuous) and total energy intake (continuous). Since tobacco consumption and alcohol intake were not associated with prostate cancer risk in this dataset, they were not included in the logistic models. Odds ratios for food groups were calculated with and without a term for total energy intake. All food groups and nutrients were tested for interaction with the following variables: total energy intake, body mass index, and age dichotomized in younger than 70 years and 70 years or more. Energy intake and body mass index were dichotomized according to the median value of the combined sample of cases and controls. Nutrients were energy-adjusted by the residuals method (Willett and Stampfer, 1986).
The test for trend after multivariate adjustment for covariates was determined by the $\chi^{2}$ statistic across the vector of indicator variables for the exposure of interest. All calculations were performed in the GLIM program (Baker and Nelder, 1985).

## RESULTS

Sociodemographic variables and family history of prostate cancer in a first-degree relative are shown in Table 1. Cases were older, lived more frequently outside Montevideo, were more frequently rural residents and were less educated than controls. Although these differences were not statistically significant, the above mentioned variables were included in all following logistic models, in order to control confounding. On the other hand, family history of prostate cancer was much more frequent among cases than controls (crude OR 9.8).
Odds ratios of prostate cancer for food groups are shown in Table 2. In the models without a term for total energy intake, intake in the uppermost quartile compared with the bottom quartile for red meat, total meat, desserts, grains and tubers displayed increased risks (OR for red meat 2.0, 95\% CI 1.1-3.8). However, reduced risks were observed for the following groups: all vegetables, all fruits and all vegetables and fruits (OR for all vegetables and fruits in the uppermost quartile of intake compared with the lower quartile was of $0.6,95 \%$ CI $0.3-1.1)$. When total energy intake was introduced in the model, red meat intake was no longer significant (OR 1.7, $95 \%$ CI $0.8-3.4, P$-value for trend 0.17 ). Desserts intake was associated with a moderate increased risk (OR 1.8, 95\% CI 0.9-3.3), whereas vegetables, and vegetables and fruits together, were associated with reduced risks (OR for all vegetables and fruits $0.5,95 \%$ CI $0.3-0.9, P$-value for linear trend 0.04).

Odds ratios of prostate cancer for nutrients are shown in Table 3. Whereas protein was not associated with risk, carbohydrate intake was associated with a reduced risk of 0.5 ( $95 \%$ CI $0.3-1.0$ ). Total fat displayed an increased risk of 1.8 for the uppermost quartile of intake ( $95 \%$ CI $0.8-3.4$ ). Saturated fat was not associated with risk, and cholesterol intake displayed an increased risk of 2.4 ( $95 \%$ CI 1.3-4.4) in the third quartile, which decreased to zero in the highest quartile of intake. Among carotenoids, only lutein

Table 2 Odds ratios of prostate cancer for food groups

| Food group | Quartile |  |  |  | P for trend |
| :---: | :---: | :---: | :---: | :---: | :---: |
|  | 1 | II | III | IV |  |
| Red meat |  |  |  |  |  |
| $1 \mathrm{IR}^{\text {c }}$ | $\leq 182$ | 183-365 | 366-378 | 379+ |  |
| Cases/Controls | 32/71 | 61/78 | 36/40 | 46/44 |  |
| OR1a | 1.0 | 1.6 | 1.8 | 2.0 |  |
| 95\% CI | - | 0.9-2.9 | 0.9-3.5 | 1.1-3.8 | 0.03 |
| OR2 ${ }^{\text {b }}$ | 1.0 | 1.5 | 1.7 | 1.7 |  |
| 95\% CI | - | 0.9-2.7 | 0.9-3.3 | 0.8-3.4 | 0.17 |
| White meat |  |  |  |  |  |
| IQR | $\leq 24$ | 25-64 | 65-104 | 105+ |  |
| Cases/Controls | 44/58 | 41/65 | 51/59 | 39/51 |  |
| OR1 | 1.0 | 0.9 | 1.2 | 1.1 |  |
| 95\% CI | - | 0.5-1.5 | 0.7-2.1 | 0.6-2.0 | 0.51 |
| OR2 | 1.0 | 0.8 | 1.1 | 0.9 |  |
| 95\% CI | - | 0.5-1.5 | 0.6-1.9 | 0.5-1.8 | 0.86 |
| Poultry |  |  |  |  |  |
| IQR | $\leq 12$ | 13-40 | 41-52 | 53+ |  |
| Cases/Controls | 45/75 | 26/32 | 64/83 | 40/43 |  |
| OR1 | 1.0 | 1.3 | 1.3 | 1.5 |  |
| 95\% CI | - | 0.7-2.6 | 0.8-2.2 | 0.8-2.6 | 0.18 |
| OR2 | 1.0 | 1.3 | 1.2 | 1.3 |  |
| 95\% CI | - | 0.7-2.5 | 0.7-2.0 | 0.7-2.4 | 0.38 |
| Fish |  |  |  |  |  |
| IQR | 0 | 1-18 | 19-52 | 53+ |  |
| Cases/Controls | 41/61 | 50/59 | 60/73 | 24/70 |  |
| OR1 | 1.0 | 1.3 | 1.4 | 0.9 |  |
| 95\% CI | - | 0.7-2.2 | 0.8-2.4 | 0.5-1.9 | 0.78 |
| OR2 | 1.0 | 1.3 | 1.3 | 0.9 |  |
| 95\% CI | - | 0.7-2.3 | 0.7-2.2 | 0.5-1.8 | 0.99 |
| Processed meat |  |  |  |  |  |
| IQR | $\leq 182$ | 183-365 | 366-378 | 379+ |  |
| Cases/Controls | 41/60 | 48/56 | 46/54 | 40/63 |  |
| OR1 | 1.0 | 1.2 | 1.1 | 0.9 |  |
| 95\% CI | - | 0.7-2.1 | 0.6-2.0 | 0.5-1.7 | 0.75 |
| OR2 | 1.0 | 1.2 | 1.0 | 0.8 |  |
| 95\% CI |  | 0.7-2.2 | 0.6-1.8 | 0.4-1.4 | 0.31 |
| Offal |  |  |  |  |  |
| IQR | 0 | 1-24 | 25-52 | $53+$ |  |
| Cases/Controls | 74/119 | 36/49 | 33/25 | 32/40 |  |
| OR1 | 1.0 | 1.2 | 2.1 | 1.2 |  |
| 95\% CI | - | 0.7-2.0 | 1.1-3.9 | 0.7-2.1 | 0.18 |
| OR2 | 1.0 | 1.3 | 2.1 | 1.1 |  |
| 95\% CI | - | 0.8-2.3 | 1.1-3.8 | 0.6-1.9 | 0.30 |
| Total meat |  |  |  |  |  |
| IQR | $\leq 422$ | 423-570 | 571-767 | 768+ |  |
| Cases/Controls | 30/72 | 53/50 | 46/58 | 46/53 |  |
| OR1 | 1.0 | 2.6 | 1.7 | 1.9 |  |
| 95\% CI | - | 1.4-4.7 | 0.9-3.1 | 1.1-3.6 | 0.11 |
| OR2 | 1.0 | 2.3 | 1.5 | 1.6 |  |
| 95\% CI | - | 1.3-4.4 | 0.8-2.9 | 0.8-3.4 | 0.59 |
| Dairy foods |  |  |  |  |  |
| IQR | $\leq 312$ | 313-469 | 470-729 | 730+ |  |
| Cases/Controls | 43/61 | 46/56 | 40/56 | 46/60 |  |
| OR1 | 1.0 | 1.1 | 1.1 | 1.1 |  |
| 95\% CI | - | 0.6-1.8 | 0.6-2.0 | 0.6-1.9 | 0.65 |
| OR2 | 1.0 | 0.9 | 0.9 | 0.8 |  |
| 95\% CI | - | 0.5-1.7 | 0.5-1.7 | 0.4-1.6 | 0.60 |
| Eggs |  |  |  |  |  |
| IQR | $\leq 48$ | 49-103 | 104-142 | $143+$ |  |
| Cases/Controls | 35/63 | 44/54 | 47/61 | 49/55 |  |
| OR1 | 1.0 | 1.5 | 1.5 | 1.6 |  |
| 95\% CI | - | 0.8-2.7 | 0.8-2.6 | 0.9-2.9 | 0.12 |
| OR2 | 1.0 | 1.4 | 1.3 | 1.4 |  |
| 95\% CI | - | 0.8-2.5 | 0.7-2.4 | 0.7-2.6 | 0.41 |

Table 2 (Cont) Odds ratios of prostate cancer for food groups

| Food group | Quartile |  |  |  | $P$ for trend |
| :---: | :---: | :---: | :---: | :---: | :---: |
|  | I | II | III | IV |  |
| Desserts |  |  |  |  |  |
| IQR | $\leq 24$ | 25-90 | 91-182 | 183+ |  |
| Cases/Controls | 41/65 | 40/62 | 41/62 | 53/44 |  |
| OR1 | 1.0 | 1.0 | 1.1 | 2.0 |  |
| 95\% CI | - | 0.6-1.8 | 0.6-1.9 | 1.1-3.6 | 0.02 |
| OR2 | 1.0 | 1.0 | 1.0 | 1.8 |  |
| 95\% Cl | - | 0.6-1.8 | 0.6-1.8 | 0.9-3.3 | 0.07 |
| Grains |  |  |  |  |  |
| IQR | $\leq 812$ | 813-924 | 925-1228 | 1229+ |  |
| Cases/Controls | 38/65 | 51/58 | 33/61 | 53/49 |  |
| OR1 | 1.0 | 1.5 | 1.0 | 2.1 |  |
| 95\% CI | - | 0.8-2.6 | 0.5-1.8 | 1.2-3.7 | 0.05 |
| OR2 | 1.0 | 1.5 | 0.9 | 1.7 |  |
| 95\% CI | - | 0.9-2.7 | 0.5-1.7 | 0.9-3.2 | 0.24 |
| Vegetables |  |  |  |  |  |
| IQR | $\leq 336$ | 337-466 | 467-696 | 697+ |  |
| Cases/Controls | 48/55 | 52/52 | 36/63 | 39/63 |  |
| OR1 | 1.0 | 1.3 | 0.7 | 0.7 |  |
| 95\% CI | - | 0.7-2.3 | 0.4-1.2 | 0.4-1.3 | 0.11 |
| OR2 | 1.0 | 1.2 | 0.6 | 0.6 |  |
| 95\% CI | - | 0.7-2.2 | 0.3-1.1 | 0.3-1.1 | 0.02 |
| Fruits |  |  |  |  |  |
| IQR | $\leq 270$ | 271-429 | 430-735 | 736+ |  |
| Cases/Controls | 46/57 | 54/47 | 35/67 | 40/62 |  |
| OR1 | 1.0 | 1.5 | 0.7 | 0.8 |  |
| 95\% CI | - | 0.8-2.6 | 0.4-1.2 | 0.5-1.6 | 0.21 |
| OR2 | 1.0 | 1.5 | 0.6 | 0.8 |  |
| 95\% CI | - | 0.8-2.7 | 0.3-1.1 | 0.4-1.4 | 0.08 |
| Vegetables and fruits |  |  |  |  |  |
| IQR | $\leq 685$ | 686-1000 | 1001-1389 | 1390+ |  |
| Cases/Controls | 55/47 | 40/63 | 38/63 | 42/60 |  |
| OR1 | 1.0 | 0.5 | 0.5 | 0.6 |  |
| 95\% CI | - | 0.3-0.9 | 0.3-0.9 | 0.3-1.1 | 0.13 |
| OR2 | 1.0 | 0.5 | 0.5 | 0.5 |  |
| 95\% CI | - | 0.3-0.8 | 0.3-0.8 | 0.3-0.9 | 0.04 |
| Legumes |  |  |  |  |  |
| IQR | $\leq 6$ | 7-24 | 25-52 | 53+ |  |
| Cases/Controls | 45/68 | 70/80 | 18/31 | 42/54 |  |
| OR1 | 1.0 | 1.4 | 0.9 | 1.2 |  |
| 95\% CI | - | 0.8-2.2 | 0.4-1.9 | 0.7-2.1 | 0.88 |
| OR2 | 1.0 | 1.4 | 0.8 | 1.1 |  |
| 95\% CI | - | 0.8-2.3 | 0.4-1.7 | 0.6-1.9 | 0.85 |
| Tubers |  |  |  |  |  |
| IQR | $\leq 168$ | 169-364 | 365-443 | 444+ |  |
| Cases/Controls | 36/70 | 48/58 | 54/56 | 42/49 |  |
| OR1 | 1.0 | 1.9 | 2.1 | 1.9 |  |
| 95\% CI | - | 1.0-3.4 | 1.1-3.7 | 1.0-3.5 | 0.04 |
| OR2 | 1.0 | 1.7 | 1.9 | 1.6 |  |
| 95\% CI | - | 0.9-3.2 | 1.0-3.4 | 0.8-3.1 | 0.17 |

${ }^{\text {a ORR }} 1$ - Adjusted for age, residence, urban/rural status, education, family history of prostate cancer in a first-degree relative and body mass index. ${ }^{\text {b }}$ OR2 -
Further adjusted for total energy intake. ${ }^{\text {IIQR - Interquartile Range in Servings. }}$
displayed a moderate decreased risk of 0.70 ( $95 \%$ CI $0.4-1.3$ ), but without a significant trend. Both vitamins C and E were associated with a protective effect (OR for vitamin C $0.4,95 \%$ CI $0.2-0.8$ ), and vitamin D displayed a moderate reduced risk of 0.7 ( $95 \%$ CI 0.4-1.2).

Odds ratios of prostate cancer for total fat and carbohydrate intakes by levels of body mass index are shown in Table 4. Whereas total fat intake was not associated with risk at low levels of body mass, a strong effect of fat was observed among more
obese patients. On the other hand, carbohydrate intake at high body mass was associated with a reduction in risk of $70 \%$ ( $95 \%$ CI 0.1-0.7).

## DISCUSSION

The present study showed increased risks of prostate cancer associated with total energy, total fat, red meat and dessert intakes. The risk associated with fat intake was more evident among obese

Table 3 Odds ratios of prostate cancer for nutrients ${ }^{\text {a }}$

| Nutrient | Quartile |  |  |  | P for trend |
| :---: | :---: | :---: | :---: | :---: | :---: |
|  | 1 | II | III | IV |  |
| Total energy |  |  |  |  |  |
| IQR ${ }^{\text {b }}$ | $\leq 1527$ | 1528-1914 | 1915-2326 | 2327+ |  |
| Cases/Controls | 38/66 | 40/59 | 46/57 | 51/51 |  |
| OR | 1.0 | 1.2 | 1.5 | 1.9 |  |
| 95\% CI | - | 0.7-2.2 | 0.9-2.7 | 1.0-3.4 | 0.03 |
| Protein |  |  |  |  |  |
| IQR ${ }^{\text {c }}$ | $\leq 62.9$ | 63.0-76.9 | 77.0-97.4 | 97.5+ |  |
| Cases/Controls | 38/64 | 43/59 | 53/49 | 41/61 |  |
| OR | 1.0 | 1.1 | 1.7 | 1.0 |  |
| 95\% CI | - | 0.6-1.9 | 0.9-3.1 | 0.6-1.8 | 0.60 |
| Carbohydrate |  |  |  |  |  |
| IQR ${ }^{\text {c }}$ | $\leq 188.5$ | 188.5-244.3 | 244.4-301.7 | 301.8+ |  |
| Cases/Controls | 48/54 | 48/54 | 48/54 | 31/71 |  |
| OR | 1.0 | 1.0 | 1.1 | 0.5 |  |
| 95\% CI | - | 0.6-1.8 | 0.6-2.0 | 0.3-1.0 | 0.13 |
| Total fat |  |  |  |  |  |
| IQR ${ }^{\text {c }}$ | $\leq 53.7$ | 53.8-66.7 | 66.8-82.2 | 82.3+ |  |
| Cases/Controls | 34/68 | 46/56 | 49/53 | 46/56 |  |
| OR | 1.0 | 1.6 | 2.0 | 1.8 |  |
| 95\% CI | - | 0.9-2.9 | 1.1-3.7 | 0.9-3.4 | 0.04 |
| Saturated fat |  |  |  |  |  |
| $1 \mathrm{IR}^{\text {c }}$ | $\leq 20.1$ | 20.2-25.8 | 25.9-32.7 | 32.8+ |  |
| Cases/Controls | 39/63 | 49/53 | 46/56 | 41/61 |  |
| OR | 1.0 | 1.4 | 1.2 | 0.9 |  |
| 95\% CI | - | 0.8-2.4 | 0.7-2.1 | 0.5-1.7 | 0.78 |
| Cholesterol |  |  |  |  |  |
| $1 \mathrm{QR}^{\text {d }}$ | $\leq 288.9$ | 289.0-398.7 | 398.8-522.6 | 522.7+ |  |
| Cases/Controls | 32/70 | 40/62 | 55/47 | 48/54 |  |
| OR | 1.0 | 1.8 | 2.4 | 1.0 |  |
| 95\% CI | - | 1.0-3.2 | 1.3-4.4 | 0.6-1.9 | 0.72 |
| Vitamin A |  |  |  |  |  |
| IQR ${ }^{\text {e }}$ | $\leq 6204$ | 6205-9460 | 9461-15838 | 15839+ |  |
| Cases/Controls | 43/59 | 49/53 | 44/58 | 39/63 |  |
| OR | 1.0 | 1.3 | 1.0 | 0.8 |  |
| 95\% CI | - | 0.8-2.4 | 0.6-1.9 | 0.4-1.4 | 0.34 |
| Dietary fibre |  |  |  |  |  |
| $\mathrm{IQR}^{\text {c }}$ | $\leq 18.2$ | 18.3-21.7 | 21.8-27.1 | $27.2+$ |  |
| Cases/Controls | 36/66 | 48/54 | 47/55 | 44/58 |  |
| OR | 1.0 | 1.6 | 1.7 | 1.5 |  |
| 95\% CI | - | 0.9-2.9 | 0.9-3.2 | 0.8-2.6 | 0.18 |
| Sucrose |  |  |  |  |  |
| IQR ${ }^{\text {c }}$ | $\leq 12.1$ | 12.2-19.2 | 19.3-29.6 | 29.7+ |  |
| Cases/Controls | 39/63 | 47/55 | 45/57 | 44/58 |  |
| OR | 1.0 | 1.2 | 1.4 | 1.0 |  |
| 95\% CI | - | 0.6-2.1 | 0.8-2.6 | 0.6-1.8 | 0.49 |
| Beta-carotene |  |  |  |  |  |
| IQR ${ }^{\text {f }}$ | $\leq 2705$ | 2706-4270 | 4271-7484 | 7485+ |  |
| Cases/Controls | 41/61 | 44/58 | 48/54 | 42/60 |  |
| OR | 1.0 | 1.2 | 1.4 | 1.0 |  |
| 95\% CI | - | 0.6-2.1 | 0.8-2.6 | 0.6-1.8 | 0.79 |
| Alpha-carotene |  |  |  |  |  |
| IQR ${ }^{\text {f }}$ | $\leq 109$ | 110-291 | 292-600 | $601+$ |  |
| Cases/Controls | 41/61 | 55/47 | 42/60 | 37/65 |  |
| OR | 1.0 | 1.8 | 1.1 | 0.9 |  |
| 95\% CI | - | 1.0-3.3 | 0.6-1.9 | 0.5-1.6 | 0.40 |
| Lycopene |  |  |  |  |  |
| IQR ${ }^{\text {t }}$ | $\leq 1300$ | 1301-2501 | 2502-3300 | 3301+ |  |
| Cases/Controls | 41/61 | 51/51 | 36/66 | 47/55 |  |
| OR | 1.0 | 1.6 | 0.8 | 1.2 |  |
| 95\% CI | - | 0.9-2.8 | 0.4-1.4 | 0.7-2.2 | 0.90 |

Table 3 (Cont) Odds ratios of prostate cancer for nutrients ${ }^{\text {a }}$

| Nutrient | Quartile |  |  |  | $P$ for trend |
| :---: | :---: | :---: | :---: | :---: | :---: |
|  | I | II | III | IV |  |
| Lutein |  |  |  |  |  |
| IQR ${ }^{\text {f }}$ | $\leq 1214$ | 1215-2086 | 2087-3593 | 3594+ |  |
| Cases/Controls | 44/58 | 51/51 | 43/59 | 37/65 |  |
| OR | 1.0 | 1.3 | 0.9 | 0.7 |  |
| 95\% CI | - | 0.7-2.3 | 0.5-1.7 | 0.4-1.3 | 0.15 |
| Vitamin C |  |  |  |  |  |
| $1 \mathrm{QR}^{\text {d }}$ | $\leq 85.8$ | 85.9-115.6 | 115.7-161.8 | 161.9+ |  |
| Cases/Controls | 55/47 | 45/57 | 39/63 | 36/66 |  |
| OR | 1.0 | 0.6 | 0.5 | 0.4 |  |
| 95\% CI | - | 0.3-1.0 | 0.3-0.8 | 0.2-0.8 | 0.008 |
| Vitamin E |  |  |  |  |  |
| $1 \mathrm{IR}^{\text {d }}$ | $\leq 5.0$ | 5.1-6.0 | 6.1-7.8 | 7.9+ |  |
| Cases/Controls | 49/53 | 52/50 | 37/65 | 37/65 |  |
| OR | 1.0 | 1.2 | 0.6 | 0.6 |  |
| 95\% CI | - | 0.7-2.1 | 0.3-1.1 | 0.3-1.1 | 0.03 |
| Vitamin D |  |  |  |  |  |
| IQRe | $\leq 75.2$ | 75.3-148.4 | 184.5-189.7 | 189.8+ |  |
| Cases/Controls | 44/58 | 52/49 | 46/57 | 33/69 |  |
| OR | 1.0 | 1.3 | 0.9 | 0.7 |  |
| 95\% CI | - | 0.7-2.5 | 0.5-1.8 | 0.4-1.2 | 0.14 |

${ }^{a}$ Adjusted for age, residence, urban/rural status, education, family history of prostate cancer, body mass index and total energy intake. ${ }^{\text {b }}$ Kcal per day; ${ }^{\circ}$ Grams per day; ${ }^{\text {dMiligrams }}$ per day; elU; ' M Mcrograms per day.

Table 4 Odds ratios of prostate cancer for fat and carbohydrate intakes according levels of body mass indexa

|  | Body mass index |  |
| :--- | :--- | :--- |
| Fat | Low | High |
| Low | 1.0 | 1.0 |
| 2 | $1.5(0.7-3.1)$ | $2.3(0.8-6.1)$ |
| 3 | $0.9(0.5-2.1)$ | $4.2(1.6-11.4)$ |
| High | $0.9(0.4-1.9)$ | $3.3(1.2-8.9)$ |
| Carbohydrate | Low | High |
| Low | 1.0 | 1.0 |
| 2 | $1.0(0.4-2.3)$ | $0.9(0.4-2.0)$ |
| 3 | $1.7(0.8-3.6)$ | $0.6(0.2-1.4)$ |
| High | $0.8(0.4-1.8)$ | $0.3(0.1-0.7)$ |
|  |  |  |

${ }^{\text {a/Adjusted for age, residence, urban/rural status and total energy intake. }}$
patients, and also after controlling for dietary fibre and vitamin E intakes (results not shown). As in previous studies (West et al, 1991; Rohan et al, 1995; Whittemore et al, 1995; Meyer et al, 1997), total energy intake was a risk factor for prostate cancer. Although it is difficult to disentangle the effects of total energy intake from the effects of energy-dense foods, the evidence suggests that high energy intake may increase the risk of prostate cancer (World Cancer Research Fund, 1997).

Previous studies and reviews have reported increased risks of prostate cancer associated with red meat intake (Kolonel and Nomura, 1992; Talamini et al, 1992; Boyle and Zaridze, 1993; Giovannucci et al, 1993; Pienta and Esper, 1993; Gann et al, 1994; Le Marchand et al, 1994). The mechanisms of red meat intake as a risk factor for this cancer site are mostly unknown, although red meat's fat content may be a factor, possibly immediated by androgenic hormones (World Cancer Research Fund, 1997). On the other hand, fried or broiled meat may be a source of heterocyclic
amines, potent mutagens in experimental studies (Weisburger et al, 1994). These chemicals have proved to be associated with cancers at other sites (De Stefani et al, 1997) and further studies on prostate cancer and heterocyclic amine intake are needed. Total fat intake was associated with risk in our study as in previous studies (West et al, 1991; Giovannucci et al, 1993; Whittemore et al, 1995).

Both vitamin A and carotenoids have been the subject of conflicting reports (Boyle and Zaridze, 1993; Pienta and Esper, 1993; Giovannucci, 1995; Kolonel et al, 1987, 1988; Le Marchand et al, 1991) and, in our study, no clear association with either was found. On the other hand, vitamin C was associated with a rather strong protective effect. Previous studies on vitamin C intake and prostate cancer (West et al, 1991; Rohan et al, 1995) reported no significant association. Also vitamin E was associated with a reduced risk of prostate cancer in our study. A recent report from a clinical trial (Heinonen et al, 1998) showed a $32 \%$ decrease in prostate cancer, associated with supplementation with $\alpha$-tocopherol. It has been suggested that this protective effect is related to the antioxidant effect of vitamin E. Thus, the protective effect of vegetables and fruits, vitamin $C$ and vitamin $E$ could be due to a mechanism against oxidative stress (Heinonen et al, 1998).

As in all hospital-based case-control studies, the present study has a number of limitations and strengths. Perhaps the major limitation is related to changes in the diet of control patients. Although studies on diseases accepted as control diseases have shown no major differences among the general population regarding intake of meat, vegetables, fruits and legumes, it is not possible to rule out the possibility of mis-classification bias, generally towards the null. Another limitation is related to the limited number of cases afflicted with prostate cancer, which precludes against strong statements in the consideration of the results. Among the strengths, the high response rate, both in cases and controls, reassures against selection bias.

In summary, this case-control study suggests an increased risk of prostate cancer associated with total energy, total fat, red meat intake and a protective effect of vegetables, fruits, vitamin C and vitamin E intakes.

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