British Journal of Cancer (1997) 76(5), 678–687

A case–control study of diet and prostate cancer

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Summary We interviewed 328 men diagnosed with prostate cancer before the age of 75 years and 328 age-matched population controls. The principal hypotheses were that risk would increase with a high intake of total or saturated fat and would decrease with a high intake of carotene (β-carotene equivalents) or lycopene. We also examined the associations of other nutrients and foods with risk. There was no evidence for an association between fat intake and risk, although the average fat intake was high and the range of fat intakes was narrow (medians of lower and upper thirds of percentage of energy from fat among controls were 34.3% and 42.9% respectively). Risk was lower in subjects with higher carotene intake: odds ratios 0.65 (95% CI 0.45–0.94) and 0.76 (0.53–1.10) in the middle and upper thirds of carotene intake respectively (*P* for trend = 0.150). Lycopene was not associated with risk. Among 13 other nutrients examined, the odds ratios in the top third of intake were below 0.8 for: potassium, 0.74 (0.51–1.09; *P* for trend = 0.054); zinc, 0.73 (0.49–1.08; *P* for trend = 0.126); iodine, 0.75 (0.51–1.11; *P* for trend = 0.077); vitamin B_6 food only, 0.77 (0.53–1.12; *P* for trend = 0.077); and vitamin B_6 including supplements, 0.70 (0.48–1.03; *P* for trend = 0.029). Among 18 foods examined, statistically significant associations were observed for: garlic as food, ≥ 2/week vs never, 0.56 (0.33–0.93); garlic including supplements, ≥ 2/week vs never, 0.60 (0.37–0.96); baked beans, ≥ 2/week vs < 1/month, 0.57 (0.34–0.95); and garden peas, ≥ 5/week vs ≤ 3/month, 0.35 (0.13–0.91). This study does not support the hypothesis that fat increases risk and is equivocal in relation to carotene. The possible relationships of vitamin B_6, garlic, beans and peas with risk for prostate cancer should be further investigated.

Keywords: prostate cancer; diet; fat; carotene; case–control study

Prostate cancer is one of the commonest cancers in Western countries, but the only definite risk factors are age, family history of the disease, and ethnic group/country of residence (Nomura and Kolonel, 1991). The large international variation in both incidence and mortality rates has suggested that environmental factors such as diet may affect risk, but no dietary risk factors have been firmly established.

We have investigated the relationship of dietary factors with risk using a population-based case–control study in England. We had two principal hypotheses. The first, generated by the international correlation between fat consumption and prostate cancer (Armstrong and Doll, 1975), was that risk is increased by a high intake of total fat or saturated fat. The second, stimulated by the suggestion that β-carotene might protect against various types of cancer (Peto et al, 1981), was that a high intake of carotene (β-carotene equivalents) may reduce risk. A subsidiary hypothesis to this, generated by the study of Giovannucci et al (1995), was that the carotenoid lycopene from tomatoes would reduce risk.

We also present results for other nutrients and for selected foods. These analyses were not testing previous hypotheses but were simply exploratory; therefore, the results should be interpreted cautiously. Variables were selected because they were thought to be important components of the diet, because there was some previous research suggesting that they might be associated with prostate cancer, or because in a preliminary examination of mean intakes of 35 nutrients there was some evidence for a difference between cases and controls.

Received 2 December 1997
Revised 17 March 1997
Accepted 17 March 1997

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MATERIALS AND METHODS

Selection of cases and controls

The study was conducted in Oxfordshire, West Berkshire and Leeds, and approved by the local ethics committees in these three districts. Between December 1989 (June 1990 in Leeds) and June 1992 we attempted to identify all men diagnosed with prostate cancer before the age of 75 years. Identification of cases was largely by searching histopathology records, supplemented by records from cytology, biochemistry, radiotherapy and cancer registries (with permission from hospital consultants). The date of diagnosis was taken as the date of the first positive histopathology report or, in the 14 cases where the diagnosis was based solely on clinical, radiological and/or biochemical evidence, the date of the first letter from the consultant giving a diagnosis of prostate cancer. Cases were contacted by a letter from their consultant, after receiving permission to do this from their general practitioner.

For each case, three potential controls were chosen from the patient list of his general practitioner. The controls were matched by age within 1 year either way. For practices with computerized records, potential controls were the three men on the general practitioner's list whose dates of birth were closest to that of the case. For practices without computerized records, potential controls were the first three men found in the alphabetical index, after skipping the first ten patients following the case, whose dates of birth were within 1 year of the date of birth of the case. Men who had a previous diagnosis of prostate cancer or who had had a radical prostatectomy were not eligible as controls. The potential controls were designated as first, second or third according to the order of identification, and the first control was then invited by letter to be interviewed for the study. If the first control refused the second and third controls were approached in turn until an interview was

Table 1 Use of nutritional supplements in cases and controls

Supplement[a]	Cases (n = 328)	Controls (n = 328)
Fish oil	58	65
Multivitamins	23	29
Vitamin C	9	13
Garlic	11	11
Vitamin B complex, brewer's yeast	3	7
Vitamin E	1	5

[a]Other formulations were taken by a total of five or fewer cases and controls.

completed. In a few instances further controls had to be approached.

The study was restricted to white men who could speak English and who were well enough to complete the interview and give a reasonable history.

Interviewing

The men were interviewed between February 1990 and July 1994. The median time between diagnosis and interview among cases was 4 months (range 1 month to 2.6 years), and 93.0% of cases were interviewed within 1 year of diagnosis. There were three female interviewers: one covering all the cases and controls in each of the three health districts. The majority of interviews were conducted in patients' homes, with the remainder at general practices or in hospital.

Data and dietary questionnaire

The interview took about 1 h and included questions on basic demographic details, smoking, family history of prostate cancer and usual food intake during the previous 5 years.

The dietary questionnaire was an adaptation of the food frequency questionnaire developed for the British component of

Table 2 Characteristics of cases and controls

Variable	Cases (n = 328)	Controls (n = 328)	Odds ratio	95% Confidence interval
Height at age 25 years (m)				
< 1.73	102	100	1.00	
1.73–1.78	122	110	1.09	0.73–1.63
1.79 +	104	118	0.87	0.59–1.28
P for trend			0.173	
Body mass index at age 25 years (kg m^{-2}) (three missing, 325 matched pairs)				
< 21.069	86	109	1.00	
21.069–23.354	126	105	1.53	1.04–2.26
23.355 +	113	111	1.30	0.879–1.90
P for trend			0.465	
Body mass index at age 45 years (kg m^{-2}) (four missing, 325 matched pairs)				
< 22.754	87	108	1.00	
22.754–25.167	115	108	1.32	0.89–1.95
25.168 +	123	109	1.39	0.95–2.02
P for trend			0.073	
Age at leaving school (years)				
≤ 14	190	190	1.00	
15–16	79	74	1.08	0.72–1.63
17 +	59	64	0.92	0.60–1.41
P for trend			0.751	
Social class				
I	35	32	1.00	
II	89	113	0.68	0.38–1.22
III non-manual	24	38	0.59	0.29–1.21
III manual	121	87	1.31	0.74–2.33
IV	44	43	0.95	0.48–1.88
V	15	15	0.89	0.37–2.14
I, II, III non-manual	148	183	1.00	
III manual, IV, V	180	145	1.63	1.17–2.27
Cigarette smoking				
Never	79	82	1.00	
Previous	193	191	1.05	0.72–1.55
Current	56	55	1.06	0.66–1.70
Father had prostate cancer				
No	321	324	1.00	
Yes	7	4	1.75	0.51–5.98
Brother had prostate cancer				
No	319	325	1.00	
Yes	9	3	3.00	0.81–11.08

Table 3 Geometric mean daily nutrient intakes in cases and controls (not including supplements)

Nutrient	Cases (n = 328)	Controls (n = 328)	P^a
Energy (mJ)	11.1	11.1	0.729
Carbohydrate (g)	303	301	0.799
Starch (g)	149	145	0.261
Sugar (g)	146	148	0.586
Protein (g)	84.6	86.5	0.184
Total fat (g)	115.6	115.9	0.910
Saturated fatty acids (g)	46.9	47.2	0.797
Monounsaturated fatty acids (g)	39.3	39.5	0.870
Polyunsaturated fatty acids (g)	18.4	18.5	0.865
Cholesterol (mg)	341	351	0.297
Alcohol[b] (g)	8.46	8.47	0.988
Non-starch polysaccharides (g)	16.5	16.9	0.231
Potassium (mg)	3602	3714	0.055
Calcium (mg)	1128	1145	0.489
Magnesium (mg)	338	346	0.172
Iron (mg)	12.9	13.2	0.338
Copper (mg)	1.51	1.51	0.933
Zinc (mg)	9.77	10.04	0.127
Manganese (mg)	4.48	4.49	0.938
Selenium (μg)	64.0	61.8	0.231
Iodine (μg)	131	136	0.078
Retinol (μg)	1298	1324	0.684
Carotene (μg)	2703	2842	0.151
Lycopene[c] (μg)	448	462	0.723
Vitamin D (μg)	4.30	4.37	0.723
Vitamin E (mg)	12.4	12.5	0.803
Thiamin (mg)	1.52	1.53	0.692
Riboflavin (mg)	2.24	2.28	0.364
Niacin (mg)	20.1	20.6	0.245
Vitamin B_6 (mg)	1.99	2.06	0.078
Vitamin B_{12} (μg)	7.36	7.63	0.312
Folate (μg)	328	331	0.542
Pantothenate (mg)	12.2	12.6	0.683
Biotin (μg)	53.7	54.2	0.624
Vitamin C (mg)	77.0	78.5	0.591

[a]Paired t-test. [b]Geometric mean of (alcohol intake + 1 g). [c]Geometric mean of (lycopene intake + 1 μg).

the European Prospective Investigation into Cancer and Nutrition (EPIC; Riboli, 1992), which was itself based on the questionnaire developed for the US Nurses' study (Willett et al, 1988). The EPIC food frequency questionnaire has been validated among women in Cambridge (Bingham et al, 1994, 1995). This showed that the questionnaire provides a reasonable estimate of usual intake of important nutrients. For example, for total fat and carotene, which were the primary interests of the current study, the correlations between the estimate of nutrient density from the food frequency questionnaire and from 28 days of weighed dietary records were 0.63 and 0.55 respectively (Bingham et al, 1995).

The food frequency questionnaire enquired about usual frequency of consumption of 83 groups of food items during the last 5 years. Average nutrient intakes were estimated using standard portion sizes, largely from the Ministry of Agriculture Fisheries and Food (1993), and nutrient contents from the fifth edition of McCance and Widdowson's *The Composition of Foods* and its supplements (Holland et al, 1991*a*, 1992*a*,*b*, 1993; Chan et al, 1994). Carotene is given as β-carotene equivalents (β-carotene + 0.5 × (α-carotene + α-cryptoxanthin + β-cryptoxanthin); Holland et al, 1991*a*). Lycopene (μg) was estimated as carotene from tomatoes and tomato products (mg) multiplied by 1.68×10^{-3} (values from Holland et al, 1991*b*).

Participants were asked whether they had regularly taken any vitamin pills or other nutritional supplements during the previous 5 years. Supplement use was slightly less frequent among cases than among controls for all supplements except garlic (Table 1). This information was used to estimate total intakes from food plus supplements of retinol, vitamin E, vitamin B_6 and vitamin C using the following assumed vitamin contents of supplements: cod liver oil or other fish oil, 800 μg retinol; multivitamins, 800 μg retinol, 10 mg vitamin E, 2 mg vitamin B_6, 50 mg vitamin C; evening primrose oil, 10 mg vitamin E; vitamin A, 800 μg retinol; vitamin B complex or Brewer's yeast, 2 mg vitamin B_6; vitamin C, 200 mg vitamin C; and vitamin E, 50 mg vitamin E. These contents were chosen to be representative of common supplements on the market in England (Proprietary Association of Great Britain, 1996).

Statistical methods

Descriptive statistics were calculated using SPSS (SPSS, Chicago, USA). Estimated nutrient intakes were logarithmically transformed to produce approximately normal distributions, and the mean values quoted are geometric means. Relative risks were estimated as odds ratios (and 95% confidence intervals), calculated with EGRET (Statistics and Epidemiological Research Corporation, 1989) using conditional logistic regression methods for individually matched case–control studies (Breslow and Day, 1980). For nutrients, odds ratios were calculated for thirds of the distribution among controls, and tests for trend were for the logarithm of actual nutrient intake; for foods, odds ratios were calculated for four categories of consumption, selected to give the most even distribution among the controls, and tests for trend were for the daily frequency of consumption. To allow for the association of fat intake with energy intake, we calculated the percentages of energy supplied by fat and fatty acids and present the odds ratios in relation to per cent energy from fat adjusted for energy intake (Willett, 1990). We also calculated energy-adjusted fat intakes by the residuals method of Willett and Stampfer (1986); these results were similar to those for the percentage energy method and are not presented.

Two-sided P-values are quoted. Tests for trend were calculated using the logarithmically transformed continuous estimates of nutrient intake.

RESULTS

Response rates

Of 425 eligible cases identified, 328 were interviewed (77.2%), 33 refused (7.8%), for 28 the consultant or general practitioner advised against contact (6.6%), 34 died before an interview could be arranged (8.0%) and two had moved outside the area (0.5%). A total of 94 cases (28.7%) had radiological or microscopic evidence of local or metastatic spread at the time of diagnosis.

Of the 328 first controls selected, 267 were interviewed (81.4%), 42 refused (12.8%) and for 19 the general practitioner advised against contact (5.8%).

Characteristics of cases and controls

The mean ages of cases and controls were identical at 68.1 years. The distributions of reported height were similar in cases and controls, but there was some evidence that risk was higher in the

Table 4 Odds ratios (ORs) and 95% confidence intervals (CIs) in relation to daily nutrient intakes

			Unadjusted		Adjusted for social class	
Nutrient and daily intake	**Cases**	**Controls**	**OR**	**95% CI**	**OR**	**95% CI**
Energy (mJ)						
< 10.2	111	109	1.00		1.00	
10.2–12.3	112	110	1.00	0.69–1.44	1.02	0.70–1.48
≥ 12.4	105	109	0.95	0.65–1.38	0.90	0.62–1.32
P for trend			0.729		0.563	
Total fat (g)						
< 103.0	111	109	1.00		1.00	
103.0–134.1	115	110	1.02	0.71–1.47	1.00	0.69–1.45
≥ 134.2	102	109	0.92	0.62–1.35	0.85	0.57–1.25
P for trend			0.909		0.574	
Saturated fatty acids (g)						
< 40.8	113	109	1.00		1.00	
40.8–54.2	111	110	0.97	0.67–1.40	0.95	0.66–1.38
≥ 54.3	104	109	0.92	0.62–1.35	0.87	0.58–1.28
P for trend			0.796		0.481	
Monounsaturated fatty acids (g)						
< 34.9	105	109	1.00		1.00	
34.9–45.2	115	110	1.08	0.75–1.56	1.06	0.73–1.55
≥ 45.3	108	109	1.03	0.70–1.53	0.96	0.64–1.43
P for trend			0.870		0.543	
Polyunsaturated fatty acids (g)						
< 15.1	118	109	1.00		1.00	
15.1–21.9	98	110	0.82	0.56–1.20	0.82	0.55–1.21
≥ 22.0	112	109	0.94	0.64–1.37	0.94	0.64–1.38
P for trend			0.865		0.765	
Total fat (per cent energy)[a]						
< 37.0	111	109	1.00		1.00	
37.0–41.1	105	110	0.94	0.64–1.39	0.86	0.58–1.28
≥ 41.2	112	109	1.02	0.69–1.49	0.93	0.63–1.38
P for trend			0.621		0.958	
Saturated fatty acids (per cent energy)[a]						
< 14.1	112	109	1.00		1.00	
14.1–16.8	88	110	0.78	0.53–1.17	0.76	0.51–1.15
≥ 16.9	128	109	1.19	0.80–1.78	1.12	0.74–1.69
P for trend			0.962		0.701	
Monounsaturated fatty acids (per cent energy)[a]						
< 12.5	108	109	1.00		1.00	
12.5–13.9	111	110	1.02	0.70–1.49	0.95	0.65–1.40
≥ 14.0	109	109	1.02	0.68–1.53	0.94	0.62–1.43
P for trend			0.667		0.950	
Polyunsaturated fatty acids (per cent energy)[a]						
< 5.0	117	109	1.00		1.00	
5.0–7.6	105	110	0.88	0.60–1.29	0.89	0.61–1.31
≥ 7.7	106	109	0.89	0.61–1.32	0.91	0.62–1.35
P for trend			0.827		0.851	
Alcohol (g)						
< 3.6	105	109	1.00		1.00	
3.6–16.5	118	110	1.12	0.76–1.63	1.13	0.77–1.66
≥ 16.6	105	109	1.01	0.69–1.47	1.04	0.71–1.54
P for trend			0.988		0.914	
Non-starch polysaccharides (g)						
< 15.0	131	109	1.00		1.00	
15.0–19.1	85	110	0.64	0.43–0.94	0.69	0.46–1.02
≥ 19.2	112	109	0.86	0.58–1.27	0.96	0.64–1.44
P for trend			0.230		0.533	
Potassium (g)						
< 3.46	125	109	1.00		1.00	
3.46–4.09	110	110	0.87	0.59–1.26	0.91	0.62–1.34
≥ 4.10	93	109	0.74	0.51–1.09	0.81	0.55–1.20
P for trend			0.054		0.164	
Copper (mg)						
< 1.35	119	108	1.00		1.00	
1.35–1.72	99	111	0.82	0.57–1.18	0.80	0.55–1.17
≥ 1.73	110	109	0.91	0.62–1.32	0.86	0.59–1.25
P for trend			0.933		0.779	

Table 4 cont.

Nutrient and daily intake	Cases	Controls	Unadjusted OR	Unadjusted 95% CI	Adjusted for social class OR	Adjusted for social class 95% CI
Zinc (mg)						
< 9.15	127	109	1.00		1.00	
9.15–10.99	106	110	0.80	0.54–1.18	0.84	0.56–1.25
≥ 11.00	95	109	0.73	0.49–1.08	0.78	0.52–1.17
P for trend			0.126		0.229	
Iodine (μg)						
< 120	122	109	1.00		1.00	
120–155	113	110	0.90	0.62–1.31	0.90	0.61–1.32
≥ 156	93	109	0.75	0.51–1.11	0.77	0.52–1.14
P for trend			0.077		0.108	
Retinol, food only (μg)						
< 944	115	109	1.00		1.00	
944–1851	105	110	0.90	0.62–1.32	0.88	0.61–1.29
≥ 1852	108	109	0.94	0.66–1.35	0.90	0.62–1.30
P for trend			0.683		0.514	
Retinol, including supplements (μg)						
< 1214	111	109	1.00		1.00	
1214–2086	117	110	1.04	0.72–1.50	1.07	0.74–1.56
≥ 2087	100	109	0.91	0.64–1.32	0.90	0.62–1.30
P for trend			0.519		0.441	
Carotene (mg)[b]						
< 2.65	137	109	1.00		1.00	
2.65–3.47	88	110	0.65	0.45–0.94	0.69	0.47–1.01
≥ 3.48	103	109	0.76	0.53–1.10	0.83	0.57–1.21
P for trend			0.150		0.351	
Lycopene (μg)						
< 402	117	109	1.00		1.00	
402–717	103	110	0.89	0.62–1.26	0.90	0.63–1.29
≥ 718	108	109	0.93	0.64–1.35	0.99	0.68–1.45
P for trend			0.727		0.882	
Vitamin B_6, food only (mg)						
< 1.90	128	109	1.00		1.00	
1.90–2.26	101	110	0.78	0.54–1.13	0.85	0.58–1.24
≥ 2.27	99	109	0.77	0.53–1.12	0.86	0.59–1.26
P for trend			0.077		0.204	
Vitamin B_6, including supplements (mg)						
< 1.93	130	107	1.00		1.00	
1.93–2.35	104	111	0.77	0.54–1.12	0.84	0.58–1.23
≥ 2.36	94	110	0.70	0.48–1.03	0.79	0.54–1.18
P for trend			0.029		0.122	
Vitamin C, food only (mg)						
< 66.1	114	109	1.00		1.00	
66.1–97.3	100	110	0.89	0.62–1.26	0.99	0.69–1.43
≥ 97.4	114	109	1.01	0.69–1.46	1.22	0.82–1.81
P for trend			0.590		0.607	
Vitamin C, including supplements (mg)						
< 67.1	107	109	1.00		1.00	
67.1–104.2	112	110	1.04	0.72–1.49	1.19	0.81–1.74
≥ 104.3	109	109	1.02	0.70–1.48	1.23	0.83–1.84
P for trend			0.390		0.818	
Vitamin E, food only (mg)						
< 9.59	116	109	1.00		1.00	
9.59–16.33	107	110	0.90	0.60–1.35	0.94	0.62–1.41
≥ 16.34	105	109	0.90	0.61–1.32	0.93	0.63–1.37
P for trend			0.803		0.890	
Vitamin E, including supplements (mg)						
< 9.94	119	109	1.00		1.00	
9.94–17.87	112	109	0.93	0.64–1.37	0.95	0.65–1.41
≥ 17.88	97	110	0.81	0.55–1.18	0.85	0.58–1.25
P for trend			0.296		0.413	

[a]Adjusted for log energy intake as a continuous variable. [b]β-Carotene equivalents (β-carotene + 0.5 × (α-carotene + α-cryptoxanthin + β-cryptoxanthin)). *P*-values for trend are for the logarithmically transformed continuous estimates of nutrient intake.

Table 5 Odds ratios (ORs) and 95% confidence intervals (CIs) in relation to frequency of consumption of selected foods

			Unadjusted		Adjusted for social class	
Food and frequency of consumption	**Cases**	**Control**	**OR**	**95% CI**	**OR**	**95% CI**
Meat of any type						
≤ 4 per week	64	61	1.00		1.00	
5–6 per week	94	84	1.06	0.67–1.67	1.05	0.66–1.67
1 per day	134	133	0.95	0.60–1.49	0.94	0.60–1.49
> 1 per day	36	50	0.66	0.37–1.18	0.64	0.36–1.14
P for trend			0.160		0.133	
Roast or grilled meat of any type						
< 1 per week	26	35	1.00		1.00	
1 per week	78	67	1.57	0.86–2.89	1.48	0.80–2.74
2–4 per week	202	202	1.35	0.77–2.38	1.29	0.73–2.29
5 + per week	22	24	1.23	0.56–2.69	1.12	0.50–2.49
P for trend			0.944		0.807	
Fatty fish[a]						
Never	58	43	1.00		1.00	
< 1 per month	52	53	0.72	0.41–1.27	0.74	0.42–1.32
1–3 per month	124	136	0.68	0.43–1.08	0.70	0.44–1.12
≥ 1 per week	94	96	0.72	0.44–1.18	0.78	0.47–1.29
P for trend			0.149		0.167	
Cooked vegetables except potatoes						
≤ 4 per week	51	45	1.00		1.00	
5–6 per week	52	50	0.90	0.51–1.57	0.87	0.49–1.54
1 per day	162	165	0.82	0.50–1.34	0.86	0.52–1.42
> 1 per day	63	68	0.68	0.33–1.41	0.71	0.34–1.48
P for trend			0.341		0.415	
Carrots						
≤ 3 per month	49	43	1.00		1.00	
1 per week	72	69	0.90	0.53–1.55	0.93	0.54–1.60
2–4 per week	175	177	0.86	0.54–1.38	0.92	0.57–1.49
≥ 5 per week	32	39	0.70	0.37–1.34	0.75	0.39–1.44
P for trend			0.324		0.495	
Dark-green leafy vegetables						
< 1 per month	93	98	1.00		1.00	
1–3 per month	71	71	1.08	0.66–1.75	1.16	0.70–1.89
1 per week	77	72	1.16	0.72–1.86	1.29	0.79–2.11
≥ 2 per week	87	87	1.08	0.70–1.65	1.24	0.79–1.94
P for trend			0.770		0.820	
Onions						
≤ 3 per month	75	79	1.00		1.00	
1 per week	72	65	1.16	0.73–1.84	1.11	0.70–1.77
2–4 per week	146	142	1.09	0.72–1.65	1.07	0.70–1.62
≥ 5 per week	35	42	0.89	0.52–1.53	0.85	0.49–1.48
P for trend			0.683		0.654	
Garlic						
Never	220	192	1.00		1.00	
< 1 per month	31	32	0.83	0.45–1.50	0.94	0.51–1.73
1–4 per month	45	56	0.70	0.45–1.08	0.77	0.49–1.20
≥ 2 per week	32	48	0.56	0.33–0.93	0.64	0.38–1.09
P for trend			0.038		0.129	
Garlic, including supplements						
Never	215	187	1.00		1.00	
< 1 per month	30	31	0.84	0.45–1.54	0.95	0.51–1.78
1–4 per month	43	54	0.69	0.44–1.08	0.75	0.48–1.19
≥ 2 per week	40	56	0.60	0.37–0.96	0.68	0.41–1.10
P for trend			0.117		0.255	
Raw tomatoes						
≤ 3 per month	75	78	1.00		1.00	
1 per week	71	63	1.18	0.74–1.90	1.27	0.78–2.05
2–4 per week	148	149	1.04	0.70–1.53	1.12	0.76–1.67
≥ 5 per week	34	38	0.93	0.53–1.64	1.06	0.55–1.62
P for trend			0.581		0.883	
Cooked tomatoes						
< 1 per month	99	91	1.00		1.00	
1–3 per month	55	66	0.77	0.49–1.21	0.77	0.49–1.22
1 per week	101	95	0.98	0.66–1.45	0.99	0.67–1.47
≥ 2 per week	73	76	0.88	0.57–1.36	0.92	0.59–1.42
P for trend			0.468		0.636	

Table 5 cont.

Food and frequency of consumption	Cases	Control	Unadjusted OR	Unadjusted 95% CI	Adjusted for social class OR	Adjusted for social class 95% CI
Raw green salad						
≤ 3 per month	92	102	1.00		1.00	
1 per week	91	83	1.20	0.80–1.79	1.21	0.80–1.81
2–4 per week	115	100	1.26	0.86–1.84	1.35	0.91–1.99
5–6 per week	30	43	0.75	0.43–1.31	0.87	0.49–1.56
P for trend			0.670		0.817	
Baked beans						
< 1 per month	92	76	1.00		1.00	
1–3 per month	91	109	0.66	0.43–1.02	0.66	0.43–1.02
1 per week	103	84	1.02	0.66–1.58	0.98	0.63–1.52
≥ 2 per week	42	59	0.57	0.34–0.95	0.52	0.31–0.88
P for trend			0.130		0.075	
Garden peas						
≤ 3 per month	63	62	1.00		1.00	
1 per week	107	93	1.17	0.74–1.87	1.14	0.71–1.83
2–4 per week	152	155	0.99	0.65–1.52	0.98	0.64–1.51
≥ 5 per week	6	18	0.35	0.13–0.91	0.35	0.13–0.94
P for trend			0.066		0.081	
Green beans, broad beans, runner beans						
< 1 per month	58	42	1.00		1.00	
1–3 per month	68	75	0.60	0.35–1.06	0.62	0.35–1.09
1 per week	96	99	0.65	0.38–1.10	0.68	0.40–1.16
≥ 2 per week	106	112	0.62	0.36–1.07	0.66	0.38–1.13
P for trend			0.362		0.469	
Dried lentils, beans, peas						
Never	202	200	1.00		1.00	
< 1 per month	31	36	0.85	0.50–1.45	0.87	0.51–1.50
1–3 per month	58	62	0.92	0.60–1.40	0.89	0.58–1.37
≥ 1 per week	37	30	1.21	0.72–2.04	1.38	0.81–2.36
P for trend			0.319		0.144	
Total legumes[b]						
< 3 per week	100	90	1.00		1.00	
3–4 per week	92	85	0.96	0.64–1.45	0.96	0.64–1.46
5–6 per week	77	89	0.76	0.49–1.18	0.78	0.50–1.21
≥ 1 per day	59	64	0.82	0.53–1.29	0.83	0.53–1.30
P for trend			0.068		0.093	
Citrus fruit						
Never	74	81	1.00		1.00	
≤ 1 per week	118	128	1.03	0.68–1.55	1.11	0.73–1.69
2–4 per week	87	75	1.29	0.82–2.03	1.41	0.89–2.24
≥ 5 per week	49	44	1.26	0.73–2.16	1.45	0.83–2.52
P for trend			0.175		0.091	
Non-citrus fruit						
< 1 per month	39	37	1.00		1.00	
1–4 per month	59	53	1.06	0.60–1.88	1.18	0.65–2.11
2–4 per week	90	84	1.01	0.58–1.76	1.15	0.65–2.02
≥ 5 per week	140	154	0.85	0.51–1.42	0.99	0.58–1.68
P for trend			0.307		0.539	
Tea (cups per day)						
< 3	66	65	1.00		1.00	
3–4	97	122	0.77	0.48–1.22	0.73	0.46–1.18
5–6	101	81	1.23	0.76–1.97	1.15	0.71–1.87
≥ 7	64	60	1.05	0.62–1.78	0.94	1.15–2.26
P for trend			0.253		0.522	
Coffee (cups per day)						
0	109	109	1.00		1.00	
1	72	81	0.88	0.58–1.34	0.92	0.60–1.42
2	72	52	1.34	0.86–2.10	1.41	0.89–2.21
≥ 3	75	86	0.85	0.54–1.35	0.94	0.59–1.51
P for trend			0.750		0.950	

[a]Question referred to 'oily fish, fresh or canned, e.g. mackerel, kippers, tuna, salmon, sardines, herring'. [b]Sum of baked beans, garden peas, green beans, broad beans, runner beans, dried lentils, beans and peas. *P* values for trend are for daily frequency as a continuous variable.

middle and top thirds of body mass index than in the lowest third, at both ages 25 and 45 (Table 2).

Age at leaving school was not associated with risk, but risk did vary significantly with social class. The pattern of variation in risk was irregular when social class was categorized in six groups, perhaps because of small numbers in some groups. Social class was therefore also categorized into two groups, non-manual and manual, and the odds ratio for the latter was 1.63 (95% CI 1.17–2.27). Restriction of the analysis to the 267 matched pairs in which the first control participated increased this estimate (odds ratio 1.86; 1.28–2.70). Social class was strongly related to the intake of many nutrients (data not shown), therefore results for nutrients and foods are presented before and after adjustment for social class (non-manual vs manual).

Risk was not significantly associated with cigarette smoking history. More cases than controls reported that their father or a brother had had prostate cancer (odds ratios 1.75; 0.51–5.98 and 3.00; 0.81–11.08 respectively). These results were not substantially altered by adjusting for social class (results not shown).

Nutrient intakes

Table 3 shows geometric mean intakes of 35 nutrients in cases and controls. None of the differences was statistically significant. The previous hypotheses related to total fat, saturated fat, carotene and lycopene. Geometric mean intakes of these nutrients were lower in cases than in controls: 0.3%, 0.6%, 4.9% ($P = 0.151$) and 3.0% for total fat, saturated fat, carotene and lycopene respectively. Differences were close to significant ($0.05 < P < 0.1$) for potassium, iodine and vitamin B_6, for which geometric mean intakes were 3.0%, 3.7% and 3.4% lower respectively in cases than in controls.

Table 4 shows the odds ratios for increasing consumption of 17 nutrients, selected because of a previous hypothesis (total fat, saturated fatty acids, carotene, lycopene), because they are related to fat intake (energy, monounsaturated fatty acids, polyunsaturated fatty acids), because we thought at the time of statistical analysis that they might be associated with prostate cancer (alcohol, non-starch polysaccharides, copper, zinc, retinol, vitamin C, vitamin E), or because the preliminary analyses summarized in Table 3 showed that the difference between cases and controls was close to significant (potassium, iodine, vitamin B_6). There was no evidence for an increase in risk with increasing consumption of total fat or of saturated, monounsaturated or polyunsaturated fatty acids, using either actual fat intake or the percentage of energy supplied by fat. There was some evidence that risk was lower in the middle and top thirds of carotene intake than in the bottom third, but the relationship was not linear and the odds ratios increased towards unity after adjusting for social class. There was no suggestion that risk was associated with lycopene. Of the other nutrients examined, the only significant trend was for vitamin B_6 including supplements; this association was reduced and no longer statistically significant after adjusting for social class. The only other nutrients for which odds ratios were less than 0.8 in the top third of intake were potassium (unadjusted for social class), zinc and iodine.

Intake of selected foods

Table 5 shows the association of risk with frequency of consumption of 18 foods and two drinks. These were selected because they were related to the nutrient hypotheses (meat, cooked vegetables, carrots, dark-green leafy vegetables, raw tomatoes, cooked tomatoes, raw salad) or because previous research had suggested that they might be associated with prostate cancer (roast meat, fatty fish, onions, garlic, baked beans, garden peas, green beans, dried lentils, total legumes, citrus fruit, non-citrus fruit, tea, coffee). The only statistically significant results were for garlic (food only or food plus supplements), baked beans and garden peas. After adjusting for social class the association with garlic was reduced and was not statistically significant, but the reductions in risk for frequent consumption of baked beans and garden peas remained significant. Odds ratios in the highest frequency category, unadjusted for social class, were also below 0.8 for meat, fatty fish, cooked vegetables, carrots, raw green salad and green beans (including broad beans and runner beans).

The calculations presented in Tables 4 and 5 were repeated, restricting the analysis to the 94 cases (and their matched controls) for whom there was radiological or microscopic evidence of local or metastatic disease spread at the time of diagnosis. None of these results was statistically significant. The odds ratios (95% confidence intervals) in the top thirds of the distribution of intake of per cent energy from fat, per cent energy from saturated fatty acids, carotene, and lycopene were 1.22 (0.63–2.37), 0.86 (0.42–1.74), 1.21 (0.61–2.40) and 1.65 (0.77–3.51) respectively.

DISCUSSION

Case–control studies of nutritional factors are susceptible to bias because of over-representation of health conscious people among the controls. It is therefore important to achieve a high response rate among controls. In this study the response rate among first controls was 81.4%. This is higher than the response rate in most previous case–control studies of nutrition and prostate cancer, but some potential for bias remains and the results should therefore be interpreted cautiously.

Another concern with epidemiological studies of prostate cancer is that some of the cases diagnosed after transurethral prostatectomy for benign prostatic enlargement have a disease that would never have progressed to clinical prostate cancer. Restricting the analysis to cases with advanced disease may reduce this problem, but may also introduce bias because of the removal of more educated case patients who may present with more localized cancers and who may be more health-conscious in their dietary habits (Whittemore et al, 1995). Whittemore et al (1995) found that restricting their analysis to cases with advanced disease (and to controls with normal serum prostate-specific antigen concentrations) increased the magnitude of the relationship they observed between saturated fat intake and risk, but in their study there was also a significant relationship between saturated fat and risk when all cases and controls were analysed. In our study the results were not materially altered by restricting the analysis to cases with radiological or microscopic evidence of local or metastatic spread of disease at the time of diagnosis.

Height was not associated with risk, but there was some evidence that risk was greater in subjects with a greater body mass index, both at age 25 years and at age 45 years. The results of previous studies have varied somewhat, but in a review of ten studies the men with the highest body mass index had on average a 25% higher risk for prostate cancer than the thinnest men (Key, 1995), and two subsequent prospective studies have also supported this association (Chyou et al, 1994; Grönberg et al, 1996). This small increase in risk in association with a high body mass index might be mediated by a decrease in the plasma concentration of sex hormone-binding globulin associated with obesity (Gann et al, 1996) or might be due to a higher muscle mass indicative of higher androgen levels (Kolonel, 1996).

Age at leaving school was not associated with risk, but risk was on average higher in the manual than the non-manual classes. The standardized mortality ratio for prostate cancer in England and Wales in 1911 was 92% higher in social class I than in social class V, but by 1971 this gradient had reversed and mortality was 26% higher in social class V than in social class I (Logan, 1982). Other studies in other countries have not established a clear socio-economic gradient for this cancer (Nomura and Kolonel, 1991). We decided to present all odds ratios, both unadjusted and adjusted for social class, but it should be borne in mind that a change in an odds ratio towards unity after adjustment for social class could mean that the factor is biologically related to risk and actually explains some of the observed variation in risk with social class.

A history of prostate cancer in fathers and brothers was associated with a two- to threefold increase in the risk for prostate cancer. This is similar to the results of other studies (Nomura and Kolonel, 1991), although the absolute rates of reporting disease in fathers and brothers were low, probably due to some under-reporting plus, for fathers, the lower incidence rates of prostate cancer in England and Wales a generation ago (Whittemore, 1994).

Eight out of ten studies reviewed in 1994 showed some increase in risk with high fat intakes (Key, 1995), and this was also observed in another large recent case–control study (Whittemore et al, 1995). In the current study, risk was not associated with the intake of total fat or of saturated, monounsaturated or polyunsaturated fatty acids. There was also no suggestion of a positive association between total meat intake and risk – indeed, the lowest odds ratio was for men who ate meat most frequently. The results for fat were not altered by adjusting for energy intake by the nutrient density method or by the residuals method of Willett and Stampfer (1986), and energy itself was not associated with risk. However, in our study the average fat intake was high and the range of fat intakes was narrow, with a median intake of 34.3% of energy from fat in the lowest third. Our results do not provide information on the relationship of low fat intakes with the risk for prostate cancer.

Nine studies reviewed in 1994 and a recent report from another prospective study showed, on average, no association between carotene intake and risk (Key, 1995; Daviglus et al, 1996). Our study suggests some reduction in risk in association with higher carotene intakes, but the trend was irregular and not statistically significant. The absence of any protective effect of β-carotene in the Alpha-Tocopherol, Beta Carotene Prevention Study (1994) or in the Physicians' Health Study (this included 1047 incident prostate cancers: Hennekens et al, 1996) suggests that this carotenoid does not reduce the risk for prostate cancer and that any consistent associations observed in observational studies are probably due to other correlated dietary factors. Giovannucci et al (1995) observed a protective association of lycopene from tomatoes. One other study has reported a protective association for tomatoes (Mills et al, 1989), but two other studies have found no association (Schuman et al, 1982; Le Marchand et al, 1991). Our results did not suggest a reduction in risk in association with estimated lycopene intake, but our estimate was crude and took no account of the wide variation in the bioavailability of lycopene between foods. In Britain, tinned baked beans (see below) may be a major effective source of lycopene because of the high bioavailability of lycopene from the tomato sauce.

Hayes et al (1996) recently reported a significant trend of increasing risk with increasing alcohol consumption in a large case–control study. However, there was no evidence for such a trend in our study or in most previous studies (Key, 1995).

The possibility that vitamin E might reduce the risk for prostate cancer was raised by the results of the Alpha-Tocopherol, Beta Carotene Prevention Study (1994), which reported 34% fewer cases of prostate cancer in the 50 mg of alpha-tocopherol per day arm of the trial. Our results for estimated vitamin E intake do not support this hypothesis, but median vitamin E intake (food and supplements) in the top third was estimated as only 23.9 mg per day. It is nevertheless intriguing that five controls but only one case reported taking vitamin E supplements.

We observed a reduction in risk with increasing consumption of vitamin B_6. This association was reduced by adjusting for social class and was not a previous hypothesis, but deficiency of this vitamin results in 'increased and prolonged nuclear uptake of steroid hormones and enhanced end-organ sensitivity to hormone action ... which may be relevant in the aetiology of cancer of the prostate' (Bender, 1994). This hypothesis deserves further investigation.

Among the foods and food groups we examined there were significant reductions in risk associated with garlic, baked beans and garden peas. The association with garlic was partly explained by social class, but the possible anti-carcinogenic effects of garlic (Steinmetz and Potter, 1991; Dorant et al, 1993) should be examined further in relation to prostate cancer. The associations with baked beans and peas are intriguing because the strongest dietary association with prostate cancer reported by Mills et al (1989) was for beans, lentils and peas, and because these foods have constituents which have been hypothesized to reduce cancer risk (Troll and Wiesner, 1983; Steinmetz and Potter, 1991). Another recent study in England produced results similar to ours, with a crude odds ratio of 0.63 for men who reported eating peas or beans more than once a week in comparison with men who ate these foods less often (Ewings and Bowie, 1996).

Tea and coffee consumption were not associated with risk. Green tea contains chemicals which can inhibit 5α-reductase (Liao and Hiipakka, 1995), and one previous study has reported a protective association for (black) tea among Japanese men in Hawaii (Heilbrun et al, 1986), but no evidence for this was found in a previous study in Britain, where tea consumption is much higher (Kinlen et al, 1988).

In conclusion, the role of nutrition in the aetiology of prostate cancer remains unclear. This study did not support the hypothesized role of fat, and is equivocal in relation to carotene. We think that the possible effects of vitamin B_6, garlic, and beans and peas should be examined further.

ACKNOWLEDGEMENTS

We thank Rosemary Brett, Elizabeth Hilton and Bette Ward for identifying and interviewing the patients and controls; the urologists, general practitioners, radiologists, pathologists, cancer registry staff and other medical staff who helped in identifying, contacting and interviewing patients and controls; and all the men who agreed to participate in this study. This study was supported by the Imperial Cancer Research Fund.

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