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Cancer incidence in British vegetarians

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Running head: Cancer incidence in British vegetarians

1   **ABSTRACT**

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3   We studied 64,409 British men and women, comprising 33,698 meat-eaters, 8,901 non meat-

4   eaters who did eat fish ("fish-eaters") and 21,810 vegetarians. After an average follow-up of

5   11.6 years there were 3,351 incident cancers: 2,205 among meat-eaters, 317 among fish-

6   eaters and 829 among vegetarians. Relative risks (RRs) were estimated by Cox regression,

7   stratified by sex and recruitment protocol and adjusted for age, smoking, alcohol, body mass

8   index, physical activity level and, for women only, parity and oral contraceptive use. There

9   was significant heterogeneity in cancer risk between groups for four cancer sites: stomach

10   cancer, RRs compared to meat-eaters of 0.29 (95% CI 0.07-1.20) in fish-eaters and 0.36

11   (0.16-0.78) in vegetarians, *P* for heterogeneity=0.007; ovarian cancer, RRs 0.37 (0.18-0.77)

12   in fish-eaters and 0.69 (0.45-1.07) in vegetarians, *P* for heterogeneity=0.007; bladder cancer,

13   RRs 0.81 (0.36-1.81) in fish-eaters and 0.47 (0.25-0.89) in vegetarians, *P* for

14   heterogeneity=0.05; and cancers of the lymphatic and haematopoietic tissues, RRs 0.85

15   (0.56-1.29) in fish-eaters and 0.55 (0.39-0.78) in vegetarians, *P* for heterogeneity=0.002. The

16   RRs for all malignant neoplasms were 0.82 (0.73-0.93) in fish-eaters and 0.88 (0.81-0.96) in

17   vegetarians, *P* for heterogeneity=0.001. The incidence of some cancers may be lower in fish-

18   eaters and vegetarians than in meat-eaters.

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INTRODUCTION

Vegetarians do not eat meat or fish. Meat has been suspected of influencing the risk for several types of cancer. For example, in the systematic review by the World Cancer Research Fund/American Institute for Cancer Research (WCRF/AICR), an expert panel concluded that both red meat and processed meat are convincing causes of colorectal cancer, and that there was some evidence suggesting that high intakes of red or processed meat increase the risk for cancers of the oesophagus, stomach, pancreas, lung, endometrium and prostate (WCRF/AICR, 2007).

A few prospective studies have been established with the aim of studying the long-term health of vegetarians, and have used recruitment methods designed to ensure that a substantial number of the participants were vegetarians. Some findings on cancer incidence rates in vegetarians have been reported from the Adventist Health Study in California (Fraser et al, 1999), the Oxford Vegetarian Study (Sanjoaquin et al, 2004), the UK Women's Cohort Study (Taylor et al, 2007) and EPIC-Oxford (Key et al, 2009). These reports included data for only a few cancer sites. To provide more information on cancer incidence in vegetarians, we report here on the incidence of malignant cancer at twenty sites or groups of sites, plus all incident malignant cancers combined, in a pooled analysis of data from two prospective studies in the UK, the Oxford Vegetarian Study (Appleby et al, 1999) and the EPIC-Oxford cohort (Davey et al, 2003).

MATERIALS AND METHODS

In the Oxford Vegetarian Study participants were recruited throughout the United Kingdom between 1980 and 1984 (Thorogood et al, 1994). Vegetarian participants were recruited

through advertisements, the news media and word of mouth, and non-vegetarian participants were recruited as friends and relatives of the vegetarian participants. A semiquantitative food frequency questionnaire was completed at recruitment, and information collected on smoking and exercise habits, alcohol drinking, social class, weight and height, and reproductive factors in women. In total 11,140 subjects were recruited.

The EPIC-Oxford cohort was recruited throughout the United Kingdom between 1993 and 1999 (Davey et al, 2003). Two methods of recruitment were used: general practice (GP) recruitment and postal recruitment. A Multi-Centre Research Ethics Committee (MREC Scotland) approved the protocol. A pilot recruitment phase was conducted by collaborating GPs in Scotland, and nurses working in GP practices in Oxfordshire, Buckinghamshire and Greater Manchester carried out further recruitment from the general population. Postal recruitment was designed to recruit as many vegetarians and vegans as possible. The main questionnaire was mailed directly to all members of The Vegetarian Society of the UK and all surviving participants in the Oxford Vegetarian Study. Respondents were invited to give names and addresses of relatives and friends who might also be interested in receiving a questionnaire. In addition, a short questionnaire was distributed to all members of The Vegan Society, enclosed in health/diet-interest magazines, and displayed on health food shop counters. The main questionnaire was then mailed to all those who returned a short questionnaire. 7,423 participants were recruited by the GP method and 58,042 participants by the postal method. The main questionnaire included a food frequency questionnaire and information on smoking and exercise habits, alcohol drinking, social class, weight and height, and reproductive factors in women.

Participants in both studies were followed until 31st December 2006 by record linkage with the United Kingdom's National Health Service Central Register, which provides information on cancer diagnoses and all deaths. Participants in the Oxford Vegetarian Study who subsequently joined EPIC-Oxford contributed person-years in the Oxford Vegetarian

Study until the date when they joined EPIC-Oxford. Malignant neoplasms were defined as codes C00-97 of the 10th Revision of the International Classification of Diseases (ICD; World Health Organization, 1992), excluding code C44 (non-melanoma skin cancer). In participants with no recorded incident malignant neoplasm but for whom a malignant neoplasm was noted on the death certificate, the cancer was taken to have occurred at the date of death.

Participants were excluded from the analysis if they were aged less than 20 or more than 89 years at recruitment, or had a previous malignant neoplasm before recruitment, or had no information for one or more of the factors age, sex, smoking and diet group. These exclusions left 64,409 participants (16,600 men, 47,809 women) who were censored on reaching the age of 90. The 64,409 participants included 2,843 persons who participated in both studies. Relative risks (RRs) and their 95% confidence intervals for twenty cancer sites or groups of sites, plus all incident malignant cancers combined, were calculated by Cox proportional hazards regression with age as the underlying time variable, stratified by study protocol (Oxford Vegetarian Study participants, EPIC-Oxford GP recruited participants, EPIC-Oxford postal recruited participants) and sex (where appropriate), and adjusted for smoking (never smoker, former smoker, <15 cigarettes/d or cigar or pipe only, 15+ cigarettes/d), alcohol consumption (<1, 1-7, 8-15, 16+ g ethanol/d, unknown) and body mass index (<20.0, 20.0-22.4, 22.5-24.9, 25.0-27.4, 27.5+ kg/m^2, unknown), physical activity level (low, high, unknown) and, for the women-only cancers, parity (none, 1-2, 3+, unknown) and oral contraceptive use (ever, never, unknown). Diet group was classified in three categories: meat-eaters, fish-eaters (participants who did not eat meat but did eat fish) and vegetarians (participants who did not eat meat or fish). Where a subject could not be categorised for a given factor (usually because the appropriate section of the questionnaire was left unanswered or incomplete) they were allocated to an "unknown" category for the analysis.

1   Statistical significance was set at the 5% level. All statistical analyses were conducted

2   using Stata Statistical Software: Release 10 (College Station, TX: StataCorp LP).

3

4   **RESULTS**

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6   The characteristics of the participants are given in Table 1. Thirty-four percent of participants

7   were vegetarians and about three-quarters were women. Mean age at recruitment was lower in

8   the fish-eaters and vegetarians than in the meat-eaters. Smoking rates were low overall, with

9   only 14.2% of meat-eaters, 11.2% of fish-eaters and 11.1% of vegetarians reporting that they

10   were smokers at the time of recruitment. Median body mass index (BMI) was 1.4 kg/m^2 lower

11   in vegetarians than in meat-eaters, and median alcohol consumption was 1.2 g/d lower in

12   vegetarians than in meat-eaters. Fish-eaters had similar mean BMI to the vegetarians and had

13   similar alcohol consumption to the meat-eaters. The proportions of men and women who

14   reported a relatively high level of physical activity were higher among fish-eaters and

15   vegetarians than among meat-eaters. The proportion of women who were nulliparous at

16   recruitment was higher among fish-eaters and vegetarians than among meat-eaters, and the

17   proportion of women who had ever used oral contraceptives was lower among fish-eaters and

18   vegetarians than among meat-eaters. Of the 2,843 persons who participated in both the Oxford

19   Vegetarian Study and EPIC-Oxford, 2,338 (82%) were allocated to the same diet group at

20   recruitment to both studies, with an average 13 years gap between recruitment dates, indicating a

21   high level of consistency in diet group. At recruitment, 67% of vegetarians reported that they

22   had followed their current diet for more than five years.

23   Table 2 shows the RRs for fish-eaters and vegetarians relative to meat-eaters for each of

24   twenty cancer sites or groups of sites, plus all malignant cancers combined. There were 3,351

25   incident cancers before age 90 among the participants up to 31st December 2006. All but 339

26   (10%) of the 3,351 incident cancers are included in the twenty cancer sites or groups of sites

shown in Table 2. There was significant heterogeneity between dietary groups for four cancer

sites: stomach cancer, RRs compared to meat-eaters of 0.29 (0.07-1.20) in fish-eaters and

0.36 (0.16-0.78) in vegetarians, *P* for heterogeneity=0.007; ovarian cancer, RRs of 0.37

(0.18-0.77) in fish-eaters and 0.69 (0.45-1.07) in vegetarians, *P* for heterogeneity=0.007;

bladder cancer, RRs of 0.81 (0.36-1.81) in fish-eaters and 0.47 (0.25-0.89) in vegetarians, *P*

for heterogeneity=0.05; and cancers of the lymphatic and haematopoietic tissues, RRs of 0.85

(0.56-1.29) in fish-eaters and 0.55 (0.39-0.78) in vegetarians, *P* for heterogeneity=0.002.

Among the three main sub-groups of sites contributing to the group of cancers of the

lymphatic and haematopoietic tissues, the difference in incidence rates between diet groups

was non-significant for leukaemia and non-Hodgkin's lymphoma and was statistically

significant for multiple myeloma (*P* for heterogeneity=0.015); for both non-Hodgkin's

lymphoma and multiple myeloma, the RRs in vegetarians (but not in fish-eaters) were

significant compared to meat-eaters (RRs 0.57 (0.35-0.95) and 0.25 (0.08-0.73),

respectively). For the other cancer sites examined, there was no significant heterogeneity

between the three dietary groups, but the RR for cancer of the cervix was significantly higher

in vegetarians than in meat-eaters (2.08 (1.05-4.12)) and the RR for prostate cancer was

significantly lower in fish-eaters than in meat-eaters (0.57 (0.33-0.99)). The RRs for all

malignant neoplasms were 0.82 (0.73-0.93) among fish-eaters and 0.88 (0.81-0.96) among

vegetarians (*P* for heterogeneity between dietary groups=0.001).

We repeated the incidence rate ratios analysis after excluding the first 2 years of

follow-up so as to exclude cases diagnosed shortly after recruitment to the studies. This

analysis included 63,659 participants among whom there were 2,934 incident cancers before

age 90. The results were very similar to those shown in Table 2. For example, the RRs for all

malignant neoplasms were 0.80 (0.70-0.92) among fish-eaters and 0.92 (0.84-1.01) among

vegetarians (*P* for heterogeneity between dietary groups=0.003), and there was significant

heterogeneity of risk between the diet groups for stomach cancer, ovarian cancer and cancers

of the lymphatic and haematopoietic tissues, and the RR for bladder cancer in vegetarians

compared with meat-eaters remained statistically significant (results not shown). We also

repeated the analyses without adjustment for alcohol consumption, body mass index, physical

activity, parity and use of oral contraceptives, and the results were similar to those of the

fully-adjusted analyses reported in Table 2 (results not shown).

DISCUSSION

Few prospective studies have examined cancer incidence among vegetarians. In the

Adventist Health Study in California, vegetarians had a significantly lower risk for cancers of

the colon and prostate than non-vegetarians, but the risk for breast cancer did not differ

significantly between these dietary groups (Fraser et al, 1999). In Britain, the Oxford

Vegetarian Study suggested no large difference in the incidence of colorectal cancer between

vegetarians and non-vegetarians (Sanjoaquin et al, 2004), whereas the UK Women's Cohort

Study suggested that women who do not eat any meat have a lower risk for breast cancer than

meat-eaters (Taylor et al, 2007). The first results from EPIC-Oxford suggested that the

incidence of breast cancer did not differ significantly between vegetarians and non-

vegetarians (Travis et al, 2008), that the incidence of colorectal cancer was higher in

vegetarians than in meat-eaters, that the incidence of lung cancer was lower in fish-eaters

than in meat-eaters, and that the risk for all malignant cancers was lower in fish-eaters and

possibly lower in vegetarians than in meat-eaters (Key et al, 2009).

In the current paper we have pooled the individual participant data from the Oxford

Vegetarian Study and EPIC-Oxford, so this includes data previously reported from these

individual studies (Sanjoaquin et al, 2004; Travis et al, 2008; Key et al, 2009). The follow-up

time has been extended and, whereas our previous reports included results for only five

cancer sites, we have reported here the results for twenty cancer sites or groups of sites. The

aim of this report is descriptive, and we did not have strong prior hypotheses as to which cancers might show differences in risk between dietary groups. The results should therefore be interpreted cautiously, and for each significant finding we simply give a brief comment in relation to prior evidence and plausibility.

Stomach cancer risk differed significantly between the dietary groups, and was significantly lower in the vegetarians than in the meat-eaters, with a similarly (non-significantly) low risk among the fish-eaters. This observation was based on only 49 cases of stomach cancer. Previous research has suggested that processed meat may increase the risk for stomach cancer, perhaps due to the presence of N-nitroso compounds (Forman and Burley, 2006). It is therefore plausible that a meat-free diet could be associated with a reduction in the risk for stomach cancer. There is also some evidence that a high intake of fruit and vegetables might reduce the risk for stomach cancer, but the data are not consistent (Forman and Burley, 2006) and, although on average vegetarians eat more fruit and vegetables than meat-eaters, the difference in intake is modest (Key et al, 2009).

The risk for cancer of the cervix was significantly higher among vegetarians than among meat-eaters, with a similarly (non-significantly) high risk among the fish-eaters. The principal cause of cervical cancer is human papillomavirus. Dietary factors have been suspected of influencing risk, but no firm conclusions have been drawn (García-Closas et al, 2005). The increased risks observed in non-meat-eaters were based on only 50 cases overall and might be due to factors such as differences in attendance for cervical cancer screening, or to chance.

The risk for ovarian cancer differed significantly between the dietary groups, and was significantly lower among fish-eaters than among meat-eaters. In a review, Schulz et al, (2004) concluded that high meat consumption may be associated with an increased risk of ovarian cancer. The likely mechanism for such an effect is not clear, and the differences in risk for ovarian cancer which we observed could be due to chance or due to differences in

reproductive factors beyond the simple categories of parity and oral contraceptive use for which we were able to adjust.

Prostate cancer risk did not differ significantly between dietary groups, although there was a significantly lower risk among fish-eaters compared to meat-eaters. The role of diet in the aetiology of prostate cancer is poorly understood; there is some evidence that high intakes of dairy products might be associated with an increase in risk (Chan et al 2005), but to explore this hypothesis further in our data we would need to examine the cancer rates among vegans, among whom there are currently too few cancers to be informative.

The risk for bladder cancer was lower among vegetarians than among meat eaters, based on 85 cancers overall. Some previous studies have suggested that certain meats such as bacon might increase the risk for bladder cancer, perhaps due to preformed nitrosamines (Lijinsky, 1999; Michaud et al, 2006), and this area deserves further investigation.

We observed a striking difference between dietary groups in the risk for the group of cancers of the lymphatic and haematopoietic tissues, based on 257 cancers overall. The risk for these cancers was not significantly reduced among fish-eaters, but among vegetarians the risk was substantially lower than that among meat-eaters. Among the three major cancer types contributing to this grouping, the risks for non-Hodgkin's lymphoma and multiple myeloma, but not leukaemia, were significantly lower in vegetarians than in meat-eaters. Previous research has inconsistently suggested that consumption of meat and/or exposure to live animals and raw meat among farmers and butchers might be associated with an increased risk for some of these cancers (Zhang et al, 1999; Alexander et al, 2007). Potential mechanisms could include mutagenic compounds and viruses (Cross and Lim, 2006; Alexander et al, 2007).

We did not observe any significant difference in the incidence of colorectal cancer between dietary groups. Our earlier publications from the Oxford Vegetarian Study and EPIC-Oxford also did not report a reduction in risk for colorectal cancer among vegetarians

1   (Sanjoaquin et al, 2004; Key et al, 2009). We also noted previously in EPIC-Oxford that the

2   incidence of colorectal cancer among vegetarians was identical to that in the general population

3   of England and Wales (standardized incidence ratio 102% (95% CI 80-129%); Key et al, 2009).

4   In the Adventist Health Study a lower risk for colon cancer was observed among vegetarians

5   compared with non-vegetarians (rectal cancer was not reported; Fraser, 1999). In our pooled

6   analysis of mortality in five prospective studies, comprising the Adventist Mortality Study, the

7   Adventist Health Study, the Health Food Shoppers Study, the Oxford Vegetarian Study, and the

8   Heidelberg study, we observed no difference between vegetarians and non-vegetarians in

9   mortality from colorectal cancer (Key et al, 1999). The 2007 report from the World Cancer

10 Research Fund/American Institute for Cancer Research concluded that the evidence that high

11 intakes of red and processed meat cause colorectal cancer is convincing (WCRF/AICR, 2007).

12 In the largest single prospective study on this relationship, Cross et al (2007) reported that the

13 risk for colorectal cancer was increased by 20% at moderate red meat intakes (equivalent to

14 about 86 g/d in men and about 44 g/d in women). Meat intake among meat-eaters in EPIC-

15 Oxford was estimated as 78.1 and 69.7 g/d in men and women respectively (Key et al, 2009),

16 lower than intakes reported in the National Diet and Nutrition Survey for the United Kingdom

17 but still providing a substantial difference in intake between meat-eaters and non-meat-eaters. It

18 is possible that the current study did not have enough power to detect a moderate reduction in

19 the risk for colorectal cancer among vegetarians, but our null findings on vegetarians suggest

20 that the relationship of meat with the risk for colorectal cancer requires further research.

21   Total cancer incidence was significantly lower among both fish-eaters and vegetarians

22 than among meat-eaters. This difference in total cancer incidence between meat-eaters and non

23 meat-eaters could not be ascribed to any one of the major cancer sites examined. We are not

24 aware of other data comparing total cancer incidence in meat-eaters and non meat-eaters, and the

25 reason for this small difference is not known. More data are needed to further our understanding

26 of this observation, which if confirmed is likely to be due to differences for specific cancer sites.

The results presented here are simply descriptive of the incidence of cancer in fish-eaters and vegetarians relative to meat-eaters. More detailed analyses of individual cancer sites are needed to explore for example whether the differences observed might be linked to particular types of meat or to other dietary or lifestyle characteristics of non-meat-eaters that were not adjusted for in the current analysis.

A potential weakness of this type of study is the accuracy of the assessment of vegetarian status. Diet group was assigned on the basis of the answer to four questions, asking specifically about whether participants ever ate meat, fish, dairy products and eggs. When diet group in EPIC-Oxford was assigned on the basis of answers to the same four questions in a follow-up questionnaire five years later, 85% of vegetarians were allocated to the same diet group as at recruitment (Key et al, 2009), suggesting that the assessment of vegetarian status is accurate and stable over at least several years, and may be a substantially more stable dietary characteristic than epidemiological estimates of nutrient intakes.

In conclusion, this study suggests that the incidence of all malignant neoplasms combined may be lower among both fish-eaters and vegetarians than among meat-eaters. The most striking finding was the relatively low risk for cancers of the lymphatic and haematopoietic tissues among vegetarians.

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TABLE 1 Baseline characteristics by gender and diet group

Characteristic	Men			Women		
	Meat-eater	Fish-eater	Vegetarian	Meat-eater	Fish-eater	Vegetarian
Number of participants	8966	1712	5922	24732	7189	15888
Person-years of follow-up	108218	19698	75295	275651	79255	191584
Age at recruitment (years; %)						
20-29	11.8	15.2	22.6	11.2	21.5	32.7
30-39	18.8	29.5	31.6	17.9	30.8	29.0
40-49	22.2	26.8	21.5	27.6	23.6	19.2
50-59	20.5	13.5	10.4	24.5	13.6	9.6
60-69	18.8	9.9	7.3	13.5	6.9	5.5
70-79	6.7	4.2	4.8	4.6	2.9	2.9
80-89	1.1	1.0	1.7	0.7	0.6	1.0
Mean (SD)	48.5 (14.8)	43.4 (13.8)	41.4 (14.8)	47.3 (13.5)	40.9 (13.3)	38.2 (14.0)
Smoking (%)						
Never smoker	45.5	53.7	55.8	60.3	60.3	64.3
Former smoker	35.8	31.3	31.1	27.1	29.4	25.3
Light smoker*	11.5	11.2	8.9	6.9	7.0	7.0
Heavy smoker*	7.2	3.7	4.2	5.7	3.3	3.4
Body mass index (kg/m^2; %)						
<20.0	5.3	8.9	13.0	10.5	17.8	21.4
20.0-22.4	22.1	33.5	34.1	29.2	37.7	36.7
22.5-24.9	33.1	32.0	29.0	26.3	23.6	22.2
25.0-27.4	22.3	15.0	13.6	15.6	10.1	9.0
≥27.5	14.4	7.4	6.8	15.6	7.7	7.1
unknown	2.7	3.3	3.4	2.8	3.1	3.6
Mean (SD)	24.4 (3.3)	23.3 (3.1)	23.0 (3.1)	24.1 (4.1)	22.7 (3.4)	22.4 (3.4)
Alcohol consumption						

(g/d; %)						
<1	10.4	12.8	23.6	17.9	17.5	25.8
1-7	29.1	28.1	29.3	46.2	42.9	41.7
8-15	25.3	25.2	20.7	22.7	24.4	20.6
≥16	33.5	31.4	24.5	11.2	13.3	10.6
unknown	1.7	2.5	2.0	2.0	1.9	1.3
Mean (SD)	15.3 (16.5)	15.1 (16.8)	12.1 (16.3)	7.5 (9.3)	8.2 (10.0)	6.9 (9.4)
Physical activity level						
(%)						
Low	63.2	54.6	55.9	66.0	57.8	60.8
High	30.4	38.5	38.5	23.1	31.9	30.6
unknown	6.4	6.9	5.5	10.9	10.3	8.6
Parity (%)						
Nulliparous	-	-	-	27.2	46.7	56.3
1-2	-	-	-	48.6	38.2	32.0
>2	-	-	-	23.2	14.1	10.3
unknown	-	-	-	1.0	1.1	1.4
Ever used oral						
contraceptives (%)						
No	-	-	-	30.6	22.4	26.6
Yes	-	-	-	68.3	77.1	72.7
unknown	-	-	-	1.2	0.5	0.6

* Heavy smokers were participants who smoked 15 or more cigarettes per day; light smokers were all other current smokers including pipe or cigar smokers.

TABLE 2 Numbers of incident malignant cancers (N) and relative risks (RR) and their 95% confidence intervals (95% CI) by diet group among 33,698 meat-eaters, 8,901 fish-eaters and 21,810 vegetarians[1]

Cancer site (ICD-10 codes)	Meat eater N	RR	Fish-eater N	RR (95% CI)	Vegetarian N	RR (95% CI)	P for heterogeneity
Upper GI tract (C00-10, 13, 15)	56	1.00	4	0.44 (0.16-1.25)	18	0.81 (0.45-1.46)	0.218
Stomach (C16)	38	1.00	2	0.29 (0.07-1.20)	9	0.36 (0.16-0.78)	0.007
Colorectum (C18-20)	243	1.00	31	0.77 (0.53-1.13)	110	1.12 (0.87-1.44)	0.177
Colon (C18)	156	1.00	17	0.68 (0.41-1.14)	66	1.12 (0.81-1.54)	0.173
Rectum (C19-20)	87	1.00	14	0.92 (0.51-1.64)	44	1.12 (0.75-1.67)	0.776
Pancreas (C25)	46	1.00	6	0.82 (0.34-1.96)	19	0.94 (0.52-1.71)	0.898
Lung (C34)	114	1.00	8	0.59 (0.29-1.23)	43	1.11 (0.75-1.65)	0.225
Melanoma (C43)	116	1.00	21	0.89 (0.55-1.45)	49	0.88 (0.61-1.28)	0.765
Female breast (C50)	654	1.00	133	1.05 (0.86-1.28)	237	0.91 (0.77-1.08)	0.383
Cervix (C53)	17	1.00	10	2.05 (0.91-4.63)	23	2.08 (1.05-4.12)	0.069
Endometrium (C54)	71	1.00	8	0.61 (0.29-1.30)	22	0.75 (0.45-1.28)	0.304
Ovary (C56)	98	1.00	8	0.37 (0.18-0.77)	34	0.69 (0.45-1.07)	0.007
Prostate (C61)	207	1.00	14	0.57 (0.33-0.99)	70	0.87 (0.64-1.18)	0.092
Kidney (C64)	37	1.00	2	0.36 (0.09-1.52)	11	0.76 (0.36-1.58)	0.252
Bladder (C67)	65	1.00	7	0.81 (0.36-1.81)	13	0.47 (0.25-0.89)	0.050
Brain (C71)	44	1.00	11	1.39 (0.69-2.80)	26	1.25 (0.72-2.16)	0.581
Lymphatic/haematopoietic tissue (C81-96)	180	1.00	28	0.85 (0.56-1.29)	49	0.55 (0.39-0.78)	0.002
Non-Hodgkin's lymphoma (C82-85)	81	1.00	13	0.86 (0.47-1.58)	23	0.57 (0.35-0.95)	0.080
Multiple myeloma (C90)	34	1.00	4	0.72 (0.25-2.10)	4	0.25 (0.08-0.73)	0.015
Leukaemia (C91-95)	51	1.00	10	1.18 (0.58-2.40)	17	0.78 (0.43-1.43)	0.565
All sites (C00-97)	2205	1.00	317	0.82 (0.73-0.93)	829	0.88 (0.81-0.96)	0.001

[1] Estimated by Cox proportional hazards regression with age as the underlying time variable, adjusted for smoking (never smoker, former smoker, light smoker (<15 cigarettes/d, or cigar or pipe smokers only), heavy smoker (15 or more cigarettes/d)), alcohol consumption (<1, 1-7, 8-15, 16+ g ethanol/d, unknown), body mass index (<20.0, 20.0-22.4, 22.5-24.9, 25.0-27.4, 27.5+ kg/m^2, unknown), physical activity level (low, high, unknown) and, for the women-only cancers, parity (none, 1-2, 3+, unknown) and oral contraceptive use (ever, never, unknown), and stratified by sex (where appropriate) and study/method of recruitment, using separate models for each end point.