Cancer in British vegetarians: updated analyses of 4998 incident cancers in a cohort of 32,491 meat eaters, 8612 fish eaters, 18,298 vegetarians, and 2246 vegans[1–4]

Timothy J Key, Paul N Appleby, Francesca L Crowe, Kathryn E Bradbury, Julie A Schmidt, and Ruth C Travis

ABSTRACT

Background: Vegetarian diets might affect the risk of cancer.

Objective: The objective was to describe cancer incidence in vegetarians and nonvegetarians in a large sample in the United Kingdom.

Design: This was a pooled analysis of 2 prospective studies including 61,647 British men and women comprising 32,491 meat eaters, 8612 fish eaters, and 20,544 vegetarians (including 2246 vegans). Cancer incidence was followed through nationwide cancer registries. Cancer risk by vegetarian status was estimated by using multivariate Cox proportional hazards models.

Results: After an average follow-up of 14.9 y, there were 4998 incident cancers: 3275 in meat eaters (10.1%), 520 in fish eaters (6.0%), and 1203 in vegetarians (5.9%). There was significant heterogeneity between dietary groups in risks of the following cancers: stomach cancer [RRs (95% CIs) compared with meat eaters: 0.62 (0.27, 1.43) in fish eaters and 0.37 (0.19, 0.69) in vegetarians; *P*-heterogeneity = 0.006], colorectal cancer [RRs (95% CIs): 0.66 (0.48, 0.92) in fish eaters and 1.03 (0.84, 1.26) in vegetarians; *P*-heterogeneity = 0.033], cancers of the lymphatic and hematopoietic tissue [RRs (95% CIs): 0.96 (0.70, 1.32) in fish eaters and 0.64 (0.49, 0.84) in vegetarians; *P*-heterogeneity = 0.005], multiple myeloma [RRs (95% CIs): 0.77 (0.34, 1.76) in fish eaters and 0.23 (0.09, 0.59) in vegetarians; *P*-heterogeneity = 0.010], and all sites combined [RRs (95% CIs): 0.88 (0.80, 0.97) in fish eaters and 0.88 (0.82, 0.95) in vegetarians; *P*-heterogeneity = 0.0007].

Conclusion: In this British population, the risk of some cancers is lower in fish eaters and vegetarians than in meat eaters. *Am J Clin Nutr* 2014;100(suppl):378S–85S.

INTRODUCTION

Comparisons of cancer rates between different countries have shown that countries with relatively high intakes of meat and other animal foods generally have relatively high rates of some types of cancer such as colorectal, breast, and prostate cancer (1). These observations have led to the hypothesis that vegetarian diets might reduce the risk of certain cancers because of the absence of meat and fish or perhaps because of the relatively high intake of plant foods. Five prospective studies have been designed to recruit a large proportion of vegetarians and to follow them for cancer incidence: the Adventist Health Study (2), the Adventist Health Study II (3), the Oxford cohort of the European Prospective Investigation into Cancer and Nutrition (EPIC)–Oxford (4), the Oxford Vegetarian Study (5), and the UK Women's Cohort Study (6). In the Adventist Health Study, vegetarians had a significantly lower risk than did nonvegetarians for colon cancer and prostate cancer (2). In the Adventist Health Study II, vegetarians and vegans had a lower risk than did nonvegetarians of all cancers combined, and vegetarians had a lower risk of cancers of the gastrointestinal tract (3). A combined analysis of EPIC-Oxford and the Oxford Vegetarian Study also reported that vegetarians (including vegans) had a lower risk than did nonvegetarians for all cancers combined, as well as a lower risk of cancers of the stomach, bladder, and cancers of the lymphatic and hematopoietic tissue, but higher a risk of cervical cancer (7). In the UK Women's Cohort Study, a vegetarian diet was not associated with the risk of breast cancer (6).

To provide more information on cancer incidence in vegetarians, we report here the incidence of malignant cancer at 20 sites or groups of sites plus all incident malignant cancers combined. The analysis pooled data from 2 prospective studies in the United Kingdom: the Oxford Vegetarian Study (5) and the EPIC-Oxford cohort (4). This analysis is an update of analyses we published in 2009 (7); with longer follow-up, the number of incident cancers has increased by almost 50%. We present 2 categorizations of diet, one comparing cancer risk in meat eaters, fish eaters, and vegetarians (including vegans) and the second separating the vegans from the other vegetarians for the 3 most common cancer sites and for all malignant cancers combined. For colorectal cancer, there is substantial evidence that high intakes of meat are associated with an increased risk (8); therefore, there

[1] From the Cancer Epidemiology Unit, Nuffield Department of Population Health, University of Oxford, Oxford, United Kingdom.

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[4] Address correspondence to TJ Key, Cancer Epidemiology Unit, Nuffield Department of Population Health, University of Oxford, Richard Doll Building, Roosevelt Drive, Oxford OX3 7LF, United Kingdom. E-mail: tim.key@ceu.ox.ac.uk.

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was a strong prior hypothesis that vegetarians would have a lower risk of colorectal cancer than meat eaters. For the other cancer sites examined, there were not strong prior hypotheses that cancer risk would differ between vegetarians and meat eaters; therefore, the results presented should be interpreted as describing the incidence of cancer in vegetarians and nonvegetarians in this large cohort rather than as tests of well-defined prior hypotheses.

SUBJECTS AND METHODS

Recruitment of subjects

Participants in the Oxford Vegetarian Study were recruited throughout the United Kingdom between 1980 and 1984 (9). Vegetarian participants were recruited through advertisements, the news media, and word of mouth. Nonvegetarian participants were recruited as friends and relatives of the vegetarian participants. In total, 11,140 subjects were recruited. At recruitment, participants completed a questionnaire on their diet and other lifestyle factors. Diet group was assigned by using 4 questions on whether or not participants consumed meat, fish, dairy products, and eggs. Overall diet was examined by using a 45-item food-frequency questionnaire, including intake of meat or liver, and total meat intake was estimated from these 2 questions by using portion sizes of 99 g for meat and 60 g for liver; these food-frequency questions did not override the classification of diet group.

The EPIC-Oxford cohort was recruited throughout the United Kingdom between 1993 and 1999 (4). 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 United Kingdom 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. In total, 7421 participants were recruited by the GP method and 57,990 participants by the postal method. The main questionnaire included 4 questions on whether or not participants consumed meat, fish, dairy products, and eggs; and these 4 questions were used to assign participants into 1 of 4 diet groups: meat eaters (participants who ate meat, irrespective of whether they ate fish, dairy products, or eggs), fish eaters (participants who did not eat meat but did eat fish), vegetarians (participants who did not eat meat or fish), and vegans (participants who did not eat meat, fish, eggs, or dairy products). The questionnaire also included a 130-item food-frequency section, which included 11 questions on meat intake used to estimate total meat intake; these food-frequency questions did not override the classification of diet group. The baseline questionnaire can be viewed online at http://www.epic-oxford.org/files/epic-baseline-PQ.pdf. Participants were sent a second questionnaire ∼5 y after recruitment, including the same 4 questions on current intakes of meat, fish, dairy products, and eggs, to enable us to classify them according to diet group and compare this with diet group at recruitment. The 5-y follow-up questionnaire can be viewed online at http://www.epic-oxford.org/files/epic-followup1vs3-200302.pdf.

Definition and ascertainment of cancer

Participants in both studies were followed until 31 December 2010 by record linkage with the UK'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* (10), excluding code C44 (nonmelanoma 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.

Statistical analysis

Participants were excluded from the analysis if they were aged <20 or >89 y at recruitment, 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 61,647 participants (15,594 men, 46,053 women) who were censored on reaching the age of 90. There were 2842 participants who contributed follow-up data to both studies. RRs and their 95% CIs for 20 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 and using a clustered sandwich variance estimator to allow for intraparticipant correlation among individuals contributing person-years of follow-up for both the Oxford Vegetarian Study and EPIC-Oxford. The analyses were stratified by study protocol (Oxford Vegetarian Study participants, EPIC-Oxford GP-recruited participants, EPIC-Oxford postal recruited participants) and sex (except for cancers of the female breast, cervix, endometrium, ovary, and prostate) and adjusted for smoking (never smoker; former smoker; current smoker: <15 cigarettes/d or cigar or pipe smoker only; current smoker: ≥15 cigarettes/d), alcohol consumption (<1, 1–7, 8–15, or ≥16 g ethanol/d; unknown), and physical activity level [low, high, or unknown: for the Oxford Vegetarian Study, high means sport/keep fit and/or running/cycling at least twice per week, low means neither of these (where known); for EPIC-Oxford, low means an average of <3.5 h/wk cycling or other physical exercise, high means more than this (where known)]. The women-only cancers were additionally adjusted for parity (none, 1–2, ≥3, or unknown) and oral contraceptive use (ever, never, or unknown). In the main analysis, vegetarians and vegans were combined into a single group. In further analyses, for the 3 most common cancers and all cancers combined, vegans were examined as a separate group; and in further analyses for colorectal cancer we examined risk in relation to the quantity of meat consumed (categories of meat intake: ≥100, 50–99, or <50 g/d; fish eaters; vegetarians). In cases in which a subject could not be

TABLE 1
Baseline characteristics by sex and diet group[1]

Characteristic	Meat eater	Fish eater	Vegetarian	Vegan
Men				
No. of participants	8474	1634	4624	862
Age at recruitment (y)	48.9 ± 14.8[2]	43.6 ± 13.8	41.7 ± 14.9	38.9 ± 14.0
Smoking (%)				
Never smoker	45.7	53.9	55.4	60.4
Former smoker	36.0	31.1	31.0	29.5
Light smoker[3]	11.2	11.3	9.2	6.8
Heavy smoker[4]	7.1	3.7	4.4	3.2
BMI (kg/m^2)	24.5 ± 3.3	23.4 ± 3.1	23.2 ± 3.2	22.4 ± 2.9
Alcohol consumption (%)				
<1 g/d	10.3	12.6	21.1	29.6
1–7 g/d	29.3	27.8	29.2	29.7
8–15 g/d	25.0	25.1	21.9	17.1
≥16 g/d	33.5	31.8	25.9	20.5
Unknown	1.8	2.6	1.9	3.1
Alcohol consumption (g/d)	15.5 ± 16.8	15.4 ± 17.1	12.9 ± 16.7	10.8 ± 16.4
Physical activity level (%)				
Low	63.0	54.2	56.6	50.1
High	30.3	38.6	37.5	43.6
Unknown	6.7	7.2	5.9	6.3
Estimated nutrient intakes[5]				
Energy (MJ/d)	9.18 ± 2.46	8.90 ± 2.43	8.79 ± 2.39	8.01 ± 2.45
Protein (% of energy)	16.0 ± 2.8	13.9 ± 2.2	13.0 ± 1.9	12.9 ± 2.2
Carbohydrate (% of energy)	46.9 ± 6.5	49.8 ± 6.6	51.2 ± 6.8	54.6 ± 7.6
Total fat (% of energy)	31.9 ± 5.8	31.1 ± 6.1	31.1 ± 6.2	28.5 ± 7.1
Saturated fat (% of energy)	11.8 ± 3.3	10.7 ± 3.3	10.8 ± 3.4	6.5 ± 2.0
Dietary fiber (NSP; g/d)	18.5 ± 6.8	21.6 ± 7.5	22.2 ± 7.6	26.7 ± 9.0
Women				
No. of participants	24,017	6978	13,674	1384
Age at recruitment (y)	47.5 ± 13.4	40.9 ± 13.3	38.2 ± 13.9	36.7 ± 14.0
Smoking (%)				
Never smoker	60.2	60.4	64.5	62.3
Former smoker	27.2	29.5	25.1	26.6
Light smoker[3]	6.9	6.9	6.9	8.7
Heavy smoker[4]	5.7	3.2	3.4	2.5
BMI (kg/m^2)	24.2 ± 4.1	22.7 ± 3.4	22.5 ± 3.5	21.8 ± 2.9
Alcohol consumption (%)				
<1 g/d	17.7	17.2	23.7	35.0
1–7 g/d	46.2	42.7	42.2	38.3
8–15 g/d	22.7	24.6	21.6	15.8
≥16 g/d	11.3	13.5	11.1	9.5
Unknown	2.1	2.0	1.4	1.4
Alcohol consumption (g/d)	7.6 ± 9.4	8.3 ± 10.0	7.2 ± 9.6	6.2 ± 10.0
Physical activity level (%)				
Low	65.7	57.3	60.5	55.7
High	23.1	32.0	30.5	35.0
Unknown	11.2	10.7	9.0	9.2
Parity (%)				
Nulliparous	27.0	46.8	55.9	65.0
1–2	48.7	38.1	32.4	25.0
>2	23.4	14.0	10.3	8.8
Unknown	1.0	1.1	1.4	1.2
Ever used oral contraceptives (%)				
No	68.6	77.9	75.0	68.3
Yes	30.2	21.6	24.4	31.1
Unknown	1.2	0.4	0.6	0.7

(Continued)

categorized for a given factor (usually because the appropriate section of the questionnaire was left unanswered or incomplete), they were allocated to an "unknown" category. The main results were not adjusted for BMI because we considered that the differences in BMI between the dietary groups are largely caused by the differences in diet and therefore that BMI may mediate some of the differences in cancer risk between dietary groups, but we do report the effects on the RRs of further adjustment for

TABLE 1 (*Continued*)

Characteristic	Meat eater	Fish eater	Vegetarian	Vegan
Estimated nutrient intakes[5]				
Energy (MJ/d)	8.02 ± 2.10	7.73 ± 2.11	7.60 ± 2.09	6.96 ± 2.15
Protein (% of energy)	17.3 ± 3.0	14.8 ± 2.3	13.8 ± 2.1	13.5 ± 2.3
Carbohydrate (% of energy)	48.3 ± 6.1	51.3 ± 6.4	52.9 ± 6.5	56.1 ± 7.7
Total fat (% of energy)	31.5 ± 5.9	30.7 ± 6.4	30.3 ± 6.5	27.8 ± 7.4
Saturated fat (% of energy)	11.5 ± 3.3	10.6 ± 3.3	10.6 ± 3.4	6.5 ± 2.2
Dietary fiber (NSP; g/d)	18.8 ± 6.7	21.1 ± 7.5	21.4 ± 7.8	25.7 ± 9.4

[1] Persons who participated in both the Oxford Vegetarian Study and EPIC-Oxford are grouped according to their characteristics at recruitment to EPIC-Oxford. EPIC, European Prospective Investigation into Cancer and Nutrition; NSP, nonstarch polysaccharides.

[2] Mean ± SD (all such values).

[3] Light smokers were all other current smokers including pipe or cigar smokers.

[4] Heavy smokers were participants who smoked ≥15 cigarettes/d.

[5] Among EPIC-Oxford participants with reliable nutrient intake data (12,258 men, 40,542 women).

BMI (in kg/m^2; <20.0, 20.0–22.4, 22.5–24.9, 25.0–27.4, ≥27.5, or unknown).

Statistical significance was set at the 5% level. All statistical analyses were conducted by using Stata Statistical Software: release 10 (StataCorp LP).

RESULTS

The characteristics of the participants in each of the 4 diet groups are given in **Table 1**. One-third of the participants were vegetarians and three-quarters were women. The mean age at recruitment was lower in fish eaters, vegetarians, and vegans than in meat eaters. Smoking rates were low overall, with only 14.1% of meat eaters, 11.0% of fish eaters, 11.2% of vegetarians, and 10.7% of vegans reporting that they were smokers at the time of recruitment. Median BMI was 1.4 units lower in vegetarians than in meat eaters and median alcohol consumption was 0.9 g/d lower in vegetarians than in meat eaters. Fish eaters had a mean BMI similar to vegetarians and their alcohol consumption was similar to that of meat eaters; vegans had the lowest mean BMI and alcohol consumption. The proportions of men and women who reported a relatively high level of physical activity were higher in fish eaters, vegetarians, and vegans than in meat eaters. The proportion of women who were nulliparous at recruitment was highest among vegans and lowest among meat eaters, and the proportion of women who had ever used oral contraceptives was lower among fish eaters and vegetarians than among meat eaters and vegans. In both men and women, vegans had the lowest intakes of energy, protein, fat, and saturated fat and the highest intakes of carbohydrate and dietary fiber; intakes of fish eaters and vegetarians were intermediate between those of meat eaters and vegans.

Of the 2842 persons who participated in both the Oxford Vegetarian Study and EPIC-Oxford, 2267 (80%) were allocated to the same diet group (meat eater, fish eater, or vegetarian) at recruitment to both studies, with an average 13-y gap between recruitment dates, indicating a high level of consistency in diet group. At recruitment, 66% of vegetarians reported that they had followed their current diet for >5 y. Of the 53,901 EPIC-Oxford participants, 35,956 completed a further questionnaire ∼5 y after recruitment and could be characterized according to diet group at this time. Of these, 31,558 (88%) were allocated to the same diet group as they had been at recruitment.

There were 4998 incident cancers before age 90 among the participants up to 31 December 2010, with a mean follow-up of 14.9 y. All but 477 (10%) of the 4998 incident cancers are included in the 20 cancer sites or groups of sites shown in **Tables 2** and **3**. The RRs for fish eaters and vegetarians (including vegans) relative to meat eaters for each of 20 cancer sites or groups of sites, plus all malignant cancers combined, are shown in Table 2. There was significant heterogeneity between dietary groups for the following cancer sites: stomach cancer [RRs (95% CIs) compared with meat eaters: 0.62 (0.27, 1.43) in fish eaters and 0.37 (0.19, 0.69) in vegetarians; *P*-heterogeneity = 0.006], colorectal cancer [RRs (95% CIs): 0.66 (0.48, 0.92) in fish eaters and 1.03 (0.84, 1.26) in vegetarians; *P*-heterogeneity = 0.033], cancers of the lymphatic and hematopoietic tissue [RRs (95% CI): 0.96 (0.70, 1.32) in fish eaters and 0.64 (0.49, 0.84) in vegetarians; *P*-heterogeneity = 0.005], and multiple myeloma [RRs (95% CIs): 0.77 (0.34, 1.76) in fish eaters and 0.23 (0.09, 0.59) in vegetarians; *P*-heterogeneity = 0.010]. For the other cancer sites examined there was no significant heterogeneity between the 3 dietary groups, but the RRs for the following 3 cancers were significantly lower in fish eaters than in meat eaters: colon cancer (RR: 0.64; 95% CI: 0.42, 0.97), ovarian cancer (RR: 0.55; 95% CI: 0.32, 0.92), and kidney cancer (RR: 0.22; 95% CI: 0.05, 0.92). There was also significant heterogeneity between dietary groups for all sites combined [RRs (95% CIs) compared with meat eaters: 0.88 (0.80, 0.97) in fish eaters and 0.88 (0.82, 0.95) in vegetarians; *P*-heterogeneity = 0.0007].

When vegans were examined as a separate group for the 3 commonest cancers, with meat eaters as the reference group, there were no significant associations with risk of colorectal, breast, or prostate cancer, but vegans had a 19% lower risk than did meat eaters for all cancers combined (Table 3).

In analyses with additional adjustment for BMI, there were small changes in RRs (Tables 2 and 3). For 2 relations, the RRs were no longer significant after additional adjustment for BMI: the RR for vegetarians compared with meat eaters changed from 0.62 to 0.65 (95% CI: 0.40, 1.03) for bladder cancer and the RR for vegans for all cancers combined changed from 0.81 to 0.82 (95% CI: 0.68, 1.00).

In further analyses of colorectal cancer, with participants with an intake of at least 100 g of meat/d as the reference group, RRs were 0.83 (95% CI: 0.65, 1.06) for participants with a meat intake

TABLE 2
Incident malignant cancers and RRs (95% CIs) by diet group among 32,491 meat eaters, 8612 fish eaters, and 20,544 vegetarians and vegans[1]

	Meat eaters		Fish eaters		Vegetarians and vegans		
Cancer site (ICD-10 codes) and model	No. of cancers	RR	No. of cancers	RR (95% CI)	No. of cancers	RR (95% CI)	*P*-heterogeneity[2]
Upper GI tract (C00–10, 13, 15)							
Basic	88	1.00	11	0.72 (0.38, 1.38)	35	0.94 (0.62, 1.43)	0.61
+BMI		1.00		0.73 (0.38, 1.39)		0.93 (0.61, 1.43)	0.62
Stomach (C16)							
Basic	53	1.00	6	0.62 (0.27, 1.43)	11	0.37 (0.19, 0.69)	0.006
+BMI		1.00		0.64 (0.27, 1.50)		0.38 (0.20, 0.71)	0.01
Colorectum (C18–20)							
Basic	382	1.00	43	0.66 (0.48, 0.92)	154	1.03 (0.84, 1.26)	0.033
+BMI		1.00		0.67 (0.48, 0.92)		1.04 (0.84, 1.28)	0.032
Colon (C18)							
Basic	246	1.00	26	0.64 (0.42, 0.97)	92	0.99 (0.76, 1.30)	0.099
+BMI		1.00		0.65 (0.43, 0.98)		1.01 (0.77, 1.33)	0.11
Rectum (C19–20)							
Basic	136	1.00	17	0.71 (0.43, 1.18)	62	1.10 (0.80, 1.50)	0.30
+BMI		1.00		0.70 (0.42, 1.17)		1.08 (0.79, 1.48)	0.30
Pancreas (C25)							
Basic	80	1.00	10	0.80 (0.41, 1.57)	22	0.73 (0.44, 1.21)	0.43
+BMI		1.00		0.77 (0.39, 1.52)		0.70 (0.42, 1.17)	0.36
Lung (C34)							
Basic	166	1.00	12	0.60 (0.33, 1.08)	58	1.16 (0.83, 1.61)	0.12
+BMI		1.00		0.59 (0.32, 1.07)		1.09 (0.78, 1.53)	0.15
Melanoma (C43)							
Basic	191	1.00	37	0.93 (0.65, 1.35)	71	0.79 (0.59, 1.07)	0.32
+BMI		1.00		0.92 (0.64, 1.34)		0.78 (0.57, 1.05)	0.27
Female breast (C50)							
Basic	900	1.00	202	1.07 (0.92, 1.26)	352	0.93 (0.82, 1.07)	0.29
+BMI		1.00		1.09 (0.93, 1.28)		0.96 (0.83, 1.10)	0.32
Cervix (C53)							
Basic	21	1.00	13	1.98 (0.96, 4.08)	27	1.78 (0.93, 3.40)	0.12
+BMI		1.00		2.11 (1.02, 4.37)		1.90 (1.00, 3.60)	0.075
Endometrium (C54)							
Basic	118	1.00	17	0.75 (0.44, 1.26)	42	0.91 (0.62, 1.33)	0.53
+BMI		1.00		0.82 (0.48, 1.38)		0.99 (0.67, 1.45)	0.74
Ovary (C56)							
Basic	148	1.00	17	0.55 (0.32, 0.92)	56	0.86 (0.61, 1.20)	0.073
+BMI		1.00		0.56 (0.33, 0.94)		0.87 (0.61, 1.22)	0.089
Prostate (C61)							
Basic	327	1.00	30	0.76 (0.52, 1.11)	100	0.84 (0.66, 1.07)	0.19
+BMI		1.00		0.74 (0.51, 1.09)		0.83 (0.64, 1.06)	0.15
Kidney (C64)							
Basic	57	1.00	2	0.22 (0.05, 0.92)	21	0.90 (0.51, 1.60)	0.12
+BMI		1.00		0.23 (0.05, 0.99)		1.02 (0.58, 1.78)	0.13
Bladder (C67)							
Basic	91	1.00	9	0.68 (0.35, 1.35)	24	0.62 (0.38, 0.99)	0.10
+BMI		1.00		0.72 (0.36, 1.43)		0.65 (0.40, 1.03)	0.15
Brain (C71)							
Basic	56	1.00	16	1.57 (0.88, 2.81)	33	1.29 (0.78, 2.13)	0.28
+BMI		1.00		1.60 (0.90, 2.85)		1.31 (0.79, 2.17)	0.25
Lymphatic/hematopoietic tissue (C81–96)							
Basic	284	1.00	49	0.96 (0.70, 1.32)	79	0.64 (0.49, 0.84)	0.005
+BMI		1.00		0.96 (0.70, 1.32)		0.64 (0.48, 0.84)	0.006
Non-Hodgkin lymphoma (C82–85)							
Basic	128	1.00	27	1.15 (0.74, 1.78)	39	0.71 (0.48, 1.05)	0.11
+BMI		1.00		1.14 (0.74, 1.77)		0.70 (0.47, 1.04)	0.11
Multiple myeloma (C90)							
Basic	53	1.00	7	0.77 (0.34, 1.76)	5	0.23 (0.09, 0.59)	0.010
+BMI		1.00		0.80 (0.35, 1.81)		0.23 (0.09, 0.60)	0.011
Leukemia (C91–95)							
Basic	86	1.00	13	0.94 (0.51, 1.74)	29	0.87 (0.55, 1.39)	0.84
+BMI		1.00		0.92 (0.50, 1.70)		0.85 (0.53, 1.36)	0.78

(Continued)

TABLE 2 (*Continued*)

Cancer site (ICD-10 codes) and model	Meat eaters No. of cancers	Meat eaters RR	Fish eaters No. of cancers	Fish eaters RR (95% CI)	Vegetarians and vegans No. of cancers	Vegetarians and vegans RR (95% CI)	*P*-heterogeneity[2]
All sites (C00–97)							
Basic	3275	1.00	520	0.88 (0.80, 0.97)	1203	0.88 (0.82, 0.95)	0.0007
+BMI		1.00		0.89 (0.81, 0.98)		0.90 (0.93, 0.96)	0.003

[1] Estimated by Cox proportional hazards regression with age as the underlying time variable. The basic model adjusted for smoking [never smoker, former smoker, light smoker (<15 cigarettes/d or cigar or pipe smokers only), heavy smoker (≥15 cigarettes/d)], alcohol consumption (<1, 1–7, 8–15, or ≥16 g ethanol/d; unknown), physical activity level (low, high, or unknown), and for the women-only cancers, parity (none, 1–2, ≥3, or unknown) and oral contraceptive use (ever, never, or unknown), stratified by sex (except for cancers of the female breast, cervix, endometrium, ovary, and prostate) and study/method of recruitment by using separate models for each endpoint. The +BMI model was further adjusted for BMI (in kg/m^2; <20, 20.0–22.4, 22.5–24.9, 25.0–27.4, ≥27.5, or unknown). GI, gastrointestinal; ICD-10, *International Classification of Diseases, 10th revision*.

[2] Test for heterogeneity of risk between the 3 diet groups.

of 50–99 g/d, 1.02 (95% CI: 0.79, 1.31) for participants with a meat intake of <50 g/d, 0.63 (95% CI: 0.44, 0.90) for fish eaters, and 0.98 (95% CI: 0.76, 1.26) for vegetarians (including vegans). The corresponding values after further adjustment for BMI were 0.83 (95% CI: 0.65, 1.06), 1.01 (95% CI: 0.79, 1.31), 0.63 (95% CI: 0.44, 0.90), and 0.98 (95% CI: 0.76, 1.27), respectively.

DISCUSSION

In the current article we pooled the individual participant data from the Oxford Vegetarian Study and EPIC-Oxford; these include data previously reported from these individual studies and the results here supersede those previously published (7, 11–13). The follow-up time was extended and we report here the results for 20 cancer sites or groups of sites; in comparison with our most recent previous article, the current analysis reports similar differences in risks of stomach cancer and cancer of the lymphatic/hematopoietic tissue between diet groups, but the previously reported difference in risk of ovarian cancer between dietary groups is no longer significant. With the use of data from these cohorts, we also report here for the first time analyses of risks in 4 distinct diet groups, including vegans.

It is plausible that a meat-free diet could be associated with a reduction in the risk of stomach cancer because previous research suggested that processed meat might increase the risk of stomach cancer (8), perhaps due to the presence of *N*-nitroso compounds (14). There is also some evidence that a high intake of fruit and vegetables might reduce the risk of stomach cancer, but the data are not consistent (14), and although on average vegetarians eat more fruit and vegetables than meat eaters, the difference in intake is modest (15). We observed that stomach cancer risk was 63% lower in vegetarians (including vegans) compared with meat eaters, although this estimate was based on a small number of cases and more research is needed to confirm this finding.

In our extended analysis we found evidence that colorectal cancer risk differed between diet groups: whereas we observed

TABLE 3
Incident malignant cancers and RRs (95% CIs) by diet group among 32,491 meat eaters, 8612 fish eaters, 18,298 vegetarians, and 2246 vegans[1]

Cancer site (ICD-10 codes) and model	Meat eaters No. of cancers	Meat eaters RR	Fish eaters No. of cancers	Fish eaters RR (95% CI)	Vegetarians No. of cancers	Vegetarians RR (95% CI)	Vegans No. of cancers	Vegans RR (95% CI)	*P*-heterogeneity[2]
Colorectum (C18–20)									
Basic	382	1.00	43	0.67 (0.48, 0.92)	135	1.00 (0.81, 1.24)	19	1.29 (0.81, 2.07)	0.047
+BMI		1.00		0.67 (0.48, 0.92)		1.01 (0.81, 1.25)		1.31 (0.82, 2.11)	0.045
Female breast (C50)									
Basic	900	1.00	202	1.07 (0.92, 1.26)	325	0.94 (0.82, 1.08)	27	0.87 (0.59, 1.28)	0.45
+BMI		1.00		1.09 (0.93, 1.28)		0.96 (0.84, 1.10)		0.91 (0.61, 1.34)	0.50
Prostate (C61)									
Basic	327	1.00	30	0.76 (0.52, 1.11)	91	0.87 (0.68, 1.12)	9	0.62 (0.31, 1.22)	0.25
+BMI		1.00		0.74 (0.51, 1.08)		0.86 (0.66, 1.11)		0.61 (0.31, 1.20)	0.20
All sites (C00–97)									
Basic	3275	1.00	520	0.88 (0.80, 0.97)	1098	0.89 (0.83, 0.96)	105	0.81 (0.66, 0.98)	0.001
+BMI		1.00		0.89 (0.81, 0.98)		0.90 (0.84, 0.97)		0.82 (0.68, 1.00)	0.006

[1] Estimated by Cox proportional hazards regression with age as the underlying time variable. The basic model adjusted for smoking [never smoker, former smoker, light smoker (<15 cigarettes/d or cigar or pipe smokers only), heavy smoker (≥15 cigarettes/d)], alcohol consumption (<1, 1–7, 8–15, or ≥16 g ethanol/d; unknown), physical activity level (low, high, or unknown), and for the women-only cancers, parity (none, 1–2, ≥3, or unknown) and oral contraceptive use (ever, never, or unknown), stratified by sex (except for cancers of the female breast, cervix, endometrium, ovary, and prostate) and study/method of recruitment by using separate models for each endpoint. The +BMI model was further adjusted for BMI (in kg/m^2; <20, 20.0–22.4, 22.5–24.9, 25.0–27.4, ≥27.5, or unknown). ICD-10, *International Classification of Diseases, 10th revision*.

[2] Test for heterogeneity of risk between the 4 diet groups.

a 34% lower risk in fish eaters than in meat eaters, colorectal cancer risk did not differ between vegetarians or vegans and meat eaters, and the risk in meat eaters with moderate and low intakes did not differ from that in meat eaters with high intakes of meat. We also noted previously in EPIC-Oxford that the incidence of colorectal cancer among vegetarians was identical to that in the general population of England and Wales [standardized incidence ratio: 102%; 95% CI: 80%, 129% (13)]. In contrast, results from studies in Seventh Day Adventists suggested that there may be a lower risk of colorectal cancer in vegetarians than in meat eaters: in the Adventist Health Study, a lower risk of colon cancer was observed among vegetarians compared with nonvegetarians (rectal cancer was not reported) (2). In the Adventist Health Study II, the risk of cancers of the gastrointestinal tract was significantly lower in lactovegetarians than in nonvegetarians and also nonsignificantly lower in the other vegetarian groups, but this is difficult to interpret because results were not reported for colorectal cancer (3). In a pooled analysis of mortality in 5 prospective studies comprising the Adventist Mortality Study, the Adventist Health Study, the Health Food Shoppers Study, the Oxford Vegetarian Study, and the Heidelberg study, there was no difference between vegetarians and nonvegetarians in mortality from colorectal cancer (16). The 2007 report from the World Cancer Research Fund/American Institute for Cancer Research concluded that the evidence that high intakes of red and processed meat cause colorectal cancer is convincing (8). This conclusion was restated in a subsequent update on colorectal cancer (17), but this review did not include the null results of a large pooled analysis reported in an abstract (18). It is possible that the current study did not have enough power to detect a moderate reduction in the risk of colorectal cancer among vegetarians, but our null findings on vegetarians suggest that the relation of meat consumption with risk of colorectal cancer requires further research.

The risk of ovarian cancer was lower in fish eaters than in meat eaters. However, a recent meta-analysis of 8 prospective studies found no evidence of an association between meat intake and the risk of ovarian cancer (19). The differences in risk of ovarian cancer that we observed could be due to chance or due to differences in reproductive and hormonal factors beyond the simple categories of parity and oral contraceptive use for which we were able to adjust.

The risk of kidney cancer was lower in fish eaters than in meat eaters, and the risk of bladder cancer was lower in vegetarians than in meat eaters, although the latter association was no longer significant after further adjustment for BMI. Meat consumption was not judged to be associated with these cancers in an expert review (8).

The risk of cancers of the lymphatic and hematopoietic tissues was 36% lower in vegetarians (including vegans) compared with meat eaters, and within this group of cancers, vegetarians had a significantly lower risk of multiple myeloma (by 77%). Previous research 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 of some of these cancers (20, 21). Potential mechanisms could include mutagenic compounds and viruses (21, 22) and perhaps phytanic acid (23). However, recent large studies have not shown an association of meat intake with risk of lymphoma (24, 25).

Total cancer incidence was 12% lower in fish eaters, 11% lower in vegetarians, and 19% lower in vegans compared with meat eaters. These differences in total cancer incidence between diet groups could not readily be ascribed to any of the major cancer sites examined. The results of the Adventist Health Study II were similar, with total cancer risk significantly lower in vegetarians and in vegans than in nonvegetarians, by 8% and 16%, respectively (3).

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 4 questions asking whether participants ever ate meat, fish, dairy products, and eggs. When the diet group in EPIC-Oxford was assigned on the basis of answers to the same 4 questions in a follow-up questionnaire 5 y later, 88% of participants who completed the follow-up questionnaire and could be characterized according to diet group were allocated to the same diet group as at recruitment, 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 epidemiologic estimates of nutrient intakes. Some participants changed diet group during the follow-up period of the study, but this would be expected to attenuate any true differences in risk between diet groups rather than cause spurious associations.

Our analyses were designed to be descriptive of differences in risk between diet groups. We adjusted for nondietary confounding factors such as smoking and other lifestyle factors, but we did not adjust the main analyses for any other aspects of diet or for BMI, because differences between groups in nutrient intake and BMI are substantially determined by diet group. Further adjustment for BMI caused only small changes to RRs.

In conclusion, this study suggests that the risk of cancer is lower in fish eaters, vegetarians, and vegans than in meat eaters. Further research is needed to determine which cancer sites and types account for this overall reduction in risk.

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