

# Mortality in British vegetarians: results from the European Prospective Investigation into Cancer and Nutrition (EPIC-Oxford)<sup>1–4</sup>

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## ABSTRACT

**Background:** Few prospective studies have examined the mortality of vegetarians.

**Objective:** We present results on mortality among vegetarians and nonvegetarians in the European Prospective Investigation into Cancer and Nutrition (EPIC-Oxford).

**Design:** We used a prospective study of men and women recruited throughout the United Kingdom in the 1990s.

**Results:** Among 64,234 participants aged 20–89 y for whom diet group was known, 2965 had died before age 90 by 30 June 2007. The death rates of participants are much lower than average for the United Kingdom. The standardized mortality ratio for all causes of death was 52% (95% CI: 50%, 54%) and was identical in vegetarians and in nonvegetarians. Comparing vegetarians with meat eaters among the 47,254 participants who had no prevalent cardiovascular disease or malignant cancer at recruitment, the death rate ratios adjusted for age, sex, smoking, and alcohol consumption were 0.81 (95% CI: 0.57, 1.16) for ischemic heart disease and 1.03 (95% CI: 0.90, 1.16) for all causes of death.

**Conclusions:** The mortality of both the vegetarians and the nonvegetarians in this study is low compared with national rates. Within the study, mortality from circulatory diseases and all causes is not significantly different between vegetarians and meat eaters, but the study is not large enough to exclude small or moderate differences for specific causes of death, and more research on this topic is required. *Am J Clin Nutr* 2009;89(suppl):1613S–9S.

## INTRODUCTION

The health status of vegetarians can be assessed through several approaches. Dietary intake and nutritional status can be measured and compared with reference values. Other indexes of health can be measured, such as body mass index (BMI; in kg/m<sup>2</sup>), serum lipid concentrations, and blood pressure, and the likely effect on health and disease risk can be estimated. The incidence of disease and mortality can also be measured directly. This is best done by conducting prospective studies in which large numbers of vegetarians are recruited and then followed over many years, during which disease rates and mortality are recorded and compared either with national rates for the country in which they are living or with nonvegetarians recruited into the same prospective study.

Several prospective studies have been set up to study the long-term health and mortality of vegetarians. In the United States, the Adventist Mortality Study was established in 1960 (1), the

Adventist Health Study was established in 1974 (2), and the Adventist Health Study-2 began in 2002 (3). In Britain, the Health Food Shoppers Study (4, 5) and the Oxford Vegetarian Study (6, 7) were established in the 1970s and 1980s, respectively; each included about 11,000 subjects and used a relatively short questionnaire. The European Prospective Investigation into Cancer and Nutrition–Oxford (EPIC-Oxford) cohort was established in the 1990s and includes about 65,000 participants (8). In this article, we describe the mortality of participants in the EPIC-Oxford cohort. We compare the mortality from major causes of death of all the participants in the study with contemporary national rates for England and Wales, and then we compare the mortality of vegetarians and meat eaters without prior disease, focusing on mortality from circulatory diseases and all causes combined.

## SUBJECTS AND METHODS

### Recruitment of participants

The EPIC-Oxford cohort was recruited between 1993 and 1999. Further details of the recruitment methods and the baseline characteristics of the participants were described elsewhere (8). The EPIC-Oxford cohort is one component of the EPIC, a collaborative study of 500,000 men and women in 10 European countries (9).

Two methods of recruitment were used: general practice (GP) recruitment and postal recruitment. A multicenter research ethics committee approved the protocol. EPIC nurses working in GP offices in Oxfordshire, Buckinghamshire, and Greater Manchester recruited people from the general population through GPs. All men and women aged 35–69 y on the list of each collaborating GP were invited to participate. Questionnaires were mailed to consenting participants, and appointments were made to attend the GP's office for an interview with the nurse. The nurse took anthropometric and blood pressure measurements, a 30-mL

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blood sample, and checked the completed questionnaire. In addition, a pilot recruitment phase was conducted by collaborating GPs in Scotland who recruited 900 women aged 40–59 y from those attending the office for other reasons such as minor ailments and menopausal symptoms. The GP method recruited 7423 participants.

Postal recruitment, aimed at those aged  $\geq 20$  y, 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 (6). Respondents were invited to give names and addresses of relatives and friends who might also be interested in receiving a questionnaire, and questionnaires were mailed to all these potential participants. In addition, a short questionnaire (or insert) was distributed to all members of the Vegan Society, enclosed in health- or diet-interest magazines, and displayed on counters of health food shops. The insert was contained on a single page, which could be folded and sealed for prepaid return mailing to the study office. The main questionnaire was then mailed to all those who returned an insert. Participants recruited by these postal methods and who completed the main questionnaire were asked if they would be willing to provide a blood sample. The participant's GP was then approached to take a blood sample on behalf of EPIC-Oxford. These postal methods recruited 58,042 participants.

### Diet group and food and nutrient intakes

Participants were categorized into 1 of 4 diet groups according to their replies to 4 questions: Do you eat meat? Do you eat fish? Do you eat dairy products? Do you eat eggs? For each of these 4 questions, participants were asked to reply yes or no, and, if they replied no, to record their age when they last ate the food group concerned. From these 4 questions, 4 diet groups were established: meat eaters (those that eat meat), fish eaters (those that do not eat meat but do eat fish), vegetarians (those that do not eat meat or fish but do eat dairy products or eggs or both), and vegans (those that eat no animal products). For the women recruited in the pilot phase of the study, and the first 1300 men and women recruited by EPIC nurses, these 4 dietary categorization questions were not asked, and diet group was assigned according to responses provided in the food-frequency questionnaire (described next). In this article, the vegans are included with the vegetarians because there were too few deaths among the vegans to report separately.

Participants completed a food-frequency questionnaire (10, 11). Each participant estimated their average frequency of intake of 130 foods and drinks during the previous 12 mo: never or  $< 1$  time/mo, 1–3 times/mo, 1 time/wk, 2–4 times/wk, 5–6 times/wk, 1 time/d, 2–3 times/d, 4–5 times/d, or  $\geq 6$  times/d. Daily mean nutrient intakes were estimated with the use of standard portion sizes, derived largely from the Ministry of Agriculture Fisheries and Food (12), and nutrient contents were estimated by using the fifth edition of *McCance and Widdowson's The Composition of Foods* (13) and its supplements. Alcoholic drinks were included in the food-frequency questionnaire; there were questions for wines, beers, fortified wines, and spirits, for which participants were asked to report their consumption (units of glass, half pint, glass, and single measure, respectively) in the same frequency categories as for all the other items.

### Nondietary characteristics

Self-reported height and weight were recorded in the main questionnaire, except for the first 2215 participants recruited by a GP or nurse for whom height and weight were directly measured. Participants were further characterized according to their smoking habits and alcohol consumption, and they were also asked to report if any of a list of specified diseases or conditions had been diagnosed and to give details of prescribed medication for any condition.

### Follow-up

All participants who could be traced were followed up by record linkage with the United Kingdom's National Health Service Central Register, which provides information on cancer diagnoses and on all deaths. In addition, participants were sent follow-up questionnaires for self-completion  $\approx 5$  and 10 y after joining the study, designed to provide information on changes in lifestyle, diet, and morbidity.

### Statistical analysis

The analyses were restricted to participants aged 20–89 y at recruitment who were followed up by record linkage and for whom diet group was unambiguous. Standardized mortality ratios (SMRs) for vegetarians and nonvegetarians were calculated from deaths before age 90 y by comparison with contemporary mortality data for England and Wales (14); the SMR is the ratio of the observed number of deaths to the number of deaths expected from the national rates, standardized for sex and age, and expressed as a percentage. Cox regression was used to calculate death rate ratios (DRRs), comparing death rates among participants with known smoking habits and no prior disease (no previous diagnosis of myocardial infarction, stroke, or cancer) with age as the underlying time variable (for convenience, DRRs are described henceforth as being adjusted for age), stratified by method of recruitment, and adjusted for sex and smoking. Participants were followed from the age in days at which they completed the dietary questionnaire to their age at exit, defined as the age of death, emigration, loss to follow-up, or end of follow-up, whichever came first. The proportional hazards assumption for each model was tested by the method of Grambsch and Therneau (15), and no significant departures were observed. Smoking was categorized as never smoker (never smoked  $\geq 1$  cigarette/d for  $\geq 1$  y), former smoker, light smoker ( $< 15$  cigarettes/d and pipe or cigar smokers), or heavy smoker ( $\geq 15$  cigarettes/d). Statistical significance was set at the 5% level, and 95% CIs were calculated for both the SMRs and DRRs. All statistical analyses were conducted with the use of STATA statistical software, release 9 (StataCorp, College Station, TX).

## RESULTS

### SMRs for the whole cohort

The SMRs for the 64,234 participants in the EPIC-Oxford study aged 20–89 who were followed by record linkage and for whom diet group was known, for various causes of death based on deaths before age 90 up to 30 June 2007, are shown in **Table 1**.

**TABLE 1**

Standardized mortality ratios (SMRs) for selected causes of death among 64,234 participants (nonvegetarians and vegetarians) in the European Prospective Investigation into Cancer and Nutrition Oxford cohort<sup>1</sup>

Cause of death (ICD9 codes)	Nonvegetarians		Vegetarians	
	Deaths	SMR (95% CI)	Deaths	SMR (95% CI)
	<i>n</i>	%	<i>n</i>	%
All malignant neoplasms (140–208)	1040	70 (66, 74)	271	69 (62, 78)
Stomach cancer (151)	24	46 (30, 69)	3	22 (4, 63)
Colorectal cancer (153–154)	97	67 (54, 82)	30	81 (55, 115)
Pancreatic cancer (157)	47	70 (52, 94)	14	85 (46, 142)
Lung cancer (162)	107	34 (28, 41)	24	31 (20, 46)
Female breast cancer (174)	186	94 (81, 109)	50	91 (68, 120)
Ovarian cancer (183)	71	96 (75, 121)	20	113 (69, 174)
Prostate cancer (185)	50	92 (68, 121)	12	75 (39, 130)
Benign and unspecified neoplasms (210–239)	14	54 (30, 91)	4	57 (15, 145)
Endocrine diseases (240–279)	22	32 (20, 49)	9	47 (21, 89)
Mental disorders (290–319)	26	36 (24, 53)	9	38 (17, 72)
Diseases of the nervous system (320–389)	64	57 (44, 73)	18	54 (32, 86)
Circulatory diseases (390–459)	742	46 (43, 49)	208	47 (41, 53)
Ischemic heart disease (410–414)	380	45 (41, 50)	94	41 (33, 50)
Cerebrovascular disease (430–438)	199	49 (42, 56)	66	57 (44, 73)
Respiratory diseases (460–519)	134	24 (20, 29)	41	26 (19, 35)
Digestive diseases (520–579)	81	38 (30, 47)	19	29 (18, 46)
Genitourinary diseases (580–629)	19	33 (20, 51)	7	42 (17, 87)
Injury and poisoning (800–999)	83	72 (57, 89)	43	81 (58, 109)
All other causes (1–139, 280–289, 630–799)	86	59 (47, 73)	25	52 (33, 76)
All causes of death (1–999)	2311	52 (50, 54)	654	52 (48, 56)

<sup>1</sup> ICD9, International Classification of Diseases, 9th revision. The 95% CIs were calculated from deaths before age 90 y by comparison with contemporary mortality data for England and Wales (14); the SMR is the ratio of the observed number of deaths to the number of deaths expected from the national rates, standardized for sex and age. All of the SMRs with 95% CIs excluding 100 are significantly different from 100 at the 5% level.

There were 2965 deaths, and the SMR for all-cause mortality for the whole cohort was 52% (95% CI: 50%, 54%).

The SMRs for cancers of the gastrointestinal tract and lung were significantly less than 100% in both vegetarians and nonvegetarians with the exception of colorectal cancer and pancreatic cancer in vegetarians. The SMRs for cancers of the female breast, ovary, and prostate were not significantly different from 100% in either diet group.

The SMRs for all circulatory disease was 47% for vegetarians and 46% for nonvegetarians. The SMR for ischemic heart disease was slightly lower, and the SMR for cerebrovascular disease was slightly higher in vegetarians than in nonvegetarians. All the SMRs for circulatory diseases were significantly less than 100%. For other causes of death the SMRs were all significantly less than 100%, except for deaths from injury and poisoning in vegetarians.

### Comparisons of characteristics and mortality in vegetarians and nonvegetarians with no prior disease

For comparisons of mortality rates between diet groups, the analyses were restricted to participants with no missing data on smoking and with full reliable data on nutrient intake, who did not report a previous myocardial infarction or stroke, and who did not have a previous malignant cancer registration or self-reported malignant cancer (except for nonmelanoma skin cancer). The characteristics of these 47,254 participants are given in **Table 2**. Thirty-four percent were vegetarians and 76% were women. Median age at recruitment was 10 y younger in the vegetarians

than in the nonvegetarians. Smoking rates were low overall, with only 10% of vegetarians and 12% of nonvegetarians reporting that they were smokers at the time of recruitment. Median BMI was lower in vegetarians than in nonvegetarians, by 1.3 among men and by 1.0 among women. Median alcohol consumption was lower in vegetarians than in nonvegetarians, by 2.2 g/d among men and by 0.5 g/d among women. Median intakes of milk were higher in nonvegetarians than in vegetarians, whereas median intakes of cheese, vegetables, and fruit were higher in vegetarians than in nonvegetarians. Median intakes of meat among meat eaters were 79 and 67 g/d among men and women, respectively (not shown in **Table 2**). Information on diet group  $\approx$ 5 y after baseline was available for 67% of participants and, among these, 89.5% of vegetarian men and 83.8% of vegetarian women still reported that they were vegetarians.

Among the 47,254 participants with known smoking habits and no prior disease at the time of recruitment there were 1513 deaths in 506,620 person-years of follow-up. The DRRs for smoking, BMI, alcohol consumption, vegetarian status, and diet group in relation to deaths from all circulatory diseases, ischemic heart disease, cerebrovascular disease, and all causes combined are shown in **Table 3**.

Smoking significantly increased the mortality rates for each of the cause of death categories examined except for cerebrovascular disease; compared with never smokers, heavy smokers had DRRs of 2.49 (95% CI: 1.57, 3.96) for circulatory diseases, 3.30 (95% CI: 1.79, 6.10) for ischemic heart disease and 3.01 (95% CI: 2.42, 3.74) for all causes combined.

**TABLE 2**Baseline characteristics of 47,254 nonvegetarians and vegetarians with no prior disease (myocardial infarction, stroke, or malignant cancer)<sup>1</sup>

Characteristic	Men		Women	
	Nonvegetarians (n = 7302)	Vegetarians (n = 4022)	Nonvegetarians (n = 23,871)	Vegetarians (n = 12,059)
Age at entry [n (%)]				
20–29 y	542 (7.4)	778 (19.3)	2913 (12.2)	3892 (32.3)
30–39 y	1279 (17.5)	1346 (33.5)	5183 (21.7)	3692 (30.6)
40–49 y	2016 (27.6)	1048 (26.1)	6634 (27.8)	2579 (21.4)
50–59 y	1663 (22.8)	434 (10.8)	5197 (21.8)	1108 (9.2)
60–69 y	1325 (18.1)	238 (5.9)	2908 (12.2)	477 (4.0)
70–79 y	413 (5.7)	128 (3.2)	905 (3.8)	226 (1.9)
80–89 y	64 (0.9)	50 (1.2)	131 (0.5)	85 (0.7)
Median age (y)	49	39	45	35
Smoking status [n (%)] <sup>2</sup>				
Never smoker	3678 (50.4)	2352 (58.5)	14,611 (61.2)	7794 (64.6)
Former smoker	2538 (34.8)	1210 (30.1)	6688 (28.0)	3057 (25.4)
Light smoker	708 (9.7)	305 (7.6)	1524 (6.4)	847 (7.0)
Heavy smoker	378 (5.2)	155 (3.9)	1048 (4.4)	361 (3.0)
BMI [n (%)] <sup>3</sup>				
<20 kg/m <sup>2</sup>	334 (4.7)	431 (11.2)	2768 (12.0)	2296 (19.8)
20–22.4 kg/m <sup>2</sup>	1541 (21.8)	1265 (32.8)	7397 (32.0)	4374 (37.7)
22.5–24.9 kg/m <sup>2</sup>	2428 (34.4)	1211 (31.4)	6285 (27.2)	2793 (24.1)
25–27.4 kg/m <sup>2</sup>	1670 (23.6)	609 (15.8)	3483 (15.0)	1180 (10.2)
≥27.5 kg/m <sup>2</sup>	1091 (15.4)	340 (8.8)	3211 (13.9)	944 (8.1)
Median BMI (kg/m <sup>2</sup> )	24.2	22.9	23.0	22.0
Alcohol consumption [n (%)]				
<1 g/d	718 (9.8)	762 (18.9)	3887 (16.3)	2647 (22.0)
1–7 g/d	2232 (30.6)	1235 (30.7)	11,027 (46.2)	5215 (43.2)
8–15 g/d	1912 (26.2)	926 (23.0)	5839 (24.5)	2741 (22.7)
≥16 g/d	2440 (33.4)	1099 (27.3)	3118 (13.1)	1456 (12.1)
Median alcohol consumption (g/d)	10.5	8.3	5.4	4.9
Daily intake of selected foods				
Total meat (g)	65 (21–106) <sup>4</sup>	—	49 (9–87)	—
Total fish (g)	34 (22–51)	—	34 (21–53)	—
Dairy milk (mL)	293 (146–439)	146 (0–439)	293 (146–439)	146 (50–293)
Dairy cheese (g)	15 (7–27)	19 (5–35)	19 (9–31)	23 (9–38)
Total vegetables (g)	207 (148–285)	246 (177–338)	243 (176–330)	268 (192–372)
Total fresh fruit (g)	181 (102–292)	198 (114–330)	238 (146–364)	240 (140–380)
Diet group at follow-up [n (%)] <sup>3</sup>				
Nonvegetarian	4915 (97.2)	262 (10.5)	16088 (97.4)	1237 (16.2)
Vegetarian	139 (2.8)	2242 (89.5)	431 (2.6)	6384 (83.8)

<sup>1</sup> The differences between nonvegetarians and vegetarians in sex, age, smoking status, BMI, and alcohol consumption were all statistically significant,  $P < 0.001$ .

<sup>2</sup> Heavy smokers smoke  $\geq 15$  cigarettes/d; light smokers include all other current smokers, including pipe or cigar smokers; never smokers are those who have never smoked  $\geq 1$  cigarettes/d for  $\geq 1$  y.

<sup>3</sup> Categories or values are unknown for some participants at follow-up.

<sup>4</sup> Median; interquartile range in parentheses (all such values).

In comparison with participants with a BMI of 20.0–22.4, participants with a BMI  $< 20$  had significantly increased mortality from all causes combined (DRR: 1.32; 95% CI: 1.10, 1.58), and participants with a BMI  $\geq 27.5$  had a significantly higher mortality from circulatory disease (DRR: 1.99; 95% CI: 1.50, 2.63), ischemic heart disease (DRR: 2.53; 95% CI: 1.66, 3.87), and all causes combined (DRR: 1.19; 95% CI: 1.01, 1.41).

Alcohol consumption was inversely associated with mortality from circulatory disease, ischemic heart disease, and all causes combined. In comparison with people who drank an average of 1–7 g/d alcohol, people who drank less than this had significantly higher mortality from circulatory diseases (DRR: 1.41; 95% CI: 1.13, 1.75) and from all causes combined (DRR: 1.14; 95% CI:

1.01, 1.30). In contrast, people who drank an average of  $\geq 16$  g/d had DRRs of 0.87 (95% CI: 0.64, 1.17) for circulatory diseases, 0.87 (95% CI: 0.58, 1.31) for ischemic heart disease, and 0.92 (95% CI: 0.78, 1.08) for all causes combined compared with people who drank an average of 1–7 g/d alcohol.

Mortality rates did not differ significantly between non-vegetarians and vegetarians or between meat eaters, fish eaters, and vegetarians. In comparison with meat eaters, the DRRs for ischemic heart disease among fish eaters and vegetarians, adjusted for age, sex, smoking, and alcohol consumption were 0.86 (95% CI: 0.53, 1.38) and 0.81 (95% CI: 0.57, 1.16), respectively; further adjustment for BMI altered these DRRs to 0.94 (95% CI: 0.58, 1.52) for fish eaters and 0.86 (95% CI: 0.60, 1.24) for

TABLE 3

Numbers of deaths and multivariate-adjusted death rate ratios (DRRs) by various factors among 47,254 participants in the European Prospective Investigation into Cancer and Nutrition Oxford cohort with no prior disease (myocardial infarction, stroke, or malignant cancer)<sup>1</sup>

Factor and category	Circulatory diseases		Ischemic heart disease		Cerebrovascular disease		All causes	
	No. of deaths	DRR (95% CI)	No. of deaths	DRR (95% CI)	No. of deaths	DRR (95% CI)	No. of deaths	DRR (95% CI)
<b>Smoking<sup>2</sup></b>								
Never smoker	225	1.00	91	1.00	87	1.00	723	1.00
Former smoker	199	1.14 (0.94, 1.39)	91	1.19 (0.88, 1.60)	66	1.04 (0.75, 1.45)	583	1.14 (1.02, 1.27)
Light smoker	35	1.97 (1.38, 2.83)	19	2.23 (1.35, 3.69)	4	0.73 (0.26, 1.99)	113	1.86 (1.52, 2.27)
Heavy smoker	20	2.49 (1.57, 3.96)	12	3.30 (1.79, 6.10)	2	0.79 (0.19, 3.21)	94	3.01 (2.42, 3.74)
<i>P</i> for heterogeneity		<0.001		0.001		0.875		<0.001
<b>BMI<sup>3</sup></b>								
<20 kg/m <sup>2</sup>	52	1.35 (0.96, 1.89)	21	1.51 (0.89, 2.58)	21	1.24 (0.73, 2.10)	181	1.32 (1.10, 1.58)
20–22.4 kg/m <sup>2</sup>	99	1.00	38	1.00	41	1.00	370	1.00
22.5–24.9 kg/m <sup>2</sup>	112	0.95 (0.72, 1.25)	49	1.02 (0.67, 1.57)	32	0.68 (0.43, 1.09)	415	0.97 (0.84, 1.12)
25–27.4 kg/m <sup>2</sup>	90	1.29 (0.97, 1.72)	42	1.42 (0.91, 2.22)	30	1.14 (0.71, 1.84)	242	0.93 (0.79, 1.09)
≥27.5 kg/m <sup>2</sup>	101	1.99 (1.50, 2.63)	53	2.53 (1.66, 3.87)	26	1.34 (0.81, 2.20)	236	1.19 (1.01, 1.41)
<i>P</i> for heterogeneity		<0.001		<0.001		0.076		0.001
<b>Alcohol consumption<sup>3</sup></b>								
<1 g/d	165	1.41 (1.13, 1.75)	69	1.37 (0.99, 1.92)	59	1.41 (0.96, 2.06)	426	1.14 (1.01, 1.30)
1–7 g/d	167	1.00	76	1.00	53	1.00	590	1.00
8–15 g/d	83	0.95 (0.73, 1.24)	32	0.73 (0.48, 1.11)	34	1.40 (0.91, 2.17)	265	0.85 (0.74, 0.99)
≥16 g/d	64	0.87 (0.64, 1.17)	36	0.87 (0.58, 1.31)	13	0.75 (0.40, 1.40)	232	0.92 (0.78, 1.08)
<i>P</i> for heterogeneity		0.002		0.022		0.071		0.003
<b>Vegetarian status<sup>4</sup></b>								
Nonvegetarian	361	1.00	168	1.00	113	1.00	1128	1.00
Vegetarian	118	0.97 (0.78, 1.21)	45	0.83 (0.59, 1.18)	46	1.10 (0.77, 1.58)	385	1.05 (0.93, 1.19)
<i>P</i> for heterogeneity		0.780		0.303		0.601		0.439
<b>Diet group<sup>4</sup></b>								
Meat eater	313	1.00	148	1.00	94	1.00	970	1.00
Fish eater	48	0.88 (0.64, 1.19)	20	0.86 (0.53, 1.38)	19	1.03 (0.62, 1.71)	158	0.89 (0.75, 1.05)
Vegetarian or vegan	118	0.95 (0.75, 1.19)	45	0.81 (0.57, 1.16)	46	1.11 (0.76, 1.62)	385	1.03 (0.90, 1.16)
<i>P</i> for heterogeneity		0.668		0.478		0.866		0.279

<sup>1</sup> DRRs were generated with Cox proportional hazards regression, using separate models for the different exposures.

<sup>2</sup> Adjusted for age and sex. Heavy smokers smoke ≥15 cigarettes/d; light smokers include all other current smokers, including pipe or cigar smokers; never smokers are those who have never smoked ≥1 cigarettes/d for ≥1 y.

<sup>3</sup> Adjusted for age, sex, and smoking. BMI was unknown for some subjects (an unknown category was added to ensure that all observations contributed to the analysis, but results for this category are not shown, and the tests for heterogeneity relate to the “known” categories).

<sup>4</sup> Adjusted for age, sex, smoking, and alcohol consumption.

vegetarians. Mortality from cerebrovascular disease was slightly but not significantly higher among both vegetarians and fish eaters than among meat eaters, and mortality from all circulatory diseases was similar for vegetarians and nonvegetarians. For all causes of death combined, mortality in fish eaters was nonsignificantly lower than in meat eaters (DRR: 0.89; 95% CI: 0.75, 1.05), and mortality in vegetarians was nonsignificantly higher than in meat eaters (DRR: 1.03; 95% CI: 0.90, 1.16).

The results reported in Table 3 were all adjusted for sex. Further analyses showed that there was no significant effect modification by sex (results not shown).

## DISCUSSION

The EPIC-Oxford study was designed to recruit as many vegetarians as possible. Because the methods used to recruit subjects were through vegetarian societies, health food shops, and magazines, it might be expected that the participants in the study would, on average, be both healthier and more “health-conscious” than the British population in general. This expectation is borne out by the low SMRs (52% for all causes of death

for the whole cohort). The low SMRs are partly due to the low prevalence of smoking and obesity and partly because people who are already very ill and therefore likely to die within a few years are much less likely to join this type of study than people who are healthy (the well-known “healthy volunteer effect”). Most of the SMRs for major causes of death were significantly less than 100% among both the vegetarians and the nonvegetarians, with the noticeable exceptions of cancers of the female breast, ovary, and prostate, for which the known risk factors are not strongly related to health-conscious behavior.

The comparisons of mortality rates according to dietary group and other factors were restricted to people who had not previously had a myocardial infarction or stroke and who had not been registered with or self-reported a previous malignant cancer. Among these participants, vegetarians had a lower BMI than did nonvegetarians and a slightly lower prevalence of smoking and lower alcohol consumption. The analyses of mortality rates within the cohort showed the expected strong associations of smoking, BMI, and alcohol consumption with mortality from the major causes of death. Smoking and both low and high BMI increased mortality, and moderate alcohol consumption

decreased mortality from circulatory diseases, ischemic heart disease, and all causes combined. These associations are well established (16).

The comparisons of death rates between diet groups showed no significant differences, although mortality from ischemic heart disease was 19% lower among vegetarians than among meat eaters. We and others have previously reported lower mortality rates from ischemic heart disease in vegetarians than in non-vegetarians or meat eaters in other studies; in the collaborative reanalysis of 5 prospective studies, we reported that mortality from ischemic heart disease was 24% (95% CI: 6%, 38%) lower among vegetarians than among nonvegetarians (17). Major established risk factors for mortality from ischemic heart disease are smoking, obesity, high LDL cholesterol, and high blood pressure (18–20). In the EPIC-Oxford study, smoking rates are low overall and differ very little between vegetarians and non-vegetarians, and all our analyses were adjusted for smoking. Mean BMI is low in the EPIC-Oxford study, but the average BMI of vegetarians is  $\approx$ 1 unit lower than that of nonvegetarians. Measurements among participants in the EPIC-Oxford study have shown that mean serum LDL cholesterol is approximately 12% lower in vegetarians than in meat eaters (21). Mean systolic blood pressure is approximately 1 mm Hg lower in vegetarians than in meat eaters, but this small difference is eliminated by adjustment for BMI (22). Previous studies have yielded estimates that the risk of ischemic heart disease is reduced by  $\approx$ 6%/1-unit reduction in BMI (19) and by about 1% for each 1% reduction in serum LDL cholesterol (20). Thus, the lower BMI and LDL cholesterol of vegetarians would be expected to reduce their rate of mortality from ischemic heart disease by  $\approx$ 17% in comparison with meat eaters. This figure is close to the observed nonsignificant difference in mortality of 19%. Thus, although the difference in rate of mortality from ischemic heart disease between vegetarians and meat eaters was moderate and not statistically significant, it is compatible with what would be predicted from the differences in known risk factors and is potentially of major public health importance.

The rate of mortality from cerebrovascular disease was slightly but not significantly higher among both vegetarians and fish eaters than among meat eaters, and the rate of mortality from all circulatory diseases was similar for vegetarians and non-vegetarians. In the collaborative analysis of 5 prospective studies, the rate of mortality from cerebrovascular disease was slightly but not significantly lower among vegetarians than among non-vegetarians (17). The numbers of deaths from cerebrovascular disease in the EPIC-Oxford study are too small for reliable interpretation.

For all causes of death combined, the rate of mortality in vegetarians was similar to that in meat eaters, and the rate of mortality in fish eaters was nonsignificantly lower than in meat eaters. In the previous collaborative analysis of 5 prospective studies, the rate of all-cause mortality was nonsignificantly lower among vegetarians than among nonvegetarians (17).

This is a study of comparisons, and the results depend on the comparison group. In the analyses of SMRs, the comparison group was the whole population of England and Wales, and some of the differences in SMRs observed may be due to differences in nondietary risk factors, especially smoking. In the comparisons within the cohort, the vegetarians were compared with all non-vegetarians or with meat eaters. Average meat intake among the

meat eaters was only moderate, at 79 g/d in men and 67 g/d in women; these intakes are much lower than those reported in the National Diet and Nutrition Survey for the United Kingdom (23). Consumption of vegetables and fruit was higher among vegetarians than among nonvegetarians, but the differences were not large (<20%). Thus, if high intakes of meat had an adverse effect and high intakes of fruit and vegetables had a beneficial effect, the relatively low meat intake and high fruit and vegetable intake of the nonvegetarians in this cohort could reduce the chance of observing lower mortality rates in the vegetarians than in the nonvegetarians.

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 specifically about whether participants ever ate meat, fish, dairy products, and eggs. However, when diet group was assigned on the basis of answers to the same 4 questions in a follow-up questionnaire 5 y later, most participants were allocated to the same diet group as at recruitment. Furthermore, cross-sectional analyses have shown that the self-reported vegetarians have a lower prevalence of obesity (24) and also lower plasma concentrations of vitamin B-12 (25), long-chain n-3 fatty acids (26), and phytanic acid (27).

In conclusion, both the vegetarians and the nonvegetarians in this British cohort have a low rate of mortality compared with the national average. Comparisons within the cohort show no significant differences in rate of mortality between vegetarians and meat eaters, but the study is not large enough to exclude small or moderate differences for specific causes of death, and more research on this topic is required. (Other articles in this supplement to the Journal include references 28–54.)

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