

**Citation:**

Key TJ, Appleby PN, Spencer EA, Travis RC, Roddam AW, Allen NE. Mortality in British vegetarians: Results from the European Prospective Investigation into Cancer and Nutrition (EPIC-Oxford). *Am J Clin Nutr.* 2009 May; 89 (5): 1,613S-1,619S. Epub 2009 Mar 18.

**PubMed ID:** [19297458](#)

**Study Design:**

Prospective cohort study

**Class:**

B - [Click here](#) for explanation of classification scheme.

**Research Design and Implementation Rating:**

POSITIVE: See Research Design and Implementation Criteria Checklist below.

**Research Purpose:**

- To compare mortality from major causes of death among vegetarians and non-vegetarians in the European Prospective Investigation into Cancer and Nutrition-Oxford (EPIC-Oxford) study
- To compare the mortality from major causes of death of all participants in the study with contemporary national rates for England and Wales.

**Inclusion Criteria:**

- Participants enrolled in the EPIC-Oxford Study
- The analyses were restricted to participants aged 20-89 years at recruitment with known smoking characteristics and for whom diet group was unambiguous.

**Exclusion Criteria:**

- No missing data on smoking
- Full reliable data on nutrient intake
- No previous myocardial infarction or stroke
- No previous malignant cancer registration or self-reported malignant cancer (except for nonmelanoma skin cancer).

**Description of Study Protocol:****Recruitment**

- The EPIC-Oxford cohort was recruited between 1993 and 1999
- Two methods of recruitment were used: General practice (GP) recruitment and postal

recruitment

- EPIC nurses working in GP offices in Oxfordshire, Buckinghamshire, and Greater Manchester performed recruitment from the general population through GPs. All men and women aged 35-69 years on the list of each collaborating GP were invited to participate. In addition, a pilot recruitment phase was conducted by collaborating GPs who recruited 900 women aged 40-59 years. The GP method recruited 7,423 participants
- Postal recruitment, aimed at those aged >20 years, 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 (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 postal methods recruited 58,042 participants.

## **Design**

Prospective study of 63,550 men and women recruited throughout the United Kingdom in the 1990s.

## **Dietary Intake/Dietary Assessment Methodology**

- Participants were categorized into one of four diet groups according to their replies to four questions:
  - Do you eat meat?
  - Do you eat fish?
  - Do you eat dairy products?
  - Do you eat eggs?
- For each of these four 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 four questions, four 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)
  - Vegans (those that eat no animal products)
- For the women recruited in the pilot phase of the study, and the first 1,300 men and women recruited by EPIC nurses, these four dietary categorization questions were not asked, and diet group was assigned according to responses provided in the food-frequency questionnaire (FFQ)
- Because there were too few deaths among the vegans to report separately, in this article the vegans are included in the vegetarian category
- Participants completed a food-frequency questionnaire, based on that used in the US Nurses' Health Study, modified for use in the United Kingdom. Each participant estimated his or her average frequency of intake of 130 foods and drinks over the previous 12 months:
  - Never or less than one time per month
  - One to three times per month
  - One time per week
  - Two to four times per week
  - Five to six times per week
  - One time per day

- Two to three times per day
- Four to five times per day
- More than six times per day
- Daily mean nutrient intakes were estimated with the use of standard portion sizes, and nutrient contents were estimated.

### **Blinding Used**

Not applicable.

### **Intervention**

Not applicable.

### **Statistical Analysis**

- Standardized mortality ratios (SMRs) of vegetarians and non-vegetarians were calculated from incident deaths before age 90 by comparison with contemporary mortality data for England; the SMR is the ratio of the observed number of deaths to the number of deaths expected from the national rates, standardized for age and sex 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 MI, stroke or cancer) with age as the underlying time variable, 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
- Statistical significance was set at the 5% level and 95% CIs were calculated for both the SMRs and DRRs.

## **Data Collection Summary:**

### **Timing of Measurements**

- Recruitment 1993-1999
- Follow-up through June 20, 2007.

### **Dependent Variables**

Mortality (causes of) by record linkage to UK's National Health Service Central Register.

### **Independent Variables**

- Vegetarian status
- Non-vegetarian status.

### **Control Variables**

- Smoking
- Age
- Sex
- Alcohol consumption.

## Description of Actual Data Sample:

- *Initial N:* 64,234
- *Attrition (final N):* 47,254 (75% women)
- *Age:* 20-89 years
- *Ethnicity:* Not specified
- *Other relevant demographics:* None
- *Anthropometrics:* None
- *Location:* United Kingdom.

## Summary of Results:

### Key Findings

- Among 64,234 participants with known diet group, 2,965 died before age 90 by 30 June 2007. The death rate among participants was lower than the national average. The standardized mortality ratio for all causes of death was 52% (95% CI: 50%, 54%) and was identical between vegetarians and non-vegetarians
- The analyses comparing diet groups were limited to 47,254 participants after applying exclusions
- Comparisons between diet groups showed NS differences in mortality rates, but the authors stated that the study was not large enough to exclude small or moderate difference for specific causes of death
- The authors also noted that the average meat intake among the meat eaters was moderate (79g per day in men, 67g per day in women) and differences in fruit and vegetable intake between vegetarians and non-vegetarians was also moderate (<20%).

**Table: 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)**

	Circulatory Diseases		Ischemic Heart Disease		Cerebrovascular Disease		All Causes	
	Number of Deaths	DRR (95% CI)	Number of Deaths	DRR (95% CI)	Number of Deaths	DRR (95% CI)	Number of Deaths	DRR (95% CI)
<b>Vegetarian status<sup>a</sup></b>								
Non-vegetarian	361	1.00	168	1.00	113	1.00	1,128	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)
P for heterogeneity		0.780		0.303		0.601		0.439
<b>Diet group<sup>a</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)
P for heterogeneity		0.668		0.478		0.866		0.279

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

### Author Conclusion:

- Mortality from circulatory diseases and all causes is NS different between vegetarians and meat eaters; however, the study is not large enough to exclude small or moderate differences for specific causes of death
- The mortality of both vegetarians and non-vegetarians in this study is low compared to national rates.

### Reviewer Comments:

### Research Design and Implementation Criteria Checklist: Primary Research

#### Relevance Questions

- |    |   |     |
|----|---|-----|
| 1. | Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies) | N/A |
| 2. | Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?   | Yes |
| 3. | Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?  | Yes |
| 4. | Is the intervention or procedure feasible? (NA for some epidemiological studies)  | N/A |

#### Validity Questions

- |      |   |     |
|------|---|-----|
| 1.   | <b>Was the research question clearly stated?</b>  | Yes |
| 1.1. | Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified? | Yes |

1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
<b>2.</b>	<b>Was the selection of study subjects/patients free from bias?</b>	Yes
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	Yes
2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
2.4.	Were the subjects/patients a representative sample of the relevant population?	Yes
<b>3.</b>	<b>Were study groups comparable?</b>	Yes
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	N/A
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	No
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	Yes
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	Yes
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	Yes
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
<b>4.</b>	<b>Was method of handling withdrawals described?</b>	N/A
4.1.	Were follow-up methods described and the same for all groups?	N/A
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	N/A
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	N/A
4.4.	Were reasons for withdrawals similar across groups?	N/A

4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
<b>5.</b>	<b>Was blinding used to prevent introduction of bias?</b>	<b>Yes</b>
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	N/A
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	N/A
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	Yes
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
<b>6.</b>	<b>Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were intervening factors described?</b>	<b>Yes</b>
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	N/A
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	Yes
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	Yes
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	N/A
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	Yes
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
<b>7.</b>	<b>Were outcomes clearly defined and the measurements valid and reliable?</b>	<b>Yes</b>
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes

7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes
7.7.	Were the measurements conducted consistently across groups?	Yes
<b>8.</b>	<b>Was the statistical analysis appropriate for the study design and type of outcome indicators?</b>	Yes
8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	N/A
8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	Yes
8.6.	Was clinical significance as well as statistical significance reported?	Yes
8.7.	If negative findings, was a power calculation reported to address type 2 error?	N/A
<b>9.</b>	<b>Are conclusions supported by results with biases and limitations taken into consideration?</b>	Yes
9.1.	Is there a discussion of findings?	Yes
9.2.	Are biases and study limitations identified and discussed?	Yes
<b>10.</b>	<b>Is bias due to study's funding or sponsorship unlikely?</b>	Yes
10.1.	Were sources of funding and investigators' affiliations described?	No
10.2.	Was the study free from apparent conflict of interest?	Yes