

## Dietary habits and mortality in 11 000 vegetarians and health conscious people: results of a 17 year follow up

Timothy J A Key, Margaret Thorogood, Paul N Appleby, Michael L Burr

### Abstract

**Objective**—To investigate the association of dietary habits with mortality in a cohort of vegetarians and other health conscious people.

**Design**—Observational study.

**Setting**—United Kingdom.

**Subjects**—4336 men and 6435 women recruited through health food shops, vegetarian societies, and magazines.

**Main outcome measures**—Mortality ratios for vegetarianism and for daily versus less than daily consumption of wholemeal bread, bran cereals, nuts or dried fruit, fresh fruit, and raw salad in relation to all cause mortality and mortality from ischaemic heart disease, cerebrovascular disease, all malignant neoplasms, lung cancer, colorectal cancer, and breast cancer.

**Results**—2064 (19%) subjects smoked, 4627 (43%) were vegetarian, 6699 (62%) ate wholemeal bread daily, 2948 (27%) ate bran cereals daily, 4091 (38%) ate nuts or dried fruit daily, 8304 (77%) ate fresh fruit daily, and 4105 (38%) ate raw salad daily. After a mean of 16.8 years follow up there were 1343 deaths before age 80. Overall the cohort had a mortality about half that of the general population. Within the cohort, daily consumption of fresh fruit was associated with significantly reduced mortality from ischaemic heart disease (rate ratio adjusted for smoking 0.76 (95% confidence interval 0.60 to 0.97)), cerebrovascular disease (0.68 (0.47 to 0.98)), and for all causes combined (0.79 (0.70 to 0.90)).

**Conclusions**—In this cohort of health conscious individuals, daily consumption of fresh fruit is associated with a reduced mortality from ischaemic heart disease, cerebrovascular disease, and all causes combined.

### Introduction

In the early 1970s interest grew in the relation between diet and health, and it was suggested that the risk of death from ischaemic heart disease might be reduced by a high intake of dietary fibre<sup>1</sup> or by a vegetarian diet. To test these hypotheses a cohort of about 11 000 British men and women was recruited between 1973 and 1979 from among the customers of health food shops and other people with an interest in health foods or vegetarianism. Diet was assessed by a short questionnaire which asked about vegetarianism and intake of a few high fibre foods. Follow up of the cohort until 1980<sup>2</sup> and 1985<sup>3</sup> showed that habitual consumption of wholemeal bread was not significantly associated with mortality but that a vegetarian diet was associated with a significant reduction in mortality from ischaemic heart disease. We report here the results of follow up until 1995. The aim of this analysis was to examine the relation of six dietary factors (vegetarian diet and consumption of wholemeal bread, bran cereals, nuts and dried fruit, fresh fruit, and raw salad) with

mortality from conditions for which associations with diet have been suggested.

### Subjects and methods

#### RECRUITMENT

Subjects were recruited by distributing a short questionnaire to customers of health food shops and clinics, subscribers to health food magazines and a Seventh Day Adventist publication, and members of vegetarian and health food societies. This questionnaire asked about current smoking, weight (but not height), and dietary habits. Subjects were asked whether they were vegetarian (this was not defined further) and to record their usual frequency of consumption of wholemeal bread, bran cereals, nuts or dried fruit, fresh fruit, and raw vegetable salads. There were three frequency categories: at least daily, less than daily but at least once a week, and less than once a week. Most subjects consumed these foods at least once a week so subjects were grouped into the two categories daily and less than daily. Subjects also provided their name and address, date and place of birth, and NHS number for tracing at the NHS central register. We recruited and successfully traced 10 977 subjects between November 1973 and November 1979.

To assess the stability of dietary patterns we interviewed 289 subjects between one and a half and six years after the recruitment questionnaire was completed. Of these subjects, 66% of those who initially reported that they were vegetarian were still eating meat or fish less than once a month, and 67% of those who initially reported consuming wholemeal bread daily were still doing so.<sup>2</sup>

#### FOLLOW UP

Participants were followed up until death (2562, 23.3%), emigration (519, 4.7%), or 31 March 1995 (7896, 71.9%). Copies of all the death certificates were obtained, and the underlying causes of death were coded according to the International Classification of Diseases (8th revision for 1973-78 and 9th revision for 1979-95).<sup>4,5</sup>

#### STATISTICAL METHODS

We analysed all deaths occurring up to age 79 in participants aged 16 years or above at recruitment. Subjects with a previous cancer registration (other than ICD 173, non-melanoma skin cancer) were excluded, as were those with missing data on smoking or diet. These exclusions left 10 771 subjects. Subjects were censored on reaching the age of 80.

We estimated the numbers of deaths expected from each cause in each sex by multiplying the number of person years at risk in each of nine age groups (16-39, 40-44, 45-49...75-79) by the corresponding national mortality for England and Wales. Numbers were calculated separately for 1973-74, 1975-79, 1980-84, 1985-89, and 1990-95. We calculated standardised mortality ratios for men and women in the whole cohort

Imperial Cancer Research Fund, Cancer Epidemiology Unit, Radcliffe Infirmary, Oxford OX2 6HE

Timothy J A Key, research scientist

Paul N Appleby, scientific officer

Department of Public Health and Policy, London School of Hygiene & Tropical Medicine, London WC1E 7HT

Margaret Thorogood, senior lecturer

Centre for Applied Public Health Medicine, University of Wales College of Medicine, Cardiff CF1 3NW

Michael L Burr, senior lecturer

Correspondence to: Dr Key.

BMJ 1996;313:775-9

**Table 1—Characteristics and intake of certain foods of men and women. Values are numbers (percentages) unless stated otherwise**

	Men (n = 4336)	Women (n = 6435)
Mean (SD) age (years)	45.7 (17.7)	45.9 (18.3)
Current smokers	1100 (25.4)	964 (15.0)
Pipe or cigars, or both	375 (8.6)	33 (0.5)
1-14 cigarettes*	373 (8.6)	579 (9.0)
≥15 cigarettes	352 (8.1)	352 (5.5)
Mean (SD) weight (kg)	70.3 (9.9)†	58.3 (8.7)‡
Vegetarian	1851 (42.7)	2776 (43.1)
Wholemeal bread daily	2732 (63.0)	3967 (61.6)
Bran cereals daily	1279 (29.5)	1669 (25.9)
Nuts or dried fruit daily	1660 (38.3)	2431 (37.8)
Fresh fruit daily	3103 (71.6)	5201 (80.8)
Raw salad daily	1486 (34.3)	2619 (40.7)

\*This includes 21 cigarette smokers (8 men and 13 women) with unknown amount smoked. †n = 4111. ‡n = 6112.

as the ratio of observed to expected deaths and 95% confidence intervals assuming that the number of observed deaths had a Poisson distribution.

We examined the associations of smoking and dietary factors with risk of death by Poisson regression using GLIM-4 to calculate mortality ratios and 95% confidence intervals. The ratios were adjusted firstly for age and sex and secondly for age, sex, and current smoking. Smoking was categorised as non-smoking, pipe or cigars only, 1-14 cigarettes a day, ≥15 cigarettes a day. If smokers did not declare how much they smoked they were put in the category 1-14 cigarettes a day (n = 21; 8 men and 13 women).

The dietary variables were dichotomised as vegetarian or non-vegetarian and as daily versus less than daily consumption of wholemeal bread, bran cereals, nuts or dried fruit, fresh fruit, and raw salad. Information on weight was available for 10 223 subjects; the relation of

weight with mortality was examined by dividing men and women into thirds of the weight distribution and calculating mortality ratios for the middle and top thirds relative to the lowest. Two sided P values are quoted.

## Results

Table 1 shows that men and women were similar in age and in the proportion who were vegetarian and ate wholemeal bread, bran cereals, or nuts or dried fruit daily. Fewer women than men smoked and more women reported eating fresh fruit or raw salad daily.

After a mean of 16.8 years of follow up (maximum 21.3 years) mortality was substantially lower than in the general population; the standardised mortality ratio for all causes of death was 0.56 (95% confidence interval 0.53 to 0.59) for men and women combined. Table 2 shows the standardised mortality ratios for major causes of death in men and women. Among men, standardised mortality ratios were significantly below one for all malignant neoplasms, cancer of the stomach, cancer of the large intestine and rectum (subsequently referred to as colorectal cancer), cancer of the bronchus and lung, diabetes mellitus, diseases of the circulatory system, diseases of the respiratory system, diseases of the digestive system, and diseases of the genitourinary system. Among women, standardised mortality ratios were significantly below one for all malignant neoplasms, cancer of the bronchus and lung, diabetes mellitus, mental disorders, diseases of the circulatory system, diseases of the respiratory system, and diseases of the digestive system.

### ASSOCIATIONS OF MORTALITY WITH SMOKING AND SIX DIETARY FACTORS

Table 3 shows the mortality ratios associated with smoking and six dietary factors for all causes of death combined and for six cause of death categories. Smoking was associated with a 52% increase in all cause mortality, increasing to 100% in people who smoked

**Table 2—Observed and expected numbers of deaths and standardised mortality ratios (95% confidence interval) for major causes of death in men and women**

Cause of death (ICD code, 9th revision)	Men			Women		
	Observed	Expected	Standardised mortality ratio	Observed	Expected	Standardised mortality ratio
All malignant neoplasms (140-208, 238.4, 289.8)*	181	360.12	0.50 (0.43 to 0.58)	270	353.45	0.76 (0.68 to 0.86)
Stomach (151)	11	29.83	0.37 (0.18 to 0.66)	12	18.30	0.66 (0.34 to 1.15)
Large intestine and rectum (153,154)	25	38.82	0.64 (0.42 to 0.95)	37	42.38	0.87 (0.61 to 1.20)
Pancreas (157)	11	13.99	0.79 (0.39 to 1.41)	15	15.06	1.00 (0.56 to 1.64)
Bronchus and lung (162)	37	134.97	0.27 (0.19 to 0.38)	22	59.43	0.37 (0.23 to 0.56)
Breast (174)†	-	-	-	65	73.94	0.88 (0.68 to 1.12)
Ovary (183)	-	-	-	21	23.36	0.90 (0.56 to 1.37)
Prostate (185)	29	27.39	1.06 (0.71 to 1.52)	-	-	-
Bladder and other urinary (188-189, except 189.0)	8	14.29	0.56 (0.24 to 1.10)	5	6.23	0.80 (0.26 to 1.87)
All benign and unspecified neoplasms (210-238.3, 238.5-239)‡	1	2.12	0.47 (0.01 to 2.63)	1	3.34	0.30 (0.01 to 1.67)
Endocrine diseases (240-279)	10	14.06	0.71 (0.34 to 1.31)	13	19.75	0.66 (0.35 to 1.13)
Diabetes mellitus (250)	4	11.39	0.35 (0.10 to 0.90)	3	14.90	0.20 (0.04 to 0.59)
Diseases of the blood (280-289.7, 289.9)§	0	1.22	0.00 (0.00 to 3.02)	2	2.19	0.91 (0.11 to 3.30)
Mental disorders (290-319)¶	2	7.24	0.28 (0.03 to 1.00)	3	10.27	0.29 (0.06 to 0.85)
Nervous system (320-389)	17	16.61	1.02 (0.60 to 1.64)	16	18.71	0.86 (0.49 to 1.39)
Circulatory system (390-459)**	344	628.35	0.55 (0.49 to 0.61)	254	508.91	0.50 (0.44 to 0.56)
Ischaemic heart disease (410-414)	224	423.97	0.53 (0.46 to 0.60)	126	273.61	0.46 (0.38 to 0.55)
Cerebrovascular disease (430-438)	68	111.08	0.61 (0.48 to 0.78)	79	139.46	0.57 (0.45 to 0.71)
Respiratory system (460-519)	47	142.41	0.33 (0.24 to 0.44)	56	99.06	0.57 (0.43 to 0.73)
Digestive system (520-579)††	10	31.11	0.32 (0.15 to 0.59)	17	36.21	0.47 (0.27 to 0.75)
Genitourinary system (580-629)	5	11.90	0.42 (0.14 to 0.98)	7	12.17	0.58 (0.23 to 1.19)
Accidents, poisonings, and violence (800-999)	43	35.88	1.20 (0.87 to 1.61)	28	29.64	0.94 (0.63 to 1.37)
All causes (000-999)	666	1276.84	0.52 (0.48 to 0.56)	677	1127.24	0.60 (0.56 to 0.65)

\*ICD code, 8th revision, 140-209. †ICD code, 8th revision, 174; women only. ‡ICD code, 8th revision, 210-239. §ICD code, 8th revision, 280-289. ¶ICD code, 8th revision, 290-315.

\*\*ICD code, 8th revision, 390-458. ††ICD code, 8th revision, 520-577.

**Table 3—Mortality ratios (95% confidence interval) for smoking and six dietary factors after adjustment for age and sex and for age, sex, and smoking**

Factor	All cause mortality		Ischaemic heart disease		Cerebrovascular disease		All malignant neoplasms		Lung cancer		Colorectal cancer		Breast cancer (women)	
	Age and sex	Age, sex, and smoking†	Age and sex	Age, sex, and smoking†	Age and sex	Age, sex, and smoking†	Age and sex	Age, sex, and smoking†	Age and sex	Age, sex, and smoking†	Age and sex	Age, sex, and smoking†	Age and sex	Age, sex, and smoking†
Current smoker:	1.52 (1.34 to 1.73)**	-	1.43 (1.11 to 1.84)**	-	1.53 (1.02 to 2.29)*	-	1.45 (1.16 to 1.82)**	-	5.43 (3.22 to 9.14)**	-	0.92 (0.45 to 1.87)	-	1.01 (0.50 to 2.02)	-
Pipe or cigars only	1.22 (0.96 to 1.55)	-	1.49 (1.02 to 2.18)*	-	1.44 (0.72 to 2.91)	-	1.07 (0.67 to 1.71)	-	1.96 (0.67 to 5.73)	-	0.72 (0.17 to 3.05)	-	§	-
1-14 cigarettes/day‡	1.39 (1.15 to 1.69)**	-	1.42 (0.97 to 2.09)	-	1.05 (0.53 to 2.06)	-	1.42 (1.03 to 1.96)*	-	3.70 (1.68 to 8.15)**	-	1.21 (0.48 to 3.01)	-	1.25 (0.57 to 2.74)	-
15 cigarettes/day	2.00 (1.66 to 2.42)**	-	1.36 (0.87 to 2.12)	-	2.42 (1.36 to 4.31)**	-	1.82 (1.30 to 2.55)**	-	11.28 (6.28 to 20.28)**	-	0.68 (0.17 to 2.79)	-	0.60 (0.16 to 2.30)	-
Vegetarian	0.98 (0.88 to 1.10)	1.04 (0.93 to 1.16)	0.82 (0.66 to 1.02)	0.85 (0.68 to 1.06)	0.91 (0.66 to 1.27)	0.96 (0.69 to 1.34)	1.07 (0.89 to 1.29)	1.12 (0.93 to 1.35)	0.79 (0.46 to 1.35)	1.07 (0.62 to 1.86)	0.79 (0.47 to 1.33)	0.78 (0.46 to 1.32)	1.64 (1.01 to 2.67)*	1.65 (1.01 to 2.70)*
Wholemeal bread daily	0.83 (0.75 to 0.93)**	0.88 (0.78 to 0.98)*	0.82 (0.66 to 1.02)	0.85 (0.68 to 1.06)	1.02 (0.72 to 1.45)	1.08 (0.75 to 1.54)	0.87 (0.61 to 1.06)	0.91 (0.75 to 1.11)	0.76 (0.45 to 1.28)	1.07 (0.63 to 1.83)	1.08 (0.63 to 1.86)	1.07 (0.62 to 1.85)	1.08 (0.65 to 1.81)	1.08 (0.64 to 1.81)
Bran cereals daily	0.97 (0.86 to 1.10)	1.00 (0.89 to 1.13)	0.98 (0.78 to 1.24)	0.99 (0.79 to 1.25)	0.91 (0.63 to 1.31)	0.93 (0.65 to 1.34)	0.85 (0.69 to 1.05)	0.87 (0.70 to 1.08)	0.40 (0.19 to 0.84)*	0.48 (0.23 to 1.01)	1.05 (0.61 to 1.81)	1.04 (0.60 to 1.80)	0.68 (0.37 to 1.24)	0.67 (0.37 to 1.24)
Nuts or dried fruit daily	0.93 (0.83 to 1.04)	0.98 (0.88 to 1.09)	0.86 (0.70 to 1.07)	0.89 (0.72 to 1.11)	0.76 (0.54 to 1.06)	0.80 (0.57 to 1.12)	0.97 (0.80 to 1.17)	1.01 (0.84 to 1.23)	0.53 (0.29 to 0.95)*	0.72 (0.40 to 1.31)	0.75 (0.44 to 1.27)	0.74 (0.43 to 1.25)	1.40 (0.86 to 2.29)	1.41 (0.86 to 2.30)
Fresh fruit daily	0.74 (0.66 to 0.84)**	0.79 (0.70 to 0.90)**	0.73 (0.58 to 0.93)**	0.76 (0.60 to 0.97)*	0.63 (0.44 to 0.91)*	0.68 (0.47 to 0.98)*	0.77 (0.62 to 0.95)*	0.81 (0.65 to 1.01)	0.40 (0.24 to 0.68)**	0.59 (0.34 to 1.02)	0.73 (0.41 to 1.30)	0.71 (0.40 to 1.27)	0.75 (0.42 to 1.34)	0.74 (0.41 to 1.32)
Raw salad daily	0.87 (0.78 to 0.97)*	0.91 (0.82 to 1.02)	0.72 (0.58 to 0.89)**	0.74 (0.59 to 0.92)**	1.15 (0.83 to 1.59)	1.21 (0.87 to 1.68)	0.92 (0.76 to 1.11)	0.96 (0.79 to 1.16)	0.67 (0.39 to 1.16)	0.90 (0.51 to 1.58)	0.79 (0.48 to 1.33)	0.78 (0.47 to 1.31)	1.15 (0.71 to 1.88)	1.15 (0.70 to 1.87)

\*Two tailed  $P < 0.05$ , \*\*  $P < 0.01$ . †Categories: non smoker; pipe and/or cigars only; 1-14 cigarettes/day;  $\geq 15$  cigarettes/day. ‡Includes current cigarette smokers, amount unknown (8 men and 13 women). §The 33 women who smoked pipe or cigar only were included in the category 1-14 cigarettes/day along with the 13 women who did not declare how much they smoked.

$\geq 15$  cigarettes a day. After smoking was adjusted for there were significant protective associations for consumption of wholemeal bread and fresh fruit. The significant reduction in mortality associated with eating fresh fruit daily remained after wholemeal bread was adjusted for (mortality ratio 0.81 (95% confidence

interval 0.71 to 0.92)), but the reduction associated with eating wholemeal bread daily was not significant after adjustment for consumption of fresh fruit (0.91 (0.81 to 1.02)).

For ischaemic heart disease the mortality ratio associated with smoking was 1.43 (1.11 to 1.84). After smoking was adjusted for, daily consumption of fresh fruit and raw salad were each associated with a significant reduction in mortality from ischaemic heart disease. An adjustment for raw salad increased the mortality ratio associated with daily consumption of fresh fruit to 0.82 (0.64 to 1.05), while adjustment for fresh fruit increased the ratio associated with daily consumption of raw salad to 0.77 (0.61 to 0.97). Smoking was also associated with an increased risk of death from cerebrovascular disease (1.53 (1.02 to 2.29)). After adjustment for smoking, daily consumption of fresh fruit had a significant protective effect (0.68 (0.47 to 0.98)).

Smoking was associated with an increased risk of death from all malignant neoplasms combined (1.45 (1.16 to 1.82)), but the dietary factors were not significant once smoking was adjusted for. Similarly no significant dietary associations were found for lung cancer after adjustment for smoking. Mortality from colorectal cancer was not significantly associated with smoking or dietary factors. Vegetarian diet was associated with an increased mortality from breast cancer in women (1.64 (1.01 to 2.67)), and this estimate was not altered by adjusting for smoking (which was not associated with breast cancer mortality).

**Table 4—Mortality ratios (95% confidence interval) for people in the middle and top thirds of body weight compared with those in the lowest third\***

	Adjusted for age and sex	Adjusted for age, sex, and smoking†
All causes:		
Middle third	1.03 (0.89 to 1.18)	1.02 (0.89 to 1.17)
Top third	1.02 (0.89 to 1.18)	1.01 (0.88 to 1.15)
Ischaemic heart disease:		
Middle third	1.14 (0.85 to 1.52)	1.13 (0.85 to 1.51)
Top third	1.30 (0.98 to 1.71)	1.28 (0.97 to 1.69)
Cerebrovascular disease:		
Middle third	1.09 (0.71 to 1.65)	1.07 (0.70 to 1.63)
Top third	1.09 (0.72 to 1.64)	1.06 (0.70 to 1.60)
All malignant neoplasms:		
Middle third	1.05 (0.83 to 1.34)	1.05 (0.83 to 1.34)
Top third	0.96 (0.75 to 1.21)	0.94 (0.75 to 1.20)
Lung cancer:		
Middle third	0.96 (0.51 to 1.80)	0.92 (0.49 to 1.73)
Top third	0.69 (0.36 to 1.35)	0.63 (0.33 to 1.23)
Colorectal cancer:		
Middle third	1.21 (0.63 to 2.30)	1.21 (0.63 to 2.31)
Top third	0.94 (0.49 to 1.82)	0.95 (0.49 to 1.83)
Breast cancer‡:		
Middle third	0.83 (0.44 to 1.59)	0.83 (0.43 to 1.58)
Top third	0.94 (0.52 to 1.72)	0.94 (0.52 to 1.71)

\*Tertiles of 65.8 and 73.1 kg in men and 54.0 and 60.4 kg in women. †Categories: non-smoker; pipe or cigars, or both only (except for breast cancer, where this category is combined with 1-14 cigarettes); 1-14 cigarettes a day (includes current cigarette smokers, amount unknown (8 men and 13 women));  $\geq 15$  cigarettes a day. ‡Breast cancer mortality is for women only and is not adjusted for sex.

ASSOCIATION OF MORTALITY WITH WEIGHT

Table 4 shows that weight was not associated with death rates for all cause mortality, cerebrovascular

disease, all malignant neoplasms combined, colorectal cancer, and breast cancer after age, sex, and smoking were adjusted for. The mortality ratio in the heaviest third was raised for ischaemic heart disease (1.28 (0.97 to 1.69)) and was low for lung cancer (0.63 (0.33 to 1.23)), but these apparent trends were not significant.

### Discussion

The low standardised mortality ratio of the cohort, 0.56 for men and women combined, is similar to that in comparable cohorts: 0.46 in the Oxford Vegetarian Study,<sup>6</sup> 0.48 in a cohort of German vegetarians and health conscious people,<sup>7</sup> and 0.56 in a cohort of Californian Seventh Day Adventists.<sup>8</sup> The low overall mortality was mostly due to low death rates for diseases of the circulatory system, diseases of the respiratory system, and cancer of the bronchus and lung compared with the general population. This is probably mainly accounted for by the low proportion of smokers in the cohort (19% smokers overall).

### LIMITATIONS

We followed the cohort for a mean of 17 years. The long follow up has the advantages of yielding a large number of deaths and of ensuring that dietary habits were recorded, on average, long before the onset of symptoms of the diseases studied. The disadvantage is that dietary habits will have changed during the follow up. The validation study suggested that subjects' diets did change during the first few years of follow up in respect to vegetarian diet and consumption of wholemeal bread, but these changes are a combination of real change plus imperfect repeatability and therefore overestimate the extent of change. Changes in dietary habits would be expected to result in underestimation of any associations found.

Another limitation is that the questionnaire was short and did not include several important food groups (for example, dairy products, fish, alcoholic drinks), did not allow us to estimate energy intake, and did not include other factors known to be associated with health (exercise, socioeconomic status, past smoking habits). We were therefore unable to explore whether the significant associations observed were partly due to confounding by other dietary or non-dietary variables.

### ASSOCIATIONS OF DIETARY FACTORS WITH MORTALITY

This study was initially set up to test the hypotheses that daily consumption of wholemeal bread (as an indicator of a high fibre diet) and vegetarian diet are associated with a reduction in mortality from ischaemic heart disease; the reduction in mortality associated with both of these dietary factors was not significant. We did, however, find that daily consumption of fresh fruit was associated with a significant reduction in mortality from ischaemic heart disease (24%), cerebrovascular disease (32%), and all causes of death combined (21%), and was associated with non-significant reductions in mortality from all the other cause of death examined.

Fruit was included on the questionnaire as a possible indicator of a high fibre diet but was not part of the original hypothesis, so caution should be applied in looking at these results in isolation. Nevertheless, our findings are broadly consistent with the results of several other studies. For all cause mortality, Kahn *et al* reported odds ratios of 0.89 and 0.72 for frequent versus infrequent consumption of fruit or fruit juice and green salad respectively,<sup>9</sup> Pandey *et al* reported a 31% reduction with a high intake of foods rich in vitamin C and in  $\beta$  carotene,<sup>10</sup> and Enstrom *et al* reported a 23% reduction associated with high vitamin C consumption.<sup>11</sup> Fruit is an important source of vitamin C. Fruits and vegetables,<sup>12,13</sup> carotene containing fruit and vegetables,<sup>14</sup> apples,<sup>15</sup> and foods rich in vitamin C and  $\beta$  caro-

### Key messages

- Diet is known to affect health but the relation is difficult to analyse.
- This study examined dietary factors associated with mortality among 11 000 health conscious people followed for an average of 17 years.
- After smoking was adjusted for, daily consumption of fresh fruit was associated with a 24% reduction in mortality from ischaemic heart disease, a 32% reduction in mortality from cerebrovascular disease, and a 21% reduction in all cause mortality compared with less frequent consumption.

tene<sup>10</sup> have all been reported to protect against ischaemic heart disease. Fruit and vegetables have also been reported to protect against stroke,<sup>16,17</sup> as have potassium<sup>18</sup> and vitamin C<sup>19</sup>—nutrients for which fruit is an important source.

We found that a vegetarian diet was associated with a 15% reduction in mortality from ischaemic heart disease. This was not significant and was less than the roughly 30% reductions reported in earlier analyses of this cohort,<sup>2,3</sup> other British vegetarians,<sup>6</sup> and Californian vegetarians.<sup>20</sup> The 0.61 mmol/l lower average total plasma cholesterol concentration reported among vegetarians than non-vegetarians in a sample of this cohort<sup>21</sup> might be expected to result in a 24% lower mortality from coronary heart disease.<sup>22</sup> Any protective effect may have been attenuated by crossover between the vegetarian and non-vegetarian groups.

A vegetarian diet was also associated with a significant increase in mortality from breast cancer. However, the confidence interval was wide, and the result might be due to chance, perhaps combined with differences in parity. In the Oxford Vegetarian Study, for example, 37% of vegetarian women aged 40 and above were nulliparous, compared with 28% of meat eating women (unpublished data). Other studies have reported no association between vegetarian diet and risk of breast cancer or mortality.<sup>23-25</sup>

Of the other associations examined, only two were significant. Daily consumption of wholemeal bread was associated with a 12% reduction in all cause mortality, but the protection was much less than that for fresh fruit (21%) and became non-significant after fruit was adjusted for. Daily consumption of raw salad was associated with a 26% reduction in mortality from ischaemic heart disease, slightly greater than that for fresh fruit (24%). After each of these variables was adjusted for the other, salad was more closely associated with mortality, but the reduction in risk associated with fruit remained substantial (18%) and both these foods may have a protective effect.

The numbers of deaths for individual cancer sites were small and the mortality ratios have wide confidence intervals. The 41% reduction in mortality from lung cancer associated with daily consumption of fresh fruit was not significant but is consistent with previous studies.<sup>26</sup> Perhaps surprisingly, none of the dietary variables was significantly associated with mortality from colorectal cancer.<sup>27</sup>

We found no significant association between weight and mortality, perhaps because of the low numbers of obese subjects. Only 3% of men were heavier than 91 kg and 2.5% of women heavier than 78 kg, the weights at which men and women of average height are considered obese.<sup>28</sup>

We thank the participants in this study, the staff of the NHS registers and the Office of Population Censuses and Surveys for tracing the subjects, and Drs Valerie Beral and Gary Fraser for commenting on the text.

Funding: Medical Research Council and Imperial Cancer Research Fund.

Conflict of interest: TJAK and PNA are members of the Vegetarian Society.

- 1 Burkitt DP. Some diseases characteristic of modern western civilisation. *BMJ* 1973;1:274-8.
- 2 Burr ML, Sweetnam PM. Vegetarianism, dietary fiber, and mortality. *Am J Clin Nutr* 1982;36:873-7.
- 3 Burr ML, Butland BK. Heart disease in British vegetarians. *Am J Clin Nutr* 1988;48:830-2.
- 4 World Health Organisation. *International classification of diseases, injuries and causes of death. 8th Revision, 1965.* Geneva: WHO, 1967.
- 5 World Health Organisation. *International classification of diseases, injuries and causes of death. 9th Revision, 1975.* Geneva: WHO, 1977.
- 6 Thorogood M, Mann J, Appleby P, McPherson K. Risk of death from cancer and ischaemic heart disease in meat and non-meat eaters. *BMJ* 1994;308:1667-71.
- 7 Chang-Claude J, Frentzel-Beyme R, Eilber U. Mortality pattern of German vegetarians after 11 years of follow-up. *Epidemiology* 1992;3:395-401.
- 8 Phillips RL, Garfinkel L, Kuzma JW, Beeson WL, Lotz T, Brin B. Mortality among California Seventh-day Adventists for selected cancer sites. *JNCI* 1980;65:1097-107.
- 9 Kahn HA, Phillips RL, Snowdon DA, Choi W. Association between reported diet and all-cause mortality. Twenty-one-year follow-up on 27,530 adult Seventh-day Adventists. *Am J Epidemiol* 1984;119:775-87.
- 10 Pandey DK, Shekelle R, Selwyn BJ, Tangney C, Stamler J. Dietary vitamin C and  $\beta$ -carotene and risk of death in middle-aged men. The Western electric study. *Am J Epidemiol* 1995;142:1269-78.
- 11 Enstrom JE, Kanim LE, Klein MA. Vitamin C intake and mortality among a sample of the United States population. *Epidemiology* 1992;3:194-202.
- 12 Gramenzi A, Gentile A, Fasoli M, Negri E, Parazzini F, La Vecchia C. Association between certain foods and risk of acute myocardial infarction in women. *BMJ* 1990;300:771-3.
- 13 Knekt P, Reunanen A, Järvinen R, Seppänen R, Heliövaara M, Aromaa A. Antioxidant vitamin intake and coronary mortality in a longitudinal population study. *Am J Epidemiol* 1994;139:1180-9.
- 14 Gaziano JM, Manson JE, Branch LG, Colditz GA, Willett WC, Buring JE. A prospective study of consumption of carotenoids in fruits and vegetables and decreased cardiovascular mortality in the elderly. *Ann Epidemiol* 1995;5:255-60.
- 15 Hertog MGL, Feskens EJM, Hollman PCH, Katan MB, Kromhout D. Dietary antioxidant flavonoids and risk of coronary heart disease: the Zutphen Elderly Study. *Lancet* 1993;342:1007-11.
- 16 Acheson RM, Williams DRR. Does consumption of fruit and vegetables protect against stroke? *Lancet* 1983;i:1191-3.
- 17 Gillman MW, Cupples LA, Gagnon D, Posner BM, Ellison RC, Castelli WP, Wolf PA. Protective effect of fruits and vegetables on development of stroke in men. *JAMA* 1995;273:1113-7.
- 18 Khaw K-T, Barrett-Connor E. Dietary potassium and stroke-associated mortality. *N Engl J Med* 1987;316:235-40.
- 19 Gale CR, Martyn CN, Winter PD, Cooper C. Vitamin C and risk of death from stroke and coronary heart disease in cohort of elderly people. *BMJ* 1995;310:563-6.
- 20 Snowdon DA, Phillips RL, Fraser GE. Meat consumption and fatal ischemic heart disease. *Preventive Medicine* 1984;13:490-500.
- 21 Burr ML, Bates CJ, Fehily AM, St Leger AS. Plasma cholesterol and blood pressure in vegetarians. *J Hum Nutr* 1981;35:437-41.
- 22 Law MR, Wald NJ, Wu T, Hackshaw A, Bailey A. Systematic underestimation of association between serum cholesterol concentration and ischaemic heart disease in observational studies: data from the BUPA study. *BMJ* 1994;308:363-6.
- 23 Mills PK, Beeson WL, Phillips RL, Fraser GE. Dietary habits and breast cancer incidence among Seventh-day Adventists. *Cancer* 1989;64:582-90.
- 24 Rao DN, Ganesh B, Desai PB. Role of reproductive factors in breast cancer in a low-risk area: a case-control study. *Br J Cancer* 1994;70:129-32.
- 25 Mills PK, Annegers JF, Phillips RL. Animal product consumption and subsequent fatal breast cancer risk among Seventh-day Adventists. *Am J Epidemiol* 1988;127:440-53.
- 26 Block G, Patterson B, Subar A. Fruit, vegetables, and cancer prevention: a review of the epidemiological evidence. *Nutr Cancer* 1992;18:1-29.
- 27 Potter JD. Risk factors for colon neoplasia—epidemiology and biology. *Eur J Cancer* 1995;31A:1033-8.
- 28 White A, Nicolaas G, Foster K, Browne F, Carey S. *Health survey for England 1991.* London: HMSO, 1993.

(Accepted 11 July 1996)

## Predictors of mortality in insulin dependent diabetes: 10 year observational follow up study

Peter Rossing, Philip Hougaard, Knut Borch-Johnsen, Hans-Henrik Parving

### Abstract

**Objective**—To evaluate the prognostic significance of microalbuminuria and overt diabetic nephropathy and other putative risk factors for cardiovascular and all cause mortality in insulin dependent diabetes.

**Design**—Ten year observational follow up study.

**Setting**—Outpatient diabetic clinic in a tertiary referral centre.

**Subjects**—All 939 adults with insulin dependent diabetes (duration of diabetes five years or more) attending the clinic in 1984; 593 had normal urinary albumin excretion ( $\leq 30$  mg/24 h), 181 persistent microalbuminuria (31–299 mg/24 h), and 165 overt nephropathy ( $\geq 300$  mg/24 h).

**Main outcome measure**—All cause and cardiovascular mortality.

**Results**—Fifteen per cent of patients (90/593) with normoalbuminuria, 25% (45/181) with microalbuminuria, and 44% (72/165) with overt nephropathy at baseline died during follow up. Cox multiple regression analysis identified the following significant predictors of all cause mortality: male sex (relative risk 2.03; 95% confidence interval 1.37 to 3.02), age (1.07; 1.06 to 1.08), height (0.96; 0.94 to 0.98), smoking (1.51; 1.09 to 2.08), social class V versus social class IV (1.70; 1.25 to 2.31),  $\log_{10}$  urinary albumin excretion (1.45; 1.18 to 1.77), hypertension (1.63; 1.18 to 2.25),  $\log_{10}$  serum creatinine concentration (8.96; 3.34 to 24.08), and haemoglobin A<sub>1c</sub> concentration (1.11; 1.03 to 1.20). Age, smoking, microalbuminuria, overt nephropathy, and hypertension were significant predictors of cardiovascular mortality. Mortality in patients with microalbuminuria was only slightly increased compared with that in patients with normoalbuminuria. Median survival

time after the onset of overt diabetic nephropathy was 13.9 years (95% confidence interval 11.8 to 17.2 years).

**Conclusions**—Abnormally increased urinary albumin excretion and other potentially modifiable risk factors such as hypertension, smoking, poor glycaemic control, and social class predict increased mortality in insulin dependent diabetes. Microalbuminuria by itself confers only a small increase in mortality. The prognosis of patients with overt diabetic nephropathy has improved, probably owing to effective antihypertensive treatment.

### Introduction

Patients with insulin dependent diabetes have increased mortality compared with the background population. The excess is due mainly to an increased risk of renal failure and cardiovascular disease in the subgroup of around 35% of patients who develop diabetic nephropathy.<sup>1</sup> Microalbuminuria is an established predictor of the later development of nephropathy in insulin dependent<sup>2-4</sup> and non-insulin dependent diabetes.<sup>5-6</sup> Microalbuminuria is also predictive of early cardiovascular and all cause mortality in non-insulin dependent diabetes<sup>7-8</sup> and possibly also insulin dependent diabetes.<sup>9-10</sup> Two small retrospective studies of microalbuminuric insulin dependent diabetic patients (n = 8 and n = 14 respectively) followed up for 23 and 18 years suggested that microalbuminuria is a strong risk marker for early death, particularly cardiovascular death.<sup>9-10</sup> We do not know, however, whether the increased mortality associated with microalbuminuria is due to the microalbuminuric state itself or due to the later development of diabetic nephropathy.

We conducted a 10 year observational follow up study of a large cohort of adult insulin dependent

Steno Diabetes Centre,  
DK 2820 Gentofte,  
Denmark

Peter Rossing, research fellow  
Hans-Henrik Parving, chief  
physician

Novo Nordisk, Statistics  
HRT/CNS/GH, Health  
Care Development,  
Bagsvaerd, Denmark  
Philip Hougaard,  
biostatistician

Centre of Preventive  
Medicine, Medical  
Department C, Glostrup  
University Hospital,  
Glostrup, Denmark  
Knut Borch-Johnsen, chief  
physician

Correspondence to:  
Dr Rossing.

*BMJ* 1996;313:779-84