

# Lifestyle Determinants and Mortality in German Vegetarians and Health-Conscious Persons: Results of a 21-Year Follow-up

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## Abstract

**Background:** The long-term observation of vegetarians in affluent countries can provide insight into the relative effects of a vegetarian diet and lifestyle factors on mortality.

**Methods:** A cohort study of vegetarians and health-conscious persons in Germany was followed-up prospectively for 21 years, including 1,225 vegetarians and 679 health-conscious nonvegetarians. Standardized mortality ratios compared with the German general population were calculated for all causes and specific causes. Within the cohort, Poisson regression modeling was used to investigate the joint effects of several risk factors on overall and cause-specific mortality.

**Results:** Standardized mortality ratios for all-cause mortality was significantly below 100: 59 [95% confidence interval (95% CI), 54-64], predominantly due to a deficit of deaths from circulatory diseases. Within the cohort, vegetarian compared with nonvegetarian diet had no effect on overall

mortality [rate ratio (RR), 1.10; 95% CI, 0.89-1.36], whereas moderate and high physical activity significantly reduced risk of death (RR, 0.62, 0.64), adjusted for age, sex, smoking, alcohol intake, body mass index, and educational level. Vegetarian diet was however associated with a reduced RR of 0.70 (95% CI, 0.41-1.18) for ischemic heart disease, which could partly be related to avoidance of meat.

**Conclusions:** Both vegetarians and nonvegetarian health-conscious persons in this study have reduced mortality compared with the general population. Within the study, low prevalence of smoking and moderate or high level of physical activity but not strictly vegetarian diet was associated with reduced overall mortality. The nonsignificant reduction in mortality from ischemic heart diseases in vegetarians compared with health-conscious persons could be explained in part by avoidance of meat intake. (Cancer Epidemiol Biomarkers Prev 2005;14(4):963-8)

## Introduction

Prospective observations of population groups adhering to particular dietary practices and lifestyle have often provided instructive insight into the effect of dietary and lifestyle factors on mortality from specific causes. In particular, vegetarians, the Seventh-Day Adventists, and the Mormons have been the objects of continuous observation. Investigations on the mortality of these relatively healthy cohorts have consistently revealed a greatly reduced mortality compared with the general population (1-5).

Besides avoiding meat, vegetarians generally exhibit other healthy lifestyle habits, such as abstinence from smoking and alcohol consumption (2, 6-8). The repeatedly asked question is whether the avoidance of meat or other dietary components plays an important role in reducing mortality. A pooled analysis of five prospective studies, including the German vegetarian study, found that vegetarians have a lower risk of dying from ischemic heart disease than nonvegetarians (5, 9). There were no significant differences in mortality from other causes of death examined. The data contributed from the German study included deaths until 1989 after 11 years of follow-up (1).

Since that time, we have completed follow-up of the cohort after 21 years. Many more deaths from specific causes of death have accumulated, rendering much greater power both for comparison of mortality rates with the general population and for a detailed examination of lifestyle characteristics of this

cohort in relation to subsequent mortality rates by internal comparison. The findings may contribute to determining which attributes of diet and lifestyle influence all-cause mortality and mortality from cancer, circulatory disease, and ischemic heart disease in persons already adhering to a healthy lifestyle.

## Subjects and Methods

The German vegetarian study has been described in detail in earlier publications (1, 6, 10). In brief, study subjects were individuals following a vegetarian or "healthy" lifestyle who were initially recruited in 1976 from readers of relevant vegetarian magazines in Germany using a short questionnaire. In 1978, a detailed study questionnaire was mailed out to those willing to participate as well as to their close family members ages  $\geq 10$  years. Data collected included information on sociodemographic characteristics, dietary habits, smoking and drinking habits, physical activity, and previous medical history. Dietary information was collected using semiquantitative questions on usual frequency of consumption (in five categories) of vegetables overall as well as specific vegetables, fruits, nuts, cereal, different milk products, eggs, fish, meat, and processed meat. Physical activity was assessed both by frequency of different leisure sport activities and by a self-evaluation of the subject's level of activity. The study abided by the guidelines in the revised version of the Declaration of Helsinki 1964. A total of 1,904 persons (858 men and 1,046 women) participated by returning the questionnaire and comprised 82.5% of those who received them. Consent was obtained separately from the participants for the release of cause of death on the event of their death. In the subsequent 10 years, contact was maintained through mailings of a short

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questionnaire regarding illness and dietary changes and reports of the mortality analysis after 5 and 11 years of follow-up (1).

Participants were categorized according to their response regarding dietary habits at the time point of enrollment. The study participants were classified into vegan (those who avoid meat, fish, eggs, and dairy products), lacto-ovo vegetarian (those who avoid meat and fish but eat eggs and/or dairy products), and nonvegetarian (those who occasionally or regularly eat meat and/or fish). In previous reports, we used the term "moderate vegetarians" instead of nonvegetarians but included also those who did not strictly avoid but seldom ate meat or fish. Self-reported height and weight were used to calculate body mass index (BMI, kg/m<sup>2</sup>). Physical activity was analyzed using the self-evaluation of the participants on a three-level scale.

The vital status of the study participants by December 31, 1999 was requested from the Registrar's Office at the last documented place of residence. Copies of the death certificates were obtained from the public health office in charge. The underlying cause of death was coded by a trained nosologist according to the ninth revision of the *International Classification of Diseases and Causes of Death*.

The mortality analysis included all deaths occurring in the cohort until December 31, 1999. Standardized mortality ratios (SMR) were calculated by comparison of observed deaths with those expected based on the age- and sex-specific mortality rates of Germany between 1975 and 1999. Within the total cohort, Poisson regression was used to investigate possible determinants of mortality by comparing death rates among study participants for various factors simultaneously including vegetarian status, age, sex, education, and BMI. The highest educational level of the parents was used for subjects under the age of 20 years who had not yet finished schooling.

Multiplicative models were fitted to appropriately cross-classified data using PROC GENMOD (SAS System version 8.0). The person-years at risk were used as offset. Maximum likelihood estimates of rate ratios (RR) for exposure variables and 95% confidence intervals (95% CI) based on exact Poisson probabilities were calculated.

## Results

Overall, 60 subjects were vegans (3.1%), 1,165 lacto-ovo vegetarians (61.2%), and 679 (35.7%) nonvegetarians. The study participants were generally highly educated, about 40% having received >12 years of schooling (Table 1). They were less likely to be obese (7%) than underweight (14%). Vegetarians had lower median BMI than nonvegetarians (20.7 versus 21.3) and reported more often a high level of physical activity. Smoking rates were very low, with only 3.9% of vegetarians and 8.0% of nonvegetarians being smokers at the time of recruitment.

By the end of 1999, 535 (28%) study participants had died, 43 had emigrated (2.3%), and only 17 (0.9%) were lost to follow-up. All-cause mortality in this cohort (SMR, 59; 95% CI, 54-64) was strongly reduced compared with the general population, predominantly due to a deficit of deaths from circulatory diseases. As shown in Table 2, the reduced mortality was more pronounced in men (SMR, 52, 95% CI, 46-59) than in women (SMR, 66; 95% CI, 59-74). For men, significantly fewer deaths than expected from both circulatory diseases and cancer (SMR, 49 and 47, respectively) and particularly from lung cancer were observed, whereas for women, significant reduction was found for mortality from circulatory diseases but not from cancer (SMR, 56 and 82, respectively). SMRs were below 100 for most other causes of death categories examined.

**Table 1. Characteristics of the study group by sex and by dietary group**

	Total (n = 1,904), n (%)	Female (n = 1,046), n (%)	Male (n = 858), n (%)	Vegetarians (n = 1,225), n (%)	Nonvegetarians (n = 679), n (%)
Gender					
Female	1,046 (54.9)	—	—	677 (55.3)	369 (54.3)
Male	858 (45.1)	—	—	548 (44.7)	310 (45.7)
Age group at entry					
≤34	586 (30.8)	280 (26.8)	306 (35.7)	369 (30.1)	217 (32.0)
35-44	334 (17.5)	181 (17.3)	153 (17.8)	211 (17.2)	123 (18.1)
45-54	239 (12.6)	138 (13.2)	101 (11.8)	145 (11.8)	94 (13.8)
55-64	255 (13.4)	176 (16.8)	79 (9.2)	151 (12.3)	104 (15.3)
65-74	302 (15.9)	170 (16.3)	132 (15.4)	198 (16.2)	104 (15.3)
≥75	188 (9.9)	101 (9.7)	87 (10.1)	151 (12.3)	37 (5.4)
Education*					
Low	367 (19.3)	242 (23.1)	125 (14.6)	238 (19.4)	129 (19.0)
Medium	702 (36.9)	459 (43.9)	243 (28.3)	461 (37.6)	241 (35.5)
High	821 (43.1)	338 (32.3)	483 (56.3)	520 (42.4)	301 (44.3)
Unknown	14 (0.7)	7 (0.7)	7 (0.8)	6 (0.5)	8 (1.2)
BMI					
Normal (>18.5-25)	1,376 (72.3)	745 (71.2)	631 (73.5)	886 (72.3)	490 (72.2)
Underweight (<18.5)	265 (13.9)	171 (16.3)	94 (11.0)	179 (14.6)	86 (12.7)
Overweight (>25)	140 (7.4)	68 (6.5)	72 (8.4)	81 (6.6)	59 (8.7)
Unknown	123 (6.5)	62 (5.9)	61 (7.1)	79 (6.4)	44 (6.5)
Median	20.9	20.6	21.3	20.7	21.3
Level of activity					
Low	139 (7.3)	68 (6.5)	71 (8.3)	87 (7.1)	52 (7.7)
Moderate	1,026 (53.9)	582 (55.6)	444 (51.8)	644 (52.6)	382 (56.3)
High	681 (35.8)	358 (34.2)	323 (37.7)	456 (37.2)	225 (33.1)
Unknown	58 (3.0)	38 (3.6)	20 (2.3)	38 (3.1)	20 (2.9)
Smoking					
Never	1,548 (81.3)	912 (87.2)	636 (74.1)	1,025 (83.7)	523 (77.0)
Former	254 (13.3)	100 (9.6)	154 (18.0)	152 (12.4)	102 (15.0)
Current	102 (5.4)	34 (3.3)	68 (7.9)	48 (3.9)	54 (8.0)
Alcohol consumption					
Never	930 (48.8)	575 (55.0)	355 (41.4)	701 (57.2)	229 (33.7)
Ever	974 (51.2)	471 (45.0)	503 (58.6)	524 (42.8)	450 (66.3)

\*Low, <10 years schooling; medium, 10 to 12 years; high, ≥13 years.

**Table 2. Mortality analysis (1978-1999) for selected causes of death by sex and dietary group**

Cause of death (ICD-9)	Males		Females		Vegetarians		Nonvegetarians	
	Deaths	SMR (95% CI)	Deaths	SMR (95% CI)	Deaths	SMR (95% CI)	Deaths	SMR (95% CI)
All causes (001-999)	243	52 (46-59)	292	66 (59-74)	380	62 (56-69)	155	52 (44-61)
Infectious diseases (010-139)	1	29 (5-164)	2	68 (19-248)	3	71 (24-209)	0	—
Malignant neoplasms (140-208)	50	47 (36-62)	74	82 (65-103)	88	69 (56-85)	36	53 (38-73)
Stomach (151)	8	79 (40-155)	8	99 (50-195)	11	91 (51-163)	5	83 (35-194)
Colon and rectum (153-154)	5	35 (15-82)	10	65 (35-120)	8	41 (21-81)	7	70 (34-144)
Lung (162)	1	4 (0-23)	2	35 (10-128)	3	16 (5-47)	0	—
Breast (174)	—	—	9	62 (33-118)	6	63 (29-137)	3	60 (20-176)
Ovary (183)	—	—	5	97 (41-227)	5	148 (63-346)	0	—
Prostate (185)	8	51 (26-101)	—	—	7	69 (33-142)	1	18 (3-102)
Bladder (188)	3	57 (19-168)	2	102 (28-371)	3	63 (21-185)	2	81 (22-295)
Benign neoplasms (210-239)	1	28 (5-159)	2	54 (14-197)	1	21 (4-119)	2	84 (23-306)
Endocrine and blood diseases (240-289)	6	69 (32-151)	6	43 (20-94)	8	53 (27-105)	4	54 (21-139)
Mental disorders (290-319)	3	78 (3-229)	4	133 (51-342)	5	112 (48-262)	2	85 (23-310)
Diseases of the nervous system (320-389)	8	132 (67-261)	5	80 (34-187)	11	137 (77-245)	2	46 (13-168)
Diseases of the circulatory system (390-459)	117	49 (41-59)	138	56 (47-66)	173	52 (45-60)	82	54 (44-67)
Ischemic heart diseases (410-414)	43	44 (33-59)	29	36 (25-52)	44	37 (28-50)	28	47 (33-68)
Cerebrovascular diseases (430-438)	31	55 (39-78)	44	66 (49-89)	52	61 (48-80)	23	62 (41-93)
Diseases of the respiratory system (460-519)	16	39 (24-63)	16	68 (42-110)	25	58 (39-86)	7	34 (16-70)
Diseases of the digestive system (520-579)	4	20 (8-51)	8	44 (22-87)	8	31 (16-61)	4	31 (12-80)
Diseases of the genitourinary system (580-629)	4	57 (22-147)	5	89 (38-208)	9	103 (54-196)	0	—
Symptoms and ill-defined conditions (780-799)	14	127 (76-213)	14	116 (69-194)	19	119 (76-186)	9	128 (67-243)
Accidents (800-999)	17	98 (61-157)	15	111 (67-183)	25	121 (82-179)	7	68 (33-140)

Abbreviation: ICD-9, ninth revision of the *International Classification of Diseases and Causes of Death*.

The reduced all-cause mortality compared with the general German population was somewhat stronger for nonvegetarians (SMR, 52; 95% CI, 44-61) than vegetarians (SMR, 62; 95% CI, 56-69), as was the significantly lower mortality from malignant neoplasms (SMR, 53 and 69, respectively). Mortality from circulatory diseases and from cerebrovascular diseases were similarly reduced in both dietary groups; however, vegetarians experienced lower mortality from ischemic heart disease than nonvegetarians. The SMRs for diseases of the respiratory system and the digestive system were also significantly decreased in both groups.

We were interested to see whether mortality changed with follow-up time. The SMRs for all causes were lowest during the first 5 years of follow-up for both sexes (Fig. 1). The reduced mortality diminished with follow-up time but remained significantly lower than in the general population even after >15 years of follow-up.

The analysis of lifestyle determinants of mortality within the cohort was restricted to the 1,724 subjects without missing data for the variables of interest (Table 3). Within the cohort, the strongest determinant of mortality was smoking, despite relatively few smokers. Compared with never smokers, smokers at entry into the study had significantly increased mortality RR for all causes (2.04; 95% CI, 1.37-3.04) and circulatory diseases (2.66; 95% CI, 1.52-4.63). Ever smokers (former or current smoker) were at significantly increased risk of dying from ischemic heart disease (2.93; 95% CI, 1.60-5.36; data not shown). A nonsignificant elevated RR for all malignant neoplasms was found also for former smokers (1.71; 95% CI, 0.95-3.06).

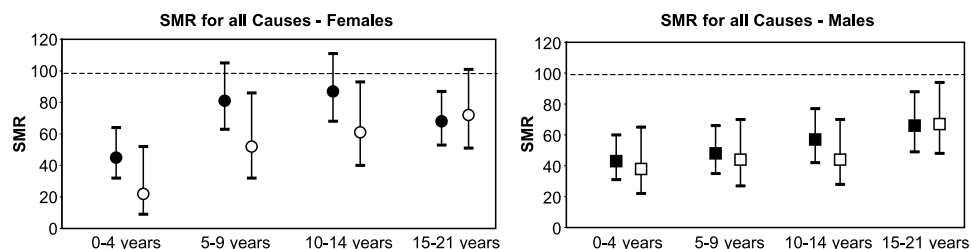
A self-reported moderate or high level of physical activity compared with low activity showed a clear protective effect on mortality from all malignant neoplasms, circulatory diseases, and ischemic heart disease, and a significant effect for all causes combined (0.62; 95% CI, 0.43-0.89 for moderate and 0.64; 95% CI, 0.44-0.93 for high level physical activity). The reduced mortality from circulatory diseases associated with high level of activity was borderline significant (0.58; 95% CI, 0.33-1.00).

Alcohol consumption was weakly associated with all-cause mortality and ischemic heart disease but significantly associated with an increased mortality risk for all malignant neoplasms (1.65; 95% CI, 1.06-2.56).

Mortality rates did not differ significantly between vegetarians and health-conscious nonvegetarians. Compared with the nonvegetarians, vegetarians had slightly higher mortality from all-cause mortality (1.10; 95% CI, 0.89-1.36), similar mortality from malignant neoplasms, but reduced mortality from circulatory disease (0.83; 95% CI, 0.62-1.12) and ischemic heart disease (0.70; 95% CI, 0.41-1.18). We also tested for possible differences between a vegan and a lacto-ovo vegetarian diet, although there were only 60 vegans and 23 deaths in this group. Being a vegan was associated with a higher mortality risk (1.59; 95% CI, 0.98-2.59) than being a lacto-ovo vegetarian (1.08; 95% CI, 0.86-1.34), when compared with nonvegetarians with moderate meat/fish consumption, accounting for all other variables (data not shown).

BMI was not strongly associated with overall mortality and cancer mortality. However, compared with a normal BMI between 18.5 and 25, BMI  $\geq$ 25 was associated with an

**Figure 1.** SMRs and their 95% CIs for all causes of death, dietary group, and 5-year follow-up period, separately for males and females. SMRs are represented by different symbols (○, female vegetarians; ●, female non-vegetarians; □, male vegetarians; ■, male non-vegetarians). Bars, 95% CI.



**Table 3. Risk factors for mortality from all causes, malignant neoplasms, circulatory diseases, and ischemic heart diseases**

	All causes (n = 456)		Malignant neoplasms (n = 107)		Circulatory diseases (n = 219)		Ischemic heart diseases (n = 60)	
	Deaths	RR* (95% CI)	Deaths	RR* (95% CI)	Deaths	RR* (95% CI)	Deaths	RR* (95% CI)
Smoking at entry								
Never	374	1	88	1	180	1	54	1
Former	52	1.13 (0.83-1.55)	16	1.71 (0.95-3.06)	23	1.06 (0.66-1.69)	6	1.81 (0.86-3.81)
Current	30	2.04 (1.37-3.04)	3	0.99 (0.30-3.24)	16	2.66 (1.52-4.63)	0	—
Level of activity								
Low	34	1	8	1	16	1	3	1
Moderate	228	0.62 (0.43-0.89)	50	0.62 (0.29-1.32)	120	0.69 (0.41-1.18)	38	0.57 (0.22-1.50)
High	194	0.64 (0.44-0.93)	49	0.84 (0.39-1.81)	83	0.58 (0.33-1.00)	19	0.58 (0.21-1.56)
Alcohol consumption								
Never	257	1	66	1	121	1	35	1
Ever	199	1.15 (0.93-1.41)	41	1.65 (1.06-2.56)	98	1.09 (0.81-1.48)	25	1.34 (0.77-2.34)
Dietary group								
Nonvegetarian	134	1	31	1	74	1	19	1
Vegetarian	322	1.10 (0.89-1.36)	76	1.04 (0.67-1.62)	145	0.83 (0.62-1.12)	41	0.70 (0.41-1.18)
BMI†								
Normal	348	1	81	1	167	1	47	1
Underweight	57	1.13 (0.85-1.51)	16	1.05 (0.61-1.81)	23	0.91 (0.58-1.42)	5	1.06 (0.47-2.40)
Overweight	51	1.12 (0.82-1.51)	10	0.98 (0.50-1.92)	29	1.40 (0.93-2.12)	8	1.90 (0.95-3.78)
Education								
Low	130	1	32	1	66	1	21	1
Medium	185	0.89 (0.71-1.12)	41	0.74 (0.46-1.18)	83	0.83 (0.59-1.15)	18	0.95 (0.52-1.75)
High	141	0.80 (0.62-1.03)	34	0.60 (0.36-1.00)	70	0.82 (0.57-1.18)	21	0.76 (0.39-1.48)

NOTE: Included are only those without missing values in all variables in the table.

\*Adjusted for age, gender, and all other variables in the table.

†BMI categories (underweight, <18.5 kg/m<sup>2</sup>; normal weight, 18.5-25.0 kg/m<sup>2</sup>; overweight, >25.0 kg/m<sup>2</sup>).

increased risk of dying from circulatory disease (1.40; 95% CI, 0.93-2.12) and from ischemic heart disease (1.90; 95% CI, 0.95-3.78).

Educational level was used as a surrogate variable for differences in socioeconomic status. Compared with a low level of education (equivalent to <10 years of schooling), medium and high levels of education were associated with nonsignificant reduced mortality from all causes and the specific causes examined.

To identify which aspects of the vegetarian diet may influence risk of death within the cohort, particularly for circulatory diseases and ischemic heart disease, we analyzed several dietary variables independent of the dietary group. Frequency of intake of vegetables, fruits, and nuts did not show an appreciable effect on all-cause and cause-specific mortality. Regular meat intake ( $\geq 3$  times/wk) was associated with a nonsignificantly increased risk of dying from circulatory diseases (RR, 2.02; 95% CI, 0.91-4.44) and a significantly increased risk of dying from ischemic heart diseases (RR, 4.78; 95% CI, 1.86-12.28), which was based on a very small number of deaths from ischemic heart diseases (Table 4). However, there was a significant trend of increasing risk with higher consumption levels of meat ( $P = 0.006$ ). A similar association between consumption of meat products and mortality from circulatory diseases and ischemic heart diseases was also observed (Table 4). Again, the trend test with increasing meat product consumption was significant only for ischemic heart diseases ( $P = 0.04$ ). The highest fish consumption category was also associated with a significantly elevated risk of dying from ischemic heart diseases.

## Discussion

The mortality of our study participants, including both vegetarians and nonvegetarian "health-conscious" persons, was very low (SMR, 59) compared with the general population in Germany after a follow-up of 21 years. This was predominantly due to a large deficit of deaths from circulatory diseases, which accounts for about 50% of all

deaths in the general population. The greater reduction of deaths from malignant neoplasms among men than in women is predominantly attributable to the large deficit of lung cancer, the leading cause of cancer deaths among men. The virtual absence of smoking in this study population probably explains much of the scarcity of deaths from lung cancer and respiratory diseases as well as in part that of circulatory diseases.

The mortality analysis by time since entry into the study indicated an initial weak healthy participant effect but the mortality remained low. The SMR for all-cause mortality increased for men over the years, whereas among women the SMR reached a plateau after 10 years. The disappearance of the self-selection effect after 5 to 10 years was similarly observed in the British vegetarian studies (11).

**Table 4. Meat and fish consumption and mortality from circulatory diseases and ischemic heart diseases**

	Circulatory diseases		Ischemic heart diseases	
	Deaths	RR* (95% CI)	Deaths	RR* (95% CI)
Meat consumption				
Never	162	1	47	1
$\leq$ Once a month	29	1.01 (0.67-1.52)	9	1.01 (0.47-2.19)
$>$ Once a month	21	1.39 (0.86-2.25)	3	1.80 (0.82-3.94)
$\geq 3$ times/wk	7	2.02 (0.91-4.44)	1	4.78 (1.86-12.28)
$P_{\text{trend}}$		0.08		0.006
Meat products consumption				
Never	178	1	51	1
$\leq$ Once a month	22	1.07 (0.73-1.56)	7	1.29 (0.68-2.43)
$>$ Once a month	19	2.38 (0.94-6.05)	2	5.24 (1.64-16.71)
$P_{\text{trend}}$		0.27		0.04
Fish consumption				
Never	147	1	40	1
$\leq$ Once a month	39	1.10 (0.76-1.59)	12	1.11 (0.56-2.23)
$>$ Once a month	33	1.24 (0.83-1.85)	8	2.11 (1.13-3.96)
$P_{\text{trend}}$		0.28		0.03

NOTE: Included are only those with nonmissing data in the variables from Table 3 and this table.

\*Adjusted for age, gender, and all other variables in Table 3 except dietary group.

Both subjects who avoided meat and fish and those who consumed moderate amounts of meat and/or fish experienced strongly reduced mortality, indicating that both groups are not representative of the general population. A similar 50% to 60% reduction in mortality has been reported for other vegetarian and health-conscious cohorts in Europe after a comparable length of follow-up time (5, 11). Several nondietary factors that differ in their prevalence in our study population and in the general population could partly explain the low mortality. A health-conscious lifestyle is more common among the better informed and well educated and is reflected in the proportion of higher educated and professionals (50%) in our study population compared with the general population (18%; ref. 12). The smoking rate was very low and this is known to explain the low mortality also among the Seventh-Day Adventists and the Mormon high priests, who generally neither smoke cigarettes nor drink alcohol (3, 7, 13, 14). In addition, <10% of the study participants were overweight. Overweight and obesity are known to be important determinants of mortality (15, 16). It is therefore not surprising that study cohorts of vegetarians and health-conscious groups generally associated with a low prevalence of obesity also have lower mortality compared with the general population (11).

Our study population was selected for leading a healthy lifestyle and was clearly not comparable with the general population. Using internal comparison, we were able to study directly the effect of lifestyle factors, accounting for different confounders simultaneously. We were nevertheless surprised to find smoking the strongest determinant of mortality in this study cohort despite the low prevalence of smoking at entry. The increased mortality risk was predominantly found for circulatory diseases rather than cancer and seemed at least as strong for ischemic heart disease. Preliminary results from EPIC-Oxford also showed a somewhat higher risk of ischemic heart disease than overall circulatory diseases associated with smoking (17). We found a moderately elevated risk for all malignant neoplasms associated with former smoking only.

A moderate or high level of physical activity had a strong protective effect on mortality in our study population, reducing circulatory disease mortality by 35% and all malignant neoplasms by 30%. Our findings corroborate epidemiologic evidence indicating that regular and vigorous physical activity is an effective means of preventing circulatory diseases and cancers at different sites (18). Regular physical exercise and adequate sleep was also found to further decrease mortality among religiously active Mormons (7). In another low-risk healthy cohort, the Adventist Health Study, exercise was associated with a similar risk reduction of about 40% for fatal coronary heart disease (19). The protective effect of regular exercise against overall mortality and coronary heart disease mortality was observed even for the oldest subjects ages  $\geq 84$  years (20). Physical activity can therefore further reduce the risk of dying among those who already follow a healthy lifestyle.

A vegetarian diet devoid of meat and fish did not have any effect on all-cause mortality and cancer mortality compared with a nonvegetarian diet in health-conscious persons. There was solely a nonsignificantly lower risk of dying from ischemic heart disease (RR, 0.70). This modest reduction in mortality from ischemic heart disease in vegetarians compared with nonvegetarian was also observed in the three British vegetarian studies albeit nonsignificant (death risk ratios of 0.85, 0.86, and 0.75 in the Health Food Shoppers Study, the Oxford Vegetarian Study, and EPIC-Oxford, respectively) but was significant with RR of 0.76 in a pooled analysis of five prospective studies, including a shorter follow-up of the German study (5, 17).

These results may be interpreted to suggest that abstinence from meat, meat products, and fish does not affect the risk of death except for ischemic heart disease. It should be pointed

out, however, that even among the nonvegetarians in our study, there were only 0.4% (1.6%) who reported consuming meat (meat products) daily, 6.5% (4.9%) frequently ( $\geq 3$  times/wk but not daily), and 28.1% (18.7%) occasionally (more than once a month but  $< 3$  times/wk). Therefore, the meat consumption was quite moderate compared with the general population (21, 22). Thus, the findings from the healthy cohorts corroborate epidemiologic findings showing increased risks for coronary heart disease. The lack of clear differences in cancer mortality between vegetarians and nonvegetarians may indicate that, for the relevant cancer sites, moderate meat consumption plays a less important role in populations or groups with a healthy lifestyle and diet high in vegetables, fruits, and grains. For ischemic heart disease, the lower mortality among vegetarians may truly be attributed to abstinence from meat. When we examined the influence of dietary variables on mortality within the cohort, taking into account all other lifestyle factors, we found regular consumption of meat, meat products, and fish to be associated with a significantly increased risk for ischemic heart disease with a clear dose-response relationship. In the Oxford Vegetarian Study, a gradient of risk in ischemic heart disease mortality was apparent with increasing intake of saturated animal fat and cholesterol (23). The highest tertile of intake was associated with a 2- to 3-fold increased risk. In that study, the association with meat consumption was not strong. However, a dose-response relationship between meat consumption and ischemic heart disease risk has been reported among the California Seventh-Day Adventists, also representing a relatively health-conscious cohort (24, 25). The average diet of the Seventh-Day Adventist vegetarians is not particularly low in fat. Vegetarians and nonvegetarians among the Adventists, however, differ in the type of fat consumed: the ratio of polyunsaturated to saturated fat was 0.83 and 0.63, respectively (25). Meat contains substantial quantities of cholesterol and saturated fats that raise low-density lipoprotein cholesterol concentration. Therefore, the findings regarding meat consumption are compatible with the hypothesis that the nature and quantity of dietary fat and cholesterol are key determinants of ischemic heart disease mortality (26-29).

We were not able to identify significant effects for intake of other food groups, such as vegetables, fruits, nuts, and grains. Both vegetarian and nonvegetarian participants of this study had high average intake levels of vegetables and fruits. The absence of an effect in our data could be due to the lack of gradient in risk at these high levels. The semiquantitative food frequency questionnaire that we used was a relatively crude instrument compared with the more sophisticated food frequency questionnaire currently employed in large epidemiologic studies. Therefore, we may not have been able to detect finer differences in dietary pattern. Furthermore, because some participants may have changed their diet during follow-up, we cannot exclude the possibility that some associations with dietary factors were not detected or overestimated due to misclassification. The associations shown had taken into account all major potential confounding factors. Restricting the data to individuals with no previous cancer or ischemic heart disease did not materially change the risk estimates.

In summary, we conclude that the recommended healthy lifestyle factors, particularly abstinence from smoking, a moderate or high level of physical activity, moderate alcohol intake, and absence of overweight, are important determinants of reduced mortality in both vegetarians and nonvegetarians who already follow a healthy lifestyle (30). Meat consumption seems to explain in part the higher mortality from ischemic heart disease in nonvegetarians compared with vegetarians. Other potentially protective foods were not identified, and this could be due to either inadequacy of the instruments used to measure dietary intake or the general high intake of vegetables and fruits in the whole cohort.

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# BLOOD CANCER DISCOVERY

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