

# Adherence to the *Dietary Guidelines for Americans* and risk of major chronic disease in women<sup>1-5</sup>

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## ABSTRACT

**Background:** Little is known about the overall health effects of adherence to the *Dietary Guidelines for Americans*. The healthy eating index (HEI), developed at the US Department of Agriculture, measures how well Americans' diets conform to these guidelines.

**Objective:** We tested whether the HEI (scores range from 0 to 100; 100 is best) calculated from food-frequency questionnaires (HEI-f) would predict risk of major chronic disease in women.

**Design:** A total of 67272 US female nurses who were free of major disease completed detailed questionnaires on diet and chronic disease risk factors in 1984 and repeatedly over 12 y. Major chronic disease was defined as fatal or nonfatal cardiovascular disease (myocardial infarction or stroke,  $n = 1365$ ), fatal or nonfatal cancer ( $n = 5216$ ), or other nontraumatic deaths ( $n = 496$ ), whichever came first. We also examined cardiovascular disease and cancer as separate outcomes.

**Results:** After adjustment for smoking and other risk factors, the HEI-f score was not associated with risk of overall major chronic disease in women [relative risk (RR) = 0.97; 95% CI: 0.89, 1.06 comparing the highest with the lowest quintile of HEI-f score]. Being in the highest HEI-f quintile was associated with a 14% reduction in cardiovascular disease risk (RR = 0.86; 95% CI: 0.72, 1.03) and was not associated with lower cancer risk (RR = 1.02; 95% CI: 0.93, 1.12).

**Conclusion:** These data suggest that adherence to the 1995 *Dietary Guidelines for Americans*, as measured by the HEI-f, will have limited benefit in preventing major chronic disease in women. *Am J Clin Nutr* 2000;72:1214-22.

**KEY WORDS** Diet, nutrition, diet quality, healthy eating index, food guide pyramid, dietary guidelines, cardiovascular disease, cancer, women, food-frequency questionnaire

## INTRODUCTION

The *Dietary Guidelines for Americans* are designed to promote good health and reduce the risk of major chronic disease in the United States (1); the food guide pyramid instructs Americans in following these guidelines (2). The utility of the guidelines has been assessed by evaluating the relation of the guidelines to chronic disease risk factors (3); however, little is known about whether risk of major chronic disease can be reduced by following the guidelines.

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The healthy eating index (HEI) is a 10-component indicator of how well Americans' diets conform to the dietary guidelines and the food guide pyramid. The HEI was developed at the US Department of Agriculture (USDA) to track the quality of the American diet over time and to guide nutrition promotion activities (4). In a prospective study of 38622 men followed for 8 y, we found that the HEI score calculated from food-frequency questionnaires (HEI-f) was associated with only a small reduction in overall incidence of major chronic disease [fatal and nonfatal cardiovascular disease (CVD) and cancer and other causes of death combined] (5). This weak inverse association was driven by a moderate inverse association with CVD risk; there was no relation to risk of cancer.

The major causes of death in women differ from those in men throughout much of adult life, with malignant neoplasms ranking highest among adult women aged 45-64 y and CVD ranking highest for men in the same age range (6). After the age of 64 y, however, heart disease is the leading cause of death in both men and women. Therefore, with use of the HEI-f, we examined the overall association between adherence to the dietary guidelines and subsequent risk of major chronic disease in 67272 women from the Nurses' Health Study cohort who were followed for 12 y.

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**TABLE 1**

Healthy eating index (HEI) scoring criteria and HEI scores in the Continuing Survey of Food Intakes by Individuals (CSFII) subset and the Nurses' Health Study (NHS) cohort<sup>1</sup>

Component	Criteria for maximum score of 10 <sup>2</sup>		Criteria for minimum score of 0	CSFII (1996)	NHS (1984)
	Women 19–50 y	Women ≥51 y		HEI score	HEI-f score
1) Grains (servings/d)	9.1	7.4	0	6.7 <sup>3</sup>	4.9 ± 2.2 <sup>4</sup>
2) Vegetables (servings/d)	4.2	3.5	0	6.3	8.7 ± 1.9
3) Fruit (servings/d)	3.2	2.5	0	3.8	7.2 ± 2.9
4) Milk (servings/d)	2.0	2.0	0	5.4	6.1 ± 2.9
5) Meat (servings/d)	2.4	2.2	0	6.4	8.3 ± 2.0
6) Total fat (% of total energy)		≤30	≥45	6.9	6.5 ± 3.0
7) Saturated fat (% of total energy)		<10	≥15	6.4	5.2 ± 3.5
8) Cholesterol (mg/d)		<300	≥450	7.9	7.4 ± 3.6
9) Sodium (mg/d)		<2400	≥4800	6.3	5.0 ± 3.2 <sup>5</sup>
10) Variety (no. of different food items over 3 d)		16	≤6	7.6	5.0 ± 3.1 <sup>6</sup>
Total score				64	64.4 ± 12.5

<sup>1</sup>HEI scoring criteria were adapted from Kennedy et al (4). The CSFII subset ( $n = 428$ ) was a subsample of women aged 37–66 y, with ≥12 y of schooling (16). Pregnant and lactating women were excluded. HEI-f, HEI score calculated from food-frequency questionnaires.

<sup>2</sup>Recommended servings for age and sex groups extrapolated from recommended energy requirements (14).

<sup>3</sup> $\bar{x}$ .

<sup>4</sup> $\bar{x} \pm$  SD.

<sup>5</sup>Sodium in deciles of NHS distribution of intake.

<sup>6</sup>Variety scored by quantile of different foods consumed per month.

## SUBJECTS AND METHODS

### Study population

The Nurses' Health Study was established in 1976 when 121 700 female nurses aged 30–55 y responded to a mailed questionnaire requesting information on medical history and risk factors for cancer and heart disease. Every 2 y, follow-up questionnaires are sent to obtain up-to-date information on smoking history, weight, leisure time activity, medication use, and other risk factors and to identify newly diagnosed diseases.

In 1980 a 61-item food-frequency questionnaire (FFQ) was mailed to participants to obtain information on diet. The FFQ was expanded to 116 items in 1984, primarily by creating individual questions for groups of nutritionally similar foods previously combined in single items. For consistency with our previous study of men, in which the expanded FFQ was used, we considered 1984 as the baseline for the present analysis.

After ≤4 mailings, 81 757 women returned the 1984 diet questionnaire. We excluded women with previously diagnosed cancer, myocardial infarction (MI), stroke, angina, or other CVD. Women with diabetes were excluded because this disorder is strongly associated with CVD and because it may have caused them to alter their usual diets. We also excluded those with unrealistically low (<2510 kJ/d) or high (>14644 kJ/d) energy intakes and those who left >70 items blank on the FFQ. The final baseline population in 1984 included 67 272 women. The study was conducted according to the ethical guidelines of Brigham and Women's Hospital, Boston.

### Dietary assessment

Dietary intake data were collected in 1984, 1986, and 1990 with use of similar questionnaires. For each item, a common serving size of food or beverage was specified (eg, 1/2 cup broccoli or 1 cup milk) and participants were asked how often, on average, they consumed this serving size of the item over the previous year. The FFQ provided 9 frequency responses ranging from "never or less than once per month" to "six or more times per day." Separate questions

were asked about types of fats and oils used in cooking and addition of salt to food at the table and during cooking. We computed nutrient intake by multiplying the frequency of consumption of each food by the nutrient content of the specified portion, and then summing nutrient contributions from all foods. Nutrient values were derived from USDA sources (7, 8) supplemented with information from food manufacturers and published research.

The development, reproducibility, and validity of the FFQ were documented in detail elsewhere (9–13). In 1986 the expanded FFQ was completed twice at a 1-y interval by a subsample of 191 women from the Nurses' Health Study cohort, many of whom participated in an earlier validation study (9). Two 1-wk diet records were also completed during this interval. The mean correlation coefficient between the energy-adjusted nutrient intakes measured by the second FFQ and the diet records, corrected for week-to-week variation, was 0.63 (L Sampson, E Rimm, G Colditz, et al, unpublished observations, 2000). The mean correlation for nutrients averaged from food records kept by these women during 1980 and 1986 with the 1986 FFQ was 0.68, indicating reasonably valid measures of current and long-term average dietary intake by the FFQ (L Sampson, E Rimm, G Colditz, et al, unpublished observations, 2000).

### The healthy eating index

We calculated an HEI score for each FFQ respondent for 1984, 1986, and 1990 by using methods similar to those used in our previous study of men (5), with *The Healthy Eating Index Final Report* (14) as a guide for these calculations. Listed in **Table 1** are the 10 equally weighted components of the HEI, which reflect dietary recommendations based on the food guide pyramid (2) and the *Dietary Guidelines for Americans* (1). Each component has a minimum score of zero (for nonadherence) and a maximum of 10 (for perfect adherence); intermediate degrees of adherence to the guidelines are calculated proportionately. The scores from the 10 components are added for a total HEI score ranging from 0 (worst) to 100 (best).

Components 1–5 quantify adherence to serving recommendations for 5 food groups: grains (includes bread, cereal, rice, and pasta), vegetables, fruit, milk (includes yogurt and cheese), and

meat (includes meat, poultry, fish, dry beans, eggs, and nuts) (15). The number of recommended servings varies by age and sex; the recommended servings used to determine the HEI scores for the women in this study are shown in Table 1. We assigned food items on the FFQ to their appropriate food groups after applying serving size conversion factors when appropriate to conform to the serving size definitions in the food guide pyramid (16).

Consistent with USDA protocol (14), we disaggregated recipes from our database and assigned foods to their appropriate groups. We totaled the average number of daily servings of foods from each food group. We did not adjust the food intakes for total energy because adjustment is not used in the USDA HEI scoring system, which accounts for differences in energy requirements by varying the recommended number of servings by sex and age.

Components 6–9 relate to nutrient intake, which we derived from our database. The total fat, saturated fat, and cholesterol components were scored according to USDA criteria. We calculated the sodium component differently because the 1984 FFQ did not ask about salt added during cooking, which resulted in an underestimate of sodium intake. We therefore divided the participants into 11 equal groups based on the distribution of reported sodium intake and assigned corresponding scores of 0–10 (higher score for less sodium consumed). Although subsequent FFQs did inquire about salt use during cooking, we used this sodium scoring method throughout for consistency.

As in our previous study of men (5), we also quantified the variety component differently. Because the FFQ does not assess foods consumed on a particular day, women were grouped into 11 equal quantiles according to the number of unique foods consumed per month (range: 22–61) and the groups were assigned scores of 0–10. For example, those with the fewest unique foods consumed per month received a score of zero and those with the most received a score of 10. Hereafter, we refer to the estimation of the HEI by the FFQ as the HEI-f. We also calculated HEI scores from food records kept during a validation study of the expanded FFQ in 127 men participating in the Health Professionals Follow-up Study (11, 12). The Pearson correlation coefficient relating the HEI-f to the HEI computed from the diet records, corrected for week-to-week variation in diet records, was 0.72 (95% CI: 0.59, 0.81). This indicates that the HEI can be estimated reasonably well from the FFQ.

For comparison, the USDA calculated HEI scores for a demographically similar subset of women from the nationwide Continuing Survey of Food Intake by Individuals (CSFII;  $n = 428$ ), using one 24-h recall and 2 food records. The women in the CSFII subset were employed, had  $\geq 12$  y education, and were of the same age range as the Nurses' Health Study participants.

### Outcome ascertainment

The primary endpoint for this study was combined major chronic disease, defined as CVD, cancer, or death, whichever came first. We also examined CVD and cancer as separate outcomes.

CVD was defined as fatal or nonfatal MI or fatal or nonfatal stroke. We asked all women who reported incident MI or stroke on any biennial follow-up questionnaire to confirm the report and provide permission to review medical records. Study physicians blinded to risk factor status reviewed the records. MI was confirmed by using the World Health Organization criteria (17). Strokes were confirmed if characterized by a typical neurologic defect of sudden or rapid onset, lasting  $\geq 24$  h, and attributable to a cerebrovascular event (18).

When a new cancer case was identified, we asked the participant (or next of kin) for permission to obtain hospital records

and pathology reports. We included all confirmed cancers except nonmelanoma skin cancer and in situ breast cancer because of the relatively low mortality from these lesions.

The major chronic disease endpoint also included all nontraumatic deaths. Deaths were reported by next of kin, coworkers, or postal authorities, or ascertained by a search for nonrespondents in the National Death Index (19). If not listed in the National Death Index, nonrespondents were assumed to be alive. We attempted to confirm the cause of each death, including fatal MI, stroke, and cancer, by using medical records or autopsy reports.

### Statistical analyses

Each participant contributed follow-up time from the return of her baseline questionnaire in 1984 until the diagnosis of CVD or cancer, until death, or until June 1, 1996, whichever came first. During follow-up, confirmed cases were censored from subsequent follow-up. Therefore, the cohort at risk included only those free of disease at the beginning of each 2-y follow-up interval. Overall follow-up based on potential person-years was  $>95\%$  complete.

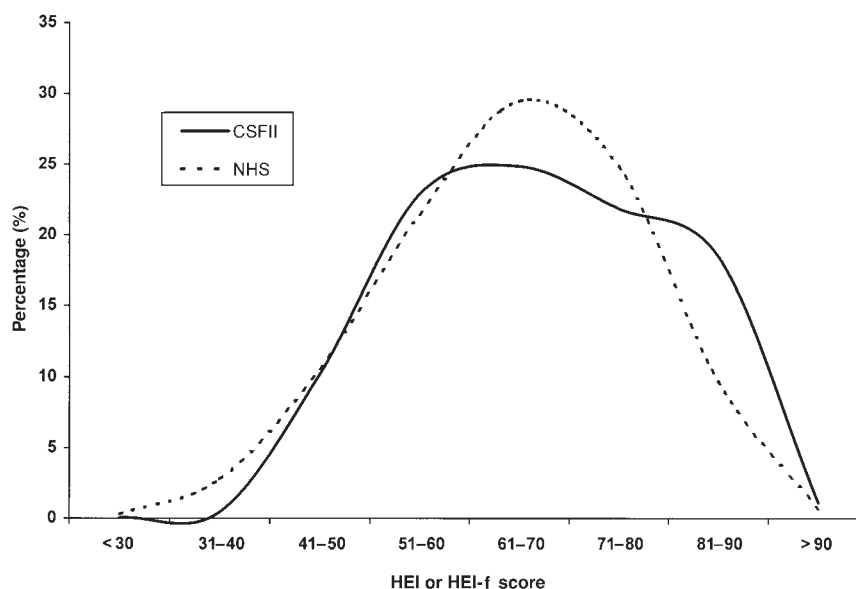
HEI-f quintiles were defined by using a cumulative-diet-average scoring method (20). This method incorporated repeated measures of diet to capture long-term intake and to reduce measurement error due to intraindividual variation in diet over time (20). With this approach, the 1984 HEI-f score was used to predict outcome in 1984–1986 and an average of the 1984 and 1986 HEI-f scores was related to outcome between 1986 and 1990. The average of the 1984, 1986, and 1990 scores was used to predict outcome from 1990–1996. If an FFQ was not completed in 1986 or 1990, the previous HEI-f score was carried forward. We did not update diet for women who reported a diagnosis of angina, hypercholesterolemia, diabetes, or hypertension during follow-up because changes in diet after development of these intermediate endpoints may have confounded the exposure-disease association. We also examined the relation between baseline diet in 1984 and risk of all outcomes.

We calculated relative risks (RRs) as the incidence rate of disease among women in each quintile of HEI-f score divided by the incident rate for women in the lowest quintile of HEI-f score. We adjusted RRs for age (5-y categories) by using the Mantel-Haenszel method (21). The Mantel extension test (22) was used to test for linear trend. To simultaneously adjust for  $\geq 2$  covariates, we used pooled logistic regression with 2-y time increments to compute odds ratios as an estimate of RR (23). This approach is regularly used in prospective cohort analyses with repeated measures of exposure and has been shown to closely approximate Cox regression analysis with time-dependent covariates (24). We tested for significant linear trends with use of multivariate logistic models by modeling median quintile values as a continuous regression variable. In addition to analysis by quintiles, we examined each outcome according to USDA-defined HEI score categories of poor ( $<51$ ), needs improvement (51–80), and good ( $>80$ ).

To examine potential interactions, we stratified by age ( $\leq 60$  and  $>60$  y at baseline), smoking status (never, past, and current), current multivitamin use (yes or no), menopausal status (pre- or postmenopausal), family history of heart disease (yes or no), and family history of cancer (yes or no). Models with and without interaction terms were compared by using likelihood ratio tests to formally test for interactions (25).

To examine the influence of individual HEI-f components on the incidence of major chronic disease, CVD, and cancer, each





**FIGURE 1.** Distribution of total healthy eating index scores calculated from food-frequency questionnaires (HEI-f) in the Nurses' Health Study (NHS) cohort ( $n = 67272$ ) and of total HEI scores in a subset of women in the Continuing Survey of Food Intakes by Individuals (CSFII) population [ $n = 428$  (16)].

of the 10 components was entered into the multivariate model as a continuous (0–10) variable. Components were entered into the models both individually and simultaneously. We also used stepwise regression to determine which HEI-f components were most strongly and independently associated with the outcomes of interest, using a  $P$  value of 0.10 as the criteria for inclusion.

We considered several covariates for inclusion in the final multivariate models. Those that remained were established risk factors and variables that changed the  $\beta$  coefficient for the HEI-f-outcome association by  $>10\%$ . The following covariates were updated biennially: age, exogenous hormone use and menopausal status, cigarette smoking, body mass index (BMI; in  $\text{kg}/\text{m}^2$ ), and multivitamin and vitamin E supplement use. Leisure time physical activity was assessed in 1986, 1988, 1992, and 1994 by inquiring about average weekly time spent performing specified activities during the past year. Activity was modeled in metabolic equivalents (METs) per week, with 7 METs equal to  $\approx 1$  h of jogging/wk. We applied 1986 reports of activity to the 1984–1986 time period and carried 1988 values forward to the 1990–1992 time period. Total energy intake and alcohol consumption were assessed in 1984, 1986, and 1990. Energy intake was updated by using the same method as for the HEI-f. A baseline diagnosis of hypercholesterolemia or hypertension was included as a covariate only in the major chronic disease and CVD multivariate models. The same baseline exclusions were used for all outcomes. We present RRs and 95% CIs. All  $P$  values are two-sided.

## RESULTS

During 757804 person-years of follow-up, we documented 7077 major chronic disease endpoints; these included 1365 first CVD events, 5216 first cancer cases, and 496 deaths not due to CVD or cancer. The most common cancers occurring after the completion of the 1984 FFQ were cancers of the breast (42.5%), colon (9.3%), uterus (8.9%), and lung (8.3%), which together accounted for almost 70% of cancers.

The mean HEI-f score at baseline (1984) was  $64.4 \pm 12.5$  and ranged from 11.7 to 99.3 (10th to 90th percentile: 47.5–80.2). Study participants had higher mean scores for vegetables, fruit, and meat and lower mean scores for grains than did the CSFII subset (16); other scores were similar (Table 1). Because the HEI-f scores for the variety and sodium components were based on their distribution in the present cohort, the mean score was 5.0 by definition. The distribution of total HEI-f scores in the cohort overlapped considerably with the HEI scores reported for the CSFII subset (Figure 1).

Baseline characteristics of the cohort are presented in Table 2. Higher HEI-f scores were associated with other healthful lifestyle behaviors: women with high scores were less likely to smoke, more likely to exercise, and more likely to take multivitamin supplements and supplemental vitamin E. In addition, energy consumption was higher (in part reflecting physical activity) and BMI slightly lower with higher HEI-f quintiles. As expected, servings of milk, fruit, vegetables, and grains and the variety of foods consumed increased across HEI-f quintiles and total fat and saturated fat decreased across HEI-f quintiles. The number of meat group servings and dietary cholesterol changed only slightly across quintiles.

The relations of other nutrients to HEI-f quintile (not energy adjusted to be consistent with the HEI) are also described in Table 2. Food sources of several antioxidants, minerals, and fiber all increased across HEI-f quintiles. Likewise, glycemic load, an indicator of blood glucose response induced by total carbohydrate intake (26), was positively associated with HEI-f score. Percentage of energy from monounsaturated and polyunsaturated fat decreased slightly across quintiles.

Lifestyle and diet characteristics of the CSFII subset are presented in Table 3 for comparison. In this group of women, median HEI quintile scores were similar to those in our study. Patterns of smoking behavior, age, BMI, energy intake, and other dietary variables were also qualitatively similar.

**TABLE 2**

Mean baseline (1984) diet and lifestyle characteristics and risk factors by quintile of healthy eating index score calculated from food-frequency questionnaires (HEI-f) for 67 272 female nurses<sup>1</sup>

	HEI-f quintile				
	1	2	3	4	5
HEI-f score (median)	48	58	65	72	80
Current smoker (%)	34	28	23	19	16
Multivitamin use (%) <sup>2</sup>	31	34	36	39	44
Vitamin E supplement use (%) <sup>2</sup>	13	15	16	18	22
Age (y)	48.7 ± 6.8 <sup>3</sup>	49.6 ± 7.0	50.3 ± 7.1	51.3 ± 7.2	52.7 ± 7.0
BMI (kg/m <sup>2</sup> )	25.2 ± 4.9	25.0 ± 4.8	24.9 ± 4.5	24.7 ± 4.4	24.5 ± 4.2
Total energy (kJ/d)	6050 ± 2008	6970 ± 2134	7380 ± 2163	7757 ± 2100	8368 ± 1966
Physical activity (METs/wk) <sup>4</sup>	11.1 ± 18.0	12.5 ± 21.4	13.5 ± 18.4	15.6 ± 21.3	18.4 ± 24.4
Alcohol intake (g/d)	5.4 ± 9.2	7.0 ± 11.4	7.4 ± 11.8	7.6 ± 12.2	7.5 ± 11.2
Contributors to HEI score					
Milk (servings/d)	1.0 ± 0.9	1.3 ± 0.9	1.4 ± 1.0	1.6 ± 1.0	1.8 ± 1.0
Fruit (servings/d)	1.2 ± 0.8	1.9 ± 1.1	2.5 ± 1.3	3.1 ± 1.5	4.0 ± 1.8
Vegetables (servings/d)	3.3 ± 1.6	3.9 ± 1.7	4.3 ± 1.8	4.7 ± 1.9	5.3 ± 2.0
Grains (servings/d)	3.1 ± 1.6	3.8 ± 1.8	4.1 ± 1.9	4.4 ± 2.0	5.0 ± 2.0
Meat (servings/d)	2.1 ± 1.0	2.2 ± 1.0	2.3 ± 0.9	2.3 ± 0.9	2.3 ± 0.8
Total fat (% of energy)	40.2 ± 5.1	36.5 ± 5.0	34.3 ± 4.5	32.3 ± 4.2	29.6 ± 3.9
Saturated fat (% of energy)	14.9 ± 2.5	13.3 ± 2.2	12.3 ± 2.0	11.4 ± 1.8	10.3 ± 1.5
Cholesterol (mg/d)	305 ± 157	310 ± 136	308 ± 127	305 ± 112	293 ± 89
Sodium (mg/d)	1909 ± 399	1821 ± 365	1786 ± 361	1762 ± 335	1689 ± 307
Variety (no. of unique foods/mo)	35.2 ± 7.2	40.4 ± 7.4	43.3 ± 7.4	46.0 ± 7.1	49.8 ± 6.5
Other nutrients <sup>5</sup>					
Monounsaturated fat (% of energy)	16.5 ± 2.4	14.9 ± 2.2	13.9 ± 2.1	13.1 ± 2.1	11.8 ± 1.9
Polyunsaturated fat (% of energy)	8.1 ± 2.3	7.6 ± 2.0	7.3 ± 1.8	7.1 ± 1.7	6.7 ± 1.6
Glycemic load	77.2 ± 30.0	98.6 ± 34.4	110 ± 37	122 ± 39	141 ± 42
Dietary fiber (g/d)	11.8 ± 4.3	15.1 ± 5.0	17.3 ± 5.5	19.7 ± 6.1	23.5 ± 7.0
Fiber from cruciferous vegetables (g/d)	0.7 ± 0.6	0.9 ± 0.7	1.0 ± 0.8	1.2 ± 0.9	1.4 ± 1.0
Fiber from cereal (g/d)	3.0 ± 1.9	3.9 ± 2.2	4.5 ± 2.5	5.1 ± 2.9	6.3 ± 3.2
Folate (μg/d)	200 ± 82	254 ± 102	290 ± 104	328 ± 117	380 ± 127
Vitamin E (mg/d)	5.5 ± 3.2	6.5 ± 4.6	7.0 ± 3.9	7.5 ± 4.7	8.4 ± 4.5
α-Carotene (μg/d)	454 ± 592	609 ± 654	739 ± 757	881 ± 898	1110 ± 1108
β-Carotene (μg/d)	2709 ± 2102	3627 ± 2422	4357 ± 2744	5137 ± 3216	6487 ± 3952
Lycopene (μg/d)	7355 ± 6371	8763 ± 6124	9730 ± 6755	10506 ± 6867	11553 ± 6794
Magnesium (mg/d)	225 ± 77	267 ± 91	293 ± 90	323 ± 97	371 ± 100
Potassium (mg/d)	2370 ± 756	2804 ± 826	3075 ± 848	3363 ± 862	3800 ± 883
Iron (mg/d)	14.4 ± 14.7	16.5 ± 14.7	18.0 ± 15.4	19.5 ± 15.2	21.8 ± 16.5
Vitamin C (mg/d)	243 ± 337	289 ± 341	329 ± 352	378 ± 375	462 ± 409

<sup>1</sup> *P* for trend < 0.001 for all variables, controlling for age.

<sup>2</sup> Multivitamin and vitamin E use represent current use.

<sup>3</sup>  $\bar{x}$  ± SD.

<sup>4</sup> Metabolic equivalents (METs) are defined for each type of physical activity as a multiple of the metabolic equivalent of sitting quietly for 1 h.

<sup>5</sup> Nutrients from food sources only.

The relation of the HEI-f score to disease, with use of cumulatively updated scores for all analyses, is presented in **Table 4**. With adjustment for only age, the risk of overall major chronic disease was 19% lower for women in the highest HEI-f quintile than for those in the lowest quintile (RR = 0.81; 95% CI: 0.75, 0.87). Control for smoking changed the RR in the highest HEI-f quintile to 0.92 (Table 4). In our final multivariate model, the association between HEI-f and major chronic disease was null. Results were similar whether or not BMI was included in the model (without BMI, RR = 0.96; 95% CI: 0.89, 1.05). Although the HEI-f score was strongly inversely associated with CVD risk with adjustment for only age (a 41% reduction in risk), this relation was markedly attenuated when smoking was added to the model (RR = 0.81; 95% CI: 0.69, 0.96). Control for additional covariates (primarily exercise) further weakened the estimate (RR = 0.86; 95% CI: 0.72, 1.03). Although a weak inverse asso-

ciation for HEI-f and total cancer risk was noted in the age-adjusted models, models controlled for smoking, activity, and other confounders showed no association. Results using baseline HEI-f scores (rather than cumulatively updated values) were similar for all outcomes. We did not observe any significant interactions by smoking status, age, menopausal status, multivitamin use, or family history of cancer or CVD.

We also examined risk according to the USDA-defined HEI score categories to see whether these (arbitrary) cutoffs predicted disease (**Table 5**). Compared with a good score as the reference, those with poor scores were not at higher risk of overall major chronic disease or cancer. However, those with poor scores had an increased risk of CVD (RR = 1.27; 95% CI: 1.01, 1.61). Women in the needs improvement category, which constituted 74% of the cohort [and 71% of the CSFII subset (15)], were not at increased risk.

**TABLE 3**Characteristics of women in the 1989–1990 Continuing Survey of Food Intakes by Individuals by healthy eating index (HEI) quintile<sup>1</sup>

Characteristic	HEI-f quintile				
	1	2	3	4	5
HEI score (median)	48.8	58.2	66.0	73.4	82.4
Current smoker (%)	30	39	23	23	12
Age (y)	43.9 ± 5.0 <sup>2</sup>	43.3 ± 4.4	44.9 ± 6.0	44.8 ± 5.8	45.1 ± 5.8
BMI (kg/m <sup>2</sup> )	26.7 ± 5.4	24.6 ± 5.2	25.6 ± 6.2	24.9 ± 5.7	24.3 ± 3.9
Total energy (kJ)	5355 ± 1728	6372 ± 1904	6405 ± 2310	6999 ± 1837	6857 ± 1473
Baseline diet					
Total fat (% of energy)	42.0 ± 5.6	38.9 ± 5.5	34.8 ± 6.4	34.0 ± 4.5	28.9 ± 5.2
Saturated fat (% of energy)	15.1 ± 3.0	13.4 ± 2.0	11.8 ± 2.6	11.3 ± 2.0	9.3 ± 1.9
Cholesterol (mg/d)	251 ± 158	227 ± 99	254 ± 128	236 ± 114	217 ± 115
Dietary fiber (g/d)	7.4 ± 3.4	10.1 ± 3.3	12.1 ± 4.5	13.9 ± 4.0	16.4 ± 4.3

<sup>1</sup>n = 428 women aged 37–66 y, with ≥12 y of schooling and employed full- or part-time (16). Results are based on complete 3-d intake. P for trend: age = 0.149, BMI = 0.047, cholesterol = 0.435, smoking = 0.022; all others < 0.001.

<sup>2</sup> $\bar{x} \pm$  SD.

The estimated changes in risk of major chronic disease for a 5-point increase in each HEI-f component, considered individually in the multivariate model and also considered simultaneously, are shown in **Table 6**. A high cholesterol score (representing lower cholesterol intake) was consistently inversely associated with major chronic disease risk. The sodium score (representing lower sodium intake) was directly associated with outcome when entered individually in the model, but was no longer significant in the model controlled for all other components. The total fat score (representing less total fat) was directly related to major chronic disease in the model controlled for all other components. When saturated and total fat were in the same model, the total fat term represented other fats (mainly polyunsaturated and monounsaturated fat); a low intake of these fats predicted a higher risk of disease. After stepwise regression, the cholesterol score (inversely) and sodium score (directly) remained in the model for major chronic disease.

For the CVD model in which all components were included simultaneously, the grain, dairy, and saturated fat scores were inversely, and the total fat score was directly, associated with risk ( $P < 0.05$ ). After stepwise regression, the grains and saturated fat components remained in the model ( $P < 0.05$ ). For cancer, the cholesterol and variety scores were inversely related to risk in the model with components entered simultaneously ( $P < 0.05$ ); after stepwise regression the cholesterol component (inversely) and the total fat component (directly) remained ( $P < 0.05$ ).

## DISCUSSION

In this large, prospective cohort study, women whose diet pattern reflected close accordance with the *Dietary Guidelines for Americans* were not at lower risk of overall major chronic disease over a 12-y follow-up period. We observed a small reduction in CVD risk in association with higher HEI-f scores, but no association with cancer risk.

**TABLE 4**

Relative risk (95% CI) of major chronic disease by quintile of healthy eating index score calculated from food-frequency questionnaires (HEI-f) for women in the Nurses' Health Study (1984–1996)

	HEI-f quintile					P for trend <sup>1</sup>
	1	2	3	4	5	
Major chronic disease (no. of cases) <sup>2</sup>	1501	1413	1389	1399	1375	—
Person-years	163902	155360	148699	147104	142740	—
Age adjusted	1.0	0.93 (0.86, 1.00)	0.91 (0.85, 0.98)	0.87 (0.81, 0.94)	0.81 (0.75, 0.87)	<0.001
Adjusted for smoking <sup>3</sup>	1.0	0.97 (0.91, 1.05)	0.98 (0.91, 1.06)	0.96 (0.89, 1.04)	0.92 (0.86, 1.00)	0.049
Multivariate adjusted <sup>4</sup>	1.0	0.99 (0.92, 1.07)	1.01 (0.93, 1.09)	1.00 (0.92, 1.08)	0.97 (0.89, 1.06)	0.580
Cardiovascular disease (no. of cases)	347	293	268	265	254	—
Person-years	168292	159955	153264	151791	147477	—
Age adjusted	1.0	0.81 (0.70, 0.95)	0.72 (0.61, 0.84)	0.66 (0.56, 0.77)	0.59 (0.50, 0.70)	<0.001
Multivariate adjusted <sup>5</sup>	1.0	0.92 (0.79, 1.08)	0.90 (0.76, 1.06)	0.88 (0.74, 1.04)	0.86 (0.72, 1.03)	0.085
Cancer (no. of cases)	1063	1038	1052	1062	1061	—
Person-years	165279	156408	149684	148136	143581	—
Age adjusted	1.0	0.98 (0.90, 1.06)	1.00 (0.92, 1.09)	0.97 (0.89, 1.06)	0.92 (0.84, 1.00)	0.134
Multivariate adjusted <sup>6</sup>	1.0	1.01 (0.92, 1.10)	1.05 (0.96, 1.14)	1.03 (0.94, 1.13)	1.02 (0.93, 1.12)	0.578

<sup>1</sup>P for trend over quintiles of HEI-f score with use of the median value per quintile.

<sup>2</sup>Major chronic disease was defined as cardiovascular disease (n = 1365), cancer (n = 5216), or death (n = 496), whichever came first (total n = 7077).

<sup>3</sup>Adjusted for age (5-y categories), smoking (never, past, 1–14 cigarettes/d, 15–24 cigarettes/d, or ≥25 cigarettes/d), and time period.

<sup>4</sup>Adjusted for variables listed above plus body mass index (quintiles), alcohol intake (7 categories), physical activity (6 categories of metabolic equivalents), history of hypertension or hypercholesterolemia at baseline, total energy intake (quintiles), postmenopausal status, and postmenopausal hormone use.

<sup>5</sup>n = 1427. Contained same covariates as major chronic disease model plus multivitamin and vitamin E supplement use.

<sup>6</sup>n = 5276. Controlled for same variables as major chronic disease model except for history of hypertension or hypercholesterolemia at baseline.

**TABLE 5**

Relative risk (95% CI) of major chronic disease, cardiovascular disease, and cancer according to US Department of Agriculture classification of healthy eating index (HEI) scores

	HEI score >80: good	HEI score of 51–80: needs improvement	HEI score <51: poor
Major chronic disease <sup>1</sup>	1.0	1.02 (0.95, 1.10)	1.01 (0.90, 1.13)
Cardiovascular disease <sup>2</sup>	1.0	1.06 (0.89, 1.26)	1.27 (1.01, 1.61)
Cancer <sup>3</sup>	1.0	0.98 (0.90, 1.07)	0.93 (0.82, 1.05)

<sup>1</sup>Adjusted for age, body mass index, smoking, alcohol intake, energy intake, physical activity, postmenopausal hormone use, and history of hypertension or hypercholesterolemia at baseline.

<sup>2</sup>Additionally controlled for multivitamin and vitamin E supplement use.

<sup>3</sup>Controlled for same variables as major chronic disease model except for history of hypertension or hypercholesterolemia at baseline.

These findings are generally comparable with those from our study of men of similar age (5). In both cohorts, the association between HEI-f and CVD risk was moderately inverse, but there was no association with cancer risk. Because CVD and cancer affect men and women at different rates throughout much of adult life, the relative proportions of CVD and cancer incidence in the populations studied will influence the relation between HEI-f and overall chronic disease. In this study of women, cancer cases exceeded CVD cases 4-fold, whereas in the male Health Professionals Follow-up Study (5), cancer cases exceeded CVD cases 1.5-fold. This difference in the relative occurrence of disease is likely to account for the small differences in associations of the HEI-f with major chronic disease in the 2 cohorts (RR = 0.89 in men and 0.97 in women, for those with the highest compared with the lowest scores).

Others reported inverse associations between indexes of recommended dietary patterns and risk of total (27–30), cardiovascular (29–31), and cancer (29–31) mortality. Huijbregts et al (29) found that an 8-component index of adherence to the World Health Organization guidelines for prevention of chronic disease was inversely associated with all-cause, cardiovascular, and cancer mortality over a 20-y period. Likewise, a Mediterranean diet index was inversely associated with all-cause mortality in Greece (27) and in Denmark (32). Kant et al (30) recently found that a recommended food score (RFS) was associated with a 30% lower risk of total mortality in a cohort of US women. The results were widely interpreted as evidence of the efficacy of the current *Dietary Guidelines for Americans*. However, the RFS, which ranged from 0 to 23, was heavily weighted by fruit and vegetables, which con-

tributed 15 points, and included no meat or refined grain products and ignored the fat and carbohydrate recommendations emphasized by the food guide pyramid. In contrast, the diet quality index (a more comprehensive measure of US dietary guidance than the RFS) was not associated with total mortality in a large cohort of men and women after important confounders were controlled for (J Seymour et al, unpublished observations, 2000).

A direct comparison of these studies with our findings is not feasible. Most used relatively crude component scores (binary or 0–2 points) and control for confounders varied. In addition, these studies used mortality as an endpoint. Because case fatality can be influenced by early diagnosis, access to optimal medical care, and compliance with treatment, the use of mortality as an endpoint is potentially confounded by behaviors that are difficult to measure and control.

Several possible explanations may account for the lack of an overall association between the HEI-f and risk of chronic disease. The HEI was originally developed for use with 24-h recalls and food records in the CSFII survey population (4). Because FFQs are designed to measure long-term dietary intake and contain a defined list of foods, our approximation of the HEI varied slightly from the original method. As noted, we defined variety according to distribution in the present cohort. Likewise, the sodium score was defined according to distribution of intake in our study population because of underestimation of sodium in 1984. Results considering 1986 as baseline (and using original HEI sodium scoring cutoffs) were not materially different. A second possibility is that the method we used to measure dietary intake did not measure actual food consumption well. However,

**TABLE 6**

Relative risk (95% CI) of major chronic disease associated with a 5-point increase in component scores

Component	Component represents	Entered individually <sup>1</sup>	Entered simultaneously <sup>2</sup>
Dairy	More dairy <sup>3</sup>	0.99 (0.94, 1.04)	0.97 (0.92, 1.02)
Fruit	More fruit	1.02 (0.97, 1.07)	1.01 (0.96, 1.08)
Vegetable	More vegetables <sup>3</sup>	1.02 (0.94, 1.10)	1.03 (0.94, 1.13)
Grain	More grains	0.94 (0.87, 1.01)	0.94 (0.87, 1.02)
Meat	More meat, poultry, and fish	1.06 (0.99, 1.15)	1.04 (0.95, 1.13)
Total fat	Less total fat	1.02 (0.98, 1.07)	1.12 (1.03, 1.22)
Saturated fat	Less saturated fat	0.99 (0.95, 1.03)	0.94 (0.88, 1.01)
Cholesterol	Less cholesterol	0.92 (0.88, 0.96)	0.91 (0.86, 0.96)
Sodium	Less sodium	1.04 (1.00, 1.09)	1.03 (0.98, 1.08)
Variety	More variety <sup>3</sup>	0.98 (0.93, 1.02)	0.95 (0.90, 1.01)

<sup>1</sup>Not controlled for other healthy eating index (HEI) components. Full models were adjusted for age (5-y categories), smoking (never, past, 1–14 cigarettes/d, 15–24 cigarettes/d, or ≥25 cigarettes/d), time period, body mass index (quintiles), alcohol intake (7 categories), physical activity (6 categories of metabolic equivalents), history of hypertension or hypercholesterolemia at baseline, total energy intake (quintiles), postmenopausal status, and postmenopausal hormone use.

<sup>2</sup>All HEI components entered simultaneously in the multivariate model.

<sup>3</sup>Test for nonlinearity was significant,  $P < 0.05$ .


the FFQ we used has been validated with use of both food records and biological markers of dietary intake (9, 11–13, 33). Moreover, the intake of several nutrients and foods increased or decreased in the expected direction across HEI-f quintiles, indicating that the index captured recommendations of the dietary guidelines, and there was a wide distribution in total HEI-f scores. In the age-adjusted models, we found strong and significant associations, especially for CVD. However, estimates were markedly attenuated after confounders, especially smoking and exercise, were controlled for. Furthermore, our validation of the HEI-f scoring method with use of data from the Health Professionals Follow-up Study cohort indicated that the total HEI score was estimated reasonably well by the FFQ.

Another strong possibility for the lack of overall association in this study is that the HEI and the dietary guidelines do not describe an optimal diet. Improvement in the HEI is likely to strengthen its association with major chronic disease, especially CVD risk. For example, the 1995 dietary guidelines emphasize reductions in total and saturated fat, cholesterol, and sodium and an increase in complex carbohydrates—recommendations influenced mainly by expected reductions in CVD risk. Some of these factors were independently predictive of disease in our analysis of individual HEI-f components. However, additional multiple and complex mechanisms are involved in the pathogenesis of CVD (34) and attention to other important dietary factors may improve the association with CVD risk. For example, other types of fat (35–40), antioxidants (34, 41), folate and vitamin B-6 (42, 43), and carbohydrate quality (26, 44) have all been associated with CVD development. In this and in our study in men (5), the total fat component score (reflecting a low-fat diet) was directly associated with disease when saturated fat was controlled for. In this context, the total fat score can be interpreted as a measure of other types of fat (eg, polyunsaturated and monounsaturated fats). Thus, these findings suggest that limiting unsaturated fats, which is usually done by increasing carbohydrate if energy intake is maintained, is detrimental. This is consistent with metabolic studies indicating that replacing unsaturated fats with carbohydrate increases triacylglycerol and decreases HDL cholesterol (40). Furthermore, low-fat, high-carbohydrate diets provide a higher glycemic load, aggravate hyperinsulinemia (45), and may thus increase the risk of diabetes and coronary artery disease (26, 39, 46).

The role of diet in the development of cancer is less well understood and is more complex than that for CVD (47). The dietary guidelines may be too nonspecific; for example, potatoes are not related to cancer risk reduction (48, 49) but contribute importantly to vegetable consumption as defined by the food guide pyramid and the HEI. Furthermore, in prospective studies (50), low-fat diets consistently have little or no relation to breast cancer risk—the predominant cancer in this cohort. The food guide pyramid also combines foods that have been directly associated with chronic disease risk with foods inversely associated with disease (eg, fish and red meat, as well as whole grains and highly refined starches) (44, 51). Because there are no upper limits on food servings in the HEI, high consumption of red meat and refined carbohydrates can yield perfect component scores (52).

This population comprised mostly white women with some college education, though the socioeconomic level of the nurses overlaps considerably with that of women in the general US population. This homogeneity increases the internal validity of the study by reducing confounding by factors that are hard to measure. However, the ability

of the HEI-f score to predict lower chronic disease risk in women of other racial and educational backgrounds should also be evaluated.

In summary, we observed no association between the HEI-f score and risk of overall major chronic disease in women. Our results may reflect a combined effect of the weak associations between dietary factors in midlife and risk of breast cancer (the major disease in our outcome measures) and the shortcomings of the HEI in defining an optimal diet for prevention of CVD and other conditions. Continued refinement of the HEI, and the dietary guidelines, may improve the ability of the HEI to predict major chronic disease in women and its usefulness as a tool for describing an optimal diet. Dietary guidelines should continue to be evaluated for their efficacy in reducing the incidence of diseases of major public health concern. 

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## REFERENCES

1. US Department of Agriculture, US Department of Health and Human Services. Nutrition and your health: dietary guidelines for Americans. Washington, DC: US Government Printing Office, 1995.
2. US Department of Agriculture. The food guide pyramid. Washington, DC: US Government Printing Office, 1992.
3. Gambera PJ, Schneeman BO, Davis PA. Use of the food guide pyramid and US dietary guidelines to improve dietary intake and reduce cardiovascular risk in active-duty Air Force members. *J Am Diet Assoc* 1995;95:1268–73.
4. Kennedy ET, Ohls J, Carlson S, Fleming K. The healthy eating index: design and applications. *J Am Diet Assoc* 1995;95:1103–8.
5. McCullough ML, Feskanich D, Rimm EB, et al. Adherence to the dietary guidelines for Americans and risk of major chronic disease in men. *Am J Clin Nutr* 2000;72:1223–31.
6. Peters KD, Kochanek KD, Murphy SL. Death: final data for 1996. In: National vital statistics reports. Vol 47, no. 9. Hyattsville, MD: National Center for Health Statistics, 1998. World Wide Web: <http://www.cdc.gov/nchs/data/nvsr479.pdf> (accessed 2 August 2000).
7. Adams CF. Nutritive value of American foods. Washington, DC: US Department of Agriculture, Agricultural Research Service, 1975. (Agricultural handbook no. 456.)
8. Consumer and Food Economics Institute. Composition of foods: handbook 8 series, 1976–1989. Washington, DC: US Department of Agriculture, 1989.
9. Willett WC, Sampson L, Stampfer MJ, et al. Reproducibility and validity of a semiquantitative food frequency questionnaire. *Am J Epidemiol* 1985;122:51–65.
10. Salvini S, Hunter DJ, Sampson L, et al. Food-based validation of a dietary questionnaire: the effects of week-to-week variation in food consumption. *Int J Epidemiol* 1989;18:858–67.
11. Feskanich D, Rimm EB, Giovannucci EL, et al. Reproducibility and validity of food intake measurements from a semiquantitative food frequency questionnaire. *J Am Diet Assoc* 1993;93:790–6.
12. Rimm EB, Giovannucci EL, Stampfer MJ, Colditz GA, Litin LB, Willett WC. Reproducibility and validity of an expanded self-administered semiquantitative food frequency questionnaire among male health professionals. *Am J Epidemiol* 1992;135:1114–26.
13. Michaud DS, Giovannucci EL, Ascherio A, et al. Associations of plasma carotenoid concentrations and dietary intake of specific carotenoids in samples of two prospective cohort studies using a new carotenoid database. *Cancer Epidemiol Biomarkers Prev* 1998;7:283–90.
14. Kennedy E, Ohls J, Carlson S, Fleming K. The healthy eating index final report. Alexandria, VA: Food and Nutrition Service, US Depart-





- ment of Agriculture, 1994. (Contract no. 53-3198-3-0381994, submitted by Mathematica Policy Research Inc, Princeton, NJ, PR 94-65.)
15. Bowman SA, Lino M, Gerrior SA, Basiotis PP. The healthy eating index: 1994–1996. Washington, DC: US Department of Agriculture, Center for Nutrition Policy and Promotion, 1998.
  16. US Department of Agriculture, Agricultural Research Service. 1995–1996 Continuing Survey of Food Intakes by Individuals and 1994–1996 Diet and Health Knowledge Survey and related materials. Riverdale, MD: US Department of Agriculture, Agricultural Research Service, 1998 (CD-ROM).
  17. Rose GA, Blackburn H. Cardiovascular survey methods. World Health Organ Monogr Ser 1982;58.
  18. Walker AE, Robins M, Weinfeld FD. The National Survey of Stroke. Clinical findings. Stroke 1981;12:113–44.
  19. Stampfer MJ, Willett WC, Speizer FE, et al. Test of the National Death Index. Am J Epidemiol 1984;119:837–9.
  20. Hu FB, Stampfer MJ, Rimm E, et al. Dietary fat and coronary heart disease: a comparison of approaches for adjusting for total energy intake and modeling repeated dietary measurements. Am J Epidemiol 1999;149:531–40.
  21. Rothman KJ. Modern epidemiology. Boston: Little, Brown & Co, 1986.
  22. Mantel N. Chi-square tests with one degree of freedom: extensions of the Mantel-Haenszel procedure. J Am Stat Assoc 1963;58:690–700.
  23. Cupples LA, D'Agostino RB, Anderson K, Kannel WB. Comparison of baseline and repeated measure covariate techniques in the Framingham Heart Study. Stat Med 1988;7:205–22.
  24. D'Agostino RB, Lee MLT, Belanger AJ, Cupples LA, Anderson K, Kannel WB. Relation of pooled logistic regression to time dependent Cox regression analysis: the Framingham Heart Study. Stat Med 1990;9:1501–15.
  25. Hosmer D, Lemeshow S. Applied logistic regression. New York: John Wiley and Sons, 1989.
  26. Salmeron J, Manson JE, Stampfer MJ, Colditz GA, Wing AL, Willett WC. Dietary fiber, glycemic load, and risk of non-insulin-dependent diabetes mellitus in women. JAMA 1997;277:472–7.
  27. Trichopoulos A, Kouris-Blazos A, Wahlqvist ML, et al. Diet and overall survival in elderly people. Br Med J 1995;311:1457–60.
  28. Nube M, Kok FJ, Vandenbroucke JP, van der Heide-Wessel C, van der Heide RM. Scoring of prudent dietary habits and its relation to 25-year survival. J Am Diet Assoc 1987;87:171–5.
  29. Huijbregts P, Feskens E, Rasanen L, et al. Dietary pattern and 20 year mortality in elderly men in Finland, Italy, and the Netherlands: longitudinal cohort study. BMJ 1997;315:13–7.
  30. Kant AK, Schatzkin A, Graubard BI, Schairer C. A prospective study of diet quality and mortality in women. JAMA 2000;283:2109–15.
  31. Kant AK, Schatzkin A, Ziegler RG. Dietary diversity and subsequent cause-specific mortality in the NHANES I Epidemiologic Follow-up Study. J Am Coll Nutr 1995;14:233–8.
  32. Osler M, Schroll M. Diet and mortality in a cohort of elderly people in a north European community. Int J Epidemiol 1997;26:155–9.
  33. Hunter DJ, Rimm EB, Sacks FM, et al. Comparison of measures of fatty acid intake by subcutaneous fat aspirate, food frequency questionnaire, and diet records in a free-living population of US men. Am J Epidemiol 1992;135:418–27.
  34. Ross R. Atherosclerosis—an inflammatory disease. N Engl J Med 1999;340:115–26.
  35. Hu FB, Stampfer MJ, Manson JE, et al. Dietary intake of  $\alpha$ -linolenic acid and risk of fatal ischemic heart disease among women. Am J Clin Nutr 1999;69:890–7.
  36. Mensink RP, Katan MB. Effect of monounsaturated fatty acids versus complex carbohydrates on high-density lipoprotein in healthy men and women. Lancet 1987;1:122–5.
  37. Dolecek TA. Epidemiological evidence of relationships between dietary polyunsaturated fatty acids and mortality in the Multiple Risk Factor Intervention Trial. Proc Soc Exp Biol Med 1992;200:177–82.
  38. Willett WC, Stampfer MJ, Manson JE, et al. Intake of *trans* fatty acids and risk of coronary heart disease among women. Lancet 1993;341:581–5.
  39. Hu FB, Stampfer MJ, Manson JE, et al. Dietary fat intake and the risk of coronary heart disease in women. N Engl J Med 1997;337:1491–9.
  40. Mensink RP, Katan MB. Effect of dietary fatty acids on serum lipids and lipoproteins: a meta-analysis of 27 trials. Arterioscler Thromb 1992;12:911–9.
  41. Stampfer MJ, Hennekens CH, Manson JE, Colditz GA, Rosner B, Willett WC. Vitamin E consumption and the risk of coronary disease in women. N Engl J Med 1993;328:1444–9.
  42. Rimm EB, Willett WC, Hu FB, et al. Folate and vitamin B<sub>6</sub> from diet and supplements in relation to risk of coronary heart disease among women. JAMA 1998;279:359–64.
  43. Robinson D, Arheart K, Refsum H, et al. Low circulating folate and vitamin B<sub>6</sub> concentrations: risk factors for stroke, peripheral vascular disease, and coronary artery disease. Circulation 1998;97:437–43.
  44. Jacobs DR Jr, Meyer KA, Kushi LH, Folsom AR. Whole-grain intake may reduce the risk of ischemic heart disease death in postmenopausal women: the Iowa Women's Health Study. Am J Clin Nutr 1998;68:248–57.
  45. Jeppesen J, Schaaf P, Jones G, Zhou MY, Chen YD, Reaven GM. Effects of low-fat, high-carbohydrate diets on risk factors for ischemic heart disease in postmenopausal women. Am J Clin Nutr 1997;65:1027–33.
  46. Reaven GM. Looking at the world through LDL-cholesterol-colored glasses. Nutrition 1986;116:1143–7.
  47. Clinton SK, Giovannucci EL. Nutrition in the etiology and prevention of cancer. In: Holland JF, Frei E, Bast RC, Kufe DW, Morton DL, Weichselbaum RD, eds. Cancer medicine. Baltimore: Williams & Wilkins, 1997.
  48. World Cancer Research Fund, American Institute for Cancer Research. Food, nutrition and the prevention of cancer: a global perspective. Washington, DC: American Institute for Cancer Research, 1997.
  49. Steinmetz KA, Potter JD. Vegetables, fruit and cancer. I. Epidemiology. Cancer Causes Control 1991;2:325–57.
  50. Hunter DJ, Spiegelman D, Adami HO, et al. Cohort studies of fat intake and the risk of breast cancer: a pooled analysis. N Engl J Med 1996;334:356–61.
  51. Giovannucci E, Rimm EB, Stampfer MJ, Colditz GA, Ascherio A, Willett WC. Intake of fat, meat, and fiber in relation to risk of colon cancer in men. Cancer Res 1994;54:2390–7.
  52. Chung S, Shih C, Lentner D, et al. The healthy eating index needs further work. J Am Diet Assoc 1996;96:751–2.

