Prospective study of major dietary patterns and risk of coronary heart disease in men[1–3]

Frank B Hu, Eric B Rimm, Meir J Stampfer, Alberto Ascherio, Donna Spiegelman, and Walter C Willett

ABSTRACT

Background: Previous studies on diet and coronary heart disease (CHD) focused primarily on individual nutrients or foods.

Objective: We examined whether overall dietary patterns derived from a food-frequency questionnaire (FFQ) predict risk of CHD in men.

Design: This was a prospective cohort study of 44875 men aged 40–75 y without diagnosed cardiovascular disease or cancer at baseline in 1986.

Results: During 8 y of follow-up, we documented 1089 cases of CHD (nonfatal myocardial infarction and fatal CHD). Using factor analysis, we identified 2 major dietary patterns using dietary data collected through a 131-item FFQ. The first factor, which we labeled the "prudent pattern," was characterized by higher intake of vegetables, fruit, legumes, whole grains, fish, and poultry, whereas the second factor, the "Western pattern," was characterized by higher intake of red meat, processed meat, refined grains, sweets and dessert, French fries, and high-fat dairy products. After adjustment for age and CHD risk factors, the relative risks from the lowest to highest quintiles of the prudent pattern score were 1.0, 0.87, 0.79, 0.75, and 0.70 (95% CI: 0.56, 0.86; *P* for trend = 0.0009). In contrast, the relative risks across increasing quintiles of the Western pattern score were 1.0, 1.21, 1.36, 1.40, and 1.64 (95% CI: 1.24, 2.17; *P* for trend < 0.0001). These associations persisted in subgroup analyses according to cigarette smoking, body mass index, and parental history of myocardial infarction.

Conclusions: These data suggest that major dietary patterns derived from the FFQ predict risk of CHD, independent of other lifestyle variables. *Am J Clin Nutr* 2000;72:912–21.

KEY WORDS Health Professionals Follow-up Study, food-frequency questionnaire, coronary heart disease, dietary patterns, men

INTRODUCTION

Distinct eating patterns reflect different dietary traditions worldwide, and they may be related to rates of coronary heart disease (CHD) in different countries (1). Mediterranean and Asian populations have very low rates of CHD compared with Western populations. These low rates are attributed to high intakes of vegetables, fruit, whole-grain products, and fish and low intakes of red meat, high-fat dairy products, and other animal products in traditional Mediterranean and Asian diets. However, the differences in CHD rates among countries may also be due to differences in other CHD risk factors, including physical activity and obesity.

Many prospective cohort studies have examined the associations between intakes of individual nutrients or foods and risk of CHD (2), but few have evaluated the relation of overall dietary patterns to the risk. Conceptually, examination of overall dietary patterns would more closely parallel the real world, where people do not eat isolated nutrients but rather meals consisting of a variety of foods with complex combinations of nutrients that may be interactive or synergistic (3). Studies of individual foods or nutrients can be difficult to interpret because of strong correlations among them. In dietary pattern analyses, the collinearity of nutrients or foods can be used to advantage because patterns are characterized on the basis of habitual food use (4). In addition, dietary interventions may be easier to implement and may be more comprehensive when initiated as a change in the overall dietary pattern (5). In clinical studies, changes in dietary patterns appeared to be more effective in lowering blood pressure than was supplementation with single nutrients (6, 7). Finally, dietary pattern analysis is potentially useful in making dietary recommendations because overall dietary patterns might be easy for the public to interpret or translate into diets (8).

A major difficulty in studying the relation between dietary patterns and disease outcomes is that dietary patterns cannot be measured directly. One commonly used statistical method for quantifying dietary patterns is factor analysis. Factor analysis is a multivariate technique (9, 10) that, in a dietary context, uses information reported on food-frequency questionnaires (FFQs) (11–13) or in dietary records (14) to identify common underlying factors (patterns) of food consumption. Recently, Slattery et al (15) showed in a case-control study that eating patterns

[1] From the Departments of Nutrition and Epidemiology, Harvard School of Public Health, Boston, and the Channing Laboratory, the Department of Medicine, Brigham and Women's Hospital, Boston.

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[3] Address reprint requests to FB Hu, Department of Nutrition, Harvard School of Public Health, 665 Huntington Ave, Boston, MA 02115. E-mail: frank.hu@channing.harvard.edu.

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identified by factor analysis were significantly associated with colon cancer risk, independent of other lifestyle variables. In a previous study (16), we showed reasonable reproducibility and validity of major dietary patterns defined by factor analysis using food consumption data collected through an FFQ. In this study, we attempted to evaluate whether these dietary patterns predicted incidence of CHD during 8 y of follow-up in the Health Professionals Follow-up Study (HPFS).

SUBJECTS AND METHODS

Subjects

The HPFS began in 1986 when 51 529 US health professionals (dentists, optometrists, pharmacists, podiatrists, and veterinarians) aged 40–75 y answered a detailed questionnaire that included a comprehensive diet survey and items on lifestyle practice and medical history. Follow-up questionnaires were sent in 1988, 1990, 1992, and 1994 to update information on potential risk factors and to identify new cases of cardiovascular and other diseases. We excluded from the analysis men who did not satisfy the a priori criteria of a reported daily energy intake between 3.3 and 17.6 MJ (800 and 4200 kcal) or who left blank >70 of a total of 131 food items on the diet questionnaire (n = 1595). We also excluded men with a prior diagnosis of myocardial infarction (MI), angina, coronary artery surgery, stroke, transient ischemic attack, or peripheral arterial disease at baseline (n = 5059). Thus, we followed 44 875 men to determine the incidence of CHD over the subsequent 8 y.

Endpoints

The endpoints were incident CHD (including nonfatal MI and fatal CHD) occurring between the return of the baseline questionnaire and 31 January 1994. We inquired about the occurrence of cardiovascular endpoints on each biennial questionnaire. Participants reporting an incident MI were asked for their permission for us to review their medical records. Nonfatal MI was confirmed by using World Health Organization (WHO) criteria: symptoms plus either typical electrocardiographic changes or increased activities of cardiac enzymes (17). MIs that required hospital admission and for which confirmatory information was obtained by interview or letter, but for which no medical records were available, were designated as probable. We included all confirmed and probable cases in the analyses because results were the same after exclusion of probable cases. The follow-up rate for nonfatal events was 97% of the total potential person-years of follow-up.

Deaths were reported by next of kin, coworkers, or postal authorities or were obtained from the National Death Index (18). Using all sources combined, we estimated that follow-up for the deaths was >98% complete. Fatal CHD was confirmed by medical records or autopsy reports or if it was the underlying cause on the death certificate and a diagnosis of CHD was confirmed by other sources. Sudden death within 1 h of the onset of symptoms in men with no other plausible cause of death (other than CHD) was also included.

Semiquantitative food-frequency questionnaire

The reproducibility and validity of the FFQ used in this study was reported previously (19, 20). The FFQ includes 131 food items with specified serving sizes that are described by using natural portions (eg, 1 banana and 2 slices of pizza) or standard weight and volume measures of the servings commonly consumed in this study population. For each food item, participants indicated their average frequency of consumption over the past year in terms of the specified serving size by checking 1 of 9 frequency categories ranging from "almost never" to "≥6 times/d." The selected frequency category for each food item was converted to a daily intake. For example, a response of "2–4 servings/wk" was converted to 0.43 servings/d (3 servings/wk).

Assessment of dietary patterns

The procedure for deriving dietary patterns by using food consumption data from the FFQ was described in detail elsewhere (16). Briefly, we first classified 131 food items in the FFQ into 40 predefined food groups (**Table 1**) to minimize within-person variations in intakes of individual foods. Individual food items were preserved if they constituted a distinct item on their own (eg, eggs, butter, margarine, pizza, soup, coffee, and tea) or if they were thought to represent a particular dietary pattern (eg, garlic, liquor, wine, beer, and French fries). In secondary analyses, we used all 131 food items to derive dietary patterns.

We conducted factor analysis (principal components) to derive dietary patterns based on the 40 foods or food groups (10). The factors were rotated by an orthogonal transformation (resulting in uncorrelated factors) to achieve a simpler structure with greater interpretability. In determining the number of factors to retain, we considered components with an eigenvalue >1, the Scree test (9), and the interpretability of the factors. We did not use the percentage of variance explained by each factor because this criterion depends largely on the total number of variables included in the analyses (9). The factor score for each pattern was constructed by summing observed intakes of the component food items weighted by factor loadings (9). The analyses were conducted by using the FACTOR PROCEDURE in SAS (21).

In a subsample of men (n = 127) in the HPFS (16), the 131-item FFQ was administered twice with a 1-y interval, and two 1-wk diet records were collected during that year. The factor analysis generated 2 major eating patterns. The first factor (the prudent pattern) was characterized by a high intake of vegetables, fruit, legumes, whole grains, fish, and poultry, whereas the second factor (the Western pattern) was characterized by a high intake of processed meat, red meat, butter, high-fat dairy products, eggs, and refined grains. The reliability correlations for the factor scores between the 2 FFQs were 0.70 for the prudent pattern and 0.67 for the Western pattern. The correlations (corrected for week-to-week variations in diet records) between the FFQ and the diet records were 0.52 for the prudent pattern and 0.74 for the Western pattern.

Statistical analysis

Participants were followed from the time the 1986 questionnaire was returned until the occurrence of a nonfatal MI or CHD death, death, or 31 January 1994. Relative risks (RRs) were calculated by dividing the incidence of CHD among men in the highest quintile of dietary pattern scores by the incidence among men in the lowest quintile of dietary pattern scores, with adjustment for age (40–44, 45–49, 50–54, 55–59, 60–64, 65–69, and ≥70 y). To adjust for other risk factors, we used pooled logistic regression with 2-y intervals (22), which is approximately equivalent to Cox regression for time-dependent covariates when the event rate is rare. Multivariate models were adjusted for total energy intake (quintiles), smoking status [never, past, current (1–14, 15–24, and ≥25 cigarettes/d)], alcohol

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TABLE 1
Food groupings used in the dietary pattern analysis

Foods or food groups	Food items
Processed meats	Processed meats, bacon, hot dogs
Red meats	Beef, pork, lamb, hamburger
Organ meats	Beef, calf, and pork liver; chicken and turkey liver
Fish and other seafood	Canned tuna fish, dark-meat fish, other fish, shrimp, lobster, scallops
Poultry	Chicken or turkey with or without skin
Eggs	Eggs
Butter	Butter
Margarine	Margarine
Low-fat dairy products	Skim or low-fat milk, sherbet or ice milk, yogurt
High-fat dairy products	Whole milk, cream, sour cream, ice cream, cream cheese, other cheese
Liquor	Liquor
Wine	Red wine, white wine
Beer	Beer
Tea	Tea
Coffee	Coffee
Fruit	Raisins or grapes, avocado, bananas, cantaloupe, watermelon, fresh apples or pears, oranges, grapefruit, strawberries, blueberries, peaches, apricots, plums
Fruit juices	Apple juice or cider, orange juice, grapefruit juice, other fruit juice
Cruciferous vegetables	Broccoli; coleslaw and uncooked cabbage; cooked cabbage; cauliflower; Brussels sprouts; kale, mustard, and chard greens; sauerkraut
Dark-yellow vegetables	Carrots, yellow (winter) squash, yams
Tomatoes	Tomatoes, tomato juice, tomato sauce
Green, leafy vegetables	Spinach, iceberg or head lettuce, romaine or leaf lettuce
Legumes	String beans, peas or lima beans, beans or lentils, tofu or soybeans, alfalfa sprouts
Other vegetables	Celery, mushrooms, green pepper, corn, mixed vegetables, eggplant, summer squash
Garlic	Garlic
Potatoes	Potatoes
French fries	French fries
Whole grains	Cooked oatmeal, other cooked breakfast cereal, dark bread, brown rice, other grains, bran added to food, wheat germ
Cold breakfast cereal	Cold breakfast cereal
Refined grains	White bread, English muffins, bagels or rolls, muffins or biscuits, white rice, pasta, pancakes or waffles
Pizza	Pizza
Snacks	Potato chips or corn chips, crackers, popcorn
Nuts	Peanuts, other nuts, peanut butter
High-energy drinks	Cola with sugar, other carbonated beverages with sugar, fruit drinks
Low-energy drinks	Low-energy cola, other low-energy carbonated beverages
Oil and vinegar salad dressing	Oil and vinegar salad dressing
Mayonnaise and other creamy salad dressings	Mayonnaise and other creamy salad dressings
Chowder or cream soup	Chowder or cream soup
Other soup	Home-made soup, ready-made soup
Sweets and desserts	Chocolate bars or pieces, candy bars, cookies, brownies, doughnuts, cake, pie, sweet roll, coffee cake, pastry
Condiments	Red chili sauce (dry or prepared), mustard, pepper, soy or Worcestershire sauce, jam, jelly, syrup, honey

consumption (0–4, 5–9, 10–14, 15–29, and ≥30 g/d), history of hypertension, history of diabetes, history of high cholesterol, parental history of MI before age 60 y, body mass index (quintiles), current vitamin E supplement use, and physical activity in metabolic equivalents per week (quintiles) (23).

RESULTS

We entered food consumption data for the 40 predefined food groups into the factor analysis procedure. The Scree plot of eigenvalues indicated 2 major patterns and 1 minor pattern. Thus, we extracted 3 factors in the final model. Factor-loading matrixes for the 2 major factors are listed in **Table 2**. The larger the loading of a given food item or group to the factor, the greater the contribution of that food item or group to a specific factor. The first factor was loaded heavily with the following foods or food groups: vegetables, legumes, whole grains, fruit, fish, and poultry; the second factor was loaded heavily with red meat, processed meat, refined grains, sweets and dessert, French fries, and high-fat dairy products. The first factor explained 10.0% of the total variance and the second factor explained 7.4% of the total variance. As with our previous study (16), we labeled the first factor as the prudent pattern and the second factor as the Western pattern. The third (minor) factor, which explained 4.4% of the total variance, did not appear to have a clear pattern of factor loadings, with a positive loading for some foods (eg, 0.36 for coffee, 0.36 for wine, 0.35 for liquor, 0.34 for beer, and 0.37 for garlic) and a negative loading for others (eg, −0.47 for low-fat dairy products, −0.43 for cold breakfast cereal, −0.31 for fruit, and −0.31 for whole-grain products). Our analyses did not suggest a significant association between this pattern and risk of CHD (data not shown).

The 2 major patterns closely resembled those identified in a validation study using data from two 1-wk diet records in a subsample of the HPFS (16). When the whole cohort was randomly divided into 2 groups, the 2 major patterns were similar for the 2 groups and closely resembled those for the overall sample. Participants with a higher prudent pattern score were more likely to take multivitamin and vitamin E supplements and to engage in exercise, were less likely to smoke cigarettes, were slightly older and leaner, and were more likely to have hypercholesterolemia (**Table 3**). This cross-sectional relation probably reflects changes in diet after a diagnosis of high cholesterol concentrations. Men with a higher prudent pattern score also had higher intakes of dietary folate, fiber, protein, and carbohydrate and lower intakes of cholesterol, saturated fat, monounsaturated fat, and *trans* fat. As expected, consumption of vegetables, fruit, fish, poultry, low-fat dairy products, and whole-grain products was directly correlated with the prudent pattern score, whereas consumption of red meat, processed meat, and sweets and dessert was inversely correlated with the prudent pattern score.

In contrast, men with a higher Western pattern score were more likely to smoke and drink alcohol and less likely to take multivitamin or vitamin E supplements and to exercise (**Table 4**). These men also had higher intakes of cholesterol, saturated fat, and monounsaturated fat and lower intakes of folate, fiber, protein, and carbohydrate. Consumption of red meat, processed meat, eggs, butter, high-fat dairy products, refined grain, and sweets and dessert was positively correlated with the Western pattern score.

During 8 y of follow-up (311 606 person-years), we documented 1089 incident cases of CHD (730 nonfatal MIs and

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TABLE 2
Factor-loading matrix for the major factors (diet patterns) identified by using food consumption data from the food-frequency questionnaire used in the Health Professionals Follow-up Study in 1986[1]

Food or food group	Factor 1 (prudent diet pattern)	Factor 2 (Western diet pattern)
Other vegetables[2]	0.75	—
Green, leafy vegetables	0.64	—
Dark-yellow vegetables	0.63	—
Cruciferous vegetables	0.63	—
Legumes	0.61	—
Fruit	0.57	—
Tomatoes	0.56	—
Fish	0.51	—
Garlic	0.42	—
Poultry	0.36	—
Whole grains	0.35	—
Red meat	—	0.63
Processed meat	—	0.59
Refined grains	—	0.49
Sweets and desserts	—	0.47
French fries	—	0.46
High-fat dairy products	—	0.45
Eggs	—	0.39
High-sugar drinks	—	0.38
Snacks	—	0.37
Condiments	—	0.36
Margarine	—	0.34
Potatoes	—	0.33
Butter	—	0.31

[1] Absolute values <0.30 were not listed in the table for simplicity. Foods or food groups with factor loadings <0.30 for both factors were excluded.
[2] *See* Table 1 for food groupings.

359 fatal cases of CHD). After adjustment for age, a higher prudent pattern score was strongly associated with a monotonic lower risk of CHD (**Table 5**). The age-adjusted RRs across increasing quintiles of prudent pattern score were 1.0, 0.84, 0.76, 0.71, and 0.66 (95% CI: 0.54, 0.80; *P* for trend < 0.0001). Further adjustment for smoking and other CHD risk factors did not change the results materially. This inverse association was similar for fatal CHD; multivariate RRs across quintiles of prudent pattern score were 1.0, 0.94, 0.78, 0.63, and 0.66 (95% CI: 0.46, 0.94; *P* for trend = 0.0003) and nonfatal MI. RRs after adjustment for smoking, BMI, and other CHD risk factors were 1.0, 0.83, 0.78, 0.81, and 0.70 (95% CI: 0.54, 0.91; *P* for trend = 0.03). The inverse association between the prudent pattern score and total CHD was persistent among subgroups of current smokers and nonsmokers, obese and nonobese individuals, and those with and without a parental history of MI (**Figure 1**).

In our analyses, intakes of fiber—especially cereal fiber (24)—and folate (25) were inversely associated with risk of CHD. To examine the degree to which the inverse association for the prudent pattern was mediated by these beneficial nutrients, we included dietary intakes of cereal fiber and folate in the multivariate model. Additional adjustment for these nutrients only slightly attenuated the inverse association for the prudent pattern score: the RR for the comparison of the highest with the lowest quintile was 0.75 (95% CI: 0.59, 0.95; *P* for trend = 0.02).

After adjustment for age, a higher Western pattern score was associated with a monotonic higher risk of CHD (**Table 6**). The age-adjusted RRs across increasing quintiles of the Western pattern score were 1.0, 1.21, 1.24, 1.24, and 1.45 (95% CI: 1.19, 1.77; *P* for trend < 0.0001). Further adjustment for smoking, alcohol use, and other coronary risk factors slightly strengthened these associations. The positive association appeared to be stronger for fatal CHD: the RRs across quintiles of the score were 1.0, 1.63, 1.49, 1.50, and 2.15 (95% CI: 1.34, 3.46; *P* for trend = 0.009) than for nonfatal MI. Corresponding RRs of nonfatal MI were 1.0, 1.12, 1.30, 1.33, 1.46 (95% CI: 1.04, 2.05; *P* for trend = 0.0007). The positive association between the Western diet pattern score and total CHD persisted in subgroup analysis according to current smoking, obesity, and parental history of MI (**Figure 2**). Additional adjustment for intakes of nutrients that were directly correlated with this pattern, such as dietary cholesterol, saturated fat, and *trans* fat, only slightly attenuated these results: RRs across quintiles of Western pattern score were 1.0, 1.21, 1.27, 1.27, and 1.43 (95% CI: 1.01, 2.01; *P* for trend = 0.004).

In an additional analysis, we subdivided breakfast cereal into whole and refined cereals using the criteria developed by Jacobs et al (26). Specifically, breakfast cereals with ≥25% whole-grain or bran content by weight were classified as whole-grain and the rest were classified as refined-grain cereals. The associations between the 2 major patterns and risk of CHD obtained from this analysis were similar to those mentioned above. The multivariate RR comparing extreme quintiles of the prudent pattern score was 0.72 (95% CI: 0.58, 0.89) and the corresponding RR for the Western pattern was 1.62 (95% CI: 1.23, 2.15).

Although the 2 dietary pattern scores were statistically independent through the orthogonal transformation procedure, it is possible for one individual to have high or low scores on the 2 patterns at the same time. We therefore examined CHD risk according to joint classifications of Western pattern and prudent pattern scores. In a multivariate analysis, the observed associations for the 2 patterns appeared to be independent of each other. Compared with those with the lowest score for the prudent pattern and highest score for the Western pattern, the RR of CHD for men in the highest category of the prudent pattern compared with the lowest category of the Western pattern was 0.50 (95% CI: 0.34, 0.74).

We conducted several sensitivity analyses to examine the robustness of our findings. Use of the maximum likelihood rather than the principal component method to extract initial factors or an alternative algorithm [oblique rotation (producing correlated factors) rather than orthogonal rotation (producing uncorrelated factors)] to rotate factors yielded similar loadings for the 2 major diet patterns. When the final factor solutions were limited to 2 rather than to 3 factors, the factor loadings for the 2 factors did not change appreciably, and neither did the associations between the factors scores and the risk of CHD. The multivariate RRs across quintiles of the prudent pattern score were 1.0, 0.95, 0.78, 0.77, and 0.72 (95% CI: 0.58, 0.89; *P* for trend = 0.0009). Corresponding RRs across quintiles of the Western pattern score were 1.0, 1.15, 1.45, 1.30, and 1.61 (95% CI: 1.24, 2.10; *P* for trend < 0.0001). Finally, we derived dietary patterns based on food consumption data from all 131 food items in the FFQ rather than from the predefined food groups. The 2 major diet patterns identified from this analysis were qualitatively similar to those identified by using predefined food groups. Additionally, the associations between the 2 major diet patterns and risk of CHD did not materially change; the multivariate RRs across quintiles of the prudent pattern score were 1.0, 0.99, 0.85, 0.78, and 0.76 (95% CI: 0.62. 0.94; *P* for trend = 0.006). Corresponding RRs

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TABLE 3
Age-standardized baseline characteristics according to quintiles of prudent pattern score in the Health Professionals Follow-up Study in 1986

	Quintile of prudent diet score				
	1 (lowest) (n = 8939)	2 (n = 9239)	3 (n = 9049)	4 (n = 9008)	5 (highest) (n = 8640)
Subject characteristics (%)					
Current smoker	16	11	9	7	6
Parental history of MI[1]	11	12	12	12	13
Multivitamin supplement use	38	39	41	44	48
Vitamin E supplement use	13	16	18	21	26
Diabetes	2	2	3	3	3
Hypertension	20	20	20	20	21
Hypercholesterolemia	8	9	10	12	13
Physical activity[2]	14	17	19	22	27
Age (y)	52 ± 9[3]	53 ± 10	54 ± 10	55 ± 10	55 ± 10
BMI (kg/m^2)	26 ± 3	26 ± 3.3	25 ± 3	25 ± 3	25 ± 3
Alcohol use (g/d)	11 ± 16	12 ± 15	12 ± 15	12 ± 15	12 ± 15
Nutrient intakes (energy-adjusted)					
Cholesterol (mg/d)	322 ± 126	311 ± 107	308 ± 106	299 ± 103	288 ± 107
Saturated fat (g/d)	29 ± 6	26 ± 5	25 ± 5	23 ± 5	21 ± 6
Monounsaturated fat (g/d)	31 ± 6	29 ± 5	27 ± 5	26 ± 5	24 ± 6
Polyunsaturated fat (g/d)	13 ± 3	13 ± 3	13 ± 3	13 ± 3	14 ± 4
Trans fat (g/d)	4 ± 1	3 ± 1	3 ± 1	3 ± 1	2 ± 1
Dietary folate (μg/d)	282 ± 94	326 ± 95	354 ± 109	381 ± 102	439 ± 123
Fiber (g/d)	15 ± 5	18 ± 5	20 ± 5	23 ± 6	28 ± 8
Protein (g/d)	85 ± 15	89 ± 15	93 ± 15	95 ± 16	100 ± 18
Carbohydrates (g/d)	223 ± 43	228 ± 40	232 ± 39	238 ± 41	249 ± 45
Food intakes (servings/d)					
Red meat	0.7 ± 0.5	0.6 ± 0.4	0.6 ± 0.5	0.6 ± 0.4	0.5 ± 0.5
Processed meat	0.5 ± 0.5	0.4 ± 0.4	0.4 ± 0.4	0.3 ± 0.4	0.3 ± 0.4
Fish	0.2 ± 0.2	0.3 ± 0.2	0.4 ± 0.2	0.4 ± 0.3	0.6 ± 0.5
Poultry	0.2 ± 0.2	0.3 ± 0.2	0.3 ± 0.2	0.4 ± 0.3	0.5 ± 0.4
Eggs	0.4 ± 0.5	0.3 ± 0.4	0.3 ± 0.4	0.3 ± 0.4	0.3 ± 0.4
Butter	0.3 ± 0.7	0.3 ± 0.7	0.3 ± 0.7	0.3 ± 0.6	0.3 ± 0.6
Low-fat dairy products	0.7 ± 0.9	0.8 ± 1.0	0.9 ± 1.0	1.0 ± 1.1	1.0 ± 1.1
High-fat dairy products	1.0 ± 1.2	1.0 ± 1.0	1.0 ± 1.0	1.0 ± 1.0	0.9 ± 1.0
Fruit	0.9 ± 0.7	1.4 ± 0.8	1.7 ± 1.0	2.2 ± 1.2	3.1 ± 2.0
Vegetables	1.3 ± 0.5	2.0 ± 0.6	2.6 ± 0.7	3.4 ± 0.8	5.4 ± 2.1
Whole grain	0.5 ± 0.7	0.8 ± 0.9	1.1 ± 1.1	1.3 ± 1.3	1.7 ± 1.7
Refined grain	1.2 ± 1.1	1.1 ± 1.1	1.1 ± 1.0	1.1 ± 1.0	1.1 ± 1.0
Sweets and dessert	1.2 ± 1.3	1.1 ± 1.2	1.1 ± 1.1	1.0 ± 1.1	0.9 ± 1.1

[1] MI, myocardial infarction.
[2] Measured as metabolic equivalent (MET). The MET value is the energy need per kilogram of body weight per hour of activity divided by the energy need per kilogram of body weight per hour at rest. Because of the large sample size, tests for trends across quintiles of the pattern score were statistically significant for all variables.
[3] $\bar{x}$ ± SD.

across quintiles of the Western pattern score were 1.0, 1.06, 1.20, 1.36, and 1.54 (95% CI: 1.19, 2.01; P for trend = 0.0003).

DISCUSSION

With the use of dietary data from an FFQ, 2 major dietary patterns emerged by factor analysis. The first factor, the prudent pattern, was characterized by high intakes of vegetables, fruit, legumes, whole grains, fish, and poultry, whereas the second factor, the Western diet pattern, was characterized by high intakes of red meat, processed meat, refined grains, sweets and dessert, French fries, and high-fat dairy products. During 8 y of follow-up, we found that as prudent pattern score increased, the risk of CHD decreased, even after adjustment for potential beneficial nutrients such as folate and cereal fiber. In contrast, as Western pattern score increased, the risk of CHD increased, even after adjustment for potential deleterious nutrients such as saturated fat, *trans* fat, and cholesterol. These data suggest that the 2 major dietary patterns derived from the FFQ predict the risk of CHD, independent of the effects of several known beneficial or deleterious nutrients.

Our data are consistent with ecologic observations. Distinct eating patterns reflecting different dietary traditions have been related to disease rates in different countries (1). The Mediterranean and Asian diets have attracted considerable interest as alternatives to the Western diet because of the extremely low rates of CHD in Greece and Japan. Compared with the typical American diet, traditional Mediterranean and Asian diets contain substantially more grains, legumes, vegetables, fruit, and fish and less red meat, high-fat dairy products, and other animal products. However, because many other potential risk factors besides diet vary among countries, one cannot confidently attribute differences in CHD rates to

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TABLE 4
Age-standardized baseline characteristics according to quintiles of Western diet score in the Health Professionals Follow-up Study in 1986

	Quintile of Western diet score				
	1 (lowest) (n = 8029)	2 (n = 9093)	3 (n = 9287)	4 (n = 9363)	5 (highest) (n = 9103)
Subject characteristics (%)					
Current smoking	7	8	9	11	14
Parental history of MI[1]	13	12	12	12	11
Multivitamin supplement use	47	44	42	41	37
Vitamin E supplement use	25	21	19	16	14
Diabetes	2	2	3	2	3
Hypertension	22	21	20	20	19
Hypercholesterolemia	14	11	10	9	8
Physical activity[2]	23	21	19	19	17
Age (y)	55 ± 10[3]	54 ± 10	54 ± 10	53 ± 10	53 ± 9
BMI (kg/m^2)	25 ± 3	25 ± 3	25 ± 3	26 ± 3	26 ± 4
Alcohol use (g/d)	10 ± 14	11 ± 15	12 ± 15	12 ± 16	13 ± 17
Nutrient intakes (energy-adjusted)					
Cholesterol (mg/d)	273 ± 101	295 ± 103	305 ± 100	317 ± 112	335 ± 126
Saturated fat (g/d)	20 ± 6	24 ± 6	25 ± 6	26 ± 5	28 ± 6
Monounsaturated fat (g/d)	23 ± 6	26 ± 6	28 ± 5	29 ± 5	30 ± 5
Polyunsaturated fat (g/d)	13 ± 4	13 ± 3	13 ± 3	13 ± 3	14 ± 3
Trans fat (g/d)	2 ± 1	3 ± 1	3 ± 1	3 ± 1	3 ± 1
Dietary folate (μg/d)	405 ± 138	372 ± 118	354 ± 112	338 ± 106	315 ± 91
Fiber (g/d)	25 ± 9	22 ± 7	20 ± 6	19 ± 6	18 ± 5
Protein (g/d)	96 ± 19	93 ± 17	92 ± 16	91 ± 15	90 ± 15
Carbohydrates (g/d)	252 ± 50	238 ± 43	232 ± 40	228 ± 38	222 ± 37
Food intakes (servings/d)					
Red meat	0.2 ± 0.2	0.4 ± 0.3	0.6 ± 0.3	0.8 ± 0.4	1.0 ± 0.6
Processed meat	0.1 ± 0.1	0.2 ± 0.2	0.3 ± 0.3	0.4 ± 0.3	0.7 ± 0.6
Fish	0.5 ± 0.4	0.4 ± 0.3	0.4 ± 0.3	0.4 ± 0.3	0.3 ± 0.3
Poultry	0.4 ± 0.3	0.3 ± 0.3	0.3 ± 0.3	0.3 ± 0.3	0.3 ± 0.3
Eggs	0.2 ± 0.2	0.2 ± 0.3	0.3 ± 0.3	0.4 ± 0.4	0.6 ± 0.6
Butter	0.1 ± 0.2	0.2 ± 0.3	0.2 ± 0.5	0.3 ± 0.6	0.6 ± 1.0
Low-fat dairy products	0.7 ± 0.9	0.8 ± 0.9	0.9 ± 1.0	0.9 ± 1.1	0.9 ± 1.2
High-fat dairy products	0.5 ± 0.4	0.7 ± 0.6	0.9 ± 0.8	1.1 ± 1.0	1.7 ± 1.5
Fruit	2.1 ± 1.7	1.9 ± 1.4	1.8 ± 1.3	1.8 ± 1.3	1.8 ± 1.3
Vegetables	3.1 ± 2.1	2.8 ± 1.8	2.8 ± 1.7	2.9 ± 1.6	3.0 ± 1.7
Whole grain	1.0 ± 1.2	1.0 ± 1.2	1.0 ± 1.2	1.1 ± 1.2	1.2 ± 1.4
Refined grain	0.6 ± 0.5	0.8 ± 0.6	1.0 ± 0.8	1.3 ± 1.0	1.9 ± 1.4
Sweets and dessert	0.4 ± 0.5	0.7 ± 0.7	1.0 ± 0.9	1.3 ± 1.2	1.9 ± 1.7

[1] MI, myocardial infarction.
[2] Measured as metabolic equivalent (MET). The MET value is the energy need per kilogram of body weight per hour of activity divided by the energy need per kilogram of body weight per hour at rest. Because of the large sample size, tests for trends across quintiles of the pattern score were statistically significant for all variables.
[3] $\bar{x}$ ± SD.

distinct dietary patterns. Nevertheless, the overlap of the prudent diet pattern identified by the factor analysis with the Mediterranean and Asian diets increases our confidence that the factor analysis identified meaningful patterns.

Relating dietary patterns to disease outcomes within a population is relatively new in nutritional epidemiology. Limited data suggest that overall dietary patterns assessed by various methods are indeed associated with risk of diseases or mortality. Using dietary data collected by a diet-history questionnaire, Slattery et al (15) derived 2 major patterns that closely resembled ours: one was a Western-type diet pattern characterized by a high intake of red meat, processed meat, fast food, refined grains, and sugar-containing foods; the second was the prudent diet pattern, characterized by high intakes of vegetables and fruit, fish, and poultry. The authors found that the prudent diet pattern was associated with a lower risk of colon cancer, whereas the Western-type diet pattern was associated with an increased risk. In a study of elderly rural Greeks (27), greater adherence to the traditional Mediterranean dietary pattern (reflected by a composite score for intakes of vegetables, fruit, legumes, ethanol, dairy products, cereal, and monounsaturated rather than saturated fat) was significantly associated with a reduction in total mortality. Similarly, Huijbregts et al (28) found that a dietary indicator of a healthy dietary pattern, based on the World Health Organization's guidelines for the prevention of chronic diseases, was significantly associated with reduced overall mortality in the Seven Countries Study. Using cluster analysis, Farchi et al (29) identified 4 distinct dietary patterns in 2 Italian rural cohorts of the Seven Countries Study. After 20 y of follow-up, they found the lowest risk of CHD in the cluster with high vegetable oil consumption and the highest risk of stroke in the cluster with high alcohol consumption. Using data from the National Health and Nutrition Examination Survey

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TABLE 5
Relative risks (95% CIs) of coronary heart disease according to quintiles of prudent pattern score[1]

	Quintile of prudent pattern score					
	1 (lowest) (n = 246)	2 (n = 233)	3 (n = 214)	4 (n = 207)	5 (highest) (n = 189)	P for trend
Person-years	62 315	64 266	62 921	62 429	59 675	
Age adjusted	1.0	0.84 (0.70, 1.00)	0.76 (0.63, 0.91)	0.71 (0.59, 0.86)	0.66 (0.54, 0.80)	<0.0001
Multivariate 1[2]	1.0	0.87 (0.73, 1.05)	0.79 (0.66, 0.96)	0.75 (0.62, 0.92)	0.70 (0.56, 0.86)	0.0009
Multivarite 2[3]	1.0	0.90 (0.74, 1.08)	0.83 (0.68, 1.01)	0.79 (0.64, 0.98)	0.75 (0.59, 0.95)	0.02

[1] n values are the number of CHD cases.
[2] Adjusted for age (40–44, 45–49, 50–54, 55–59, 60–64, 65–69, and ≥70 y), BMI (quintiles), time period (four 2-y periods), cigarette smoking [never, past, and current smoking (1–14, 15–24, and ≥25 cigarettes/d)], parental history of myocardial infarction before age 60, multivitamin and vitamin E supplement use, alcohol consumption (0–4, 5–9, 10–14, 15–29, and ≥30 g/d), history of hypertension, physical activity (quintiles of metabolic equivalents), total energy intake (quintiles), and profession.
[3] Adjusted for the variables listed above and for dietary intakes of cereal fiber and folate.

Epidemiologic Follow-up Study, Kant et al found inverse associations between dietary diversity (a score counting the number of food groups consumed daily: dairy, meat, grain, fruit, and vegetable) and subsequent overall mortality (30) and cause-specific mortality (31). In addition, Slattery et al (32) found that diet diversity in plant intake, but not in meat intake, was associated with lower risk of colon cancer. However, the dietary diversity score is a crude measure of dietary patterns because it does not distinguish the effects of different types of foods.

In contrast with the traditional analytic approach used in nutritional epidemiology, dietary pattern analysis considers overall diet rather than individual nutrients or foods. This

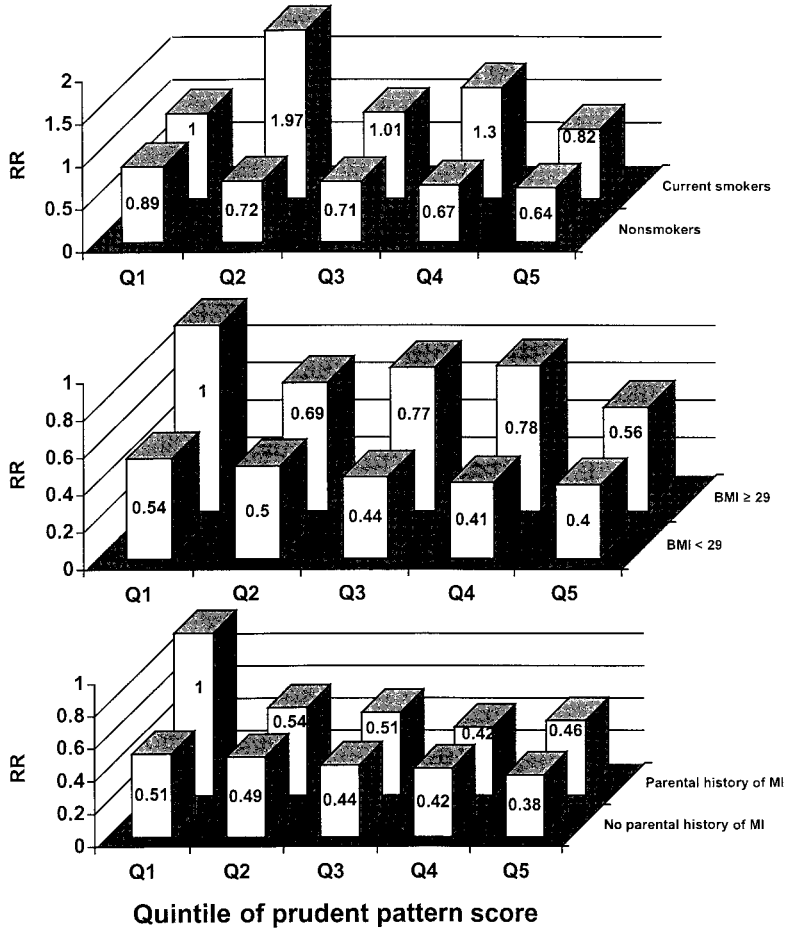

FIGURE 1. Multivariate relative risks (RRs) of coronary heart disease according to quintiles (Q1–Q5) of prudent pattern score by smoking status, BMI, and parental history of myocardial infarction (MI). The models include all the nondietary covariates listed in Table 4 except the stratifying variable. Note that the scale of the y axis for the smoking subgroups is different from that of the other 2 panels.

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TABLE 6
Relative risks (95% CIs) of coronary heart disease according to quintiles of Western pattern score[1]

	Quintile of Western pattern score					
	1 (lowest) (n = 173)	2 (n = 226)	3 (n = 228)	4 (n = 223)	5 (highest) (n = 239)	P for trend
Person-years	55 476	63 128	64 355	65 039	63 337	
Age adjusted	1.0	1.21 (0.99, 1.48)	1.24 (1.02, 1.52)	1.24 (1.02, 1.52)	1.45 (1.19, 1.77)	<0.0001
Multivariate 1[2]	1.0	1.25 (1.02, 1.54)	1.36 (1.08, 1.70)	1.40 (1.10, 1.79)	1.64 (1.24, 2.17)	<0.0001
Multivariate 2[3]	1.0	1.21 (0.98, 1.50)	1.27 (0.99, 1.63)	1.27 (0.99, 1.69)	1.43 (1.01, 2.01)	0.004

[1] n values are the number of CHD cases.
[2] Adjusted for age (40–44, 45–49, 50–54, 55–59, 60–64, 65–69, and ≥70 y), BMI (quintiles), time period (four 2-y periods), cigarette smoking [never, past, and current smoking (1–14, 15–24, and ≥25 cigarettes/d)], parental history of myocardial infarction before age 60 y, multivitamin and vitamin E supplement use, alcohol consumption (0–4, 5–9, 10–14, 15–29, and ≥30 g/d), history of hypertension, physical activity (quintiles of metabolic equivalents), total energy intake (quintiles), and profession.
[3] Adjusted for the variables listed above and for dietary cholesterol, saturated fat, and *trans* fat.

approach would more closely parallel the real world, where dietary intakes consist of nutrients that occur together in common foods. It can take into account complicated interactions among nutrients and nonnutrient substances in studies of free-living people. On the other hand, because there are many potential differences in nutrients between dietary patterns, this approach cannot be specific about the particular nutrients responsible for the observed differences in disease risk, and thus it may not be very informative about biological relations between dietary components and disease risk. However, our findings are consistent with associations between intakes of nutrients and foods identified in previous epidemiologic studies. In particular,

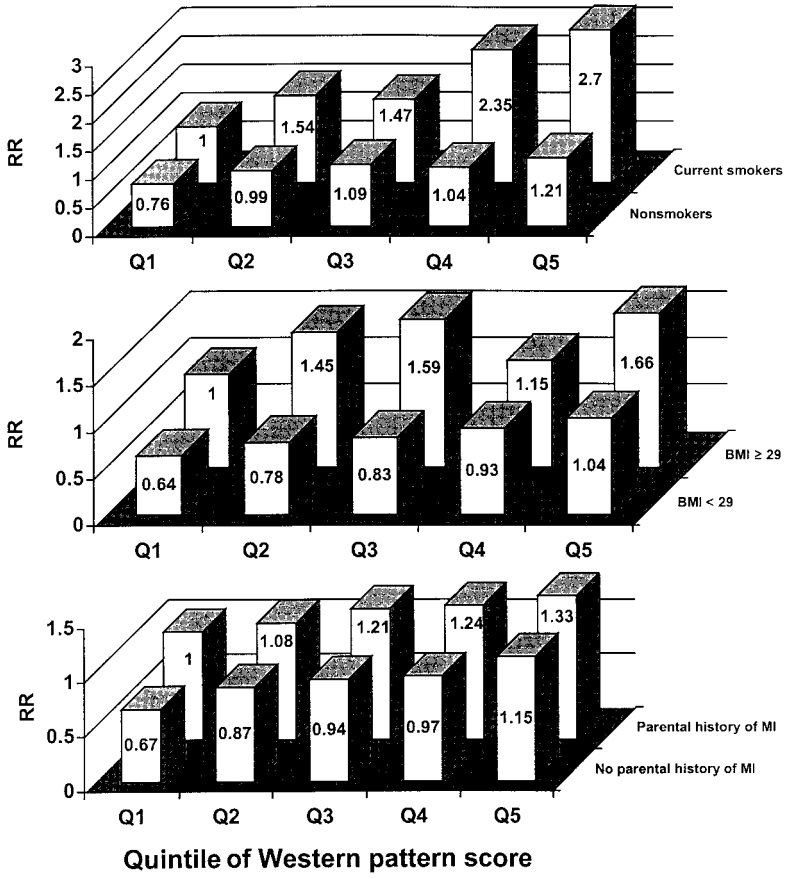

FIGURE 2. Multivariate relative risks (RRs) of coronary heart disease according to quintiles (Q1–Q5) of Western pattern score by smoking status, BMI, and parental history of myocardial infarction (MI). The models include all the nondietary covariates listed in Table 4 except the stratifying variable. Note that the scale of the y axis for the smoking subgroups is different from that of the other 2 panels.

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higher consumption of fruit and vegetable (33), whole-grain products (26, 34, 35), and fish (36–38) has been associated with a reduced risk of CHD. Intakes of nutrients that are directly correlated with the prudent diet pattern, including folate (25), vitamin E (39–41), and fiber (24, 42, 43) are protective against CHD. On the other hand, red meat consumption was associated with increased CHD risk (44, 45). Intake of heme iron, primarily from red meat, was significantly related to an increased risk of MI (46). Whole milk rather than skim milk consumption has been associated with increased risk of CHD (34). Carbohydrate-containing foods with a high glycemic index, such as white bread and mashed potatoes, have been associated with an increased risk of type 2 diabetes (47, 48) and CHD (49).

Statistical methods used to define dietary patterns such as factor analysis are somewhat subjective (50) because decisions on the number of factors are usually based on empirical guidelines rather than on an exact quantitative solution (9, 10). In determining the number of factors, we adhered to established empirical guidelines as closely as possible. Meanwhile, multiple sensitivity analyses suggested the robustness of our findings on both the derived major patterns and their relations with CHD. Additionally, in our previous study (16), we showed reasonable reproducibility over time and comparability between the FFQs and diet records in characterizing dietary patterns in a subsample of the HPFS. The same procedures for defining food groups and deriving dietary patterns were used in this study.

A previous study (51) found that patients with hypercholesterolemia consuming a National Cholesterol Education Program Step I diet containing primarily lean red meats or lean white meats (poultry and fish) had similar reductions in LDL-cholesterol cholesterol. It is possible that lean red meats and fat meats may belong to different eating patterns and have different associations with risk of CHD. We were unable to separate lean red meats from fat meats in the dietary pattern analysis because our FFQ only asked about overall meat consumption. Nevertheless, in our previous analysis of the Nurses' Health Study (52), overall red meat consumption was associated with a modest increase in CHD risk, whereas white meat consumption was associated with a lower risk. Substitution of white meat for red meat was associated with significantly reduced risk of CHD.

Dietary patterns are likely to vary by sex, socioeconomic status, ethnic group, and culture. Thus, it is necessary to replicate the results of our study in other populations. Additionally, because of changes in food preferences and food availability, the meaning of dietary pattern could change over time. Finally, the 2 major diet patterns derived from our data explained < 20% of total variance, suggesting the potential existence of other patterns. In a previous study (15), the Western and prudent diet patterns explained 19% of the variance in men and 15% of the variance in women. However, the percentage of variance explained by the factors should be interpreted with caution because it depends heavily on the total number of variables used in the factor analysis (9).

In conclusion, our data suggest that 2 dietary patterns derived from food consumption data assessed by the FFQ significantly predict the incidence of CHD, independent of other lifestyle variables. This study provided strong evidence that a diet high in vegetables, fruit, legumes, whole grains, fish, and poultry and low in red meat, processed meat, high-fat dairy products, and refined grains may reduce the risk of CHD. Our findings may provide practical guidance for nutrition intervention and education because overall patterns of dietary intake might be easy for the public to interpret or translate into diets.

REFERENCES

1. Willett WC. Diet and health: what should we eat? Science 1994; 264:532–7.
2. Willett WC. Nutritional epidemiology. 2nd ed. New York: Oxford University Press, 1998.
3. Randall E, Marshall JR, Brasure J, Graham S. Dietary patterns and colon cancer in western New York. Nutr Cancer 1992;18:265–76.
4. Wirfalt AKE, Jeffery RW. Using cluster analysis to examine dietary patterns: nutrient intakes, gender, and weight status differ across food pattern clusters. J Am Diet Assoc 1997;97:272–9.
5. Sacks FM, Obarzanek E, Windhauser MM, et al. Rational and design of the Dietary Approaches to Stop Hypertension Trial (DASH): a multicenter controlled-feeding study of dietary patterns to lower blood pressure. Ann Epidemiol 1994;5:108–18.
6. Appel L, Moore TJ, Obarzanek E, et al. A clinical trial of the effects of dietary patterns on blood pressure. N Engl J Med 1997;336:1117–24.
7. The Trials of Hypertension Prevention Collaborative Research Group. The effects of nonpharmacologic interventions on blood pressure of persons with high normal levels. JAMA 1992;267:1213–20.
8. National Research Council, Committee on Diet and Health. Diet and health. implications for reducing chronic disease risk. Washington, DC: National Academy Press, 1989.
9. Kim J-O, Mueller CW. Factor analysis: statistical methods and practical issues. Thousand Oaks, CA: Sage Publications, Inc, 1978.
10. Kleinbaum DG, Kupper LL, Muller KE. Variable reduction and factor analysis. Applied regression analysis and other multivariable methods. Boston: PWS-KENT Publishing Company, 1988:595–640.
11. Nicklas TA, Webber LS, Thompson B, Berenson GS. A multivariate model for assessing eating patterns and their relationship to cardiovascular risk factors: the Bogalusa Heart Study. Am J Clin Nutr 1989;49: 1320–7.
12. Herbert JR, Kabat GC. Implications for cancer epidemiology of differences in dietary intake associated with alcohol consumption. Nutr Cancer 1991;15:107–19.
13. Randall E, Marshall JR, Graham S, Brasure J. Patterns in food use and their associations with nutrient intakes. Am J Clin Nutr 1990;52:739–45.
14. Barker ME, McClean SI, Stain JJ, Thompson KA. Dietary behavior and health in Northern Ireland: an exploration of biochemical and haematological associations. J Epidemiol Community Health 1992;46:151–6.
15. Slattery ML, Boucher KM, Caan BJ, Potter JD, Ma KN. Eating patterns and risk of colon cancer. Am J Epidemiol 1998;148:4–16.
16. Hu FB, Rimm E, Smith-Warner SA, et al. Reproducibility and validity of dietary patterns assessed with a food-frequency questionnaire. Am J Clin Nutr 1999;69:243–9.
17. Rose GA, Blackburn H. Cardiovascular survey methods. World Health Organ Monogr Ser 1982;56.
18. Stampfer MJ, Willett WC, Speizer FE, et al. Test of the National Death Index. Am J Epidemiol 1984;119:837–9.
19. 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.
20. 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.
21. SAS Institute Inc. SAS/STAT user's guide, version 6. 4th ed. Vol 2. Cary, NC: SAS Institute Inc, 1989.
22. D'Agostino RB, Lee M-L, 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.
23. Chasan-Taber S, Rimm EB, Stampfer MJ, et al. Reproducibility and validity of a self-administered physical activity questionnaire for male health professionals. Epidemiology 1996;7:81–6.

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24. Rimm EB, Ascherio A, Giovannucci E, Spiegelman D, Stampfer MJ, Willett WC. Vegetable, fruit, and cereal fiber intake and risk of coronary heart disease among men. JAMA 1996;275:447–51.
25. Rimm E, Willett W, Hu FB, et al. Folate and vitamin B6 from diet and supplements in relation to risk of coronary heart disease among women. JAMA 1998;279:359–65.
26. 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.
27. Trichopoulou A, Kouris-Blazos A, Wahlqvist M, et al. Diet and overall survival in elderly people. BMJ 1995;311:1457–60.
28. 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.
29. Farchi G, Mariotti S, Menotti A, Seccareccia F, Torsello S, Fidanza F. Diet and 20-y mortality in two rural population groups of middle-aged men in Italy. Am J Clin Nutr 1989;50:1095–103.
30. Kant AK, Schatzkin A, Harris TB, Ziegler RG, Block G. Dietary diversity and subsequent mortality in the First National Health and Nutrition Examination Survey Epidemiologic Follow-up Study. Am J Clin Nutr 1993;57:434–40.
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. Slattery ML, Berry TD, Potter J, Caan B. Diet diversity, diet composition, and risk of colon cancer (United States). Cancer Causes Control 1997;8:872–82.
33. Ness AR, Powles J. Fruit and vegetables, and cardiovascular disease: a review. Int J Epidemiol 1997;26:1–13.
34. Fraser GE, Sabate J, Beeson WL, Strahan TM. A possible protective effect of nut consumption on risk of coronary heart disease. The Adventist Health Study. Arch Intern Med 1992;152:1416–24.
35. Liu S, Stampfer MJ, Hu FB, et al. Whole grain consumption and risk of coronary heart disease: results from the Nurses' Health Study. Am J Clin Nutr 1999;70:412–9.
36. Kromhout D, Bosscheiter EB, de Lezenne Coulander C. The inverse relation between fish consumption and 20-year mortality from coronary heart disease. N Engl J Med 1985;312:1205–9.
37. Daviglus ML, Stamler J, Orencia AJ, et al. Fish consumption and the 30-year risk of fatal myocardial infarction. N Engl J Med 1997;336: 1046–53.
38. Albert CM, Hennekens CH, O'Donnell CJ, et al. Fish consumption and risk of sudden cardiac death. JAMA 1998;279:23–8.
39. Rimm EB, Stampfer MJ, Ascherio A, et al. Vitamin E consumption and the risk of coronary heart disease in men. N Engl J Med 1993; 328:1450–6.
40. Stampfer MJ, Hennekens CH, Manson JE, Colditz GA, Rosner B, Willett WC. A prospective study of vitamin E consumption and risk of coronary disease in women. N Engl J Med 1993;328: 1444–9.
41. Kushi LH, Folsom AR, Prineas RJ, Mink PJ, Wu Y, Bostick RM. Dietary antioxidant vitamins and death from coronary heart disease in postmenopausal women. N Engl J Med 1996;334:1156–62.
42. Kushi LH, Lew RA, Stare FJ, et al. Diet and 20-year mortality from coronary heart disease: The Ireland-Boston Diet-Heart study. N Engl J Med 1985;312:811–8.
43. Khaw KT, Barrett-Connor E. Dietary fiber and reduced ischemic heart disease mortality rates in men and women: a 12-year prospective study. Am J Epidemiol 1987;126:1093–102.
44. Snowdon DA, Phillips RL, Fraser GE. Meat consumption and fatal ischemic heart disease. Prev Med 1984;13:490–500.
45. Snowdon DA. Animal product consumption and mortality because of all causes combined, coronary heart disease, stroke, diabetes, and cancer in Seventh-day Adventists. Am J Clin Nutr 1988;48(suppl): 739S–48S.
46. Ascherio A, Willett WC, Rimm EB, Giovannucci EL, Stampfer MJ. Dietary iron intake and risk of coronary heart disease among men. Circulation 1994;89:969–74.
47. 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.
48. Salmeron J, Ascherio A, Rimm EB, et al. Dietary fiber, glycemic load, and risk of NIDDM in men. Diabetes Care 1997;20:545–50.
49. Fraser GE. Diet and coronary heart disease: beyond dietary fats and low-density-lipoprotein cholesterol. Am J Clin Nutr 1994;59(suppl): 1117S–23S.
50. Martinez ME, Marshall JR, Sechrest L. Invited commentary: factor analysis and the search for objectivity. Am J Epidemiol 1998;148: 17–9.
51. Davidson MH, Hunninghake D, Maki KC, Kwiterovich PO Jr, Kafonek S. Comparison of the effects of lean red meat vs lean white meat on serum lipid levels among free-living persons with hypercholesterolemia: a long-term, randomized clinical trial. Arch Intern Med 1999;159:1331–8.
52. Hu FB, Stampfer MJ, Manson JE, et al. Dietary saturated fats and their food sources in relation to the risk of coronary heart disease in women. Am J Clin Nutr 1999;70:1001–8.

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