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A Possible Protective Effect of Nut Consumption on Risk of Coronary Heart Disease

The Adventist Health Study

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• *Background.*—**Although dietary factors are suspected to be important determinants of coronary heart disease (CHD) risk, the direct evidence is relatively sparse.**

Methods.—**The Adventist Health Study is a prospective cohort investigation of 31 208 non-Hispanic white California Seventh-Day Adventists. Extensive dietary information was obtained at baseline, along with the values of traditional coronary risk factors. These were related to risk of definite fatal CHD or definite nonfatal myocardial infarction.**

Results.—**Subjects who consumed nuts frequently (more than four times per week) experienced substantially fewer definite fatal CHD events (relative risk, 0.52; 95% confidence interval [CI], 0.36 to 0.76) and definite nonfatal myocardial infarctions (relative risk, 0.49; 95% CI, 0.28 to 0.85), when compared with those who consumed nuts less than once per week. These findings persisted on covariate adjustment and were seen in almost all of 16 different subgroups of the population. Subjects who usually consumed whole wheat bread also experienced lower rates of definite nonfatal myocardial infarction (relative risk, 0.56; 95% CI, 0.35 to 0.89) and definite fatal CHD (relative risk, 0.89; 95% CI, 0.60 to 1.33) when compared with those who usually ate white bread. Men who ate beef at least three times each week had a higher risk of definite fatal CHD (relative risk, 2.31; 95% CI, 1.11 to 4.78), but this effect was not seen in women or for the nonfatal myocardial infarction end point.**

Conclusion.—**Our data strongly suggest that the frequent consumption of nuts may protect against risk of CHD events. The favorable fatty acid profile of many nuts is one possible explanation for such an effect.**

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Dietary practices are important personal behaviors. Health researchers have recognized the social and psychological associations of diet but have also long recognized that the foods we eat have physiologic effects and change the cellular environment, hence potentially causing or preventing disease.

For editorial comment see p 1371.

Dietary determinants of risk factors for coronary heart disease (CHD) are known. Dietary fats, cholesterol, and soluble fiber influence serum cholesterol levels.[1-3] Dietary fat affects both the aggregability of platelets and coagulation factors,[4-8] whereas sodium, potassium, alcohol, possibly calcium, and fat consumption are suspected to change blood pressure levels.[9]

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Reported associations directly linking *CHD events* to diet are relatively few. Such nutrients as cholesterol and polyunsaturated and saturated fats have demonstrated associations with either risk of fatal CHD or all incident CHD events in both a cohort study[10] and clinical trials.[11-13] Similarly, dietary fiber has been linked to decreased risk of CHD death, although the associations weakened or disappeared on multivariate adjustment.[14,15] Other studies correlating diet and CHD mortality between whole populations also reported findings consistent with those above,[16,17] but such studies are susceptible to confounding by the numerous dietary and nondietary differences of different cultural and geographic settings.[18]

A few individual foods (or nutrients from specific foods), such as starch from peas and beans,[19] cereal fiber,[20] and possibly fish,[21-27] have also been associated with risk of CHD events. An assumption seems to have been that nutrients are the active agents and that they should be the variables of investigation in such research. While this undoubtedly has some validity, the nutrient emphasis ignores the possibility that the biologic activity of one nutrient may depend on the presence or absence of other substances. A number of such situations are well known.[28-34] Foods are unique combinations of complex chemicals, many of which have unknown biologic activ-

ity. A clear advantage of investigating individual foods is that the health education message is usually quite simple. People usually shop for foods rather than nutrients and can more easily translate such research to effective dietary changes.

The California Seventh-day Adventist population has previously provided information on an apparent protective association between the lacto-ovovegetarian diet and risk of coronary artery disease from an older data set. Specifically, it was shown that meat consumption may increase the age-adjusted risk of CHD in both men and women.[35] The present report is the first, with CHD incidence as the end point, from a more recent prospective study of Adventists. These data allow more detailed dietary analyses from 31 208 non-Hispanic white Adventist subjects followed up for 6 years.

The population is ideally suited to the investigation of diet and heart disease, being well educated and intensely interested in diet and health. There is a virtual absence of current cigarette smoking, a very low consumption of alcohol, and frequent adherence to a lacto-ovovegetarian diet.[36] The relative homogeneity with respect to cigarette smoking and alcohol removes or diminishes their potential confounding effect in these analyses. We report herein on associations between consumption of a number of specific foods or food groups and risk of incident fatal and nonfatal CHD events.

SUBJECTS AND METHODS

The Adventist Health Study population and design have been described in detail elsewhere.[36] Briefly, a census questionnaire was mailed in 1974 to all Adventist households in the state of California. This census identified 59 081 Adventists from different ethnic backgrounds aged 25 years or older. In August 1976, a detailed life-style questionnaire, which included a food frequency section, was mailed to all cohort members. Other information relevant to CHD included previous physician-diagnosed heart disease, diabetes, and hypertension, height, weight, previous and current cigarette smoking, and exercise habits. Exercise was categorized as low, moderate, or high on the basis of work and leisure-time activities. Vegetarian status was defined as the consumption of flesh foods (red meat, fish, or poultry) less than once each week.

We confine this report to data from non-Hispanic white Adventists. All subjects who at study baseline had a previous or unknown history of heart disease and all diabetics were excluded. Thus, all events counted from the remaining 26 473 subjects were first events.

Diet Ascertainment

A semiquantitative food frequency questionnaire was developed and pretested[37] for this population, which has unique dietary patterns.[38] The subjects were asked to report on the frequency of current use of 65 food items, which included also beverages and vitamin supplements. Most foods were evaluated on a scale of 1 to 8, ranging from "never consume" to "more than once per day." The questions read "Mark the box that comes closest to how frequently you now use each food when following your usual routine." There followed a list of foods, each with the eight possible response categories. Foods pertinent to these analyses included "nuts (except those used in recipes)," "beef—steak," "beef—hamburger," "other beef or veal," "fish," "poultry (chicken or turkey)," "pork products," "regular coffee (not decaffeinated)," "cheese (except cottage cheese)," "dried or canned beans, lentils, split peas, etc," "canned or frozen fruit," "raisins, dates, and other dried fruits," "fresh citrus fruit (*not* juice)," "fresh fruit commonly available in winter (apples, bananas, pears, etc)," and "other fresh fruit." For bread, the question read "What one type of bread do you use most of the time?" with options being "white," "100% whole wheat or whole grain," "sprouted wheat or wheat berry," and "other (rye, cracked wheat, pumpernickel, soy, etc)." Responses for the various fruit and beef questions were summed to form fruit and beef indexes.

The validity of our dietary data from this epidemiologic study was tested by comparison with a detailed dietary substudy conducted on a random sample of local study subjects. One hundred forty-seven such participants completed a food frequency/portion size questionnaire containing questions identical to those subsequently used in the epidemiologic study. They also gave five 24-hour recalls on random days during a 3-month period. With the average of the 24-hour recalls used as the standard, correlation coefficients between the corresponding food frequency and 24-hour recall items were calculated. These correlation coefficients were corrected for error in the standard,[39] and the 24-hour recall data were also log transformed to improve normality. Pertinent results include a corrected coefficient for nut consumption of .46 ($P<.001$) and for beef consumption, .63 ($P<.001$). Subjects who stated on the food frequency questionnaire that they mostly consumed white bread on average consumed 23.6 g of white bread per day, using the 24-hour recall data, whereas the corresponding figure for those who stated that they mainly consumed whole wheat bread was only 11.5 g of white bread per day ($P<.025$). Such validity results are comparable with reports by others who have investigated a broad range of foods evaluated with the food frequency method.[40-42]

The proportion of missing values for the food frequency dietary variables of the Adventist Health Study varied from 2% to 8%. We gave particular attention to missing dietary data, since in this population some sensitive questions were strongly tied to church recommendations on health (avoiding alcohol, coffee, meat, etc). However, these sensitive questions had response rates similar to those for nonsensitive items.[36]

Identification of Cases

For a period of 6 years (1977 through 1982), annual questionnaires were mailed to all participants as a screening mechanism to identify new cases of CHD. Information on any hospitalization in the previous 12-month period was requested by this questionnaire, and permission to review any relevant medical records was obtained. Pertinent portions of the hospital records were microfilmed by study field representatives to allow confirmation of the diagnosis by Adventist Health Study physicians. All electrocardiograms were microfilmed, and cardiac enzyme results were abstracted to a special form. Follow-up in this fashion was completed for 97% of the participants. All electrocardiograms were also Minnesota coded.[43] Two batches of approximately 100 electrocardiograms each were sent to the Minnesota Coding Laboratory as an aid to quality control. These were timed at about one third and two thirds of the way through the coding process.

A diagnosis of nonfatal myocardial infarction was confirmed if the international diagnostic criteria[44] were met. In summary, these require a diagnostic series of electrocardiographic changes, or elevation of cardiac enzyme levels plus either prolonged cardiac pain or static electrocardiographic abnormalities. Fatal CHD was also defined by the international diagnostic criteria[44] as either "definite fatal myocardial infarction" or "other definite fatal CHD." Definite fatal myocardial infarction required death within 28 days of a myocardial infarction confirmed by hospital records as described above, or fresh myocardial infarction recorded at autopsy. Other definite fatal CHD required *International Classification of Diseases* codes 410 through 414 as underlying or immediate cause of death on the death certificate, provided there were no other likely lethal causes on the certificate. In addition, for this diagnosis, a history of CHD, autopsy findings of severe coronary disease, or symptoms compatible with a coronary cause of death were necessary. For comparison with previous studies,[35,45] a classification titled "all coronary deaths" is displayed that re-

Table 1.—Selected Demographic Characteristics of Participants in the Adventist Health Study

	Men (n = 10 003)	Women (n = 16 740)
Age, y	51.3 ± 16.0	53.2 ± 16.6
Body mass index, kg/m²	24.8 ± 3.5	24.1 ± 4.6
Hypertension, %	21	15
Smoking, %		
Current	2	1
Past	29	13
Never	69	86
Exercise, %		
Low	31	46
Moderate/high	69	54
Education, %		
High school only	26	35
Some college	31	43
College graduate	33	22

quired only that *International Classification of Diseases* codes 410 through 414 be the underlying or immediate cause of death on the death certificate.

Deaths were ascertained for the total study population by computer-assisted linkage with the California death certificate file, the National Death Index, and also the use of church records. For any possible case of fatal CHD, relatives were contacted to elicit information pertinent to the circumstances of death. Also, when available, autopsy reports were procured.

For the few subjects who had both a definite nonfatal myocardial infarction and subsequently a definite fatal CHD event, both events were counted as end points. However, when all definite CHD events were combined (Figure), only the nonfatal myocardial infarction (the first event) was counted.

Data Analysis

Distributions of the food variables under study were examined before analysis began, to create categories of exposure that were biologically meaningful and that included adequate numbers of person-years at risk in each exposure category for analysis. Associations between diet and CHD events were explored by two methods, Mantel-Haenszel stratified analyses and the Cox proportional hazards method.

The analysis was based on person-time incidence rates. For all subjects, person-months at risk were computed after the return of the life-styles questionnaire until an end point, death, unavailability for follow-up, or end of the study (December 31, 1982). Where possible, three or more categories of exposure were examined to detect dose-response gradients between a dietary exposure and CHD end points. Tests of null hypotheses used either Mantel-Haenszel or likelihood ratio χ^2 statistics.

RESULTS

The characteristics of the study population are shown in Tables 1 and 2. The average age was 51 years for men and 53 years for women. The proportion of subjects whose physicians had diagnosed them as hypertensive was close to that expected for an adult population. Although a modest number of subjects admitted to past cigarette smoking (usually before joining the Adventist church), there were virtually no current smokers in this cohort. A relatively large proportion claimed to exercise with at least moderate frequency, and the population was well educated. Table 2 illustrates the tendency toward low consumption of fish and beef and the relatively frequent consumption of nuts, whole wheat bread, fruits, and salads. Indeed, 45% consumed meat products (red meat, fish, or poultry) less than once per week.

Table 2.—Reported Frequency of Use of Selected Foods in the Adventist Health Study Population

Food Item	Frequency of Use	% of Subjects
Cheese	<1 ×/wk	32
	1-2 ×/wk	37
	≥3 ×/wk	31
Nuts	<1 ×/wk	34
	1-4 ×/wk	42
	≥5 ×/wk	24
Beef index	None	39
	>0, <3 ×/wk	40
	≥3 ×/wk	21
Fish	None	43
	>0, <1 ×/wk	47
	≥1 ×/wk	10
Coffee	None	65
	>0, 1 ×/d	26
	≤2 ×/d	9
Bread	White	9
	Mixed	14
	Whole wheat	77
Fruit index	<1 ×/d	19
	1-2 ×/d	32
	>2 ×/d	49
Legumes	<1 ×/wk	40
	1-2 ×/wk	37
	>2 ×/wk	23

We identified 134 cases of incident definite nonfatal myocardial infarction, 260 cases of incident definite fatal CHD, and a total of 463 cases of incident coronary deaths (*International Classification of Diseases* 410 through 414 on death certificate).

Using Mantel-Haenszel stratified analyses, we tested associations between a number of foods and risk of CHD events. These were foods for which we had formulated hypotheses either from the work of others or from basic science considerations. Preliminary analyses stratifying only on age and sex identified two foods that showed strong and consistent protective effects. The first food was nuts, where frequent consumption (more than five times per week) was associated with relative risks of 0.42 and 0.47 for nonfatal myocardial infarction and definite fatal CHD, respectively, when compared with those eating nuts less than once each week. Consumption of whole wheat as compared with white bread was also associated with relative risks of 0.39 and 0.70 for the same two syndromes.

Table 3 shows the results of stratified analyses where the strata are all combinations of age (four categories), sex, smoking (never, past, current), exercise (low, moderate, high), relative weight (tertiles), and hypertension (yes/no), thus controlling confounding by these factors. No important associations were found between risk of coronary events and consumption of beef, fish, coffee, cheese,

Table 3.—Associations Between Selected Foods and Risk of Three Coronary Heart Disease End Points*

Food Item	Frequency of Use	RR (95% CI) Definite Nonfatal Myocardial Infarction†	Definite Fatal CHD†	Fatal CHD as Determined by Death Certificate†
Nuts	<1/wk	1	1	1
	1-4/wk	0.74 (0.49-1.11)	0.73 (0.54-0.99)	0.77 (0.61-0.98)
	≥5/wk	0.52 (0.30-0.87)‡§	0.62 (0.44-0.90)§‖	0.67 (0.51-0.88)‖
Bread	White	1	1	1
	Mixed	0.51 (0.27-0.96)	0.87 (0.53-1.41)	0.72 (0.50-1.04)
	Whole wheat	0.45 (0.28-0.71)‖	0.82 (0.55-1.21)	0.78 (0.58-1.03)
Beef index	Never	1	1	1
	<3/wk	1.14 (0.74-1.75)	0.99 (0.72-1.35)	1.12 (0.88-1.41)
	≥3/wk	0.98 (0.64-1.50)	0.98 (0.64-1.50)	1.19 (0.87-1.62)
Cheese	<1/wk	1	1	1
	1-2/wk	1.97 (1.27-3.04)	0.90 (0.67-1.21)	1.03 (0.83-1.30)
	≥3/wk	1.23 (0.71-2.12)‖	0.72 (0.48-1.1)	0.84 (0.62-1.14)
Fish	Never	1	1	1
	<1/wk	1.11 (0.75-1.66)	1.01 (0.76-1.35)	1.10 (0.89-1.37)
	≥1/wk	1.04 (0.55-1.96)	0.74 (0.42-1.33)	1.09 (0.73-1.61)
Coffee	Never	1	1	1
	≤1/d	0.93 (0.60-1.44)	1.07 (0.77-1.48)	0.85 (0.66-1.11)
	≥2/d	1.13 (0.61-2.10)	1.07 (0.60-1.92)	0.92 (0.58-1.46)
Legumes (beans and peas)	<1/wk	1	1	1
	1-2/wk	0.90 (0.58-1.40)	1.07 (0.78-1.47)	0.98 (0.77-1.24)
	≥3/wk	1.16 (0.72-1.85)	1.26 (0.90-1.78)	1.06 (0.81-1.37)
Fruit index	<1/d	1	1	1
	1-2/d	1.10 (0.57-2.61)	1.30 (0.80-2.12)	1.17 (0.79-1.73)
	>2/d	1.07 (0.58-1.96)	1.08 (0.67-1.75)	1.18 (0.82-1.70)

*Stratified on age, sex, smoking, exercise, relative weight, and high blood pressure. CHD indicates coronary heart disease; RR, relative risk; and CI, confidence interval.
†See text for definitions.
‡Overall χ^2 $P<.05$.
§χ^2 trend $P<.01$.
‖Overall χ^2 $P<.01$.

or legumes. The negative associations with consumption of whole wheat bread were still seen but were reduced in magnitude and were significantly only for nonfatal myocardial infarction.

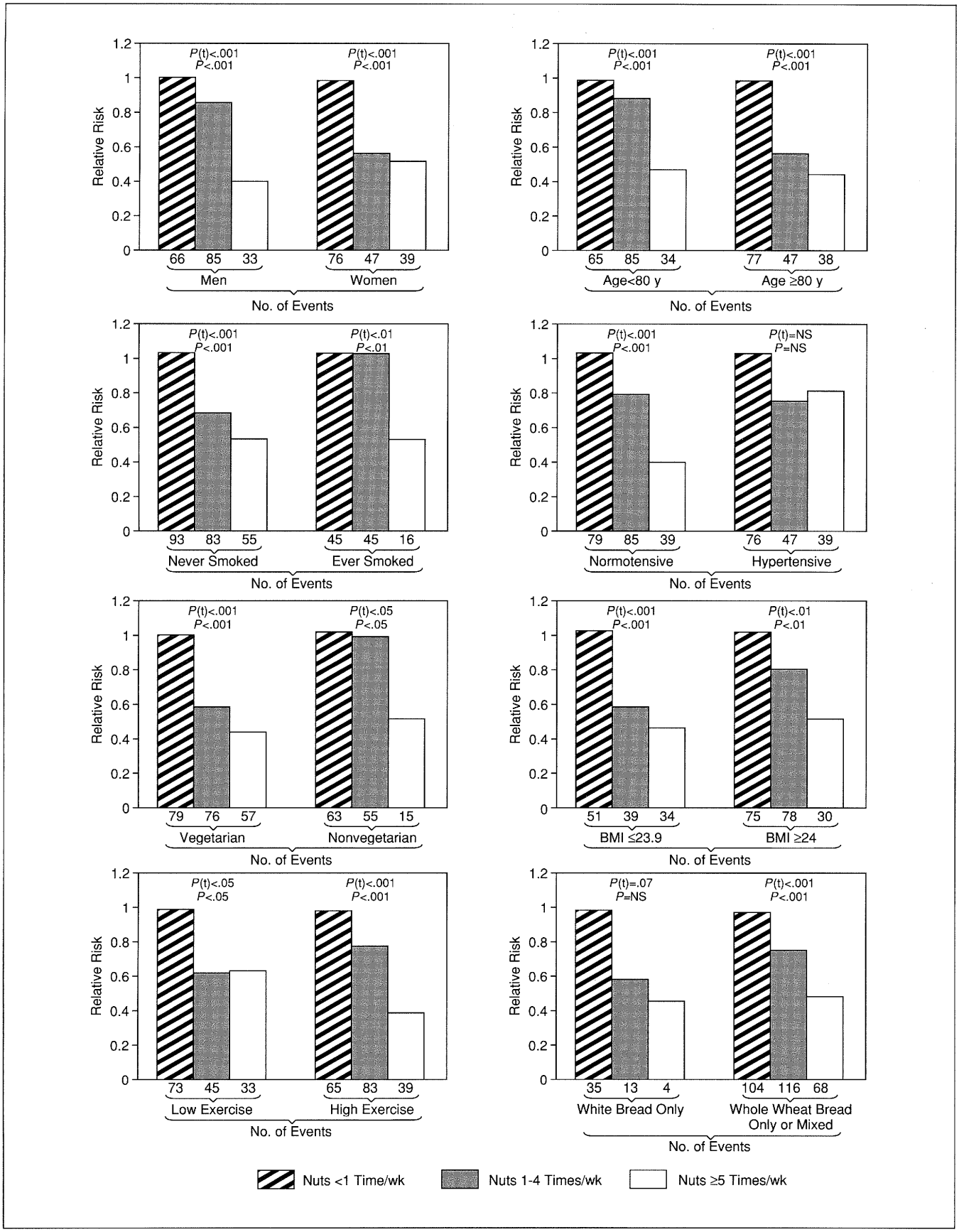
However, the consistent strong negative associations between consumption of nuts and risk of coronary disease remained. Although the relative risks were now of slightly lesser magnitude, statistical significance was retained, suggesting that these results were unlikely to be chance observations. An analysis using the proportional hazards model with the same variables coded to identical categories gave relative risk estimates very similar to those in Table 3.

As it is possible that there was confounding between some of the foods of interest, we examined results of a proportional hazards analysis adjusting for the other seven selected foods as well as the traditional risk factors (Table 4). Results are shown where nuts, bread, and beef (separately analyzed for men, women, and both sexes combined) are the exposures of interest. None of the other foods not shown were significantly related to risk of CHD events. However, again the apparent protective associations seen with higher consumption of nuts and use of whole wheat bread were essentially unchanged. Table 4 also presents the apparently different effects of higher beef consumption on risk of fatal CHD between men and women.

The consistency of the association between nut consumption and risk of coronary events was further explored by the use of age- and sex-stratified analyses within a number of subgroups of the population (Figure). Such analyses inevitably suffer from smaller numbers of events; hence, we combined the two definite categories of event, definite nonfatal myocardial infarction and definite fatal CHD, as the outcome variables in these analyses. A highly consistent negative association between risk of CHD and nut consumption is demonstrated in the Figure, with most analyses retaining statistical significance.

A proportional hazards analysis was restricted to subjects over 80 years of age, with covariates of sex, nut consumption, and age (by individual year). Among these elderly subjects, the relative risks of nut consumption were 1.00, 0.71, 0.46 for the three consumption categories. Thus, the association was undiminished in the elderly and not confounded by the possibly lower consumption of nuts in the extremely old.

As it is possible that persons consuming more nuts may have other distinctive dietary patterns, correlation coefficients were calculated between the frequency of consumption of nuts and other foods, with the following values being found: cheese (−.06), beef (−.30), fish (−.19), coffee (−.19), legumes (.34), poultry (−.26), fruit (.36), and eggs (−.07). The level of multicollinearity between these foods (including nuts) was measured by the



Age- and sex-stratified analyses of associations between the consumption of nuts and definite coronary heart disease events in different subgroups of the population in the Adventist Health Study. P(t) *is the* P *value for a test of trend;* P *is the* P *value for the overall test of difference between categories. NS indicates not significant; BMI, body-mass index.*

Table 4.—Proportional Hazard Analyses Associating Consumption of Beef, Nuts, and Bread With Risk of Three Coronary Heart Disease End Points*

Food Item	Frequency of Use	RR (95% CI) Definite Nonfatal Myocardial Infarction†	Definite Fatal CHD†	Fatal CHD as Determined by Death Certificate†
Nuts	<1/wk	1	1	1
	1-4/wk	0.78 (0.51-1.18)	0.76 (0.56-1.04)	0.82 (0.65-1.04)
	≥5/wk	0.49 (0.28-0.85)‡	0.52 (0.36-0.76)§	0.59 (0.45-0.78)§
Bread	White	1	1	1
	Mixed	0.59 (0.32-1.07)	0.96 (0.60-1.54)	0.77 (0.54-1.08)
	Whole wheat	0.56 (0.35-0.89)‖	0.89 (0.60-1.33)‡	0.74 (0.56-0.99)§
Beef index (men only)	Never	1	1	1
	<3/wk	1.00 (0.56-1.80)	1.93 (1.12-3.33)	1.50 (1.00-2.26)
	≥3/wk	0.71 (0.32-1.59)	2.31 (1.11-4.78)¶	1.74 (1.01-3.01)¶
Beef index (women only)	Never	1	1	1
	<3/wk	0.92 (0.36-2.04)	0.81 (0.50-1.32)	1.13 (0.79-1.61)
	≥3/wk	0.86 (0.22-2.59)	0.76 (0.37-1.56)	1.28 (0.76-2.16)#
Beef index (Both sexes)	Never	1	1	1
	<3/wk	0.92 (0.57-1.49)	1.08 (0.76-1.55)	1.20 (0.92-1.56)
	≥3/wk	0.72 (0.37-1.40)	1.16 (0.70-1.93)¶	1.42 (0.98-2.06)§

*Adjusting for nondietary risk factors and consumption of other foods. All food variables are entered simultaneously into the Cox model, along with age, sex, smoking, exercise, relative weight, and high blood pressure. CHD indicates coronary heart disease; RR, relative risk; and CI, confidence interval.

†See text for definitions.

‡Overall χ^2 $P<.005$.

§Overall χ^2 $P<.0001$.

‖Overall χ^2 $P<.01$.

¶Overall χ^2 $P\leq.001$.

#Overall χ^2 $P<.02$.

tolerance and had a value of 0.77, indicating only mild multicollinearity.

COMMENT

The above analyses suggest that frequent consumption of nuts may be protective for both fatal and nonfatal CHD events. The study has a number of strengths enabling an effective investigation of this question. First, this is a very large cohort with extensive exposure data gathered from each subject. The population includes both men and women with a broad age range. Perhaps of greatest importance is the wide range of frequency of nut consumption in the Adventists, which has undoubtedly increased statistical power. As can be seen from Table 2, 34% of the subjects consumed nuts less than once each week, but 24% consumed nuts at least five times each week. Corresponding figures from other cohort studies are not easy to find, but data from a large study of women[46] will serve as some comparison. Seventy percent of these women consumed nuts less than once per week, and only 5% consumed nuts five or more times per week.

The potential limitations of our study design must also be considered. These include the possibilities of selection bias, misclassification of exposure, and confounding. The data were collected on Seventh-Day Adventists. Can results be applied to the general population? Although various sociocultural selective factors undoubtedly operated, it seems improbable that these would alter metabolic responsiveness and thus change exposure disease associations. Indeed, associations between the traditional risk factors and CHD risk in this population seem very similar[47] to those repeatedly found elsewhere. Although the dietary data must be gathered by questionnaire in a population of this size, we have demonstrated adequate validity for the major foods used in these analyses. Some misclassification is inevitable, but this should not differ between persons who will or will not subsequently develop CHD. Such nondifferential misclassification in a cohort study biases the relative risk toward the null.[48] Despite this, the reported associations persist.

Of greatest concern in the interpretation of these data is the possibility of confounding. Could the consumption of nuts, whole wheat bread, or beef be markers for other true causal factors? We used the techniques of stratification and adjustment in the analyses to adjust for a wide variety of such variables, but the apparent effect of these foods on risk persists. One obvious concern is whether the apparent protective effect of nuts may be due to this variable acting as a surrogate for the vegetarian status. However, our analyses indicate that this is improbable. The proportional hazards analysis in Table 4, with nut consumption as the exposure of interest, included beef consumption as a covariate. In addition, the Figure shows the continuing effect of nut consumption in both vegetarians and nonvegetarians separately. The correlation analyses between nuts and other foods indicated that, although the higher nut consumers tended in the direction of a more vegetarian diet, these correlations are not close to the magnitude that would interfere with isolation of independent effects in multivariate analyses. Despite

this, and the large number of exposure variables in this data set, it remains possible that some other causal variable not included is confounding the observed associations.

Although we have found evidence associating only three foods with coronary disease events, this in no way denies the possibility that other foods not showing clear associations in our data set could still have causal effects. Statistical power depends heavily on the range of intake of foods and the accuracy with which the consumption information for that food is gathered. Both of these can vary substantially in different populations, with different questionnaire designs, and for different foods.

There is little previous research on the effect of nut consumption on cardiovascular risk factors or heart disease events. Our dietary data did not distinguish between different kinds of nuts. However, the dietary substudy of 147 randomly selected local subjects from the same population showed that 32% of the nuts consumed were peanuts, 29% were almonds, 16% were walnuts, and 23% were other nuts. Thus, it seems probable that the effect of interest is at least represented in some or all of peanuts, almonds, and walnuts, and perhaps also other nuts. Peanuts are botanically classified as legumes, rather than nuts, but the nutrient content of all nuts share many similarities and are quite unique among natural foods.

Nuts commonly eaten in California have a high polyunsaturated/saturated fat ratio (eg, peanuts, 2.3; almonds, 2.2; hazelnuts, 1.30; and English walnuts, 7.1). They also have a very high percentage of total fat as monounsaturated fat (eg, peanuts, 49%; almonds, 65%; hazelnuts, 78%; and English walnuts, 23%), whereas the percentage of fat as saturated fat is relatively low (eg, peanuts, 14%; almonds, 10%; hazelnuts, 7%; and English walnuts, 9%).[49] The fiber content is high, ranging from 5.2% to 14.3% by weight.[50]

We can only speculate on the possible mechanisms of a protective effect of nuts in humans, but the unique fat and fiber content described above suggests several possibilities. It is of interest that the 24-hour recall data (five recalls per subject) from the dietary substudy indicated that subjects who consumed nuts at least three times each week obtained 4.5% of their saturated fatty acids, 13.9% of oleic acid, and 11.7% of linoleic acid from the nuts. Walnuts (and to a lesser extent other nuts) are an important source of linolenic acid, the main nonmarine omega-3 fatty acid in the diet.[49] These same subjects obtained 19.3% of this fatty acid from the nuts. The effect of dietary fiber and polyunsaturated and monounsaturated fats on serum lipid levels is well known.[1-3]

Nuts have 73% to 90% of calories as fat. This raises some concern that frequent consumption of these foods may produce obesity. However, consumption of fat also stimulates satiety, and obesity generally has stronger associations with physical inactivity[51] than consumption of individual foods. In our data set, we found a statistically significant *negative* association between consumption of nuts and the Quetelet index of obesity, showing that the higher nut consumers in this population were less obese.

If nuts contain one or more active substances that are protective for CHD, this is a finding of great interest, but contrary to expectations based on well-known animal work with peanut oil. It is commonly held that peanut oil is unusually atherogenic in rabbits, rats, and monkeys. However, as pointed out by Alderson et al,[52] this needs closer scrutiny. The majority of such studies have used diets containing a high concentration of dietary cholesterol.[53-56] Other studies using peanut oil with diets low in cholesterol or free of cholesterol have shown less consistent findings.[57-59] One recent study of cynomolgus monkeys[52] fed several concentrations of peanut oil included evidence of significant negative associations between concentration of this oil and serum cholesterol level and aortic and coronary atherosclerosis.

The effects of a whole food may possibly be different than those of one extracted part. Several examples can be cited.[60-62] Nuts are more than nut oils, and it has been shown, for instance, that peanut meal is hypocholesterolemic in rabbits.[63] It is of interest that other work also suggests a cholesterol-lowering effect of raw almonds and/or almond oil in both animals[64,65] and humans.[66,67] Additional studies of the possible effects of nut consumption on CHD risk factors would provide useful information regarding mechanisms of action and improve the strength of causal inference.

The finding that consumption of whole grain as compared with white bread is associated with decreased risk of CHD (especially myocardial infarction) does not have an immediate or obvious explanation. However, others have also found associations between grains[68] or cereal fibers[20] and risk of CHD. While a role for the antioxidant vitamin E in the prevention of coronary heart disease has long been controversial, there has been recent epidemiological and basic science evidence suggesting this may be worth further investigation.[69,70] Thus, it is of interest that whole wheat bread (containing the wheat germ), and also many nuts, have a high content of this vitamin.[71] Wheat fiber is largely insoluble and does not lower serum cholesterol level.[72,73] However, a feeding study showed that a combination of whole grains did significantly lower levels of low-density lipoprotein and total cholesterol as compared with a supplement of sucrose with equal energy content.[74] The small fat content of wheat is found in the germ and hence is not retained in white bread. Fat represents only 5.4% of energy in whole wheat, but it has a polyunsaturated-saturated ratio of 3.0.[75,76] As usual, the possibility that whole wheat bread consumption is a marker for some other protective factor not measured in this study must be considered.

In conclusion, an epidemiologic investigation of 26 473 subjects found evidence of a substantial protective effect of higher consumption of nuts on fatal and nonfatal CHD events. This effect was consistent among several population subgroups and was also consistent among different clinical expressions of coronary artery disease. It was independent of traditional coronary risk factors and other foods that were available for analysis. A reduction in incidence of nonfatal myocardial infarction was also demonstrated for those who consumed only whole wheat bread. The results for nuts and whole wheat bread were seen in both stratified and proportional hazards multivariate analyses. No obvious source of confounding to provide alternative explanations for those associations could be identified in our data.

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