Plant-based foods and prevention of cardiovascular disease: an overview1–4

Frank B Hu

ABSTRACT Evidence from prospective cohort studies indicates that a high consumption of plant-based foods such as fruit and vegetables, nuts, and whole grains is associated with a significantly lower risk of coronary artery disease and stroke. The protective effects of these foods are probably mediated through multiple beneficial nutrients contained in these foods, including mono- and polyunsaturated fatty acids, n−3 fatty acids, antioxidant vitamins, minerals, phytochemicals, fiber, and plant protein. In dietary practice, healthy plant-based diets do not necessarily have to be low in fat. Instead, these diets should include unsaturated fats as the predominant form of dietary fat (eg, fats from natural liquid vegetable oils and nuts), whole grains as the main form of carbohydrate, an abundance of fruit and vegetables, and adequate n−3 fatty acids. Such diets, which also have many other health benefits, deserve more emphasis in dietary recommendations to prevent chronic diseases. Am J Clin Nutr 2003;78(suppl):544S–51S.

KEY WORDS Fruit, vegetables, whole grains, nuts, fat, carbohydrate, glycemic index, n−3 fatty acids, dietary patterns, cardiovascular disease, coronary artery disease

INTRODUCTION

Plant-based foods such as fruit and vegetables, nuts, natural vegetable oils, and whole grains are important components of traditional diets in Mediterranean and Asian regions (1). Such diets have been associated with low rates of cardiovascular disease (CVD) and mortality in these regions. In recent years, growing interest in preventing CVD using plant-based foods has generated numerous epidemiologic and clinical studies (2). Such studies are important in extending our understanding of diet-CVD relations beyond what we already know about individual nutrients. Additionally, practical dietary advice based on health effects of specific foods or food groups is much easier for the public to understand and implement than arbitrary numerical criteria for macronutrients (eg, 30% of energy from total fat). Here we summarize epidemiologic studies on plant-based foods and dietary patterns in relation to risk of CVD.

FRUIT AND VEGETABLES

Because many nutrients in fruit and vegetables, such as dietary fiber, folate, potassium, flavonoids, and antioxidant vitamins, have been associated with reduced risk for CVD, it is widely believed that higher consumption of fruit and vegetables is protective against CVD. A number of prospective cohort studies have examined this relation, and most found protective effects for total fruit and vegetables (Figure 1) (3–10). In a study of 5133 Finnish men and women, Knekt et al (3) found an inverse association between intake of both vegetables and risk of coronary artery disease (CAD). When the highest and lowest tertiles of vegetable intake were compared, the multivariate relative risks (RRs) for CAD death were 0.66 (95% CI: 0.46, 0.96) for men and 0.66 (95% CI: 0.35, 1.23) for women. The RRs comparing the highest and lowest tertiles of fruit intake were 0.77 (95% CI: 0.52, 1.12) for men and 0.66 (95% CI: 0.36, 1.22) for women. A subsequent analysis (11) found significant inverse associations between flavonoid intake and major food sources of flavonoids (eg, apple, berries, onions) and CAD death. In the Framingham Heart Study (4), a significant inverse association was observed between total vegetable and fruit consumption as assessed by a single 24-h recall instrument and incidence of ischemic stroke among 832 men [multivariate RR of stroke for each increment of 3 servings per day of fruit and vegetables was 0.75 (95% CI: 0.57, 1.00)]. In the Physicians’ Health Study (9), Liu et al found an inverse association between vegetables rich in carotenoids (eg, broccoli, carrots, spinach, lettuce, yellow squash, tomatoes) and risk of CAD. The multivariate RR comparing men who consumed ≥2.5 servings/d of these vegetables with those consuming <1 serving/d was 0.77 (95% CI: 0.60, 0.98; P for trend = 0.03). A weaker inverse association was observed (8) between intakes of fruit and vegetables and risk of CVD in the Women’s Health Study (RR comparing extreme quintiles: 0.85; 95% CI: 0.61, 1.17). However, the association was strengthened by excluding women with history of diabetes, high cholesterol, or hypertension at baseline (who may have changed their diets after these conditions were diagnosed); the multivariate RR comparing extreme quintiles was 0.45 (95% CI: 0.22, 0.91).

The largest study so far was performed by Joshipura et al (7), who conducted pooled analyses of the Nurses’ Health Study and the Health Professionals’ Follow-up Study, including 2190 incident cases of CAD and 570 cases of ischemic stroke (6). The

1 From the Department of Nutrition, Harvard School of Public Health, Boston.
2 Presented at the Fourth International Congress on Vegetarian Nutrition, held in Loma Linda, CA, April 8–11, 2002.
3 Supported by research grants HL34594, HL60712, and HL35464 from the National Institutes of Health. FBH was partly supported by an Established Investigator Award from the American Heart Association.
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multivariate RRs comparing extreme quintiles of fruit and vegetable intake were 0.80 (95% CI: 0.69, 0.92) for CAD and 0.69 (95% CI: 0.52, 0.91) for ischemic stroke. The inverse association between fruit and vegetables and CAD appears to be graded in a dose-response fashion, and intake of at least 8 servings/d is associated with the lowest risk. For stroke, the risk reduction plateaus at levels of ≥4 servings/d. Among individual items, green leafy vegetables contributed most to the protective effects for CAD, whereas cruciferous vegetables, citrus fruit and juices, and vitamin C–rich fruit and vegetables contributed most to the protective effects for stroke (Table 1). Thus, while research efforts should continue to investigate the biological effects of individual fruit and vegetables, from a public health point of view, an increase in consumption of all types of fruit and vegetables should be encouraged. However, there was a suggestion of increased risk of both CAD and stroke with higher consumption of potatoes and French fries, probably because of their ability to induce high glycemic and insulimemic responses (12). Another potential explanation for this positive association is that higher consumption of potatoes and French fries represents a Western dietary pattern, which has been associated with an increased risk of CAD (discussed below).

No clinical trials have been conducted to examine the effects of increased consumption of fruit and vegetables on CVD endpoints. However, the Lyon Diet Heart Study (13) showed that a Mediterranean diet rich in fruit and vegetables and α-linolenic acid substantially reduced the recurrence of myocardial infarction (MI) and mortality compared with a regular low-fat diet. The beneficial effects of increased fruit and vegetables on blood pressure have been demonstrated in several clinical trials (14, 15). Because fruit and vegetables contain a myriad of nutrients and compounds that may be beneficial for CVD, it is virtually impossible to pinpoint the exact nutrients or substances that are responsible for these protective effects. Several clinical trials have definitely ruled out any beneficial effects of supplementation with high doses of β-carotene on CVD (16–19). This raises the question of whether the antioxidants coming from supplements—in high doses and not part of a balanced mix of antioxidants—function in the same way as those derived from diet.

### NUTS

A decade of epidemiologic investigation (Figure 1) and clinical studies has transformed the image of nuts from a fattening snack food to a wholesome and heart-healthy food (20–25). The first epidemiologic study on frequent nut consumption and risk of CAD was based on the Adventist Health Study with 6 y of follow-up (20). After adjustments were made for age, sex, smoking, exercise, relative weight, and high blood pressure, the RRs of nonfatal MI across categories of nut consumption (<1/wk, 1–4/wk, ≥5/wk) were 1.0, 0.74, and 0.52 (95% CI: 0.30, 0.87). The corresponding RRs for definite fatal CAD were 1.0, 0.73, and 0.62

### TABLE 1

Multivariate relative risks (RRs) of coronary artery disease (CAD) based on a comparison of the highest and the lowest quintiles of fruit and vegetable intakes in the pooled analyses of the Nurses’ Health Study and the Health Professionals’ Follow-up Study.

<table>
<thead>
<tr>
<th>Food</th>
<th>RR (95% CIs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All fruit</td>
<td>0.80 (0.69, 0.92)</td>
</tr>
<tr>
<td>All vegetables</td>
<td>0.82 (0.71, 0.94)</td>
</tr>
<tr>
<td>Total citrus fruit</td>
<td>0.88 (0.77, 1.00)</td>
</tr>
<tr>
<td>Citrus fruit juices</td>
<td>1.06 (0.85, 1.32)</td>
</tr>
<tr>
<td>Cruciferous vegetables</td>
<td>0.86 (0.75, 0.99)</td>
</tr>
<tr>
<td>Green leafy vegetables</td>
<td>0.72 (0.63, 0.83)</td>
</tr>
<tr>
<td>Vitamin C–rich fruit and vegetables</td>
<td>0.91 (0.79, 1.04)</td>
</tr>
<tr>
<td>Legumes</td>
<td>1.06 (0.91, 1.24)</td>
</tr>
<tr>
<td>Potatoes (including French fries)</td>
<td>1.15 (0.78, 1.70)</td>
</tr>
</tbody>
</table>

1 Adapted from references 6 and 7. The RRs were adjusted for standard cardiovascular disease risk factors.
but lose a substantial amount of dietary fiber, vitamins, minerals, and the germ. The resulting refined-grain products contain more starch and other nutrients. Thus, it has been proposed that the antiatherogenic effect of nuts might be related in part to the arginine-NO pathway (29). In addition, higher consumption of whole grains was associated with a lower risk of type 2 diabetes in women (27).

Nuts are high in fat, but most of the fat is monounsaturated and polyunsaturated (Table 2). Numerous metabolic studies have found that a diet high in nuts (peanuts, walnuts, or almonds) significantly lowers LDL cholesterol and decreases the ratio of total to HDL cholesterol (28). Besides the favorable effects on blood lipids, nuts may protect against CAD through other mechanisms. Most nuts are rich in arginine, which is the precursor of endothelium-derived relaxing factor, nitric oxide (NO). NO is a potent vasodilator that can inhibit platelet adhesion and aggregation. Thus, it has been proposed that the antiatherogenic effect of nuts might be related in part to the arginine-NO pathway (29). In addition, walnuts are high in α-linolenic acid (7%). Higher intake of α-linolenic acid has been associated with reduced risk of CAD in several prospective studies (30), possibly because of its antithrombotic and antiarrhythmic effects. Other postulated explanations for a benefit of nuts include their high content of magnesium, copper, folic acid, potassium, fiber, and vitamin E.

### TABLE 2

<table>
<thead>
<tr>
<th>Total fat</th>
<th>Saturated fat</th>
<th>Monounsaturated fat</th>
<th>Polyunsaturated fat</th>
<th>Ratio of unsaturated to saturated fat</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>g</td>
<td>g</td>
<td>g</td>
<td></td>
</tr>
<tr>
<td>Almonds</td>
<td>14.5</td>
<td>1.5</td>
<td>10</td>
<td>8.7</td>
</tr>
<tr>
<td>Brazil nuts</td>
<td>19</td>
<td>5.0</td>
<td>7.0</td>
<td>2.8</td>
</tr>
<tr>
<td>Cashews</td>
<td>13</td>
<td>2.5</td>
<td>8.0</td>
<td>4.2</td>
</tr>
<tr>
<td>Hazelnuts</td>
<td>18</td>
<td>1.0</td>
<td>15.0</td>
<td>8.4</td>
</tr>
<tr>
<td>Macadamia</td>
<td>20</td>
<td>2.5</td>
<td>16.5</td>
<td>7.0</td>
</tr>
<tr>
<td>Peanuts</td>
<td>13.5</td>
<td>2.0</td>
<td>7.0</td>
<td>5.8</td>
</tr>
<tr>
<td>Pecans</td>
<td>19</td>
<td>2.0</td>
<td>12</td>
<td>5.0</td>
</tr>
<tr>
<td>Pistachios</td>
<td>14</td>
<td>2.0</td>
<td>8.0</td>
<td>7.0</td>
</tr>
<tr>
<td>Walnuts</td>
<td>18</td>
<td>2.0</td>
<td>5.0</td>
<td>8.0</td>
</tr>
<tr>
<td>Average</td>
<td>16.6</td>
<td>2.3</td>
<td>9.8</td>
<td>4.4</td>
</tr>
</tbody>
</table>

1. Adapted from reference 26. All values are for dried or dry roasted nuts.

WHOLE GRAINS

Grains are staple foods in most societies. In traditional diets, grains were typically consumed either in whole intact form or as coarse flours produced from stone grinding. Grinding or milling using modern technology produces fine flours with very small particle size. Milling also removes the outer bran layer and much of the germ. The resulting refined-grain products contain more starch but lose a substantial amount of dietary fiber, vitamins, minerals, essential fatty acids, and phytochemicals. Because of loss of the bran and pulverization of the endosperm, refined grains are digested and absorbed more rapidly than whole-grain products and tend to cause more rapid and larger increases in concentrations of blood glucose and insulin. Thus, whole-grain products such as whole-wheat breads, brown rice, oats, and barley usually have lower glycemic index (GI) values than refined grains do (12). Whole grains are also rich in fiber, antioxidant vitamins, magnesium, and phytochemicals.

Several studies have found an inverse association between whole-grain consumption and risk of CVD (Figure 1) (20, 31–33). In the Iowa Women’s Health Study (31), after adjustment for CVD risk factors, the RRs were 1.0, 0.96, 0.71, 0.64, and 0.70 in ascending quintiles of whole-grain intake (P for trend = 0.02). The lower risk associated with higher whole-grain intake was independent of intake of fiber or several other constituents of whole grains. The Nurses’ Health Study observed a 25% lower risk of CAD among women who ate nearly 3 servings of whole grains a day compared with those who ate less than a serving per week (32). In addition, higher consumption of whole grains was associated with a lower risk of ischemic stroke (33), independent of known CVD risk factors (multivariate RR comparing the highest with the lowest quintile of intake: 0.69; 95% CI: 0.50, 0.98). The inverse association with CVD remained even after adjustment for intakes of folate, fiber, and vitamin E, suggesting that the protective effects of whole grains are not entirely mediated through these nutrients.

In the United States, cereal grains are generally highly processed before they are used; only 2% of the 150 pounds of wheat flour consumed per capita in 1997 was whole-wheat flour, and the average American gets less than 1 serving of whole grains a day (34). Thus, there is great potential to reduce risk of CVD through increased consumption of whole-grain products.

### DIETARY PATTERNS

In contrast to the traditional analytic approach used in nutritional epidemiology, which focuses on individual nutrients or foods, dietary pattern analysis considers overall diet. This approach more closely approximates the real world, where people eat meals consisting of a variety of foods instead of isolated nutrients. Thus, it can take into account complicated interactions among nutrients and nonnutrient substances in studies of free-living people.
Although numerous studies have examined the relation between intake of individual nutrients or foods and risk of CAD, few data are available on the effects of overall dietary patterns (35). Recently, we examined the associations between major eating patterns derived from factor analysis and risk of CAD in 2 large ongoing cohort studies, the Nurses’ Health Study (36) and the Health Professionals’ Follow-up Study (37). In both studies, we identified 2 major dietary patterns—prudent and Western—and calculated factor scores of each pattern for individuals in the cohorts. The prudent pattern was characterized by higher intakes of fruit, vegetables, legumes, fish, poultry, and whole grains, while the Western pattern was characterized by higher intakes of red and processed meats, sweets and desserts, French fries, and refined grains (Figure 2). In the Nurses’ Health Study (36), after coronary risk factors were adjusted for, the prudent diet score was associated with an RR of 0.76 (95% CI: 0.60, 0.98; \(P\) for trend = 0.03) comparing the highest with the lowest quintile. Extreme-quintile comparison yielded an RR of 1.46 (95% CI: 1.07, 1.99; \(P\) for trend = 0.02) for the Western pattern.

We found similar associations in the Health Professionals’ Follow-up Study (37). After adjustment for age, smoking, body mass index, and other coronary risk factors, the RRs 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 RRs 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 MI.

In a separate study, we examined the relation between the major eating patterns and biochemical markers of CAD and obesity (38). We observed significant positive correlations between the Western pattern score and tissue-type plasminogen activator antigen (0.19, \(P<0.01\)), fasting insulin (0.32, \(P<0.01\)), C-peptide (0.31, \(P<0.01\)), leptin (0.28, \(P<0.0001\)), C-reactive protein (0.22, \(P<0.0001\)), and homocysteine (0.23, \(P<0.01\)) after adjustment for various potential confounders. In addition, a significant inverse correlation was observed between plasma folate (−0.39, \(P<0.0001\)) and the
that replacement of 5% of energy from saturated fat by unsaturated fat would reduce risk of CAD by 42% (95% CI: 23, 56; \( P < 0.001 \)) and replacement of 2% of energy from \textit{trans} fat by nonhydrogenated unsaturated fat would reduce risk by 53% (95% CI: 34, 67; \( P < 0.001 \)). These findings suggest that replacing saturated and \textit{trans} fat with nonhydrogenated mono- and polysaturated fats is more effective than reducing overall fat intake in preventing CAD.

The strong inverse association between polysaturated fat and CAD observed in the Nurses’ Health Study cohort is consistent with previous findings. In prospective cohort studies among men, a strong inverse association for polysaturated fat was found in the Western Electric Study (43), and borderline significant associations were found in both the Ireland-Boston Diet Heart Study (44) and the usual care group of the Multiple Risk Factor Intervention Trial (45). Numerous metabolic studies have shown strong cholesterol-lowering effects for vegetable oils rich in linoleic acid when substituted for animal fat (46). Also, dietary intervention trials using high-polyunsaturated-fat diets have been more effective than those using low-fat–high-carbohydrate diets in lowering both total serum cholesterol and risk of CAD (30).

Compared with most Western populations, in Mediterranean countries where olive oil (a major source of oleic acid) is the primary source of fat, CAD mortality rate is very low, suggesting potential beneficial effects of monounsaturated fat on CAD. Prospective cohort studies on the association between intake of monounsaturated fat and CAD risk are sparse. Two studies found an increased risk of CAD with higher intake of monounsaturated fat in younger but not older participants (47, 48). However, neither study adjusted for intake of other types of fat. A Finnish study found an inverse association for monounsaturated fat after adjustment for intake of other types of fat (49). Because monounsaturated fat in the US diet comes mainly from beef, dairy fats, and partially hydrogenated vegetable oils, intake of monounsaturated fat is strongly correlated with saturated and \textit{trans} fats. Thus, the association for monounsaturated fat intake not adjusted for saturated and \textit{trans} fats is likely to be seriously confounded. In the Nurses’ Health Study (42), after other fats were adjusted for, monounsaturated fat intake was inversely associated with risk of CAD, although the association was weaker than that for polyunsaturated fat. In metabolic studies, replacing carbohydrates with monounsaturated fat raised HDL without affecting LDL (50); this replacement also improved glucose tolerance and insulin sensitivity among patients with diabetes mellitus (51). In addition, monounsaturated fat is resistant to oxidative modification (52).

The major nonanimal sources of monounsaturated fat include olive and canola oils, nuts, and avocados. Both canola oil and nuts are also important sources of polyunsaturated fat. In dietary practice, natural liquid vegetable oils can be used to replace animal fat, stick margarine, and hydrogenated vegetable shortenings for frying, cooking, and baking. Another advantage of liquid vegetable oils is that they generally contain higher amounts of vitamin E, whereas animal fats contain few antioxidants. Some vegetable oils (such as canola and soybean oils) contain high amounts of \( \alpha \)-linolenic acid, an essential \( n-3 \) fatty acid important in the prevention of CVD. In a previous analysis of the Nurses’ Health Study (53), we found that higher consumption of oil-and-vinegar salad dressings (a major source of \( \alpha \)-linolenic acid in the US diet) was strongly associated with a lower risk of CAD. Women who consumed oil-and-vinegar salad dressing frequently (\( \geq 5-6 \) times/wk) had \( \approx 50\% \) lower fatal CAD risk than those who rarely consumed this type of salad dressing, even after adjustment for CVD risk factors and intake of vegetables (Figure 3). Full-fat salad dressing
products are typically made with soybean oil, which contains \( \approx 7\% \) \( \alpha \)-linolenic acid if it is not hydrogenated. Thus, eating vegetable salads dressed with natural vegetable oils is a nutritious and palatable way to reduce risk of CAD. Unfortunately, many salad dressings nowadays are low-fat or fat-free as a result of the food industry’s enthusiastic response to the low-fat campaign. This not only reduces n-6 and n-3 essential fatty acids in the diets but can adversely affect the taste of the salads (which would not be helpful in increasing vegetable intake).

**PLANT-BASED DIETS AND OBESITY**

Concern exists that higher consumption of high-fat foods such as nuts and vegetable oils would result in weight gain because of their high energy density. However, in both the Adventist Health Study (20) and the Nurses’ Health Study (22), persons who consumed more nuts tended to weigh less, indicating that in practice, the energy contained in nuts can readily be balanced by reductions in other sources of energy or increased physical activity.

Although the conventional wisdom holds that a low-fat diet would reduce body weight, long-term clinical trials have provided no convincing evidence that reducing dietary fat can lead to substantial weight loss (54). Such absence of evidence, combined with the dramatic increase in prevalence of obesity in the United States despite a decrease in percentage of energy from fat, leads us to believe that too much emphasis on reducing dietary fat as an effort to prevent obesity and CVD may have been counterproductive.

Increasing attention has been paid to the role of carbohydrates in the development of obesity (55). Emerging evidence from experimental studies suggests that a high-GI diet may play a role in obesity (56, 57). In animal studies (58), high-GI diets induced an increase in fat synthesis over isocaloric low-GI diets, even when the total body weight remained constant. Consumption of low-GI foods and liquids was directly associated with a reduction in subsequent hunger, increased satiety, or both in most of the short-term feeding studies in humans (lasting for a single meal or a single day) (57). Thus, voluntary energy intake increased after consumption of high-GI meals as compared with consumption of low-GI meals (57). These observations suggest that in the long term, high-GI diets may promote excess energy consumption and thus contribute to weight gain and obesity (56). On the other hand, a diet moderately high in protein and lower in refined carbohydrate may improve blood lipids (59, 60), facilitate weight loss (61), and lower the risk of CAD (62). Thus, high-GI starch and sugar can be partially replaced by plant protein from nuts and legumes or animal protein from fish or poultry. In such a diet, dietary protein can provide \( \approx 20–25\% \) of total energy intake.

**CONCLUSIONS**

The past decade has seen an expansion of epidemiologic and clinical research on the role of plant-based foods and eating patterns in the prevention of CVD. This research has revolutionized our thinking about heart-healthy foods and the biological mechanisms linking dietary factors and CVD. Some foods once deemed to be unhealthy simply because of their fat content (eg, nuts) have become important parts of diets designed to lower blood pressure (14) and serum cholesterol (63), to control weight (64), and to achieve secondary prevention of CAD (13), besides adding flavor, variety, and texture to dishes. On the other hand, higher consumption of some foods that form the basis of the US Department of Agriculture Food Guide Pyramid, such as white bread and refined cereals, may have long-term adverse effects on insulin resistance and CAD because they contain mostly rapidly digestible starch (55). Plant-based diets and vegetarian diets are not necessarily healthy unless the right types of carbohydrates and fats are the predominant sources of energy. In addition, animal products such as fish, poultry, and low-fat dairy can be included as part of plant-based diets unless a strict vegetarian diet is followed.

In conclusion, substantial evidence indicates that plant-based diets including whole grains as the main form of carbohydrate, unsaturated fats as the predominate form of dietary fat, an abundance of fruit and vegetables, and adequate n-3 fatty acids can play an important role in preventing CVD. Such diets—which have other health benefits, including the prevention of other chronic diseases—deserve more emphasis in dietary recommendations.

The author had no conflict of interest.

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