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Healthful and unhealthful plant-based diets and the risk of coronary heart disease in US adults

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Abstract

Background—Plant-based diets are recommended for coronary heart disease (CHD) prevention. However, not all plant foods are necessarily beneficial for health.

Objectives—To examine associations between plant-based diet indices and CHD incidence.

Methods—We included 73,710 women in Nurses' Health Study (NHS) (1984–2012), 92,329 women in NHS2 (1991–2013), and 43,259 men in Health Professionals Follow-up Study (1986–2012), free of chronic diseases at baseline. We created an overall plant-based diet index (PDI) from repeated semi quantitative food-frequency questionnaire data, by assigning positive scores to plant foods and reverse scores to animal foods. We also created a healthful PDI (hPDI) where healthy plant foods (whole grains, fruits/vegetables, nuts/legumes, oils, tea/coffee) received positive scores, while less-healthy plant foods (juices/sweetened beverages, refined grains, potatoes/fries, sweets) and animal foods received reverse scores. To create an unhealthful PDI (uPDI), we gave positive scores to less-healthy plant foods and reverse scores to animal and healthy plant foods.

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Results—Over 4,833,042 person-years of follow-up, we documented 8,631 incident CHD cases. In pooled multivariable analysis, higher adherence to PDI was independently inversely associated with CHD (HR comparing extreme deciles: 0.92, 95% CI: 0.83–1.01; p trend=0.003). This inverse association was stronger for hDPI (HR: 0.75, 95% CI: 0.68–0.83; p trend<0.001). Conversely, uPDI was positively associated with CHD (HR: 1.32, 95% CI: 1.20–1.46; p trend<0.001).

Conclusions—Higher intake of a plant-based diet index rich in healthier plant foods is associated with substantially lower CHD risk, while a plant-based diet index that emphasizes less-healthy plant foods is associated with higher CHD risk.

Keywords

Diet; nutrition; dietary pattern; coronary heart disease; prospective cohort study; epidemiology

Introduction

Plant-based diets have been associated with a lower risk of various diseases,(1–3) including coronary heart disease (CHD),(4–9) the leading global cause of death.(10) However, these studies suffer from key limitations. With the exception of a recent investigation,(3) prior studies(4–9) have defined plant-based diets as 'vegetarian' diets, which constitute a family of dietary patterns that exclude some or all animal foods. As recommendations based on incremental dietary changes are easier to adopt, it is important to understand how gradual reductions in animal food intake with concomitant increases in consumption of plant foods affect cardiovascular health. Additionally, in studies of vegetarian diets all plant foods are treated equally, even though certain plant foods, such as refined grains and sugar-sweetened beverages (SSBs) are associated with higher cardio-metabolic risk.(11–13)

To overcome these limitations, we have created three versions of plant-based diet indices using a graded approach – an overall plant-based diet index (PDI) which emphasizes consumption of all plant food while reducing animal food intake; a healthful plant-based diet index (hPDI) which emphasizes intake of healthy plant foods associated with improved health outcomes such as whole grains, fruits, and vegetables; and an unhealthful plant-based diet index (uPDI) which emphasizes consumption of less healthy plant foods known to be associated with a higher risk of several diseases.(14) In three US cohorts, we previously documented that the PDI was inversely associated with type 2 diabetes risk with a stronger inverse association for hPDI, and a positive association for uPDI(14). In the present study, we examined the associations of these plant-based diet indices with CHD incidence in more than 200,000 male and female health professionals in the US.

Methods

Study population

The Nurses' Health Study (NHS) started in 1976 with 121,701 female registered nurses (aged 30–55 years), the NHS2 started in 1989 with 116,686 female registered nurses (aged 25–42 years), and the Health Professionals Follow-Up Study (HPFS) started in 1986 with 51,529 male health professionals (aged 40–75 years). Participants receive a follow-up questionnaire every two years on lifestyle, health behaviors, and medical history, with a response rate of ~90% at each cycle. Participants with CHD at baseline were excluded. Participants with cancer (except nonmelanoma skin cancer), stroke, and coronary artery surgery at baseline were also excluded, as diagnosis with these conditions can change diet. Lastly, individuals with implausible energy intake at baseline (<600 or >3500 kcal/day for women and <800 or >4200 kcal/day for men) were excluded. The final baseline sample included 73,710 women in NHS, 92,320 women in NHS2, and 43,259 men in HPFS (1984 for NHS, 1991 for NHS2, and 1986 for HPFS).

Study protocols for all cohorts were approved by the institutional review boards of Brigham and Women's Hospital and the Harvard T.H. Chan School of Public Health; completion of the self-administered questionnaire was considered to imply informed consent.

Dietary assessment and the plant-based diet indices

Dietary data were collected using a semi-quantitative food frequency questionnaire every 2–4 years. Participants were asked how often, on average, they consumed a defined portion of ~130 food items over the previous year. There were 9 response categories ranging from "never or less than once/month" to "≥6 times/day". The reliability and validity of the questionnaires have been described previously.(15–18)

Using this dietary data, we created three versions of a plant-based diet for each food frequency questionnaire cycle for each cohort: an overall plant-based diet index (PDI), a healthful plant-based diet index (hPDI), and an unhealthful plant-based diet index (uPDI).(14) We created 18 food groups based on nutrient and culinary similarities within the larger categories of healthy plant foods, less healthy plant foods, and animal foods (Table 1). Given that alcoholic beverages have different directions of association for various health outcomes, and margarine's fatty acid composition has changed over time from high trans to high unsaturated fats, we did not include these foods in the indices, but adjusted for them in the analysis. Food groups were ranked into quintiles, and given positive or reverse scores. With positive scores, participants above the highest quintile of a food group received a score of 5, following on through to participants below the lowest quintile who received a score of 1. With reverse scores, this pattern of scoring was inversed. For creating PDI, plant food groups were given positive scores, while animal food groups were given reverse scores. For creating hPDI, positive scores were given to healthy plant food groups, and reverse scores to less healthy plant food groups and animal food groups. Finally, for uPDI, positive scores were given to less healthy plant food groups, and reverse scores to healthy plant food groups and animal food groups. The 18 food group scores were summed to obtain the indices. Higher intake of all indices reflected lower animal food intake (e.g. 5–6 vs. 3 servings/day comparing extreme PDI deciles).

Outcome ascertainment

CHD was defined as non-fatal myocardial infarction and fatal CHD. Participants self-reporting newly diagnosed CHD on the biennial questionnaires were asked permission to access their medical records to confirm diagnosis, which was done through blinded review by study physicians. To confirm diagnosis of nonfatal MI, we used the World Health Organization criteria(19) of the presence of typical symptoms plus either elevated enzymes or diagnostic electrocardiographic findings. Cases that required hospital admission and were confirmed by interview or letter but for which medical records were unobtainable were included in the analysis as "probable".

Reports from next of kin or postal authorities were used to identify deaths, in addition to searching the National Death Index. Classification of CHD as the cause of death was done by examining autopsy reports, hospital records, or death certificates, using International Classification of Diseases, ninth revision(20) codes 410–412. CHD deaths were considered confirmed if fatal CHD was established through medical records or autopsy reports, or if CHD was listed as the cause of death on the death certificate with prior medical record of CHD. If CHD was listed as the cause of death on the death certificate, but medical records were unavailable and no prior knowledge of CHD existed, the CHD death was included in the analysis as "probable".

Assessment of covariates

We obtained updated information on participants' smoking status, multivitamin use, CHD family history, and physical activity through self-report on the biennial questionnaires. Among women, information was assessed on menopausal status, post-menopausal hormone use, and oral contraceptive use (NHS2 only). Self-reported data on height were collected at baseline, with updated information on weight assessed every two years through the questionnaires. We also collected updated information on self-reported diagnosis of diseases such as hypertension, hypercholesterolemia, and diabetes, and on medication use.

Statistical analysis

We used Cox proportional-hazards regression to estimate hazard ratios and 95% confidence intervals evaluating, separately, the associations of deciles of each index with CHD. Person-time was calculated from questionnaire return date till CHD diagnosis, death, or end of follow-up (30th June 2012 in NHS, 30th June 2013 in NHS2, and 1st January 2012 in HPFS). We used age (in years) as the time scale, with stratification by calendar time (in 2-year intervals). We adjusted for time-varying covariates including smoking status, alcohol intake, physical activity, CHD family history, multivitamin use, aspirin use, energy intake, margarine intake, body mass index (BMI), postmenopausal status and hormone use (women), and oral contraceptive use (NHS2). We additionally adjusted for baseline self-reported hypertension, hypercholesterolemia, and diabetes.

Indices were cumulatively averaged over follow-up to better capture long-term diet; for instance, for the 2001–2003 risk set, plant-based diet index scores in 1991, 1995, and 1999 were averaged to predict CHD risk Because diagnosis of conditions such as type 2 diabetes, stroke, and cancer could change an individual's diet and potentially be associated with the underlying risk of CHD, we stopped updating diet upon diagnosis of these conditions. Values of other covariates were updated every 2 years to account for changes over time. A continuous variable for each index was created by assigning the median value to each decile and conducting tests for linear trend. To examine potential deviation from linearity, we fit restricted cubic splines to the fully adjusted model with the indices entered as continuous variables. The proportional hazards assumption was tested by including interaction terms between the indices, and age and calendar year. We examined potential effect modification by gender, BMI, physical activity, family history of CHD, and smoking status. We also evaluated the independent associations of the three food categories which constituted the diet indices (healthy plant foods, less healthy plant foods, animal foods) with CHD risk by entering all three simultaneously into the model in place of the diet indices. We also created a healthy omnivorous diet, by assigning positive scores to healthy plant foods and healthy animal foods [dairy products (except ice cream), egg, fish], and reverse scores to less healthy plant foods and less healthy animal foods [animal fat, ice cream, meat, miscellaneous animal-based foods]. The analysis was carried out separately for each cohort, and combined using a fixed effects model; heterogeneity was examined using the Cochrane Q statistic(21) and the I^2 statistic.(22) All analyses were performed using SAS software (version 9.2; SAS Institute Inc.), and statistical significance was set at a 2-tailed p value<0.05.

Results

At baseline, the indices ranged from a median of 42–44 in the lowest decile, to 66–68 in the highest decile (Online Table 1). Participants with higher scores on PDI and hPDI were older, more active, leaner, and less likely to smoke than participants with lower scores. Conversely, high consumers of uPDI were younger, less active, and more likely to smoke then low consumers. The proportion of participants with a history of diabetes decreased with increasing deciles of PDI and uPDI, but increased with higher hPDI intake. Animal food intake ranged from 5–6 servings/day in the highest decile to 3–4 servings/day in the lowest decile of the indices.

Over 4,833,042 person-years of follow-up, 8,631 participants developed CHD (3,233 cases over 1,876,942 person-years in NHS; 667 cases over 1,999,945 person-years in NHS2; and 4731 cases over 956,155 person-years in HPFS). In the fully adjusted model, PDI was modestly inversely associated with CHD incidence (HR comparing extreme deciles: 0.92, 95% CI: 0.83–1.01; HR per 10-unit increase: 0.93, 95% CI: 0.90–0.97; p trend=0.003) (Table 2). When we analyzed hPDI (Table 3) and uPDI (Table 4) separately, we found a stronger inverse association between hPDI and CHD incidence (HR comparing extreme deciles: 0.75, 95% CI: 0.68–0.83; HR per 10-unit increase: 0.88, 95% CI: 0.85–0.91; p trend<0.001) and a positive association for uPDI (HR comparing extreme deciles: 1.32, 95% CI: 1.20–1.46; HR per 10-unit increase: 1.10, 95% CI: 1.06–1.14; p trend<0.001). The association of uPDI with CHD was non-linear (p for test of curvature=0.01; p for non-linear association<0.001) (Central Illustration panel A and Online Figure 1). We found no evidence of deviation from linearity for PDI and hPDI (p for test of curvature>0.20 for both; p for linearity=0.001 for PDI, and <0.001 for hPDI). Further adjustment for ethnicity, marital status, recent physical exam, diet beverage intake, and indicators of socioeconomic status did not appreciably alter the results [pooled HR for extreme deciles of (PDI, 0.93; 95% CI, 0.84–1.03; p trend=0.01) (hPDI, 0.76; 95% CI, 0.69–0.84; p trend<0.001) (uPDI, 1.30; 95% CI, 1.18–1.44; p trend<0.001)].

The associations of hPDI and uPDI with risk of CHD were consistently observed across strata defined by age, BMI, family history of CHD, and sex (Figure 1). Associations of both indices were significantly stronger among more active relative to less active participants (p interaction=0.002 for both); the association of uPDI with CHD was slightly stronger among ever smokers compared with never smokers (p interaction=0.04). There was no evidence of significant effect modification by calendar year in any of the cohorts for hPDI or uPDI (all p values for interaction>0.20).

When, in place of the indices, we entered variables for the three food categories together into the fully adjusted model, we found an inverse association for healthy plant foods, and positive associations for animal foods and less healthy plant foods (Central Illustration panel B and Online Table 2). To quantify the benefit of hPDI that was due to lower intake of red meat or SSBs, we individually adjusted for these foods in the final model. The results were largely unchanged upon red meat adjustment: [pooled HR for extreme deciles of (PDI, 0.93; 95% CI, 0.84–1.03; p trend=0.01) (hPDI, 0.76; 95% CI, 0.68, 0.84; p trend<0.001) (uPDI, 1.32; 95% CI, 1.19, 1.46; p trend<0.001)], and changed in expected directions with SSB adjustment [pooled HR for extreme deciles of (PDI, 0.90; 95% CI, 0.81–0.99; p trend=0.001) (hPDI, 0.79; 95% CI, 0.71, 0.88; p trend<0.001) (uPDI, 1.22; 95% CI, 1.10, 1.36; p trend=0.005)]. Given the previously observed inverse association between fish intake and CHD,(23) we modified hPDI to score fish intake positively, and found similar results (pooled HR for extreme deciles, 0.74; 95% CI, 0.67–0.81; p trend<0.001). The results were slightly attenuated when we modified hPDI to score healthy animal foods positively (dairy except ice cream, egg, and fish) (HR comparing extreme deciles: 0.78, 95% CI: 0.71–0.86; HR per 10-unit increase: 0.91, 95% CI: 0.89–0.94; p trend<0.001).

Sensitivity analyses

The associations of PDI, hPDI and uPDI with risk of CHD did not vary based on how we modeled diet. For example, we found similar results when we continuously updated the indices throughout follow-up, used baseline values of the indices, used the most recent index scores before CHD diagnosis, and stopped updating the indices once intermediate conditions such as hypertension and hypercholesterolemia developed (Online Table 3). When we created the plant-based diet indices with quintiles of energy-adjusted food groups (instead of with quintiles of unadjusted food groups as we had originally done), the association of PDI with CHD became slightly stronger, but that of uPDI with CHD was slightly attenuated (Online Table 4). Removing potential intermediates (BMI and aspirin use) from the model strengthened the association of PDI with CHD [pooled HR for extreme deciles of (PDI, 0.86; 95% CI, 0.78–0.95; p trend<0.001) (hPDI, 0.73; 95% CI, 0.66–0.81; p trend<0.001) (uPDI, 1.27; 95% CI, 1.15, 1.40; p trend<0.001)]. Adjustment for additional potential intermediates in the causal pathway, (updated history of hypertension, hypercholesterolemia, and diabetes instead of baseline history) slightly attenuated associations of hPDI and uPDI with CHD [pooled HR for extreme deciles of (PDI, 0.92; 95% CI, 0.83–1.02; p trend=0.003) (hPDI, 0.80; 95% CI, 0.73–0.89; p trend<0.001) (uPDI, 1.24; 95% CI, 1.12, 1.37; p trend=0.001); proportion of the association with hPDI explained by these intermediates ranged from 9.5% in NHS to 4.9% in HPFS, with all p values<0.01]. Finally, the results did not change when we excluded participants who had diabetes at baseline [pooled HR for extreme deciles of (PDI, 0.93; 95% CI, 0.84–1.03; p trend=0.002) (hPDI, 0.74; 95% CI, 0.66–0.82; p trend<0.001) (uPDI, 1.35; 95% CI, 1.21, 1.50; p trend<0.001)], or when we pooled results across the cohorts using a random-effects model [pooled HR for extreme deciles of (PDI, 0.92; 95% CI, 0.83–1.01; p trend=0.01) (hPDI, 0.71; 95% CI, 0.57–0.88; p trend<0.001) (uPDI, 1.40; 95% CI, 1.13, 1.73; p trend<0.001)].

Discussion

In three ongoing prospective cohort studies, higher adherence to an overall plant-based diet index (PDI) was modestly associated with lower CHD incidence [HR comparing extreme deciles: 0.92 (0.83–1.01)]. This inverse association was considerably stronger for adherence to a healthier version (hPDI) [0.75 (0.68–0.83)], but positive for adherence to a less healthy version (uPDI) [1.32 (1.20–1.46)] of a plant-based diet index. These associations remained robust to adjustment for multiple confounders and were consistently observed in various subgroups.

In a previous analysis,(14) we found similar associations of these three indices with type 2 diabetes. Our current analysis extends the potentially protective association with hPDI to CHD. The mechanisms through which hPDI could reduce CHD risk are likely shared with the mechanisms for type 2 diabetes risk reduction.(2, 24–32) Specifically, greater adherence to hPDI would lead to diets high in dietary fiber, antioxidants, unsaturated fat, and micronutrient content, and low in saturated fat and heme iron content (Online Table 1), all of which could aid in weight loss/maintenance, enhance glycemic control and insulin regulation, improve lipid profile, reduce blood pressure, improve vascular health, decrease inflammation, and foster more favorable diet- gut microbiome interactions (e.g. through lowered levels of trimethylamine N-oxide), thereby lowering CHD risk. Greater adherence to uPDI, on the other hand, leads to diets with higher glycemic load and index, and added sugar, and lower levels of dietary fiber, unsaturated fats, micronutrients, and antioxidants, which could result in higher CHD risk through the above-mentioned pathways. This is also illustrated in the fact that the associations of hPDI and uPDI with CHD incidence were slightly attenuated upon adjustment for some of these pathways, specifically hypercholesterolemia, hypertension, and diabetes.

Prospective cohort studies examining the association of plant-based diets with CHD have focused on CHD mortality. Most of these studies have been carried out in Europe, with only three studies in the US (Adventist Health Studies(7)). A pooled analysis of five of the above cohorts found a 24% lower risk of CHD mortality (95% CI: 6%–38%) comparing vegetarians with non-vegetarians.(5) A recent meta-analysis found similar results with vegetarians experiencing a 29% lower risk of CHD mortality (95% CI: 13%–43%) relative to non-vegetarians.(6) The EPIC-Oxford study, one of the few studies to examine the association of a vegetarian diet with CHD incidence in addition to mortality, found a 32% lower 11-year CHD incidence (95% CI: 19%–42%) among vegetarians relative to non-vegetarians.(8)

The above studies have defined plant-based diets dichotomously as being vegetarian or not. Our study adds to the evidence base by examining the association of gradations of adherence to an overall plant-based diet index with CHD incidence. For instance, those in the lowest decile of PDI consumed 5–6 servings of animal foods per day, while those in the highest decile consumed 3 servings of animal foods per day. This approach has the advantage of being easily translatable, as we found that even a slightly lower intake of animal foods combined with higher intake of healthy plant foods is associated with lower CHD risk. One other studies adopted this approach with respect to cardiovascular disease mortality and found similar results.(3) However, these studies have examined plant-based diets at a single time point, making it difficult to fully capture the association of a time-varying exposure such as diet on the development of CHD which has a long etiologic period. Our study adds to the existing literature by demonstrating the associations of long-term cumulative intake of a plant-based diet index with more than 20-year CHD incidence.

We also found that a healthier version of a plant-based diet index, which emphasizes plant foods known to be associated with improved health outcomes, is associated with substantially lower CHD risk. Contrarily, when intake of less healthy plant foods is emphasized, the opposite association was observed. When we examined associations of the three food categories with CHD risk, less healthy plant foods and animal foods were both associated with increased risk, with a potentially stronger association for less healthy plant foods. This highlights the wide variation in nutritional quality of plant foods, making it crucial to consider the quality of plant foods consumed in plant-rich diets.

When we examined a diet which emphasized both healthy plant and healthy animal foods, the association with CHD was only slightly attenuated relative to that with hPDI. Thus, the moderate reductions in animal foods suggested here can be largely achieved by lowering intake of less healthy animal foods such as red and processed meats. The results of this study are in line with the recently released 2015 Dietary Guidelines for Americans,(33) which recommends higher consumption of high quality plant foods. Dietary recommendations based on the hPDI would also be environmentally sustainable, as plant-based food systems use fewer resources than food systems that are heavily reliant on animal foods.(34)

Potential study limitations

This is one of the largest prospective investigations of plant-based diet indices and incident CHD in the world, with periodic data on diet, lifestyle, and medical history collected over more than two decades. However, measurement error in diet assessment is likely, although evaluating cumulatively averaged intake reduces random errors(17) while allowing for the examination of long-term dietary intake. Given the observational nature of the study, residual and unmeasured confounding are possible; thus, we should interpret modest effect sizes such as those we observed for PDI with caution. However, the results were largely unchanged when we adjusted for additional covariates, including markers of socio-economic status. Additionally, randomized controlled trial evidence showing the protective effect of plant-based diets on intermediate outcomes, including weight change, lipid profile, glycemic control, and blood pressure lends further support to our findings.(35–38)

Conclusions

We found a modest inverse association of higher adherence to an overall plant-based diet index with CHD incidence in three prospective cohort studies in the US. While this inverse association was stronger for a plant-based diet index that emphasized healthy plant foods, CHD risk was significantly elevated for a plant-based diet index that emphasized less healthy plant foods.

Dietary guidelines and lifestyle interventions could recommend increasing intake of healthy plant foods, while reducing intake of less healthy plant foods and certain animal foods for improved cardio-metabolic health.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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ABBREVIATIONS & ACRONYMS

BMI	Body Mass Index
CHD	Coronary Heart Disease
CI	Confidence Interval
hPDI	Healthful Plant-based Diet Index
HPFS	Health Professionals Follow-up Study
HR	Hazard Ratio
NHS	Nurses' Health Study
PDI	Overall Plant-based Diet Index
SSB	Sugar-Sweetened Beverages
uPDI	Unhealthful Plant-based Diet Index

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Condensed abstract

Plant-based diets are recommended for coronary heart disease (CHD) prevention, but not all plant foods have health benefits. We examined prospective associations of graded plant-based diet indices [overall (PDI), healthful (hPDI), and unhealthful (uPDI)] with CHD in 209,298 participants. Higher adherence to PDI was inversely associated with CHD [HR comparing extreme deciles: 0.92 (0.83–1.01)], with a stronger inverse association for hDPI [0.75 (0.68–0.83)], but a positive association for uPDI [1.32 (1.20–1.46)]. Patients should be encouraged to increase healthy plant food intake (e.g. whole grains, fruits, vegetables), while reducing intake of animal foods and less-healthy plant foods (e.g. refined grains, sweets).

PERSPECTIVES

Competency in patient care

Medical and health professionals should guide patients to increase intake of healthy plant foods such as whole grains, fruits, vegetables, and nuts, and reduce intake of animal foods and less healthy plant foods such as sugar-sweetened beverages for CHD prevention.

Translational outlook

Future research should replicate these findings in other racial/ethnic, occupational, and socio-economic groups, and explore biological mechanisms involved in the potentially cardio-protective effects of healthful plant-based diet indices to identify personalized clinical interventions and therapies for CHD prevention.

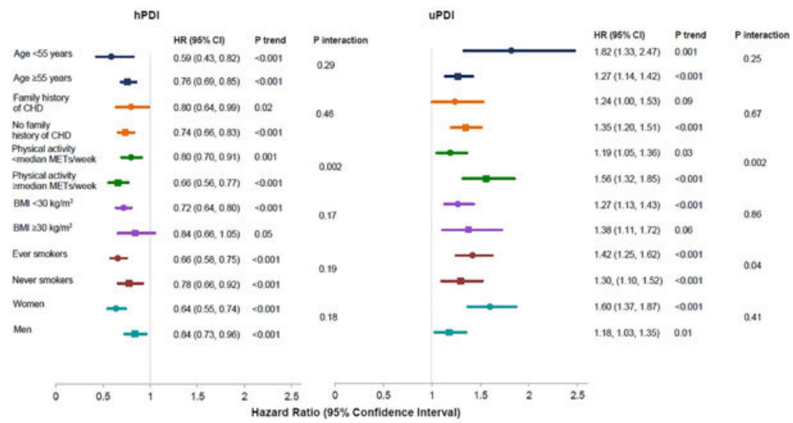
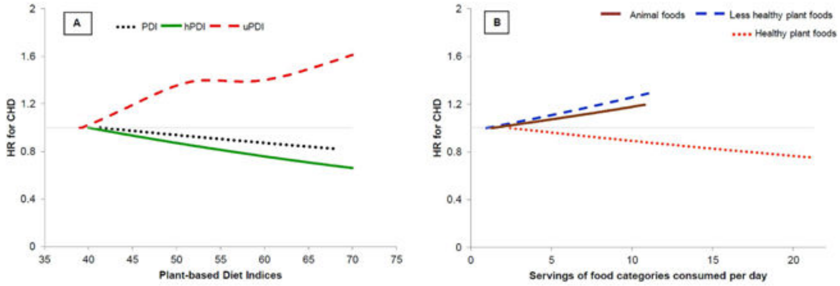


Figure 1. Pooled HRs (95% CI) for CHD comparing extreme deciles of the plant-based diet indices, stratified by selected characteristics

The HRs and P values for men and women were obtained after combining all three cohorts. All other HRs and P values were obtained by pooling estimates from the three cohorts using a fixed-effects model.

Adjusted for age, smoking status, physical activity, alcohol intake, multivitamin use, aspirin use, family history of CHD, margarine intake, energy intake, baseline hypertension, hypercholesterolemia, and diabetes, and updated body mass index. Also adjusted for postmenopausal hormone use in NHS & NHS2, and for oral contraceptive use in NHS2.

Abbreviations: BMI, Body Mass Index; CHD, Coronary Heart Disease; hPDI, Healthful Plant-based Diet Index; MET, Metabolic Equivalent Task; uPDI, Unhealthful Plant-based Diet Index



Central Illustration. Dose-response relationship of (A) the Plant-based Diet Indices and (B) animal, healthy plant, and less healthy plant foods with CHD incidence

Analysis carried out after combining all three cohorts Adjusted for age, smoking status, physical activity, alcohol intake, multivitamin use, aspirin use, family history of CHD, margarine intake, baseline hypertension, hypercholesterolemia, and diabetes, and updated body mass index. Also adjusted for postmenopausal hormone use in NHS & NHS2, and for oral contraceptive use in NHS2. Energy intake was additionally adjusted when analyzing the plant-based diet indices. The three plant-based diet indices were examined in separate models. The three food categories (healthy and less healthy plant foods, and animal foods) were simultaneously included in the same model.

For uPDI, p for test of curvature=0.01 and p for non-linear association<0.001. P for test of curvature for PDI=0.25, for hPDI=0.82, for animal foods=0.58, for healthy plant foods=0.99, and for less healthy plant foods=0.74; P for linearity=0.004 for animal foods, 0.001 for PDI, and <0.001 for hPDI, less healthy plant foods, and healthy plant foods.

Abbreviations: CHD, Coronary Heart Disease; hPDI, Healthful Plant-based Diet Index; PDI, Overall Plant-based Diet Index; uPDI, Unhealthful Plant-based Diet Index

Table 1

Examples of food items constituting the 18 food groups (from the 1984 NHS FFQ)

		PDI	*hPDI*	*uPDI*
Plant Food Groups				
Healthy				
Whole grains	Whole grain breakfast cereal, other cooked breakfast cereal, cooked oatmeal, dark bread, brown rice, other grains, bran, wheat germ, popcorn	Positive scores	Positive scores	Reverse scores
Fruits	Raisins or grapes, prunes, bananas, cantaloupe, watermelon, fresh apples or pears, oranges, grapefruit, strawberries, blueberries, peaches or apricots or plums	Positive scores	Positive scores	Reverse scores
Vegetables	Tomatoes, tomato juice, tomato sauce, broccoli, cabbage, cauliflower, Brussels sprouts, carrots, mixed vegetables, yellow or winter squash, eggplant or zucchini, yams or sweet potatoes, spinach cooked, spinach raw, kale or mustard or chard greens, iceberg or head lettuce, romaine or leaf lettuce, celery, mushrooms, beets, alfalfa sprouts, garlic, corn	Positive scores	Positive scores	Reverse scores
Nuts	Nuts, peanut butter	Positive scores	Positive scores	Reverse scores
Legumes	String beans, tofu or soybeans, beans or lentils, peas or lima beans	Positive scores	Positive scores	Reverse scores
Vegetable oils	Oil-based salad dressing, vegetable oil used for cooking	Positive scores	Positive scores	Reverse scores
Tea & Coffee	Tea, coffee, decaffeinated coffee	Positive scores	Positive scores	Reverse scores
Less healthy				
Fruit juices	Apple cider (non-alcoholic) or juice, orange juice, grapefruit juice, other fruit juice	Positive scores	Reverse scores	Positive scores
Refined grains	Refined grain breakfast cereal, white bread, English muffins or bagels or rolls, muffins or biscuits, white rice, pancakes or waffles, crackers, pasta	Positive scores	Reverse scores	Positive scores
Potatoes	French fries, baked or mashed potatoes, potato or corn chips	Positive scores	Reverse scores	Positive scores
Sugar sweetened beverages	Colas with caffeine & sugar, colas without caffeine but with sugar, other carbonated beverages with sugar, non-carbonated fruit drinks with sugar	Positive scores	Reverse scores	Positive scores
Sweets and Desserts	Chocolates, candy bars, candy without chocolate, cookies (home-baked & ready-made), brownies, doughnuts, cake (home-baked & ready-made), sweet roll (home-baked & ready-made), pie (home-baked & ready-made), jams or jellies or preserves or syrup or honey	Positive scores	Reverse scores	Positive scores
Animal Food Groups				
Animal fat	Butter added to food, butter or lard used for cooking	Reverse scores	Reverse scores	Reverse scores
Dairy	Skim low fat milk, whole milk, cream, sour cream, sherbet, ice cream, yogurt, cottage or ricotta cheese, cream cheese, other cheese	Reverse scores	Reverse scores	Reverse scores
Egg	Eggs	Reverse scores	Reverse scores	Reverse scores
Fish or Seafood	Canned tuna, dark meat fish, other fish, shrimp or lobster or scallops	Reverse scores	Reverse scores	Reverse scores
Meat	Chicken or turkey with skin, chicken or turkey without skin, bacon, hot dogs, processed meats, liver, hamburger, beef or pork or lamb mixed dish, beef or pork or lamb main dish	Reverse scores	Reverse scores	Reverse scores
Misc. animal-based foods	Pizza, chowder or cream soup, mayonnaise or other creamy salad dressing	Reverse scores	Reverse scores	Reverse scores

Abbreviations: hPDI, Healthful Plant-based Diet Index; PDI, Overall Plant-based Diet Index; uPDI, Unhealthful Plant-based Diet Index

Table 2

Hazard Ratios (95% CI) for Coronary Heart Disease according to deciles of the Overall Plant-based Diet Index

	Decile 1	Decile 2	Decile 3	Decile 4	Decile 5	Decile 6	Decile 7	Decile 8	Decile 9	Decile 10	HR (95% CI) per 10 units	*P* Trend*
Nurses' Health Study												
Median	45.3	48.7	50.7	52.2	53.7	55.0	56.5	58.0	60.0	63.5		
Cases/PY	354/187576	345/182392	342/188258	295/175859	352/200856	272/183715	337/192344	298/184899	326/190404	312/190640		
Age-adjusted	1.00	0.96 (0.83, 1.11)	0.92 (0.80, 1.07)	0.83 (0.71, 0.97)	0.86 (0.75, 1.00)	0.71 (0.61, 0.84)	0.82 (0.70, 0.95)	0.74 (0.64, 0.87)	0.78 (0.67, 0.90)	0.70 (0.60, 0.82)	0.81 (0.76, 0.87)	<0.001
Multivariable adjusted	1.00	1.02 (0.88, 1.18)	1.04 (0.90, 1.21)	0.97 (0.83, 1.13)	1.01 (0.87, 1.18)	0.88 (0.75, 1.03)	0.97 (0.83, 1.13)	0.92 (0.79, 1.09)	0.95 (0.81, 1.12)	0.87 (0.74, 1.03)	0.92 (0.85, 0.98)	0.04
Nurses' Health Study 2												
Median	45.0	48.5	50.7	52.3	53.8	55.0	56.8	58.5	60.7	64.0		
Cases/PY	91/195183	75/194826	75/204890	73/197879	63/187964	67/202075	56/215822	51/201307	60/200824	56/199175		
Age-adjusted	1.00	0.84 (0.62, 1.15)	0.77 (0.57, 1.05)	0.78 (0.58, 1.07)	0.67 (0.48, 0.92)	0.69 (0.51, 0.95)	0.54 (0.39, 0.76)	0.51 (0.36, 0.71)	0.59 (0.43, 0.82)	0.54 (0.39, 0.75)	0.69 (0.60, 0.79)	<0.001
Multivariable adjusted	1.00	0.95 (0.70, 1.29)	0.91 (0.67, 1.24)	0.95 (0.69, 1.29)	0.80 (0.58, 1.12)	0.89 (0.64, 1.23)	0.71 (0.50, 1.01)	0.66 (0.46, 0.95)	0.80 (0.56, 1.13)	0.77 (0.54, 1.11)	0.81 (0.70, 0.95)	0.02
Health Professionals Follow-Up Study												
Median	45.0	48.0	50.4	52.0	54.0	55.3	57.0	58.5	60.8	64.2		
Cases/PY	492/86581	441/87892	409/88955	471/97460	434/86993	449/94437	369/80989	435/89147	397/92546	463/92145		
Age-adjusted	1.00	0.90 (0.79, 1.02)	0.80 0.70, 0.91)	0.83 (0.73, 0.94)	0.86 (0.75, 0.97)	0.81 (0.71, 0.92)	0.73 (0.64, 0.84)	0.79 (0.69, 0.90)	0.69 (0.60, 0.79)	0.79 (0.70, 0.90)	0.88 (0.84, 0.92)	<0.001
Multivariable adjusted	1.00	0.97 (0.85, 1.10)	0.88 (0.77, 1.01)	0.91 (0.80, 1.04)	0.98 (0.86, 1.12)	0.92 (0.81, 1.05)	0.85 (0.74, 0.98)	0.91 (0.80, 1.04)	0.82 (0.71, 0.94)	0.95 (0.83, 1.09)	0.96 (0.90, 1.01)	0.10
Pooled results (fixed effects model)												
Age-adjusted	1.00	0.92 (0.84, 1.01)	0.85 (0.78, 0.94)	0.83 (0.76, 0.91)	0.85 (0.78, 0.93)	0.77 (0.70, 0.84)	0.76 (0.69, 0.84)	0.75 (0.68, 0.82)	0.71 (0.65, 0.78)	0.75†‡ (0.68, 0.82)	0.84†∥ (0.81, 0.87)	<0.001†∥
Multivariable adjusted	1.00	0.99 (0.91, 1.09)	0.96 (0.87, 1.05)	0.94 (0.86, 1.04)	0.99 (0.90, 1.08)	0.91 (0.83, 1.00)	0.90 (0.82, 0.99)	0.90 (0.82, 0.99)	0.87 (0.79, 0.96)	0.92 (0.83, 1.01)	0.93 (0.90, 0.97)	0.003

Multivariable adjusted model: Adjusted for age (years), smoking status (never, past, current [1–14, 15–24, or ≥25 cigarettes/day]), physical activity (<3, 3–8.9, 9–17.9, 18–26.9, or ≥27 metabolic equivalent task hours/week), alcohol intake (0, 0.1–4.9, 5–9.9, 10–14.9, or ≥15 g/day), multivitamin use (yes/no), aspirin use (yes/no), family history of CHD (yes/no), margarine intake (quintiles), energy intake (quintiles), baseline hypertension, hypercholesterolemia, and diabetes (yes/no), and updated body mass index (<21, 21–22.9, 23–24.9, 25–26.9, 27–29.9, 30–32.9, 33–34.9, 35–39.9, or ≥40 kg/m2). Also adjusted for postmenopausal hormone use in NHS & NHS2 (premenopausal, postmenopausal current, past or never user), and for oral contraceptive use in NHS2 (never, past, or current user).

* P value when we assigned the median value to each decile and entered this as a continuous variable in the model

†P value for Q-statistic for heterogeneity <0.05, indicating statistically significant heterogeneity in HRs among the three studies

‡I^2 statistic=60–69%;

§I^2 statistic=70–79%;

‖I^2 statistic=80–89%

Table 3

Hazard Ratios (95% CI) for Coronary Heart Disease according to deciles of the Healthful Plant-based Diet Index

	Decile 1	Decile 2	Decile 3	Decile 4	Decile 5	Decile 6	Decile 7	Decile 8	Decile 9	Decile 10	HR (95% CI) per 10 units	*P* trend*
Nurses' Health Study												
Median	44.3	48.0	50.5	52.4	54.0	55.8	57.5	59.3	61.7	65.5		
Cases/PY	359/18835 2	323/186140	327/190716	327/187664	313/183877	322/191819	306/188145	330/187373	322/184367	304/188490		
Age-adjusted	1.00	0.85 (0.73, 0.99)	0.80 (0.69, 0.93)	0.78 (0.67, 0.91)	0.74 (0.64, 0.86)	0.71 (0.61, 0.83)	0.66 (0.57, 0.77)	0.70 (0.60, 0.81)	0.66 (0.57, 0.77)	0.57 (0.49, 0.67)	0.80 (0.75, 0.84)	<0.001
Multivariable adjusted	1.00	0.91 (0.78, 1.06)	0.90 (0.77, 1.05)	0.88 (0.75, 1.02)	0.87 (0.74, 1.01)	0.83 (0.71, 0.97)	0.76 (0.65, 0.90)	0.83 (0.71, 0.98)	0.78 (0.67, 0.92)	0.68 (0.57, 0.80)	0.86 (0.81, 0.91)	<0.001
Nurses' Health Study 2												
Median	44.0	48.0	50.5	52.3	54.0	55.8	57.3	59.2	61.6	65.6		
Cases/PY	79/203121	72/192054	78/220042	61/187944	76/207405	70/201138	60/196640	65/199695	62/192381	44/199524		
Age-adjusted	1.00	0.90 (0.66, 1.24)	0.87 (0.64, 1.19)	0.74 (0.53, 1.03)	0.84 (0.61, 1.15)	0.76 (0.55, 1.05)	0.67 (0.47, 0.93)	0.67 (0.48, 0.93)	0.65 (0.47, 0.91)	0.42 (0.29, 0.61)	0.72 (0.64, 0.81)	<0.001
Multivariable adjusted	1.00	0.98 (0.71, 1.35)	0.97 (0.71, 1.34)	0.85 (0.60, 1.19)	0.98 (0.71, 1.35)	0.87 (0.62, 1.21)	0.78 (0.55, 1.11)	0.80 (0.57, 1.13)	0.77 (0.54, 1.09)	0.53 (0.36, 0.79)	0.79 (0.69, 0.90)	0.001
Health Professionals Follow-Up Study												
Median	43.0	47.2	50.0	52.0	53.8	55.5	57.2	59.2	62.0	66.0		
Cases/PY	413/88274	452/89330	404/92920	486/93019	425/88417	448/89543	425/89922	431/85604	424/91479	452/88635		
Age-adjusted	1.00	0.96 (0.84, 1.10)	0.84 (0.73, 0.96)	0.95 (0.83, 1.08)	0.84 (0.74, 0.97)	0.86 (0.75, 0.98)	0.79 (0.69, 0.90)	0.82 (0.72, 0.94)	0.74 (0.65, 0.85)	0.77 (0.67, 0.88)	0.88 (0.84, 0.92)	<0.001
Multivariable adjusted	1.00	0.99 (0.87, 1.14)	0.87 (0.76, 1.00)	0.99 (0.86, 1.13)	0.89 (0.78, 1.03)	0.91 (0.79, 1.04)	0.84 (0.73, 0.97)	0.89 (0.77, 1.02)	0.80 (0.70, 0.93)	0.84 (0.73, 0.97)	0.90 (0.86, 0.95)	<0.001
Pooled results (fixed effects model)												
Age-adjusted	1.00	0.90 (0.82, 0.99)	0.82 (0.74, 0.90)	0.86 (0.78, 0.94)	0.79 (0.72, 0.87)	0.78 (0.71, 0.85)	0.72 (0.66, 0.79)	0.75 (0.68, 0.82)	0.70 (0.63, 0.76)	0.66†// (0.60, 0.73)	0.84†// (0.81, 0.86)	<0.001†//
Multivariable adjusted	1.00	0.95 (0.86, 1.04)	0.88 (0.80, 0.97)	0.92 (0.84, 1.01)	0.88 (0.80, 0.97)	0.86 (0.78, 0.95)	0.80 (0.73, 0.88)	0.85 (0.77, 0.94)	0.79 (0.71, 0.87)	0.75 (0.68, 0.83)	0.88 (0.85, 0.91)	<0.001

Multivariable adjusted model: Adjusted for age (years), smoking status (never, past, current [1–14, 15–24, or ≥25 cigarettes/day]), physical activity (<3, 3–8.9, 9–17.9, 18–26.9, or ≥27 metabolic equivalent task hours/week), alcohol intake (0, 0.1–4.9, 5–9.9, 10–14.9, or ≥15 g/day), multivitamin use (yes/no), aspirin use (yes/no), family history of CHD (yes/no), margarine intake (quintiles), energy intake (quintiles), baseline hypertension, hypercholesterolemia, and diabetes (yes/no), and updated body mass index (<21, 21–22.9, 23–24.9, 25–26.9, 27–29.9, 30–32.9, 33–34.9, 35–39.9, or ≥40 kg/m2). Also adjusted for postmenopausal hormone use in NHS & NHS2 (premenopausal, postmenopausal current, past or never user), and for oral contraceptive use in NHS2 (never, past, or current user).

* P value when we assigned the median value to each decile and entered this as a continuous variable in the model

[†] P value for Q-statistic for heterogeneity <0.05, indicating statistically significant heterogeneity in HRs among the three studies

[‡] I^2 statistic=60–69%;

[§] I^2 statistic=70–79%;

[‖] I^2 statistic=80–89%

Table 4

Hazard Ratios (95% CI) for Coronary Heart Disease according to deciles of the Unhealthful Plant-based Diet Index

	Decile 1	Decile 2	Decile 3	Decile 4	Decile 5	Decile 6	Decile 7	Decile 8	Decile 9	Decile 10	HR (95% CI) per 10 units	*P* trend*
Nurses' Health Study												
Median	43.5	47.6	50.0	52.0	53.7	55.5	57.3	59.3	62.0	66.0		
Cases/PY	274/187546	311/195345	359/177785	267/183572	343/191298	334/191430	341/191659	322/187773	325/186951	357/183583		
Age-adjusted	1.00	1.12 (0.95, 1.32)	1.41 (1.20, 1.65)	1.03 (0.87, 1.22)	1.28 (1.10, 1.51)	1.26 (1.07, 1.47)	1.32 (1.13, 1.55)	1.26 (1.08, 1.49)	1.30 (1.11, 1.53)	1.49 (1.27, 1.74)	1.14 (1.08, 1.20)	<0.001
Multivariable adjusted	1.00	1.20 (1.02, 1.41)	1.52 (1.30, 1.78)	1.13 (0.96, 1.34)	1.41 (1.20, 1.66)	1.36 (1.16, 1.61)	1.43 (1.21, 1.68)	1.34 (1.13, 1.58)	1.34 (1.13, 1.58)	1.49 (1.26, 1.76)	1.13 (1.06, 1.19)	<0.001
Nurses' Health Study 2												
Median	43.5	47.5	50.0	52.0	54.0	56.0	58.0	60.0	62.5	66.5		
Cases/PY	52/205047	77/197734	65/198432	71/214560	58/196690	71/205961	61/192014	80/194172	60/204436	72/190899		
Age-adjusted	1.00	1.57 (1.10, 2.23)	1.35 (0.93, 1.94)	1.49 (1.04, 2.13)	1.26 (0.87, 1.83)	1.52 (1.06, 2.17)	1.40 (0.97, 2.03)	1.85 (1.30, 2.62)	1.40 (0.96, 2.03)	1.81 (1.26, 2.58)	1.19 (1.06, 1.32)	0.01
Multivariable adjusted	1.00	1.67 (1.17, 2.38)	1.45 (1.01, 2.10)	1.56 (1.09, 2.25)	1.29 (0.88, 1.89)	1.59 (1.10, 2.30)	1.46 (0.99, 2.14)	1.91 (1.32, 2.75)	1.37 (0.93, 2.03)	1.77 (1.21, 2.59)	1.16 (1.03, 1.31)	0.04
Health Professionals Follow-Up Study												
Median	44.0	48.0	50.0	52.0	54.0	55.6	57.3	59.0	61.5	65.2		
Cases/PY	456/90508	454/90758	415/86415	409/89136	461/92660	449/89599	447/94149	416/87472	410/87604	443/88847		
Age-adjusted	1.00	1.01 (0.89, 1.15)	1.02 (0.89, 1.16)	0.98 (0.86, 1.12)	1.10 (0.97, 1.26)	1.11 (0.97, 1.26)	1.07 (0.94, 1.22)	1.10 (0.96, 1.25)	1.11 (0.97, 1.27)	1.22 (1.07, 1.40)	1.09 (1.04, 1.14)	<0.001
Multivariable adjusted	1.00	1.04 (0.92, 1.19)	1.07 (0.94, 1.22)	1.05 (0.91, 1.20)	1.18 (1.04, 1.35)	1.15 (1.01, 1.32)	1.10 (0.96, 1.25)	1.14 (0.99, 1.31)	1.14 (0.99, 1.31)	1.21 (1.05, 1.39)	1.08 (1.03, 1.14)	0.003
Pooled results (fixed effects model)												
Age-adjusted	1.00	1.09 (0.99, 1.20)	1.17[†‖] (1.07, 1.29)	1.05 (0.95, 1.15)	1.17 (1.07, 1.29)	1.18 (1.08, 1.30)	1.20 (1.10, 1.32)	1.19[†§] (1.08, 1.31)	1.19 (1.08, 1.31)	1.35[†‡] (1.22, 1.48)	1.11 (1.08, 1.15)	<0.001
Multivariable adjusted	1.00	1.14[†‡] (1.04, 1.25)	1.24[†‖] (1.13, 1.37)	1.12 (1.01, 1.23)	1.26 (1.14, 1.39)	1.25 (1.13, 1.37)	1.25 (1.13, 1.38)	1.23[†§] (1.11, 1.36)	1.21 (1.09, 1.34)	1.32[†§] (1.20, 1.46)	1.10 (1.06, 1.14)	<0.001

Multivariable adjusted model: Adjusted for age (years), smoking status (never, past, current [1–14, 15–24, or ≥25 cigarettes/day]), physical activity (<3, 3–8.9, 9–17.9, 18–26.9, or ≥27 metabolic equivalent task hours/week), alcohol intake (0, 0.1–4.9, 5–9.9, 10–14.9, or ≥15 g/day), multivitamin use (yes/no), aspirin use (yes/no), family history of CHD (yes/no), margarine intake (quintiles), energy intake (quintiles), baseline hypertension, hypercholesterolemia, and diabetes (yes/no), and updated body mass index (<21, 21–22.9, 23–24.9, 25–26.9, 27–29.9, 30–32.9, 33–34.9, 35–39.9, or ≥40 kg/m2).

Also adjusted for postmenopausal hormone use in NHS & NHS2 (premenopausal, postmenopausal current, past or never user), and for oral contraceptive use in NHS2 (never, past, or current user).

[*] P value when we assigned the median value to each decile and entered this as a continuous variable in the model

[†] P value for Q-statistic for heterogeneity <0.05, indicating statistically significant heterogeneity in HRs among the three studies

[‡] I^2 statistic=60–69%;

[§] I^2 statistic=70–79%;

[//] I^2 statistic=80–89%