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Healthy Plant-Based Diets Are Associated with Lower Risk of All-Cause Mortality in US Adults

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Abstract

Background: Plant-based diets, often referred to as vegetarian diets, are associated with health benefits. However, the association with mortality is less clear.

Objective: We investigated associations between plant-based diet indexes and all-cause and cardiovascular disease mortality in a nationally representative sample of US adults.

Methods: Analyses were based on 11,879 participants (20–80 y of age) from NHANES III (1988–1994) linked to data on all-cause and cardiovascular disease mortality through 2011. We constructed an overall plant-based diet index (PDI), which assigns positive scores for plant foods and negative scores for animal foods, on the basis of a food-frequency questionnaire administered at baseline. We also constructed a healthful PDI (hPDI), in which only healthy plant foods received positive scores, and a less-healthful (unhealthy) PDI (uPDI), in which only less-healthful plant foods received positive scores. Cox proportional hazards models were used to estimate the association between plant–based diet consumption in 1988–1994 and subsequent mortality. We tested for effect modification by sex.

Results: In the overall sample, PDI and uPDI were not associated with all-cause or cardiovascular disease mortality after controlling for demographic characteristics, socioeconomic factors, and health behaviors. However, among those with an hPDI score above the median, a 10-unit increase in hPDI was associated with a 5% lower risk in all-cause mortality in the overall study population (HR: 0.95; 95% CI: 0.91, 0.98) and among women (HR: 0.94; 95% CI: 0.88, 0.99), but not among men (HR: 0.95; 95% CI: 0.90, 1.01). There was no effect modification by sex (P-interaction > 0.10).

Conclusions: A nonlinear association between hPDI and all-cause mortality was observed. Healthy plant-based diet scores above the median were associated with a lower risk of all-cause mortality in US adults. Future research exploring the impact of quality of plant-based diets on long-term health outcomes is necessary. *J Nutr* 2018;148:624–631.

Keywords: diet indexes, mortality, NHANES III, plant-based diets, sex

Introduction

Systematic reviews and meta-analyses have shown multiple health benefits of plant-based diets, including low risk of obesity, hypertension, type 2 diabetes, and ischemic heart disease (1–3). Plant-based diets emphasize a high intake of foods of plant origin and limit the intake of animal products such as red and processed meats, poultry, and fish (4–6). Plant-based diets are increasingly popular among young people (7) and are considered to be a more sustainable choice for the environment than are diets containing meat (8). As such, delineating the long-term health consequences of plant-based diets represents an important area of research (8).

Many cohort studies showed that the consumption of plant foods such as fruit, vegetables, whole grains, and nuts is associated with a lower risk of all-cause and cardiovascular disease mortality, whereas animal foods such as red and processed meat are associated with an elevated risk (9–12). A recent study on specific sources of protein showed that, within the context of an isocaloric diet, the substitution of 3% of energy from animal foods with plant protein was associated with a lower risk of all-cause and cardiovascular disease mortality (13). However, an important question remains whether an overall plant-based dietary pattern is associated with a lower risk of mortality.

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Abbreviations used: eGFR, estimated glomerular filtration rate; hPDI, healthy plant-based diet index; PDI, plant-based diet index; uPDI, less-healthy (unhealthy) plant-based diet index.

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Studies that examined the associations between diets high in plant foods and low in animal foods have shown mixed results concerning mortality risk. A longitudinal study of Seventh Day Adventists in the United States and Canada reported that following a vegetarian diet was associated with a 12% reduced risk of death compared with a nonvegetarian diet (5). In contrast, a study in the United Kingdom and Australia found no significant association between a vegetarian diet and all-cause, cerebrovascular, or ischemic heart disease mortality (14, 15).

Three key challenges remain in the study of plant-based diets and mortality, namely choice of study population, consideration of sex, and definitions of plant-based diets. Previous studies have specifically recruited vegetarians, vegans, health-conscious controls, Adventists, and Buddhist monks (5, 14, 16–19). These study populations have healthier lifestyles than the general population [e.g., the former populations abstain from alcohol and tobacco use (20, 21)]; thus, the results from these studies are not generalizable to the overall US population. It appears that there has been only one population-based study in vegetarians, the 45 and Up Study, which was conducted in Australia; however, the study excluded cause-specific deaths due to a short follow-up period of 6 y (15).

Only a few studies have reported sex-specific results and tested for effect modification by sex (5, 22). Given that men have a higher baseline risk of cardiovascular disease than do women, weaker associations between plant-based diets and mortality would be expected among men more than among women (23). However, a meta-analysis reported that the risk of ischemic heart disease was significantly reduced for vegetarians compared with nonvegetarians among both men and women, but that the reduced risk of cerebrovascular disease and all-cause mortality for vegetarians compared with nonvegetarians was significant only among men (22). The Adventist Health Study found effect modification by sex on cardiovascular disease mortality, and only men who were vegetarians had a lower risk of death from all causes and cardiovascular disease compared with nonvegetarians (5).

Definitions of plant-based diets need refinement, because previous studies have not been sufficiently nuanced. When individuals increase their consumption of plant foods, while decreasing their intake of animal foods (24), there may be increased consumption of less-healthy plant foods (e.g., sugar-sweetened beverages and refined grains) that are associated with a greater burden of chronic diseases (25–27). However, most previous studies defined plant-based diets as a dichotomous or ordinal variable (i.e., semivegetarians, lacto-ovo-vegetarians) by assessing the frequency of animal food consumption (15, 17, 28). None of the studies on vegetarians' diet considered the presence of less-healthy plant foods (5).

Thus, we used established plant-based diet indexes (29, 30), which provide different scores for animal foods, healthy plant foods, and less-healthy plant foods, to investigate the associations between plant-based diets, all-cause mortality, and cardiovascular disease mortality. Furthermore, the present study addresses the methodologic limitations discussed above with the use of a nationally representative sample of US adults (Third National Health and Nutrition Examination Survey (NHANES III), 1988–1994), and by examining effect modification by sex.

Methods

Study population. Analyses were conducted among adult participants from the NHANES III (1988–1994). This study used multistage, stratified, clustered probability sampling to provide a nationally representative estimate of noninstitutionalized civilians in the United States (31). Older adults, non-Hispanic blacks, and Mexican Americans were oversampled. Participants completed a household interview, provided biospecimens for laboratory measurements, and completed physical examinations. Details of the study design have been reported previously (31).

The present study included men and women (20–80 y of age; $n = 17{,}287$) with complete information on dietary intake based on an FFQ and vital status ($n = 17{,}264$). We excluded those individuals with a history of stroke, heart attack, or ischemic heart disease ($n = 1303$); cancer ($n = 498$); diabetes (self-reported diabetes, taking diabetes medication, or fasting glucose >126 mg/dL; $n = 3260$); or chronic kidney disease [estimated glomerular filtration rate (eGFR) <60 mL · min^{-1} · 1.73 m^{-2}; $n = 324$] at baseline, because dietary patterns may change after a diagnosis of a chronic disease. The analytic sample size was 11,879.

Dietary assessment. At baseline, participants completed an 81-item FFQ that assessed their usual intake of foods and beverages in the past month. Portion sizes were not assessed in this questionnaire. The NHANES III Nutrition Methodology Working Group, a group of experts from academic research institutions, government agencies, and industry, had reviewed the literature and determined that an FFQ should be used to rank participants by the intake of food groups and foods (31).

With the use of the approaches outlined in Satija et al. (29), we used frequency of consumption of each food item to create 3 indexes: an overall plant-based diet index (PDI), a healthy PDI (hPDI), and a less-healthy (unhealthy) PDI (uPDI). Briefly, each food item was categorized into 1 of 17 food groups, and food groups were classified as animal products, healthful plant foods (i.e., fruit, vegetables, whole grains), and less-healthful plant foods (i.e., sugar-sweetened beverages, sweets and desserts, potatoes, refined grains) (**Supplemental Table 1**). Healthful and less-healthful plant foods are differentiated by their reported associations with a number of chronic conditions (i.e., obesity, hypertension, type 2 diabetes, and cardiovascular disease) in the literature (29). We excluded vegetable oil as a food group because the questionnaire only assessed margarine intake, which may be high in *trans* fats (30). We controlled for margarine intake in our multivariable models.

Quintiles of consumption were calculated for each of the 17 food groups and were assigned a score from 1 to 5. For the PDI, in each plant food category, participants in the highest quintile of consumption received a score of 5, whereas those in the lowest quintile of consumption received a score of 1. Participants received a score of 1 for the highest quintile of consumption of animal products (reverse scores). For the hPDI, only the healthful plant foods received a score of 5 for the highest quintile of consumption, whereas less-healthy plant foods and animal foods received reverse scores. For the uPDI, only the less-healthy plant foods received positive scores, and healthy plant foods and animal foods received reverse scores (**Supplemental Figure 1**). All 3 indexes were divided into deciles for analysis.

Each 10-unit increase in PDI score represented more-frequent consumption of healthful plant foods and less-healthful plant foods. Each 10-unit increase in hPDI score represented more-frequent consumption of healthful plant foods and a less-frequent consumption of less-healthful plant foods. Each 10-unit increase in hPDI score represented a higher intake of healthful plant foods and a lower intake of less-healthful plant foods. Each 10-unit increase in uPDI score represented a less-frequent consumption of healthy plant foods and more frequent consumption of less-healthy plant foods. Each 10-unit increase in the score of all 3 indexes represented less-frequent consumption of animal foods.

In addition to the FFQ, participants completed in-person 24-h recalls by trained interviewers (31). We used information derived from participants' 24-h recalls, including total energy intake (covariate in regression models) and nutrients, to examine whether there were differences in nutritional factors according to deciles of PDIs.

Outcomes. We obtained data on all-cause and cardiovascular disease mortality from the NHANES III mortality files. The National Center for Health Statistics tracked survey participants' vital status and cause of death through 31 December 2011 with the use of probabilistic matching

and by matching their records with the National Death Index records, using several criteria including social security number, name, sex, and date of birth. Details of the linkage methods can be found elsewhere (32). In the present study, the follow-up period was calculated as the time from the NHANES examination (NHANES III, 1988–1994) until the date of death or censoring. Cardiovascular disease mortality was defined as codes I00–I69 by the *International Classification of Diseases, 10th Edition* (33).

Covariates. Participants self-reported 13 covariates: age (continuous), sex (male or female), race/ethnicity (non-Hispanic white, non-Hispanic black, Mexican American, or other), educational level (less than high school, high school, or more than high school), income (poverty-income ratio: <130%, 130–350%, or >350%), marital status (married; widowed, separated or divorced; or never married), smoking status (current, former, or never smoker), physical activity (continuous), alcohol consumption (quintiles), margarine intake (quintiles), total energy intake (continuous), baseline hypertension (systolic blood pressure ≥140 mm Hg, diastolic blood pressure ≥90 mm Hg, or antihypertensive medication use), and menopausal status (premenopausal or postmenopausal).

For physical activity, participants reported if they engaged in activities such as walking, running, jogging, bicycling, swimming, aerobics, dancing, gardening, or lifting weights, and estimated the frequency of each activity performed per week. Each activity was assigned a metabolic equivalent of task, which quantified energy costs associated with the activity (34). Participants' physical activity was derived by multiplying the frequency and intensity of each activity performed per week.

Standing height (centimeters) and weight (kilograms) were measured by a trained examiner using standardized methods (31). BMI (in kg/m^2) was calculated and was categorized as underweight (<18.5), normal weight (18.5 to <25), overweight (25 to <30), and obese (≥30). Three sets of systolic and diastolic blood pressure were measured with a mercury sphygmomanometer, according to the standardized protocol, and the measurements were averaged (31). Total serum cholesterol was measured with the use of previously described enzymatic methods (35). eGFR was calculated with the use of the 2009 Chronic Kidney Disease Epidemiology Collaboration equation, after serum creatinine measurements were calibrated to reference values at the Cleveland Clinic Research Laboratory (36, 37). In regression models, physical activity, total serum cholesterol, and eGFR were used as continuous variables. The proportion of the population with missing covariates was low in this sample (0–8%). The analysis was conducted among participants without missing covariates.

Statistical analyses. All of the analyses accounted for the complex survey design of NHANES III with the use of survey weights (31). We examined the characteristics of our overall study population, and separately for men and women, according to deciles of PDI, hPDI, and uPDI. To test for differences by deciles of each index, we used weighted chi-square tests for categorical variables and weighted 2-tailed *t* tests for continuous variables (38).

To investigate the association between plant-based diet indexes (PDI, hPDI, and uPDI) and all-cause and cardiovascular disease mortality, we used Cox proportional regression models to estimate HRs and 95% CIs using length of follow-up as a time metric. For the associations between the 3 plant-based diet indexes and all-cause mortality and cardiovascular disease mortality, we tested for departures from linearity (39). We found a significant nonlinear association between hPDI and all-cause mortality (*P*-nonlinear association = 0.01). Because there was evidence of nonlinearity, we then modeled the association between hPDI and outcomes by using 2 linear spline terms with a knot at the median value (less than the median, median or higher).

We used 3 nested models for multivariate analyses. Model 1 adjusted for age, sex, race/ethnicity, and total energy intake. Model 2 further adjusted for socioeconomic factors (education, federal poverty level, and marital status), and health behaviors (smoking status, physical activity, alcohol consumption, and margarine intake). We considered model 2 as our main results. Model 3 adjusted for variables in model 2, plus clinical factors including BMI, baseline hypertension, serum cholesterol, eGFR, and menopausal status. In model 3, we included these potential mediating variables to investigate if plant-based diets are associated with mortality independent of mediators.

We tested for effect modification by sex to evaluate whether the associations between plant-based diet indexes and the outcomes of interest were constant across sex strata. As a post hoc analysis, we also tested for effect modification by age (20–39, 40–64, and ≥65 y of age).

In addition, we modeled components of PDIs in fully adjusted models. To estimate the risk of mortality in the fully adjusted models, instead of the indexes, we used animal foods, healthy plant foods, and less-healthy plant foods simultaneously. Stata statistical software version 13.0 was used for all statistical analyses (StataCorp LP).

Results

Baseline characteristics of the study population. In the total sample, the PDI ranged from 24 to 75 (median: 49; 10th–90th percentile range: 43–58), the hPDI ranged from 28 to 78 (median: 51; 10th–90th percentile range: 43–60), and the uPDI ranged from 31 to 78 (median: 52; 10th–90th percentile range: 44–61).

When considered by sex, the PDI in men ranged from 30 to 75 (median: 49; 10th–90th percentile range: 43–59) and in women from 24 to 72 (median: 51; 10th–90th percentile range: 42–60); the hPDI ranged in men from 29 to 71 (median: 50; 10th–90th percentile range: 42–60) and in women from 28 to 78 (median: 51; 10th–90th percentile range: 43–61); and the uPDI ranged in men from 33 to 73 (median: 52; 10th–90th percentile range: 44–60) and in women from 31 to 78 (median: 52; 10th–90th percentile range: 44–61).

Participants with a higher PDI score were more likely to be women, non-Hispanic white, older, and married; more likely to have higher levels of education; less likely to smoke; and more likely to be physically active than participants with a lower PDI score (**Table 1**). For the hPDI, the patterns were similar for age, sex, race, marital status, and education (**Supplemental Table 2**), and when stratified by sex.

Participants with a higher uPDI score were more likely to be non-Hispanic black and younger, less likely to be married, and more likely to be at <130% of the federal poverty level (**Supplemental Table 3**). Participants with a higher PDI or hPDI score tended to be more overweight or obese, have hypertension, higher serum cholesterol, and lower eGFR. Participants with higher uPDI scores had significantly higher eGFR levels than those with lower uPDI scores.

Dietary intake of nutrients. Participants in the highest decile of PDI and hPDI consumed greater amounts of fiber, vitamin C, and folate and lower amounts of dietary cholesterol, sodium, saturated fat, and monounsaturated fat as a percentage of energy (**Supplemental Table 4**). In general, participants in the highest decile of uPDI consumed lower amounts of micronutrients and fiber and higher amounts of carbohydrates as a percentage of energy. There were no significant differences across deciles of uPDI with respect to intakes of fat and cholesterol when expressed in terms of nutrient density. Men and women in the highest decile of PDI and hPDI consumed fruit, vegetables, and whole grains more frequently than did those in the lowest decile (**Supplemental Figures 2** and **3**). The PDI and hPDI were positively correlated with each other ($r = 0.33$, $P<0.001$), whereas the uPDI was negatively correlated with the PDI ($r = -0.06$, $P = 0.003$) and with the hPDI ($r = -0.12$, $P<0.001$).

TABLE 1 Demographic, socioeconomic, and health characteristics for all participants and men and women separately for the overall PDI: NHANES III, 1988–1994[1]

	Total ($n = 11,879$)				Men ($n = 5620$)				Women ($n = 6259$)			
Characteristic	Decile 1 ($n = 1454$)	Decile 5 ($n = 1543$)	Decile 10 ($n = 1169$)	*P*	Decile 1 ($n = 741$)	Decile 5 ($n = 716$)	Decile 10 ($n = 564$)	*P*	Decile 1 ($n = 713$)	Decile 5 ($n = 827$)	Decile 10 ($n = 605$)	*P*
Median score	41	50	61		41	50	61		41	50	61	
Female, %	44	55	52	<0.001								
Race/ethnicity, %				<0.001				0.003				0.003
Non-Hispanic white	74	77	74		76	78	71		73	75	77	
Non-Hispanic black	14	9	7		12	9	8		16	10	7	
Mexican American	3	6	10		3	6	11		3	5	8	
Other	10	8	8		9	6	10		8	10	7	
Age, y	35 ± 0.3	41 ± 0.6	48 ± 0.8	<0.001	35 ± 0.6	40 ± 0.7	46 ± 1.2	<0.001	36 ± 0.7	41 ± 0.7	49 ± 0.9	<0.001
Education, %				0.003				0.02				0.004
Less than high school	26	18	25		27	21	26		25	17	24	
High school	37	34	29		33	33	23		41	35	35	
More than high school	37	46	46		39	46	52		34	48	41	
Federal poverty level, %				0.09				0.25				0.21
<130%	19	14	20		19	15	20		21	19	21	
130–350%	46	45	44		45	44	42		47	44	45	
>350%	34	41	36		36	41	39		32	37	34	
Marital status, %				<0.001				0.009				0.04
Married	59	70	70		59	73	78		61	65	64	
Widowed, separated, or divorced	16	14	16		12	8	7		21	22	24	
Never married	24	16	14		29	19	15		20	12	12	
BMI (kg/m^2) category, %				0.30				0.23				0.05
Underweight (<18.5)	3	2	3		1	1	2		5	3	4	
Normal weight (18.5 to <25)	47	45	45		47	38	40		48	50	48	
Overweight (25 to <30)	32	34	36		38	44	42		25	25	31	
Obese (≥30)	18	20	16		14	17	16		22	22	16	
Smoking status, %				<0.001				<0.001				<0.001
Current smoker	46	29	15		51	31	13		39	27	18	
Former smoker	14	23	31		15	27	42		13	19	21	
Never smoker	40	48	54		34	42	45		48	53	62	
Physical activity, METs/wk	21 ± 1.3	24 ± 1.3	32 ± 1.8	<0.001	27 ± 2.0	26 ± 1.7	33 ± 2.0	0.20	15 ± 1.0	18 ± 1.0	30 ± 1.3	<0.001
Alcohol consumption, times/mo	6.6 ± 0.1	5.8 ± 0.1	4.6 ± 0.1	<0.001	8.2 ± 0.2	7.7 ± 0.2	6.5 ± 0.2	0.29	4.4 ± 0.2	4.0 ± 0.3	2.5 ± 0.1	<0.001
Hypertension, %	21	25	31	<0.001	24	27	33	0.14	19	24	30	0.002
Serum cholesterol, mg/dL	197 ± 1.4	204 ± 2.0	206 ± 2.6	<0.001	200 ± 2.2	204 ± 3.6	201 ± 3.3	0.77	194 ± 2.0	203 ± 2.7	209 ± 2.9	<0.001
eGFR, mL · min^{-1} · 1.73 m^{-2}	108 ± 0.6	103 ± 0.8	98 ± 0.8	<0.001	108 ± 0.9	102 ± 0.9	97 ± 1.2	<0.001	109 ± 0.9	104 ± 1.5	98 ± 1.2	<0.001

[1]Values are means ± SEs unless otherwise indicated. All analyses accounted for the complex survey design of NHANES III and included survey weights. eGFR, estimated glomerular filtration rate; MET, metabolic equivalent task; PDI, plant-based diet index.

Plant-based diets and mortality. Over a median follow-up of 19 y, 2228 deaths occurred, 543 of which were from cardiovascular diseases. Neither the PDI nor the uPDI was associated with all-cause mortality in the overall sample in model 2 (HR per 10-unit increase in PDI: 1.01; 95% CI: 0.98, 1.03; HR per 10-unit increase in uPDI: 1.00; 95% CI: 0.98, 1.04) or model 3 (HR per 10-unit increase in PDI: 1.01; 95% CI: 0.98, 1.03; HR per 10-unit increase in uPDI: 1.00; 95% CI: 0.98, 1.04) (Table 2).

In the overall study population, a 10-unit increase in hPDI was not associated with all-cause mortality (HR per 10-unit increase in hPDI: 1.05; 95% CI: 0.98, 1.11) in model 2 among those with hPDI scores below the median. These results did not change when potentially mediating variables were further adjusted (model 3; HR per 10-unit increase in hPDI: 1.04; 95% CI: 0.97, 1.12).

However, a 10-unit increase in hPDI was associated with a lower risk of all-cause mortality among those with hPDI scores above the median (HR per 10-unit increase in hPDI: 0.95; 95% CI: 0.91, 0.98) in model 2 (**Supplemental Figure 4**). There was a similar result for model 3 (HR per 10-unit increase in hPDI: 0.95; 95% CI: 0.91, 0.98) as for model 2. When analyzed according to deciles, there was a lower risk of death for deciles 6–10 relative to decile 1 (**Supplemental Table 5**).

There was no significant effect modification by sex on the association between the PDI (*P*-interaction = 0.16), hPDI (*P*-interaction = 0.11), or uPDI (*P*-interaction = 0.55) and all-cause mortality. After stratifying by sex, the results for women were similar to those observed in the overall study population (**Supplemental Figures 5** and **6**). Neither the PDI nor the uPDI was associated with the risk of death among men or women.

The PDI, hPDI, and uPDI were not associated with deaths from cardiovascular diseases (Table 3). There was no significant effect modification by sex on the association between the PDI (*P*-interaction = 0.74), the hPDI (*P*-interaction = 0.43), or the uPDI (*P*-interaction = 0.53) and cardiovascular disease mortality. We also did not find effect modification by age (*P*-interaction > 0.20) for all-cause mortality or cardiovascular disease mortality.

TABLE 2 Associations between PDIs, per 10-unit increase, and all-cause mortality among participants of NHANES III[1]

			HR (95% CI)		
	Participants, *n*	Deaths, *n*	Model 1	Model 2	Model 3
PDI					
All	11,879	2228	0.98 (0.96, 1.01)	1.01 (0.98, 1.03)	1.01 (0.98, 1.03)
Men	5620	1258	1.00 (0.97, 1.03)	1.04 (1.01, 1.07)	1.04 (0.99, 1.07)
Women	6259	970	0.96 (0.94, 0.99)	0.97 (0.94, 1.00)	0.98 (0.95, 1.00)
hPDI					
All	11,879	2228			
Less than median	5159	710	0.99 (0.93, 1.06)	1.05 (0.98, 1.11)	1.04 (0.97, 1.12)
Median or higher	6720	1518	0.94 (0.91, 0.97)	0.95 (0.91, 0.98)	0.95 (0.91, 0.98)
Men	5620	1258			
Less than median	2679	466	0.97 (0.89, 1.04)	1.00 (0.93, 1.09)	1.01 (0.92, 1.10)
Median or higher	2941	792	0.95 (0.90, 0.99)	0.95 (0.90, 1.01)	0.95 (0.89, 1.01)
Women	6259	970			
Less than median	2479	244	1.04 (0.95, 1.14)	1.09 (0.99, 1.20)	1.09 (0.98, 1.19)
Median or higher	3780	726	0.94 (0.89, 0.98)	0.94 (0.88, 0.99)	0.94 (0.88, 0.99)
uPDI					
All	11,879	2228	1.04 (1.02, 1.07)	1.00 (0.98, 1.04)	1.00 (0.98, 1.04)
Men	5620	1258	1.04 (1.01, 1.08)	1.01 (0.98, 1.05)	1.01 (0.98, 1.06)
Women	6259	970	1.04 (1.01, 1.08)	1.01 (0.99, 1.05)	1.01 (0.98, 1.05)

[1]Values were derived with the use of a Cox proportional hazards regression model. Model 1 was adjusted for race, sex, age, and total energy intake; model 2 was adjusted for covariates in model 1 plus education, federal poverty level, marital status, smoking status, physical activity, alcohol consumption, and margarine intake; model 3 was adjusted for covariates in model 2 plus BMI, baseline hypertension, serum cholesterol, and eGFR. Among women, model 3 was adjusted for the covariates in model 3 plus menopause. eGFR, estimated glomerular filtration rate; hPDI, healthy plant-based diet index; PDI, plant-based index; uPDI, less-healthy (unhealthy) plant-based diet index.

When we modeled components of PDIs, no individual component was significantly associated with all-cause mortality or cardiovascular disease mortality in the fully adjusted models. For all of the analyses, model 3 showed results similar to model 2.

Discussion

To the best of our knowledge, the present study is the first to use a nationally representative sample to investigate the association between plant-based diets and all-cause and cardiovascular disease mortality. In this sample of US men and women without any chronic diseases at baseline, we found a reduced risk of death from all causes among those with healthful plant-based diet score above the median (after adjustment for demographic characteristics, socioeconomic factors, health behaviors, and clinical factors). In stratified analyses, women had a lower risk of all-cause mortality with higher healthful plant-based diet scores above the median. No significant association was observed for men, and we found no effect modification by sex or age.

Studies in vegetarians have typically defined vegetarian diet status by the restriction of types of animal foods (meat, fish,

TABLE 3 Associations between PDIs, per 10-unit increase, and cardiovascular disease mortality among participants of NHANES III[1]

			HR (95% CI)		
	Participants, *n*	Deaths, *n*	Model 1	Model 2	Model 3
PDI					
All	11,879	543	1.01 (0.96, 1.07)	1.05 (0.99, 1.11)	1.05 (0.99, 1.12)
Men	5620	306	1.01 (0.94, 1.10)	1.08 (0.98, 1.17)	1.08 (0.99, 1.17)
Women	6259	237	1.01 (0.95, 1.07)	1.02 (0.97, 1.09)	1.03 (0.96, 1.10)
hPDI					
All	11,879	543	1.00 (0.95, 1.06)	1.03 (0.97, 1.08)	1.02 (0.97, 1.08)
Men	5620	306	1.00 (0.92, 1.10)	1.03 (0.96, 1.10)	1.03 (0.96, 1.10)
Women	6259	237	0.99 (0.94, 1.06)	1.00 (0.94, 1.07)	1.00 (0.93, 1.07)
uPDI					
All	11,879	543	1.06 (1.00, 1.12)	1.03 (0.97, 1.08)	1.02 (0.96, 1.08)
Men	5620	306	1.07 (0.99, 1.15)	1.04 (0.96, 1.13)	1.04 (0.96, 1.13)
Women	6259	237	1.05 (0.99. 1.13)	1.03 (0.96, 1.11)	1.03 (0.95, 1.10)

[1]Values were derived with the use of a Cox proportional hazards regression model. Model 1 was adjusted for race, sex, age, and total energy intake; model 2 was adjusted for covariates in model 1 plus education, federal poverty level, marital status, smoking status, physical activity, alcohol consumption, and margarine intake; model 3 was adjusted for covariates in model 2 plus BMI, baseline hypertension, serum cholesterol, and eGFR. Among women, model 3 was adjusted for the covariates in model 3 plus menopause. eGFR, estimated glomerular filtration rate; hPDI, healthy plant-based diet index; PDI, plant-based diet index; uPDI, less-healthy (unhealthy) plant-based diet index.

milk, or eggs), failing to distinguish between healthy and less-healthy plant foods (5, 15, 28). However, in our present study, we conceptualized plant-based diets differently, because plant-based diets are characterized as consisting predominantly of foods of plant origin (which may be healthy or less healthy), with a secondary characteristic of limiting animal foods (4, 6, 40). Thus, a more comprehensive assessment of this dietary pattern is provided by the use of an overall PDI, which accounts for both plant foods and animal foods. We found no association between the PDI and all-cause mortality, which is similar to previous studies in vegetarians (3, 8, 14, 15, 17, 22, 41–43).

Our study extends previous findings by presenting results for hPDIs and uPDIs to represent the quality of plant foods, in addition to the overall PDI. Importantly, our nuanced approach showed that among individuals with hPDI scores above the median, a 10-unit increase in hPDI was associated with a lower risk of death, whereas no association was observed below the median.

Several prospective studies of diet scores and mortality or cardiovascular disease outcomes reported a nonlinear relation (44–46). A recent meta-analysis also showed a nonlinear dose-response relation between different food groups such as fruit, vegetables, nuts, eggs, and dairy and all-cause mortality (9). Our study builds upon findings from these previous studies by adding that a nonlinear association exists between hPDI scores and all-cause mortality in adults.

Our findings also suggest that there may be a minimum level of plant-based diets that needs to be achieved for health benefits to be evident. Our results differ from the studies in nurses and health care professionals, in which there was no departure from linearity for the hPDI and diabetes and coronary artery disease risk (29, 30). Considering the use of sample-based scores, it is possible that the diets of the general population may be less healthy (or less plant-rich) than those of health care professionals. In our sample, individuals who were at or above the median of the hPDI consumed fruit, vegetables, whole grains, and tea and coffee more frequently than individuals who were below the median of hPDI and consumed sugar-sweetened beverages, red and processed meat, and dairy less frequently. However, because serving size was not measured in NHANES III, it is difficult to interpret our results in terms of health risks associated with the consumption of an absolute amount of animal food and less-healthy plant food. Future research is needed to explore the optimal amount of consumption of these foods in the context of an overall plant-based diet.

Our sex-specific results showed that an hPDI above the median was associated with a lower risk of death from all causes in women. Studies have hypothesized that diet and some food items have a differential effect on circulating sex hormones or blood lipid concentrations (47–50) in men and women. However, the evidence has been inconsistent (51, 52), and we did not find a significant interaction. More studies on dietary patterns and health outcomes should test for effect modification by sex to clarify if the associations truly differ between men and women.

We did not observe significant results for the healthy plant-based diets and cardiovascular disease mortality in the overall study population, or in sex-specific strata. We expected to find an inverse association between healthy plant-based diets and cardiovascular disease mortality, given that high fiber intake and decreased saturated fat intake are associated with a reduced risk of cardiovascular disease events, all-cause mortality, and cardiovascular disease mortality (53–56). Either there is no association or the absence of detecting an association may be due to inaccuracies in cause-of-death information on death certificates, particularly for cardiovascular diseases (57, 58), or the possibility that healthy plant-based diets are associated with a reduced risk of other related chronic disease outcomes, such as type 2 diabetes (29, 30), which we excluded. In addition, those participants with a diagnosis of cardiovascular disease may be more likely to be treated for their condition, possibly decreasing the risk of death due to these conditions.

In the present study, associations between less-healthy plant-based diets and mortality outcomes were not significant. Less-healthy plant-based diets were low in healthy plant foods and animal foods and high in less-healthy plant foods, which may be considered less healthful than both the overall plant-based diets and healthy plant-based diets. Previous studies reported an elevated risk of all-cause and cardiovascular disease mortality with higher intakes of red and processed meat (59, 60) and a higher risk of type 2 diabetes and coronary artery disease with greater adherence to less-healthy plant-based diets (29, 30). An evaluation of the risk of chronic diseases with the use of a similar index for less-healthy plant-based diets in other study populations is warranted to confirm our results.

To our knowledge, this is the first nationally representative study with a long duration of follow-up that examined the association between plant-based diets and mortality and assessed effect modification by sex. The study had minimal loss to follow-up (0.1%) because probabilistic matching to the National Death Index was used to ascertain vital status. We used an FFQ to define plant-based diets, which allowed us to examine specific food groups and food items of interest. The use of sample-based scores enabled us to assess the diets of the entire study population.

Nonetheless, there are several limitations of this study. Dietary intake was self-reported; thus, the possibility of reporting error remains. The NHANES III used an FFQ without a validation study, but a shorter version of the questionnaire (61) and a similar instrument without portion sizes were validated (62). In addition, we found similar trends in macro- and micronutrient intakes across levels of plant-based diet scores when we compared nutrient intakes in our study with the previous study that used a semiquantitative FFQ (30), suggesting that the FFQ used in NHANES III classified participants reasonably well to different deciles as the semiquantitative FFQ. There may be exposure misclassification, but it would be expected to be nondifferential and to bias our results toward the null (63). Diet was assessed only at baseline; thus, repeated assessments of dietary intake were not available and it is not known whether participants maintained their baseline diet throughout the follow-up period. A previous study has shown that the duration of time consuming plant-based diets may be an important consideration (43), but unfortunately, NHANES III does not have this information. Studies with repeated measurements of dietary intake are necessary to better understand the association.

Although we adjusted for multiple confounding factors, the possibility of residual confounding remains, because there may be unmeasured covariates or errors in the measured confounding factors. Last, we adjusted for several potential mediating variables, including BMI, in the fully adjusted model. As such, the results may be overadjusted and underestimate the true association between plant-based diets and mortality.

In conclusion, in a representative sample of US adults, we found that diets with greater intakes of healthy plant foods showed a nonlinear association with all-cause mortality. A 10-unit increase in the hPDI above the median was associated with a moderately lower risk of death. In stratified analyses, we found

a similar pattern in women with higher adherence to healthy plant-based diets, but no significance was observed for men. We also observed no effect modification by sex. Future research should explore the impact of the quality of plant-based diets on long-term health outcomes, by considering the intake of less-healthy plant foods.

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