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Plant-based diets and the incidence of cardiovascular disease: the Million Veteran Program

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ABSTRACT

Background A healthful plant-based diet was associated with lower risks of coronary heart disease and type 2 diabetes, and a favourable profile of adiposity-associated biomarkers, while an unhealthful plant-based diet was associated with elevated risk of cardiometabolic disease in health professional populations. However, little is known about the associations between plant-based dietary patterns and risk of cardiovascular disease (CVD) in US veterans.

Methods The study population consisted of 148 506 participants who were free of diabetes, CVD and cancer at baseline in the Veterans Affairs (VA) Million Veteran Program. Diet was assessed using a Food Frequency Questionnaire at baseline. We calculated an overall Plant-Based Diet Index (PDI), a healthful PDI (hPDI) and an unhealthful PDI (uPDI). The CVD endpoints included non-fatal myocardial infarction (MI) and acute ischaemic stroke (AIS) identified through high-throughput phenotyping algorithms approach and fatal CVD events identified by searching the National Death Index.

Results With up to 8 years of follow-up, we documented 5025 CVD cases. After adjustment for confounding factors, a higher PDI was significantly associated with a lower risk of CVD (HR comparing extreme quintiles=0.75, 95% CI 0.68 to 0.82, $P_{trend}<0.0001$). We observed an inverse association between hPDI and the risk of CVD (HR comparing extreme quintiles=0.71, 95% CI 0.64 to 0.78, $P_{trend}<0.001$), whereas uPDI was positively associated with the risk of CVD (HR comparing extreme quintiles=1.12, 95% CI 1.02 to 1.24, $P_{trend}<0.001$). We found similar associations of hPDI with subtypes of CVD; a 10-unit increment in hPDI was associated with HRs (95% CI) of 0.81 (0.75 to 0.87) for fatal CVD, 0.86 (0.79 to 0.94) for non-fatal MI and 0.86 (0.78 to 0.95) for non-fatal AIS.

Conclusions Plant-based dietary pattern enriched with healthier plant foods was associated with a substantially lower CVD risk in US veterans.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Vegetarian diets, compared with omnivorous diets, were associated with beneficial effects on various pathways underlying cardiovascular diseases. However, studies that examined associations between plant-based diets and stroke mortality largely yielded null results.

WHAT THIS STUDY ADDS

⇒ In this large cohort of US veterans, we observed that overall plant-based diet was significantly associated with a lower risk of cardiovascular diseases and was consistent for both myocardial infarction and stroke.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ These findings support recommending plant-based diet rich in healthier plant foods for the prevention of cardiovascular diseases.

BACKGROUND

Plant-based diets have been associated with lower risk of coronary heart disease (CHD),[1] stroke and cardiovascular disease (CVD) risk factors.[2–6] Various dietary guidelines, including the Dietary Guidelines for Americans,[7] recommend a dietary pattern with higher consumption of plant foods and lower consumption of animal foods for the prevention of CVD. However, a majority of earlier studies was limited by a dichotomous definition of plant-based diet, that is, entirely excluding certain groups of (eg, red meat and poultry) or all animal foods. This definition limited the applicability of study findings in US populations given the fact less than 3% of US population are vegetarians.[8] Dietary indices that can evaluate the gradients of adherence to a plant-based diet are warranted to study the health effects of this dietary pattern in general populations.

Previous studies linking plant-based diets to CVD outcomes focused more on ischaemic heart disease[1 9]; fewer studies have investigated cerebrovascular diseases.[10] Recently, the European Prospective Investigation into Cancer and Nutrition (EPIC)-Oxford study reported that participants who consumed a vegetarian diet that completely excluded intake of meat and fish showed an increased risk of stroke as compared with meat eaters.[11]

This finding, conflicting with the evidence that supports cardioprotective effects of plant-based diets,[1 9 12] could be explained by the fact that this vegetarian diet treated all plant foods equally and did not distinguish different plant foods with divergent health effects; some plant foods, such as white rice[13] and sugar-sweetened beverages,[14] are associated with higher cardiometabolic risk. To overcome the aforementioned limitations, we previously developed three plant-based diet indices, an overall Plant-Based Diet Index (PDI), a healthful PDI (hPDI) and an unhealthful PDI (uPDI), to quantify the degree of adherence to plant-based diets with consideration of quality of plant foods, and linked the indices to the risk of type 2 diabetes and CHD in health professional populations.[1 6 15] However, the earlier studies were conducted in populations that consist of older and predominantly White participants, mostly women and relatively high socioeconomic status. To address the limitations of the previous studies, we proposed to examine the PDIs in relation to the risk of CVD including non-fatal myocardial infarction (MI) and acute ischaemic stroke (AIS), and fatal CVD in the Veterans Affairs (VA) Million Veteran Program (MVP), a newly launched prospective cohort study that enrolled mostly male participants with a wide age range and diverse socioeconomic and racial/ethnic backgrounds.

METHODS

Study population

The MVP is a nationally representative, prospective cohort study of veterans designed to study genetic and non-genetic determinants of chronic diseases. The enrolment of MVP began in early 2011. The MVP enrolled individuals receiving routine primary care in the US Department of Veterans Affairs Healthcare System, which collected data from self-reported surveys and electronic health records. Details of the study design of MVP can be found elsewhere.[16]

As of 2020, 790 116 veterans were enrolled, and 351 892 participants had completed the baseline Lifestyle Survey that included a semiquantitative Food Frequency Questionnaire (sFFQ) with a total of 61 food items. For this current analysis, we excluded participants who did not provide dietary information; or who reported implausible dietary data (total energy intake: <400 or ≥4000 kcal/day of female; <450 or ≥4500 kcal/day of male); or who had more than 30 blanks on sFFQ at baseline. After this exclusion, a total of 327 702 participants were included. We then excluded 11 561 participants who responded to the lifestyle questionnaire after December 2018 and 167 635 participants who had a history of diabetes (n=73 803), cancer (n=85 055) and/or CVD (n=74 160) at baseline, yielding an analytical population of 148 506 relatively heathy participants.

Assessment of exposure and covariates

Participants self-reported their dietary intake at baseline through sFFQ, which has been demonstrated reasonably well validity in assessing intakes of individual foods in other cohorts [17–20] Participants were asked how often, on average, they consumed a standard portion of each food in the past year. Frequencies and portions of each individual food item were converted to average daily intake for each participant. We calculated the overall PDI, hPDI and uPDI to quantify each participant's adherence to plant-based diets. Details of the scoring systems can be found in our previous publications.[21] Briefly, we first created 16 food groups on the basis of nutrient and culinary similarities of individual foods. Healthful plant food groups included whole grains, fruits, vegetables, nuts, legumes and tea/coffee. Less healthful plant food groups included fruit juices, sugar-sweetened beverages, refined grains, potatoes and sweets/desserts. Animal food groups included animal fats, dairy, eggs, fish/seafood and meat (poultry and red meat). Then, we calculated quintiles of intake for each of the 16 food groups and assigned component score for each food group. For PDI, participants received scores from 5 to 1 for their intake levels from the highest to the lowest quintiles of each plant food group (positive scoring). For animal foods, we reversed the scoring: participants received scores from 5 to 1 for their intake levels from the highest to the lowest quintiles of each animal food group (reverse scoring). For hPDI, we applied positive scoring to healthy plant food groups, and reverse scoring to less healthy plant food groups and animal food groups. For uPDI, positive scoring was applied to less healthy plant food groups, and reverse scoring was applied to healthy plant food groups and animal food groups (more detail in online supplemental table 1 of scoring method and online supplemental table 2 of illustrations). Finally, we summed up component scores across the 16 food groups to obtain the indices with theoretical range of each index ranging from 16 to 80.

Daily total energy intake was estimated by multiplying the frequency of consumption for each item by its energy content from the Harvard University Food Composition Database[22] and summing across all foods. Participants self-reported information on age, sex, race, family income, education, body mass index, alcohol consumption, exercise, smoking and baseline comorbidities, including hypercholesterolaemia and hypertension at baseline.

Assessment of CVDs

The outcomes of interest in the current study included fatal CVD and non-fatal CVD, the latter included non-fatal MI and AIS, based on the linked data from the VA Corporate Data Warehouse (CDW) with data from the Centers for Medicaid & Medicare Services and National Death Index data bases using scrambled social security numbers.[23–27]

MI and AIS cases were identified by applying the Surrogate-Assisted Feature Extraction method, a validated high-throughput phenotyping algorithms approach, using a combination of International Classification of Diseases (ICD) codes from both VA and Center for Medicare & Medicaid Services data sources, natural language

processing and medical record review labels.[28 29] Fatal CVD was defined based on the ICD, 10th Revision, Clinical Modification codes I00–I99.

Statistical analysis

Person-years of follow-up were calculated from sFFQ assessment to the earliest of time of the first occurrence of MI or AIS, death, or last visit recorded in the CDW. We used Cox proportional hazards models to estimate HRs with 95% CIs comparing higher quintiles to the lowest quintile of dietary indices with simultaneous adjustment for covariates. Covariates included age (continuous), sex (male or female), race/ethnicity (non-Hispanic white (European Americans), African American or other), education level (≤high school or GED, some colleague or college or above), income level (<US$30 000, US$30 000–US$59 000 or ≥US$60 000), marital status (currently married or not), smoking status (current, former or never smoking), frequency of alcohol consumption (never, <1 times/week or ≥1 times/week), frequency of vigorous exercise (never/rarely, 1–4 times/month, 2–4 times/week or ≥5 times/week), body mass index (<23.0, 23.0–24.9, 25.0–29.9, 30.0–34.9 or ≥35.0 kg/m^2) and histories of

Table 1 Baseline characteristics of 148 506 participants in the Million Veteran Program according to PDI scores

	Quintiles of PDI			Quintiles of hPDI			Quintiles of uPDI		
	Q1	Q3	Q5	Q1	Q3	Q5	Q1	Q3	Q5
N	32 164	35 761	32 965	30 162	32 609	28 796	31 835	29 426	28 781
PDI score	38.9	47.5	56.1	46.6	47.3	48.9	47.4	47.8	47.1
hPDI score	47.3	48.4	49.7	38.7	48.5	58.4	52.1	48.4	45.0
uPDI score	47.7	47.9	47.3	51.3	47.9	43.5	37.3	47.5	58.4
Age, years	60.9	61.1	61.8	60.2	61.4	62.1	61.9	61.7	59.7
Men, %	87.1	88.0	89.0	91.5	88.5	83.1	85.8	88.9	88.7
European Americans, %	80.6	81.7	81.7	79.5	81.5	83.4	85.8	81.2	77.2
African American, %	14.0	12.8	12.7	15.5	13.0	10.6	9.1	12.9	17.1
Married, %	53.4	58.2	60.8	55.3	58.7	57.5	61.0	59.0	51.6
Education level, %									
≤High school or GED	23.4	20.6	18.5	24.8	20.8	16.7	13.8	19.9	28.4
Some colleague	30.6	29.4	28.3	32.2	29.5	26.2	26.6	29.6	31.2
College or above	46.0	50.0	53.2	42.9	49.7	57.0	59.5	50.5	40.4
Annual family income, %									
<30 000	35.0	31.9	31.3	36.8	31.7	29.8	27.2	32.1	38.6
30 000–59 000	33.4	34.5	34.8	35.0	34.6	33.1	33.2	34.5	34.8
≥60 000	31.6	33.6	33.9	28.2	33.6	37.1	39.6	33.4	26.6
Smoking status, %									
Current smoking	24.7	23.3	21.6	29.5	23.3	16.6	17.7	23.2	28.5
Former smoker	44.7	44.9	45.0	40.4	45.0	49.0	49.7	45.3	39.3
Never smoking	30.6	31.8	33.4	30.1	31.6	34.4	32.6	31.4	32.2
Vigorously exercise*, %									
Never/rarely	31.5	26.2	20.9	17.7	23.2	28.5	17.5	25.0	36.9
1–4 times/month	26.2	26.6	26.2	28.1	27.3	23.1	23.5	27.0	27.4
2–4 times/week	28.4	31.9	34.9	27.4	31.9	36.4	38.4	33.2	24.5
≥5 times/week	13.9	15.3	18.0	12.4	14.7	20.4	20.6	14.7	11.2
Alcohol drinking, %									
Never	35.1	37.3	38.9	39.2	36.1	36.8	30.9	36.6	44.6
<1 times/week	26.8	28.3	29.0	28.9	28.1	26.9	27.4	28.4	29.0
≥1 times/week	38.1	34.4	32.1	31.9	35.7	36.3	41.7	35.0	26.4
BMI, kg/m^2	29.7	29.0	28.3	29.2	29.1	28.5	29.2	29.0	28.8
Hypertension, %	38.7	37.6	37.0	37.6	38.9	36.8	37.2	38.5	37.5
Hypercholesterolaemia	33.6	35.0	35.9	32.4	35.3	36.8	35.3	35.7	33.4

Unless otherwise indicated, data are expressed as means.
*Exercise vigorously enough to work up a sweat.
GED, General Educational Development; hPDI, healthful PDI; PDI, plant-based diet index; uPDI, unhealthful PDI.

hypertension and hypercholesterolaemia at baseline (yes vs no). To quantify a linear trend of relative risk of CVD across quintiles, we assigned the median within each quintile and modelled this variable continuously; the Wald test was used to assess statistical significance. We also tested for potential non-linearity in the association between PDIs and the risk of CVD. Restricted cubic spline regression with three knots were applied to flexibly model the association between the dietary indices and risk of CVD with the first percentile of each dietary score as the reference level.[30] Non-linearity in the dose–response relationship of the dietary indices with the risk of CVD was evaluated by comparing the model with the linear term to the model with the linear and cubic spline terms using the likelihood ratio test. In a secondary analysis, we examined the associations between PDIs and the risk of CVD in white, Africa American and other racial/ethnic group separately. We performed stratified analyses to examine the associations between PDIs and the risk of CVD outcomes across different subgroups defined by sex, age, smoking, exercise, BMI, family income and baseline diseases/conditions. We tested for interactions between the dietary indices and the variables of stratification by adding a product term of the two variables in addition to their main effects in the multivariable model.

RESULTS

Table 1 presents baseline characteristics of participants according to quintiles of PDI, hPDI and uPDI. Participants with high PDI and hPDI were more likely to be married and more physically active and had higher education and income levels. A higher uPDI was associated with younger age, less educated, less likely married, lower physical activity level and higher prevalence of current smoking (table 1).

During a mean follow-up of 3.8 years (1–8 years), we documented 5025 CVD events, including 2167 fatal CVD and 2858 non-fatal CVD events; the latter included 1676 MI and 1261 AIS cases (79 participants developed both MI and AIS). After adjustment for known and suspected confounding variables and risk factors, a higher PDI was significantly associated with a lower risk of CVD (HR comparing extreme quintiles=0.75, 95% CI 0.68 to 0.82, P_{trend}<0.001). We observed an inverse association between hPDI and the risk of total CVD (HR comparing extreme quintiles=0.71, 95% CI 0.64 to 0.78, P_{trend}<0.001), whereas uPDI was positively associated with total CVD (HR comparing extreme quintiles=1.12, 95% CI 1.02 to 1.284, P_{trend}<0.001). A 10-unit increment in the indices was associated with a 17% lower risk of CVD (HR 0.83, 95% CI 0.78 to 0.88) for PDI and a 16% lower risk of CVD (HR

Table 2 Associations of Plant-Based Diet Indices (PDIs) and cardiovascular diseases in 148 506 participants from the Million Veteran Program (2011–2018)

	Quintiles of dietary indices						HR (95% CI) for
	Q1	Q2	Q3	Q4	Q5	P_{trend}	10-unit increment in PDIs
				PDI			
Median	40	44	48	51	55		
Cases	1191	810	1172	788	1064		
PYs	114 031	88 574	135 734	92 542	132 883		
Model1	1.0 (ref.)	0.85 (0.78, 0.93)	0.79 (0.73, 0.86)	0.76 (0.69, 0.83)	0.68 (0.63, 0.74)	<0.001	0.78 (0.74 to 0.83)
Model2	1.0 (ref.)	0.89 (0.81, 0.97)	0.84 (0.77, 0.91)	0.82 (0.74, 0.90)	0.75 (0.68, 0.82)	<0.001	0.83 (0.78 to 0.88)
				Healthful PDI			
Median	39	45	48	52	58		
Cases	1161	1038	1170	886	770		
PYs	112 031	108 093	123 713	108 193	111 734		
Model1	1.0 (ref.)	0.88 (0.81, 0.96)	0.86 (0.79, 0.93)	0.74 (0.68, 0.81)	0.62 (0.56, 0.67)	<0.001	0.78 (0.74 to 0.81)
Model2	1.0 (ref.)	0.94 (0.86, 1.02)	0.92 (0.85, 1.01)	0.82 (0.75, 0.90)	0.71 (0.64, 0.78)	<0.001	0.84 (0.80 to 0.88)
				Unhealthful PDI			
Median	38	44	48	52	58		
Cases	970	820	1003	1169	1063		
PYs	118 613	98 890	112 256	123 747	110 258		
Model1	1.0 (ref.)	1.01 (0.92, 1.11)	1.10 (1.01, 1.20)	1.22 (1.12, 1.33)	1.31 (1.20, 1.43)	<0.001	1.16 (1.11 to 1.21)
Model2	1.0 (ref.)	0.98 (0.89, 1.08)	1.03 (0.94, 1.13)	1.10 (1.01, 1.20)	1.12 (1.02, 1.24)	<0.001	1.07 (1.03 to 1.12)

Model 1 adjusted for age (continuous) and sex (male or female).
Model 2 further adjusted for race/ethnicity (European Americans, African American or other), education level (≤high school or GED, some colleague, or college or above), income level (<US$30 000, US$30 000–US$59 000 or ≥US$60 000) and marital status (currently married or not), smoking status(current, former or never smoking), frequency of alcohol consumption (never, <1 times/week or ≥1 times/week), frequency of exercise vigorously (never/rarely, 1–4 times/month, 2–4 times/week or ≥5 times/week, total energy intake (in quintiles), body mass index (<23.0, 23.0–24.9, 25.0–29.9, 30.0–34.9 or ≥35.0 kg/m^2) and histories of hypertension and hypercholesterolaemia at baseline (yes vs no).
PYs, person-years.

Table 3 Associations of Plant-Based Diet Index (PDI) and subtypes of cardiovascular disease in 148 506 participants from the Million Veteran Program (2011–2018)

		Quintile of dietary indices						HR (95% CI) for
		Q1	Q2	Q3	Q4	Q5	P_{trend}	10-unit increment in PDIs
PDI								
Fatal CVD	Cases	499	336	509	343	480		
	Model 1	1.0 (ref.)	0.81 (0.71, 0.93)	0.78 (0.69, 0.88)	0.72 (0.63, 0.83)	0.66 (0.58, 0.75)	<0.0001	0.77 (0.71 to 0.83)
	Model 2	1.0 (ref.)	0.86 (0.75, 0.99)	0.83 (0.73, 0.953)	0.79 (0.69, 0.91)	0.73 (0.64, 0.84)	<0.0001	0.82 (0.75 to 0.89)
Non-fatal CVD	Cases	692	474	663	445	584		
	Model 1	1.0 (ref.)	0.87 (0.78, 0.98)	0.79 (0.71, 0.88)	0.77 (0.68, 0.87)	0.69 (0.62, 0.77)	<0.0001	0.79 (0.73 to 0.84)
	Model 2	1.0 (ref.)	0.91 (0.81, 1.02)	0.84 (0.75, 0.93)	0.83 (0.73, 0.94)	0.75 (0.66, 0.84)	<0.0001	0.83 (0.77 to 0.89)
Non-fatal MI	Cases	389	298	385	264	340		
	Model 1	1.0 (ref.)	0.98 (0.84, 1.14)	0.82 (0.71, 0.95)	0.81 (0.70, 0.95)	0.72 (0.62, 0.83)	<0.0001	0.80 (0.73 to 0.87)
	Model 2	1.0 (ref.)	1.02 (0.87, 1.18)	0.87 (0.75, 1.01)	0.88 (0.75, 1.04)	0.80 (0.68, 0.93)	0.001	0.85 (0.77 to 0.94)
Non-fatal AIS	Cases	325	190	288	198	260		
	Model 1	1.0 (ref.)	0.74 (0.62, 0.89)	0.73 (0.63, 0.86)	0.73 (0.61, 0.87)	0.65 (0.55, 0.77)	<0.0001	0.77 (0.70 to 0.85)
	Model 2	1.0 (ref.)	0.77 (0.65, 0.98)	0.77 (0.66, 0.91)	0.78 (0.65, 0.93)	0.69 (0.58, 0.82)	<0.0001	0.80 (0.72 to 0.90)
Healthful PDI								
Fatal CVD	Model 1	1.0 (ref.)	0.88 (0.77, 0.99)	0.77 (0.68, 0.87)	0.72 (0.63, 0.82)	0.57 (0.49, 0.65)	<0.0001	0.75 (0.70 to 0.80)
	Model 2	1.0 (ref.)	0.94 (0.83, 1.07)	0.85 (0.74, 0.96)	0.81 (0.71, 0.94)	0.65 (0.56, 0.76)	<0.0001	0.81 (0.75 to 0.87)
Non-fatal CVD	Model 1	1.0 (ref.)	0.89 (0.79, 0.99)	0.93 (0.84, 1.04)	0.76 (0.68, 0.86)	0.67 (0.59, 0.76)	<0.0001	0.81 (0.77 to 0.86)
	Model 2	1.0 (ref.)	0.93 (0.83, 1.04)	0.99 (0.89, 1.11)	0.83 (0.74, 0.95)	0.76 (0.67, 0.86)	<0.0001	0.86 (0.81 to 0.92)
Non-fatal MI	Model 1	1.0 (ref.)	0.89 (0.77, 1.03)	0.96 (0.84, 1.11)	0.80 (0.69, 0.93)	0.67 (0.57, 0.78)	<0.0001	0.82 (0.76 to 0.88)
	Model 2	1.0 (ref.)	0.92 (0.79, 1.07)	1.01 (0.87, 1.17)	0.86 (0.73, 1.01)	0.74 (0.62, 0.88)	<0.0001	0.86 (0.79 to 0.94)
Non-fatal AIS	Model 1	1.0 (ref.)	0.86 (0.72, 1.01)	0.88 (0.75, 1.04)	0.71 (0.59, 0.85)	0.66 (0.55, 0.78)	<0.0001	0.80 (0.73 to 0.87)
	Model 2	1.0 (ref.)	91 (0.77, 1.08)	0.96 (0.81, 1.14)	0.80 (0.66, 0.96)	0.76 (0.63, 0.92)	0.003	0.86 (0.78 to 0.95)
Unhealthful PDI								
Fatal CVD	Model 1	1.0 (ref.)	1.03 (0.89, 1.19)	1.12 (0.98, 1.28)	1.32 (1.16, 1.50)	1.39 (1.22, 1.59)	<0.0001	1.21 (1.13 to 1.28)
	Model 2	1.0 (ref.)	1.01 (0.87, 1.16)	1.06 (0.93, 1.22)	1.21 (1.05, 1.38)	1.21 (1.05, 1.39)	<0.0001	1.12 (1.05 to 1.20)
Non-fatal CVD	Model 1	1.0 (ref.)	0.99 (0.88, 1.12)	1.08 (0.96, 1.22)	1.14 (1.02, 1.27)	1.23 (1.11, 1.38)	<0.0001	1.12 (1.06 to 1.18)
	Model 2	1.0 (ref.)	0.95 (0.84, 1.08)	1.00 (0.89, 1.13)	1.02 (0.90, 1.14)	1.05 (0.93, 1.19)	0.297	1.03 (0.97 to 1.09)
Non-fatal MI	Model 1	1.0 (ref.)	0.98 (0.84, 1.16)	1.13 (0.98, 1.32)	1.15 (0.99, 1.33)	1.21 (1.04, 1.41)	0.003	1.11 (1.04 to 1.19)
	Model 2	1.0 (ref.)	0.94 (0.80, 1.11)	1.05 (0.90, 1.22)	1.03 (0.88, 1.20)	1.03 (088, 1.21)	0.51	1.03 (0.95 to 1.11)
Non-fatal AIS	Model 1	1.0 (ref.)	1.02 (0.85, 1.22)	1.05 (0.88, 1.25)	1.13 (0.95, 1.34)	1.29 (1.08, 1.53)	0.002	1.14 (1.05 to 1.23)
	Model 2	1.0 (ref.)	0.98 (0.82, 1.18)	0.98 (0.82, 1.17)	1.02 (0.85, 1.22)	1.10 (0.91, 1.32)	0.295	1.05 (0.96 to 1.15)

Model 1 and 2 (same as note of table 2).
AIS, acute ischaemic stroke; CVD, cardiovascular disease; MI, myocardial infarction.

0.84, 95% CI 0.80 to 0.88) for hPDI, while a 10-unit increment in uPDI was associated a 7% increase in the risk of CVD (HR 1.07, 95% CI 1.03 to 1.12) (table 2).

We found similar associations of hPDI with subtypes of CVD. A 10-unit increment in hPDI was associated with HRs (95% CI) of 0.81 (0.75 to 0.87) for fatal CVD, 0.86 (0.79 to 0.94) for non-fatal MI and 0.86 (0.78 to 0.95) for non-fatal AIS. We identified a significant positive association of uPDI with risk of fatal CVD (HR per 10-unit increment=1.12; 95% CI 1.05 to 1.20; P trend<0.001, table 3).

We observed linear dose–response association between PDI and the risk of CVD in both European Americans and African Americans (both Ps for linear trend<0.001, figure 1). The association between PDIs and CVD was consistent across subgroups defined by sex, smoking status, body weight status, family income and baseline health conditions. There was no evidence of significant interaction between the dietary indices and the stratification variables (all p values for interaction>0.05, figure 2).

DISCUSSION

In this large cohort of US veterans, we observed that overall plant-based diet was significantly associated with a lower risk of CVD, which was consistent across racial/ethnic groups. We also assessed participants' adherence to two plant-based dietary patterns that distinguished the healthfulness of plant foods. A healthful plant-based diet was significantly associated with a lower risk of total CVD, while a greater adherence to an unhealthful plant-based

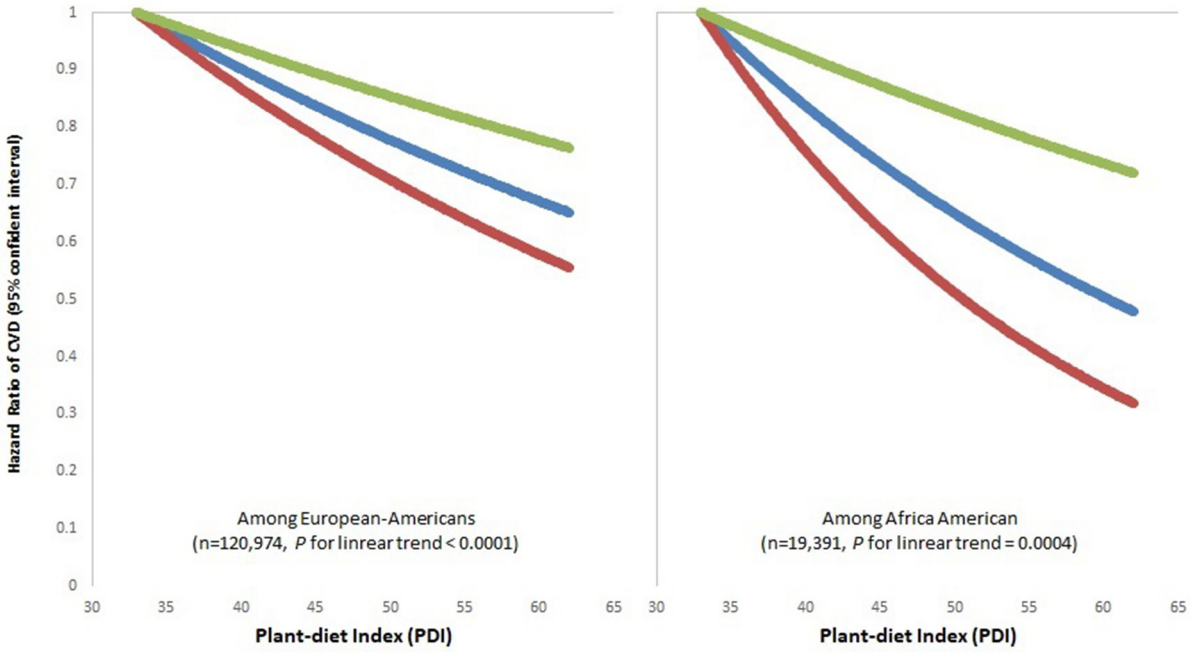

Figure 1 Dose–response relationship between PDI and cardiovascular diseases (CVD) in the entire study population and subgroups of European Americans, African American and other racial/ethnic participants. Dose–response relationship between PDI and CVD was estimated by restricted cubic spline Cox proportional-hazards model adjusted for age (continuous), sex (male or female), race/ethnicity (European Americans, African American or other, only for ALL), education level (≤high school or GED, some colleague or college or above), income level (<US$30 000, US$30 000–US$59 000 or ≥US$60 000) and marital status (currently married or not), smoking status(current, former or never smoking), frequency of alcohol consumption (never, <1 times/week or ≥1 times/week), frequency of exercise vigorously (never/rarely, 1–4 times/month, 2–4 times/week or ≥5 times/week), total energy intake, fruit, vegetable and sugar sweetened beverage (all in quintiles), body mass index (<23.0, 23.0–24.9, 25.0–29.9, 30.0–34.9 or ≥35.0 kg/m^2) and histories of hypertension and hypercholesterolaemia at baseline (yes vs no). The dose–response relationship was quantified by Cox proportional hazards models with restricted cubic spline with three knots specified. The first percentile of each dietary score was used as reference level for calculating HRs. We tested non-linearity in the dose–response relationship of the dietary indices with the risk of CVD by comparing the model with only the linear term to the model with the linear and the cubic spline terms and using the likelihood ratio test (blue line: HR between PDI and CVD; green line: upper 95% CI of HR; red line: lower 95% CI of HR). GED, General Educational Development.

diet was associated with a greater risk of CVD. The inverse association of a healthy plant-based diet with CVD endpoint was consistent for both MI and AIS.

Our findings were consistent with previous cohort studies that defined plant-based diets dichotomously (ie, 'vegetarian' vs 'non-vegetarian') in which vegetarian diets showed protective associations with CVD morbidity and mortality compared with non-vegetarian diets.[5 10] Recent systematic review and meta-analysis indicated that vegetarian diets, compared with omnivorous diets, were associated with beneficial effects on various pathways underlying CVD, such blood pressure reduction,[4] weight loss and modulation of blood lipids,[5 10] supporting the biological plausibility of an important role of plant-based diet in the dietary prevention of CVDs.[5] However, studies that examined associations between plant-based diets and stroke mortality largely yielded null results.[5 10] More recently, the EPIC-Oxford study found a significantly higher risk of stroke among vegetarians as compared with meat eaters in a UK population.[11] In contrast, our study found a significant inverse association between a plant-based diet enriched with healthier plant foods and risk of stroke, which is consistent with the Tzu χ Health Study and the Tzu χ Vegetarian Study that reported a significantly lower risk of stroke among Taiwanese vegetarians.[31] The discrepancies in these findings might be due to the fact that the prior studies essentially treated all plant foods equally and did not distinguish the quality of plant foods. It has been clear that several food groups, especially those with high glycaemic index and load, although plant-sourced, were associated with higher risk of chronic diseases.[13]

Our study added to the evidence base by applying dietary indices capable of quantifying the gradient of adherence to plant-based diets.[1 21] The PDIs mimicked gradual reductions in animal food intake with concomitant increases in consumption of plant foods. While hPDI positively weighed healthy plant foods (eg, whole grains, fruits, vegetables, nuts, legumes) and negatively weighed less healthy plant foods (eg, refined grains, potatoes, sugar-sweetened beverages) and animal foods, uPDI positively weighed less healthy plant foods and negatively weighed healthy plant foods and animal foods. Compared with vegetarian diets that partially or fully excluded certain foods, a healthful plant-based diet with gradual changes

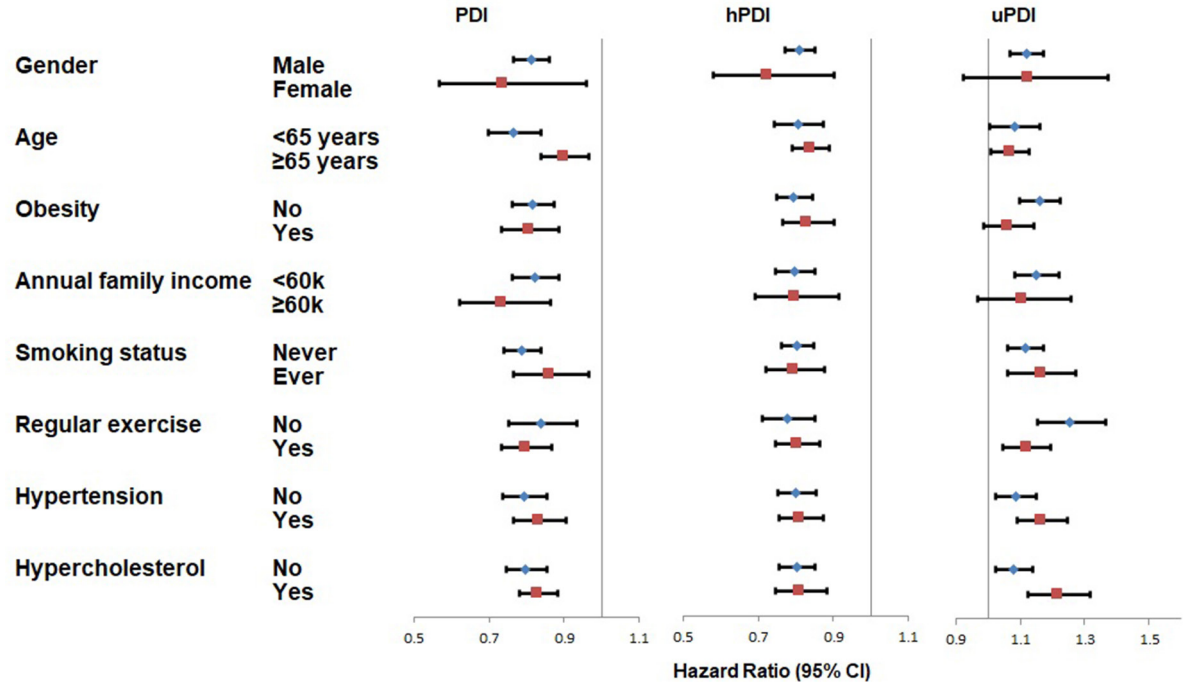

Figure 2 Association of plant-based diet indexand cardiovascular diseases in subgroups. Models adjusted for age (continuous) and sex (male or female), race/ethnicity (European Americans, African American or other), education level (≤high school or GED, some colleague or college or above), income level (<US$30,000, US$30 000–US$59 000 or ≥US$60 000) and marital status (currently married or not), smoking status(current, former or never smoking), frequency of alcohol consumption (never, <1 times/week or ≥1 times/week), frequency of exercise vigorously (never/rarely, 1–4 times/month, 2–4 times/week or ≥5 times/week), total energy intake (in Quintiles), body mass index (<23.0, 23.0–24.9, 25.0–29.9, 30.0–34.9 or ≥35.0 kg/m^2) and histories of hypertension and hypercholesterolaemia at baseline (yes vs no) except the variables of stratification. GED, General Educational Development; hPDI, healthful PDI; PDI, Plant-Based Diet Index; uPDI, unhealthful PDI.

to healthy plant-based diet without necessarily excluding any food group would be flexible, desirable and easier to implement because it allows individuals to make gradual changes to their diets. Such as in a population, if anyone ate foods in amount of median level of all 16 food groups, then he/she would have all PDIs score of 48 (3 for each food group whether positively or negatively ranking). We could improve the hPDI from 48 to 52 by increasing the legume and nuts intake from median to quintile 4 levels and reduce the red meat intake and the refine grain intakes from median to quintile 2 levels, no need to be exclusive of any food.[6 15 21 32] While, for a vegetarian diet, we could substitute unhealthy plant foods with healthy plant foods to improve the dietary quality, just less flexible with less foods to choose. Our findings in this US veteran population with diverse socioeconomic and racial/ethnic backgrounds were consistent with the findings of three large cohort studies of US health professionals that reported lower CVD risk with plant-based diets.[1 12] Our findings were also in line with studies applying the same PDIs that found a greater adherence to hPDI was associated with significantly lower risk of weight gain,[21] diabetes,[6] as well as total and cardiovascular mortality[15]; whereas the associations for uPDI were in the opposite direction: greater adherence to uPDI was associated with significantly more weight gain,[21] and significantly higher risk of diabetes,[6] total and cardiovascular mortality.[15]

Strengths of our study include the prospective design with a large sample size, a large number of confirmed cases, careful adjustment for many potential confounders and the generalisability of our findings to populations with diverse socioeconomic and racial/ethnic backgrounds. We acknowledge several limitations. First, our study population was only veterans of MVP, with comparable demographic characteristic to the national data from the Veterans Health Administration[23 33]; but had a relatively higher proportion of elders than the general US population[34] and the majority of the study population were male. However, we did not observe and would not expect measures of effect to be different across populations and genders, though the magnitude of effect may vary considerably given potential differences in the prevalence of the PDI scores, and more easily accessed counselling and health services by VA members in comparison to other US populations. Also, although the majority of Veterans were male, we had data on 17 674 women to show a similar relation. Second, we were limited to a single assessment of dietary intake, change in dietary habits over time was not assessed, and measurement errors in dietary assessment are inevitable. However, we applied sFFQ, a tool that best captures long-term usual diet, to measure dietary intake. Third, considering the high prevalence of chronic diseases of study population at baseline, participants who were concerned about a serious illness might

change towards a diet generally perceived to be healthier, which may potentially bias the results. However, this would be less of a concern as we excluded participants with major chronic disease at baseline and performed statistical adjustment for hypertension and dyslipidaemia. Fourth, the ascertainment of MI and AIS events may not be complete, as we lack information on CVD events that occurred in non-VA hospitals, although VA health records typically documented the event when the Veteran returned to the VA Healthcare System for follow-up care. However, this limitation likely led to conservative effect estimates of the associations between the dietary indices and CVD endpoints. Lastly, we were not able to examine the association between PDIs and haemorrhagic stroke, which will be undertaken in a future project.

In conclusion, in this large cohort of US veterans, significantly lower risk of incident cardiovascular events, including fatal CVD, non-fatal MI and non-fatal AIS in participants who consumed a dietary pattern enriched with plant foods, particularly healthy plant foods such as whole grains, whole fruit and vegetables. However, adherence to a plant-based dietary pattern that includes many unhealthy plant foods, such as sugar-sweetened beverages and refined grains, could lead to higher risk of fatal CVD. These findings support recommending plant-based diet rich in healthier plant foods for the prevention of CVD.

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Competing interests None declared.

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Ethics approval This study involves human participants and was approved by ethics committee(s) or institutional board(s): VA Central Institutional Review BoardID: MVP000. The study was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures involving research study participants were approved by the VA Central Institutional Review Board, Washington DC (protocol: MVP000, date of approval: 2010). Participants gave informed consent to participate in the study before taking part.

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Data availability statement Data cannot be shared publicly because of VA policies regarding data privacy and security. Data contain potentially identifying and sensitive patient information. All relevant summary level data are included in the manuscript. For investigators with appropriate authorisations within the Department of Veterans Affairs, requests for data access can be made.

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