




Degree of adherence to plant-based diet and total and cause-specific mortality: prospective cohort study in the Million Veteran Program

Dong D Wang^{1,2,3,*}, Yanping Li^{1,3} , Xuan-Mai T Nguyen^{1,4,5}, Rebecca J Song^{1,6}, Yuk-Lam Ho¹, Frank B Hu^{2,3,7}, Walter C Willett^{2,3,7}, Peter Wilson^{8,9}, Kelly Cho^{1,4,5}, J Michael Gaziano^{1,4,5}, Luc Djoussé^{1,3,4,5} and on behalf of the Million Veteran Program

¹Massachusetts Veterans Epidemiology Research and Information Center (MAVERIC), VA Boston Healthcare System, Boston, MA, USA; ²The Channing Division of Network Medicine, Department of Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, MA 02115, USA; ³Departments of Nutrition, Harvard T. H. Chan School of Public Health, Boston, MA, USA; ⁴Department of Medicine, Division of Aging, Brigham and Women's Hospital, Boston, MA, USA; ⁵Harvard Medical School, Boston, MA, USA; ⁶Department of Epidemiology, Boston University School of Public Health, Boston, MA, USA; ⁷Department of Epidemiology, Harvard T. H. Chan School of Public Health, Boston, MA, USA; ⁸Atlanta VA Medical Center, Atlanta, GA, USA; ⁹Emory Clinical Cardiovascular Research Institute, Atlanta, GA, USA

Submitted 2 September 2021: Final revision received 28 February 2022: Accepted 14 March 2022: First published online 21 March 2022

Abstract

Objective: To examine the association between adherence to plant-based diets and mortality.

Design: Prospective study. We calculated a plant-based diet index (PDI) by assigning positive scores to plant foods and reverse scores to animal foods. We also created a healthful PDI (hPDI) and an unhealthful PDI (uPDI) by further separating the healthy plant foods from less-healthy plant foods.

Setting: The VA Million Veteran Program.

Participants: 315 919 men and women aged 19–104 years who completed a FFQ at the baseline.

Results: We documented 31 136 deaths during the follow-up. A higher PDI was significantly associated with lower total mortality (hazard ratio (HR) comparing extreme deciles = 0.75, 95 % CI: 0.71, 0.79, $P_{\text{trend}} < 0.001$). We observed an inverse association between hPDI and total mortality (HR comparing extreme deciles = 0.64, 95 % CI: 0.61, 0.68, $P_{\text{trend}} < 0.001$), whereas uPDI was positively associated with total mortality (HR comparing extreme deciles = 1.41, 95 % CI: 1.33, 1.49, $P_{\text{trend}} < 0.001$). Similar significant associations of PDI, hPDI and uPDI were also observed for CVD and cancer mortality. The associations between the PDI and total mortality were consistent among African and European American participants, and participants free from CVD and cancer and those who were diagnosed with major chronic disease at baseline.

Conclusions: A greater adherence to a plant-based diet was associated with substantially lower total mortality in this large population of veterans. These findings support recommending plant-rich dietary patterns for the prevention of major chronic diseases.

Keywords
Plant-based diet
Mortality
Public health

What is already known on this topic?

Previous studies support the benefits of consuming plant-based diets for preventing cardiometabolic diseases such as coronary heart disease and type 2 diabetes and

intermediate outcomes including obesity and adiposity-associated plasma biomarkers. However, studies on plant-based diets and mortality have been inconclusive and limited, especially for findings on cause-specific mortality due to cardiovascular disease and cancer.

*Corresponding author. Email dow471@mail.harvard.edu

© The Author(s), 2022. Published by Cambridge University Press on behalf of The Nutrition Society. This is an Open Access article, distributed under the terms of the Creative Commons Attribution licence (<https://creativecommons.org/licenses/by/4.0/>), which permits unrestricted re-use, distribution, and reproduction in any medium, provided the original work is properly cited.



What this study adds

We found an inverse association between adherence to plant-based diets and mortality in a large cohort of US veterans. The association was stronger for the plant-based diet that emphasised healthy plant foods, and the risk of mortality was significantly elevated in participants with greater adherence to a plant-based diet that emphasised less-healthy plant foods. Our findings supported current dietary guidelines to increase intake of healthy plant foods at the expense of less-healthy plant foods and certain animal foods.

Plant-based diets are defined as a low frequency of consumption of animal foods and higher consumption of plant foods⁽¹⁾. Previous studies support the benefits of consuming plant-based diets for preventing cardiometabolic disease end points such as coronary heart disease (CHD) and type 2 diabetes and intermediate outcomes including obesity and adiposity-associated plasma biomarkers^(2–8). Various authorities, including the American Heart Association (AHA)⁽⁹⁾ and the 2015 Dietary Guidelines for Americans⁽¹⁰⁾, recommend diets rich in plant foods to prevent major chronic diseases. To address the role of plant-based diets in overall health, analysis of total and cause-specific mortality as outcomes would be informative. However, studies on plant-based diets and mortality have been inconclusive and limited, especially for findings on cause-specific mortality due to cardiovascular disease (CVD) and cancer^(6,8,11–13).

Earlier studies defined plant-based diets dichotomously as ‘vegetarian’ *v.* ‘non-vegetarian’ by completely excluding certain groups of (e.g. red meat and poultry) or all animal foods^(7,8). However, it is challenging to study the health effects of vegetarian diets in US populations given the very low prevalence of vegetarianism (approximately 3%)⁽¹⁴⁾. Alternatively, several recent studies employed *a priori* defined dietary indices to examine gradations of adherence to a plant-based diet^(2,3,15). The advantage of the indices is their broader applicability in US populations because recommendations of moderate, incremental dietary changes towards vegetarianism may be easier to adopt than more extreme, complete exclusion of animal foods. In addition, earlier investigations of vegetarian diets did not distinguish plant foods with divergent health effects, despite the fact that certain plant foods, such as refined grains⁽¹⁶⁾, potatoes^(17–19) and sugar-sweetened beverages^(20,21), were associated with an elevated risk of CVD, diabetes and mortality. To overcome this limitation, Satija *et al.* developed three plant-based diet indices (PDI), an overall PDI, a healthful PDI (hPDI) and an unhealthful PDI (uPDI), to assess the adherence to plant-based diets with consideration of the quality of plant foods and linked the indices to the risk of type 2 diabetes and CHD in health professional populations^(2,3,6). However, the earlier studies were conducted in populations that consist of older and predominantly White participants,

mostly women and relatively high socio-economic status^(2–6). To address the limitations of the previous studies, we conducted this study in the VA Million Veteran Program (MVP), a newly launched prospective cohort study that consists primarily of male participants with a wide age range (19–104 years) and diverse socio-economic and racial/ethnic backgrounds. We hypothesise that PDI, hPDI and uPDI are divergently associated with total and cause-specific mortality in more than 0.3 million MVP participants with detailed dietary information.

Methods

Study population

MVP is a nationally representative, prospective cohort study of veterans designed to study genetic and non-genetic determinants of chronic diseases. MVP combines data from self-reported surveys, electronic health records and biospecimens. Details of the study design of MVP can be found elsewhere⁽²²⁾. The enrolment of MVP participants began in 2011. As of 2020, 790 116 veterans were enrolled, and 351 892 participants have completed the baseline diet and lifestyle survey. Information on age, sex, race, education, body weight and height, alcohol consumption, physical activity and smoking status was collected through a self-reported survey at baseline. Health conditions, co-morbidities and medication use were obtained through Veterans Health Administration (VHA) electronic health records. We defined the baseline of this study as the time a participant completed the first lifestyle survey and the end of follow-up as the end of December 2018. All participants signed informed consent, and the Veterans Affairs Central Institutional Review Board approved the study protocol. We first excluded participants who did not provide dietary information, reported implausible dietary data (total energy intake < 1674 or > 16 736 kJ/d) or had more than 30 blanks on semi-quantitative food frequency questionnaire (SFFQ) at baseline. After this exclusion, a total of 327 480 participants were included. We then excluded 11 561 participants with relatively short follow-up, that is, those who responded to the lifestyle questionnaire after 2018. After the exclusions, the study population consisted of 315 919 participants (see online supplementary material, Supplementary Fig. 1).

Dietary assessment

Dietary information was collected at baseline with an extensively validated SFFQ of sixty-one food items⁽²³⁾. We asked how often, on average, the participant had consumed a specified portion size of each food over the preceding year on the SFFQ, with nine prespecified responses: ‘never or less than once a month’, ‘1–3 per month’, ‘once a week’, ‘2–4 per week’, ‘5–6 per week,



'once a day', '2–3 per day', '4–5 per day' and '6+ per day'. We converted frequencies and portions of each food item to the average daily intake for each participant. We then calculated the average daily total energy intake by multiplying the frequency of consumption of each item by its energy content from the Harvard University Food Composition Database⁽²⁴⁾ and summing across all foods. The SFFQ demonstrated reasonably well validity in assessing intakes of individual foods in our previous validation studies in the Health Professionals Follow-Up Study (HPFS) and the Nurses' Health Study (NHS)^(25,26). For example, the average Pearson correlation coefficients corrected for within-person weekly variation comparing SFFQ-measured intakes to those measured by multiple 7-d food records (7DDR) ranged from 0.45 for nuts to 0.85 for tea/coffee in the HPFS⁽²⁵⁾. In addition, we recently validated SFFQ-measured PDI against the indices measured by 7DDR; the correlations were 0.63 for PDI, 0.78 for hPDI and 0.73 for uPDI in the NHS, and 0.65 for PDI, 0.74 for hPDI and 0.77 for uPDI in the HPFS⁽²⁷⁾.

Definitions of plant-based diet indices

We applied the overall PDI, hPDI and uPDI to quantify each participant's gradations of adherence to plant-based diets. Details of these indices can be found in our previous publications⁽³⁾. Briefly, we created sixteen food groups based on nutrient and culinary similarities of individual foods (see online supplementary material, Supplemental Table 1). The categorisation of healthy and less-healthy plant foods was based on the most recent empirical evidence of their associations with cardiometabolic disease (type 2 diabetes and CVD), certain cancers and intermediate conditions (obesity, hypertension, lipids and inflammation)^(10,17–21). All food groups within the same categories were given equal weight regardless of the strength of the evidence or the association of the individual foods with chronic disease risk. Healthy plant food groups included whole grains, fruits, vegetables, nuts, legumes and tea/coffee. Less-healthy plant food groups included fruit juices, sugar-sweetened beverages, refined grains, potatoes and sweets/desserts. Animal food groups included butter and lard, dairy, eggs, fish/seafood and meat (poultry and red meat). Third, we calculated quintiles of intake for each of the sixteen food groups and assigned component scores for each food group. For PDI, participants received 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. 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. Finally, we summed up component

scores across the sixteen food groups to obtain the indices with the theoretical range of each index ranging from 16 to 80.

Outcome ascertainment

The primary outcome of this study was total mortality. Deaths were identified through the National Death Index⁽²⁸⁾. We defined three cause-specific mortality outcomes: deaths due to CVD, cancer (non-metastatic skin cancers excluded) and other causes. CVD mortality was defined based on the International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) codes I00 to I99. Cancer mortality was defined based on ICD-10-CM codes C00–C97.

Statistical analysis

We categorised PDI, hPDI and uPDI into deciles based on their population distributions. Person-years of follow-up were calculated from baseline to the earliest time of death, loss to follow-up or the end of follow-up (which was December 2018). Cox proportional hazards models were applied to estimate hazard ratios (HR) and their 95% CI of mortality, comparing participants in each category to the lowest category of a dietary index with simultaneous adjustment for covariables. For cause-specific mortality, we performed competing risk analysis using Cox proportional hazards models with a data augmentation method⁽²⁹⁾. Multivariable model was adjusted for age (years: < 60, 60–70, > 70) and sex (male or female), race/ethnicity (non-Hispanic European American, African American or other), education level (\leq high school or GED, some college or college or above), income level (< \$30 000, \$30 000–\$59 000 or \geq \$60 000) and marriage status (currently married or not), smoking status (current, former or never smoking), frequency of alcohol consumption (never, < 1 times/week or \geq 1 times/week), frequency of exercise vigorously (never/rarely, 1–4 times/month, 2–4 times/week or \geq 5 times/week), total energy intake (in quintiles) and BMI (<23.0, 23.0–24.9, 25.0–29.9, 30.0–34.9 or \geq 35.0 kg/m²). In a separate model, we additionally adjusted for histories of hypertension, hypercholesterolemia, diabetes, cancer and CVD at baseline.

We used the median within each decile as a score variable and included it as a continuous variable in the model to quantify a linear trend; the Wald test was used for calculating *P*-values for linear trend. We also modelled the dietary indices continuously and calculated HR associated with every 10-unit increment in PDI, hPDI and uPDI. For example, an increase in nut and legume intake from 0 to 1 serving/d or a reduction in red and processed meat consumption from 1.5 servings to little consumption per d will result in a 10-unit improvement in the indices. To quantify non-linear dose–response relationship, restricted cubic splines with three knots were applied to flexibly model the association between the dietary indices and risk of

mortality with the first percentile of each dietary score as the reference level⁽³⁰⁾. We tested non-linearity in the dose–response relationship of the dietary indices with mortality by comparing the model with the linear term to the model with the linear and cubic spline terms using the likelihood ratio test.

We repeated the analyses on the associations of PDI scores with total mortality in European and African American groups separately and among participants who were free from and with histories of major chronic diseases, including diabetes, CVD and cancer at baseline. In addition, we conducted secondary analyses to test the robustness of our findings by examining the associations of PDI, hPDI and uPDI with total mortality in subgroups defined by smoking status, baseline age, baseline BMI and baseline histories of CVD, cancer, hypercholesterolemia, diabetes and hypertension. In another sensitivity analysis, we quantified associations of dietary scores with total mortality after excluding deaths within the first year of follow-up and participants with less than 1-year follow-up. The data analyses were performed using SAS software version 9.4 (SAS Institute, North Carolina) at a two-tailed α value of 0.05.

Patient and public involvement

This research was done without patient involvement. Patients and the public were not invited to comment on the study design and were not consulted to develop patient-relevant outcomes or interpret the results. Patients and the public were not invited to contribute to the writing or editing of this document for readability or accuracy. The study did not receive funds to train or involve members of the community in the study design or interpretation of the results.

Results

Population characteristics

During a mean follow-up of 4 years, we documented 31 136 deaths, including 9751 deaths due to CVD, 9510 deaths due to cancer and 11 875 deaths due to other causes. At baseline, the study population had a mean age of 65.5 years (age range: 19 to 104 years) and consisted of 91.9% men and 9.9% African Americans (Table 1). Compared to the participants with a lower PDI, participants with a higher PDI were older, more physically active, and less likely to smoke, drink alcohol and have diabetes and hypertension. They also had higher education and income levels and a lower BMI at baseline.

Total mortality

PDI was inversely associated with total mortality after multivariable adjustment for known and suspected

confounding variables and risk factors (HR comparing extreme deciles = 0.75, 95% CI: 0.71, 0.79, $P_{\text{trend}} < 0.001$; Table 2). Every 10-unit increment in PDI was associated with a 13% lower total mortality (HR = 0.87, 95% CI: 0.85, 0.89). Compared to the association for PDI, the inverse association of hPDI with total mortality was stronger; the highest decile of hPDI was associated with an HR of 0.64 (95% CI: 0.61, 0.68, $P_{\text{trend}} < 0.001$) compared to the lowest decile. For uPDI, we observed a significant positive association with total mortality (HR comparing extreme deciles = 1.41, 95% CI: 1.33, 1.49, $P_{\text{trend}} < 0.001$). When modelled continuously, every 10-unit increment in hPDI was associated with an HR of 0.81 (95% CI: 0.80, 0.83), whereas every 10-unit increment in uPDI was associated with an HR of 1.15 (95% CI: 1.13, 1.17). We observed slightly stronger associations for PDI, hPDI and uPDI in a subpopulation free from diabetes, CVD and cancer at baseline; the HR (95% CI) of total mortality associated with a 10-unit increment in the indices were 0.82 (0.79, 0.86) for PDI, 0.79 (0.77, 0.83) for hPDI and 1.15 (1.11, 1.19) for uPDI (see online supplementary material, Supplemental Table 2). We found similar but slightly attenuated associations of PDI, hPDI and uPDI with total mortality in participants with baseline histories of diabetes, CVD and cancer (Fig. 1). The associations between the dietary indices and total mortality were not materially different between European American and Africa American participants (Fig. 2): P for interaction between the dietary indices and racial groups (European American or Africa American) was 0.03 for PDI, 0.39 for hPDI and 0.79 for uPDI. In addition, the associations between the dietary indices and total mortality in Hispanic participants were comparable to those in the overall study population (see online supplementary material, Supplemental Fig. 2). The observed associations were generally consistent across subgroups defined by sex, age, family income, smoking status, alcohol consumption, physical activity level, weight status, and baseline histories of hypertension and hypercholesterolemia (see online supplementary material, Supplemental Fig. 2). In a sensitivity analysis that excluded deaths occurring during the first year of follow-up and participants who were followed for less than 1 year, the associations of PDI, hPDI and uPDI with mortality risks were similar to those in the primary analyses (see online supplementary material, Supplemental Table 3).

Cause-specific mortality

The PDI was inversely associated with cancer mortality (HR per 10-unit increment = 0.85, 95% CI: 0.82, 0.88, $P_{\text{trend}} < 0.0001$) and CVD mortality (HR per 10-unit increment = 0.88, 95% CI: 0.85, 0.91, $P_{\text{trend}} < 0.0001$, Table 3). A higher hPDI was significantly associated with lower mortality due to CVD (HR comparing extreme deciles = 0.69, 95% CI: 0.63, 0.76, $P_{\text{trend}} < 0.001$) and

**Table 1** Baseline characteristics of 315 919 participants in the Million Veteran Program across deciles of plant-based diet indices

| | Deciles of plant-based diet indices | | | | | |
|-------------------------------------|-------------------------------------|-----------|----------|-----------|----------|-----------|
| | PDI | | hPDI | | uPDI | |
| | Decile 1 | Decile 10 | Decile 1 | Decile 10 | Decile 1 | Decile 10 |
| <i>n</i> | 34510 | 27498 | 34736 | 29651 | 30746 | 27976 |
| PDI | 37.6 | 59.3 | 45.7 | 51.6 | 48.1 | 47.5 |
| uPDI | 48.7 | 47.6 | 52.4 | 43.7 | 35.4 | 61.6 |
| hPDI | 44.8 | 50.9 | 36.3 | 59.6 | 51.7 | 43.9 |
| Age, years | 64.7 | 66.9 | 64.4 | 66.0 | 65.9 | 64.0 |
| Men, % | 91.7 | 92.5 | 94.2 | 88.2 | 89.6 | 91.7 |
| European American, % | 83.0 | 86.1 | 83.7 | 85.7 | 88.6 | 82.6 |
| Married, % | 55.6 | 64.6 | 58.5 | 60.1 | 64.7 | 54.2 |
| Education level, % | | | | | | |
| ≤High school or GED | 27.4 | 20.2 | 28.1 | 18.5 | 14.7 | 33.3 |
| Some colleague | 31.4 | 28.4 | 31.6 | 27.3 | 27.9 | 30.3 |
| College or above | 41.3 | 51.4 | 40.3 | 54.2 | 57.4 | 36.4 |
| Annual family income, % | | | | | | |
| <\$30 000 | 37.1 | 32.9 | 37.9 | 31.9 | 28.1 | 41.1 |
| \$30 000–\$59 000 | 35.1 | 36.3 | 36.3 | 34.3 | 34.5 | 35.7 |
| ≥\$60 000 | 27.9 | 30.9 | 25.8 | 33.8 | 37.4 | 23.2 |
| Smoking status, % | | | | | | |
| Current smoking | 6.1 | 5.3 | 7.3 | 4.3 | 5.1 | 7.0 |
| Former smoker | 65.7 | 63.2 | 64.3 | 63.9 | 64.7 | 62.8 |
| Never smoking | 28.2 | 31.5 | 28.4 | 31.8 | 30.2 | 30.2 |
| Frequency of exercise vigorously, % | | | | | | |
| Never/rarely | 38.3 | 23.3 | 38.3 | 22.7 | 20.7 | 43.6 |
| 1–4 times/month | 25.5 | 24.4 | 26.8 | 21.8 | 23.1 | 25.3 |
| 2–4 times/week | 24.6 | 34.1 | 23.8 | 34.9 | 36.9 | 21.0 |
| ≥ 5 times/week | 11.7 | 18.2 | 11.1 | 20.6 | 19.3 | 10.2 |
| Frequency of alcohol drinking, % | | | | | | |
| Never | 42.0 | 44.5 | 44.9 | 44.4 | 36.9 | 51.3 |
| <1 times/week | 25.2 | 26.5 | 27.2 | 25.5 | 27.0 | 25.8 |
| ≥1 times/week | 32.8 | 28.9 | 27.9 | 30.2 | 36.1 | 22.9 |
| BMI, kg/m ² | 29.6 | 27.5 | 28.8 | 28.0 | 29.2 | 28.2 |
| Diabetes, % | 28.2 | 17.2 | 19.8 | 24.8 | 29.9 | 17.5 |
| Hypertension, % | 58.0 | 52.5 | 53.6 | 53.7 | 56.6 | 52.6 |
| Hypercholesterolemia, % | 50.2 | 50.4 | 47.2 | 52.0 | 51.6 | 47.5 |
| Cancer, % | 24.7 | 28.9 | 25.7 | 27.0 | 28.3 | 23.9 |
| Cardiovascular disease, % | 23.9 | 23.6 | 23.2 | 22.8 | 22.1 | 23.6 |
| Food intake, servings/d | | | | | | |
| Whole grains | 0.2 | 0.7 | 0.2 | 0.5 | 0.7 | 0.1 |
| Fruit | 0.6 | 2.1 | 0.9 | 2.0 | 2.2 | 0.5 |
| Vegetables | 0.8 | 2.2 | 0.9 | 2.0 | 2.6 | 0.4 |
| Nuts | 0.2 | 0.7 | 0.3 | 0.6 | 0.7 | 0.2 |
| Legume | 0.2 | 0.8 | 0.3 | 0.7 | 0.9 | 0.2 |
| Tea or coffee | 1.2 | 2.3 | 1.2 | 2.2 | 2.5 | 0.9 |
| Fruit juice | 0.1 | 0.5 | 0.4 | 0.1 | 0.2 | 0.3 |
| Sugar-sweetened beverages | 0.2 | 0.6 | 0.9 | 0.1 | 0.1 | 0.8 |
| Refined grains | 0.5 | 1.3 | 1.4 | 0.5 | 0.7 | 1.0 |
| Potatoes | 0.3 | 0.8 | 0.9 | 0.3 | 0.4 | 0.6 |
| Sweets and cake | 0.3 | 1.3 | 1.3 | 0.4 | 0.6 | 1.0 |
| Butter | 0.5 | 0.2 | 0.7 | 0.1 | 0.7 | 0.2 |
| Dairy | 1.7 | 1.6 | 2.2 | 1.1 | 2.3 | 1.0 |
| Eggs | 0.6 | 0.3 | 0.6 | 0.3 | 0.8 | 0.2 |
| Fish | 0.2 | 0.2 | 0.2 | 0.2 | 0.3 | 0.1 |
| All meat | 1.7 | 1.7 | 2.4 | 1.0 | 2.2 | 1.2 |
| Chicken | 0.5 | 0.5 | 0.6 | 0.4 | 0.8 | 0.3 |
| Red meat | 0.7 | 0.7 | 1.1 | 0.4 | 0.9 | 0.5 |
| Processed meat | 0.5 | 0.4 | 0.7 | 0.2 | 0.5 | 0.3 |

PDI, plant-based diet index; hPDI, healthful PDI; uPDI, unhealthful PDI.
Unless otherwise indicated, data are expressed as means.

cancer (HR comparing extreme deciles = 0.67, 95% CI: 0.61, 0.74, $P_{\text{trend}} < 0.001$). We found significant positive associations between uPDI and both CVD and cancer mortality. Across extreme deciles, the uPDI was associated with CVD mortality (HR = 1.41 (95% CI: 1.28, 1.55,

$P_{\text{trend}} < 0.001$) and cancer mortality (HR = 1.36 (95% CI: 1.24, 1.50, $P_{\text{trend}} < 0.001$). In a sensitivity analysis, we examined the associations of PDI with the risk of death due to specific cancer types (see online supplementary material, Supplemental Table 4). The associations with

Table 2 Association of plant-based diet indices with total mortality in 315 919 participants from the Million Veteran Program

| | Deciles of plant-based diet indices | | | | | | | | | | | | | | | | | | | HR per 10-unit increment | | | |
|------------------------------------|-------------------------------------|---------|------------|---------|------------|---------|------------|---------|------------|---------|------------|---------|------------|---------|------------|---------|------------|---------|------------|--------------------------|---------------------------|------------|--------|
| | D1 | | D2 | | D3 | | D4 | | D5 | | D6 | | D7 | | D8 | | D9 | | D10 | | <i>P</i> _{trend} | HR | 95% CI |
| | HR | 95% CI | HR | 95% CI | HR | 95% CI | HR | 95% CI | HR | 95% CI | HR | 95% CI | HR | 95% CI | HR | 95% CI | HR | 95% CI | | | | | |
| Plant-based diet index | | | | | | | | | | | | | | | | | | | | | | | |
| Median | 38 | 42 | | 44 | | 46 | | 48 | | 49 | | 50 | | 52 | | 55 | | 59 | | | | | |
| Deaths | 3500 | 2374 | | 3053 | | 3634 | | 3945 | | 1874 | | 3597 | | 3048 | | 3342 | | 2769 | | | | | |
| PY | 124 765 | 88 673 | | 118 051 | | 142 841 | | 154 256 | | 77 511 | | 147 355 | | 125 608 | | 137 259 | | 115 365 | | | | | |
| Model 1 | Ref. | 0.94 | 0.90, 0.99 | 0.88 | 0.84, 0.93 | 0.85 | 0.81, 0.89 | 0.85 | 0.81, 0.89 | 0.79 | 0.75, 0.84 | 0.78 | 0.75, 0.82 | 0.77 | 0.73, 0.80 | 0.75 | 0.72, 0.79 | 0.71 | 0.67, 0.74 | <0.0001 | 0.84 | 0.83, 0.86 | |
| Model 2 | Ref. | 0.96 | 0.91, 1.01 | 0.90 | 0.86, 0.95 | 0.88 | 0.84, 0.92 | 0.88 | 0.84, 0.92 | 0.82 | 0.78, 0.87 | 0.81 | 0.77, 0.85 | 0.79 | 0.76, 0.84 | 0.78 | 0.74, 0.82 | 0.72 | 0.68, 0.76 | <0.0001 | 0.85 | 0.84, 0.87 | |
| Model 3 | Ref. | 0.96 | 0.91, 1.01 | 0.91 | 0.87, 0.96 | 0.89 | 0.85, 0.94 | 0.89 | 0.85, 0.93 | 0.84 | 0.79, 0.89 | 0.83 | 0.79, 0.87 | 0.82 | 0.78, 0.86 | 0.80 | 0.76, 0.84 | 0.75 | 0.71, 0.79 | <0.0001 | 0.87 | 0.85, 0.89 | |
| Healthful plant-based diet index | | | | | | | | | | | | | | | | | | | | | | | |
| Median | 37 | 41 | | 44 | | 46 | | 47 | | 48 | | 50 | | 52 | | 55 | | 59 | | | | | |
| Cases | 3904 | 3824 | | 3254 | | 3625 | | 1896 | | 3690 | | 3299 | | 2661 | | 2689 | | 2294 | | | | | |
| PY | 129 480 | 129 832 | | 118 381 | | 136 162 | | 71 395 | | 146 069 | | 136 218 | | 117 293 | | 126 253 | | 120 603 | | | | | |
| Model 1 | Ref. | 0.93 | 0.89, 0.97 | 0.85 | 0.81, 0.89 | 0.82 | 0.78, 0.86 | 0.81 | 0.77, 0.86 | 0.76 | 0.73, 0.80 | 0.73 | 0.70, 0.77 | 0.69 | 0.66, 0.72 | 0.64 | 0.61, 0.67 | 0.57 | 0.54, 0.60 | <0.0001 | 0.77 | 0.76, 0.79 | |
| Model 2 | Ref. | 0.98 | 0.94, 1.03 | 0.92 | 0.87, 0.96 | 0.90 | 0.86, 0.94 | 0.89 | 0.84, 0.94 | 0.84 | 0.81, 0.88 | 0.82 | 0.78, 0.86 | 0.78 | 0.74, 0.82 | 0.73 | 0.69, 0.77 | 0.65 | 0.62, 0.69 | <0.0001 | 0.82 | 0.81, 0.84 | |
| Model 3 | Ref. | 0.98 | 0.94, 1.03 | 0.91 | 0.87, 0.96 | 0.89 | 0.85, 0.93 | 0.88 | 0.83, 0.93 | 0.83 | 0.80, 0.87 | 0.81 | 0.77, 0.85 | 0.77 | 0.73, 0.81 | 0.72 | 0.68, 0.76 | 0.64 | 0.61, 0.68 | <0.0001 | 0.81 | 0.80, 0.83 | |
| Unhealthful plant-based diet index | | | | | | | | | | | | | | | | | | | | | | | |
| Median | 36 | 40 | | 43 | | 46 | | 48 | | 49 | | 51 | | 53 | | 56 | | 61 | | | | | |
| Cases | 2440 | 2533 | | 3677 | | 2933 | | 3132 | | 3240 | | 3006 | | 2801 | | 4211 | | 3163 | | | | | |
| PY | 118 512 | 113 242 | | 154 425 | | 119 798 | | 125 746 | | 122 922 | | 114 878 | | 103 248 | | 150 641 | | 108 271 | | | | | |
| Model 1 | Ref. | 1.07 | 1.01, 1.13 | 1.14 | 1.08, 1.19 | 1.17 | 1.11, 1.23 | 1.20 | 1.14, 1.27 | 1.27 | 1.21, 1.34 | 1.29 | 1.23, 1.37 | 1.36 | 1.29, 1.44 | 1.42 | 1.36, 1.50 | 1.56 | 1.48, 1.64 | <0.0001 | 1.20 | 1.18, 1.22 | |
| Model 2 | Ref. | 1.06 | 1.00, 1.12 | 1.11 | 1.06, 1.17 | 1.14 | 1.08, 1.20 | 1.14 | 1.08, 1.21 | 1.20 | 1.13, 1.26 | 1.20 | 1.14, 1.27 | 1.24 | 1.17, 1.31 | 1.27 | 1.21, 1.34 | 1.32 | 1.25, 1.39 | <0.0001 | 1.12 | 1.10, 1.14 | |
| Model 3 | Ref. | 1.07 | 1.01, 1.13 | 1.14 | 1.08, 1.20 | 1.17 | 1.11, 1.23 | 1.19 | 1.13, 1.25 | 1.24 | 1.18, 1.31 | 1.25 | 1.18, 1.32 | 1.30 | 1.23, 1.37 | 1.34 | 1.28, 1.42 | 1.41 | 1.33, 1.49 | <0.0001 | 1.15 | 1.13, 1.17 | |

HR, hazard ratio; PY, person-year.

Model 1 adjusted for age (years: < 60, 60–70, > 70) and sex (male or female).

Model 2 further adjusted for race/ethnicity (non-Hispanic European American, African American or other), education level (≤ high school or GED, some college, or college or above), income level (< \$30 000, \$30 000–\$59 000 or ≥ \$60 000) and marriage 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) and BMI (< 23.0, 23.0–24.9, 25.0–29.9, 30.0–34.9 or ≥ 35.0 kg/m²).

Model 3 further adjusted for histories of diabetes, hypertension, hypercholesterolemia, cancer and CVD at baseline (yes v. no).

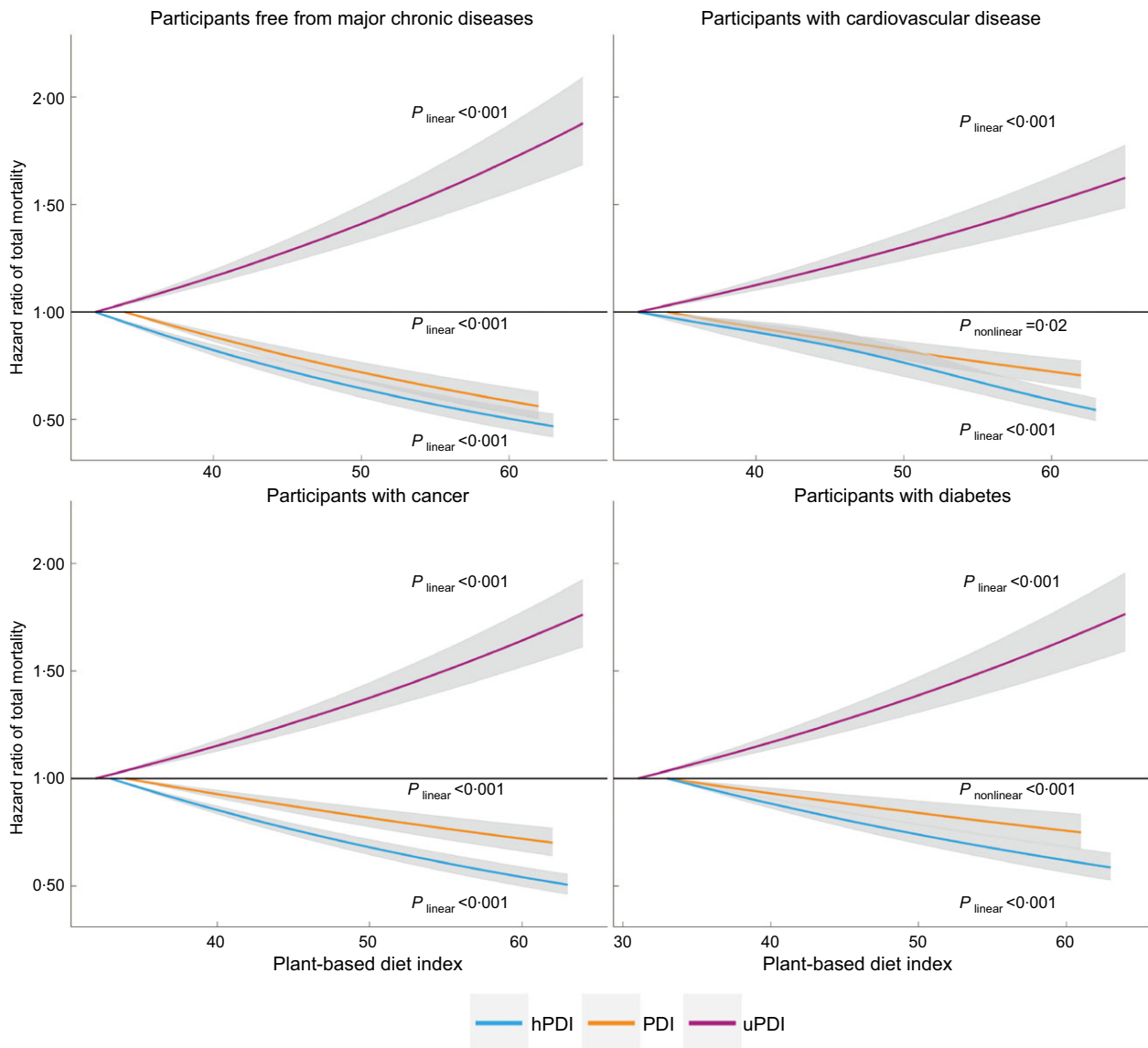


Fig. 1 Dose–response relationship of plant-based diet indices with total mortality among participants free from and among those with a history of diabetes, CVD or cancer at baseline. The dose–response relationship was quantified by Cox proportional hazards models with restricted cubic spline with three knots specified. The first percentile of each dietary score was used as reference level for calculating hazard ratios. We tested non-linearity in the dose–response relationship 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. All the models simultaneously adjusted for age (years: <60, 60–70, >70) and sex (male or female), race/ethnicity (non-Hispanic European American, African American or other), education level (\leq high school or GED, some college, or college or above), income level (< \$30 000, \$30 000–\$59 000 or \geq \$60 000) and marriage status (currently married or not), smoking status (current, former or never smoking), frequency of alcohol consumption (never, < 1 times/week or \geq 1 times/week), frequency of exercise vigorously (never/rarely, 1–4 times/month, 2–4 times/week or \geq 5 times/week), total energy intake (in quintiles), BMI (< 23.0, 23.0–24.9, 25.0–29.9, 30.0–34.9 or \geq 35.0 kg/m²), histories of hypertension, hypercholesterolemia, diabetes, cancer and CVD at baseline (yes v. no) (except among the same patients). The sample sizes were 148 244, 73 799, 74 213 and 85 149 for the analyses in participants free from major chronic diseases, with a history of diabetes, CVD or cancer at baseline, respectively. PDI, plant-based diet index; hPDI, healthful PDI; uPDI, unhealthful PDI

mortality due to four major cancer types, including digestive tract cancers, liver cancer, lung cancer and prostate cancer (in men only), were generally similar to that with mortality due to total cancer. In addition, we observed inverse associations of PDI and hPDI and positive association of uPDI with cancer mortality among cancer patients and CVD mortality among CVD patients, similar to the

findings among participants without major chronic disease at baseline (see online supplementary material, Supplemental Table 5). In another secondary analysis, we found the associations of the dietary indices with the risk of death due to causes other than cancer and CVD were generally similar to those for total mortality (see online supplementary material, Supplemental Table 4).

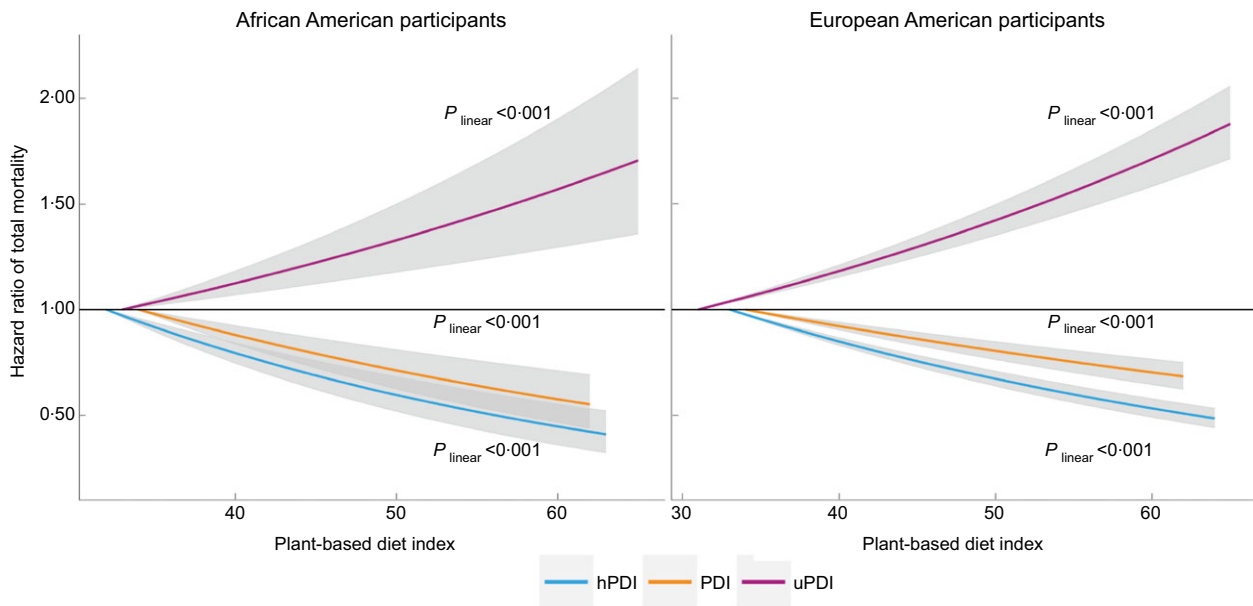


Fig. 2 Dose–response relationship of plant-based diet indices with total mortality in African and European American participants. The dose–response relationship was quantified by Cox proportional hazards models with restricted cubic spline with three knots specified. The first percentile of each dietary score was used as reference level for calculating hazard ratios. We tested nonlinearity in the dose–response relationship of the dietary indices with mortality 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. All the models simultaneously adjusted for age (years: < 60, 60–70, > 70) and sex (male or female), race/ethnicity (non-Hispanic European American, African American or other), education level (\leq high school or GED, some college or college or above), income level (< \$30 000, \$30 000–\$59 000 or \geq \$60 000) and marriage status (currently married or not), smoking status (current, former or never smoking), frequency of alcohol consumption (never, < 1 times/week or \geq 1 times/week), frequency of exercise vigorously (never/rarely, 1–4 times/month, 2–4 times/week or \geq 5 times/week), total energy intake (in quintiles), BMI (< 23.0, 23.0–24.9, 25.0–29.9, 30.0–34.9, or \geq 35.0 kg/m²), histories of hypertension, hypercholesterolemia, diabetes, cancer and CVD at baseline (yes v. no) (except among the same patients). The sample sizes were 28 018 and 241 374 for the analyses in African and European American participants, respectively. PDI, plant-based diet index; hPDI, healthful PDI; uPDI, unhealthful PDI

Discussion

Our study represents the largest investigation of plant-based diets and mortality in a multi-ethnic cohort with diverse socio-economic backgrounds. In this population of more than 0.3 million US veterans, greater adherence to a plant-based diet was associated with lower risk of total, cancer and CVD mortality. We found that the associations of plant-based diets with mortality depend on the quality of plant foods. A higher hPDI was associated with a lower mortality risk, whereas a higher uPDI was associated with a higher mortality rate. Our findings were robust and remain largely unchanged among participants free from CVD and cancer and those diagnosed with major chronic disease at baseline. In addition, our results were consistent across different sex, age and racial/ethnic groups, supporting the generalisability of recommending plant-based diets in the US population.

Previous data on plant-based diets and total mortality have been inconclusive and limited^(6,8,11–13). Consistent with our findings, a recent study in NHS and HPFS found that 10-unit increases in PDI and hPDI during 12 years were associated with 8% (HR = 0.92, 95% CI: 0.89, 0.95) and 10% (HR = 0.90, 95% CI: 0.88, 0.93) lower total mortality, respectively, whereas a 10-unit increase in uPDI during 12

years was associated a 9% (HR = 1.09, 95% CI: 1.06, 1.12) higher total mortality⁽⁵⁾. In the Adventist Health Study 2, vegetarians, compared to non-vegetarians, had a 12% lower risk of all-cause death during a follow-up of 7 years⁽¹¹⁾. In contrast, in the National Health and Nutrition Examination Survey (NHANES) III and the European Prospective Investigation into Cancer and Nutrition Study (EPIC), neither the PDI nor the comparison between vegetarian and non-vegetarian diets was associated with total mortality^(8,13). These inconsistencies may be partly due to different population characteristics and variability in the adherence to plant-based diets in different studies. In line with previous studies that employed various nutritional metrics, such as glycaemic index, glycaemic load, fibre content and food sources of carbohydrate, to distinguish the healthfulness of plant foods^(16,31,32), we found that greater adherence to plant-based diets with emphasis on healthy plant foods (hPDI) was associated with a substantially lower risk of total mortality. In contrast, significantly higher total mortality was observed in participants with a higher uPDI. These divergent associations between the two versions of PDI highlighted the importance of considering the quality of plant foods when consuming and recommending plant-based diets.



Table 3 Association of plant-based diet indices with cause-specific mortality in 315 919 participants from the Million Veteran Program

| | | Deciles of dietary indices | | | | | | | | | | | | | | | | | | HR per 10-unit increment | | | | |
|-------------------------------|-------|----------------------------|------------|------|------------|------|------------|------|------------|------|------------|------|------------|------|------------|------|------------|------|------------|--------------------------|------|---------------------------|----|--------|
| | | D1 | | D2 | | D3 | | D4 | | D5 | | D6 | | D7 | | D8 | | D9 | | D10 | | <i>P</i> _{trend} | HR | 95% CI |
| | | HR | 95% CI | HR | 95% CI | HR | 95% CI | HR | 95% CI | HR | 95% CI | HR | 95% CI | HR | 95% CI | HR | 95% CI | HR | 95% CI | | | | | |
| CVD Mortality | | | | | | | | | | | | | | | | | | | | | | | | |
| PDI | Cases | 1107 | 709 | 949 | | 1093 | | 1270 | | 566 | | 1144 | | 947 | | 1045 | | 921 | | | | | | |
| | Ref. | 0.90 | 0.82, 0.99 | 0.89 | 0.82, 0.97 | 0.84 | 0.77, 0.92 | 0.89 | 0.82, 0.97 | 0.79 | 0.71, 0.87 | 0.82 | 0.75, 0.89 | 0.79 | 0.72, 0.86 | 0.78 | 0.71, 0.84 | 0.77 | 0.70, 0.84 | <0.0001 | 0.88 | 0.85, 0.91 | | |
| hPDI | Cases | 1176 | 1171 | 1029 | | 1113 | | 598 | | 1164 | | 1046 | | 848 | | 863 | | 743 | | | | | | |
| | Ref. | 1.00 | 0.92, 1.08 | 0.95 | 0.88, 1.04 | 0.91 | 0.83, 0.98 | 0.92 | 0.83, 1.01 | 0.87 | 0.80, 0.94 | 0.84 | 0.78, 0.92 | 0.81 | 0.74, 0.89 | 0.76 | 0.69, 0.83 | 0.69 | 0.63, 0.76 | <0.0001 | 0.84 | 0.81, 0.87 | | |
| uPDI | Cases | 757 | 826 | 1114 | | 933 | | 969 | | 1054 | | 909 | | 904 | | 1314 | | 971 | | | | | | |
| | Ref. | 1.13 | 1.02, 1.24 | 1.11 | 1.02, 1.22 | 1.20 | 1.09, 1.32 | 1.19 | 1.08, 1.31 | 1.30 | 1.19, 1.43 | 1.22 | 1.11, 1.35 | 1.35 | 1.23, 1.49 | 1.36 | 1.24, 1.49 | 1.41 | 1.28, 1.55 | <0.0001 | 1.14 | 1.13, 1.19 | | |
| Cancer mortality | | | | | | | | | | | | | | | | | | | | | | | | |
| PDI | Cases | 1017 | 739 | 936 | | 1175 | | 1252 | | 605 | | 1085 | | 925 | | 972 | | 804 | | | | | | |
| | Ref. | 1.03 | 0.95, 1.13 | 0.96 | 0.88, 1.05 | 0.99 | 0.91, 1.08 | 0.97 | 0.89, 1.05 | 0.92 | 0.84, 1.02 | 0.85 | 0.78, 0.93 | 0.85 | 0.77, 0.93 | 0.79 | 0.73, 0.87 | 0.74 | 0.68, 0.82 | <0.0001 | 0.85 | 0.82, 0.88 | | |
| hPDI | Cases | 1164 | 1156 | 957 | | 1124 | | 583 | | 1141 | | 1031 | | 804 | | 844 | | 706 | | | | | | |
| | Ref. | 1.00 | 0.92, 1.08 | 0.90 | 0.82, 0.98 | 0.93 | 0.85, 1.01 | 0.91 | 0.82, 1.00 | 0.87 | 0.80, 0.94 | 0.85 | 0.78, 0.92 | 0.78 | 0.71, 0.86 | 0.76 | 0.69, 0.83 | 0.67 | 0.61, 0.74 | <0.0001 | 0.83 | 0.81, 0.86 | | |
| uPDI | Cases | 788 | 753 | 1129 | | 898 | | 914 | | 960 | | 947 | | 874 | | 1265 | | 982 | | | | | | |
| | Ref. | 0.99 | 0.89, 1.09 | 1.08 | 0.99, 1.19 | 1.11 | 1.01, 1.22 | 1.08 | 0.98, 1.18 | 1.14 | 1.04, 1.25 | 1.22 | 1.11, 1.34 | 1.26 | 1.14, 1.38 | 1.25 | 1.15, 1.37 | 1.36 | 1.24, 1.37 | <0.0001 | 1.14 | 1.11, 1.19 | | |
| Mortality due to other causes | | | | | | | | | | | | | | | | | | | | | | | | |
| PDI | Cases | 1376 | 926 | 1168 | | 1366 | | 1423 | | 703 | | 1368 | | 1176 | | 1325 | | 1044 | | | | | | |
| | Ref. | 0.95 | 0.87, 1.03 | 0.88 | 0.81, 0.95 | 0.85 | 0.78, 0.91 | 0.81 | 0.75, 0.87 | 0.79 | 0.72, 0.86 | 0.79 | 0.73, 0.85 | 0.79 | 0.73, 0.85 | 0.79 | 0.73, 0.85 | 0.70 | 0.65, 0.76 | <0.0001 | 0.85 | 0.83, 0.88 | | |
| hPDI | Cases | 1564 | 1497 | 1268 | | 1388 | | 715 | | 1385 | | 1222 | | 1009 | | 982 | | 845 | | | | | | |
| | Ref. | 0.96 | 0.89, 1.03 | 0.88 | 0.82, 0.95 | 0.85 | 0.79, 0.91 | 0.82 | 0.75, 0.90 | 0.78 | 0.72, 0.84 | 0.74 | 0.69, 0.80 | 0.72 | 0.67, 0.79 | 0.65 | 0.60, 0.70 | 0.59 | 0.54, 0.64 | <0.0001 | 0.78 | 0.75, 0.80 | | |
| uPDI | Cases | 895 | 954 | 1434 | | 1102 | | 1249 | | 1226 | | 1150 | | 1023 | | 1632 | | 1210 | | | | | | |
| | Ref. | 1.10 | 1.00, 1.20 | 1.21 | 1.11, 1.32 | 1.20 | 1.10, 1.31 | 1.29 | 1.19, 1.41 | 1.28 | 1.18, 1.40 | 1.31 | 1.20, 1.43 | 1.29 | 1.18, 1.42 | 1.43 | 1.31, 1.55 | 1.48 | 1.36, 1.62 | <0.0001 | 1.16 | 1.13, 1.19 | | |

PDI, plant-based diet index; hPDI, healthful plant-based diet index; uPDI, unhealthful plant-based diet index.

Models adjusted for age (years: < 60, 60–70, > 70) and sex (male or female), race/ethnicity (non-Hispanic European American, African American or other), education level (≤ high school or GED, some colleague, or college or above), income level (< \$30 000, \$30 000–\$59 000 or ≥ \$60 000) and marriage 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), BMI (< 23.0, 23.0–24.9, 25.0–29.9, 30.0–34.9 or ≥ 35.0 kg/m²) and histories of diabetes, hypertension, hypercholesterolemia, cancer and CVD at baseline (yes v. no).



Our data support the hypothesis that adherence to plant-based diets, particularly a plant-based diet with emphasis on healthy plant foods, reduces the risk of cancer mortality. Although limited studies have examined plant-based diets with total cancer outcomes⁽⁶⁾, substantial and consistent evidence from epidemiologic studies suggested that a dietary pattern rich in plant foods or a vegetarian diet was protective against colorectal cancer^(33,34). In addition, findings on hallmarks of a healthy plant-based diet with cancer risk have been consistent across studies. For example, based on extensive literature review, an updated report from the World Cancer Research Fund/American Institute for Cancer Research (WCRF/AICR) concluded with high gradings, that is, either as 'convincing' or 'probable', for evidence that low intakes of red/processed meat and high intakes of whole grains, non-starchy vegetables and fruit, and foods high in dietary fibres decrease the risk for cancer⁽³⁵⁾. Our finding of an association between a higher PDI and improved cancer survival was consistent with previous data on healthy dietary patterns and mortality among cancer patients^(36–38) and provided additional evidence supporting the promotion of healthy eating as a means to ameliorate the adverse effects of cancer and its treatment, as recommended by various organisations such as the American Cancer Society (ACS) and WCRF/AICR^(35,39). In addition, we found a significant positive association between plant-based diets rich in less-healthy plant foods (uPDI) and cancer mortality. Such a finding is biologically plausible because an unhealthy plant-based diet is typically high in glycaemic load and index and added sugar, and low in dietary fibre, unsaturated fats and antioxidants, potentially leading to systemic inflammation that predisposes to the development of cancer and promotes all stages of tumorigenesis⁽⁴⁰⁾.

When plant foods known to be associated with health benefits were emphasised, hPDI was associated with a lower risk of CVD mortality. Conversely, when the intake of less-healthy plant foods was emphasised, the opposite association with CVD mortality was observed. Our findings were broadly consistent with previous studies on both incidence and mortality of CVD^(2,6). For example, Satija *et al.* found that every 10-unit increment in hPDI was associated with a 12% lower risk of CHD (HR = 0.88, 95% CI: 0.85, 0.91), whereas every 10-unit increment in uPDI was associated with a 10% higher risk of CHD (HR = 1.10, 95% CI: 1.06, 1.14). There are several mechanisms through which a healthful plant-based diet could lower CVD risk. Such a diet is usually rich in dietary fibre, polyphenols, unsaturated fatty acids, micronutrients such as Mg, and low in saturated fat, Na:K ratio and glycaemic index. Thus, adherence to a healthful plant-based diet could lead to a lower risk of CVD through improving glycaemic control⁽³²⁾, modulating lipid profile⁽⁴¹⁾ and decreasing chronic inflammation^(42,43). To our knowledge, our study is the first to report of a protective association between a plant-based diet and mortality

among CVD patients. Previously studies reported that greater adherence to a Mediterranean diet, a dietary pattern that contains a variety of plant foods, was associated with less recurrence of myocardial infarction and longer survival in individuals with high cardiovascular risk^(44–46). Furthermore, our findings in both baseline CVD-free participants and CVD patients (Fig. 1) highlight the important role of a healthy plant-based diet in the management of CVD and emphasise how healthy eating patterns may influence prognosis of CVD.

Our secondary analysis revealed that the associations of PDI with the non-CVD and non-cancer mortality were similar to the associations for total mortality. The associations for deaths due to diabetes and respiratory disease were consistent with previous findings on healthy dietary patterns and the incident disease outcomes^(3,47), whereas the results for deaths due to chronic liver disease and cirrhosis, and renal failure are novel and therefore require confirmation in further studies.

Our study has several limitations. First, reverse causation is a possible explanation for our findings because people with chronic disease and poor health might change their habitual diet. However, our results remain unchanged in a subpopulation free from known major chronic diseases at baseline. Also, participants with a severe illness might change their diets towards ones generally perceived to be healthier and had a higher risk of mortality, leading to an attenuation in the associations between healthy diets and mortality, which would not explain away our findings. Second, the follow-up of our study was relatively short, which may not sufficiently capture the induction period of diet–mortality association. However, our study employed SFFQ to assess long-term usual diet and focused on overall dietary patterns rather than individual foods and nutrients. Usual dietary intake, especially dietary patterns, tends to be stable during adulthood. Therefore, the PDI represent the adherence to plant-based dietary patterns formed in early adulthood beyond the diet patterns captured at the start of follow-up. In addition, our findings were consistent with other studies of PDI with the incident disease during decades-long follow-ups^(2,6,48) and barely changed in the sensitivity analysis that excluded deaths during the first year of follow-up. Third, because our study is observational in nature, we are unable to establish causality. Fourth, although we carefully adjusted for many potential confounders, residual confounding could not be ruled out. Fifth, measurement errors are inevitable in estimates of dietary intakes. However, our adjustment for energy intake reduced the impact of measurement errors and controlled for potential confounding due to energy intake⁽⁴⁹⁾. Lastly, the majority of the study participants were male. However, we found similar associations between PDI and mortality in men *v.* women. Strengths of the present study include the large sample size and high rates of follow-up. In addition, we addressed generalisability, a key limitation of previous work on plant-based diet^(2–6), by



studying a population with a large proportion of men, a wide age range and diverse socio-economic and racial/ethnic backgrounds and testing the consistency of findings across various subgroups.

Conclusions

We found an inverse association of higher adherence to PDI with mortality in a large cohort of US veterans. This inverse association was stronger for a PDI that emphasised healthy plant foods, and the risk of mortality was significantly elevated in participants with greater adherence to a plant-based diet that emphasised less-healthy plant foods. Increasing intakes of healthy plant foods at the expense of less-healthy plant foods and certain animal foods in the diet can confer substantial health benefits and should be a key message in the current dietary guidelines. Our findings strengthen the guidelines by addressing their generalisability in a unique study population with a wide age range and diverse socio-economic and racial/ethnic backgrounds.

Acknowledgements

Acknowledgements: This research is based on data from the VA Million Veteran Program supported by award MVP#000, MVP001 and VA Merit Award I01-CX001025 from the Department of Veterans Affairs. This publication does not represent the views of the Department of Veterans Affairs or the US government. **Financial support:** None of the authors have financial with the work reported in this manuscript. **Conflicts of interest:** None of the authors have conflicts of interest with the work reported in this manuscript. We acknowledge the Support for VA/CMS data provided by the Department of Veterans Affairs, VA Health Services Research and Development Service, VA Information Resource Center (Project Numbers SDR 02-237 and 98-004) and important contributions by the Million Veteran Program (MVP) Consortium. **Authorship:** W.D., H. F., W.C.W., P.W., K.C., J.M.G. and L.D. designed the study; Li Y, Song R, Ho Y and Nguyen X provided statistical expertise; DW wrote the manuscript, had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis; and all authors conducted the research, contributed to the interpretation of the results and critical revision of the manuscript for important intellectual content and read and approved the final manuscript. **Ethics of human subject participation:** 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). Written informed consent was obtained from all subjects/patients.

Supplementary material

For supplementary material/s referred to in this article, please visit <https://doi.org/10.1017/S1368980022000659>

References

- Li D (2014) Effect of the vegetarian diet on non-communicable diseases. *J Sci Food Agric* **94**, 169–173.
- Satija A, Bhupathiraju SN, Spiegelman D *et al.* (2017) Healthful and unhealthful plant-based diets and the risk of coronary heart disease in US adults. *J Am Coll Cardiol* **70**, 411–422.
- Satija A, Bhupathiraju SN, Rimm EB *et al.* (2016) Plant-based dietary patterns and incidence of type 2 diabetes in US men and women: results from three prospective cohort studies. *PLoS Med* **13**, e1002039.
- Satija A, Malik V, Rimm EB *et al.* (2019) Changes in intake of plant-based diets and weight change: results from 3 prospective cohort studies. *Am J Clin Nutr* **110**, 574–582.
- Baden MY, Satija A, Hu FB *et al.* (2019) Change in plant-based diet quality is associated with changes in plasma adiposity-associated biomarker concentrations in women. *J Nutr* **149**, 676–686.
- Baden MY, Liu G, Satija A *et al.* (2019) Changes in plant-based diet quality and total and cause-specific mortality. *Circulation* **140**, 979–991.
- Huang T, Yang B, Zheng J *et al.* (2012) Cardiovascular disease mortality and cancer incidence in vegetarians: a meta-analysis and systematic review. *Ann Nutr Metab* **60**, 233–240.
- Key TJ, Fraser GE, Thorogood M *et al.* (1999) Mortality in vegetarians and nonvegetarians: detailed findings from a collaborative analysis of 5 prospective studies. *Am J Clin Nutr* **70**, 516s–524s.
- Van Horn L, Carson JAS, Appel LJ *et al.* (2016) Recommended dietary pattern to achieve adherence to the American Heart Association/American College of Cardiology (AHA/ACC) guidelines: a scientific statement from the American Heart Association. *Circulation* **134**, e505–e29.
- U.S. Department of Health and Human Services & U.S. Department of Agriculture (2015) 2015–2020 Dietary Guidelines for Americans. <https://health.gov/our-work/food-nutrition/previous-dietary-guidelines/2015> (accessed July 2021).
- Orlich MJ, Singh PN, Sabaté J *et al.* (2013) Vegetarian dietary patterns and mortality in Adventist Health Study 2. *JAMA Intern Med* **173**, 1230–1238.
- Dinu M, Abbate R, Gensini GF *et al.* (2017) Vegetarian, vegan diets and multiple health outcomes: a systematic review with meta-analysis of observational studies. *Crit Rev Food Sci Nutr* **57**, 3640–3649.
- Sotos-Prieto M, Bhupathiraju SN, Mattei J *et al.* (2017) Association of changes in diet quality with total and cause-specific mortality. *N Engl J Med* **377**, 143–153.
- Juan W, Yamini S & Britten P (2015) Food intake patterns of self-identified vegetarians among the US population, 2007–2010. *Procedia Food Sci* **4**, 86–93.
- Martínez-González MA, Sanchez-Tainta A, Corella D *et al.* (2014) A provegetarian food pattern and reduction in total mortality in the Prevención con Dieta



- Mediterránea (PREDIMED) study. *Am J Clin Nutr* **100**, 320S–328S.
16. Liu S, Willett WC, Stampfer MJ *et al.* (2000) A prospective study of dietary glycemic load, carbohydrate intake, and risk of coronary heart disease in US women. *Am J Clin Nutr* **71**, 1455–1461.
 17. Veronese N, Stubbs B, Noale M *et al.* (2017) Fried potato consumption is associated with elevated mortality: an 8-year longitudinal cohort study. *Am J Clin Nutr* **106**, 162–167.
 18. Halton TL, Willett WC, Liu S *et al.* (2006) Potato and french fry consumption and risk of type 2 diabetes in women. *Am J Clin Nutr* **83**, 284–290.
 19. Muraki I, Rimm EB, Willett WC *et al.* (2016) Potato consumption and risk of type 2 diabetes: results from three prospective cohort studies. *Diabetes Care* **39**, 376–384.
 20. Li Y, Guo L, He K *et al.* (2021) Consumption of sugar-sweetened beverages and fruit juice and human cancer: a systematic review and dose-response meta-analysis of observational studies. *J Cancer* **12**, 3077–3088.
 21. Narain A, Kwok C & Mamas M (2016) Soft drinks and sweetened beverages and the risk of cardiovascular disease and mortality: a systematic review and meta-analysis. *Int J Clin Pract* **70**, 791–805.
 22. Gaziano JM, Concato J, Brophy M *et al.* (2016) Million veteran program: a mega-biobank to study genetic influences on health and disease. *J Clin Epidemiol* **70**, 214–223.
 23. Willett W (2012) *Nutritional Epidemiology*. Oxford: Oxford University Press.
 24. HSPH. Harvard University Food Composition Table: Nutrition Department at the Harvard T.H. Chan School of Public Health. <https://regepi.bwh.harvard.edu/health/nutrition/> (Posted 2015; extracted 2020; accessed March 2015).
 25. Salvini S, Hunter DJ, Sampson L *et al.* (1989) Food-based validation of a dietary questionnaire: the effects of week-to-week variation in food consumption. *Int J Epidemiol* **18**, 858–867.
 26. Feskanich D, Rimm EB, Giovannucci EL *et al.* (1993) Reproducibility and validity of food intake measurements from a semiquantitative food frequency questionnaire. *J Am Diet Assoc* **93**, 790–796.
 27. Yue Y, Yuan C, Wang DD *et al.* (2021) Reproducibility and validity of diet quality scores derived from food frequency questionnaires. *Am J Clin Nutr* **115**, 843–853.
 28. Center of Excellence for Suicide Prevention. Joint Department of Veterans Affairs (VA) & Department of Defense (DoD) Suicide Data Repository – National Death Index (NDI). <http://vaww.virec.research.va.gov/Mortality/Overview.htm> (extracted 2018; accessed June 2021).
 29. Lunn M & McNeil D (1995) Applying cox regression to competing risks. *Biom* **51**, 524–532.
 30. Govindarajulu US, Malloy EJ, Ganguli B *et al.* (2009) The comparison of alternative smoothing methods for fitting non-linear exposure-response relationships with Cox models in a simulation study. *Int J Biostat* **5**, 2.
 31. Fan J, Song Y, Wang Y *et al.* (2012) Dietary glycemic index, glycemic load, and risk of coronary heart disease, stroke, and stroke mortality: a systematic review with meta-analysis. *PLoS One* **7**, e52182.
 32. Willett W, Manson J & Liu S (2002) Glycemic index, glycemic load, and risk of type 2 diabetes. *Am J Clin Nutr* **76**, 274S–280S.
 33. Tantamango-Bartley Y, Jaceldo-Siegl K, Fan J *et al.* (2013) Vegetarian diets and the incidence of cancer in a low-risk population. *Cancer Epidemiol Biomarkers Prev* **22**, 286–294.
 34. Godos J, Bella F, Sciacca S *et al.* (2017) Vegetarianism and breast, colorectal and prostate cancer risk: an overview and meta-analysis of cohort studies. *J Hum Nutr Diet* **30**, 349–359.
 35. World Cancer Research Fund/American Institute for Cancer Research (2007) *Food, Nutrition and the Prevention of Cancer: A Global Perspective*. Washington, DC: AIRC.
 36. Kim EH, Willett WC, Fung T *et al.* (2011) Diet quality indices and postmenopausal breast cancer survival. *Nutr Cancer* **63**, 381–388.
 37. Saxe GA, Rock CL, Wicha MS *et al.* (1999) Diet and risk for breast cancer recurrence and survival. *Breast Cancer Res Treat* **53**, 241–253.
 38. Thomson CA, Crane TE, Wertheim BC *et al.* (2014) Diet quality and survival after ovarian cancer: results from the Women's Health Initiative. *JNCI: J Natl Cancer Inst* **106**, dju314.
 39. Doyle C, Kushi LH, Byers T *et al.* (2006) Nutrition and physical activity during and after cancer treatment: an American Cancer Society guide for informed choices. *CA: Cancer J Clin* **56**, 323–353.
 40. Zitvogel L, Pietrocola F & Kroemer G (2017) Nutrition, inflammation and cancer. *Nat Immunol* **18**, 843–850.
 41. Mensink RP, Zock PL, Kester AD *et al.* (2003) Effects of dietary fatty acids and carbohydrates on the ratio of serum total to HDL cholesterol and on serum lipids and apolipoproteins: a meta-analysis of 60 controlled trials. *Am J Clin Nutr* **77**, 1146–1155.
 42. Wang DD (2018) Dietary *n*-6 polyunsaturated fatty acids and cardiovascular disease: epidemiologic evidence. *Prostaglandins Leukotrienes Essent Fatty Acids* **135**, 5–9.
 43. Tangney CC & Rasmussen HE (2013) Polyphenols, inflammation, and cardiovascular disease. *Curr Atheroscler Rep* **15**, 324.
 44. Trichopoulos A, Bamia C, Norat T *et al.* (2007) Modified Mediterranean diet and survival after myocardial infarction: the EPIC-Elderly study. *Eur J Epidemiol* **22**, 871–881.
 45. de Lorgeril M, Salen P, Martin JL *et al.* (1999) Mediterranean diet, traditional risk factors, and the rate of cardiovascular complications after myocardial infarction: final report of the Lyon Diet Heart Study. *Circulation* **99**, 779–785.
 46. Estruch R, Ros E, Salas-Salvadó J *et al.* (2013) Primary prevention of cardiovascular disease with a Mediterranean diet. *N Engl J Med* **368**, 1279–1290.
 47. Varraso R, Chiuve SE, Fung TT *et al.* (2015) Alternate Healthy Eating Index 2010 and risk of chronic obstructive pulmonary disease among US women and men: prospective study. *BMJ* **350**, h286.
 48. Loeb S, Fu BC, Bauer SR *et al.* (2021) Association of plant-based diet index with prostate cancer risk. *Am J Clin Nutr* **115**, 662–670.