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Association Between Healthy Eating Patterns and Risk of Cardiovascular Disease

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Supplemental content

IMPORTANCE The 2015-2020 Dietary Guidelines for Americans recommend multiple healthy eating patterns. However, few studies have examined the associations of adherence to different dietary patterns with long-term risk of cardiovascular disease (CVD).

OBJECTIVE To examine the associations of dietary scores for 4 healthy eating patterns with risk of incident CVD.

DESIGN, SETTING, AND PARTICIPANTS Prospective cohort study of initially healthy women from the Nurses' Health Study (NHS) (1984-2016) and the NHS II (1991-2017) and men from the Health Professionals Follow-up Study (HPFS) (1986-2012). The dates of analysis were July 25 to December 4, 2019.

EXPOSURES Healthy Eating Index–2015 (HEI-2015), Alternate Mediterranean Diet Score (AMED), Healthful Plant-Based Diet Index (HPDI), and Alternate Healthy Eating Index (AHEI).

MAIN OUTCOMES AND MEASURES Cardiovascular disease events, including fatal and nonfatal coronary heart disease (CHD) and stroke.

RESULTS The final study sample included 74 930 women in the NHS (mean [SD] baseline age, 50.2 [7.2] years), 90 864 women in the NHS II (mean [SD] baseline age, 36.1 [4.7] years), and 43 339 men in the HPFS (mean [SD] baseline age, 53.2 [9.6] years). During a total of 5 257 190 person-years of follow-up, 23 366 incident CVD cases were documented (18 092 CHD and 5687 stroke) (some individuals were diagnosed as having both CHD and stroke). Comparing the highest with the lowest quintiles, the pooled multivariable-adjusted hazard ratios (HRs) of CVD were 0.83 (95% CI, 0.79-0.86) for the HEI-2015, 0.83 (95% CI, 0.79-0.86) for the AMED, 0.86 (95% CI, 0.82-0.89) for the HPDI, and 0.79 (95% CI, 0.75-0.82) for the AHEI (*P* for trend <.001 for all). In addition, a 25-percentile higher dietary score was associated with 10% to 20% lower risk of CVD (pooled HR, 0.80 [95% CI, 0.77-0.83] for the HEI-2015; 0.90 [95% CI, 0.87-0.92] for the AMED; 0.86 [95% CI, 0.82-0.89] for the HPDI; and 0.81 [95% CI, 0.78-0.84] for the AHEI). These dietary scores were statistically significantly associated with lower risk of both CHD and stroke. In analyses stratified by race/ethnicity and other potential risk factors for CVD, the inverse associations between these scores and risk of CVD were consistent in most subgroups.

CONCLUSIONS AND RELEVANCE In 3 large prospective cohorts with up to 32 years of follow-up, greater adherence to various healthy eating patterns was consistently associated with lower risk of CVD. These findings support the recommendations of the 2015-2020 Dietary Guidelines for Americans that multiple healthy eating patterns can be adapted to individual food traditions and preferences.

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Dietary modifications have been established as one of the most important strategies for population prevention of cardiovascular disease (CVD),[1,2] the primary cause of death in the United States and worldwide.[3,4] Multiple studies have evaluated the associations of individual nutrients or foods with CVD risk.[5] However, nutrients and foods are not consumed in isolation but in numerous and multifaceted combinations. Therefore, approaches that combine various nutrients and foods into "dietary patterns" could reflect real-world dietary practices and integrate potentially interactive and cumulative associations of different dietary components.[6,7] In addition, dietary patterns more closely mimic real-world scenarios of nutrient and food combinations, which facilitates translation of findings into dietary recommendations.[8]

The 2015-2020 Dietary Guidelines for Americans[9] highlight a shift from focusing on individual nutrients or foods to emphasizing healthy eating patterns as a whole and recommend multiple healthy dietary patterns to provide dietary choices for all Americans with diverse cultural and personal food traditions or preferences. However, few studies[10-13] have comprehensively examined whether adherence to different dietary patterns could be associated with lower risk of incident CVD. Therefore, using 3 large prospective cohorts with up to 32 years of follow-up with data on repeated measures of dietary habits, we derived dietary scores for 4 healthy dietary patterns, including the Healthy Eating Index–2015 (HEI-2015), Alternate Mediterranean Diet Score (AMED), Healthful Plant-Based Diet Index (HPDI), and Alternate Healthy Eating Index (AHEI). We then examined their associations with risk of CVD, including coronary heart disease (CHD) and stroke.

Key Points

Question Are there associations of different healthy eating patterns with long-term risk of cardiovascular disease?

Findings In this cohort study of individuals from the Nurses' Health Study, Nurses' Health Study II, and Health Professionals Follow-up Study (165 794 women and 43 339 men) with up to 32 years of follow-up, greater adherence to various healthy eating patterns was associated with lower risk of cardiovascular disease. The associations between dietary scores and risk of cardiovascular disease were consistent across different subgroups.

Meaning These findings support the recommendations of the 2015-2020 Dietary Guidelines for Americans that multiple healthy eating patterns can be adapted to individual food traditions and preferences.

Methods

Study Population

Data used in this prospective cohort study were from the Nurses' Health Study (NHS) (1984-2016), NHS II (1991-2017), and Health Professionals Follow-up Study (HPFS) (1986-2012). The dates of analysis were July 25 to December 4, 2019. The NHS is a prospective cohort study of 121 700 female registered nurses aged 30 to 55 years that began in 1976. The NHS II was established in 1989 and consists of 116 671 younger female registered nurses, aged 25 to 42 years. The HPFS is a prospective cohort study of 51 529 male health professionals aged 40 to 75 years that began in 1986. The follow-up rates in all 3 cohorts exceed 90%.[14-17] The institutional review boards of Harvard T.H. Chan School of Public Health and Brigham and Women's Hospital approved the study protocol. The return of the questionnaires was considered to imply informed consent.

For the present analysis, baseline was defined as the year when the diet was first assessed with a validated semiquantitative food frequency questionnaire (FFQ) with more than 110 items in the cohorts (1984 in the NHS, 1991 in the NHS II, and 1986 in the HPFS). Of the participants who completed the baseline FFQ (84 199 in the NHS, 97 813 in the NHS II, and 51 529 in the HPFS), we excluded those participants who reported CVD, cancer, or diabetes at baseline (8127 in the NHS, 3792 in the NHS II, and 6547 in the HPFS) because the diagnoses of these conditions might have led to changes in diet. We also excluded participants with missing age at baseline (45 in the NHS, 224 in the NHS II, and 27 in the HPFS) and those who had daily energy intakes less than 600 or greater than 3500 kcal for women (1097 in the NHS and 2951 in the NHS II) and less than 800 or greater than 4200 kcal for men (1616 in the HPFS).

Assessment of Dietary Scores

Dietary information was collected every 2 to 4 years.[18] Participants were asked how often, on average, they consumed a standard portion size of each food in the past year. The frequency responses ranged from never or less than 1 time per month to at least 6 times per day. The reproducibility and validity of the FFQs have been described in detail elsewhere,[18-21] showing reasonably good correlation between nutrients assessed by the FFQs and multiple weeks of food records or biomarkers of diet. Using the nutrient and food components, we calculated the HEI-2015, AMED, HPDI, and AHEI to measure adherence to different dietary patterns. These dietary scores have been evaluated in previous studies and have been widely applied in numerous epidemiological studies on diet patterns associated with the risk of chronic diseases.[22-25] The components and scoring criteria in detail for each dietary score are summarized in the eAppendix and eTables 1-4 in the Supplement. The HEI-2015 included 13 components, with the total score ranging from 0 to 100. The AMED included 9 components, with the total score ranging from 9 to 45. The HPDI included 18 components, with the total score ranging from 18 to 90. The AHEI included 10 components, with the total score ranging from 0 to 100. Higher dietary scores represented greater adherence to individual healthy eating patterns.

Assessment of CVD

This study included incident cases of CVD, defined as fatal and nonfatal CHD (including nonfatal myocardial infarction and coronary artery bypass graft surgery) and fatal and nonfatal stroke. When a participant reported an incident event on each biennial questionnaire, permission was requested to examine medical records, which were reviewed by study investigators blinded to the participant's risk factor status. Nonfatal

Table 1. Baseline Characteristics of Participants According to Quintiles of the Healthy Eating Index–2015 (HEI-2015), Alternate Mediterranean Diet Score (AMED), Healthful Plant-Based Diet Index (HPDI), and Alternate Healthy Eating Index (AHEI)[a]

	HEI-2015 quintile			AMED quintile			HPDI quintile			AHEI quintile		
Variable	1	3	5	1	3	5	1	3	5	1	3	5
NHS (1984)												
No. of participants	15 279	14 977	14 588	16 116	14 887	13 590	15 829	15 560	13 550	15 238	14 956	14 743
Dietary score, mean (SD)	50.8 (4.8)	64.4 (1.3)	75.5 (3.3)	19.5 (2.2)	27.0 (0.8)	35.3 (2.2)	44.6 (3.1)	54.4 (1.1)	65.4 (3.2)	29.3 (3.5)	42.0 (1.5)	57.8 (5.8)
Age, mean (SD), y	48.2 (7.0)	50.0 (7.1)	52.6 (6.8)	48.8 (7.1)	50.1 (7.1)	51.7 (7.0)	48.1 (7.0)	50.2 (7.1)	52.4 (6.8)	48.4 (7.1)	50.2 (7.1)	52.1 (6.8)
Non-Hispanic white race/ethnicity	97.9	97.7	97.4	98.0	98.0	97.4	98.4	97.7	97.4	98.7	97.8	96.5
Body mass index, mean (SD)[b]	25.1 (5.2)	25.0 (4.6)	24.4 (4.1)	25.1 (5.0)	24.9 (4.6)	24.6 (4.3)	25.4 (5.2)	24.9 (4.6)	24.2 (4.0)	25.1 (5.0)	25.0 (4.7)	24.4 (4.2)
Physical activity, mean (SD), MET-h/wk	9.5 (16.1)	12.9 (18.2)	17.3 (24.3)	9.5 (15.1)	12.6 (19.0)	17.7 (23.8)	10.4 (15.8)	12.7 (19.1)	16.9 (24.4)	9.4 (14.2)	12.7 (19.0)	18.0 (25.8)
Never												
Smoker	40.4	45.9	44.2	40.7	44.5	45.6	45.4	44.9	41.3	43.7	44.2	42.7
Drinker	36.6	29.4	27.7	42.7	29.5	20.2	31.2	30.2	30.4	34.4	29.8	29.7
Premenopausal	41.2	42.1	40.9	41.3	41.6	41.4	42.7	41.5	40.3	42.1	42.0	40.8
Married	65.1	70.0	70.1	64.9	69.6	71.2	67.9	69.0	69.6	68.7	68.9	68.5
Live alone	9.9	9.3	10.5	10.4	9.6	9.8	9.6	9.5	10.6	8.7	9.5	11.3
Family history of MI	25.2	24.7	25.8	25.4	25.1	26.1	24.4	24.9	26.3	25.0	25.3	25.8
Total energy intake, mean (SD), kcal/d	2029 (566)	1746 (490)	1454 (413)	1524 (488)	1727 (506)	2019 (525)	2079 (504)	1721 (495)	1445 (434)	1936 (492)	1730 (536)	1580 (505)
Multivitamin use	29.2	37.6	45.1	30.4	36.0	45.1	32.2	36.9	42.6	30.7	36.0	44.9
Aspirin use	71.3	71.5	68.3	69.9	71.4	71.0	72.8	71.4	68.2	72.7	71.3	68.0
NHS II (1991)												
No. of participants	18 190	18 213	18 086	20 381	17 915	15 951	16 975	14 430	17 868	18 278	18 159	18 105
Dietary score, mean (SD)	49.5 (4.9)	64.1 (1.4)	75.6 (3.3)	19.5 (2.2)	27.0 (0.8)	35.4 (2.2)	44.6 (3.2)	55.0 (0.8)	65.6 (3.4)	30.0 (3.9)	43.5 (1.6)	59.2 (5.4)
Age, mean (SD), y	35.5 (4.7)	36.1 (4.6)	36.8 (4.5)	35.7 (4.8)	36.0 (4.7)	36.6 (4.5)	35.0 (4.7)	36.1 (4.7)	37.0 (4.4)	35.3 (4.8)	36.1 (4.7)	36.9 (4.5)
Non-Hispanic white race/ethnicity	95.8	96.5	96.7	96.5	96.6	96.3	96.4	96.3	96.6	97.4	96.6	95.5
Body mass index, mean (SD)[b]	25.2 (6.2)	24.5 (5.1)	23.9 (4.5)	25.2 (5.8)	24.6 (5.2)	23.8 (4.7)	25.3 (6.1)	24.6 (5.2)	23.9 (4.5)	25.2 (6.0)	24.6 (5.1)	23.9 (4.7)
Physical activity, mean (SD), MET-h/wk	15.2 (22.9)	20.3 (25.6)	27.7 (32.5)	15.2 (22.0)	20.3 (26.7)	29.0 (34.2)	16.2 (21.6)	20.2 (26.6)	27.5 (33.6)	14.3 (19.6)	19.8 (25.3)	30.0 (35.3)
Never												
Smoker	63.8	67.2	65.0	64.4	66.5	65.0	68.6	66.1	62.1	66.9	66.5	63.7
Drinker	49.9	58.5	62.4	43.0	57.6	72.6	53.1	57.1	61.4	49.4	58.4	62.9
Premenopausal	96.2	96.5	96.5	96.4	96.3	96.7	96.6	96.4	96.3	96.3	96.6	96.6
Married	77.8	79.6	74.4	76.9	79.3	76.6	79.8	78.8	74.5	81.9	79.1	71.6
Live alone	8.2	7.5	9.7	8.8	7.5	8.3	7.15	7.6	9.7	6.2	7.7	10.9
Family history of MI	43.1	42.0	41.9	43.1	42.3	41.5	42.5	41.9	42.5	43.0	42.8	41.9
Total energy intake, mean (SD), kcal/d	2024 (580)	1795 (524)	1536 (441)	1503 (485)	1774 (504)	2131 (526)	2146 (520)	1759 (513)	1517 (456)	1969 (521)	1765 (550)	1677 (528)
Multivitamin use	37.6	44.0	50.0	36.2	44.0	52.2	41.4	43.5	46.5	38.9	43.8	49.0
Aspirin use	12.4	11.2	10.2	11.6	11.2	11.0	11.5	11.0	11.2	12.0	11.1	10.6

(continued)

myocardial infarction was confirmed according to the World Health Organization criteria,[26] and nonfatal stroke was confirmed according to the National Survey of Stroke criteria.[27] Information on coronary artery bypass graft surgery was based on unconfirmed self-reports.[28] Death was identified from the next of kin, postal authorities, or a search of the National Death Index, and at least 98% of deaths could be ascertained in each cohort.[29] Fatal CHD or stroke was defined as CHD or stroke listed as the cause of death on the death certificate.

Assessment of Covariates

Information on age, weight, physical activity, smoking status, multivitamin use, and aspirin use was assessed and updated every 2 to 4 years via the questionnaires throughout

Table 1. Baseline Characteristics of Participants According to Quintiles of the Healthy Eating Index–2015 (HEI-2015), Alternate Mediterranean Diet Score (AMED), Healthful Plant-Based Diet Index (HPDI), and Alternate Healthy Eating Index (AHEI)[a] (continued)

	HEI-2015 quintile			AMED quintile			HPDI quintile			AHEI quintile		
Variable	1	3	5	1	3	5	1	3	5	1	3	5
HPFS (1986)												
No. of participants	9076	8700	8072	9658	10642	8709	9985	8803	7313	9072	8714	8167
Dietary score, mean (SD)	52.5 (5.1)	67.1 (1.4)	79.1 (3.2)	19.3 (2.4)	27.5 (1.1)	35.7 (2.5)	44.5 (3.2)	54.5 (1.1)	65.6 (3.3)	32.2 (4.2)	46.7 (1.6)	62.6 (5.2)
Age, mean (SD), y	51.5 (9.3)	53.3 (9.6)	55.1 (9.5)	51.7 (9.4)	53.4 (9.5)	54.5 (9.6)	51.0 (9.3)	53.3 (9.6)	55.4 (9.4)	51.3 (9.3)	53.3 (9.6)	55.1 (9.5)
Non-Hispanic white race/ethnicity	91.0	90.3	91.2	90.9	90.4	91.8	92.0	90.5	90.7	92.0	90.6	91.2
Body mass index, mean (SD)[b]	25.7 (3.5)	25.6 (3.4)	24.8 (3.0)	25.8 (3.4)	25.5 (3.2)	25.0 (3.3)	25.6 (3.4)	25.6 (3.3)	25.1 (3.2)	25.8 (3.5)	25.6 (3.3)	25.0 (3.2)
Physical activity, mean (SD), MET-h/wk	14.7 (23.1)	19.1 (26.5)	24.7 (31.8)	13.6 (20.2)	18.7 (26.3)	25.6 (30.5)	16.5 (23.6)	18.1 (22.4)	23.9 (31.7)	14.1 (21.1)	18.5 (24.7)	25.0 (31.0)
Never												
Smoker	45.0	50.8	54.9	46.0	50.1	53.1	51.2	50.0	47.9	46.4	51.1	52.4
Drinker	27.3	21.5	21.8	32.2	21.6	14.9	22.9	22.3	24.3	24.7	22.4	22.2
Married	88.5	91.4	89.7	88.5	90.5	90.9	89.6	90.1	90.3	89.9	90.4	90.4
Live alone	7.0	5.5	6.5	7.2	5.8	5.5	6.5	6.1	6.2	6.3	6.0	5.7
Family history of MI	29.6	32.4	34.9	30.0	32.3	34.2	30.5	31.3	34.8	30.0	32.2	34.9
Total energy intake, mean (SD), kcal/d	2290 (676)	1982 (578)	1700 (489)	1769 (568)	1983 (601)	2270 (618)	2331 (619)	1943 (580)	1705 (518)	2119 (594)	1981 (637)	1895 (589)
Multivitamin use	34.9	41.0	51.5	35.4	41.6	50.3	36.1	42.3	48.3	35.6	41.5	49.9
Aspirin use	27.4	26.5	26.2	25.4	28.0	28.1	26.9	26.7	27.3	27.4	26.5	25.9

Abbreviations: HPFS, Health Professionals Follow-up Study; MET, metabolic equivalent task; MI, myocardial infarction; NHS, Nurses' Health Study.

[a] Data are percentages unless otherwise indicated. All variables, except age, are age standardized.

[b] Calculated as weight in kilograms divided by height in meters squared.

follow-up. Among women, information was also assessed on menopausal status, postmenopausal hormone use, and oral contraceptive use (NHS II only). Self-reported data on height and weight were used to calculate body mass index (BMI). Every 2 to 4 years, alcohol intake was updated on the FFQs. Information on Hispanic ethnicity was available in the NHS and the NHS II. If covariate information was missing, we imputed the mean values for continuous variables or used a missing indicator approach for categorical variables.

Statistical Analysis

This study calculated each individual's person-years from the date of the return of the baseline questionnaire to the date of CVD diagnosis, death, or end of follow-up (June 2016 for the NHS, June 2017 for the NHS II, and January 2012 for the HPFS), whichever occurred first. We did not censor participants lost to active follow-up because fatal events were included in the outcomes.

The cumulative average dietary scores were calculated by averaging the repeated measurements to better represent long-term dietary habits and to minimize within-person variation. For instance, for the 1994-1995 risk set in the HPFS, dietary scores in 1986, 1990, and 1994 were averaged to estimate subsequent CVD risk. We stopped updating dietary scores on a report of incident cancer, diabetes, or angina because changes in diet after development of these conditions may confound the association between diet and chronic diseases. This study used Cox proportional hazards models with time-varying covariates and age as the underlying timescale, with stratification by calendar time (in 2-year intervals), to assess the association between the 4 dietary scores and the subsequent risk of CVD. The proportional hazards assumption was evaluated with a likelihood ratio test comparing the model with and without an interaction term between age and dietary scores. In multivariable analysis, we adjusted for the updated potential confounders, including age, race/ethnicity, BMI, physical activity, smoking status, alcohol intake, postmenopausal status and postmenopausal hormone use (NHS and NHS II), oral contraceptive use (NHS II), marital status, living alone or with others, family history of CHD, total energy intake, multivitamin use, and aspirin use. Tests for linear trend across quintiles were conducted by assigning a median value to each quintile of dietary score, producing a single continuous variable used in the model. All 3 cohorts had greater than 90% power to detect a hazard ratio (HR) of 0.90 with $\alpha = .05$. In addition, a 25-percentile difference in each dietary score (25 points for the HEI-2015, 9 points for the AMED, 18 points for the HPDI, and 25 points for the AHEI) was calculated from the range of total dietary score (0-100 points for the HEI-2015, 9-45 points for the AMED, 18-90 points for the HPDI, and 0-100 points for the AHEI). Separate analyses were conducted for CVD, CHD, and stroke per a 25-percentile difference in each dietary score. All analyses were performed separately for each cohort and then were pooled with the use of fixed-effects meta-analysis with inverse-variance weighting.

Table 2. Pooled Hazard Ratios of Cardiovascular Disease According to Quintiles of the Healthy Eating Index–2015 (HEI-2015), Alternate Mediterranean Diet Score (AMED), Healthful Plant-Based Diet Index (HPDI), and Alternate Healthy Eating Index (AHEI)

	Quintile of dietary score				
Variable[a]	1	2	3	4	5
HEI-2015					
Median score					
NHS	55	62	67	71	76
NHS II	52	60	65	69	75
HPFS	55	63	68	72	78
Deaths/person-years	4864/1 023 862	4715/1 055 329	4734/1 065 029	4590/1 066 708	4463/1 046 262
Age-adjusted HR (95% CI)	1 [Reference]	0.86 (0.83-0.90)	0.81 (0.78-0.85)	0.75 (0.72-0.78)	0.68 (0.65-0.71)
Multivariable-adjusted HR (95% CI)[b]	1 [Reference]	0.93 (0.89-0.97)	0.91 (0.87-0.95)	0.86 (0.83-0.90)	0.83 (0.79-0.86)
AMED					
Median score					
NHS	20	24	27	30	34
NHS II	20	24	27	30	34
HPFS	20	24	27	31	35
Deaths/person-years	4858/1 034 832	4780/1 038 118	4839/1 076 122	4630/1 083 871	4259/1 024 246
Age-adjusted HR (95% CI)	1 [Reference]	0.89 (0.85-0.92)	0.83 (0.80-0.87)	0.78 (0.75-0.82)	0.71 (0.68-0.74)
Multivariable-adjusted HR (95% CI)[b]	1 [Reference]	0.94 (0.90-0.98)	0.90 (0.87-0.94)	0.88 (0.84-0.92)	0.83 (0.79-0.86)
HPDI					
Median score					
NHS	47	52	55	59	64
NHS II	47	52	55	59	64
HPFS	46	51	55	59	64
Deaths/person-years	4731/1 072 015	4829/1 109 660	4913/1 083 866	4740/1 055 658	4153/935 991
Age-adjusted HR (95% CI)	1 [Reference]	0.92 (0.88-0.96)	0.87 (0.83-0.90)	0.85 (0.82-0.88)	0.78 (0.75-0.81)
Multivariable-adjusted HR (95% CI)[b]	1 [Reference]	0.95 (0.91-0.99)	0.91 (0.87-0.95)	0.90 (0.86-0.94)	0.86 (0.82-0.89)
AHEI					
Median score					
NHS	34	41	46	51	59
NHS II	33	40	45	50	59
HPFS	35	42	48	53	61
Deaths/person-years	5110/1 063 578	4966/1 090 162	4840/1 077 328	4541/1 046 139	3909/979 984
Age-adjusted HR (95% CI)	1 [Reference]	0.87 (0.84-0.90)	0.82 (0.79-0.86)	0.76 (0.73-0.79)	0.68 (0.65-0.71)
Multivariable-adjusted HR (95% CI)[b]	1 [Reference]	0.91 (0.87-0.95)	0.88 (0.85-0.92)	0.84 (0.81-0.88)	0.79 (0.75-0.82)

Abbreviations: HPFS, Health Professionals Follow-up Study; HR, hazard ratio; NHS, Nurses' Health Study.

[a] *P* for trend <.001 for all age-adjusted HR rows and multivariable-adjusted HR rows.

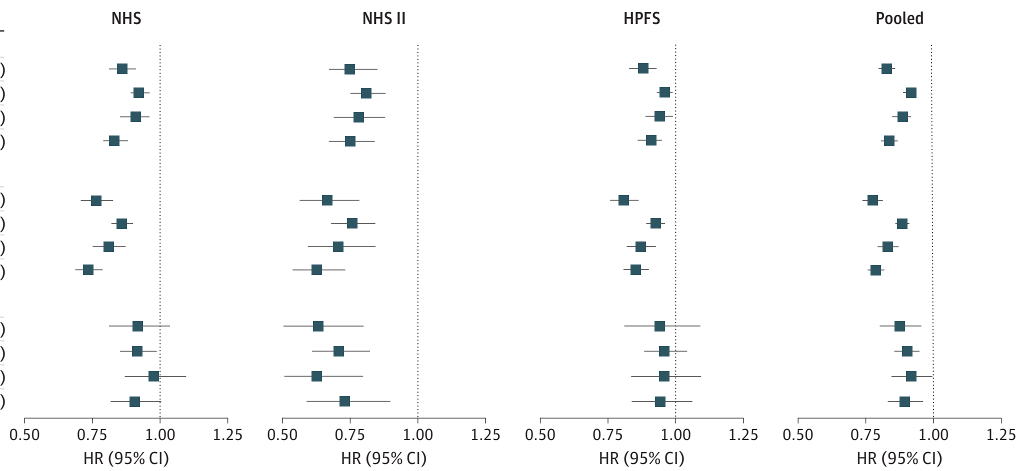
[b] Multivariable adjusted for age (continuous), race/ethnicity (non-Hispanic white, non-Hispanic black, or Hispanic [NHS and NHS II only]), body mass index (calculated as weight in kilograms divided by height in meters squared [<21, 21-24.9, 25-29.9, 30-34.9, or ≥35]), physical activity (quintile), smoking status (never, former, or current [1-14, 15-24, or ≥25 cigarettes per day]), alcohol intake (0, 0.1-4.9, 5.0-14.9, 15.0-19.9, 20.0-29.9, or ≥30 g/d), menopausal status (premenopausal or postmenopausal [never, past, or current postmenopausal hormone use]), oral contraceptive use (never, past, or current [NHS II only]), marital status (married, divorced/separated/single, or widowed), living alone or with others (alone or not), family history of myocardial infarction (yes or no), total energy intake (quintile), multivitamin use (yes or no), and aspirin use (yes or no).

Heterogeneity was assessed with the I^2 statistic, and low to moderate heterogeneity was observed ($I^2 < 60\%$ for all). In addition, random-effects meta-analysis yielded similar results.

We conducted stratified analyses that were defined a priori by race/ethnicity (NHS and NHS II) and other potential risk modifiers, including age, sex, BMI, physical activity, smoking status, alcohol intake, menopausal status, multivitamin use, aspirin use, and history of hypertension and hypercholesterolemia. The interactions between covariates and the 4 dietary scores were examined using the likelihood ratio test. Given a large number of tests being performed for subgroup analyses, we adjusted the *P* value for multiple testing using Bonferroni correction, and statistical significance was set at $P \le .001$ (.05 ÷ [11 subgroups × 4 dietary scores]) to account for type I error. Several sensitivity analyses were performed to test the robustness of our findings. First, we did not include self-reported cases of coronary artery bypass graft surgery as an end point and reanalyzed the associations of the 4 dietary scores with the risk of total CVD and CHD. Second, to test whether our results were biased by selectively not updating dietary scores after an intermediate outcome, we continu-

Figure 1. Hazard Ratios of Cardiovascular Disease (CVD), Coronary Heart Disease (CHD), and Stroke per 25-Percentile Increment in the 4 Dietary Scores[a]

	Pooled HR (95% CI)
CVD	
HEI-2015	0.80 (0.77-0.83)
AMED	0.90 (0.87-0.92)
HPDI	0.86 (0.82-0.89)
AHEI	0.81 (0.78-0.84)
CHD	
HEI-2015	0.78 (0.74-0.82)
AMED	0.89 (0.86-0.91)
HPDI	0.84 (0.80-0.87)
AHEI	0.79 (0.76-0.82)
Stroke	
HEI-2015	0.88 (0.81-0.96)
AMED	0.90 (0.86-0.95)
HPDI	0.92 (0.85-1.00)
AHEI	0.90 (0.83-0.97)



The multivariable analysis was adjusted for age (continuous), race/ethnicity (non-Hispanic white, non-Hispanic black, or Hispanic [NHS and NHS II only]), body mass index (calculated as weight in kilograms divided by height in meters squared [<21, 21-24.9, 25-29.9, 30-34.9, or ≥35]), physical activity (quintile), smoking status (never, former, or current [1-14, 15-24, or ≥25 cigarettes per day]), alcohol intake (0, 0.1-4.9, 5.0-14.9, 15.0-19.9, 20.0-29.9, or ≥30 g/d), menopausal status (premenopausal or postmenopausal [never, past, or current postmenopausal hormone use]), oral contraceptive use (never, past, or current [NHS II only]), marital status (married, divorced/separated/single, or widowed), living alone or with others (alone or not), family history of myocardial infarction (yes or no), total energy intake (quintile), multivitamin use (yes or no), and aspirin use (yes or no). Results were pooled using the fixed-effect model with inverse-variance weighting. AHEI indicates Alternate Healthy Eating Index; AMED, Alternate Mediterranean Diet Score; HEI-2015, Healthy Eating Index–2015; HPDI, Healthful Plant-Based Diet Index; HPFS, Health Professionals Follow-up Study; HR, hazard ratio; and NHS, Nurses' Health Study.

[a] Calculated per 25-percentile increment in the 4 dietary scores (25 points for the HEI-2015, 9 points for the AMED, 18 points for the HPDI, and 25 points for the AHEI).

ously updated dietary scores until the end of follow-up. Third, instead of using repeated measures of dietary habits, we analyzed the associations of baseline dietary scores with the incidence of CVD. All analyses were performed with the SAS statistical package (version 9.4; SAS Institute Inc). All statistical tests were 2-sided, and *P* < .05 was considered to indicate statistical significance.

Results

The final study sample included 74 930 women in the NHS (mean [SD] baseline age, 50.2 [7.2] years), 90 864 women in the NHS II (mean [SD] baseline age, 36.1 [4.7] years), and 43 339 men in the HPFS (mean [SD] baseline age, 53.2 [9.6] years). **Table 1** lists age and the age-adjusted characteristics of study participants at baseline according to quintiles of the 4 dietary scores. In all cohorts, participants with higher dietary scores tended to be older, have a lower BMI, be more likely to exercise, and be less likely to smoke (Table 1). Total energy intake was higher in participants with higher AMED but lower in those with higher HEI-2015, HPDI, and AHEI. The unadjusted Spearman rank correlation coefficients between the 4 dietary scores ranged from 0.35 to 0.75 (*P* < .001 for all), with the weakest correlation between the AMED and the HPDI and the strongest correlation between the HEI-2015 and the AHEI (eTable 5 in the Supplement).

During a total of 5 257 190 person-years of follow-up, 23 366 incident CVD cases were documented (18 092 CHD and 5687 stroke) (some individuals were diagnosed as having both CHD and stroke). After accounting for multiple potential confounding factors, the multivariable analyses showed statistically significant inverse associations across quintiles of the 4 dietary scores with risk of CVD in each cohort (eTable 6 in the Supplement). The tests for the proportional hazards assumption did not indicate a violation in any cohort. Comparing the highest with the lowest quintiles, the pooled multivariable-adjusted HRs of CVD were 0.83 (95% CI, 0.79-0.86) for the HEI-2015, 0.83 (95% CI, 0.79-0.86) for the AMED, 0.86 (95% CI, 0.82-0.89) for the HPDI, and 0.79 (95% CI, 0.75-0.82) for the AHEI (*P* for trend <.001 for all) (**Table 2**). In addition, a 25-percentile higher dietary score was associated with 10% to 20% lower risk of CVD (pooled HR, 0.80 [95% CI, 0.77-0.83] for the HEI-2015; 0.90 [95% CI, 0.87-0.92] for the AMED; 0.86 [95% CI, 0.82-0.89] for the HPDI; and 0.81 [95% CI, 0.78-0.84] for the AHEI) (**Figure 1**). We further examined the associations of dietary scores with CHD and stroke separately (Figure 1). For CHD, the pooled HRs per 25-percentile increment were 0.78 (95% CI, 0.74-0.82) for the HEI-2015, 0.89 (95% CI, 0.86-0.91) for the AMED, 0.84 (95% CI, 0.80-0.87) for the HPDI, and 0.79 (95% CI, 0.76-0.82) for the AHEI. For stroke, the pooled HRs per 25-percentile increment were 0.88 (95% CI, 0.81-0.96) for the HEI-2015, 0.90 (95% CI, 0.86-0.95) for the AMED, 0.92 (95% CI, 0.85-1.00) for the HPDI, and 0.90 (95% CI, 0.83-0.97) for the AHEI.

Among women in the NHS and the NHS II, differences in dietary scores were observed by race/ethnicity over time (eFigure 1 and eFigure 2 in the Supplement). For example, the HEI-2015 was

Table 3. Pooled Hazard Ratios of Cardiovascular Disease According to the 4 Dietary Scores Across Racial/Ethnic Groups in the Nurses' Health Study and Nurses' Health Study II[a]

Variable[b]	Cases/person-years	HR (95% CI)	*P* value for interaction[c]
HEI-2015			
Non-Hispanic white	11 793/4 068 772	0.68 (0.64-0.72)	NA
Minority racial/ethnic group	798/288 861	0.71 (0.55-0.91)	.74
Non-Hispanic black	144/52 982	0.62 (0.33-1.15)	.77
Hispanic	92/55 008	0.48 (0.22-1.07)	.39
Other	562/180 871	0.77 (0.58-1.03)	.41
AMED			
Non-Hispanic white	11 793/4 068 772	0.80 (0.77-0.84)	NA
Minority racial/ethnic group	798/288 861	0.79 (0.68-0.92)	.88
Non-Hispanic black	144/52 982	0.86 (0.59-1.27)	.71
Hispanic	92/55 008	0.74 (0.46-1.20)	.75
Other	562/180 871	0.78 (0.66-0.93)	.78
HPDI			
Non-Hispanic white	11 793/4 068 772	0.78 (0.74-0.83)	NA
Minority racial/ethnic group	798/288 861	0.70 (0.55-0.89)	.39
Non-Hispanic black	144/52 982	0.76 (0.41-1.40)	.93
Hispanic	92/55 008	0.82 (0.40-1.68)	.89
Other	562/180 871	0.67 (0.51-0.89)	.30
AHEI			
Non-Hispanic white	11 793/4 068 772	0.70 (0.66-0.74)	NA
Minority racial/ethnic group	798/288 861	0.72 (0.58-0.88)	.80
Non-Hispanic black	144/52 982	0.78 (0.45-1.34)	.70
Hispanic	92/55 008	0.50 (0.26-0.98)	.32
Other	562/180 871	0.74 (0.58-0.94)	.66

Abbreviations: AHEI, Alternate Healthy Eating Index; AMED, Alternate Mediterranean Diet Score; HEI-2015, Healthy Eating Index–2015; HPDI, Healthful Plant-Based Diet Index; HR, hazard ratio; NA, not applicable.

[a] Results from the Nurses' Health Study (NHS) and the NHS II were pooled using the fixed-effect model with inverse-variance weighting per 25-percentile increment in the 4 dietary scores (25 points for the HEI-2015, 9 points for the AMED, 18 points for the HPDI, and 25 points for the AHEI). Multivariable analysis adjusted for age, body mass index, physical activity, smoking status, alcohol intake, menopausal status, oral contraceptive use (NHS II only), calendar year marital status, living alone or with others, family history of myocardial infarction, total energy intake, multivitamin use, aspirin use, and family history of diabetes.

[b] Non-Hispanic white includes non-Hispanic women with southern European/Mediterranean ancestry, Scandinavian ancestry, and other Caucasian ancestry. Minority racial/ethnic groups include non-Hispanic black, Hispanic, and other racial/ethnic women. Other includes women not classified as non-Hispanic white, non-Hispanic black, or Hispanic, such as Asian and American Indian.

[c] Interaction between non-Hispanic white and total minority racial/ethnic group or individual racial/ethnic group.

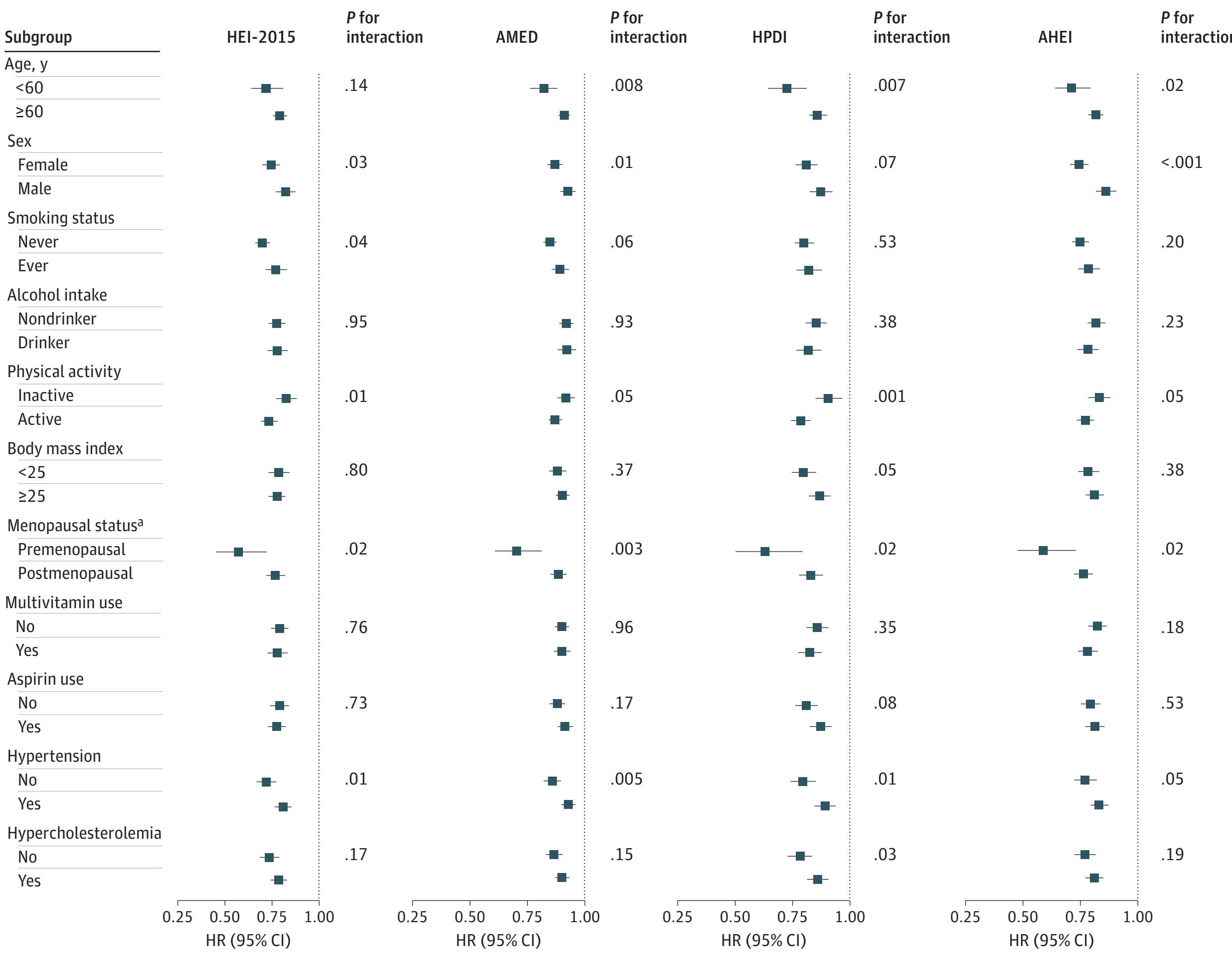
higher in Hispanic individuals than in other racial/ethnic groups. However, in stratified analyses by race/ethnicity, the associations between dietary patterns and risk of CVD did not differ statistically significantly; the HRs of CVD per 25-percentile difference in the HEI-2015 were 0.68 (95% CI, 0.64-0.72) in non-Hispanic white individuals and 0.71 (95% CI, 0.55-0.91) in overall minority racial and ethnic groups (*P* for interaction = .74) (**Table 3**). Similarly, there were no statistically significant differences in the associations of the other 3 dietary scores with CVD risk across racial/ethnic groups (Table 3). Consistent inverse associations were also observed in other subgroup analyses (**Figure 2**). In sensitivity analyses, the associations remained similar when we excluded self-reported cases of coronary artery bypass graft surgery as an end point (eFigure 3 in the Supplement). The inverse associations per 25-percentile increase in each dietary score with CVD risk were attenuated but remained statistically significant when the baseline dietary data were used and the dietary scores were continuously updated until the end of follow-up (eFigure 4 in the Supplement).

Discussion

In 3 large prospective cohorts, greater adherence to various dietary patterns was associated with lower CVD risk. Similar inverse associations were observed for incident CHD and stroke. The associations between dietary scores and risk of CVD were consistent across racial/ethnic and other subgroups.

Our results are broadly consistent with previous studies[23-25] that reported inverse associations between healthy dietary scores and risk of incident CVD. To date, only 1 study[30] has examined the associations between the HEI-2015 and risk of CVD among US adults. With data from the Atherosclerosis Risk in Communities Study, Hu and colleagues[30] simultaneously investigated the associations of the HEI-2015 and other dietary scores with CVD risk and found similar inverse associations in direction and magnitude for the HEI-2015, AMED, and AHEI. The Dietary Patterns Methods Project also found that better diet quality (as assessed by the HEI-2010, AMED, AHEI, and

Figure 2. Pooled Hazard Ratios of Cardiovascular Disease According to the 4 Dietary Scores Across Subgroups



The multivariable analysis was adjusted for age (continuous), race/ethnicity (non-Hispanic white, non-Hispanic black, or Hispanic [Nurses' Health Study and Nurses' Health Study II only]), body mass index (calculated as weight in kilograms divided by height in meters squared [<21, 21-24.9, 25-29.9, 30-34.9, or ≥35]), physical activity (quintile), smoking status (never, former, or current [1-14, 15-24, or ≥25 cigarettes per day]), alcohol intake (0, 0.1-4.9, 5.0-14.9, 15.0-19.9, 20.0-29.9, or ≥30 g/d), menopausal status (premenopausal or postmenopausal [never, past, or current postmenopausal hormone use]), oral contraceptive use (never, past, or current [Nurses' Health Study II only]), marital status (married, divorced/separated/single, or widowed), living alone or with others (alone or not), family history of myocardial infarction (yes or no), total energy intake (quintile), multivitamin use (yes or no), and aspirin use (yes or no). Results were pooled using the fixed-effect model with inverse-variance weighting. AHEI indicates Alternate Healthy Eating Index; AMED, Alternate Mediterranean Diet Score; HEI-2015, Healthy Eating Index–2015; HPDI, Healthful Plant-Based Diet Index; and HR, hazard ratio.

[a] Calculated per 25-percentile increment in the 4 dietary scores (25 points for the HEI-2015, 9 points for the AMED, 18 points for the HPDI, and 25 points for the AHEI). These results are from the Nurses' Health Study and Nurses' Health Study II.

other scores) was associated with 18% to 26% lower risk of all-cause and CVD mortality.[12,13] These dietary scores share several components, including higher intake of whole grains, vegetables, fruits, legumes, and nuts,[31] all of which have been associated with lower risk of CVD.[32-35] The high correlations in the indexes, except between the AMED and the HPDI, also suggested a high degree of agreement. However, these dietary scores also differ in some specific components and scoring methods. None of the indexes were perfectly correlated, indicating that each dietary score represents a unique combination of dietary constituents. Our findings provide support for the recommendations of the current Dietary Guidelines for Americans[9] that it is not necessary to conform to a single dietary plan to achieve healthy eating.

To facilitate a comparison of the associations between the 4 dietary scores of healthy eating patterns, we reported a 25-percentile increment in each dietary score as a common unit that was associated with a statistically significantly lower CVD risk (20% for the HEI-2015, 10% for the AMED, 14% for the HPDI, and 19% for the AHEI). The HEI-2015 and the AHEI appear to have stronger inverse associations with CVD than the AMED and the HPDI. These differences were mainly attributable to associations with CHD (22% for the HEI-2015, 11% for the AMED, 16% for the HPDI, and 21% for the AHEI) because all 4 dietary scores showed similar associations with risk of stroke (12% for the HEI-2015, 10% for the AMED, 8% for the HPDI, and 10% for the AHEI). These results were in line with previous findings of stronger associations for improved adherence to the AHEI than the AMED with subsequent risk of CHD incidence and CVD.[36] Although the 4 dietary scores share several common healthy components, there are some differences in the specific components included in each dietary score, which may partly explain the differences in their associations with CVD risk. For example, fish intake, which has been associated with lower risk of CVD,[37,38] was included as a positive contributor (higher intake receiving higher score) in the AMED but as a negative contributor (higher intake receiving lower score) in the HPDI. In addition, compared with the categorization scales used in the calculations of the AMED and the HPDI, the continuous scales used in the calculations of the HEI-2015 and the AHEI may have the advantage of capturing stronger associations. Because of the differences in the scoring systems, it is difficult to conclude that 1 healthy eating pattern is superior to another.

Previous studies[39,40] with nationally representative data indicated differences across population groups in overall dietary patterns. In our study, the magnitude of the inverse associations between dietary scores and CVD risk was similar across racial/ethnic groups of women. These findings are consistent with those observed in the Multiethnic Cohort[13] and the Atherosclerosis Risk in Communities Study,[30] which showed a reduction in risk of CVD mortality according to higher HEI, AMED, and AHEI among several racial/ethnic groups. In addition, statistically significant inverse associations were consistently observed between these dietary scores and risk of CVD in subgroup analyses stratified by multiple potential risk factors for CVD, such as lifestyle factors (including physical activity, smoking status, and alcohol intake), aspirin use, and baseline prevalence of hypertension and hypercholesterolemia. We believe that the consistent associations in several sensitivity analyses also highlighted the robustness of our findings. These results support the notion that individuals could choose different healthy eating patterns based on their personal food traditions or preferences for prevention of CVD.

Strengths and Limitations

The strengths of this study include the prospective design, large sample size, long-term follow-up with a high retention rate, and repeated assessments of diet and lifestyle. However, several limitations should be noted. First, because the dietary assessment was based on self-reports, measurement error and misclassification were inevitable. However, the FFQs used in the study were extensively validated against diet records and biomarkers. Furthermore, repeated measures of dietary habits during the follow-up allowed us to calculate the cumulative average dietary scores, which reflect long-term dietary habits and reduce measurement errors. Second, although we controlled for several repeated measurements of lifestyle factors, the possibility of residual and unmeasured confounding could not be completely ruled out because of the observational nature of the study. Third, the dietary scores used in this study could not fully represent the healthy eating patterns. However, these scores were adapted in nutritional epidemiology studies[22-25] to evaluate dietary adherence to healthy dietary patterns in free-living populations. Fourth, the generalizability of our findings may be limited because participants in our study were all health professionals and predominantly non-Hispanic white individuals. However, our findings are broadly consistent across different racial/ethnic groups and with results from other populations.

Conclusions

Greater adherence to various healthy eating patterns was consistently associated with lower risk of CVD. Our findings support the 2015-2020 Dietary Guidelines for Americans, which recommend multiple healthy eating patterns for individuals to adapt according to personal food traditions and preferences.

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