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Original Contribution

Adherence to a Healthy Diet According to the World Health Organization Guidelines and All-Cause Mortality in Elderly Adults From Europe and the United States

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The World Health Organization (WHO) has formulated guidelines for a healthy diet to prevent chronic diseases and postpone death worldwide. Our objective was to investigate the association between the WHO guidelines, measured using the Healthy Diet Indicator (HDI), and all-cause mortality in elderly men and women from Europe and the United States. We analyzed data from 396,391 participants (42% women) in 11 prospective cohort studies who were 60 years of age or older at enrollment (in 1988–2005). HDI scores were based on 6 nutrients and 1 food group and ranged from 0 (least healthy diet) to 70 (healthiest diet). Adjusted cohort-specific hazard ratios were derived by using Cox proportional hazards regression and subsequently pooled using random-effects meta-analysis. During 4,497,957 person-years of follow-up, 84,978 deaths occurred. Median HDI scores ranged from 40 to 54 points across cohorts. For a 10-point increase in HDI score (representing adherence to an additional WHO guideline), the pooled adjusted hazard ratios were 0.90 (95% confidence interval (CI): 0.87, 0.93) for men and women combined, 0.89 (95% CI: 0.85, 0.92) for men, and 0.90 (95% CI: 0.85, 0.95) for women. These estimates translate to an increased life expectancy of 2 years at the age of 60 years. Greater adherence to the WHO guidelines is associated with greater longevity in elderly men and women in Europe and the United States.

aging; cohort; Consortium on Health and Ageing: Network of Cohorts in Europe and the United States; diet; longevity; meta-analysis

Abbreviations: BMI, body mass index; CHANCES, Consortium on Health and Ageing: Network of Cohorts in Europe and the United States; CI, confidence interval; EPIC-Elderly, European Prospective Investigation Into Cancer and Nutrition–Elderly; HAPIEE, Health, Alcohol, and Psychosocial Factors in Eastern European Countries; HDI, Healthy Diet Indicator; NIH-AARP, National Institutes of Health–AARP Diet and Health; PUFA, polyunsaturated fatty acids; SENECA, Survey in Europe on Nutrition and the Elderly, a Concerted Action; WHO, World Health Organization.

The elderly population is growing, and we need to understand which factors contribute to an increase in lifespan (1). Diet plays an important role in extending life expectancy (2), but more research is required to quantify the magnitude of its role. Studying diet by means of dietary pattern analysis is an appealing method to assess the association with longevity because humans do not consume single foods or nutrients, but rather complex diets (3). A well-known example of a healthy dietary pattern is the Mediterranean diet, which is known to reduce the risk of premature death (4). The latest scientific evidence on the association of diet with chronic diseases and death is summarized in population-specific dietary

guidelines, which aim to help people make informed "healthy" choices. The adherence to dietary guidelines can be measured by diet quality indices. One example of a dietary index is the American Healthy Eating Index, which defines adherence to the US dietary guidelines (5). The Healthy Eating Index–2010 was found to be inversely associated with all-cause mortality in elderly participants in the United States (6). However, studies on an international level require the operationalization of globally applicable dietary guidelines. Therefore, the 1990 World Health Organization (WHO) guidelines for a healthy diet for the prevention of chronic diseases and subsequent increase of life expectancy (7) were translated into the Healthy Diet Indicator (HDI) (8, 9).

In 2003, the WHO updated the dietary guidelines according to the latest scientific evidence (10). The association between survival and a healthy diet that accords with the latest WHO guidelines has not been quantified. Combining all causes of death as a single outcome measure is of great interest for the population under study, because comorbid conditions frequently prevent identification of the primary causes of death (11). Our hypothesis was that greater adherence to the WHO guidelines is associated with greater longevity. We tested this hypothesis and quantified the number of years of life gained by following the WHO guidelines in 11 prospective cohort studies of participants aged 60 years or older from Europe and the United States.

METHODS

We conducted a meta-analysis of individual participant data from 11 population-based cohorts of the Consortium on Health and Ageing: Network of Cohorts in Europe and the United States (CHANCES). Its aim is to combine and integrate prospective cohort studies to produce, improve, and clarify the evidence on the distribution and risk factors of chronic diseases in the elderly and their socioeconomic implications (www.chancesfp7.eu). The CHANCES cohorts were chosen because all variables needed for this project were harmonized according to predefined rules. The harmonization rules were discussed among the CHANCES partners until a consensus was reached.

We included participants 60 years of age or older from the European Prospective Investigation Into Cancer and Nutrition–Elderly (EPIC-Elderly) Study (12) from Spain, the Netherlands, Greece, Sweden, and Denmark; the Health, Alcohol, and Psychosocial Factors in Eastern European Countries (HAPIEE) Study (13) from Czech Republic, Russia, and Poland; the National Institutes of Health–AARP Diet and Health (NIH-AARP) Study from the United States (14); the Rotterdam Elderly Study (RES) (15) from the Netherlands; and the Survey in Europe on Nutrition and the Elderly, a Concerted Action (SENECA) Study (16) from Europe. Baseline data were collected between 1988 and 2005. Before the analysis, we excluded participants with incomplete follow-up information relevant for the analysis. We also excluded participants with missing information on age or death status, as well those who had missing or unrealistic information on body mass index (BMI) (weight (kg)/height $(m)^2$) (i.e., BMI values of >60 or <10) at baseline and those with extreme energy intakes. The RES and the NIH-AARP Study had dietary intake outliers that we removed by Box-Cox transformation.

Main characteristics of the cohorts have been previously described in the literature (12–15, 17–19) and are summarized in Web Table 1, available at http://aje.oxfordjournals.org/. In all cohorts, the collaborative research procedures were in accordance with the ethical standards of the responsible institutional or regional committees on human experimentation, and all participants gave written informed consent.

All-cause mortality

Information on vital status was almost complete across cohorts (Web Table 1). The start of follow-up was defined as age at baseline, and the end of follow-up was defined as the age of the participant at last linkage with the death registry.

Dietary assessment

Different dietary assessment methods were used in each cohort. Most cohorts applied a validated food frequency questionnaire (12–18). The SENECA Study used a validated dietary history method (19). The total numbers of food frequency questionnaire or dietary history items, reference periods, and interview-derived or self-reported dietary assessments differed across cohorts. Translation of foods into nutrients was performed by using cohort-specific food composition tables.

Healthy Diet Indicator

We substituted the WHO guidelines on the HDI score that were introduced by Huijbregts et al. (8) with the updated WHO guidelines from 2003 on diet and nutrition to prevent chronic diseases. The initial dichotomous scoring system (8) was replaced by a continuous scoring system, because this deals more efficiently with between-person variation and can better reveal diet-disease associations (20). WHO components, as updated in 2003, and HDI scoring standards are shown in Table 1. All cohorts had information on 9 nutrients and 1 food group of the 14 WHO guideline goals. Five of the 11 cohorts (3 cohorts of the HAPIEE Study plus the NIH-AARP Study and the RES) had information on all dietary intake goals. To improve the comparability with previous studies (6), we focused on the following 7 HDI components, which were available in all cohorts: percentages of energy intake from saturated fatty acids, polyunsaturated fatty acids (PUFAs), mono- and disaccharides, and protein; and intakes of cholesterol (mg/day), fruits and vegetables combined (g/day), and either total dietary fiber or nonstarch polysaccharides (g/day). The intakes of *n*-3 PUFAs, *n*-6 PUFAs, *trans*-fatty acids, and sodium were not included in the score for the main analysis. Furthermore, as suggested before (8), we excluded total fat and total carbohydrates from the HDI score calculation to avoid duplicating weights for these 2 components. We did not include monounsaturated fatty acids because the WHO guidelines do not take them into account. Dietary fiber was used for the HDI score calculation in all cohorts except the HAPIEE Study, in which only information on intake of nonstarch polysaccharide was available. Data on intake of free sugars were not available in all cohorts and were replaced

Table 1. Healthy Diet Indicator Components Based on the World Health Organization's 2003 Dietary Guidelines[a,b] and Operationalization as Applied in the Consortium on Health and Ageing: Network of Cohorts in Europe and the United States, 1988–2011

HDI Component	Standard (Lower Limit) for Minimum HDI Score of 0 Points[c]	Standard for Maximum HDI Score of 10 Points[d]	Standard (Upper Limit) for Minimum HDI Score of 0 Points[e]
"Moderation" components			
Saturated fatty acids, energy %[f,g]	NA	<10	>15
Mono-and disaccharides, energy %[g,h]	NA	<10	>30
Cholesterol, mg/day	NA	<300	>400
"Moderation range" components			
Polyunsaturated fatty acids, energy %[g]	0	6–10	>10
Protein, energy %[g]	0	10–15	>20
"Adequacy" components			
Total dietary fiber, g/day[i]	0	>25	NA
Fruits and vegetables, g/day	0	>400	NA

Abbreviations: HDI, Healthy Diet Indicator; NA, not applicable; WHO, World Health Organization.

[a] WHO guidelines for total fat and carbohydrates were not scored because of overlap with included components.

[b] WHO guidelines for monounsaturated fatty acids, *n*-6 and *n*-3 polyunsaturated fatty acids, *trans*-fatty acids, and sodium were not scored because of lack of information.

[c] Points for dietary intake between the lower limit and the standard intake for maximum number of points were calculated as follows: (intake / standard lower limit) × 10.

[d] Standard in accordance with WHO guidelines. The joint WHO Food and Agriculture Organization of the United Nations guidelines of 2003 do not clearly indicate fiber cutoff values. Fulfillment of the fruit and vegetable recommendation and consumption of whole grains should sum to 20 g of nonstarch polysaccharides, which equals approximately 25 g of dietary fiber.

[e] The upper cutoff value at which a participant could score more than 0 points was based on the 85th percentile of the population's intake distribution. Calculation of points for dietary intake between the upper limit and the standard intake for maximum number of points was as follows: 10 – (intake – 10) × 10 / standard upper limit – 10).

[f] Calculated without energy from alcohol.

[g] "Energy %" represents percentage of energy intake from that dietary component.

[h] Free sugars were replaced by mono- and disaccharides.

[i] Data on fiber were not available for Health, Alcohol, and Psychosocial Factors in Eastern European Countries (HAPIEE) participants. Therefore, we instead applied nonstarch polysaccharides for that cohort with a standard maximum score of 20.

Table 2. Follow-up Information on 396,391 Participants in the Consortium on Health and Ageing: Network of Cohorts in Europe and the United States, 1988–2011

CHANCES Cohort	Region	Start of Follow-up	End of Follow-up	Median Follow-up, years
EPIC-Elderly	Spain	1992–1996	2009	14
	Netherlands	1993–1997	2009	13
	Greece	1994–1999	2011	11
	Sweden	1992–1996	2009	14
	Denmark	1993–1997	2007	12
HAPIEE	Czech Republic	2002–2005	2011	8
	Russia	2002–2005	2010	7
	Poland	2002–2005	2009	5
NIH-AARP	United States	1995–1996	2008	13
RES	Netherlands	1989–1993	2010	15
SENECA	Europe	1988	1998	10

Abbreviations: CHANCES, Consortium on Health and Ageing: Network of Cohorts in Europe and the United States; EPIC-Elderly, European Prospective Investigation Into Cancer and Nutrition–Elderly Study; HAPIEE, Health, Alcohol, and Psychosocial Factors in Eastern European Countries Study; NIH-AARP, National Institutes of Health–AARP Diet and Health Study; RES, Rotterdam Elderly Study; SENECA, Survey in Europe on Nutrition and the Elderly, a Concerted Action.

Table 3. Baseline Characteristics of 396,391 Consortium on Health and Ageing: Network of Cohorts in Europe and the United States Participants, 1988–2011

Characteristic	No. of Participants										
	EPIC-Elderly					HAPIEE			NIH-AARP (United States)	RES (Netherlands)	SENECA (Europe)
	Spain	Netherlands	Greece	Sweden	Denmark	Czech Republic	Russia	Poland			
Participants prior exclusions	5,185	6,896	9,863	3,364	15,355	3,442	3,796	3,877	349,047	4,320	2,251
Participants eligible for analysis	5,168	6,730	9,531	3,263	15,264	3,376	3,794	3,859	339,182	4,160	2,064
Cause of death											
Cancer	284	408	608	193	973	193	131	136	27,034	NA	169
CVD	179	295	932	154	556	153	319	102	22,993	707	286
All deaths	643	1,010	2,006	499	2,438	411	590	305	73,883	2,397	796
Male sex	2,228	309	3,824	1,541	7,083	1,642	1,755	1,967	205,174	1,709	1,028
Disease at baseline											
Cancer	74	489	336	NA	193	235	128	235	6,374	NA	38
CHD	71	211	388	90	536	281	401	495	57,309	604	324
Diabetes	592	300	1,373	100	449	569	275	612	34,221	428	174
Stroke	71	127	246	NA	339	167	275	126	8,806	91	51
Educational level[a]											
Low	4,423	2,252	8,664	1,802	6,280	499	693	655	2,747	1,514	1,356
Medium	841	3,710	522	1,069	6,558	2,402	2,134	2,213	90,079	2,310	537
High	318	735	304	363	2,384	460	967	987	23,6076	314	167
Alcohol intake[b]											
Low	2,136	1,492	3,306	418	439	1,248	2,867	2,706	85,066	852	762
Medium	2,351	4,333	5,772	2,844	11,514	1,701	855	803	221,760	2,878	1,048
High	681	905	453	1	3,311	366	71	316	32,356	430	254
Smoking											
Never	3,460	3,178	6,439	1,952	4,685	1,628	2,475	1,792	115,863	1,427	1,069
Former	841	2,349	1,739	691	5,472	1,090	546	1,224	176,036	1,825	604
Current	862	1,175	1,093	535	5,063	633	773	829	34,619	883	364
Vigorous physical activity[c]											
Yes	268	3,810	1,949	NA	6,821	2,245	1,180	2,596	161,882	865	519
No	4,864	2,695	7,434		2,651	996	2,612	1,065	173,492	1,068	1,016

Abbreviations: CHANCES, Consortium on Health and Ageing: Network of Cohorts in Europe and the United States; CHD, coronary heart disease; CVD, cardiovascular disease; EPIC-Elderly, European Prospective Investigation Into Cancer and Nutrition–Elderly Study; HAPIEE, Health, Alcohol, and Psychosocial Factors in Eastern European Countries Study; NA, not available (no data were supplied); NIH-AARP, National Institutes of Health–AARP Diet and Health Study; RES, Rotterdam Elderly Study; SENECA, Survey in Europe on Nutrition and the Elderly, a Concerted Action.

[a] Low, primary school or less; medium, more than primary school but less than college or university; high, college or university.

[b] Low, 0 g of alcohol per day; medium, >0–40 g/day for men and >0–20g/day for women; high, >40 g/day for men and >20 g/day for women.

[c] Yes, being vigorous physically active; no, not being vigorous physically active.

by data on mono- and disaccharides. In accordance with the WHO guidelines, all macronutrients were expressed as a percentage of energy intake. For the calculation of nutrient densities, we excluded energy provided by ethanol (8).

The HDI includes 3 categories of guidelines ("moderation," "moderation range," and "adequacy") with accompanying scoring systems (Table 1). The maximum score of 10 points was allocated if the intake was in accordance with the

WHO guidelines. For the moderation category, (saturated fatty acids, mono- and disaccharides, and cholesterol) participants with higher intakes than recommended received proportionally fewer points, with a minimum of 0 points at the upper limit. The upper limit was defined as the 85th percentile of the combined cohort-specific population distribution (21). The "moderation range" components (6%–10% of energy intake from PUFAs and 10%–15% from protein) were scored with a maximum of 10 points if intake was within the recommended range. A score of 0 corresponded to an intake of 0 at the lower limit or the 85th percentile at the upper limit. Regarding PUFAs, 85% of our participants met the WHO guidelines (i.e., the upper limit was included in the recommended range). Therefore, all participants with PUFA intakes above the recommended range received 0 points. For the "adequacy" components (>25 g/day of fiber and >400 g/day of fruits and vegetables), participants with lower intakes were allocated proportionately fewer points, with 0 g/day as the minimum.

After all individual scores were summed, participants received the maximum HDI score of 70 points if all guidelines were met; the minimum HDI score was 0.

Covariates

We used similar statistical models for each of the cohorts. Data on measured height and weight were available for EPIC-Elderly Study, the RES, and the SENECA Study; self-reported data were used for the NIH-AARP Study and the HAPIEE Study. In the RES, no baseline measurements of physical activity were available. As a proxy measure, physical activity assessed 6 years after baseline was used. Information on physical activity in the Swedish cohort of the EPIC-Elderly Study was not provided. Potential confounding variables were selected based on their associations with dietary patterns and all-cause mortality.

Statistical analysis

This meta-analysis of individual participant data followed a 2-step approach by first analyzing each of the 11 CHANCES cohorts individually using the same analysis script, and then conducting meta-analyses of the obtained hazard ratio estimates. We applied Cox proportional hazard models, using age as the underlying time variable, to assess the association between the continuously scored HDI (per 10-point increment) and all-cause mortality. Hazard ratio estimates were summarized by random-effects meta-analysis to take into account differences in sample size and the possibility of statistical heterogeneity among the studies. Between-study heterogeneity was determined by I^2 statistics (22). The final hazard ratio was adjusted for sex; educational level (primary or less (low), more than primary but less than college or university (medium), or college or university (high)); alcohol consumption (low (0 g/day), medium (for men, >0–40 g/day; for women, >0–20 g/day), or high (for men, >40 g/day; for women, >20 g/day); smoking status (never, former, or current); energy intake (kcal/day); and vigorous physical activity (yes or no). Participants with missing data for the confounding variables were assigned to a separate category for each of these

Table 4. Medians and Interquartile Ranges of the Healthy Diet Indicator Score and Its Components for 396,391 Consortium on Health and Ageing: Network of Cohorts in Europe and the United States Participants, 1988–2011

HDI Component	Median (IQR) HDI Component Score by Cohort										
	EPIC-Elderly					HAPIEE			NIH-AARP (United States	RES (Netherlands)	SENECA (Europe)
	Spain	Netherlands	Greece	Sweden	Denmark	Czech Republic	Russia	Poland			
Saturated fatty acids	9 (4, 10)	2 (0, 5)	6 (3, 9)	2 (0, 5)	1 (0, 5)	3 (0, 6)	2 (0, 5)	1 (0, 5)	10 (7, 10)	0 (0, 4)	1 (0, 8)
Polyunsaturated fatty acids	8 (6, 10)	10 (8, 10)	7 (6, 8)	7 (6, 8)	9 (8, 10)	10 (9, 10)	10 (0, 10)	8 (7, 9)	10 (8, 10)	9 (6, 10)	7 (5, 10)
Protein	0 (0, 4)	4 (0, 7)	9 (6, 10)	10 (7, 10)	3 (0, 7)	5 (1, 8)	5 (2, 9)	3 (0, 6)	8 (4, 10)	6 (2, 10)	10 (6, 10)
Mono- and disaccharides	6 (4, 8)	2 (0, 4)	7 (5, 8)	5 (3, 6)	5 (3, 7)	5 (3, 8)	7 (5, 8)	5 (3, 7)	3 (0, 5)	4 (2, 6)	6 (3, 8)
Cholesterol	8 (0, 10)	10 (10, 10)	10 (10, 10)	10 (10, 10)	1 (0, 10)	10 (5, 10)	2 (0, 10)	6 (0, 10)	10 (10, 10)	10 (10, 10)	10 (3, 10)
Fiber	9 (7, 10)	9 (7, 10)	8 (6, 9)	7 (6, 9)	10 (8, 10)	9 (7, 10)	8 (7, 10)	9 (7, 10)	7 (5, 9)	6 (5, 8)	8 (6, 10)
Fruits and vegetables	10 (9, 10)	9 (6, 10)	10 (10, 10)	5 (3, 9)	8 (5, 10)	10 (9, 10)	10 (7, 10)	10 (8, 10)	10 (10, 10)	10 (8, 10)	10 (9, 10)
Total HDI score (maximum 70 points)	46 (40, 51)	45 (40, 49)	54 (49, 59)	46 (41, 51)	40 (35, 45)	48 (42, 53)	42 (37, 47)	42 (37, 47)	53 (47, 57)	44 (39, 48)	47 (42, 53)

Abbreviations: EPIC-Elderly, European Prospective Investigation Into Cancer and Nutrition–Elderly Study; HAPIEE, Health, Alcohol, and Psychosocial Factors in Eastern European Countries Study; HDI, Healthy Diet Indicator; IQR interquartile range; NIH-AARP, National Institutes of Health–AARP Diet and Health Study; RES, Rotterdam Elderly Study; SENECA, Survey in Europe on Nutrition and the Elderly, a Consorted Action.

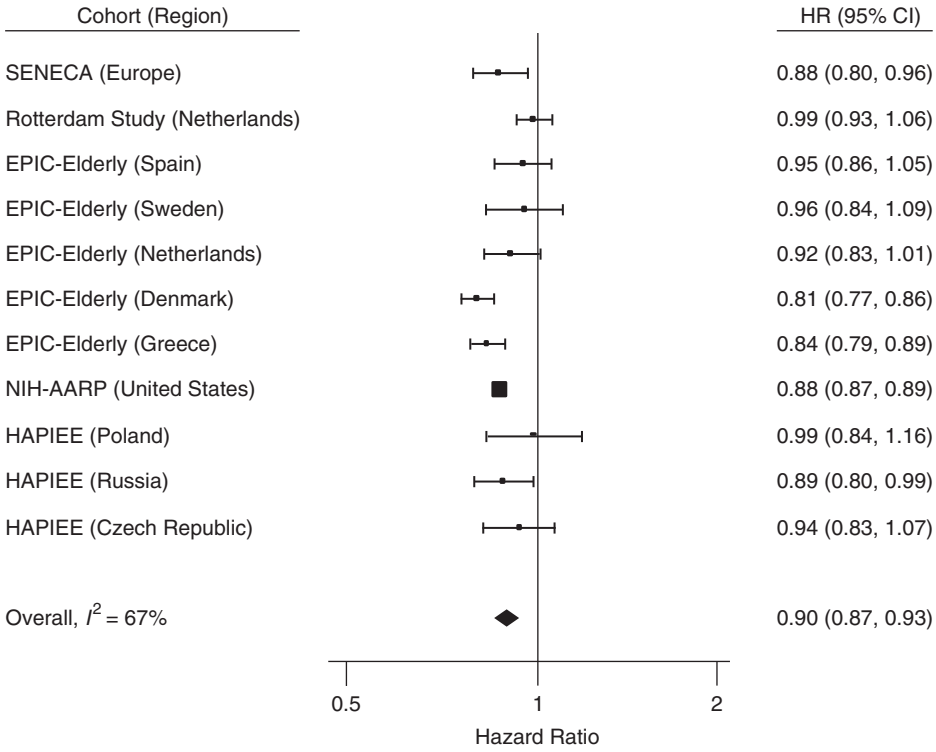


Figure 1. Cohort-specific and pooled hazard ratios (HRs) of all-cause mortality in relation to a 10-point increase in Healthy Diet Indicator (HDI) score, adjusted for sex, educational level, smoking status, energy intake, alcohol consumption, and physical activity level in the Consortium on Health and Ageing: Network of Cohorts in Europe and the United States (CHANCES), 1988–2011. Bars, 95% confidence intervals (CIs). Cohorts are ordered according to year of baseline assessment, beginning with the oldest. I^2 value is expressed as the percentage of total variability caused by heterogeneity. All data were obtained from CHANCES (www.chancesfp7.eu). EPIC-Elderly, European Prospective Investigation Into Cancer and Nutrition–Elderly Study; HAPIEE, Health, Alcohol, and Psychosocial Factors in Eastern European Countries Study; NIH-AARP, National Institutes of Health–AARP Diet and Health Study; SENECA, Survey in Europe on Nutrition and the Elderly, a Concerted Action.

variables. BMI and BMI^2 (to account for a potential U-shaped association with death) were not included in the main model for their potential influence on the association as a mediator, but additional analyses showed that inclusion of BMI and BMI^2 did not change the hazard ratio estimate. We included study center for the HAPIEE Study and the EPIC-Elderly multicenter cohorts (Spain, the Netherlands, and Denmark) and region for the SENECA Study in all models to adjust for potential differences in baseline hazards across centers or regions.

Potential effect modifications by age, sex, BMI (<27 or ≥27), which is considered the upper range of normal for elderly persons (23)), smoking, educational level, alcohol consumption, and chronic disease at baseline were investigated by including an interaction term in the models and by conducting stratified analysis. To examine the importance of excluded HDI components (*n*-3 and *n*-6 as separate components, *trans*-fatty acids, and sodium) to the association between WHO guidelines and all-cause mortality, we additionally investigated the complete HDI score based on 10 WHO components in the HAPIEE Study, the NIH-AARP Study, and the RES. Sensitivity analyses were performed by excluding missing covariates, data on chronic diseases at baseline, and data from participants who died during the first 2 years of follow-up. To examine the relative importance of the single HDI components, we excluded 1 HDI component at a time while including this component as a covariate in the model. Finally, we calculated population-attributable risk (24) and life expectancy (25). To estimate the years gained by adhering to a healthy diet, we used data on life expectancy at age 60 years for Europeans in the year 2000 from the WHO data base (26).

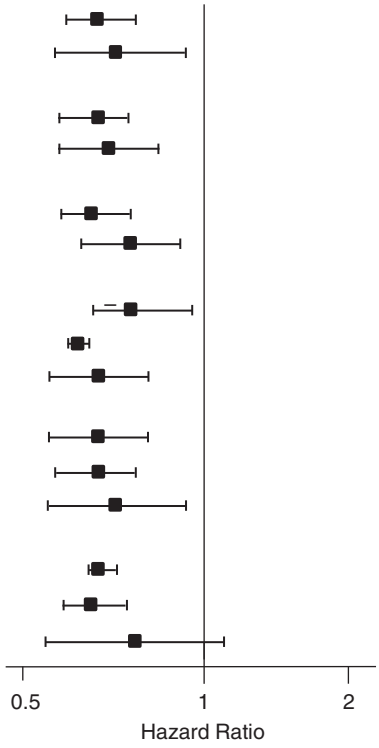
Cohort-specific data were analyzed using SAS, version 9.2, software (SAS Institute, Inc., Cary, North Carolina). For random-effects meta-analysis, we used the *metafor* package in R, version 2.15.0 (R Foundation for Statistical Computing, Vienna, Austria). *P* values of less than 0.05 were considered statistically significant.

RESULTS

Median length of follow-up ranged from 5 to 15 years across cohorts (Table 2). During that time, a total of 84,978 deaths occurred (Table 3). Median HDI scores ranged from 40 (interquartile range, 35–45) in the EPIC-Elderly cohort in Denmark to 54 (interquartile range, 49–59) in the EPIC-Elderly cohort in Greece. We obtained low (unhealthy) median HDI component scores for saturated fatty acids for all

A)

Potential Effect Modifier	No. of Deaths	HR (95% CI)	I^2
Age category, years			
60–70	76,070	0.89 (0.86, 0.93)	58
>70	8,908	0.91 (0.85, 0.98)	64
Sex			
Male	56,095	0.89 (0.85, 0.92)	42
Female	28,883	0.90 (0.85, 0.95)	66
BMI			
<27	45,720	0.88 (0.85, 0.92)	43
≥27	39,258	0.92 (0.87, 0.97)	70
Smoking			
Never	20,292	0.92 (0.88, 0.98)	51
Former	44,872	0.87 (0.86, 0.88)	<1
Current	16,452	0.89 (0.84, 0.94)	52
Educational level			
Low	6,720	0.89 (0.84, 0.94)	49
Medium	25,783	0.89 (0.85, 0.93)	28
High	49,423	0.91 (0.84, 0.98)	20
Alcohol intake			
None	74,758	0.89 (0.88, 0.91)	0
Medium	50,143	0.88 (0.85, 0.92)	54
High	9,722	0.93 (0.84, 1.02)	56



B)

Cohort-Specific Characteristic	Cohort	HR (95% CI)	I^2
Location			
United States	NIH-AARP	0.89 (0.88, 0.90)	NA
Europe	EPIC-E (all), RES, SENECA	0.90 (0.84, 0.96)	78
Eastern Europe	HAPIEE	0.93 (0.86, 0.99)	0
Median follow-up, years			
≤10	HAPIEE (all), SENECA	0.91 (0.86, 0.96)	0
>10	EPIC-E (all), NIH-AARP, RES	0.90 (0.85, 0.94)	78
% Deaths between baseline and end of follow-up			
≤15	EPIC-E (SP, NL, SW), HAPIEE (CZ, PL)	0.94 (0.90, 0.99)	0
>15	EPIC-E (GR, DK), HAPIEE (RU), NIH-AARP, RES, SENECA	0.89 (0.84, 0.92)	79
Dietary assessment self-report	EPIC-E (NL, DK), HAPIEE (CZ, PL), NIH-AARP, RES	0.88 (0.84, 0.93)	66
Dietary intake assess via interview	EPIC-E (SP, GR, SW), HAPIEE (RU), SENECA	0.92 (0.87, 0.97)	31
HDI score			
Based on 7 components	HAPIEE (all), NIH-AARP,RES	0.93 (0.87, 0.99)	49
Based on 10 components	HAPIEE (all), NIH-AARP, RES	0.95 (0.89, 1.02)	83

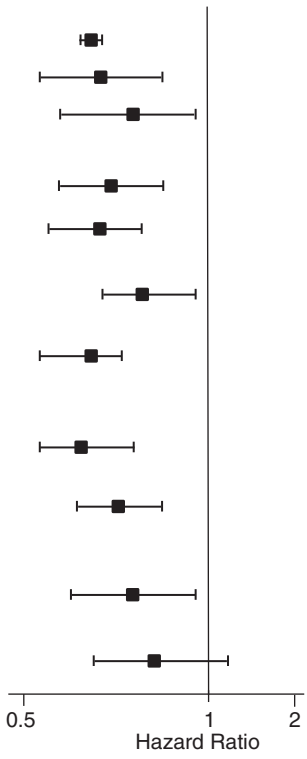


Figure 2 continues

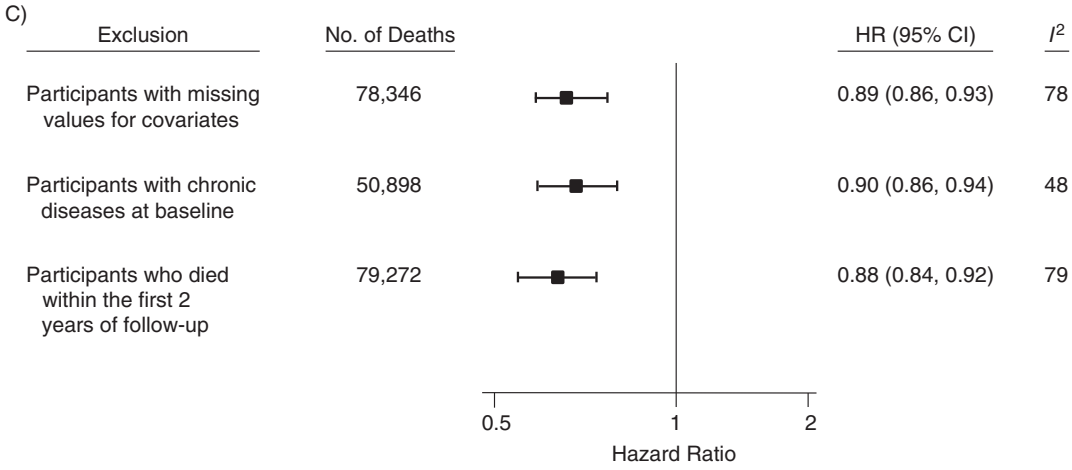


Figure 2. Adjusted hazard ratios (HRs) and 95% confidence intervals (CIs) in the Consortium on Health and Ageing: Network of Cohorts in Europe and the United States (CHANCES), 1988–2011, for the association between a 10-point increase in Healthy Diet Indicator (HDI) score and all-cause mortality A) stratified for potential effect modifiers; B) stratified for cohort-specific characteristics; and C) after several exclusion criteria have been applied. Body mass index (BMI) is weight (kg)/height (m)^2. I^2 values are expressed as percentages of total variability caused by heterogeneity. CZ, Czech Republic; DK, Denmark; EPIC-E, European Prospective Investigation into Cancer and Nutrition–Elderly Study; GR, Greece; HAPIEE, Health, Alcohol, and Psychosocial Factors in Eastern European Countries Study; NA, not applicable; NIH-AARP, National Institutes of Health–AARP Diet and Health Study; NL, Netherlands; PL, Poland; RES, Rotterdam Elderly Study; RU, Russia; SENECA, Survey in Europe on Nutrition and the Elderly, a Concerted Action; SP, Spain; SW, Sweden.

cohorts except the EPIC-Elderly cohorts in Spain and Greece and the NIH-AARP cohort. A low score for dietary cholesterol was observed in the EPIC-Elderly cohort in Denmark and the HAPIEE cohort in Russia. Protein scores ranged from very low (0 points) in the EPIC-Elderly cohort in Spain to very high (10 points) in the EPIC-Elderly cohort in Sweden and in the SENECA cohort. All cohorts scored high on PUFAs, dietary fiber, and fruits and vegetables combined, except the EPIC-Elderly cohort in Sweden, with a score of 5 points for fruits and vegetables, and the RES cohort, with a low score for dietary fiber (Table 4).

Mean age at baseline ranged from 60 years in the EPIC-Elderly cohort in Sweden to 73 years in the SENECA cohort (data not shown). In all cohorts, mean age, BMI values, and proportions of men and women were comparable across HDI quartiles (Web Table 2). Participants in the highest HDI quartile (representing the greatest adherence to WHO guidelines) were more likely to be highly educated, never or former smokers, and physically active, and they were less likely to drink large amounts of alcohol. The associations between HDI and mean energy intake and mean scores for PUFAs and mono- and disaccharides differed across cohorts.

Figure 1 shows the hazard ratios after adjustment for sex, educational level, smoking status, energy intake, alcohol consumption, and physical activity. The hazard ratios per 10 units ranged from 0.81 for the EPIC-Elderly cohort in Denmark to 0.99 for the RES cohort. Overall, the results showed a 10% reduction (hazard ratio = 0.90, 95% CI: 0.87, 0.93, I^2 = 67%) in all-cause mortality for each 10-point increase in HDI score. The inclusion of the covariates weakened the association slightly compared with the age- and sex-adjusted model (hazard ratio = 0.86, 95% CI: 0.82, 0.90, I^2 = 85%).

Stratifying the included cohorts by potential effect modifiers (Figure 2A) and cohort-specific characteristics (Figure 2B), as well as excluding participants with chronic diseases at baseline or those who died within the first 2 years of follow-up (Figure 2C) produced hazard ratios similar to the summary hazard ratio of 0.90. However, inclusion of all 10 HDI components changed the pooled hazard ratio estimate slightly, which had wider confidence intervals and a greater level of heterogeneity (Figure 2B). Excluding single components of the HDI and adding them instead as confounders produced little difference in pooled hazard ratio estimates compared with the overall result. All summary estimates remained statistically significant, ranging from 0.87 (95% CI: 0.86, 0.88) to 0.93 (95% CI: 0.90, 0.97) (Web Table 3).

Finally, the calculation of the population-attributable risk based on the adjusted analyses showed that 2% (in the RES) to 18% (in the EPIC-Elderly cohort in Denmark) of deaths could be attributed to unhealthy diets. The overall population-attributable risk estimate across cohorts derived by meta-analysis was 10% (95% CI: 0.08, 0.12). On the basis of WHO life expectancy data, the overall hazard ratio of 0.90 would translate to an increase in life expectancy of approximately 2 years for someone who was 60 years of age in 2000.

DISCUSSION

Our study included 11 cohorts from Europe and the United States and comprised a total sample of 396,391 elderly participants with 84,978 deaths. Overall, we found that a healthier diet according to WHO guidelines was associated with lower risk of death. These results did not appear to be explained by other risk factors or by specific components of the HDI, and they were

similar among different age groups, between men and women, and across geographical locations. Excluding participants with chronic diseases at baseline did not change the overall pooled association between HDI score and all-cause mortality. Depending on the cohort, up to 18% of deaths could be attributed to unhealthy diet, and an increase in 10 HDI points was associated with a 2-year increase in life expectancy for a person 60 years of age.

An increase of 10 HDI points represents adherence to 1 additional WHO guideline. However, improving dietary quality should be achieved by following a balanced diet. For example, avoiding the consumption of potato chips and sweets, reducing the consumption of meat during the main meal by introducing 1 (additional) day of fish intake, and replacing full-fat milk with low-fat milk would add approximately 6 points to the total HDI score (2 points for saturated fat, 1 point for PUFAs, 2 points for mono- and disaccharides, and 1 point for cholesterol). Together with eating 2 additional servings of fruits or vegetables daily (approximately 2 points) and replacing white rolls and cereals with whole-grain alternatives (approximately 2 points for fiber), this would result in an increase of 10 HDI points. Our results show that such a difference in dietary quality would translate to a 10% lower mortality rate in an elderly population. Three previous studies (8, 9, 27) assessed the WHO recommendations from 1990, measured by the original dichotomous HDI scoring system, in relation to all-cause mortality. Huijbregts et al. (8) included a population-based random sample of 3,045 men aged 50–70 years from the Finnish, Italian, and Dutch cohorts of the Seven Countries Study, who were followed for 20 years. The pooled hazard ratio was 0.87 (95% CI: 0.77, 0.98) when comparing the bottom tertile versus the top tertile. Knoops et al. (9) analyzed data from Healthy Ageing: a Longitudinal Study in Europe, including 3,117 men and women aged 70–90 years who were followed for 10 years. The HDI scores showed an inverse association with mortality risk of 0.89 (95% CI: 0.81, 0.98) comparing HDI scores above the median with those below the median. Finally, Sjögren et al. (27) reported an inverse but nonsignificant hazard ratio estimate of 0.96 (95% CI: 0.77, 1.19) per 1–standard deviation increase between the HDI score and total mortality risk in a population of elderly Swedish men after 10 years of follow-up. Our results strengthen these findings by using updated dietary guidelines and enlarging the cohort size by pooling and extending the coverage of the countries across Europe and the United States. Also, we applied a continuous HDI score and not a dichotomous one as in the previous HDI studies, which might have improved the power of our study (20). Combining prospective cohort studies in a meta-analysis to examine the association between nutrient-based dietary patterns and all-cause mortality typically introduces heterogeneity (28). Reasons for this might be related to, for example, the use of different dietary questionnaires (assessment of dietary intake) and food composition tables (translation of food groups into nutrients). As expected, the levels of heterogeneity and uncertainty increased after the additional inclusion of *n*-6 PUFAs, *n*-3 PUFAs, *trans*-fatty acids, and sodium. We considered the result of our main analysis on the association between the HDI and all-cause mortality based on 7 instead of 10 HDI components to be reliable and more precise. An advantage of the current meta-analysis was the use of the same analysis script across cohorts and the use of harmonized variables, enabling the reduction of heterogeneity. The overall I^2 value was interpreted as being moderate in size. All hazard ratio estimates pointed in the same direction, which shows that the level of heterogeneity was driven by differences in strength of the association rather than by the direction (29). Another advantage of the present study is the large sample size and diversity of the populations.

Limitations of our study are partly related to differences in cohort design, such as differences in length of follow-up, dietary assessment methods, and comparability of specific dietary variables. However, despite cohort differences, we found similar results across cohorts, which strengthens our overall finding. We performed stratified analyses by region to ensure that the large NIH-AARP Study did not dominate the overall result, and we found stable significant inverse associations between HDI and all-cause mortality across strata.

A single dietary intake measurement at baseline assumes a constant diet over time. To partially reduce potential bias from dietary changes between baseline and follow-up, we excluded all deaths occurring within 2 years after baseline in an additional analysis. This resulted in a slightly stronger association between the HDI score and all-cause mortality, which might indicate an underestimation of our overall association. We tried to differentiate between a healthy diet and a healthy lifestyle by including the most important risk factors for all-cause mortality. However, residual confounding by unmeasured or imprecisely measured covariates remains possible. The HDI score, as a measure of dietary quality, appears to be a useful tool for international comparison studies, but its associations with health outcomes may be weaker compared with associations with specifically tailored diet scores such as, for instance, the Dietary Approaches to Stop Hypertension diet (30) to prevent cardiometabolic diseases or a score tailored to a specific study population, such as the Healthy Eating Index (31, 32). In addition, our results need to be confirmed in future studies examining non-Western populations, such as those from Asia, Africa, and South America, with different dietary patterns.

The results of the present study showed that a healthy diet based on the globally defined dietary guidelines of the WHO is associated with greater survival in elderly populations in Europe and the United States. This analysis confirms that the WHO dietary guidelines are valuable to promote overall good health.

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