Alternate Healthy Eating Index 2010 and risk of chronic obstructive pulmonary disease among US women and men: prospective study

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ABSTRACT

OBJECTIVE

To investigate the association between the Alternate Healthy Eating Index 2010 (AHEI-2010)—a measure of diet quality—and the risk of chronic obstructive pulmonary disease (COPD).

DESIGN

Prospective cohort study.

SETTING

Participants in the Nurses' Health Study and the Health Professionals Follow-up Study, United States.

PARTICIPANTS

73 228 female nurses from 1984 to 2000 and 47 026 men from 1986 to 1998, who completed biennial questionnaires.

MAIN OUTCOME MEASURES

The primary outcome was the self report of newly diagnosed COPD. Multivariable Cox proportional hazards models were adjusted for age, physical activity, body mass index, total energy intake, smoking, second hand tobacco exposure (only in the Nurses' Health Study), race/ethnicity, physician visits, US region, spouse's highest educational attainment (only in the Nurses' Health Study), and menopausal status (only in the Nurses' Health Study).

RESULTS

Over the study period, 723 cases of newly diagnosed COPD occurred in women and 167 in men. In the pooled analysis, a significant negative association was seen between the risk of newly diagnosed COPD and fifths of the AHEI-2010: hazard ratios were 0.81 (95% confidence interval 0.51 to 1.29) for the second fifth, 0.98 (0.80 to 1.18) for the third fifth, 0.74 (0.59 to 0.92) for the fourth fifth, and 0.67 (0.53 to 0.85) for participants who ate the healthiest diet according to the AHEI-2010 (that is, were in the highest fifth), compared with those who ate the less healthy diet (participants in the lowest fifth). Similar findings were observed among ex-smokers and current smokers.

CONCLUSIONS

A higher AHEI-2010 diet score (reflecting high intakes of whole grains, polyunsaturated fatty acids, nuts, and long chain omega-3 fats and low intakes of red/processed meats, refined grains, and sugar sweetened drinks) was associated with a lower risk of COPD in both women and men. These findings support the importance of a healthy diet in multi-interventional programs to prevent COPD.

WHAT IS ALREADY KNOWN ON THIS TOPIC

The Alternate Healthy Eating Index 2010 (AHEI-2010), a new measure of diet quality based on current scientific knowledge, has been linked to risk of major chronic diseases, such as cardiovascular disease, diabetes, and cancer

The role of dietary scores in risk of chronic obstructive pulmonary disease (COPD) is unknown

Previous studies have found a lower risk of COPD associated with increased intake of antioxidants and a greater risk of COPD associated with increased intake of processed meats

WHAT THIS STUDY ADDS

A high AHEI-2010 diet score (reflecting high intakes of whole grains, polyunsaturated fatty acids, nuts, and long chain omega-3 fats and low intakes of red/processed meats, refined grains, and sugar sweetened drinks) was associated with a lower risk of COPD

This finding supports the importance of a healthy diet in multi-interventional programs to prevent COPD

Regarding public health, this finding extends the relevance of the AHEI-2010 dietary score to another chronic disease, COPD

Introduction

Chronic respiratory diseases remain a worldwide public health problem. Respiratory health and lung function strongly predict general health status and all cause mortality.[1] In the 2010 Global Burden of Disease report, chronic obstructive pulmonary disease (COPD) was the third most common cause of death worldwide.[2] The predominant risk factor for COPD in the developed world is cigarette smoking, but up to one third of COPD patients have never smoked, suggesting that other factors are involved. Apart from smoking, relatively little attention has been paid to other modifiable risk factors that might decrease the risk of developing COPD. Diet is one of such factor, but prospective data on the association between diet and the risk of COPD remain scarce,[3] compared with the extensive literature on cardiovascular diseases or cancer. A potential positive association of a diet rich in antioxidants with better lung function and reduced long term mortality due to COPD has been reported, as well as a negative association with a Western diet, and more precisely with cured meat intake.[4–8]

Several diet quality indices, usually based on established nutrient requirements and well publicized dietary guidelines, have been developed to evaluate the healthfulness of individual diets. These scores, reflecting overall diet quality, can help researchers to sort through the nutrient and food specific findings and provide a measure of diet that incorporates nutrient and food interactions of likely biological importance.[9–11] Moreover, the

scores are easy for clinicians and dietitians to use for recording people's diet in the clinic setting. Recently, a new measure of diet quality was proposed that is more accurate than previous scores as it is based on current scientific knowledge: the Alternate Healthy Eating Index 2010 (AHEI-2010).[12] This diet score, including 11 components, was associated with a 16% lower risk of major chronic diseases (cardiovascular disease, diabetes, and cancer).[12] Several studies have confirmed the relevance of the AHEI-2010 diet score as being associated with lower risk of total prostate cancer,[13] lower incidence of obesity,[14] healthy ageing and wellbeing,[15] lower risk of hip fracture,[16] and a reduced risk of all cause, cardiovascular, and cancer mortality.[17]

In the context of tackling chronic diseases, public health initiatives to improve lung function through dietary advice are particularly relevant and timely. We therefore investigated prospectively the association between the AHEI-2010 and the risk of newly diagnosed COPD in two large prospective US cohorts, the Nurses' Health Study and the Health Professionals Follow-up Study.[18 19]

Methods

Overview

The Nurses' Health Study began in 1976, when 121 701 female nurses aged 30–55 years and living in 11 US states responded to a mailed health questionnaire.[18] The Health Professionals Follow-up Study began in 1986 when 51 529 male US health professionals aged 40–75 years answered a detailed mailed questionnaire that included a diet survey and items on lifestyle practice and medical history.[19] In both the Nurses' Health Study and the Health Professionals Follow-up Study, follow-up questionnaires were sent every two years thereafter to update information on smoking habits, physical activity, weight, and other risk factors and to ask about newly diagnosed medical conditions. Participants also completed a food frequency questionnaire in 1984 for the Nurses' Health Study and at baseline (1986) for the Health Professionals Follow-up Study. Similar food frequency questionnaires were sent every two to four years thereafter (see web appendix 1).

We used several exclusion criteria in our analysis. The first category was related to the analysis of dietary data,[20] and the second category was related to the analysis of cohort data. Regarding dietary data, we excluded participants without a completed food frequency questionnaire at baseline and participants with unreasonably high (>3500 kcal/day for women and >4200 kcal/day for men) or low intakes (<500 kcal/day for women and <800 kcal/day for men) to take care of outliers, as well as those who had left more than 70 items blank.[20] We also excluded women and men who reported a diagnosed asthma or COPD at baseline. The final baseline population included 73 228 women and 47 026 men.

Assessment of dietary intake

Dietary intake information was collected by a food frequency questionnaire designed to assess average food intake over the previous 12 months. Standard portion sizes were listed with each food. For each food item, participants indicated their average frequency of consumption over the previous year in terms of the specified serving size by checking one of nine frequency categories ranging from "almost never" to "at least six times/day." The selected frequency category for each food item was converted to a daily intake. For example, a response of "one serving/week" was converted to 0.14 servings/day.

Scoring criteria for the Alternate Healthy Eating Index 2010 are described in detail elsewhere.[12] Briefly, the AHEI-2010 is based on 11 components: six components for which the highest intakes were supposed to be ideal (vegetables, fruit, whole grains, nuts and legumes, long chain omega-3 fats (docosahexaenoic acid and eicosapentaenoic acid), and polyunsaturated fatty acids), one component for which moderate intake was supposed to be ideal (alcohol), and four components for which avoidance or lowest intake were supposed to be ideal (sugar sweetened drinks and fruit juice, red and processed meat, trans fat, and sodium). Each component is given a minimal score of 0 and a maximal score of 10, with intermediate values scored proportionally, and has the potential to contribute 0–10 points to the total score. All the component scores are summed to obtain a total AHEI-2010 score, which ranges from 0 to 110, with a higher score representing a healthier diet (see web appendix 2 for the distribution of the baseline score in each cohort—that is, AHEI-2010 calculated in 1984 for the Nurses' Health Study and in 1986 for the Health Professionals Follow-up Study).

We identified the AHEI-2010 score from each food frequency questionnaire administrated in 1984, 1986, 1990, 1994, and 1998 in the Nurses' Health Study and in 1986, 1990, and 1994 in the Health Professionals Follow-up Study. To reduce measurement errors and to represent long term dietary intake, we calculated the cumulative average of AHEI-2010, divided it into fifths, and used it as a time dependent variable. The cumulative average incorporated repeated measures of diet. For example, by using this method in the Health Professionals Follow-up Study, we used the 1986 AHEI-2010 to predict newly diagnosed COPD in 1986–90, an average of the 1986 and 1990 AHEI-2010 to predict COPD in 1990–94, and the average of the 1986, 1990, and 1994 AHEI-2010, to predict COPD from 1994 to 1998.

Assessment of respiratory phenotypes

In 1998 and 2000 a supplemental questionnaire on COPD was sent to every participant who reported a physician's diagnosis of emphysema or chronic bronchitis before 1996 (on the biennial questionnaire). The specific questionnaire included, among other data, information confirming a physician's diagnosis of emphysema, chronic bronchitis, or COPD, as well as the dates of symptom onset and diagnosis and the tests performed to confirm the diagnosis or symptoms consistent with a diagnosis of chronic bronchitis. Self reported COPD was defined by the affirmative response

to a physician's diagnosis of chronic bronchitis or emphysema and by the report of a diagnostic test at diagnosis (that is, pulmonary function testing, chest radiograph, or chest computed tomography was performed). This epidemiologic definition was validated in a random sample of COPD cases in the Nurses' Health Study.[21] We obtained participants' medical records, and a physician reviewed them in a blinded fashion. The diagnosis of COPD was confirmed in 80% of 218 cases that met this case definition and 88% of cases that met this definition and denied a physician's diagnosis of asthma. Results of pulmonary function testing were available in the medical records of 71% of confirmed cases; the mean forced expiratory volume in one second (FEV_1) in this group was 50% of predicted.

Asthma was also self reported and was defined by a doctor's diagnosis of asthma and the use of drugs for asthma within the previous 12 months. We validated the self reported incidence of asthma against medical records for a random sample of 100 cases in a related study of female nurses and confirmed that all carried a physician's diagnosis of asthma.[22]

Assessment of others variables

When possible, covariates were obtained from the baseline questionnaire (1984 in Nurses' Health Study, and 1986 in Health Professionals Follow-up Study) and updated every two years. Variables included time varying covariates such as age, physical activity, body mass index, total energy intake, smoking status, pack years of smoking, and menopausal status (only in the Nurses' Health Study) and fixed covariates such as second hand tobacco exposure (only in the Nurses' Health Study), race/ethnicity, physician visits, US region, and spouse's highest educational attainment (only in the Nurses' Health Study).

Physical activity, including a variety of activities such as walking, cycling, swimming, or playing tennis, was measured in metabolic equivalents per week and used as a continuous variable. Body mass index (calculated as kg/m^2) was updated biennially and categorized in four categories (< 20.0, 20.0–24.9, 25.0–29.9, and ≥ 30.0). Total energy intake was estimated through the food frequency questionnaire, expressed in kilocalories per day, and used as a continuous variable. Smoking status was categorized as never smoker, ex-smoker, or current smoker. Pack years of smoking were calculated among ever-smokers. Second hand tobacco exposure was defined by an exposure at home, work, or both. Race/ethnicity was categorized in two groups (white, non-white). Examination by a physician in the previous two years was categorized in three classes (no visit, screening visit, symptoms related visit), and US region was categorized in six classes (New England, Mid-Atlantic, East North Central, South Atlantic, West South Central, Pacific). Among women, spouse's educational attainment was categorized in three classes (high school, college, or graduate school), and menopausal status was categorized in five categories as pre/postmenopausal and according to whether estrogen or progesterone replacement (oral or patch) had been or was being used (premenopause, postmenopause and never hormone replacement therapy use, postmenopause and past user of replacement therapy, postmenopause and estrogen replacement therapy, post-menopause and estrogen-progesterone replacement therapy).

Bias

Residual confounding by smoking remains an important source of possible bias in studies of respiratory diseases and diet. In our particular study, in which both smoking and COPD were self reported, we faced an unusually high risk of residual confounding. As smoking is the major risk factor for COPD, we further investigated the association among ex-smokers and current smokers (the number of newly diagnosed COPD cases among never smokers was too small to conduct a meaningful analysis). We also excluded participants with previous comorbidities (cardiovascular diseases and cancer). To avoid potential for preclinical COPD leading to reverse causation, we did "lagged" analyses, by omitting the cases from the initial four years of follow-up, and further examined the long latency of COPD, by omitting the cases from the initial eight years of follow-up.

Statistical analysis

We analyzed the association between the risk of COPD and the cumulative average of the AHEI-2010 score (that is, time varying exposure) by using a stratified proportional Cox hazards model adjusted for time varying variables (physical activity, body mass index, total energy intake, smoking status, pack years of smoking, pack years^2 of smoking, and menopausal status (only in the Nurses' Health Study)) and fixed variables (second hand tobacco exposure (only in the Nurses' Health Study), race/ethnicity, physician visits, US region, and spouse's highest educational attainment (only in the Nurses' Health Study)). The proportional hazards model was stratified according to age (in months) to provide finer control for age. In addition, we analyzed each individual component of the AHEI-2010 diet score by using Cox proportional hazards model adjusted for the same potential confounders plus the other AHEI-2010 components.

To minimize missing continuous covariates (physical activity, total energy intake, and pack years of smoking), we replaced missing data on these three covariates with the last valid values. For missing data on these continuous covariates at baseline, we created a dummy variable when making categories for these continuous covariates. Similarly, we used missing indicator variables to include participants with missing categorical variables, including smoking status, second hand tobacco exposure (Nurses' Health Study only), body mass index, menopausal status (Nurses' Health Study only), race/ethnicity, physician visits, US region, and spouse's highest educational attainment (Nurses' Health Study only). In the Nurses' Health Study, the percentage of missing values at baseline was 0.3% for smoking, 1.5% for second hand tobacco exposure, 4.9% for body mass index, 10.2% for menopausal status,

0.8% for race/ethnicity, 11.2% for physician visits, 0% for US region, and 24.1% for spouse's educational attainment. In the Health Professionals Follow-up Study, the percentage of missing values at baseline was 3.8% for smoking, 0% for body mass index, 0.2% for race/ethnicity, 14.2% for physician visits, and 0% for US region. In both cohorts, after adjustments for pack years and pack years^2 of smoking, the missing smoking status category was not associated with the risk of newly diagnosed COPD.

We calculated a test for trend across the fifths of the AHEI-2010 score by treating the categories as an ordinal variable in a proportional hazards model. After calculating sex specific hazard ratios, we combined the $\log_e$ hazard ratios, weighted by the inverse of their variances, by using a random effects model.[23] We tested for between studies heterogeneity by using the Q statistic, which gives information about the presence versus the absence of heterogeneity, and we also provided the I^2 index to quantify the degree of heterogeneity between studies, expressed as a percentage of total variance.[23] We calculated two sided 95% confidence intervals. We used SAS version 9.3 for all analyses.

Results

Characteristics of population

Tables 1 and 2 shows characteristics of women and men according to fifths of the AHEI-2010. Among both women and men, those with the highest score for AHEI-2010 (highest fifth, healthy diet) were more physically active, less often obese, and less likely to be current smokers than those with the lowest AHEI-2010 score (lowest fifth, unhealthy diet). Among women, those with the highest scores for AHEI-2010 were less exposed to secondhand smoke at work and at home than were those with the lowest scores for AHEI-2010. In the Nurses' Health Study, 45% of the women were never smokers at baseline, 32% were former smokers, and 23% were current smokers. Among former smokers, 62% had quit smoking at least 10 years before; only 10% had quit in the previous two years. In the Health Professionals Follow-up Study, 47% of the men were never smokers at baseline, 43% were former smokers, and only 10% were current smokers. Among former smokers, 72% had quit smoking at least 10 years before; only 8% had quit in the previous two years.

Alternate Healthy Eating Index 2010 and COPD

Among women in the Nurses' Health Study, we documented 723 cases of newly diagnosed COPD between 1984 and 2000 (from 1 137 106 person years); among men in the Health Professionals Follow-up Study, 167 cases were reported between 1986 and 1998 (from 521 764 person years). The incidence rate for newly diagnosed COPD was 64 per 100 000 person years in the Nurses' Health Study and 32 per 100 000 person years in the Health Professionals Follow-up Study.

In the pooled analysis, the risk of newly diagnosed COPD was inversely associated with the AHEI-2010 diet score: the age adjusted hazard ratio for the highest compared with the lowest fifth of AHEI-2010 score was 0.32 (95% confidence interval 0.25 to 0.40; P for trend < 0.001), with no heterogeneity between studies (P = 0.50). After control for several potential confounders (Table 3), the risk of newly diagnosed COPD was one third lower in participants who ate the healthiest diet according to the AHEI-2010 (highest fifth) compared with those who ate the least healthy diet (lowest fifth): the multivariable hazard ratio was 0.67 (0.53 to 0.85). In both women and men, the healthiest diet was associated with a reduced risk of newly diagnosed COPD: multivariable hazard ratios for the highest compared with the lowest fifth of AHEI-2010 score were 0.69 (0.53 to 0.90) in women and 0.60 (0.34 to 1.03) in men, with no heterogeneity between studies (P = 0.63).

We also investigated the association between AHEI-2010 and the risk of newly diagnosed COPD in ex-smokers and current smokers (Table 4). In the pooled analysis, after control for several potential confounders, the risk of newly diagnosed COPD was inversely associated with the AHEI-2010 diet score both in ex-smokers (P for trend = 0.002) and in current smokers (P for trend = 0.03). The hazard ratio for the highest compared with the lowest fifth of AHEI-2010 score in ex-smokers was 0.50 (0.33 to 0.75), and in current smokers it was 0.69 (0.49 to 0.98). The findings were similar in women and men. Among ever smokers, we further investigated the interaction between the AHEI-2010 score and pack years of smoking, but the association was not significant (P = 0.42).

In a sensitivity analysis looking at a study population without cancer or cardiovascular disease at baseline (n = 105 220 participants, with 771 cases of newly diagnosed COPD), we observed similar associations between AHEI-2010 and the risk of newly diagnosed COPD. In the pooled analysis, after adjustments for potential confounders, the healthiest diet was associated with a reduced risk of newly diagnosed COPD: the multivariable hazard ratio for the highest compared with the lowest fifth of AHEI-2010 score was 0.71 (0.55 to 0.92) (P for trend = 0.007; P for between studies heterogeneity = 0.62).

We also did lagged analyses, firstly by excluding cases occurring in the first four years (n = 207). We again observed a strong negative association between the AHEI-2010 and the risk of newly diagnosed COPD: the pooled multivariable hazard ratio for the highest compared with the lowest fifth of AHEI-2010 score was 0.65 (0.49 to 0.85) (P for trend < 0.001; P for between studies heterogeneity = 0.62). When we excluded COPD cases occurring within the first eight years (n = 538), we again observed a negative association between the AHEI-2010 and the risk of newly diagnosed COPD: the pooled multivariable hazard ratio for the highest compared with the lowest fifth of AHEI-2010 score was 0.63 (0.25 to 1.63) (P for trend < 0.001; P for between studies heterogeneity = 0.65).

Component score of Alternate Healthy Eating Index 2010 and COPD

To better understand the individual role of each component score of the AHEI-2010, we examined the association

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Table 1| Age **standardized baseline characteristics in women (Nurses' Health Study; n = 73 228) according to fifths of Alternate Healthy Eating Index 2010 (AHEI-2010). Values are percentages (standardized to age distribution of study population) unless stated otherwise**

Characteristic	Lowest fifth (less healthy diet) (n = 14 466)	Second fifth (n = 14 662)	Third fifth (n = 14 667)	Fourth fifth (n = 14 698)	Highest fifth (healthiest diet) (n = 14 735)
Median score on AHEI-2010	34.3	41.5	47.1	53.0	62.1
AHEI-2010 score range	15.6–38.4	38.5–44.3	44.4–49.9	50.0–56.8	56.9–98.7
Mean (SD) age, years	48.6 (7.2)	49.5 (7.2)	50.3 (7.1)	51.0 (7.0)	52.1 (6.8)
Mean (SD) physical activity, METs/week*	9.3 (15.0)	11.7 (16.1)	13.5 (20.6)	15.8 (21.7)	20.8 (28.0)
Mean (SD) body mass index, kg/m^2	25.4 (5.2)	25.2(4.9)	25.1 (4.7)	24.8 (4.4)	24.2 (4.0)
Body mass index (kg/m^2):					
< 20.0	8.2	6.9	6.9	6.8	8.0
20.0–24.9	47.6	48.8	49.1	51.3	54.9
25.0–29.9	24.7	25.5	26.0	25.9	24.0
≥ 30.0	14.9	13.7	13.1	11.2	8.0
Missing	4.6	5.1	4.9	4.8	5.1
Mean (SD) total energy, kcal/day	1910 (516)	1794 (528)	1730 (527)	1665 (521)	1598 (501)
Smoking habits:					
Never smokers	47.8	46.8	45.5	43.3	41.1
Former smokers	22.8	27.7	31.2	36.0	42.4
Current smokers	29.2	25.3	23.1	20.4	16.1
Missing	0.2	0.2	0.2	0.3	0.4
Mean (SD) pack years among ever smokers†	24.8 (19.0)	22.4 (17.9)	21.1 (17.2)	19.6 (15.7)	18.0 (15.7)
Exposure to secondhand smoke at work and/or home	60.6	60.2	59.0	57.0	54.0
White race/ethnicity	98.4	98.2	97.8	97.3	97.0
Physician examination:					
No physician visits	12.4	11.2	10.1	9.6	9.4
Screening visits	56.7	61.1	62.9	64.7	65.6
Symptom related visits	16.2	16.1	15.7	15.0	14.7
Missing	14.7	11.6	11.3	10.7	10.3
US region:					
New England	12.8	14.3	14.9	15.2	15.0
Mid-Atlantic	47.1	45.1	43.6	41.8	38.6
East North Central	23.9	21.6	19.4	17.3	14.7
South Atlantic	5.6	5.8	5.9	6.1	5.8
West South Central	4.4	4.9	5.1	5.0	4.3
Pacific	6.2	8.3	11.1	14.6	21.6
Spouse's educational attainment:					
High school	41.5	38.2	34.7	31.9	26.9
College	19.3	21.6	22.6	23.0	24.9
Graduate school	12.9	16.1	18.2	21.0	24.9
Missing	26.3	24.1	24.5	24.1	23.3
Menopausal status:					
Premenopause	54.0	49.1	45.0	41.9	35.5
Postmenopause and never HRT use	21.6	23.7	24.8	25.4	27.3
Postmenopause and past user of HRT	8.5	10.0	10.8	11.9	13.1
Postmenopause and estrogen replacement therapy	6.7	7.2	8.3	9.6	11.7
Postmenopause and estrogen-progesterone replacement therapy	0.5	0.6	0.8	1.0	1.3
Missing	8.7	9.4	10.3	10.2	11.1
Component of AHEI-2010 score:					
Vegetables (score)	4.1 (1.9)	4.9 (2.2)	5.4 (2.3)	5.9 (2.4)	6.8 (2.4)
Fruit	2.3 (1.7)	2.9 (1.9)	3.4 (2.2)	3.9 (2.4)	4.9 (2.6)
Whole grains	1.2 (1.1)	1.5 (1.3)	1.7 (1.4)	2.1 (1.7)	2.8 (2.2)
Sugar sweetened drinks and fruit juice	1.5 (2.8)	2.3 (3.3)	2.8 (3.5)	3.5 (3.7)	4.8 (4.0)
Nuts and legumes	1.8 (1.7)	2.3 (2.1)	2.5 (2.3)	2.9 (2.6)	3.8 (3.2)
Red and processed meat	1.5 (2.2)	2.5 (2.6)	3.3 (2.8)	4.3 (2.9)	6.1 (2.7)
Trans fat	5.2 (1.7)	5.5 (1.6)	5.9 (1.6)	6.2 (1.6)	7.0 (1.5)
Long chain fats	4.2 (2.7)	5.5 (3.0)	6.3 (3.1)	7.0 (3.0)	8.0 (2.7)
Polyunsaturated fatty acids	5.2 (1.8)	5.5 (1.9)	5.6 (2.0)	5.7 (2.0)	5.9 (2.2)
Sodium	4.1 (3.0)	4.7 (3.1)	5.0 (3.1)	5.4 (3.2)	5.8 (3.1)
Alcohol	3.7 (2.5)	4.5 (2.9)	5.1 (3.0)	5.6 (3.1)	6.2 (3.2)

HRT = hormone replacement therapy.
*Sum of average time per week spent in each activity multiplied by metabolic equivalent (MET) value of each activity.
†Number of packs smoked per day multiplied by number of years smoked, among previous and current smokers.

Table 2| Age standardized baseline characteristics in men (Health Professionals Follow-up Study; n = 47 026) according to fifths of Alternate Healthy Eating Index 2010 (AHEI-2010). Values are percentages (standardized to age distribution of study population) unless stated otherwise

Characteristics	Lowest fifth (less healthy diet) (n = 9364)	Second fifth (n = 9414)	Third fifth (n = 9390)	Fourth fifth (n = 9430)	Highest fifth (healthiest diet) (n = 9428)
Median score on AHEI-2010	39.6	47.4	53.1	59.0	67.4
AHEI-2010 score range	14.8–44.3	44.4–50.5	50.6–56.0	56.1–62.6	62.3–94.5
Mean (SD) age, years	51.9 (9.5)	53.2 (9.7)	54.0 (9.8)	54.8 (9.7)	56.0 (9.5)
Mean (SD) physical activity, METs/week*	15.1 (22.7)	18.0 (26.9)	20.5 (28.5)	23.5 (30.7)	28.4 (35.7)
Mean (SD) body mass index (kg/m^2)	25.3 (5.2)	25.2 (5.0)	25.0 (5.0)	24.8 (4.8)	24.3 (5.0)
Body mass index (kg/m^2):					
< 20.0	3.8	3.2	3.4	3.3	4.2
20.0–24.9	39.5	40.8	42.3	45.7	51.5
25.0–29.9	46.4	47.3	46.3	44.1	38.7
≥ 30.0	10.3	8.7	8.0	6.9	5.6
Missing	0.0	0.0	0.0	0.0	0.0
Mean (SD) total energy, kcal/day	2129 (611)	2027 (627)	1972 (625)	1909 (613)	1882 (585)
Smoking habits:					
Never smokers	44.7	45.7	45.0	45.0	45.1
Former smokers	35.7	39.7	42.4	44.3	46.2
Current smokers	16.3	10.9	8.6	6.5	4.4
Missing	3.3	3.7	4.0	4.2	4.3
Pack years among ever smokers†	29.7 (21.2)	26.5 (19.7)	24.6 (18.4)	23.0 (17.8)	21.3 (16.7)
White race/ethnicity	91.9	91.0	90.6	90.0	90.8
Physician examination:					
No physician visits	24.5	21.9	22.5	22.1	22.2
Screening visits	42.2	47.9	49.5	51.3	53.0
Symptom related visits	13.2	13.3	13.1	13.3	12.9
Missing	20.1	16.9	14.9	13.3	11.9
US region:					
New England	20.8	21.5	20.8	21.9	21.7
Mid-Atlantic	21.7	18.4	16.0	14.2	13.2
East North Central	15.5	17.9	19.8	21.7	25.6
South Atlantic	37.0	36.4	36.5	35.5	32.8
West South Central	0.2	0.1	0.3	0.2	0.2
Pacific	4.8	5.7	6.6	6.5	6.5
Component of AHEI-2010 score:					
Vegetables (score)	4.2 (2.1)	5.2 (2.3)	5.7 (2.4)	6.2 (2.5)	7.2 (2.5)
Fruit	2.3 (1.8)	3.1 (2.1)	3.7 (2.4)	4.4 (2.6)	5.6 (2.8)
Whole grains	1.4 (1.2)	1.9 (1.5)	2.3 (1.8)	2.8 (2.0)	3.8 (2.5)
Sugar sweetened drinks and fruit juice	1.4 (2.7)	2.0 (3.1)	2.5 (3.4)	2.9 (3.6)	4.3 (3.9)
Nuts and legumes	2.7 (2.4)	3.5 (2.8)	4.0 (3.1)	4.6 (3.2)	5.7 (3.4)
Red and processed meat	1.2 (2.0)	2.2 (2.6)	3.1 (2.8)	4.1 (3.0)	5.4 (3.0)
Trans fat	6.9 (1.5)	7.4 (1.3)	7.7 (1.3)	8.2 (1.2)	8.8 (1.0)
Long chain fats	5.4 (3.2)	7.1 (3.1)	7.9 (2.8)	8.6 (2.5)	9.1 (2.0)
Polyunsaturated fatty acids	4.1 (1.6)	4.5 (1.7)	4.8 (1.8)	4.9 (1.9)	5.2 (2.1)
Sodium	3.9 (3.0)	4.5 (3.1)	5.0 (3.1)	5.5 (3.1)	6.1 (3.0)
Alcohol	4.2 (2.9)	5.3 (3.2)	5.9 (3.3)	6.5 (3.3)	7.1 (3.2)

*Sum of average time per week spent in each activity multiplied by metabolic equivalent (MET) value of each activity.

between each individual component and the risk of COPD (Table 5). High scores on the whole grains and fruit components were associated with a lower risk of newly diagnosed COPD: 30% (significant) and 19% (borderline significant), respectively. These associations were similar among women and men (web appendix 3; P for heterogeneity = 0.52 and 0.91, respectively). For the sugar sweetened drinks and fruit juice component, the test for heterogeneity was borderline significant (P = 0.08); in women a high score (that is, a low dietary intake close to avoidance) was associated with a 21% lower risk of newly diagnosed COPD (P for trend = 0.02), whereas in men the association was statistically non-significant but positive (P for trend = 0.06). For the red and processed meat component, heterogeneity was not significant (P for between studies heterogeneity = 0.10); however, we found no significant association in women (P for trend = 0.22), whereas in men a high score on the red and processed meat component (that is, a low dietary intake close to avoidance) was associated with a 53% lower risk of newly diagnosed COPD (P for trend = 0.03). For vegetables, nuts, trans fat, polyunsaturated fatty acids, long chain fats, sodium, and alcohol, we found no significant associations with the risk of COPD, and no significant heterogeneity existed between men and women.

Alternate Healthy Eating Index 2010 and asthma

In the Nurses' Health Study, 1742 new cases of adult onset asthma were reported between 1984 and 2000 and met our epidemiologic definition. In the Health

Table 3| Association **between Alternate Healthy Eating Index 2010 (AHEI-2010) and risk of newly diagnosed chronic obstructive pulmonary disease in women (Nurses' Health Study) and men (Health Professionals Follow-up Study)**

	Women			Men			Total			
AHEI-2010	No	Person years	Hazard ratio (95% CI)*	No	Person years	Hazard ratio (95% CI)*	No	Hazard ratio (95% CI)*	P value†	I^2‡
Lowest fifth§	198	221 312	1.00 (referent)	53	103 567	1.00 (referent)	251	1.00 (referent)		
Second fifth	168	226 830	0.98 (0.80 to 1.21)	27	104 165	0.61 (0.38 to 0.97)	195	0.81 (0.51 to 1.29)	0.07	81.0
Third fifth	161	228 007	1.01 (0.81 to 1.25)	34	104 398	0.85 (0.55 to 1.33)	195	0.98 (0.80 to 1.18)	0.50	0.0
Fourth fifth	104	229 754	0.70 (0.54 to 0.89)	33	104 817	0.90 (0.57 to 1.43)	137	0.74 (0.59 to 0.92)	0.33	0.0
Highest fifth§	92	231 204	0.69 (0.53 to 0.90)	20	104 818	0.60 (0.34 to 1.03)	112	0.67 (0.53 to 0.85)	0.63	0.0
P for trend			<0.001			0.27		<0.001		

*Multivariable hazard ratios adjusted for age, physical activity, body mass index, total energy intake, smoking status, pack years of smoking, pack years^2 of smoking, secondhand tobacco exposure (only in Nurses' Health Study), race/ethnicity, physician visits, US region, spouse's highest educational attainment (only in Nurses' Health Study), and menopausal status (only in Nurses' Health Study).
†Test for between studies heterogeneity.
‡Degree of heterogeneity between studies expressed as percentage of total variance.
§Lowest fifth corresponds to least healthy diet according to AHEI-2010 diet score; highest fifth corresponds to healthiest diet.

Table 4| Association **between Alternate Healthy Eating Index 2010 (AHEI-2010) and risk of newly diagnosed chronic obstructive pulmonary disease in women (Nurses' Health Study) and men (Health Professionals Follow-up Study), according to smoking status**

	Women			Men			Total			
AHEI-2010	No	Person years	Hazard ratio (95% CI)*	No	Person years	Hazard ratio (95% CI)*	No	Hazard ratio (95% CI)*	P value†	I^2‡
Ex-smokers										
Lowest fifth§	42	65 259	1.00 (referent)	20	36 519	1.00 (referent)	62	1.00 (referent)		
Second fifth	27	78 161	0.56 (0.34 to 0.91)	12	40 597	0.52 (0.25 to 1.08)	39	0.55 (0.36 to 0.82)	0.89	0.0
Third fifth	50	86 439	0.94 (0.62 to 1.43)	18	42 480	0.83 (0.43 to 1.60)	68	0.91 (0.64 to 1.29)	0.76	0.0
Fourth fifth	28	98 266	0.48 (0.29 to 0.78)	14	44 514	0.60 (0.30 to 1.23)	42	0.52 (0.35 to 0.78)	0.60	0.0
Highest fifth§	35	111 919	0.52 (0.32 to 0.84)	10	46 066	0.44 (0.20 to 0.97)	45	0.50 (0.33 to 0.75)	0.72	0.0
P for trend			0.009			0.09	0.002			
Current smokers										
Lowest fifth§	143	48 618	1.00 (referent)	32	26 174	1.00 (referent)	175	1.00 (referent)		
Second fifth	120	41 638	1.08 (0.85 to 1.39)	12	20 752	0.55 (0.28 to 1.09)	132	0.84 (0.44 to 1.58)	0.07	84.8
Third fifth	91	36 645	0.97 (0.74 to 1.28)	13	19 585	0.73 (0.38 to 1.43)	104	0.93 (0.73 to 1.20)	0.44	0.0
Fourth fifth	64	31 219	0.81 (0.59 to 1.10)	14	17 756	1.03 (0.53 to 2.00)	78	0.84 (0.64 to 1.11)	0.52	0.0
Highest fifth§	39	23 021	0.70 (0.48 to 1.02)	6	16 641	0.64 (0.26 to 1.61)	45	0.69 (0.49 to 0.98)	0.86	0.0
P for trend			0.03			0.64			0.03	

*Multivariable hazard ratios adjusted for age, physical activity, body mass index, total energy intake, pack years of smoking, pack-years^2 of smoking, secondhand tobacco exposure (only in Nurses' Health Study), race/ethnicity, physician visits, US region, spouse's highest educational attainment (only in Nurses' Health Study), and menopausal status (only in Nurses' Health Study).
†Test for between studies heterogeneity.
‡Degree of heterogeneity between studies expressed as percentage of total variance.
§Lowest fifth corresponds to least healthy diet according to AHEI-2010 diet score; highest fifth corresponds to healthiest diet.

Professionals Follow-up Study, 228 new cases of adult onset asthma were reported between 1984 and 1998.

Owing to the potential overlap between COPD and asthma, we also investigated the association between the AHEI-2010 and the risk of adult onset asthma (Table 6). In men, in women, and in the pooled analysis, the AHEI-2010 was not associated with the risk of adult onset asthma: the pooled multivariable hazard ratio for the highest compared with the lowest fifth of AHEI-2010 score was 1.04 (0.90 to 1.21).

Discussion

In this prospective cohort analysis of more than 120 000 US women and men, we found that a higher AHEI-2010 diet score, reflecting high intakes of whole grains, polyunsaturated fatty acids, nuts, and long chain omega-3 fats and low intakes of red and processed meats, refined grains, and sugar sweetened drinks, was associated with a lower risk of newly diagnosed COPD. The association was consistent in several sub-populations and after adjustment for several potential confounders. By contrast, the AHEI-2010 diet score was completely unrelated to incident asthma in this large, prospective cohort analysis. These findings extend the relevance of this new dietary score to target chronic diseases and support the importance of diet in the pathogenesis of COPD. As the lungs exist in a high oxygen environment, it is reasonable to posit that certain exposures (and local inflammation) can further increase the burden of oxidants. The balance between these potentially toxic substances and the protective actions of antioxidant defenses, including those derived from diet, may play a role in the loss of lung function over time and the eventual development of COPD.

Comparison with other studies

To our knowledge, our study is the first to investigate the association between diet assessed through a priori dietary scores and the risk of newly diagnosed COPD. Several dietary scores have been proposed in the literature over the decades since the Mediterranean diet score was published.[24] The diet scores approach is

Table 5| Association between each component of Alternate Healthy Eating Index 2010 (AHEI-2010) and risk of newly diagnosed chronic obstructive pulmonary disease, pooled analysis (Nurses' Health Study and Health Professionals Follow-up Study)

AHEI-2010	Median (range) in women	Median (range) in men	No	Pooled hazard ratio* (95% CI)	P for trend	P value†	I²‡
Vegetables score							
Lowest fifth	3.0 (0.0–4.2)	2.7 (0.0–3.6)	211	1.00 (referent)	0.73		
Second fifth	4.6 (4.3–5.5)	4.2 (3.7–5.0)	183	0.92 (0.75 to 1.12)		0.34	0.0
Third fifth	5.9 (5.6–6.8)	5.5 (5.1–6.3)	190	0.96 (0.78 to 1.19)		0.36	0.0
Fourth fifth	7.3 (6.9–8.2)	7.1 (6.4–8.3)	148	0.82 (0.65 to 1.03)		0.59	0.0
Highest fifth§	9.1 (8.3–10.0)	9.5 (8.4–10.0)	158	1.02 (0.80 to 1.32)		0.65	0.0
Fruit score							
Lowest fifth	1.1 (0.0–2.0)	1.1 (0.0–1.9)	285	1.00 (referent)	0.08		
Second fifth	2.3 (2.1–3.1)	2.3 (2.0–3.1)	181	0.82 (0.63 to 1.06)		0.24	38.0
Third fifth	3.4 (3.2–4.1)	3.5 (3.2–4.3)	172	0.90 (0.74 to 1.11)		0.33	0.0
Fourth fifth	4.6 (4.2–5.6)	5.0 (4.4–6.1)	132	0.79 (0.63 to 1.00)		0.33	0.0
Highest fifth§	6.8 (5.7–10.0)	7.7 (6.2–10.0)	120	0.81 (0.63 to 1.05)		0.91	0.0
Whole grains score							
Lowest fifth	0.5 (0.0–1.2)	0.5 (0.0–1.2)	279	1.00 (referent)	0.01		
Second fifth	1.1 (1.3–1.9)	1.4 (1.3–2.0)	193	0.91 (0.75 to 1.10)		0.50	0.0
Third fifth	1.7 (2.0–2.3)	2.2 (2.1–2.9)	172	0.85 (0.60 to 1.29)		0.10	75.1
Fourth fifth	2.6 (2.4- 3.6)	3.3 (3.0–4.2)	145	0.80 (0.51 to 1.26)		0.10	74.8
Highest fifth§	4.1 (3.7–10.0)	5.2 (4.3–10.0)	101	0.70 (0.55 to 0.90)	0.52	0.0	
Sugar sweetened drinks and fruit juice score							
Lowest fifth	0.0 (0.0–0.0)	0.0 (0.0–0.0)	233	1.00 (referent)	0.86		
Second fifth	0.1 (0.1–1.6)	0.1 (0.1–0.3)	138	0.97 (0.74 to 1.27)		0.31	8.9
Third fifth	2.2 (1.7–3.6)	1.4 (0.4–2.7)	161	0.92 (0.75 to 1.14)		0.77	0.0
Fourth fifth	5.0 (3.7–7.2)	4.3 (2.8–6.5)	166	0.83 (0.67 to 1.03)		0.97	0.0
Highest fifth§	8.6 (7.3–10.0)	8.6 (6.6–10.0)	192	0.97 (0.58 to 1.60)		0.08	79.3
Nuts and legumes score							
Lowest fifth	0.7 (0.0–1.2)	0.7 (0.0–1.6)	184	1.00 (referent)	0.59		
Second fifth	1.4 (1.3–2.0)	2.1 (1.7–2.8)	194	1.09 (0.89 to 1.34)		0.73	0.0
Third fifth	2.2 (2.1–3.0)	3.4 (2.9–4.3)	176	1.04 (0.84 to 1.29)		0.70	0.0
Fourth fifth	3.5 (3.1–4.6)	5.4 (4.4–7.1)	174	1.03 (0.83 to 1.28)		0.68	0.0
Highest fifth§	6.1 (4.7–10.0)	9.1 (7.2–10.0)	162	0.95 (0.74 to 1.20)		0.34	0.0
Red and processed meat score							
Lowest fifth	0.0 (0.0–1.3)	0.0 (0.0–0.0)	234	1.00 (referent)	0.15		
Second fifth	1.5 (1.4–3.2)	0.9 (0.1–2.2)	198	1.11 (0.91 to 1.36)		0.88	0.0
Third fifth	3.5 (3.3–5.0)	3.2 (2.3–4.7)	178	0.98 (0.80 to 1.21)		0.32	0.0
Fourth fifth	5.5 (5.1–6.7)	5.5 (4.8–6.7)	155	0.90 (0.72 to 1.14)		0.38	0.0
Highest fifth§	7.6 (6.8–10.0)	7.7 (6.8–9.7)	125	0.70 (0.39 to 1.25)		0.10	76.6
Trans fat score							
Lowest fifth	4.9 (0.0–6.1)	5.8 (0.0–6.7)	194	1.00 (referent)	0.31		
Second fifth	6.2 (6.2–6.8)	7.1 (6.8–7.6)	173	0.95 (0.77 to 1.17)		0.56	0.0
Third fifth	6.9 (6.9–7.5)	7.8 (7.7–8.3)	171	0.98 (0.78 to 1.22)		0.31	4.7
Fourth fifth	7.6 (7.6–8.2)	8.5 (8.4–9.0)	187	0.96 (0.62 to 1.50)		0.14	68.8
Highest fifth§	8.5 (8.3–10.0)	9.4 (9.1–10.0)	165	1.11 (0.86 to 1.44)		0.79	0.0
Long chain fats score							
Lowest fifth	2.8 (0.0–4.2)	3.2 (0.0–5.1)	192	1.00 (referent)	0.75		
Second fifth	4.8 (4.3–6.0)	6.2 (5.2–8.0)	203	1.12 (0.81 to 1.53)		0.19	54.7
Third fifth	6.8 (6.1–7.8)	8.8 (8.1–9.8)	167	1.03 (0.83 to 1.27)		0.87	0.0
Fourth fifth	8.5 (7.9–9.8)	9.9 (9.9–9.9)	183	1.22 (0.98 to 1.52)		0.58	0.0
Highest fifth§	10.0 (9.9–10.0)	10.0 (10.0–10.0)	145	0.95 (0.75 to 1.21)		0.74	0.0
Polyunsaturated fatty acids score							
Lowest fifth	3.1 (0.0–3.9)	2.6 (0.0–3.3)	197	1.00 (referent)	0.37		
Second fifth	4.2 (4.0–4.9)	3.7 (3.4–4.1)	167	0.98 (0.79 to 1.21)		0.97	0.0
Third fifth	5.0 (5.0–5.7)	4.5 (4.2–5.0)	169	0.97 (0.64 to 1.48)		0.13	68.5
Fourth fifth	5.8 (5.8–7.2)	5.3 (5.1–6.1)	178	1.10 (0.87 to 1.38)		0.39	0.0
Highest fifth§	7.3 (7.3–10.0)	6.8 (6.2–10.0)	179	1.07 (0.84 to 1.36)		0.69	0.0
Sodium score							
Lowest fifth	1.2 (0.0–2.5)	1.0 (0.0–2.0)	187	1.00 (referent)	0.91		
Second fifth	3.2 (2.6–4.2)	3.0 (2.1–4.0)	181	0.92 (0.74 to 1.15)		0.51	0.0
Third fifth	5.0 (4.3–6.0)	5.0 (4.1–6.0)	184	0.96 (0.75 to 1.23)		0.53	0.0
Fourth fifth	6.8 (6.1–8.0)	7.0 (6.1–8.0)	171	0.98 (0.75 to 1.29)		0.37	0.0
Highest fifth§	9.0 (8.1–10.0)	9.0 (8.1–10.0)	167	0.98 (0.71 to 1.34)		0.44	0.0

(*Continued*)

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Table 5| Continued

AHEI-2010	Median (range) in women	Median (range) in men	No	Pooled hazard ratio* (95% CI)	P for trend	P value†	I²‡
Alcohol score							
Lowest fifth	2.5 (0.0–2.5)	2.5 (0.0–2.5)	279	1.00 (referent)	0.71		
Second fifth	3.1 (2.6–3.8)	3.7 (2.6–4.2)	104	1.08 (0.85 to 1.36)		0.63	0.0
Third fifth	4.9 (3.9–5.0)	5.0 (4.3–6.3)	168	1.01 (0.83 to 1.23)		0.46	0.0
Fourth fifth	5.0 (5.1–7.5)	7.5 (6.4–8.3)	158	1.06 (0.79 to 1.41)		0.24	41.8
Highest fifth§	10.0 (7.6–10.0)	10.0 (8.4–10.0)	181	1.08 (0.71 to 1.63)		0.08	75.9

*Multivariable hazard ratios adjusted for age, physical activity, body mass index, total energy intake, smoking status, pack years of smoking, pack years^2 of smoking, secondhand tobacco exposure (only in Nurses' Health Study), race/ethnicity, physician visits, US region, spouse's highest educational attainment (only in Nurses' Health Study), menopausal status (only in Nurses' Health Study), and other AHEI-2010 components.
†Test for between studies heterogeneity.
‡Degree of heterogeneity between studies expressed as percentage of total variance.
§Reflects healthier intake of that component.

based on prevailing hypotheses and guidance about the role of nutrients in disease prevention, and the diet is assessed for compliance with this guidance.[9] The other approach to deriving dietary patterns is data driven, with dietary exposure summarized using statistical techniques. Using this data driven approach, five studies have investigated the association of dietary patterns with spirometry or with symptoms or incidence of COPD[25–29]; we acknowledge that two of these studies included the same participants as our analysis.[28 29] Three of the five studies reported a "protective" association for a "prudent" dietary pattern characterized by a high intake of fruit, vegetables, fish, and whole grain cereals, consistent with the dietary antioxidant or anti-inflammatory properties hypothesis. Moreover, four of the five studies also reported a deleterious role of a "Western" diet characterized by a high intake of chicken, pork, fish, rice and noodle dishes, and preserved foods among a population of Chinese Singaporeans[27]; by a high intake of cured and red meat, potato, boiled vegetables, added fat, coffee, and beer among Dutch adults[26]; and by a high intake of cured and red meats, refined grains, desserts, sweets, French fries, and high fat dairy products among US adults.[28 29] Now, in addition to these data driven approaches, we report similar findings by using a diet score based on foods and nutrients consistently associated with a lower risk of cardiovascular diseases, diabetes, or cancer. These findings support the importance of the AHEI-2010 diet score to also target COPD.

Recent studies have suggested that COPD patients with multimorbidity represent the norm rather than the exception and that COPD is just one component of multimorbidity in patients with COPD.[30] Results of epidemiologic studies have shown that COPD is frequently associated with cardiovascular disease, lung cancer, osteoporosis, muscle weakness, and cachexia. Mechanistically, environmental risk factors such as smoking, unhealthy diet, exacerbations, and physical inactivity or inherent factors such as genetic background and ageing contribute to these associations.[31] When we excluded participants with previous comorbidities (cancer and cardiovascular diseases), we observed similar associations between the AHEI-2010 and the risk of COPD, suggesting that a healthy diet may play a role beyond its association with others chronic diseases.

Sex differences in susceptibility to COPD are probably multifactorial, and many unanswered questions remain.[32] With the growing number of female smokers around the world (and the epidemic of COPD in the female population), a pressing need exists to answer these and other questions relevant to sex differences in COPD.[32] In our study, the number of newly diagnosed COPD cases was twice as high in women as in men, but women were also twice as likely as men to be current smokers. Food choices are also an area in which research has shown consistent behavioral sex differences. Studies conducted in modern Western societies report consistent associations between sex and choice

Table 6| Association between Alternate Healthy Eating Index 2010 (AHEI-2010) and risk of adult onset of asthma in women (Nurses' Health Study) and men (Health Professionals Follow-up Study)

	Women			Men			Total			
AHEI-2010	No	Person years	Hazard ratio (95% CI)*	No	Person years	Hazard ratio (95% CI)*	No	Hazard ratio (95% CI)*	P value†	I²‡
Lowest fifth§	376	224 672	1.00 (referent)	36	103 187	1.00 (referent)	412	1.00 (referent)		
Second fifth	330	228 814	0.88 (0.76 to 1.02)	49	103 857	1.33 (0.86 to 2.05)	379	1.03 (0.69 to 1.53)	0.07	85.3
Third fifth	320	229 261	0.86 (0.74 to 1.00)	57	104 248	1.57 (1.02 to 2.39)	377	1.12 (0.62 to 2.01)	0.009	93.5
Fourth fifth	354	230 904	0.96 (0.83 to 1.12)	43	104 598	1.19 (0.76 to 1.88)	397	0.98 (0.85 to 1.13)	0.38	0.0
Highest fifth§	362	231 409	1.03 (0.88 to 1.20)	43	104 689	1.22 (0.77 to 1.94)	405	1.04 (0.90 to 1.21)	0.48	0.0
P for trend			0.47			0.64		0.40		

*Multivariable hazard ratios adjusted for age, physical activity, body mass index, total energy intake, smoking status, pack years of smoking, pack years^2 of smoking, secondhand tobacco exposure (only in Nurses' Health Study), race/ethnicity, physician visits, US region, spouse's highest educational attainment (only in Nurses' Health Study), and menopausal status (only in Nurses' Health Study).
†Test for between studies heterogeneity.
‡Degree of heterogeneity between studies expressed as percentage of total variance.
§Lowest fifth corresponds to least healthy diet according to AHEI-2010 diet score; highest fifth corresponds to healthiest diet.

of specific foods; for example, meat, alcohol, and hearty portion sizes are associated with masculinity, whereas vegetables, fruit, fish, and sour dairy products are associated with femininity.[33] We found similar associations among men and women, but statistical power was lower among men owing to the relatively limited number of COPD cases in men.

Strengths and limitations of study

Our study has a few potential limitations. Firstly, newly diagnosed COPD was defined by a self reported physician's diagnosis of COPD, and lung function measures were not available for these large national cohorts. However, our questionnaire based definition of newly diagnosed COPD was validated in a subset of registered nurses,[21] and we are confident that the accuracy of reporting also extends to the male health professionals. The main source of disease misclassification is probably misdiagnosis of asthma. Women who had a high dietary score and who developed COPD may have preferentially been diagnosed as having adult onset asthma, a potential bias that would create the appearance of an association between AHEI-2010 and COPD. However, our findings for AHEI-2010 and asthma were completely null, which suggests that misdiagnosis with asthma is an unlikely explanation. We also acknowledge that misclassification of AHEI-2010 assessed by the food frequency questionnaire intake is likely. Although we acknowledge the potential for some misclassification, these data allowed us to investigate the relations between diet and COPD in a very large sample, with repeated assessments of both diet and newly diagnosed COPD. Furthermore, this AHEI-2010 dietary score predicts other chronic diseases in the same cohorts.[12] Secondly, we acknowledge that the association between AHEI-2010 and COPD may be due, in part, to a residual confounding by cigarette smoking, which is a powerful risk factor. To minimize this possibility, multivariable models were adjusted with multiple time varying measures of tobacco exposure (smoking habits, pack years, and pack years^2), which were assessed biennially from 1976, and analyses were stratified according to smoking status. An inverse association between AHEI-2010 and risk of COPD remained even after we controlled for all of these factors, and analyses in ex-smokers yielded comparable results. Regarding statistics and our models, we acknowledge a possible effect size of the sample, and even though we controlled for several potential and known cofounders, our results might still be explained by some leftover confounding as well as by other healthy lifestyle factors. Finally, even though our cohorts consisted of female and male health professionals (that is, a relatively homogenous group as regards education level), residual differences in socioeconomic status might have contributed to the observed results.

We also recognize that our results obtained among health professionals are not necessarily generalizable to the whole population, as differences in health awareness, socioeconomic status, and smoking behavior might differ significantly between the general population and our study population. Lastly, our study population was mainly non-Hispanic white, which might limit generalizability of our results to other racial/ethnic populations. We encourage replication of our prospective findings on AHEI-2010 and COPD in other populations.

Conclusions and policy implications

In summary, a high AHEI-2010 dietary score was associated with a lower risk of newly diagnosed COPD, a novel finding that supports the importance of diet in the pathogenesis of COPD. This finding extends the relevance of the AHEI-2010 dietary score to another major chronic disease, COPD. Although efforts to prevent COPD should continue to focus on smoking cessation, these prospective findings support the importance of a healthy diet in multi-interventional programs to prevent COPD. Our results encourage clinicians to consider the potential role of the combined effect of foods in a healthy diet in promoting lung health. Although a single study is unlikely to change clinical practice, our paper provides further support for non-traditional risk factors for COPD.

AUTHOR AFFILIATIONS

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Transparency declaration: The lead author (the manuscript's guarantor) affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

Data sharing: Requests for access to data, statistical code, questionnaires, and technical processes may be made by contacting the corresponding author at raphaelle.varraso@inserm.fr.

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