THE ASSOCIATION OF DIETARY PATTERN WITH LUNG FUNCTION DECLINE IN A PROSPECTIVE COHORT STUDY

A thesis

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Master of Science

by

William Alexander Vonderschmidt

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ABSTRACT

Background

Diet has been found to be associated with lung function outcomes. However, few studies have investigated longitudinal associations of dietary components (individual foods and/or nutrients) with lung function, and we believe no investigation of the association of dietary pattern as a whole with longitudinal lung function has been conducted.

Objective

We aimed to investigate if a higher dietary pattern score would attenuate the decline of lung function with age and if this association is modified by smoking status.

Design

We estimated the association of 2 dietary pattern scores, the Healthy Eating Index 2015 (HEI-2015) and Alternate Mediterranean Diet (AMED), with 3 lung function outcomes, FEV_1, FVC, and FEV_1/FVC, in two separate cohorts. Stratified analyses were performed in relevant groups, namely among never vs. ever smokers. We performed a meta-analysis to assess the strength of evidence across the cohorts.

Results

The two cohorts comprise 5,409 participants who met inclusion criteria for analysis. In meta-analysis, a 10-point higher HEI-2015 score was statistically significantly associated with a 16 mL higher FEV_1 and a 1-point higher AMED score was statistically significantly associated with a 5 mL higher FEV_1 at any point during follow-up. For ever smokers, these associations persisted and increased in magnitude to 24 mL and 6 mL, respectively. Little to no association was found between dietary pattern and the longitudinal rate of decline in lung function.

Conclusion

We found that dietary pattern has an association with lung function cross-sectionally, but not longitudinally. These associations were modified by smoking status such that a healthier dietary pattern had a stronger positive association in lung function in smokers. While smoking cessation should remain the primary prevention and treatment for lung function decline, our findings provide limited evidence that a healthier dietary pattern associates with better lung health.

BIOGRAPHICAL SKETCH

Alexander Vonderschmidt was born and raised in Mission, Kansas, where he resided until moving to Manhattan (The *Little* Apple) to attend Kansas State University. There, Alex received two bachelor's degrees: a Bachelor of Science in dietetics and a Bachelor of Arts in French language. Following his undergraduate studies, Alex moved to Ithaca, New York to work toward a Registered Dietitian Nutritionist credential from Cornell University before finishing his graduate studies in nutritional epidemiology. Moving forward, Alex plans to pursue a career in policy, translational research, and population health in the hopes of transforming our food systems to better align with environmental sustainability targets and human health. Throughout his life, Alex always makes time to prioritize the arts: singing, music, and theatre; cultural enrichment through traveling and learning languages; and personal growth through running, yoga, and being surrounded by the people he loves.

To science: ad astra per aspera

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BACKGROUND

Pulmonary function is essential for the diagnosis, staging, and monitoring of chronic obstructive pulmonary disease (COPD).[1,2] COPD is a chronic disease that is characterized by incurable, progressive airflow restriction, which manifests in various clinical forms including emphysema and chronic bronchitis.[3] While there is currently no cure for this common disease, there are treatments that help manage the disease in persons with COPD.[4–6] Exposure to cigarette smoke (and pipe and cigar smoke) is the prevailing risk factor for COPD, and emerging studies suggest possible associations between electronic cigarettes and lung function outcomes.[7–10] Smoking cessation is considered the number one modifiable factor to mitigate lung function decline and reduce the risk of COPD.[11–13] However, some proportion of smokers do not develop COPD and non-smokers develop COPD, implying that there are other factors at play in the causal network.[14] Aside from smoking, known risk factors that are associated with decreased lung function and COPD risk include genetics[15–17], non-smoking inhalation exposures[18–25], sex and gender[26–28], socioeconomic status[29–31], and diet[32–38]. These potential risk factors, which influence lung function and risk of COPD, include modifiable risk factors that offer an opportunity to mitigate lung function decline and to reduce the risk of COPD.

In 2019, chronic lower respiratory diseases ranked as the 4th leading cause of death in the United States[39] and COPD ranked as the 3rd leading cause of death worldwide.[40] Between 1990 and 2017, the total number of deaths due to chronic respiratory diseases increased by 18%, to an estimated 3.91 (3.79 – 4.04) million deaths in 2017 (7% of all deaths worldwide).[41] Researchers recently found that lung function decline was inversely associated with health-related quality of life (HRQOL)[42,43], supporting the idea that loss in lung function leads to morbidity. In 2017, the

Global Burden of Disease Study 2017 estimated the Disability-Adjusted Life Years (DALYs; the number of years of life lost to ill-health, disability, or death) due to chronic respiratory diseases to be between 97.2 to 112.3 million per year.[44,45] There is substantial economic burden from COPD; for example, in the United States, the total estimated costs of COPD were more than $50B in 2010 comprising $32B in direct costs (hospitalization, medication, treatment, etc.) and $20B in indirect costs (i.e., due to lost productivity and/or wages, etc.).[46]

Lung function is measured by spirometry to yield two primary measurements, the forced expiratory volume in the 1st second (FEV_1; a measure (in liters) of the maximum volume of air that an individual can exhale in the first second following a maximal inhalation)[47–49] and the forced vital capacity (FVC; a measure (in liters) of the greatest voluntary expiration following a maximal inhalation, expelled at maximum speed and effort).[50,51] The landmark reference for the progression of lung function over the lifespan, which described the Fletcher-Peto Curve, showed that the rate of decline in FEV_1 accelerates as age increases, with more rapid acceleration in those with pulmonary obstruction.[52,53] However, accelerated decline in FEV_1 among patients with COPD can be highly variable and heterogenous, depending on the stage of COPD.[54] The ratio of FEV_1/FVC is used in the diagnosis of obstructive and restrictive lung disease. A greater reduction of FEV_1 compared to FVC may be due to increased airway resistance to expiratory flow. Thus, a lower ratio is indicative of obstruction, or COPD, as the main cause of limited airflow. Conversely, in diseases that result in chest wall deformities and pulmonary fibrosis, the FVC may be more decreased than the FEV_1, resulting in an increased ratio, indicating restriction as the main cause of limited airflow.[47] Both FEV_1 and FVC have been found to be predictive of all-cause mortality in the general population.[55] Thus, interventions to mitigate lung function decline have the potential to both prevent COPD occurrence, and to prevent mortality.

While smoking cessation remains the primary preventive approach in preserving lung function and reducing COPD risk, other risk factors are still under study. There is a consistent body of evidence on the association of nutrient intake and dietary components with lung function outcomes. Observational studies have investigated the associations of individual nutrient intake/serum biomarkers of nutrient status with lung function, namely nutrients with antioxidant properties (Vitamin A, beta-cryptoxanthin, Vitamin C, Vitamin D, Vitamin E); which are hypothesized to combat the oxidative damage that may occur in the lungs.[56–77] This may be even more effective in smokers who have greater oxidative stress and inflammatory load than non-smokers.[78–82] Randomized controlled trials have also studied the role of supplementing individual nutrients to attenuate lung function decline and prevent COPD, with mixed results.[83,84] However, when investigating the associations among food intake, nutrient intake, and lung function, it's important to consider the complexity in the diet with the understanding that no food is eaten in isolation and there is a high degree of collinearity among foods that could lead to possible synergistic effects of foods eaten in combination. A shift to study dietary patterns to capture a more complete representation of overall diet has led to the identification of clear associations of dietary pattern with chronic disease endpoints.[85–87] Emerging, but limited, research has identified positive associations of dietary pattern with lung function. A "prudent" dietary pattern (high in consumption of fruits, vegetables, fish, and wholegrains) was associated with higher FEV_1, FVC, and FEV_1/FVC outcomes [88–90] and with a lower risk, i.e., inverse association of COPD diagnosis.[91] Conversely, a "western" dietary pattern (high in consumption of processed foods (high in trans and saturated fats), refined carbohydrates, cured and red meats, and desserts) was associated with lower lung function and increased risk of respiratory symptoms and prevalent COPD.[89,91,92] More recently, researchers have found that the Healthy Eating

Index 2005 (HEI-2005) and certain dietary sub-components of the HEI-2005 had positive associations with the FEV_1/FVC ratio.[93]

While prior studies investigated the association of dietary pattern and nutrients with lung function using a cross-sectional study design[56–65,67,72–76,88–91,93], and while few studies have investigated the association of nutrient intake (typically nutrients with antioxidant properties) with longitudinal change in lung function [70,77,83,94–101], to the best of our knowledge, no study has investigated the overall dietary pattern with longitudinal change in lung function. We aimed to investigate dietary pattern in relation to the longitudinal change in pulmonary function parameters. We hypothesized that if participants have higher HEI-2015 and (separately) higher Alternate Mediterranean Diet (AMED) scores, then lung function decline over time will be less steep. Our primary aim was to estimate the association of dietary pattern with rate of decline in function decline. Our secondary aim was to investigate whether the association of dietary pattern with lung function decline differs between smokers and non-smokers given the key role of smoking on lung function decline, and the hypothesis that dietary intake may attenuate the oxidative or inflammatory effects of inhalation exposures, such as smoking.[102–105]

METHODS

Study Population

Health, Aging, and Body Composition (Health ABC) Study

The National Institute of Aging's (NIA) Health ABC study is a longitudinal cohort study that recruited 3,075 community-dwelling volunteer men (48.4%) and women (51.6%) between April 1997 and June 1998. Participants were 70 – 79 years of age at baseline and 45% of the women

and 33% of the men were Black; the remaining participants were White. Participants were recruited from a random sample of White Medicare-eligible residents and all the Black Medicare-eligible residents in the Pittsburgh, PA and Memphis, TN metropolitan areas. Participants were eligible if they reported no difficulty walking one-fourth of a mile, climbing up 10 steps, or performing basic activities of daily living; were free of life-threatening illness; planned to remain in the geographic area for ≥3 years; and were not enrolled in lifestyle intervention trials.[106] More detailed information on the Health ABC cohort is available from the NIA including an overview of the cohort, disease outcomes, all datasets and documentation for the 16 years follow-up, and an operations manual.[107]

Yearly clinic examinations were conducted for 6 years with phone calls on alternate 6 months to update functional and health status. Phone calls continued every 6 months with additional clinic examinations at years 8 and 10. Ultimately, follow-up was extended to 16 years.[108]

All participants provided written informed consent. The institutional review boards (IRB) of the University of Tennessee (Memphis, TN) and the university of Pittsburgh (Pittsburgh, PA) approved the study.

Respiratory Ancillary Study (RAS)

The RAS study was nested within the Selenium and Vitamin E Cancer Prevention Trial (SELECT). SELECT was an intergroup Phase III, randomized, double-blind, placebo-controlled, population-based clinical trial of 35,533 men testing the efficacy of selenium and vitamin E supplementation alone and/or in combination to prevent prostate cancer. SELECT eligibility included ≥ 55 y (≥ 50 y for Black participants), serum prostate-specific antigen ≤ 4

ng/mL, and no clinical evidence of prostate cancer. SELECT enrolled men in the United States and Canada between 2001 – 2004. RAS used a post-randomization design; thus, pre-randomization lung function was not measured, but rate of lung function decline was captured over the intervention period through repeated measurements of lung function. RAS enrolled 2,920 men from the 16 SELECT sites with the greatest number of current cigarette smokers to test hypotheses that the effect of supplements on lung function decline was modified by cigarette smoking.[83]

The RAS was approved by local IRBs at each of the 16 study site locations and by the Cornell University IRB.

The analyses presented in this thesis used de-identified data from both cohorts and the study was approved by Cornell University's IRB.

Measurements

Dietary Intake and Derived Dietary Pattern Indices

Health ABC Cohort

To estimate usual energy intake, habitual dietary intake (the frequency and quantity of the foods and beverages consumed over the past 12 months) was assessed via a modified version of the Block food frequency questionnaire (FFQ) (Block Dietary Data Systems, Berkeley, CA).[109] The Block FFQ is a quantitative, validated FFQ, and was administered by trained interviewers at the 12-month follow-up examination (1998 – 99; year 2). The FFQ food list was developed specifically for this cohort, using NHANES III 24-hr recalls from ≥ 65 y non-Hispanic White

and Black adults residing in the Northeast or South. Trained interviewers used wood blocks, food models, standard kitchen measures, and flash cards to help participants estimate portion sizes for each food. Interviews were periodically monitored throughout the study to ensure the quality and consistency of the data collection procedures. The Health ABC FFQ was analyzed for micronutrient and macronutrient content by Block Dietary Data Systems.[110] All Health ABC participants who attended the year 2 visit and have no missing FFQ dietary data were eligible for inclusion in this analysis (n = 2,527). Missing data were assumed to be missing at random, given very low drop-out rates.

RAS Cohort

Participants completed the 120-item self-administered Nutrition Assessment shared resource (NASR) FFQ developed in 2001 by the Fred Hutchinson Cancer research Center (Seattle, WA)[111], based on questionnaires originally developed for the Women's Health Initiative.[112,113] The FFQ was administered at study baseline and assessed the average food and beverage intake over the prior 12 months. Each participant recorded their average frequency of consumption for each food item in the survey and specified the amount of each item typically consumed using the categories provided. There were nine frequency categories and three portion sizes to choose from. All RAS men with ≥1 PFT and no missing dietary data (n = 2,882) were included in this analysis. Missing data were assumed to be missing at random, given very low drop-out rates.

Healthy Eating Index-2015 (HEI-2015)

The HEI-2015 is the current version of the Healthy Eating Index (HEI; updated every 5 years) and it is a measure of adherence to the dietary pattern laid out in the 2015 – 2020 Dietary Guidelines for Americans. The index comprises 13 food components, including 9 adequacy

components describing foods or nutrients where greater consumption is considered as a positive attribute and 4 components describing foods or nutrients to be consumed in moderation where greater consumption is considered a negative attribute.

The consumption of each component is estimated from the FFQ data and is expressed relative to total calories consumed. Thus, the portion sizes of each FFQ item were translated into cup or ounce (depending on the component) equivalents (e.g., 1 apple = ½ cup of apple) per 1,000 kilocalories consumed per day. Relative density of foods or nutrients consumed (cup or ounce equivalents per 1,000 kilocalories) "uncouples diet quality from diet quantity;" allowing for the assessment of the quality of the overall mix of foods and nutrients consumed, rather than the absolute amount of food consumed, which varies from person to person and is affected by factors such as age, sex, and physical activity.[114]

The maximum score for each of the 13 components is either 5 or 10 points. Adequacy components are scored higher when consumption is higher and moderation components are scored higher when consumption is lower. For all components, intakes defined by the criteria set for minimum or maximum are scored as 0 and 5 or as 0 and 10 points, depending on the component. Scores between the minimum and maximum values are prorated linearly; the reported intake amount (per 1,000 kilocalories) is divided by the maximum criteria and multiplied by the maximum score (5 or 10) for that component.[114] For example, if a participant eats 1 apple (0.5 cup equivalents) per day as their whole fruit consumption out of a total of 2,000 kilocalories consumed, they would have a density of 0.25 cup equivalents of whole fruit consumed per 1,000 kilocalories consumed. Since this does not meet the minimum (no whole fruit consumed, scored as 0) or the maximum (>0.4 cup equivalents of whole fruit per 1,000

kilocalories per day, scored as 5) criteria for the whole fruit component (Appendix 1), the score is derived by prorating linearly. Thus, the 0.25 cup equivalents is divided by 0.4 cup equivalents (the maximum criteria for that component) and multiplied by 5 (the maximum score for that component) to calculate the score (calculated score is 3.125). Once each of the 13 components are scored (by summing the cup/ounce equivalents across all foods consumed in that component), the components scores are summed to yield the total HEI-2015 score, which ranges from a theoretical minimum score of 0 to a theoretical maximum score of 100.[115] Appendix 1 provides further information on the scoring of the HEI-2015. More detailed information on the development of the HEI-2015 and how it is scored, including example code for computational purposes is available at the National Cancer Institute, National Institutes of Health.[116]

Alternate Mediterranean Diet Index (AMED)

The AMED index, with 9 components developed by Fung, et al.[117], was modified from the Mediterranean diet scale of Trichopoulou et al.[118–120] to more fully represent eating behaviors that are associated with a lower risk of chronic disease in both clinical and epidemiological studies.[117]

While the AMED score does not account for caloric density (amount of food or nutrient consumed per 1,000 kilocalories), we accounted for density to create consistency between the dietary pattern scores under investigation. Thus, as with the HEI-2015 scoring, the portion sizes of each FFQ item were translated into cup or ounce (depending on the component) equivalents (e.g., 1 apple = ½ cup of apple) per 1,000 kilocalories consumed per day, before being scored.

Each of the 9 components has a total score of 1. For most components, intakes greater than the cohort median for the component are set equal to 1, and intakes less than or equal to the cohort median are set equal to 0. For the red and processed meat component, the reverse is true: intakes less than the cohort median are set equal to 1 and intakes greater than or equal to the cohort median are set equal to 0. In light of a discrepancy in the reporting of the alcohol range in Fung et al., (both 5 – 15 g/d and 5 – 25 g/d were reported in the paper as the indicated range of alcohol consumption, with no sex differentiation noted), we set 5 – 15 g/d and 10 – 25 g/d as the range of alcohol intake for women and men, respectively, based on prior publications reporting the AMED dietary pattern scores.[121] Thus, for the alcohol component, intakes within the gender-specific range (5 – 15 g/d for women and 10 – 25 g/d for men) are set equal to 1, all other intake values (both greater than and less than the defined range) are set equal to 0, and are not dependent on median values of the cohort. The component scores are summed to yield the total AMED score, which ranges from a theoretical minimum score of 0 to a theoretical maximum score of 9. Appendix 2 provides further details on the components and scoring of the AMED.

Both dietary indices were computed in Health ABC and RAS using the FFQ data. FFQ items were sorted into the corresponding HEI-2015 or AMED components. Some FFQ items specified exact cup or ounce equivalents per serving of food (e.g., 1 apple = ½ cup apple). For the items that did not specify an exact cup or ounce equivalent, we used the USDA's nutrient database, FoodData Central, to estimate a typical portion size and the associated cup or ounce equivalent of that portion size. All estimated portion sizes were based on this database. Some FFQ items included foods that contained ingredients that could be subdivided between dietary pattern components (e.g., spaghetti, lasagna, and other pasta with meat sauce). These items were internally labeled as "mixed dishes." For all mixed dishes, the USDA's MyPlace Kitchen was

used to source recipes for each mixed dish. These USDA standardized recipes also included information on the food group equivalents (vegetables, grains, protein, dairy, fruit) per portion of the recipe. These recipes were used to estimate how a given mixed dish should be divided across dietary score components (e.g., spaghetti, lasagna, and other pasta with meat sauce dishes were estimated to contain 50% refined grains, 30% total protein, 15% total vegetable, and 5% dairy). When applicable, multiple recipes were considered and an average across the recipes was used for that individual FFQ item. Further details about the coding of mixed dishes, and the cup or ounce equivalent estimations is provided in the appendix (Appendix 3).

Lung Function

The lung function measurements that were included for these analyses were: FEV_1, FVC, and the ratio of the two, FEV_1/FVC.

Health ABC Cohort

Lung function data were collected at the year 1 (baseline), year 5, year 8, and year 10 clinic examinations using a horizontal dry rolling seal HF6 Spirometer (Sensor Medics Corporation, Yorba Linda, CA) according to standard guidelines. The spirometers were adjusted at the National Institute of Occupational Safety and Health (Morgantown, WV) and connected to a software used in the 3rd National Health and Nutrition Examination Survey.[122] The spirometers were calibrated daily by trained and certified technicians, using a 3.0-liter syringe. Between 3 – 5 tracings were obtained from each subject. In participants with bronchodilator medicines, spirometry tracings were collected 10 minutes after use and any bronchodilator medication use in the 4 hours preceding the exam was recorded. A four-point scoring system was used for FEV_1 and FVC values; a score of 2 indicated that American Thoracic Society (ATS) criteria for

acceptability and reproducibility of spirometry were met and a score of 3 or 4 meant those criteria were exceeded.[123] Starting at the year 8 clinic examination, the EasyOne Worldspirometer Model 2001 diagnostic spirometer (NDD Medizintechnik AG, Zurich, Switzerland) was used in home visits.[124] A total of 7,846 spirometry measurements were completed on 2,886 participants.

RAS Cohort

Lung function measures were collected at 3 out of the 4 annual clinical visits that spanned 3 years. However, the final pulmonary function test was available for only 57% of the participants due to early termination of SELECT, and this is assumed to be an unbiased sample given the randomness of the termination date. SELECT clinical research nurses were trained in spirometry methods by the RAS staff and bi-annual refresher sessions were required.[83] All pulmonary function tests followed ATS guidelines[123] for the standardization of spirometry in epidemiologic studies and used the EasyOne handheld flow-sensing spirometer, which yields valid and reproducible results.[125] A total of 9,660 spirometry measurements were completed on 2,912 participants.

Covariates

We included known predictors of the outcome and potentially confounding factors as covariates in the analysis. The variables adjusted in all the models included: sex (male and female, Health ABC only), race (self-reported Black, White, Hispanic non-Black*, Hispanic Black*, Other* (*RAS only)), age (years), height (cm), the residual of height-squared (cm^2), smoking status (never, former, intermittent, persistent), pack-years of smoking, and study site. Education was described as a characteristic, to provide information about the cohort participants, but was not included in

the final analyses as it is likely to be a proxy for dietary pattern, or other variables related to socioeconomic status. Both the HEI-2015 and the AMED scores were computed to account for caloric density (food or nutrient amount per 1,000 kilocalories), hence total caloric intake was not included as a covariate. In computing the HEI-2015 dietary pattern score, scores with decimal values are possible, whereas the AMED score is comprised of integers only. Furthermore, an increase of one on the HEI-2015 scale conveys a much smaller change compared to a one-point increase on the AMED scale. Smoking status was recorded at each clinic examination as never, former, or current smoking status. For the RAS cohort, any participant with a smoking status recorded as "unknown" was removed from analyses. These categories were then coded into longitudinal smoking status: never, former, current-intermittent, current-persistent. If participants consistently reported as never or former smokers at every examination, they were labeled accordingly. If participants consistently reported current smoking status at every examination, they were categorized as current-persistent. If participants reported to starting, resuming, or quitting smoking at any point during follow-up, they were categorized as current-intermittent.

Statistical Analysis

We analyzed the association of HEI-2015 and AMED, separately, with repeated measures of FEV_1, FVC, and the ratio of FEV_1/FVC using a multivariate linear mixed effects regression model using the unstructured covariance matrix to estimate the linear, longitudinal associations. The analysis included baseline age and a continuous time variable that represented the elapsed time between the baseline and each lung function measurement (clinic examination visit) in years. The coefficient for the elapsed time variable provides the estimate of rate of change in lung

function per unit of time, i.e., year (mL/year). The statistical model we used for analysis followed the basic pattern of:

$$PFT_{ij} = \alpha + \beta 1 * t_{ij} + \beta n * X_i + \beta 3 * D_i + \beta 4 * t_{ij} * D_i + \alpha_i + e_{ij},$$

where PFT_{ij} is the pulmonary function test (FEV_1, FVC, or FEV_1/FVC) for participant i at the j^{th} measurement; α represents the fixed population intercept; α_i is the deviation of each participant i from the fixed intercept; e_{ij} represents the independent random error term, its values assumed to be normally distributed; t_{ij} is the elapsed time variable for the j^{th} PFT for participant i; $\beta 1$ is the fixed coefficient for time, and an estimate of the rate of decline across all participants; βn is the fixed coefficient for each covariate, X, used in the model; $\beta 3$ is the fixed cross-sectional effect of diet, D; and $\beta 4$ is the fixed effect of diet, D, on the longitudinal rate of decline.

All variables in the model were estimated as fixed effects, and the model specified a random effect for the intercept. The linear mixed effects regression model allows for the inclusion of participants with only one lung function measurement as well as participants with ≥1 lung function measurement to leverage all available data.

Two adjusted models were estimated for each dietary pattern indicator and each lung function outcome. The first model was minimally-adjusted and included the covariates sex (male, female), race (White, Black, Hispanic non-Black*, Hispanic Black*, Other* (*RAS only)), height (cm), the residual of height-squared (cm^2), age at study baseline (yrs), and elapsed time (yrs). The second model further adjusted for smoking status (categories of never, former, intermittent during study period, persistent during study period), packyears of smoking, and study site. The beta coefficient for each covariate, including HEI-2015 and AMED, conveys the estimated associate of the

variable with lung function at a point in time. To estimate the associate of a variable with the rate of change in lung function, models are extended to include the interaction of the variable with elapsed time. Thus, the dietary pattern score*time coefficient conveys the association of dietary pattern score with the rate of change in lung function over time.

We explored whether the association of dietary pattern with rate of change in lung function differed by other characteristics. Specifically, we investigated effect modification by smoking status (never vs. ever), sex (male vs. female), race (Black vs. White vs. Hispanic non-Black* vs. Hispanic Black* vs. Other* (*RAS only)), and by overall dietary quality (upper 2 quartiles of dietary pattern score by cohort, [healthy] vs. lower 2 quartiles, [unhealthy]). To test whether the association of dietary pattern with each lung function outcome differed by group, we tested the 3-way interaction coefficients for smoking status, sex, race and diet; thus, for example, for sex, we tested the sex by dietary pattern score by time coefficient to identify the statistical support for modification of the association of dietary pattern score on the rate of decline in lung function (for FEV_1, FVC, and FEV_1/FVC) (Appendix 4). If the statistical significance threshold of $p < 0.1$ was exceeded, we used a stratified analysis to estimate the dietary pattern–lung function association for each subgroup.

To assess the strength of evidence across the two cohorts, we performed a random effects meta-analysis with inverse-variance weighting to combine effect estimates for the main estimates of the association of dietary pattern with lung function (for FEV_1, FVC, and FEV_1/FVC). Additional meta-analysis was performed on the estimates of the association of dietary pattern with lung function (for FEV_1, FVC, and FEV_1/FVC) from stratified analyses where there were consistent directions in the effect estimates across the two cohorts. Q tests were performed to detect

heterogeneity across the results (Appendix 5). The meta-analyses were performed in RStudio 1.3 using the "metafor" package.

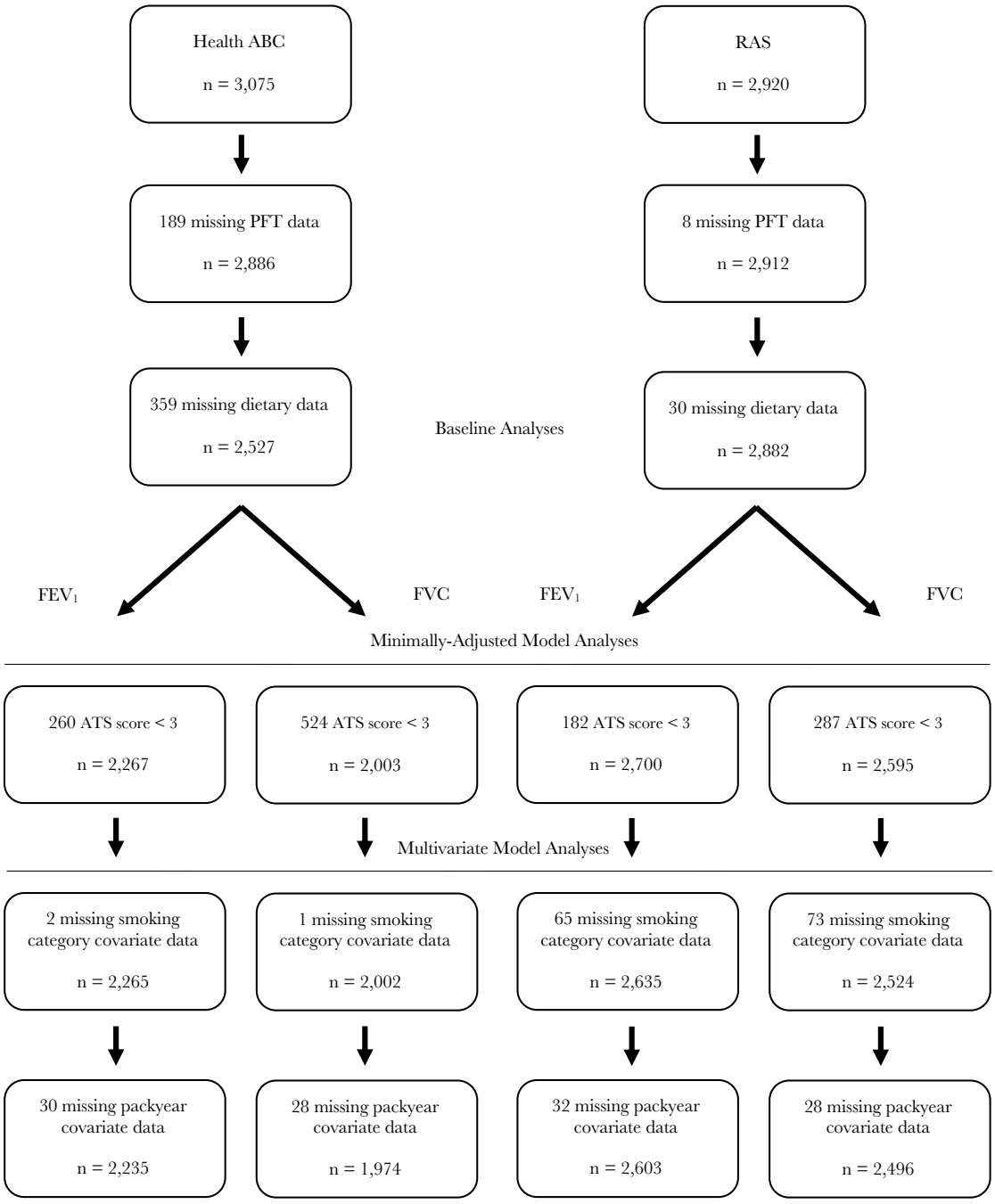
All coding was performed using SAS 9.4 and RStudio 1.3. Coding of all FFQ dietary data into dietary scores and code for all analyses were reviewed and mirrored by an independent analyst to assure validity of all findings.

RESULTS

Characteristics of Study Population

Health ABC and RAS enrolled 3,075 and 2,920 participants, respectively. Due to its rigorous design, RAS had very minimal missing data and loss to follow-up, both among PFTs (n = 8) and dietary information (n = 30), resulting in a final population to use for baseline characteristic analysis of n = 2,882. In the observational prospective cohort study, Health ABC, loss to follow-up and missing data were a bit higher for PFTs (n = 189) and dietary data (n = 359), yielding a final population of n = 2,527 for baseline characteristic analyses. For the main regression analyses, only FEV_1 and FVC values with a quality control score of 3 or more (indicating that ATS criteria for acceptability and reproducibility were exceeded upon measurement)[123] were used (Figure 1).

Figure 1 – Flow Chart of Participants from Health ABC and RAS Cohorts For Study Analyses



*Abbreviations, Figure 1: Health ABC: Health, Aging, and Body Composition Study; RAS, Respiratory Ancillary Study; PFT, pulmonary function test; ATS, American Thoracic Society; FEV_1, forced expiratory volume in the first second; FVC, forced vital capacity

Table 1 provides the baseline characteristics in both cohorts. At baseline, the Health ABC cohort had a relatively older population (73.59 ±2.85) than the RAS cohort (64.78 ±6.56) and thus, had

relatively lower FEV_1 (2,173.92 ±642.31 vs. 2,956.67 ±694.12) and FVC (2,932.74 ±806.00 vs. 4059.06 ±913.96) values. Both cohorts had a high proportion of Black participants (38.2%, 23.7%) compared to the general U.S. population.[126] The RAS cohort specifically enrolled participants from site locations with a higher proportion of smokers and in both cohorts about half of participants were ever smokers (former + intermittent + persistent). Both cohorts had very similar average dietary pattern scores both for the HEI-2015 (67.11 ±11.01, 66.53 ±10.49) and AMED (4.10 ±1.67, 4.07 ±1.92) indices. The Health ABC cohort had a lower proportion of participants with postsecondary education (44.6% vs. 70.4%).

Table 1 – Baseline Characteristics of Study Participants in the Health ABC and Respiratory Ancillary Study Cohorts†

Characteristic	Health ABC n = 2527	missing %	RAS n = 2882	missing %
Measurements, mean (SD)				
Age (years)	73.59 (±2.85)	0	64.78 (±6.56)	0
Height (cm)	166.37 (±9.31)	0	176.10 (±8.22)	0
FEV_1 (mL)	2173.92 (±642.31)	0	2956.67 (±694.12)	0
FVC (mL)	2932.74 (±806.00)	3.7	4059.06 (±913.96)	0
FEV_1/FVC	74.47 (±8.02)	3.7	72.98 (±9.20)	0
Pack Years‡	34.22 (±29.44)	1.4	25.84 (±23.45)	3.4
HEI-2015 Score	67.11 (±11.01)	0	66.53 (±10.49)	0
AMED Score	4.10 (±1.67)	0	4.07 (±1.92)	0
Race/Ethnicity		0		0
White	1563 (61.9)		1983 (68.8)	
Black	964 (38.2)		683 (23.7)	
Hispanic (non-Black)	-		92 (3.2)	
Hispanic (Black)	-		19 (0.7)	
Other	-		105 (3.6)	
Sex		0		0
Male	1250 (50.5)		2882 (100)	
Female	1277 (49.5)		-	
Smoking status		0.1		3.2
Never	1115 (44.2)		965 (34.6)	
Former	1147 (45.4)		1288 (46.2)	
Intermittent	122 (4.8)		216 (7.7)	

Persistent	140 (5.6)		320 (11.5)	
Education		0		0
< High School*	576 (22.8)		214 (7.5)	
High School/GED*	821 (32.6)		634 (22.1)	
Postsecondary	1125 (44.6)		2017 (70.4)	
Site location§		0		0
Memphis	1219 (48.2)		-	
Pittsburgh	1308 (51.8)		-	

†Number (percent) unless otherwise noted.
‡Among ever-smokers (persistent, intermittent, and former smokers) only; Health ABC: n = 1376, RAS: n = 1818.
*In Health ABC, "vocational training" was accounted for in two separate variables: high school graduate with vocational training and less than high school with vocational training, hence they were divided in < High School and High School/GED accordingly. However, in RAS, no such delineation was made for vocational education. To maintain congruency, RAS participants with vocational training were categorized into "High School/GED."
§RAS site locations included in regression analyses, but not displayed in Table 1.

The average dietary pattern in groups defined by other characteristics showed expected trends (Table 2). With race, there was a slightly lower score in both HEI-2015 and AMED for Black compared to White participants in both cohorts, with the magnitude of differences by race less pronounced in Health ABC than in RAS. In the Health ABC cohort, there was a substantially lower score in men (65.05 ±11.14, 3.95 ±1.66) compared to women (69.14 ±10.49, 4.26 ±1.66 $p<0.001$) across both dietary pattern scores. In both cohorts, there was a pattern of higher dietary score in higher educational status categories. Similarly, there was a pattern of higher dietary score in subgroups with less exposure to cigarette smoke. The bivariate associations among potentially confounding variables and diet confirm the importance of accounting for these variables in regression models given known associations of all variables with the pulmonary outcomes.

Table 2 – Healthy Eating Index-2015 (HEI-2015) and Alternate Mediterranean Diet (AMED) Scores by Cohort and by Covariates†

	Health ABC		RAS	
Characteristic	HEI-2015	AMED	HEI-2015	AMED
Race/Ethnicity				

White	67.66 (±10.63)	4.23 (±1.66)	67.15 (±10.62)	4.21 (±1.96)
Black	66.23 (±11.57)	3.90 (±1.66)	64.14 (±9.91)	3.58 (±1.79)
Hispanic (non-Black)	-	-	68.24 (±9.71)	4.28 (±1.75)
Hispanic (Black)	-	-	66.26 (±9.04)	3.58 (±1.74)
Other	-	-	68.97 (±10.14)	4.44 (±1.73)
P-value¤	<0.001	<0.001	<0.001	<0.001
Sex				
Male	65.05 (±11.14)	3.95 (±1.66)	66.53 (±10.49)	4.07 (±1.92)
Female	69.14 (±10.49)	4.26 (±1.66)	-	-
P-value¤	<0.001	<0.001	-	-
Smoking status				
Never	68.68 (±10.55)	4.31 (±1.62)	68.78 (±10.20)	4.37 (±1.88)
Former	66.79 (±11.04)	4.09 (±1.67)	66.69 (±10.39)	4.13 (±1.96)
Intermittent	62.11 (±10.71)	3.34 (±1.54)	63.23 (±10.26)	3.58 (±1.73)
Persistent	61.77 (±11.48)	3.26 (±1.59)	60.96 (±9.31)	3.19 (±1.64)
P-value¤	<0.001	<0.001	<0.001	<0.001
Education				
< High School*	64.41 (±11.43)	3.66 (±1.59)	64.26 (±11.16)	3.57 (±1.83)
High School/GED*	66.50 (±11.16)	3.96 (±1.67)	64.53 (±10.42)	3.65 (±1.84)
Postsecondary	68.94 (±10.35)	4.44 (±1.64)	67.40 (±10.32)	4.26 (±1.92)
P-value¤	<0.001	<0.001	<0.001	<0.001
Site location§				
Memphis	67.77 (±10.92)	4.06 (±1.56)	-	-
Pittsburgh	66.51 (±11.06)	4.14 (±1.76)	-	-
P-value¤	<0.001	<0.001	<0.001	<0.001

†All numbers reported in mean (SD).
¤Chi-square test for no difference was used to evaluate if the means of the HEI-2015 and AMED dietary pattern scores across the levels of the categorical covariates differed significantly. A P-value of <0.05 indicates statistically significant differences between categories.
*In Health ABC, "vocational training" was accounted for in two separate variables: high school graduate with vocational training and less than high school with vocational training, hence they were divided in < High School and High School/GED accordingly. However, in RAS, no such delineation was made for vocational education. To maintain congruency, RAS participants with vocational training were categorized into "High School/GED."
§RAS site locations included in regression analyses, but not displayed in Table 2.

The Association of Dietary Pattern with Lung Function

The primary results describing the association of dietary pattern with lung function outcomes of FEV_1, FVC, and FEV_1/FVC are in Table 3. For the purposes of interpretation, the HEI-2015–PFT associations are presented for a change of 10 in HEI-2015 score, which corresponds to about 1 standard deviation in HEI-2015 score. In the minimally-adjusted model that adjusts for the covariates age, sex, race, height, and residual of height-squared, both dietary pattern scores

were significantly positively associated with all 3 lung function parameters. Findings were consistent in both cohorts, with the exception of the AMED–FVC association in the Health ABC cohort (10.74 mL increase per 1 point, p = 0.087). These associations indicate that at any point in time in the follow-up, there are positive associations of dietary pattern and pulmonary function. However, there was little to no association of dietary pattern with the rate of decline in the lung function parameters, meaning there was little to no evidence of a longitudinal association of dietary pattern with subsequent change in lung function For example, in the Health ABC cohort, a 10-point increase in HEI-2015 score was associated with a 30 mL higher FEV_1 (p <0.001). Similarly, a 1-point higher AMED score was associated with a 19 mL higher FEV_1 (p = 0.001). The multivariate model further accounted for smoking status, packyears of smoking, and study site, the positive associations of HEI-2015 and FEV_1 persisted, though results were less consistent across all outcomes and both cohorts. At any point in follow-up, a 10-point higher HEI-2015 was associated with a 21 mL higher FEV_1 in the RAS cohort (p = 0.045). Similarly, a 10-point higher HEI-2015 was associated with a greater FEV_1/FVC ratio in the Health ABC cohort (0.30 higher ratio with 10-point higher HEI-2015, p = 0.030).

The results of the meta-analyses for the association of dietary pattern with FEV_1 confirmed the interaction between dietary pattern and FEV_1 cross-sectionally, with statistically significant results across both of the dietary pattern scores in the minimally-adjusted model. For the association of dietary pattern and FEV_1 in the multivariate model, where there was little statistically significant association between dietary pattern and FEV_1 cross-sectionally among the two cohorts, the meta-analysis revealed that there was consistent associations in direction and magnitude, confirmed by statistically significant results for both dietary pattern scores with FEV_1. A very similar pattern emerged for FVC in that the meta-analysis confirmed statistical

significance cross-sectionally in the AMED dietary pattern score in both models. The HEI-2015 score for the meta-analysis had P-values of 0.053 and 0.051 for the minimally-adjusted and multivariate models, respectively, showing near-statistical significance. For the FEV_1/FVC ratio, no statistically significant results emerged from the meta-analysis. No statistically significant or meaningful results emerged from the meta-analysis in regard to the association of dietary pattern on lung function decline longitudinally in any of the 3 lung function parameters. Q tests revealed moderate levels of heterogeneity in the minimally-adjusted model and low levels of heterogeneity in the multivariate model (Appendix 5).

Table 3 – Estimates from Regression Models for the Association of Dietary Pattern with FEV_1 (mL/year), FVC (mL/year), and the ratio of FEV_1/FVC (FEV_1%)

	Minimally-Adjusted Model			Multivariate Model		
	ß	SE	P-value	ß	SE	P-value
FEV_1						
Health ABC (n = 2,267 | n = 2,235)						
HEI-2015	**3.01**	**0.87**	**<0.001**	1.21	0.86	0.161
HEI-2015 * Time	$1.56 \cdot 10^{-2}$	$6.14 \cdot 10^{-2}$	0.799	$2.24 \cdot 10^{-2}$	$6.15 \cdot 10^{-2}$	0.716
AMED	**18.68**	**5.69**	**0.001**	4.59	5.61	0.414
AMED * Time	-0.20	0.39	0.662	-1.67	0.39	0.672
RAS (n = 2,700 | n = 2,603)						
HEI-2015	**6.20**	**1.06**	**<0.001**	**2.11**	**1.05**	**0.045**
HEI-2015 * Time	$1.92 \cdot 10^{-2}$	0.14	0.892	$1.40 \cdot 10^{-2}$	0.14	0.921
AMED	**23.82**	**5.75**	**<0.001**	5.23	5.63	0.353
AMED * Time	1.20	0.78	0.121	1.31	0.78	0.094
Meta-Analysis of Health ABC and RAS						
HEI-2015	**4.58**	**1.59**	**0.004**	**1.62**	**0.69**	**0.019**
HEI-2015 * Time	$1.67 \cdot 10^{-2}$	0.21	0.936	$1.98 \cdot 10^{-2}$	0.21	0.924
AMED	**21.24**	**2.57**	**<0.001**	**4.91**	**1.68**	**0.003**
AMED * Time	0.36	0.69	0.599	-0.25	1.49	0.869
FVC						
Health ABC (n = 2,003 | n = 1,974)						
HEI-2015	**1.89**	**0.96**	**0.049**	0.88	0.97	0.367
HEI-2015 * Time	$-6.36 \cdot 10^{-2}$	$8.58 \cdot 10^{-2}$	0.459	$-6.75 \cdot 10^{-2}$	$8.63 \cdot 10^{-2}$	0.434
AMED	10.74	6.27	0.087	2.51	6.33	0.692

AMED * Time	-0.42	0.55	0.444	-0.47	0.55	0.394
RAS (n = 2,595 | n = 2,496)						
HEI-2015	**5.84**	**1.26**	**<0.001**	2.19	1.27	0.084
HEI-2015 * Time	$-3.05 \cdot 10^{-2}$	0.26	0.906	$3.09 \cdot 10^{-2}$	0.25	0.901
AMED	**24.46**	**6.79**	**<0.001**	5.45	6.78	0.422
AMED * Time	0.55	1.41	0.694	1.00	1.36	0.462
Meta-Analysis of Health ABC and RAS						
HEI-2015	3.83	1.97	0.053	1.45	0.74	0.051
HEI-2015 * Time	$-5.54 \cdot 10^{-2}$	0.25	0.827	$-4.22 \cdot 10^{-2}$	0.25	0.868
AMED	**17.58**	**6.86**	**0.010**	**3.93**	**1.81**	**0.030**
AMED * Time	-0.15	0.63	0.814	$-1.05 \cdot 10^{-2}$	0.68	0.988
FEV_1/FVC						
Health ABC (n = 2,003 | n = 1,974)						
HEI-2015	$\mathbf{7.06 \cdot 10^{-2}}$	$\mathbf{1.59 \cdot 10^{-2}}$	**<0.001**	$\mathbf{3.10 \cdot 10^{-2}}$	$\mathbf{1.54 \cdot 10^{-2}}$	**0.044**
HEI-2015 * Time	$-2.5 \cdot 10^{-4}$	$1.47 \cdot 10^{-3}$	0.885	$2.87 \cdot 10^{-4}$	$1.47 \cdot 10^{-3}$	0.845
AMED	**0.43**	**0.10**	**<0.001**	0.13	0.10	0.204
AMED * Time	$-1.39 \cdot 10^{-3}$	$9.39 \cdot 10^{-3}$	0.907	$1.71 \cdot 10^{-3}$	$9.39 \cdot 10^{-3}$	0.855
RAS (n = 2,595 | n = 2,496)						
HEI-2015	$\mathbf{5.85 \cdot 10^{-2}}$	$\mathbf{1.59 \cdot 10^{-2}}$	**<0.001**	$1.85 \cdot 10^{-2}$	$1.51 \cdot 10^{-2}$	0.223
HEI-2015 * Time	$4.30 \cdot 10^{-3}$	$3.60 \cdot 10^{-3}$	0.235	$-3.90 \cdot 10^{-3}$	$3.60 \cdot 10^{-3}$	0.272
AMED	**0.20**	$\mathbf{8.57 \cdot 10^{-2}}$	**0.017**	$5.64 \cdot 10^{-2}$	$8.10 \cdot 10^{-2}$	0.487
AMED * Time	$1.01 \cdot 10^{-2}$	$1.97 \cdot 10^{-2}$	0.609	$1.20 \cdot 10^{-2}$	$1.97 \cdot 10^{-2}$	0.541
Meta-Analysis of Health ABC and RAS						
HEI-2015	$6.45 \cdot 10^{-2}$	$8.92 \cdot 10^{-2}$	0.469	$2.47 \cdot 10^{-2}$	$8.73 \cdot 10^{-2}$	0.777
HEI-2015 * Time	$1.10 \cdot 10^{-3}$	$3.23 \cdot 10^{-2}$	0.974	$-9 \cdot 10^{-4}$	$3.23 \cdot 10^{-2}$	0.977
AMED	0.31	0.21	0.154	$8.93 \cdot 10^{-2}$	0.21	0.673
AMED * Time	$2.30 \cdot 10^{-3}$	$7.97 \cdot 10^{-2}$	0.977	$5.00 \cdot 10^{-3}$	$7.97 \cdot 10^{-2}$	0.950

Modification of the Association of Dietary Pattern with Lung Function

Potential effect modification of the association of dietary pattern with lung function was explored through stratified analyses where there was sufficient evidence for effect modification ($p < 0.1$, Appendix 4). There was not sufficient evidence for effect modification by race, with no evidence among the multivariate models. Testing revealed potential evidence for modification of the association of dietary pattern with lung function in stratification by smoking status, sex, and diet quality (Appendix 4). In instances where there was sufficient evidence for effect modification by stratification for only one cohort, stratified analyses were completed for both cohorts.

There was evidence for modification of the association of dietary pattern with lung function by smoking status. In ever smokers, across every lung function outcome, for both dietary pattern scores, and in both cohorts, there was a positive association of dietary pattern score and lung function outcomes at any point in time, but little to no association in the never smoking group (Table 4).

There was limited evidence for an association of dietary pattern with rate of decline in lung function. In ever smokers, a higher AMED score was significantly associated with an accelerated decline in the rate of change in FVC by 1.93 mL/yr (minimally-adjusted model, $p = 0.020$) and 2.01 mL/yr (multivariate model, $p = 0.016$) (Table 4).

The meta-analyses of the smoking-stratified association of dietary pattern with FEV_1 and FVC revealed that among ever smokers, there were statistically significant associations among the findings across both cohorts, but the association of dietary pattern with rate of change in lung function was not statistically significant in the meta-analysis. The meta-analyzed findings for FEV_1/FVC found little to no association of pattern with lung function outcomes in both models across both groups (Table 4). For both never smokers and ever smokers, Q tests revealed moderate levels of heterogeneity in the minimally-adjusted model and low levels of heterogeneity in the multivariate model (Appendix 5).

Stratification of analyses by sex was only possible in the Health ABC cohort (Appendix 6). The analysis for the modification of the association of dietary pattern with lung function by sex did not yield clear results. However, a paradoxical pattern emerged; in men in Health ABC, a higher

HEI-2015 and AMED dietary pattern score was significantly associated with an accelerated rate of decline in both FEV_1 and FVC longitudinally in the multivariate model. To investigate these findings, additional analyses were performed, stratifying the Health ABC men by smoking status (Appendix 7). In the group of smoking men in Health ABC, the inverse association of dietary pattern with rate of decline in FVC persisted in the multivariate model for both HEI-2015 ($p = 0.006$) and AMED ($p = 0.011$).

Final stratification by dietary pattern was performed on those with a healthy vs. unhealthy diet quality (upper 2 vs. lower 2 quartiles of dietary pattern score for each cohort, respectively) (Appendix 8). No clear pattern emerged within these stratifications. Cross-sectionally, among those with an unhealthy diet, there were significant associations with HEI-2015 and AMED on FEV_1 and FEV_1/FVC in the Health ABC cohort. In the RAS cohort, there were significant cross-sectional increases among those with an unhealthy diet in all 3 lung function outcomes associated with the HEI-2015 dietary pattern score.

Table 4 –Association of Dietary Pattern with FEV_1 (mL/year), FVC (mL/year), and FEV_1/FVC (FEV_1%), Stratified by Smoking Status (Never vs. Ever)

	Never Smokers						Ever Smokers					
	Minimally-Adjusted Model			Multivariate Model			Minimally-Adjusted Model			Multivariate Model		
	ß	SE	P-value	ß	SE	P-value	ß	SE	P-value	ß	SE	P-value
FEV_1												
Health ABC (n = 987 | n = 987; n = 1,278 | n = 1,248)												
HEI-2015	-0.69	1.18	0.558	-0.55	1.17	0.641	**4.86**	**1.23**	**<0.001**	**2.61**	**1.24**	**0.035**
HEI-2015 * Time	$2.02 \cdot 10^{-2}$	$8.93 \cdot 10^{-2}$	0.821	$2.07 \cdot 10^{-2}$	$8.93 \cdot 10^{-2}$	0.817	$1.24 \cdot 10^{-2}$	$8.50 \cdot 10^{-2}$	0.884	$1.25 \cdot 10^{-2}$	$8.54 \cdot 10^{-2}$	0.884
AMED	4.96	7.53	0.510	4.02	7.49	0.592	**23.00**	**8.18**	**0.005**	5.44	8.17	0.506
AMED * Time	0.57	0.56	0.310	0.58	0.56	0.297	-0.77	0.55	0.160	-0.85	0.55	0.126
RAS (n = 914 | n = 914; n = 1,721 | n = 1,687)												
HEI-2015	3.27	1.74	0.060	1.70	1.75	0.330	**6.29**	**1.33**	**<0.001**	2.15	1.32	0.105
HEI-2015 * Time	-0.11	0.25	0.651	-0.11	0.25	0.649	$3.83 \cdot 10^{-2}$	0.17	0.827	$3.12 \cdot 10^{-2}$	0.17	0.859
AMED	10.01	9.36	0.285	3.60	9.44	0.703	**25.44**	**7.14**	**<0.001**	5.95	7.03	0.398
AMED * Time	0.38	1.36	0.778	0.38	1.36	0.779	1.65	0.97	0.088	1.62	0.97	0.094
Meta-Analysis of Health ABC and RAS												
HEI-2015	1.22	1.98	0.538	0.45	1.12	0.690	**5.55**	**0.80**	**<0.001**	**2.39**	**0.80**	**0.003**
HEI-2015 * Time	$-1.41 \cdot 10^{-2}$	0.26	0.956	$-1.37 \cdot 10^{-2}$	0.26	0.957	$2.10 \cdot 10^{-2}$	0.24	0.930	$1.88 \cdot 10^{-2}$	0.24	0.937
AMED	**7.30**	**2.52**	**0.004**	3.83	2.04	0.061	**24.30**	**1.95**	**<0.001**	**5.71**	**1.94**	**0.003**
AMED * Time	0.51	0.63	0.414	0.52	0.63	0.408	0.35	1.21	0.770	0.30	1.23	0.808
FVC												
Health ABC (n = 850 | n = 850 ; n = 1,152 | n = 1,124)												
HEI-2015	-0.26	1.48	0.859	-0.14	1.48	0.926	**3.32**	**1.32**	**0.012**	2.00	1.35	0.140
HEI-2015 * Time	$1.77 \cdot 10^{-2}$	0.13	0.892	$1.96 \cdot 10^{-2}$	0.13	0.881	-0.20	0.13	0.119	-0.20	0.13	0.122
AMED	4.65	9.44	0.622	4.04	9.70	0.668	12.84	8.73	0.142	2.42	8.91	0.786
AMED * Time	0.59	0.81	0.468	0.61	0.81	0.450	**-1.93**	**0.83**	**0.020**	**-2.01**	**0.84**	**0.016**
RAS (n = 865 | n = 865; n = 1,657 | n = 1,629)												
HEI-2015	**4.80**	**2.25**	**0.033**	1.68	2.22	0.450	**5.30**	**1.54**	**0.001**	2.11	1.55	0.174
HEI-2015 * Time	$-9.97 \cdot 10^{-2}$	0.42	0.815	$-8.78 \cdot 10^{-2}$	0.43	0.836	$6.39 \cdot 10^{-2}$	0.31	0.836	$8.00 \cdot 10^{-4}$	0.31	0.998
AMED	20.28	12.13	0.095	3.51	12.05	0.771	**22.27**	**8.26**	**0.007**	5.51	8.24	0.504
AMED * Time	-0.65	2.35	0.782	-0.55	2.35	0.814	1.79	1.68	0.288	1.47	1.69	0.382
Meta-Analysis of Health ABC and RAS												
HEI-2015	2.19	2.53	0.386	0.59	0.94	0.533	**4.25**	**0.99**	**<0.001**	**2.05**	**0.85**	**0.016**
HEI-2015 * Time	$1.00 \cdot 10^{-2}$	0.32	0.975	$-5.30 \cdot 10^{-3}$	0.32	0.987	-0.12	0.30	0.687	-0.14	0.30	0.642

AMED	12.38	7.81	0.113	3.80	2.32	0.101	**17.58**	**4.71**	**<0.001**	4.03	2.07	0.052
AMED * Time	0.27	0.78	0.726	0.31	0.78	0.687	-0.18	1.86	0.921	-0.39	1.74	0.821
FEV_1/FVC												
Health ABC (n = 850 | n = 850 ; n = 1,152 | n = 1,124)												
HEI-2015	$-6.21 \cdot 10^{-3}$	$2.00 \cdot 10^{-2}$	0.756	$-4.86 \cdot 10^{-3}$	$2.00 \cdot 10^{-2}$	0.808	**0.11**	**$2.26 \cdot 10^{-2}$**	**<0.001**	**$5.94 \cdot 10^{-2}$**	**$2.24 \cdot 10^{-2}$**	**0.008**
HEI-2015 * Time	$-1.50 \cdot 10^{-3}$	$2.13 \cdot 10^{-3}$	0.480	$-1.47 \cdot 10^{-3}$	$2.13 \cdot 10^{-3}$	0.489	$3.41 \cdot 10^{-3}$	$1.95 \cdot 10^{-3}$	0.080	$3.79 \cdot 10^{-3}$	$1.96 \cdot 10^{-3}$	0.060
AMED	$2.32 \cdot 10^{-2}$	0.13	0.855	$1.64 \cdot 10^{-2}$	0.13	0.897	**0.66**	**0.15**	**<0.001**	**0.29**	**0.15**	**0.049**
AMED * Time	$7.69 \cdot 10^{-3}$	$1.32 \cdot 10^{-2}$	0.560	$8.06 \cdot 10^{-3}$	$1.32 \cdot 10^{-2}$	0.5411	$-8.81 \cdot 10^{-3}$	$1.25 \cdot 10^{-2}$	0.4798	$-9.18 \cdot 10^{-3}$	$1.26 \cdot 10^{-2}$	0.465
RAS (n = 865 | n = 865; n = 1,657 | n = 1,629)												
HEI-2015	$-6.60 \cdot 10^{-3}$	$2.16 \cdot 10^{-2}$	0.761	$1.10 \cdot 10^{-2}$	$2.15 \cdot 10^{-2}$	0.609	**$7.04 \cdot 10^{-2}$**	**$2.07 \cdot 10^{-2}$**	**0.001**	$2.26 \cdot 10^{-2}$	$2.03 \cdot 10^{-2}$	0.197
HEI-2015 * Time	$-7.10 \cdot 10^{-3}$	$6.00 \cdot 10^{-3}$	0.238	$-7.50 \cdot 10^{-3}$	$6.00 \cdot 10^{-3}$	0.212	$4.50 \cdot 10^{-3}$	$4.60 \cdot 10^{-2}$	0.326	$-3.20 \cdot 10^{-3}$	$4.5 \cdot 10^{-3}$	0.482
AMED	-0.12	0.12	0.303	$1.00 \cdot 10^{-2}$	0.12	0.932	**0.28**	**0.11**	**0.011**	$9.60 \cdot 10^{-2}$	0.11	0.374
AMED * Time	$3.00 \cdot 10^{-3}$	$3.32 \cdot 10^{-2}$	0.928	$2.00 \cdot 10^{-4}$	$3.32 \cdot 10^{-2}$	0.995	$1.30 \cdot 10^{-2}$	$2.48 \cdot 10^{-2}$	0.600	$1.54 \cdot 10^{-2}$	$2.46 \cdot 10^{-2}$	0.532
Meta-Analysis of Health ABC and RAS												
HEI-2015	$-6.40 \cdot 10^{-3}$	0.10	0.950	$2.80 \cdot 10^{-3}$	0.10	0.978	$8.93 \cdot 10^{-2}$	0.10	0.390	$4.01 \cdot 10^{-2}$	0.10	0.698
HEI-2015 * Time	$-3.00 \cdot 10^{-3}$	$3.96 \cdot 10^{-2}$	0.940	$-3.00 \cdot 10^{-3}$	$3.96 \cdot 10^{-2}$	0.939	$3.50 \cdot 10^{-3}$	$4.33 \cdot 10^{-2}$	0.936	$1.70 \cdot 10^{-3}$	$3.70 \cdot 10^{-2}$	0.964
AMED	$-5.13 \cdot 10^{-3}$	0.25	0.837	$1.31 \cdot 10^{-2}$	0.25	0.958	0.44	0.25	0.080	0.18	0.25	0.480
AMED * Time	$6.40 \cdot 10^{-3}$	$9.72 \cdot 10^{-2}$	0.948	$5.80 \cdot 10^{-3}$	$9.72 \cdot 10^{-2}$	0.952	$-1.5 \cdot 10^{-3}$	$9.12 \cdot 10^{-2}$	0.987	$-9.00 \cdot 10^{-4}$	$9.40 \cdot 10^{-2}$	0.993

DISCUSSION

In a population-based observational cohort and a randomized controlled trial of older adults, we investigated if dietary pattern, measured by the HEI-2015 and AMED indices, is associated with lung function (FEV_1, FVC, and FEV_1/FVC), including the longitudinal decline in lung function. We demonstrated that dietary pattern is statistically significantly associated with lung function, cross-sectionally, and this association differs by smoking status and by sex. The effect estimates for the association of dietary pattern with lung function were greater in ever smokers compared to never smokers. The results of the meta-analysis confirmed these findings for FEV_1 and FVC, with statistically significant results across both dietary pattern scores, cross-sectionally. Associations of dietary pattern with the ratio of FEV_1 and FVC, were less consistent across the cohorts and there was no evidence of association through meta-analysis. We found very limited evidence for an association of dietary pattern with longitudinal changes in lung function.

When stratifying by sex in the Health ABC group, there was a paradoxical but statistically significant association between higher dietary pattern score and an acceleration in lung function decline, longitudinally in men (Appendix 7). This pattern was not present in the all-male RAS cohort. To explore whether this persisted when stratified by smoking status, an additional stratified analysis of the Health ABC males by smoking status was performed. The inverse association of dietary pattern with lung function decline persisted in the ever-smoking males but was not statistically significant in never-smoking males. These results may be due to unforeseen and/or unmeasured covariates or factors unique to the Health ABC cohort.

There are a limited number of studies that have examined the association of overall dietary pattern, or components therein, with rate of decline of lung function. Thus, this study contributes new evidence and shows little to no association of dietary pattern with lung function decline. There is one exception; in Health ABC ever smokers, a higher AMED score was significantly associated with an accelerated decline in the rate of change in FVC by 1.93 mL/yr (minimally-adjusted model, p = 0.020) and 2.01 mL/yr (multivariate model, p = 0.016) (Table 4). Within our analyses, smoking and aging remain to be the primary factors that contribute to lung function decline (Appendix 9). We observed a positive association of dietary pattern with lung function cross-sectionally, and found little to no evidence for an association of dietary pattern with the longitudinal change in lung function; this pattern has been noted in many prior studies of diet–lung function associations.[56–65,67,72–77,83,88–91,93,98,100,101] In the literature, it appears as though any significant associations of dietary pattern and longitudinal change in lung function occurred with single food or nutrient associations.[94–97] Thus, potentially this lack of association seen in dietary pattern with lung function decline may be due to decreased analytical power with increased variability in the exposure effect when looking at the entire dietary pattern compared to single foods or nutrients. These analyses could be completed in a larger cohort to test this hypothesis. Furthermore, while significance arose from single food or nutrient associations with lung function decline in the past, it is important to consider overall diet as this is a more accurate representation of typical eating behaviors.

The internal validity of this study is high and there is little to no concern about selection bias given high rates of participation across both Health ABC and RAS. Similarly, there is little to no concern about confounding bias as the models considered the main confounders, and the minimally-adjusted to multivariate models confirmed that associations persist cross-sectionally

and are highly modified by smoking status. The information bias in this study may contribute to the lack of association of dietary pattern with rate of decline in lung function, particularly surrounding the collection of dietary data in the form of FFQ, which is prone to human error in the under- and overestimation of the consumption of foods or nutrients. Since the FFQs used in both cohorts are validated and well tested, this concern is mitigated and at the very least, any errors that may have arisen in this manner would are assumed to be random across each cohort.

The average estimated annual decline in FEV_1 is 30 mL/yr for healthy never smokers, 60 mL/yr for current smokers, and 90 mL/yr for "extreme situations."[127] With this in mind, the effect estimates of our findings were clinically meaningful across both cohorts and both dietary pattern scores. For example, in our meta-analysis of the multivariate model association of dietary pattern with FEV_1, we found that a 10-point higher HEI-2015 score (approximately 1 SD from the mean, representing a meaningful change in dietary pattern) was associated with a 16 mL higher FEV_1 ($p=0.019$) and a 1-point increase in AMED score was associated with a 5 mL higher FEV_1 ($p=0.003$) at any point in time during follow-up (Table 3). This association was even more pronounced among ever smokers. In the meta-analysis for the multivariate model association of dietary pattern with FEV_1 stratified by smoking status (never vs. ever), we found that a 10-point higher HEI-2015 score was associated with a 24 mL higher FEV_1 ($p=0.003$) and that a 1-point higher AMED score was associated with a 6 mL higher FEV_1 ($p=0.003$) (Table 4). These findings suggest that dietary pattern (HEI-2015 and AMED) can have a clinically meaningful impact on lung function. While these associations were found in cohorts of predominately older adults, the cohorts were diverse in regard to race, smoking status, education, geographic location, and sex (Health ABC only). Thus, we suggest these findings to be relatively generalizable to the older adult U.S. population.

One of the main strengths of this research is the use of multiple cohorts, with meta-analysis of findings across the cohorts to increase the study power and to confirm the consistency of the findings. Furthermore, the cohorts were both included a diverse set of participants, with higher proportions of Black participants than the population average in the United States. The diversity of the cohorts meant that a large proportion were smokers, which supported examining whether smoking modified the association of dietary pattern with lung function. Another strength was the use of multiple dietary pattern scores in the analysis of dietary pattern, which complements and potentially accounts for any shortcomings of each score, individually. We calculated the Pearson correlation between the two dietary pattern scores and found coefficients of 0.56 in the Health ABC cohort ($P<0.001$) and 0.68 in the RAS cohort ($P<0.001$), indicating significant shared variance between the two dietary pattern scores in both cohorts. However, there is not perfect agreement, which suggests that these measures capture different aspects of dietary pattern. The dietary pattern scores used are well documented in the literature and the HEI-2015 is the latest of the HEI series, well tested and validated, based on the Dietary Guidelines for Americans.

There are a few limitations of this study worth noting. Dietary data collected by FFQ can be unreliable because it is prone to human error in the under- and overestimation of certain food items or nutrients. This concern is mitigated through the use of standardized, validated, interview-guided FFQs, and the use of physical food models. Another limitation is that diet data were collected at only one point in time, not accounting for any changes in diet that could have occurred after this point. While one-time dietary data collection is common, and not unique to either of these cohorts, it may introduce errors, potentially among participants who may have quit smoking and then used other strategies to better their health in attempt to mitigate health

concerns (like adopting healthier diets). As with all observational studies, residual confounding can be present. We tried to control for this as much as possible by accounting for confounding variables in analysis. Some potentially confounding variables that were not measured, but that may have affected lung function decline and may be associated with dietary pattern are air quality, exposure to indoor or outdoor pollutants, and genetics. Certain limitations exist in the calculation of the dietary pattern scores as well. The scoring of the AMED index components is not based on pre-defined numerical ranges, rather the scores are dependent on the median consumption frequencies of the cohort. Thus, if the cohort had an overall better or worse dietary habit, this would be reflected in the scores of the AMED index. This is somewhat accounted for by additional use of the HEI-2015, which is scored based on pre-defined criterion values, and additionally by use of meta-analysis between the cohorts.

There are important considerations given the pattern of results supports a cross-sectional association of dietary pattern and lung function, but little to no association with longitudinal rate of decline. While the results of past studies are mixed with regard to longitudinal findings, several studies reported statistically significant associations of single nutrients and/or foods with longitudinal changes in lung function.[77,94–97,99–101] With a small, but high quality set of studies identifying single nutrient—longitudinal lung function associations, more work is needed to better understand the null finding for the dietary pattern—longitudinal lung function associations in these two cohorts. While the dietary pattern score includes many of the foods and nutrients reported in past studies as attenuating lung function decline, the pattern overall had little to no association. Further work to investigate the components of the pattern score, particularly the components of the HEI-2015, could be informative.

In any epidemiologic study, measurement error in the exposure variable, specifically low validity and/or reliability of the measurement, could lead to a bias in the estimate of the effect. The HEI-2015 dietary pattern has been shown to be valid and reliable[128]; previous versions of the HEI series (HEI-2005, HEI-2010) also had high validity and reliability.[129–131] However, to our knowledge, evaluation of the AMED index for validity and reliability is not available, although AMED is widely used to measure adherence to the Mediterranean dietary pattern. The dietary pattern indices are calculated from dietary intake data, and measurement error in the collection of dietary data may also be a concern. FFQs capture long-term, habitual dietary intake, which likely accounts for food items that are not consumed often, and that would potentially be missed in short-term dietary intake methods such as the 24-hour food recall or the 3-day food record. However, as FFQs only capture consumption of a pre-determined and defined list of food items, which means they may miss some of the foods consumed, especially in groups consuming culturally/ethnically-diverse foods. This risk is mitigated in the Health ABC cohort because the FFQ was designed specifically for this cohort using NHANES III data. Furthermore, the FFQs used in both cohorts were validated and tested, which reduces concerns about measurement error. Finally, a recent meta-analysis of FFQ reproducibility found that FFQs that include more questions (≥ 120 items) and that cover at least a 12-month recall window (compared to a shorter recall window) were more likely to have higher correlations with nutrient estimations.[132] With these considerations, the measurement error in the FFQ and in the derived dietary pattern indices is expected to be non-differential and unrelated to the outcome. This pattern of measurement error would add noise to the finding, and thus bias it towards the null value.

Given the pattern of findings, i.e., a cross-sectional dietary pattern—lung function association, but null findings for the association of pattern with subsequent longitudinal decline in lung

function, there are a few considerations. Firstly, this pattern of findings may indicate that no causal relation exists between dietary pattern and lung function. However, since past studies have found significant associations between certain foods and/or nutrients with longitudinal change in lung function, this raises questions about whether overall dietary pattern or sub-components of dietary pattern are more informative. It is possible that the current approach to estimating dietary pattern is not accurately capturing the aspects of dietary pattern that are salient for lung function outcomes. For example, if the consumption of foods with anti-inflammatory properties is key, perhaps overall dietary pattern is not a good reflection of this consumption pattern. New methods to measure dietary intake that include updated technologies may enhance dietary data collection and lead to better accuracy and reliability compared to older methods.[133] Longitudinal associations reported for single foods and/or nutrients, but the lack of findings for overall dietary pattern raises the possibility that pattern does not accurately capture the synergistic effects of foods consumed. A recent and novel study suggested that dietary synergy, captured using machine learning algorithms, may have a role in pregnancy outcomes.[134] Perhaps the study hypothesis needs further refinement to investigate the synergistic effect of foods consumed in combination (dietary pattern). Alternatively, the finding of a cross-sectional association in the absence of a longitudinal association raises the possibility of reverse causality between dietary pattern and lung function. In other words, rather than dietary pattern having an effect on lung function, it is possible that persons with lower lung function consume a lower quality diet, potentially related to decreased appetite that may arise with decreased physical condition as well as decreased engagement in other health-promoting activities. Our findings do not allow us to reach a conclusion on reverse causality, and it worth noting that prior studies have identified associations of certain foods and/or nutrients with longitudinal lung function. More research to investigate the longitudinal association of dietary pattern with lung function is needed,

particularly work that looks at aspects of pattern to see if signals exist with subcomponents of the overall dietary pattern.

Finally, a major source of bias in observational epidemiologic studies is confounding bias and confounding by smoking in estimating the association of dietary pattern with lung function is a key consideration. However, the consideration of smoking as a confounding variable is moot if it is an effect modifier, and here is clear evidence that the dietary pattern—lung function associations differ by smoking status, indicating that effect modification is the key consideration. Furthermore, the stratum-specific association in ever smokers confirms both the statistically significant cross-sectional findings of an association of dietary pattern with lung function, and the finding of little to no longitudinal associations. This pattern of findings needs further investigation as described above.

The cessation of smoking remains the primary public health measure to avoid lung function disease outcomes such as COPD and cancer. However, there is a growing body of evidence on diet and lung function, and our findings show a consistent and positive association of dietary pattern with lung function in ever smokers. These findings confirm that persons consuming diets associated with a higher HEI-2015 and AMED score have better lung function, particularly in smokers. The lack of an association of dietary pattern with lung function decline raises questions about whether changes in diet would lead to better outcomes. However, for the general population, there are no negative health consequences in taking steps to improve dietary intake as outlined in the Dietary Guidelines for Americans such as increasing fresh fruit (especially whole fruit) and vegetable consumption, consuming whole grains in place of refined grains, and opting for lean sources of protein foods such as seafood and legumes.[135] So, improving dietary

intake should always be recommended at every stage of life, but there is the potential for this to be even more important for those who have ever smoked.

Moving forward, continued research that investigates dietary pattern's potential association with lung function decline will be important. To improve the strength of evidence, we recommend, when feasible, to continue to collect dietary data in a way that contributes to the most accurate representation of a participant's diet. For example, using newer collection methods that are specifically designed to capture dietary patterns may lead to better exposure assessment. To more accurately capture longitudinal associations that may exist, cohorts that are able to implement multiple points of dietary data collection would increase the strength of evidence, and potentially be able to capture a more accurate representation of a person's diet over time. Other factors that are noteworthy to explore in future research would be genetics and non-smoking inhalation, especially as increased air pollution continues to be a major concern for many regions around the world.[136]

CONCLUSIONS

This study investigated the association of dietary pattern with lung function. In most instances, a higher dietary pattern score was associated with higher lung function, cross-sectionally, but there was little to no evidence for an of association of dietary pattern with longitudinal lung function decline. These associations were modified by smoking status. While smoking cessation should remain the primary prevention and treatment for lung function decline, our findings provide limited evidence that a healthier dietary pattern associates with better lung health. Further studies are needed to investigate the association of dietary pattern and longitudinal lung function decline.

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APPENDIX

Healthy Eating Index 2015, HEI-2015 (Appendix 1)

Healthy Eating Index 2015[1]

HEI-2015 Component	Max Score	Criteria for Max Score†	Criteria for Min Score
Adequacy Components			
Total Fruits[2]	5	≥ 0.8 c equiv./1,000 kcal	No fruit
Whole Fruits[3]	5	≥ 0.4 c equiv./1,000 kcal	No whole fruit
Total Vegetables[4]	5	≥ 1.1 c equiv./1,000 kcal	No vegetables
Greens and Beans[4]	5	≥ 0.2 c equiv./1,000 kcal	No greens and beans
Whole Grains	10	≥ 1.5 oz equiv./1,000 kcal	No whole grains
Dairy[5]	10	≥ 1.3 c equiv./1,000 kcal	No dairy
Total Protein Foods[4]	5	≥ 2.5 oz equiv./1,000 kcal	No protein foods
Seafood and Plant Proteins[6]	5	≥ 0.8 oz equiv./1,000 kcal	No seafood or plant proteins
Fatty Acids[7]	10	(PUFAs + MUFAs)/SFAs ≥ 2.5	(PUFAs + MUFAs)/SFAs ≤ 1.2
Moderation Components			
Refined Grains	10	≤ 1.8 oz equiv./1,000 kcal	≥ 4.3 oz. equiv./1,000 kcal
Sodium	10	≤ 1.1 g/1,000 kcal	≥ 2.0 g/1,000 kcal
Added Sugars	10	≤ 6.5% of energy	≥ 26% of energy
Saturated Fats	10	≤ 8% of energy	≥ 16% of energy

†Cup = c; Ounce = oz; Kilocalories = kcal; Gram = g; Equivalents = equiv.
1: Intakes between the minimum and maximum are scored proportionately.
2: Includes 100% fruit juice.
3: Includes all forms except juice.
4: Includes legumes (beans and peas).
5: Includes all milk products, such as fluid milk, yogurt, and cheese, as well as fortified soy beverages.
6: Includes seafood, nuts, seeds, soy products (other than beverages), and legumes (beans and peas).
7: Ratio of poly- and monounsaturated fatty acids (PUFAs and MUFAs) to saturated fatty acids (SFAs).

Alternate Mediterranean Diet Index, AMED (Appendix 2)

Alternate Mediterranean Diet Index

Components	Description	Criteria for 1 point*
Vegetables	All vegetables except potatoes	> cohort median intake
Legumes	Tofu, string beans, peas, beans	> cohort median intake
Fruit	All fruit and juices	> cohort median intake
Nuts	Nuts, peanut butter	> cohort median intake
Whole grains	Whole-grain ready-to eat cereals dark breads, brown rice, other grains, wheat germ, bran, popcorn	> cohort median intake
Red and Processed Meat	Hot dogs, deli meat, bacon, hamburger	< cohort median intake
Fish	Fish and shrimp, breaded fish	> cohort median intake
Fatty Acid Ratio	Ratio of monounsaturated to saturated fat	> cohort median intake
Ethanol	Wine, beer, liquor	5 – 15 g/d (women) 10 – 25 g/d (men)

*If criteria are not met, score is set equal to 0 for that component; Gram = g; Day = d.

Mixed Dish Coding and Cup/Ounce Equivalent Estimations (Appendix 3)

Cup or Ounce Equivalent Estimations – RAS only

Food Frequency Questionnaires (FFQ) collected data on intake of food items, which sometimes required the assignment of a cup or ounce equivalent (cup or ounce per stated portion size) if the information on cups or ounces in the portion size were not specified in the FFQ. In these instances, listed below, the cup or ounce equivalent values were derived from the USDA nutrient database, FoodData Central.* All other cup and ounce equivalents were defined within the FFQ.

FFQ Item Name and Description in the Questionnaire	**cup, c/ounce, oz equiv.**
Granola bars and cereal bars such as Nutri-Grain bars (1 bar)*	1/3 c/1.3 oz
Bananas (1 medium ~ 4 oz. at least 7" in length)	3/4 c
Apricots (fresh, canned, or dried) (2 medium or 4 halves)	1/2 c
Oranges, grapefruits, and tangerines (not juice)	1/2 c
Cantaloupe, orange melon, mango (in season)	1 c
Watermelon and red melon (1 large slice)	1 c
Pizza (1/2 of a 12" pizza)	2 c
Burritos, tacos, tostados, and quesadillas (2 medium)	2 c
Enchiladas and tamales (2 medium)	2 c
Fresh tomatoes (1 medium ~5 oz. or 4 slices)	3/4 c
Yams and sweet potatoes (1 medium ~4 oz.)	3/4 c
Fresh garlic, including in cooking (1 clove)	1/48 c
Dark breads, including dark bagels and rolls (2 slices or 1 medium)	3 oz
Sports or meal replacement bars such as Power Bars and Clif Bars (1 bar)*	2.4 oz
Plain popcorn (no butter) or low-fat microwave popcorn (8 handfuls)	1.5 oz
Eggs (2 eggs)	4.25 oz
Bacon and breakfast sausage (3 strips or 2 links)	2.25 oz
Lunch meats such as ham, turkey, and low-fat bologna (2 slices)	4 oz
All other lunch meat such as bologna, salami, and Spam (2 slices)	4 oz
Canned tuna, tuna salad, and tuna casserole (1 can tuna)	5 oz
Fried chicken, including nuggets and tenders (2 large pieces or 9 nuggets)	8 oz
Chicken and turkey (roasted, stewed, or broiled) (2 large or 4 small pieces)	8 oz
Asian-style noodles and rice, such as chow mein, fried rice, and Pad Thai	12 oz
Pancakes, French toast, and waffles (2 medium pieces)	3 oz
Muffins, scones, croissants, and biscuits (1 medium piece)	4 oz
White breads, including bagels, rolls, and English muffins (2 slices or 1 medium)	3 oz
Cornbread and corn muffins (2 slices or 1 medium)	3 oz
Low- or non-fat crackers, such as saltines and SnackWells (12 medium)*	1.5 oz
Regular crackers, such as Ritz and Wheat Thins (12 medium)*	1.5 oz
Doughnuts, pies, and pastries (1 piece)	3 oz
Cookies and cakes (3 medium cookies or 1 piece of cake)	3 oz

*When a name-brand was referenced, information was taken directly from the manufacturer label(s) and averaged when multiple brands were referenced.

Mixed Dish Coding

Some FFQ items were labeled as "mixed dishes," denoting that a subdivision of the item into multiple dietary score components would be necessary. For all mixed dishes, the USDA's MyPlace Kitchen was used to source recipes for the appropriate mixed dish.* In addition to the itemized ingredient breakdown, these USDA standardized recipes include information of the amount of MyPlate food group equivalents (vegetables, grains, protein, dairy, fruit) per portion. These recipes were used to estimate how a given mixed dish should be subdivided across dietary score components. When applicable, multiple recipes were considered and an average across the recipes was used for that particular FFQ item.

FFQ Item Name	**Component Subdivision†**
RAS FFQ	
Meal replacement drinks and shakes such as Slim-Fast and Ensure*	D: 100%
Granola bars and cereal bars such as Nutri-Grain Bars*	R: 95%, F: 5%
Sports or meal replacement bars such as Power Bars and Clif Bars*	R: 80%, P: 20%
Fried chicken, including nuggets and tenders	P: 75%, R: 25%
Fried fish, fish sandwich, and fried shellfish (shrimp and oysters)	P/S: 75%, R: 25%
Stew, pot pie, curries, and casseroles with meat or chicken	P: 50%, V: 25%, R: 25%
Chili with meat and beans	P: 66%, V: 33%
Spaghetti, lasagna, and other pasta with meat sauce	R: 50%, P: 30%, V: 15%, D: 5%
Spaghetti and other pasta with tomato sauce (no meat)	R: 50%, V: 50%
Spaghetti and other pasta with oil, cheese, or cream sauce (mac n' cheese)	R: 66%, D: 33%
Asian-style noodles and rice, such as chow mein, fried rice, and Pad Thai	R: 40%, P: 40%, V: 20%
Pizza	R: 50%, D: 25%, V: 15%, P: 10%
Tofu, tempeh, and products such as tofu hot dogs, soy burgers, and tofu cheese	P/S: 100%
Burritos, tacos, tostadas, and quesadillas	R: 60%, P: 20%, D: 15%, V: 5%
Enchiladas and tamales	P: 50%, R: 25%, D: 15%, V: 10%
Potato, macaroni, and pasta salads made with mayonnaise or oil	R: 50%, V: 25%, D: 25%
Rice, noodles, and other grains (as a side dish)§	R: 95%, W: 5%
Health ABC FFQ‡	
Vegetable soup, vegetable beef, chicken vegetable, or tomato soup	V: 75%, P: 25%
Other soups, chicken noodle, chowder	P: 40%, R: 25%, D: 20%, V: 15%

*When a name-brand was referenced, information was taken directly from the manufacturer label(s) and averaged when multiple brands were referenced.
†F: Total Fruit, V: Total Vegetable, D: Dairy, W: Whole Grain, P: Total Protein, S: Seafood and Plant Protein, R: Refined Grain
§Researchers at Iowa State University found, through multiple nationally representative surveys of food consumed by individuals in the United States, that the rice consumption of Americans is, on average, 5% brown rice and 95% white rice. (Batres-Marquez SP, Jensen HH, Upton J. Rice consumption in the United States: recent evidence from food consumption surveys. J Am Diet Assoc. 2009 Oct;109(10):1719-27. doi: 10.1016/j.jada.2009.07.010. PMID: 19782171.)
‡Health ABC FFQ items that were similar or identical in name to the items listed in the RAS FFQ section have been omitted from this table.

P-Value Results of 3-Way Interaction Analysis by Stratification (Appendix 4)

Appendix 4 Table – P-Value Results of 3-Way Interaction Analysis by Stratification†

	Minimally-Adjusted Model			Multivariate Model		
	FEV_1	FVC	FEV_1/FVC	FEV_1	FVC	FEV_1/FVC
Smoking Status (Never vs. Ever)						
Health ABC						
HEI-2015	0.933	0.257	0.132	0.941	0.253	0.111
AMED	0.101	**0.036**	0.300	**0.080**	**0.029**	0.291
RAS						
HEI-2015	0.638	0.749	0.785	0.669	0.865	0.656
AMED	0.458	0.402	0.824	0.478	0.487	0.761
Race						
Health ABC (White vs. Black)						
HEI-2015	0.804	0.955	0.235	0.725	0.992	0.236
AMED	0.677	0.745	0.294	0.809	0.641	0.304
RAS (White vs. Black vs. Hispanic Black vs. Hispanic Non-Black vs. Other)						
HEI-2015	0.636	0.128	0.352	0.742	0.401	0.314
AMED	0.443	**0.058**	0.929	0.533	0.293	0.927
RAS (White vs. Black)*						
HEI-2015	0.278	**0.061**	0.603	0.367	0.314	0.602
AMED	0.234	**0.034**	0.630	0.331	0.309	0.731
Sex (Health ABC Only; Male vs. Female)						
Health ABC						
HEI-2015	**0.029**	**0.014**	0.225	**0.017**	**0.011**	0.386
AMED	**0.040**	**0.037**	0.253	**0.022**	**0.025**	0.387
Diet Quality (Healthy vs. Unhealthy)						
Health ABC						
HEI-2015	**0.024**	**0.034**	0.661	**0.032**	**0.027**	0.481
AMED	0.520	0.700	0.282	0.668	0.716	0.167
RAS						
HEI-2015	0.946	0.432	**0.003**	0.999	0.174	**0.001**
AMED	0.202	0.395	0.224	0.271	0.153	0.169

†A P-value of <0.1 indicates a statistically significant 3-way interaction between the stratified groups.
*Since very little significant results arose from the 3-way interaction test on the race variable using all 5 categories, an analysis was performed with only White vs. Black to potentially increase power to capture any potential effect modification that may exist in the White vs. Black participants. Only White and Black participants included in test, participants of any other race (Hispanic (Black), Hispanic (Non-Black), and Other) were removed.

Heterogeneity Considerations for Meta-Analysis of Estimates (Appendix 5)

Appendix 5 Table – Heterogeneity Considerations for Meta-Analysis of Estimates of the Association of Dietary Pattern with FEV_1 (mL/year), FVC (mL/year), and the ratio of FEV_1/FVC (FEV_1%)†

	Minimally-Adjusted Model			Multivariate Model		
	FEV_1	FVC	FEV_1/FVC	FEV_1	FVC	FEV_1/FVC
Main Analysis						
HEI-2015	**81 (0.022)**	**86 (0.008)**	0 (0.946)	0 (0.515)	0 (0.381)	0 (0.943)
HEI-2015 * Time	**0 (<0.001)**	0 (0.955)	0 (0.949)	**0 (<0.001)**	0 (0.865)	0 (0.953)
AMED	57 (0.129)	**93 (<0.001)**	0 (0.594)	0 (0.849)	0 (0.417)	0 (0.863)
AMED * Time	40 (0.196)	0 (0.488)	0 (0.946)	**87 (0.006)**	12 (0.288)	0 (0.952)
Smoking Status (Never)						
HEI-2015	**81 (0.021)**	**85 (0.009)**	0 (0.999)	42 (0.188)	0 (0.344)	0 (0.938)
HEI-2015 * Time	0 (0.823)	0 (0.874)	0 (0.951)	0 (0.823)	0 (0.886)	0 (0.947)
AMED	34 (0.219)	**91 (0.001)**	0 (0.775)	0 (0.919)	0 (0.910)	0 (0.990)
AMED * Time	0 (0.891)	0 (0.486)	0 (0.983)	0 (0.885)	0 (0.514)	0 (0.971)
Smoking Status (Ever)						
HEI-2015	0 (0.372)	27 (0.242)	0 (0.849)	0 (0.774)	0 (0.948)	0 (0.859)
HEI-2015 * Time	0 (0.959)	0 (0.691)	0 (0.996)	0 (0.971)	0 (0.762)	0 (0.931)
AMED	0 (0.533)	**81 (0.022)**	0 (0.456)	0 (0.896)	0 (0.456)	0 (0.704)
AMED * Time	**74 (0.050)**	**82 (0.019)**	0 (0.910)	**75 (0.045)**	**79 (0.029)**	0 (0.899)

†All numbers presented as I^2% (P-value)

Stratified Analysis by Sex (Male vs. Female) (Appendix 6)

Appendix 6 Table –Association of Dietary Pattern with FEV_1 (mL/year), FVC (mL/year), and FEV_1/FVC (FEV_1%), Stratified by Sex (Male vs. Female, Health ABC Only)

	Male						Female					
	Minimally-Adjusted Model			Multivariate Model			Minimally-Adjusted Model			Multivariate Model		
	ß	SE	P-value	ß	SE	P-value	ß	SE	P-value	ß	SE	P-value
FEV_1												
Health ABC (n = 1,135 | n = 1,118; n = 1,132 | n = 1,117)												
HEI-2015	**4.09**	**1.43**	**0.004**	2.06	1.41	0.142	**2.10**	**0.98**	**0.033**	0.58	0.98	0.555
HEI-2015 * Time	**-0.21**	**0.10**	**0.049**	**-0.22**	**0.11**	**0.038**	$5.83 \cdot 10^{-2}$	$6.91 \cdot 10^{-2}$	0.399	$7.20 \cdot 10^{-2}$	$6.93 \cdot 10^{-2}$	0.298
AMED	**19.35**	**9.52**	**0.042**	2.20	9.39	0.815	**18.76**	**6.27**	**0.003**	8.47	6.20	0.172
AMED * Time	-1.29	0.66	0.052	**-1.38**	**0.67**	**0.040**	0.26	0.44	0.548	0.36	0.44	0.414
FVC												
Health ABC (n = 1,034 | n = 1,018; n = 969 | n = 956)												
HEI-2015	2.28	1.56	0.143	1.34	1.57	0.395	1.51	1.12	0.175	0.27	1.13	0.809
HEI-2015 * Time	**-0.35**	**0.15**	**0.018**	**-0.37**	**0.15**	**0.014**	$8.00 \cdot 10^{-2}$	$9.50 \cdot 10^{-2}$	0.400	$8.38 \cdot 10^{-2}$	$9.52 \cdot 10^{-2}$	0.379
AMED	5.30	10.33	0.608	-3.27	10.49	0.755	**15.94**	**7.10**	**0.025**	8.53	7.11	0.231
AMED * Time	-1.80	0.95	0.057	**-1.97**	**0.96**	**0.040**	0.48	0.60	0.424	0.51	0.60	0.399
FEV_1/FVC												
Health ABC (n = 1,034 | n = 1,018; n = 969 | n = 956)												
HEI-2015	**$8.83 \cdot 10^{-2}$**	**$2.32 \cdot 10^{-2}$**	**<0.001**	$4.12 \cdot 10^{-2}$	$2.21 \cdot 10^{-2}$	0.063	**$4.93 \cdot 10^{-2}$**	**$2.17 \cdot 10^{-2}$**	**0.023**	$2.05 \cdot 10^{-2}$	$2.14 \cdot 10^{-2}$	0.339
HEI-2015 * Time	$1.45 \cdot 10^{-3}$	$2.15 \cdot 10^{-3}$	0.499	$1.36 \cdot 10^{-3}$	$2.16 \cdot 10^{-3}$	0.530	$-2.43 \cdot 10^{-3}$	$2.05 \cdot 10^{-3}$	0.236	$-1.40 \cdot 10^{-3}$	$2.04 \cdot 10^{-3}$	0.494
AMED	**0.54**	**0.15**	**<0.001**	0.19	0.15	0.207	**0.30**	**0.14**	**0.032**	$7.28 \cdot 10^{-2}$	0.14	0.591
AMED * Time	$1.02 \cdot 10^{-2}$	$1.36 \cdot 10^{-2}$	0.456	$1.01 \cdot 10^{-2}$	$1.38 \cdot 10^{-2}$	0.464	$-1.37 \cdot 10^{-2}$	$1.30 \cdot 10^{-2}$	0.291	$-7.86 \cdot 10^{-3}$	$1.29 \cdot 10^{-2}$	0.542

Stratified Analysis by Smoking Status (Never vs. Ever) Among Men in Health ABC (Appendix 7)

Appendix 7 Table –Association of Dietary Pattern with FEV_1 (mL/year), FVC (mL/year), and FEV_1/FVC (FEV_1%), Stratified by Smoking Status (Never vs. Ever) Among Men in Health ABC

	Never-Smoking Males						Ever-Smoking Males					
	Minimally-Adjusted Model			Multivariate Model			Minimally-Adjusted Model			Multivariate Model		
	ß	SE	P-value	ß	SE	P-value	ß	SE	P-value	ß	SE	P-value
FEV_1												
Health ABC (n = 337 | n = 337; n = 797 | n = 781)												
HEI-2015	3.61	2.42	0.136	3.48	2.41	0.149	**4.53**	**1.66**	**0.006**	2.28	1.65	0.166
HEI-2015 * Time	-0.37	0.19	0.056	-0.37	0.19	0.056	-0.14	0.12	0.247	-0.17	0.12	0.167
AMED	15.28	15.97	0.339	13.26	15.99	0.407	15.37	11.24	0.172	-2.40	11.16	0.830
AMED * Time	-0.59	1.26	0.640	-0.59	1.26	0.638	-0.86	0.79	0.275	-1.10	0.79	0.168
FVC												
Health ABC (n = 302 | n = 302; n = 731 | n = 716)												
HEI-2015	2.65	2.92	0.365	2.55	2.92	0.383	2.09	1.77	0.237	1.03	1.80	0.568
HEI-2015 * Time	-0.22	0.26	0.403	-0.21	0.26	0.406	**-0.44**	**0.17**	**0.009**	**-0.48**	**0.17**	**0.006**
AMED	6.50	19.32	0.737	4.65	19.35	0.810	3.14	11.94	0.792	-5.74	12.16	0.637
AMED * Time	-0.71	1.67	0.669	-0.71	1.67	0.672	**-2.53**	**1.11**	**0.023**	**-2.85**	**1.13**	**0.011**

Stratified Analysis by Diet Quality (Healthy vs. Unhealthy) (Appendix 8)

Appendix 8 Table –Association of Dietary Pattern with FEV_1 (mL/year), FVC (mL/year), and FEV_1/FVC (FEV_1%), Stratified by Diet Quality ("Healthy" vs. "Unhealthy"*)

	Healthy Diet						Unhealthy Diet					
	Minimally-Adjusted Model			Multivariate Model			Minimally-Adjusted Model			Multivariate Model		
	ß	SE	P-value	ß	SE	P-value	ß	SE	P-value	ß	SE	P-value
FEV_1												
Health ABC (n = 1,153 | n = 1,137; n = 1,114 | n = 1,098)												
HEI-2015	-2.04	2.24	0.364	-2.63	2.23	0.240	**4.81**	**1.92**	**0.012**	2.44	1.84	0.186
HEI-2015 * Time	**0.37**	**0.15**	**0.017**	**0.38**	**0.15**	**0.014**	-0.11	0.14	0.412	$-7.09 \cdot 10^{-2}$	0.14	0.611
AMED	-3.79	17.26	0.826	-15.41	16.89	0.362	**44.20**	**12.19**	**<0.001**	**30.20**	**11.96**	**0.012**
AMED * Time	1.87	1.12	0.097	1.64	1.13	0.147	0.50	0.88	0.572	0.64	0.88	0.472
RAS (n = 1,333 | n = 1,290; n = 1,365 | n = 1,311)												
HEI-2015	**8.04**	**2.86**	**.005**	2.93	2.75	0.287	**6.62**	**2.32**	**<0.001**	**4.62**	**2.26**	**0.041**
HEI-2015 * Time	-0.25	0.38	0.511	-0.15	0.38	0.683	-0.16	0.31	0.602	$-7.86 \cdot 10^{-2}$	0.31	0.803
AMED	18.61	15.65	0.235	6.10	15.04	0.685	9.10	13.55	0.502	-9.92	13.06	0.448
AMED * Time	**4.96**	**2.15**	**0.021**	**4.62**	**2.15**	**0.031**	1.08	1.82	0.552	1.37	1.83	0.455
FVC												
Health ABC (n = 1,026 | n = 1,011; n = 977 | n = 963)												
HEI-2015	-2.83	2.55	0.27	-3.00	2.57	0.242	2.66	2.06	0.198	1.30	2.06	0.528
HEI-2015 * Time	**0.45**	**0.22**	**0.038**	**0.48**	**0.22**	**0.027**	-0.13	0.19	0.488	-0.12	0.19	0.548
AMED	2.68	19.32	0.890	-4.32	19.25	0.823	24.19	13.28	0.069	16.96	13.42	0.207
AMED * Time	2.14	1.57	0.172	1.92	1.58	0.224	1.19	1.24	0.336	1.09	1.25	0.381
RAS (n = 1,294 | n = 1,244; n = 1,299 | n = 1,250)												
HEI-2015	**8.58**	**3.42**	**0.012**	2.79	3.31	0.400	**8.91**	**2.72**	**0.001**	**5.88**	**2.74**	**0.032**
HEI-2015 * Time	-0.29	0.70	0.682	0.17	0.65	0.789	-0.86	0.56	0.125	-0.86	0.57	0.130
AMED	18.00	18.71	0.336	-4.05	18.19	0.824	8.76	15.88	0.581	-11.05	15.80	0.484
AMED * Time	4.62	3.89	0.236	6.56	3.59	0.068	-0.61	3.27	0.851	-0.60	3.29	0.855
FEV_1/FVC												
Health ABC (n = 1,026 | n = 1,011; n = 977 | n = 963)												
HEI-2015	$4.45 \cdot 10^{-4}$	$4.10 \cdot 10^{-2}$	0.991	$-1.37 \cdot 10^{-2}$	$4.07 \cdot 10^{-2}$	0.736	**$9.43 \cdot 10^{-2}$**	**$3.48 \cdot 10^{-2}$**	**0.007**	$3.89 \cdot 10^{-2}$	$3.24 \cdot 10^{-2}$	0.230
HEI-2015 * Time	$-1.67 \cdot 10^{-3}$	$3.64 \cdot 10^{-3}$	0.646	$-1.90 \cdot 10^{-3}$	$3.67 \cdot 10^{-3}$	0.605	$-1.80 \cdot 10^{-4}$	$3.34 \cdot 10^{-3}$	0.958	$1.04 \cdot 10^{-3}$	$3.32 \cdot 10^{-3}$	0.755
AMED	$-4.46 \cdot 10^{-2}$	0.30	0.882	-0.26	0.29	0.378	**1.05**	**0.23**	**<0.001**	**0.70**	**0.22**	**0.001**
AMED * Time	$-3.05 \cdot 10^{-2}$	$2.63 \cdot 10^{-2}$	0.246	$-3.25 \cdot 10^{-2}$	$2.65 \cdot 10^{-2}$	0.219	$-3.51 \cdot 10^{-3}$	$2.15 \cdot 10^{-2}$	0.900	$6.09 \cdot 10^{-3}$	$2.14 \cdot 10^{-2}$	0.776

RAS (n = 1,294 | n = 1,244; n = 1,299 | n = 1,250)

HEI-2015	**$8.40 \cdot 10^{-2}$**	**$4.10 \cdot 10^{-2}$**	**0.041**	$3.59 \cdot 10^{-2}$	$3.81 \cdot 10^{-2}$	0.346	**$7.26 \cdot 10^{-2}$**	**$3.60 \cdot 10^{-2}$**	**0.044**	$3.57 \cdot 10^{-2}$	$3.38 \cdot 10^{-2}$	0.291
HEI-2015 * Time	**$-2.28 \cdot 10^{-2}$**	**$9.50 \cdot 10^{-3}$**	**0.016**	**$-2.55 \cdot 10^{-2}$**	**$9.28 \cdot 10^{-3}$**	**0.006**	$1.23 \cdot 10^{-2}$	$8.20 \cdot 10^{-3}$	0.132	$1.34 \cdot 10^{-2}$	$8.24 \cdot 10^{-3}$	0.104
AMED	$7.84 \cdot 10^{-2}$	0.23	0.730	0.15	0.21	0.478	$-4.57 \cdot 10^{-3}$	0.21	0.982	$-7.99 \cdot 10^{-2}$	0.19	0.678
AMED * Time	$2.80 \cdot 10^{-3}$	$5.36 \cdot 10^{-2}$	0.959	$3.59 \cdot 10^{-3}$	$5.29 \cdot 10^{-2}$	0.946	**$9.34 \cdot 10^{-2}$**	**$4.66 \cdot 10^{-2}$**	**0.045**	**0.10**	**$4.68 \cdot 10^{-2}$**	**0.031**

*A participant was categorized as having either a healthy or unhealthy diet quality if their HEI-2015 or AMED score was in the upper 2 or lower 2 quartiles within the cohort, respectively.

Full Report of Estimates of the Association of Dietary Pattern with Lung Function (Appendix 9)

Appendix 9 Table –Full Report of the Estimates of the Association of Dietary Pattern with FEV_1 (mL/year), FVC (mL/year), and FEV_1/FVC (FEV_1%) for both cohorts (HEI-2015 Only)

	FEV_1						FVC						FEV_1/FVC					
	Minimally-Adjusted Model			Multivariate Model			Minimally-Adjusted Model			Multivariate Model			Minimally-Adjusted Model			Multivariate Model		
Covariates	ß	SE	P-value	ß	SE	P-value	ß	SE	P-value	ß	SE	P-value	ß	SE	P-value	ß	SE	P-value
Health ABC																		
Intercept	137.58	346.00	0.691	306.60	341.29	0.369	-543.76	382.89	0.156	-546.64	386.93	0.159	82.15	6.31	<0.001	89.75	6.09	<0.001
Time	-40.82	4.24	<0.001	-41.26	4.25	<0.001	-27.10	5.93	<0.001	-26.87	5.96	<0.001	-0.54	0.10	<0.001	-0.58	0.10	<0.001
Age (Baseline)	-20.34	3.21	<0.001	-22.06	3.11	<0.001	-25.81	3.47	<0.001	-26.28	3.46	<0.001	$-3.14 \cdot 10^{-2}$	$5.71 \cdot 10^{-2}$	0.583	$-9.10 \cdot 10^{-2}$	$5.41 \cdot 10^{-2}$	0.093
Height	21.69	1.28	<0.001	22.52	1.28	<0.001	33.91	1.45	<0.001	34.66	1.48	<0.001	$-6.50 \cdot 10^{-2}$	$2.40 \cdot 10^{-2}$	0.007	$-5.59 \cdot 10^{-2}$	$2.34 \cdot 10^{-2}$	0.015
Height-Squared	0.28	$6.24 \cdot 10^{-2}$	<0.001	0.25	$6.22 \cdot 10^{-2}$	<0.001	0.25	$7.50 \cdot 10^{-2}$	0.001	0.22	$7.58 \cdot 10^{-2}$	0.004	$-1.63 \cdot 10^{-3}$	$1.25 \cdot 10^{-3}$	0.193	$1.81 \cdot 10^{-3}$	$1.22 \cdot 10^{-3}$	0.137
White	0	-	-	0	-	-	0	-	-	0	-	-	0	-	-	0	-	-
Black	-250.80	18.92	<0.001	-256.05	18.65	<0.001	-366.90	20.46	<0.001	-374.18	20.72	<0.001	0.83	0.34	0.013	0.84	0.32	0.009
Male	0	-	-	0	-	-	0	-	-	0	-	-	0	-	-	0	-	-
Female	-379.81	25.73	<0.001	-409.68	25.68	<0.001	-549.43	28.39	<0.001	-561.65	29.01	<0.001	1.42	0.47	0.003	0.499	0.456	0.274
Memphis	-	-	-	0	-	-	-	-	-	0	-	-	-	-	-	0	-	-
Pittsburgh	-	-	-	95.41	17.87	<0.001	-	-	-	77.19	19.81	<0.001	-	-	-	1.43	0.31	<0.001
Never Smoker	-	-	-	0	-	-	-	-	-	0	-	-	-	-	-	0	-	-
Former Smoker	-	-	-	-11.69	23.00	0.611	-	-	-	5.69	25.42	0.823	-	-	-	-0.97	0.40	0.015
Intermittent Smoker	-	-	-	-220.14	45.96	<0.001	-	-	-	-119.49	50.71	0.019	-	-	-	-5.50	0.79	<0.001
Persistent Smoker	-	-	-	-211.52	45.52	<0.001	-	-	-	-75.42	50.84	0.138	-	-	-	-6.20	0.80	<0.001
Packyears	-	-	-	-3.29	0.41	<0.001	-	-	-	-2.14	0.46	<0.001	-	-	-	$-6.04 \cdot 10^{-2}$	$4.15 \cdot 10^{-3}$	<0.001
HEI-2015	3.01	0.87	<0.001	1.21	0.86	0.161	1.89	0.96	0.049	0.88	0.97	0.367	$7.06 \cdot 10^{-2}$	$1.59 \cdot 10^{-2}$	<0.001	$3.10 \cdot 10^{-2}$	$1.54 \cdot 10^{-2}$	0.044
HEI-2015 * Time	$1.56 \cdot 10^{-2}$	$6.14 \cdot 10^{-2}$	0.799	$2.24 \cdot 10^{-2}$	$6.15 \cdot 10^{-2}$	0.716	$-6.38 \cdot 10^{-2}$	$8.58 \cdot 10^{-2}$	0.459	$-6.75 \cdot 10^{-2}$	$8.63 \cdot 10^{-2}$	0.434	$-2.50 \cdot 10^{-4}$	$1.47 \cdot 10^{-3}$	0.867	$2.87 \cdot 10^{-4}$	$1.47 \cdot 10^{-3}$	0.845
RAS																		
Intercept	3059.52	219.60	<0.001	2811.05	226.95	<0.001	1712.34	203.22	<0.001	1357.13	306.78	<0.001	89.37	3.91	<0.001	94.87	3.77	<0.001
Time	-39.62	9.28	<0.001	-39.36	9.28	<0.001	-38.15	17.01	0.025	-41.44	16.37	0.011	$7.00 \cdot 10^{-2}$	0.24	0.769	$5.09 \cdot 10^{-2}$	0.236	0.830
Age (Baseline)	-41.95	1.68	<0.001	-38.50	1.68	<0.001	-44.36	1.94	<0.001	-39.70	1.99	<0.001	-0.24	$2.43 \cdot 10^{-2}$	<0.001	-0.24	$2.33 \cdot 10^{-2}$	<0.001
Height	13.35	0.98	<0.001	13.68	0.97	<0.001	28.37	1.43	<0.001	27.66	1.41	<0.001	$-2.39 \cdot 10^{-2}$	$1.86 \cdot 10^{-2}$	0.199	$-2.67 \cdot 10^{-2}$	$1.76 \cdot 10^{-2}$	0.130
Height-Squared	0.16	$1.67 \cdot 10^{-2}$	<0.001	0.17	$1.69 \cdot 10^{-2}$	<0.001	0.34	$2.66 \cdot 10^{-2}$	<0.001	0.35	$2.64 \cdot 10^{-2}$	<0.001	$-4.00 \cdot 10^{-4}$	$4.00 \cdot 10^{-4}$	0.324	$-4.00 \cdot 10^{-4}$	$4.00 \cdot 10^{-4}$	0.297
White	0	-	-	330.67	55.39	<0.001	0	-	-	378.84	65.51	<0.001	0	-	-	0.54	0.77	0.485
Black	-555.22	25.89	<0.001	-55.61	63.68	0.383	-617.63	29.91	<0.001	-174.42	75.57	0.021	-2.68	0.37	<0.001	0.74	0.89	0.405
Hispanic (Non-Black)	-186.52	62.13	0.003	155.44	81.05	0.055	-301.86	73.96	<0.001	93.35	95.70	0.330	2.42	0.93	0.009	2.26	1.12	0.044
Hispanic (Black)	-359.29	150.98	0.017	240.84	209.79	0.251	-573.79	192.08	0.003	6.70	283.28	0.981	5.41	2.41	0.025	7.29	3.37	0.031
Other	-299.14	56.94	<0.001	0	-	-	-354.98	65.74	<0.001	0	-	-	-0.012	0.82	0.880	0	-	-
Never Smoker	-	-	-	0	-	-	-	-	-	0	-	-	-	-	-	0	-	-
Former Smoker	-	-	-	15.77	25.95	0.544	-	-	-	47.24	30.68	0.124	-	-	-	-0.34	0.36	0.346
Intermittent Smoker	-	-	-	-78.02	46.05	0.090	-	-	-	15.31	54.34	0.778	-	-	-	-2.32	0.63	<0.001
Persistent Smoker	-	-	-	-179.51	42.26	<0.001	-	-	-	-6.78	49.90	0.892	-	-	-	-4.28	0.58	<0.001
Packyears	-	-	-	-5.67	0.56	<0.001	-	-	-	-4.42	0.67	<0.001	-	-	-	$-6.61 \cdot 10^{-2}$	$7.80 \cdot 10^{-3}$	<0.001
HEI-2015	6.20	1.06	<0.001	2.11	1.05	0.045	1.89	0.96	0.049	2.19	1.27	0.084	$7.06 \cdot 10^{-2}$	$1.59 \cdot 10^{-2}$	<0.001	0.019	0.015	0.223
HEI-2015 * Time	$1.92 \cdot 10^{-2}$	0.14	0.892	$1.40 \cdot 10^{-2}$	0.14	0.921	$-6.36 \cdot 10^{-2}$	$8.58 \cdot 10^{-2}$	0.459	$3.09 \cdot 10^{-2}$	0.25	0.901	$-2.5 \cdot 10^{-4}$	$1.47 \cdot 10^{-3}$	0.885	$-3.90 \cdot 10^{-3}$	$3.60 \cdot 10^{-3}$	0.272