

Title: The Relationship between Dietary Fiber Intake and Lung Function in NHANES

Authors:

Corrine Hanson, PhD, RD
University of Nebraska Medical Center, School of Allied Health Professions
Medical Nutrition Education
984045 Nebraska Medical Center, Omaha, NE 68198-4045
ckhanson@unmc.edu

Elizabeth Lyden, MS
University of Nebraska Medical Center, College of Public Health
984375 Nebraska Medical Center, Omaha, NE 68198-4375
elyden@unmc.edu

Stephen Rennard, MD
Department of Internal Medicine, Division of Pulmonary, Critical Care, Sleep and Allergy
University of Nebraska Medical Center
srennard@unmc.edu

David M. Mannino, M.D.
University of Kentucky College of Public Health
111 Washington Avenue Suite 220
Lexington, KY 40536
dmannino@uky.edu

Erica P.A. Rutten, PhD
Program Development Centre, Centre of Expertise for Chronic Organ Failure (CRIO+)
Horn, The Netherlands
ericarutten@ciro-horn.nl

Raewyn Hopkins
Department of Respiratory Services, Auckland City Hospital
Auckland, New Zealand
rhopkins@adhb.govt.nz

Robert Young BMedSc, MBChB, DPhil (Oxon), FRCP, FRACP
Department of Medicine, University of Auckland
Auckland, New Zealand
roberty@adhb.govt.nz

Corresponding author and request for reprints:

Corrine Hanson, PhD, RD

University of Nebraska Medical Center, School of Allied Health Professions
Medical Nutrition Education
984045 Nebraska Medical Center, Omaha, NE 68198-4045
ckhanson@unmc.edu

Sources of Support: None

Authors' contribution to manuscript: RY, CH, SR, RH, ER, DM and EL designed the research, CH, RY, and EL conducted the research, EL performed statistical analysis, CH, RY, RH, SR, DM, ER wrote the paper, and all authors read and approved the final manuscript.

Author Disclaimers: Conflict of Interest disclosure: CH, EL, DM, ER, RH, RY have nothing to disclose. SR has received reimbursement for attending a symposium, speaking and/or consulting from: ABIM, Able Associates, Advantage Healthcare, Align2Action, Almirall, APT, ATS, AstraZeneca, Baxter, Boehringer-Ingelheim, Chiesi, CIPLA, ClearView Healthcare, Cleveland Clinic, CME Incite, Complete Medical Group, COPDFoundation, Cory Paeth, CSA, CSL, CTS Carmel, Dailchi Sankyo, Decision Resources, Dunn Group, Easton Associates, Elevation Pharma, FirstWord, Forest, Frankel Group, Gerson, GlaxoSmithKline, Gilead, Grifols, GroupH, Guidepoint Global, Haymarket, HealthStar, Huron Consulting, Incite, Inthought, IntraMed (Forest), Johnson & Johnson, LEK, McKinsey, Medical Knowledge, Mediummune, Methodist Health System, Dallas, Navigant, NCI Consulting, Novartis Nuvis, Pearl, Penn Technology, Pfizer, PlanningShop, Prescott, Pro Ed Comm, ProiMed, PSL FirstWord, Pulmatrix, Quadrant, Qwessential, Regeneron, Saatchi and Saatchi, Schlesinger Associates, Strategic North, Synapse, Takeda, Theron, WebMD

Running Head: Fiber and Lung Function in NHANES

Descriptor: 6.3 Diet, Obesity, and Lung Disease

Keywords: Diet, airflow limitation, spirometry grade-undefined (SGU)

Word Count: 2,920

Abstract

Purpose: Extensive research supports a protective effects of a high fiber diet in certain disease states; however, little is known about its relationship to lung health. The National Health and Nutrition Examination Surveys (NHANES) contain spirometry measures and dietary intake information, allowing us to assess this relationship.

Methods: Participants included 1,921 adults who had spirometry measurements and fiber intake available. The primary outcomes were lung function measurements, including FEV₁, FVC, and percent predicted FEV₁ and FVC. We also conducted acategorical analysis of fiber intake and airflow restriction and obstruction based on GOLD and Spirometry Grade (SG) classifications. Multivariable regression models were used to look at the association of lung function measurements with dietary fiber intake after adjustment for relevant confounders. All analyses accounted for the weighted data and complex design of the NHANES sample.

Results: Subjects in the highest quartile intake of fiber had mean FEV₁ and FVC measurements that were 82 mL and 129 mL higher that the lowest quartile of intake ($p=0.05$ and 0.01 , respectively), and mean percent predicted FEV₁ and FVC values that were 2.4 and 2.8 percentage points higher ($p=0.07$ and 0.02 , respectively). In the categorical analysis, higher fiber intake was associated with a higher percentage of of those with normal lung function ($p=0.001$) and a significant decline in the proportion of participants with airflow restriction ($p=0.001$).

Conclusion: Low fiber intake was associated with reduced measures of lung function. A diet rich in fiber-containing foods may play a role in improving lung health.

Keywords: Diet, fiber, lung function, restrictive lung disease, obstructive lung disease

Introduction Lung diseases are a major public health problem, with chronic obstructive pulmonary disease (COPD) now the third leading cause of death in the world [1]. Lung function is a predictor of mortality in the general population as well as in patients with lung disease [2], making maintaining lung function an important goal in the prevention of COPD and a major public health objective [3]. Despite this, few preventative interventions other than smoking cessation have been identified. While smoking remains an important risk factor, it has become clear that other factors contribute to the risk of lung disease, and evidence has revealed that diet may be an important consideration in lung health [4-17].

There is extensive research supporting the protective effects of a high fiber diet in certain disease states, including heart disease and cancer [18-20]. However, little is known about fiber and its relationship to lung health. Dietary fiber has been shown to exhibit both anti-inflammatory and anti-oxidant properties [18,21-26] which have been implicated in both the development and progression of lung disease [27-29].

The National Health and Nutrition Examination Surveys (NHANES) include spirometry measures and dietary intake information, allowing us to test the hypothesis that lower fiber intake will be associated with reduced lung function in a sample of United States adults. Therefore, the purpose of this study was to examine if intake of dietary fiber is associated with measures of lung function and presence of airflow restriction or obstruction in a United States adult population, and possible mediators of this relationship, including systemic inflammation reflected in differences in C-reactive protein (CRP) measurements. Some of the results of this study have been previously reported in the form of an abstract [30].

Methods

Subjects This analysis includes adults 40 to 79 years of age in the NHANES cycle 2009-2010 who had pre-bronchodilator spirometry measurements available. Subjects with self-reported

energy intake outside a plausible range (women: <600 or >6,000 kcal/day; men: <800 or >8,000 kcal/day) were excluded. Detailed methods and protocols for the NHANES study have been previously reported, including informed consent procedures for all participants [31]. As the data used in our study is freely available in the public domain, the study was exempt from human subjects review.

Lung Function Outcomes Pre-bronchodilator spirometry was offered to participants aged 6-79 years in NHANES 2007-2010. Protocols for these measurements have been summarized elsewhere [32-25]. Only spirometry measurements conforming to the American Thoracic Society standards were used in this analysis. Lung function was also expressed as a percent of predicted using the spirometric reference values from the third NHANES [35].

Respiratory Phenotype Determination: The Global Initiative for Chronic Obstructive Lung Disease (GOLD) classification of COPD was used to establish the presence and severity of airflow obstruction according to GOLD groups [36]. Alternate classification methods for COPD have also been proposed, including the COPD Foundation Spirometry Grade (SG) classification where those with no airflow obstruction are sub-classified according to normal lung function and those with submaximal spirometry ($FEV_1/FVC \geq 0.70$, $FEV_1 < 80\%$ predicted) [37]. Our analysis therefore included three comparator groups: 1). a group with normal spirometry ($FEV_1/FVC \geq 0.70$, $FEV_1 \geq 80\%$ predicted); 2). a group who met the criteria for classification for a “restrictive” spirometric pattern; ($FEV_1/FVC \geq 0.70$, $FEV_1 < 80\%$ predicted); and 3). those with airflow obstruction ($FEV_1/FVC < 0.70$) where severity was defined according to $FEV_1\%$ predicted into SG 1-3 or GOLD 1-4. The definitions and distributions of these classifications are presented in Table 1.

Dietary Assessment Dietary intake in the NHANES survey was determined from 2 interviewer administered 24 hour recalls, developed and validated by the U.S. Department of Agriculture.

Participants' dietary intake of total fiber in grams per day was calculated [16,38]. The use of fiber supplements was not included because of limited information.

Other Covariates To assess smoking status, survey participants were asked about current and past tobacco use. Smoking status was defined as: never, former (smoked >100 cigarettes in lifetime but does not currently smoke), and current (smoked >100 cigarettes in lifetime and smokes currently). Subject height and weight were measured during the clinical examination and were used to calculate body mass index (BMI). BMI categories were created based on the World Health Organization BMI classifications [39] and participants were categorized as follows: underweight: <18.5, normal range: 18.5-24.9, overweight: 25-30, and obese: >30. The ratio of family income to poverty levels variable was used to adjust for socioeconomic status. C-reactive protein (CRP) concentrations were included in the analysis as a biomarker of inflammation.

Statistical Analysis Mean and standard errors were used for descriptive statistics. To incorporate the complex, multistage sampling design of the NHANES in the statistical analysis, the SAS procedures SURVEYFREQ, SURVEYMEANS, SURVEYREG, and SURVEYLOGISTIC were used. Univariate and multivariable regression models were used to look at the association of lung function measurements and respiratory phenotypes with quartiles of dietary fiber intake. The multivariable regression models were adjusted for the possible confounders of height, age, gender, BMI, smoking, socioeconomic status, CRP, and energy intake. On the basis of other literature, we also adjusted for the following factors: intakes of vitamin E, alpha-carotene, beta-carotene, beta-cryptoxanthin, lycopene, lutein + zeaxanthin, vitamin C, and cured meat [28,29,40]. Odds ratios and 95% confidence intervals were determined using PROC SURVEYFREQ.

As smoking remains the most important cause of respiratory disease, we analyzed the interaction between fiber intake and smoking status. A similar analysis was performed for BMI

based on the BMI categories described above. In addition, recent literature has indicated that diet may affect lung function differently based on gender [16], therefore a test for interaction between fiber intake and gender was conducted and analysis was stratified based on gender for variables with a positive interaction signal. All analyses accounted for the weighted data and complex design of the NHANES sample. A p -value < 0.05 was considered statistically significant.

Results The final number of eligible participants was 1,921. Overall, the cohort was 50.2% male and 49.8% female. The mean age of the participants was 52.8 years with a mean BMI of 29.2. Participants with a higher fiber intake tended to have a lower BMI, a higher intake of fruits, vegetables, and whole grains, lower CRP, and higher energy intake than those with lower fiber intakes. Lower intake of fiber was also associated with smoking. The demographic characteristics of the sample by quartile of fiber intake are given in Table 2.

There was a statistically significant relationship between lung function measurements and dietary fiber intake in both univariate models (data not shown) and multivariable models (Table 3). After adjusting for confounders (age, height, BMI, gender, energy intake, smoking status, socioeconomic status, CRP, height and intake of other vitamins), participants in the highest quartile intake of fiber intake (>17.5 gms/day) had mean FEV₁ and FVC measurements that were 82 mL and 129 mL higher than the lowest quartile of intake (<10.5 gms/day) ($p=0.05$ and 0.01 , respectively). Mean percent predicted FEV₁ and FVC values were 2.4 and 2.8 percentage points higher (respectively) in participants with the highest quartile intake when compared to participants in the lowest fiber intake quartile ($p=0.07$ and 0.01 , respectively). In contrast to the other lung function parameters, where we found no gender effect with daily fiber intake, for FVC an effect was found ($p=0.003$ for males but not females ($p=0.84$)). There was no association between fiber intake and FEV₁/FVC ratio.

To determine if associations differed by source of fiber, additional analysis was conducted for servings/day of fruits/vegetables/legumes (cups/day) and daily whole grain intake (ounce equivalents/day). Significant associations were present for intake of fruit/vegetables/legume (Table 3), with participants who were in the highest quartile for daily fruit/vegetable/legume intake having mean FEV₁ and FVC 107 mL and 127 mL higher, respectively, than those in the lowest quartile (p=0.001, p=0.006), and mean percent predicted FEV₁ and FVC values that were 3.3% and 2.8% higher than participants in the lowest quartile intake (p=0.0009 and 0.007, respectively). There was no association between lung function measurements and daily whole grain intake (data not shown).

To investigate whether smoking status modified the associations of fiber with lung function, each of the lung function outcomes were evaluated with fiber intake, smoking classification, and the interaction between smoking and fiber intake. There was no significant interaction between smoking and fiber for any of the outcomes (interaction terms p>0.10). Similar results were found for BMI, with no statistically significant interactions found between BMI and fiber intake related to any of the lung function outcomes.

There was evidence of relationship between fiber intake, normal lung function and airflow restriction. With increasing daily fiber intake, the percentage of those with normal lung function increased (50.1% vs. 68.3% for Q1 vs. Q4, p=0.001) although the effect was attenuated at quartiles 3 and 4 (Figure 1). For increasing daily fiber intake, there was a significant decline in the proportion of participants with airflow restriction (29.8% vs. 14.8% for Q1 vs. Q4, p=0.001) which again was attenuated at the higher quartiles (Figure 2). There was no relationship between daily fiber intake and severity of airflow obstruction (data not shown).

Discussion

In this analysis of the population-based NHANES study, we found that low fiber intake was associated with lower lung function. These associations were consistent across sub-categories of smoking and BMI. Of note, the beneficial association of high dietary fiber intake was independent of antioxidant intake, intake of cured meat, and other possible dietary risks associated with lung function decline. While we found no effect of dietary fiber on the prevalence of airflow obstruction (SG-1-3 or GOLD 1-4) we did find a greater prevalence of airflow restriction group in those with lowest dietary fiber intake ($p=0.0001$). We believe the failure to identify an association with spirometric-defined airflow obstruction may be the consequence of the low smoking exposure in this group and the overall low prevalence of COPD. Our results are consistent with other cross-sectional studies showing there is a strong fiber-smoking interaction on FEV₁ that is considerably weaker when never smokers are analyzed [9]. Our results build upon similar associations in earlier studies, including an analysis of the Atherosclerosis Risk in Communities (ARIC) study that found participants in the highest quintile of fiber intake had higher lung function measurements than those in the lowest quintile [28]. Varraso and Hirayama have both reported significant, independent associations between total fiber intake and risk of COPD [29,41]. Other studies have demonstrated that higher fiber intakes are associated with 40-50% reduction in respiratory related deaths, compared to 25-30% reductions for cardiovascular disease [42,43]. Taken together, these findings suggest dietary fiber has considerable relevance to lung health, notably impaired lung function and reduced respiratory mortality.

Intake of fruits, vegetables and legumes were associated with lung function in our study independent of intake of antioxidants previously associated with lung function [44]. Several studies have found stronger associations with intakes of whole fruit when compared to individual fruit-related nutrients [6,11,45,46] such as vitamin C, suggesting that other compounds, or the interaction of these compounds, may be more relevant. Dietary fiber has been one of the

compounds speculated to contribute to the positive effect of fruits and vegetables on preserving lung function [9]. Indeed adjustment for fiber has eliminated univariate associations between fruit intake and FEV₁ [47]. Interestingly, our results did not show an association between intakes of whole grain foods and lung function, however whole grain intake may be poorly estimated in only 2 days of diet recalls. The lack of this relationship in our study conflicts with previous studies of fiber intake and COPD which stratified by fiber source and found the effects were due mainly to cereal fibers [29]. The relationship between healthy diet and better lung health in relation to COPD was reported by Varraso and colleagues using a “Healthy Eating Index” [16]. Current evidence is not conclusive about which fiber containing foods are most beneficial for COPD. Fiber occurs in both soluble and insoluble forms, and studies attempting to stratify by fiber type have faced the challenge that foods usually contain a mix of both soluble and insoluble fibers, making it difficult to determine if one type is more accountable.

There are several plausible mechanisms through which intake of fiber may impact lung function and predispose to airflow restriction, and risk of COPD. Systemic inflammation is considered an important sub-phenotype of COPD [48,49], and there are a growing number of studies that show CRP is a marker of systemic inflammation, activation of the innate immune system and a possible effector molecule in vascular disease [50-52]. Higher intakes of dietary fiber have been associated with reduced systemic inflammation and CRP levels [53], and CRP levels have been shown to have an inverse relationship with lung function and respiratory morbidity [50,54-60]. Consistent with other studies we did find that a higher fiber intake was associated with lower CRP (Table 2) [61].

Attenuation of systemic inflammation may be only one of the mechanisms through which fiber impacts lung function. Dietary fiber has been shown to change the composition of the gut microbiome, in particular altering the ratio of Firmicutes to Bacteroidetes [61], consequently increasing the concentrations of short-chain fatty acids (SCFA). These by-products of fiber

fermentation in the gastrointestinal tract are found in the systemic circulation and have several relevant protective functions with regard to lung function and COPD, including regulation of neutrophils [62], and attenuating pulmonary inflammation and epithelial-based protection against bacterial infection [63].

Our finding showing a trend toward a greater prevalence of those classified as airflow restriction with low dietary fiber intake is novel. This airflow restrictive subgroup, which constituted 22.6% of our older NHANES sample, includes those with a normal FEV₁/FVC ratio but proportionately reduced FVC and FEV₁. This group has also been called PRISm, for Preserved Ratio Impaired Spirometry, and has a reported prevalence of 5-18% in other studies (12% in COPDGene) [64,65]. This group is highly heterogeneous as much as three sub-phenotypes defined in COPDGene as “restrictive”, “early COPD” and “metabolic” [66]. Recent evidence shows that many of the people in this subgroup have systemic inflammation, poor exercise capacity and emphysema on computed tomography scanning, with or without airway inflammation [64]. This group remains poorly characterized and invariably excluded from studies of COPD. It is possible this group represents a separate and unique pulmonary phenotype which is, according to this study, significantly over-represented in those with low dietary fiber intake. To our knowledge, this is the first study to examine the association between dietary fiber intake and lung function with regards to this otherwise poorly understood subgroup. As this subgroup has a high prevalence of co-morbid conditions, and is highly symptomatic despite not meeting traditional COPD criteria, they may represent a group that might benefit from targeted dietary interventions to improve overall outcomes. However, it is also possible that evidence of this relationship given was driven by residual confounding from obesity that was not well captured by BMI. BMI is an imprecise measure of obesity and may not fully account for factors such as distribution of fat mass. As truncal adiposity has been associated with lung function, it is possible this may explain some of the the association between diet and a restrictive airflow pattern [66-68].

Our study has several limitations. First, the NHANES data we analyzed is cross-sectional so we cannot evaluate any temporal relationships, such as dietary fiber effects on lung function decline, nor can we establish causality. It could be proposed that fiber is a surrogate measure for an overall healthy lifestyle. Indeed, the recent study by Varraso and colleagues serves to stress the importance of the overall diet quality in pulmonary health [16]. Studies have also shown that increased intake of catechins and flavonoids are positively associated with FEV₁[69]. Improving the overall quality of the diet may drive an individual's intake towards a more plant-based diet, which would also be a diet rich in other beneficial nutrients such as phytochemicals, antioxidants, flavonoids, or ligands. These nutrients may work in a synergistic fashion and are much less likely to be accurately captured in current dietary studies where recall over relatively short time periods are traditionally used to assess long-term intake. As lung function reflects both maximal lung function attained in early adulthood and lung function lost with aging [70], it is surprising we find an association at all between dietary fiber intake and contemporaneous lung function measurements. Second, serum levels of nutritional antioxidants have been associated with lung function [71,72], and other studies of dietary fiber intake and lung function have adjusted for this [73]. Serum levels of anti-oxidant nutrients were not available for this NHANES cycle; however, we did include adjustment for intakes of these nutrients in our models. Adjustment for physical activity, which is relevant to dietary choices, was not adjusted for in this analysis and remains a potential source of confounding. Third, this study used pre-bronchodilator measurements for lung function rather than post-bronchodilator values so it is harder to extrapolate our findings on dietary fiber intake and lung function in this study to COPD. In this study we have used the fixed ratio (FEV₁/FVC) to define the presence of airflow limitation, consistent with other dietary studies, and found comparable results using the lower limit of normal. Our study does have a major strength in our ability to use spirometry measurements for identifying the presence of airflow limitation and accurately distinguish those

with sub-normal lung function, as opposed to the self-reported diagnosis of COPD used in many epidemiological studies.

Conclusions Low dietary fiber intake was associated with reduced measures of lung function, an increased prevalence of participants with airway restriction. A diet rich in fiber-containing foods may play a role in improving lung health.

Conflict of Interest disclosure: CH, EL, DM, ER, RH, RY have nothing to disclose. SR has received reimbursement for attending a symposium, speaking and/or consulting from: ABIM, Able Associates, Advantage Healthcare, Align2Action, Almirall, APT, ATS, AstraZeneca, Baxter, Boehringer-Ingelheim, Chiesi, CIPLA, ClearView Healthcare, Cleveland Clinic, CME Incite, Complete Medical Group, COPDFoundation, Cory Paeth, CSA, CSL, CTS Carmel, Dailchi Sankyo, Decision Resources, Dunn Group, Easton Associates, Elevation Pharma, FirstWord, Forest, Frankel Group, Gerson, GlaxoSmithKline, Gilead, Grifols, GroupH, Guidepoint Global, Haymarket, HealthStar, Huron Consulting, Incite, Inthought, IntraMed (Forest), Johnson & Johnson, LEK, McKinsey, Medical Knowledge, Mediummune, Methodist Health System, Dallas, Navigant, NCI Consulting, Novartis Nuvis, Pearl, Penn Technology, Pfizer, PlanningShop, Prescott, Pro Ed Comm, ProMed, PSL FirstWord, Pulmatrix, Quadrant, Qwessential, Regeneron, Saatchi and Saatchi, Schlesinger Associates, Strategic North, Synapse, Takeda, Theron, WebMD

Literature Cited

1. **The top 10 causes of death.** World Health Organization Web site.
<http://www.who.int/mediacentre/factsheets/fs310/en/>. Updated 2014. Accessed 3/25, 2015.
2. Young RP, Hopkins R, Eaton TE. Forced expiratory volume in one second: Not just a lung function test but a marker of premature death from all causes. *Eur Respir J.* 2007;30(4):616-622.

3. Young RP, J Hopkins R. Primary and secondary prevention of chronic obstructive pulmonary disease: Where to next? *Am J Respir Crit Care Med.* 2014;190(7):839-840.
4. Hanson C, Sayles H, Rutten E, Wouters E, MacNee W, Calverley P, Meza J, Rennard S. The association between dietary intake and the phenotypical characteristics of COPD in the ECLIPSE cohort. *Chronic Obstructive Pulmonary Diseases: The Journal of the COPD Foundation.* 2014;1(1):115-1247.
5. Grievink L, Smit HA, Ocke MC, van 't Veer P, Kromhout D. Dietary intake of antioxidant (pro)-vitamins, respiratory symptoms and pulmonary function: The MORGEN study. *Thorax.* 1998;53(3):166-171.
6. Smit HA, Grievink L, Tabak C. Dietary influences on chronic obstructive lung disease and asthma: A review of the epidemiological evidence. *Proc Nutr Soc.* 1999;58(2):309-319.
7. Britton JR, Pavord ID, Richards KA, et al. Dietary antioxidant vitamin intake and lung function in the general population. *Am J Respir Crit Care Med.* 1995;151(5):1383-1387.
8. Hu G, Cassano PA. Antioxidant nutrients and pulmonary function: The Third National Health and Nutrition Examination survey (NHANES III). *Am J Epidemiol.* 2000;151(10):975-981.
9. Tabak C, Smit HA, Heederik D, Ocke MC, Kromhout D. Diet and chronic obstructive pulmonary disease: Independent beneficial effects of fruits, whole grains, and alcohol (the MORGEN study). *Clin Exp Allergy.* 2001;31(5):747-755.
10. Tabak C, Smit HA, Rasanen L, et al. Dietary factors and pulmonary function: A cross sectional study in middle aged men from three European countries. *Thorax.* 1999;54(11):1021-1026.

11. Tabak C, Feskens EJ, Heederik D, Kromhout D, Menotti A, Blackburn HW. Fruit and fish consumption: A possible explanation for population differences in COPD mortality (the Seven Countries Study). *Eur J Clin Nutr.* 1998;52(11):819-825.
12. McKeever TM, Lewis SA, Cassano PA, et al. Patterns of dietary intake and relation to respiratory disease, forced expiratory volume in 1 s, and decline in 5-y forced expiratory volume. *Am J Clin Nutr.* 2010;92(2):408-415.
13. McKeever TM, Scrivener S, Broadfield E, Jones Z, Britton J, Lewis SA. Prospective study of diet and decline in lung function in a general population. *Am J Respir Crit Care Med.* 2002;165(9):1299-1303.
14. Bentley AR, Kritchevsky SB, Harris TB, et al. Dietary antioxidants and forced expiratory volume in 1 s decline: The health, aging and body composition study. *Eur Respir J.* 2012;39(4):979-984.
15. Schwartz J, Weiss ST. Dietary factors and their relation to respiratory symptoms. The second National Health and Nutrition Examination Survey. *Am J Epidemiol.* 1990;132(1):67-76.
16. Varraso R, Chiuve SE, Fung TT, et al. Alternate Healthy Eating Index 2010 and risk of chronic obstructive pulmonary disease among US women and men: Prospective study. *BMJ.* 2015;350:h286.
17. Young RP, Hopkins RJ. The Hispanic paradox further unraveled? *Thorax.* 2014;69(2):184-185.
18. Ning H, Van Horn L, Shay CM, Lloyd-Jones DM. Associations of dietary fiber intake with long-term predicted cardiovascular disease risk and C-reactive protein levels (from the National Health and Nutrition Examination survey data [2005-2010]). *Am J Cardiol.* 2014;113(2):287-291.

19. Lairon D, Arnault N, Bertrais S, et al. Dietary fiber intake and risk factors for cardiovascular disease in French adults. *Am J Clin Nutr.* 2005;82(6):1185-1194.
20. Ludwig DS, Pereira MA, Kroenke CH, et al. Dietary fiber, weight gain, and cardiovascular disease risk factors in young adults. *JAMA.* 1999;282(16):1539-1546.
21. King DE, Mainous AG,3rd, Egan BM, Woolson RF, Geesey ME. Fiber and C-reactive protein in diabetes, hypertension, and obesity. *Diabetes Care.* 2005;28(6):1487-1489.
22. Galisteo M, Duarte J, Zarzuelo A. Effects of dietary fibers on disturbances clustered in the metabolic syndrome. *J Nutr Biochem.* 2008;19(2):71-84.
23. King DE, Mainous AG,3rd, Egan BM, Woolson RF, Geesey ME. Effect of psyllium fiber supplementation on C-reactive protein: The Trial to Reduce Inflammatory Markers (TRIM). *Ann Fam Med.* 2008;6(2):100-106.
24. King DE, Egan BM, Woolson RF, Mainous AG,3rd, Al-Solaiman Y, Jesri A. Effect of a high-fiber diet vs a fiber-supplemented diet on C-reactive protein level. *Arch Intern Med.* 2007;167(5):502-506.
25. Ma Y, Griffith JA, Chasan-Taber L, et al. Association between dietary fiber and serum C-reactive protein. *Am J Clin Nutr.* 2006;83(4):760-766.
26. Ma Y, Hebert JR, Li W, et al. Association between dietary fiber and markers of systemic inflammation in the Women's Health Initiative Observational Study. *Nutrition.* 2008;24(10):941-949.
27. Toraldo D, De Nuccio F, Scoditti E. Systemic inflammation in chronic obstructive pulmonary disease: May diet play a therapeutic role? *J All Ther.* 2013.

28. Kan H, Stevens J, Heiss G, Rose KM, London SJ. Dietary fiber, lung function, and chronic obstructive pulmonary disease in the Atherosclerosis Risk in Communities Study. *Am J Epidemiol.* 2008;167(5):570-578.
29. Varraso R, Willett WC, Camargo CA, Jr. Prospective study of dietary fiber and risk of chronic obstructive pulmonary disease among US women and men. *Am J Epidemiol.* 2010;171(7):776-784.
30. Hanson C, Lyden E, Hopkins R, Rennard S, Mannino D, Young R. The relationship between dietary fiber and lung function in NHANES. American Thoracic Society International Congress; 2015 May 15-20; Denver, CO AJRCC (191) 2015; abstract nr.A5405.
31. National Center for Health Statistics, National Health and Nutrition Examination Survey (NHANES). <http://www.cdc.gov/nchs/nhanes.htm>. Accessed November, 2014.
32. Centers for Disease control and Prevention. Spirometry-1st test & 2nd test bronchodilator studies. Centers for Diseases Control and Prevention website. http://www.cdc.gov/nchs/nhanes/nhanes2009-20110/SPX_F.htm. Accessed November 1, 2014.
33. Ford ES, Mannino DM, Wheaton AG, Giles WH, Presley-Cantrell L, Croft JB. Trends in the prevalence of obstructive and restrictive lung function among adults in the United States: Findings from the National Health and Nutrition Examination Surveys from 1988-1994 to 2007-2010. *Chest.* 2013;143(5):1395-1406.
34. Mannino DM, Ford ES, Redd SC. Obstructive and restrictive lung disease and markers of inflammation: Data from the third National Health and Nutrition Examination. *Am J Med.* 2003;114(9):758-762.
35. Hankinson JL, Odencrantz JR, Fedan KB. Spirometric reference values from a sample of the general U.S. population. *Am J Respir Crit Care Med.* 1999;159(1):179-187.

36. Vestbo J, Hurd SS, Agusti AG, et al. Global strategy for the diagnosis, management and prevention of chronic obstructive pulmonary disease, GOLD executive summary. *Am J Respir Crit Care Med*. 2012.
37. Rennard S, Thomashow B, Crapo J, et al. Introducing the COPD foundation guide for diagnosis and management of COPD, recommendations of the COPD foundation. *COPD*. 2013;10(3):378-389.
38. Anand J, Bodner-Montville J, Ahuja JKC, Goldman JD, Heendeniya KY, Moshfegh AJ. What we eat in america, NHANES 2007-2008: Comparing day 1 and day 2 dietary data. *FASEB J*. 2011;25.
39. World Health Organization. Obesity and overweight. Obesity and Overweight Web site. www.who.int/mediacentre. Updated March 2013. Accessed 12/6/2013, 2013.
40. Varraso R, Jiang R, Barr RG, Willett WC, Camargo CA, Jr. Prospective study of cured meats consumption and risk of chronic obstructive pulmonary disease in men. *Am J Epidemiol*. 2007;166(12):1438-1445.
41. Hirayama F, Lee AH, Binns CW, et al. Do vegetables and fruits reduce the risk of chronic obstructive pulmonary disease? A case-control study in Japan. *Prev Med*. 2009;49(2-3):184-189.
42. Chuang SC, Norat T, Murphy N, et al. Fiber intake and total and cause-specific mortality in the European Prospective Investigation into Cancer and Nutrition cohort. *Am J Clin Nutr*. 2012;96(1):164-174.
43. Park Y, Subar AF, Hollenbeck A, Schatzkin A. Dietary fiber intake and mortality in the NIH-AARP Diet and Health study. *Arch Intern Med*. 2011;171(12):1061-1068.

44. Hanson C, Rutten EP, Wouters EF, Rennard S. Diet and vitamin D as risk factors for lung impairment and COPD. *Transl Res*. 2013;162(4):219-236.
45. Walda IC, Tabak C, Smit HA, et al. Diet and 20-year chronic obstructive pulmonary disease mortality in middle-aged men from three European countries. *Eur J Clin Nutr*. 2002;56(7):638-643.
46. Romieu I, Trenga C. Diet and obstructive lung diseases. *Epidemiol Rev*. 2001;23(2):268-287.
47. Butler LM, Koh WP, Lee HP, Yu MC, London SJ. Dietary fiber and reduced cough with phlegm: A cohort study in Singapore. *Am J Respir Crit Care Med*. 2004;170(3):279-287.
48. Sinden NJ, Stockley RA. Systemic inflammation and comorbidity in COPD: A result of 'overspill' of inflammatory mediators from the lungs? Review of the evidence. *Thorax*. 2010;65(10):930-936.
49. Broekhuizen R, Wouters EF, Creutzberg EC, Schols AM. Raised CRP levels mark metabolic and functional impairment in advanced COPD. *Thorax*. 2006;61(1):17-22.
50. Gan WQ, Man SF, Senthilselvan A, Sin DD. Association between chronic obstructive pulmonary disease and systemic inflammation: A systematic review and a meta-analysis. *Thorax*. 2004;59(7):574-580.
51. Yende S, Waterer GW, Tolley EA, et al. Inflammatory markers are associated with ventilatory limitation and muscle dysfunction in obstructive lung disease in well functioning elderly subjects. *Thorax*. 2006;61(1):10-16.
52. Young RP, Hopkins R, Eaton TE. Pharmacological actions of statins: Potential utility in COPD. *Eur Respir Rev*. 2009;18(114):222-232.

53. Ajani UA, Ford ES, Mokdad AH. Dietary fiber and C-reactive protein: Findings from National Health and Nutrition Examination survey data. *J Nutr*. 2004;134(5):1181-1185.
54. Pinto-Plata VM, Mullerova H, Toso JF, et al. C-reactive protein in patients with COPD, control smokers and non-smokers. *Thorax*. 2006;61(1):23-28.
55. Rasmussen F, Mikkelsen D, Hancox RJ, et al. High-sensitive C-reactive protein is associated with reduced lung function in young adults. *Eur Respir J*. 2009;33(2):382-388.
56. Ahmadi-Abhari S, Kaptoge S, Luben RN, Wareham NJ, Khaw KT. Longitudinal association of C-reactive protein and lung function over 13 years: The EPIC-norfolk study. *Am J Epidemiol*. 2014;179(1):48-56.
57. Bolton CE, Schumacher W, Cockcroft JR, et al. The CRP genotype, serum levels and lung function in men: The Caerphilly prospective study. *Clin Sci (Lond)*. 2011;120(8):347-355.
58. Jiang R, Burke GL, Enright PL, et al. Inflammatory markers and longitudinal lung function decline in the elderly. *Am J Epidemiol*. 2008;168(6):602-610.
59. Hancox RJ, Poulton R, Greene JM, et al. Systemic inflammation and lung function in young adults. *Thorax*. 2007;62(12):1064-1068.
60. Shaaban R, Kony S, Driss F, et al. Change in C-reactive protein levels and FEV1 decline: A longitudinal population-based study. *Respir Med*. 2006;100(12):2112-2120.
61. Trompette A, Gollwitzer ES, Yadava K, et al. Gut microbiota metabolism of dietary fiber influences allergic airway disease and hematopoiesis. *Nat Med*. 2014;20(2):159-166.
62. Meijer K, de Vos P, Priebe MG. Butyrate and other short-chain fatty acids as modulators of immunity: What relevance for health? *Curr Opin Clin Nutr Metab Care*. 2010;13(6):715-721.

63. Fukuda S, Toh H, Hase K, et al. Bifidobacteria can protect from enteropathogenic infection through production of acetate. *Nature*. 2011;469(7331):543-547.
64. Wan ES, Castaldi PJ, Cho MH, et al. Epidemiology, genetics, and subtyping of preserved ratio impaired spirometry (PRISm) in COPDGene. *Respir Res*. 2014;15:89-014-0089-y.
65. Kurth L, Hnizdo E. Change in prevalence of restrictive lung impairment in the U.S. population and associated risk factors: The National Health and Nutrition Examination Survey (NHANES) 1988-1994 and 2007-2010. *Multidiscip Respir Med*. 2015;10(1):7-015-0003-6. eCollection 2015.
66. Leone N, Courbon D, Thomas F, et al. Lung function impairment and metabolic syndrome: The critical role of abdominal obesity. *Am J Respir Crit Care Med*. 2009;179(6):509-516.
67. Chen Y, Rennie D, Cormier YF, Dosman J. Waist circumference is associated with pulmonary function in normal-weight, overweight, and obese subjects. *Am J Clin Nutr*. 2007;85(1):35-39.
68. Canoy D, Luben R, Welch A, et al. Abdominal obesity and respiratory function in men and women in the EPIC-Norfolk study, United Kingdom. *Am J Epidemiol*. 2004;159(12):1140-1149.
69. Tabak C, Arts IC, Smit HA, Heederik D, Kromhout D. Chronic obstructive pulmonary disease and intake of catechins, flavonols, and flavones: The MORGEN study. *Am J Respir Crit Care Med*. 2001;164(1):61-64.
70. Lange P, Celli B, Agusti A, et al. Lung-function trajectories leading to chronic obstructive pulmonary disease. *N Engl J Med*. 2015;373(2):111-122.

71. Thyagarajan B, A Meyer K, Smith LJ, et al. Serum carotenoid concentrations predict lung function evolution in young adults: The coronary artery risk development in young adults (CARDIA) study. *Am J Clin Nutr.* 2011;94(5):1211-1218.
72. McKeever TM, Lewis SA, Smit HA, Burney P, Cassano PA, Britton J. A multivariate analysis of serum nutrient levels and lung function. *Respir Res.* 2008;9:67.
73. Varraso R, Fung TT, Barr RG, Hu FB, Willett W, Camargo CA, Jr. Prospective study of dietary patterns and chronic obstructive pulmonary disease among US women. *Am J Clin Nutr.* 2007;86(2):488-495.

Table 1: Comparison of population distributions according to definitions of SG grade and GOLD classification based on pre-bronchodilator spirometry.

Category	Spirometry Grade (SG) classification				GOLD classification			
	SG classification	Spirometry definition	N (%)	Subtotals	GOLD classification	Spirometry definition	N (%)	Subtotals
Normal	SG-0	FEV ₁ /FVC ≥0.7 and FEV ₁ ≥80% predicted	1196 (62.3%)	1196 (62.3%)	Normal	FEV ₁ /FVC ≥0.7	1628 (84.7%)	1628 (84.7%)
Airflow Retriction	SG-U*	FEV ₁ /FVC ≥0.7 and FEV ₁ <80% of predicted FEV ₁	432 (22.5%)					
Airflow obstruction	SG-1	FEV ₁ /FVC <0.7 and FEV ₁ ≥60% predicted	238 (12.4%)	293 (15.3%)	GOLD 1	FEV ₁ /FVC <0.7 and FEV ₁ ≥80% predicted	128 (6.7%)	293 (15.3%)
					GOLD 2	FEV ₁ /FVC <0.7 and 50% ≤ FEV ₁ < 80% predicted	136 (7.0%)	
	SG-2	FEV ₁ /FVC <0.7, 30% ≤ FEV ₁ <60% predicted	53 (2.8%)		GOLD 3	FEV ₁ /FVC <0.7 and 30% ≤ FEV ₁ <50 % predicted	27 (1.4%)	
	SG-3	FEV ₁ /FVC <0.7, FEV ₁ <30% predicted	2 (0.1%)		GOLD 4	FEV ₁ /FVC <0.7 and FEV ₁ <30 % of predicted	2 (0.1%)	
	Totals		1921	1921			1921	1921

* Also called "unclassified"

Table 2: Participant characteristics stratified by energy-adjusted fiber intake quartile

Characteristic:	Fiber Intake Quartile Mean (SE)				P-value
	<10.75 grams/day (n=360)	10.75- <13.46 grams/day (n=461)	13.46-17.5 grams/day (n=529)	>17.5 grams/day (n=571)	
Continuous variables Mean (SD)					
Age, yr	52.9 (0.5)	53.1 (0.5)	52.8 (0.5)	52.5 (0.3)	0.76
FEV ₁ (L)	2.6 (0.04)	3.0 (0.04)	3.1 (0.05)	3.2 (0.05)	<0.0001
FEV ₁ , %pred	80.9 (0.8)	86.6 (0.8)	89.0 (1.0)	90.6 (0.5)	<0.0001
FVC (L)	3.3 (0.04)	3.9 (0.05)	4.1 (0.06)	4.3 (0.06)	<0.0001
FVC, %pred	82.3 (0.7)	87.2 (0.8)	90.0 (0.9)	92.7 (0.6)	<0.0001
FEV ₁ /FVC ratio	0.76 (0.005)	0.77 (0.005)	0.76 (0.003)	0.76 (0.003)	0.079
Socioeconomic Status (income:poverty status ratio)	2.96	3.55	3.56	3.68	0.007
Fruit/vegetable/legume intake (cups/day)	1.5 (0.04)	2.1 (0.03)	2.8 (0.04)	3.6 (0.04)	<0.0001
Whole grain intake (ounces/day)	0.22 (0.02)	0.47 (0.03)	0.89 (0.04)	2.4 (0.04)	<0.0001
C-Reactive protein (mg/dL)	0.47 (0.5)	0.41 (0.06)	0.31 (0.04)	0.31 (0.05)	0.01
Energy intake (kcal/day)	1868.4 (48.8)	2076.7 (46.6)	2224.9 (48.5)	2368.9 (42.3)	<0.0001
Cured meat intake (times per day)	0.22 (0.3)	0.25 (0.01)	0.27 (0.01)	0.26 (0.01)	0.37
Vitamin E intake (as α - tocopherol, mg)	6.7 (0.38)	7.9 (0.3)	9.2 (0.3)	9.3 (0.3)	<0.0001
Alpha-carotene intake (mcg)	325.9 (45.5)	323.3 (27.2)	505.6 (114.2)	533.8 (27.7)	0.0005
Beta-carotene intake (mcg)	1982.1 (284.5)	2053.9 (161.6)	2742.3 (312.6)	2863.5 (27.7)	0.019
Beta-cryptoxanthin intake (mcg)	55.5 (10.4)	73.4 (7.8)	77.4 (5.5)	126.9 (20.0)	0.026
Lycopene intake (mcg)	3565.7 (468.3)	5105.0 (634.2)	6331.4 (591.9)	6156.9 (653.0)	0.001
Lutein + zeaxanthin intake (mcg)	1402.5 (277.9)	1692.4 (192.5)	1972.8 (191.5)	1965.5 (241.5)	0.32
Vitamin C intake (mg)	59.0 (6.8)	87.3 (7.9)	86.0 (1.9)	106.5 (6.4)	0.002
BMI	29.8 (0.5)	29.8 (0.4)	28.9 (0.3)	28.4 (0.04)	0.035
Discrete variables	N (%)				
BMI Category:					
Underweight: <18.5	3 (0.6)	5 (1.1)	7 (2.3)	6 (1.6)	0.026
Normal range: 18.5-24.6	83 (28.1)	84 (21.0)	112 (22.8)	125 (26.5)	
Overweight: 25-30	107 (28.7)	163 (36.1)	192 (38.0)	224 (38.7)	
Obese: >30	167 (42.6)	208 (41.8)	218 (36.9)	215 (33.2)	
Gender					
Male	79 (18.4)	215 (45.2)	300 (54.9)	376 (64.9)	<0.0001
Female	283 (81.6)	246 (54.8)	232 (45.1)	198 (35.1)	
Smoking					
Never	162 (45.6)	239 (55.7)	275 (52.8)	313 (57.0)	0.0031

Former	97 (27.6)	125 (29.7)	154 (30.7)	163 (28.5)	
Current	103 (26.8)	97 (14.6)	103 (16.5)	98 (14.5)	
Spirometry Grade					
Classificaitons:					
Normal airflow	183 (50.1)	269 (50.1)	354 (67.0)	390 (68.3)	<0.0001
Airflow restriction	122 (29.8)	125 (29.7)	85 (14.1)	95 (14.8)	
Airway obstruction	55 (20.1)	67 (16.9)	90 (18.9)	86 (17.0)	
GOLD:					
Normal	305 (80.0)	394 (85.9)	444 (81.1)	485 (83.1)	0.35
Airflow obstruction	55 (20.1)	67 (14.1)	85 (18.9)	86 (16.9)	

Table 3: Results of Multivariable Regression Models of Fiber Intake Quartiles and Lung Function Measurements*

Daily Fiber Intake Quartile (grms/d)	FEV ₁ (mL)		FVC (mL)		% Pred FEV ₁		% Pred FVC	
	β	p-value	β	p-value	β	p-value	β	p-value
<10.75	Reference							
10.75≤13.46	36.8	0.28	25.3	0.45	1.4	0.23	0.75	0.34
13.46≤17.5	82.3	0.04	115.2	0.003	2.7	0.03	2.7	0.003
≥17.5	81.7	0.05	128.9	0.01	2.4	0.07	2.8	0.02
Daily Fruit/veg/legume Intake (cups/day)	FEV ₁ (mL)		FVC (mL)		% Pred FEV ₁		% Pred FVC	
	β	p-value	β	p-value	β	p-value	β	p-value
<1.69	Reference							
1.69-<2.31	68.1	0.06	46.3	0.32	1.9	0.07	1.0	0.32
2.31-<3.07	28.0	0.47	75.1	0.18	0.96	0.43	1.5	0.23
≥3.07	106.7	0.001	127.0	0.006	3.3	0.0009	2.8	0.007

*Models adjusted for age, BMI, energy intake, smoking status, height, gender, socioeconomic status, CRP, and intakes of alpha-tocopherol, alpha-carotene, beta-carotene, beta-cryptoxanthin, lycopene, lutein+zeaxanthin, vitamin C, and cured meat.

Figure Legend: Figure 1 Percent of participants with a normal airflow pattern according to the spirometry grading classification by each fiber intake quartile. Fiber intake key: Q1= <10.75 g/day, Q2= $10.75-13.46$ g/day, Q3= $13.46-17.5$ g/day, Q4= >17.5 g/day

Figure Legend: Figure 2 Percent of participants with a restrictive airflow pattern according to the spirometry grading classification by each fiber intake quartile. Fiber intake key: Q1= <10.75 g/day, Q2= $10.75-13.46$ g/day, Q3= $13.46-17.5$ g/day, Q4= >17.5 g/day

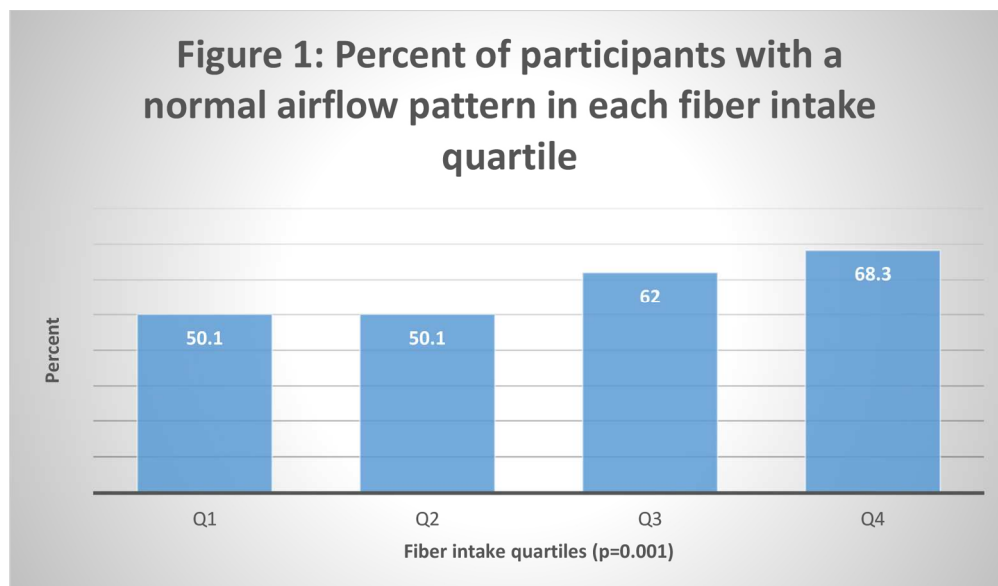


Figure 1 Percent of participants with a normal airflow pattern according to the spirometry grading classification by each fiber intake quartile. Fiber intake key: Q1=<10.75 g/day, Q2=10.75-<13.46 g/day, Q3=13.46-17.5 g/day, Q4=>17.5 g/day
152x89mm (300 x 300 DPI)

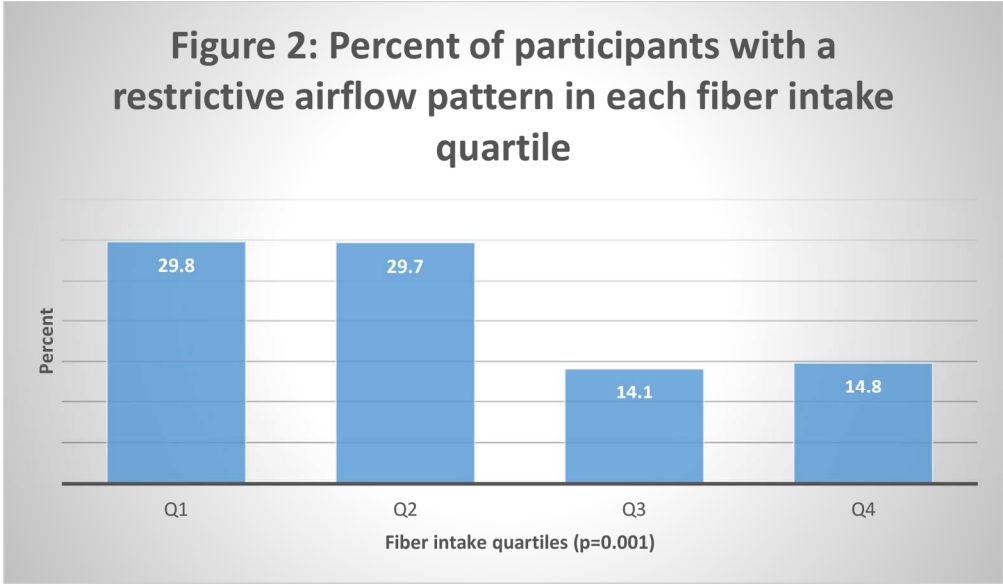


Figure 2 Percent of participants with a restrictive airflow pattern according to the spirometry grading classification by each fiber intake quartile. Fiber intake key: Q1=<10.75 g/day, Q2=10.75-<13.46 g/day, Q3=13.46-17.5 g/day, Q4=>17.5 g/day
152x89mm (300 x 300 DPI)