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## Original Contribution

# Prospective Study of Dietary Fiber and Risk of Chronic Obstructive Pulmonary Disease Among US Women and Men

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Little is known about the relation between dietary fiber intake and the incidence of respiratory diseases, especially chronic obstructive pulmonary disease (COPD). The authors investigated this issue among 111,580 US women and men (Nurses' Health Study and Health Professionals Follow-up Study), with 832 cases of newly diagnosed COPD being reported between 1984 and 2000. The cumulative average intake of total fiber and of fiber from specific sources (cereal, fruit, and vegetables) was calculated from food frequency questionnaires and a food composition database and divided into quintiles. After adjustment for 11 factors (age, sex, smoking, energy intake, body mass index, US region, physician visits, physical activity, diabetes, and intakes of omega-3 and cured meat), total dietary fiber intake was negatively associated with risk of newly diagnosed COPD (for highest vs. lowest intake, relative risk = 0.67, 95% confidence interval: 0.50, 0.90; $P_{\text{trend}} = 0.03$). For specific fiber sources (cereal, fruit, and vegetables), only cereal fiber was significantly associated with newly diagnosed COPD independently of other fiber sources (for highest vs. lowest intake, relative risk = 0.77, 95% confidence interval: 0.59, 0.99; $P_{\text{trend}} = 0.04$). These data suggest that a diet high in fiber, and possibly specifically cereal fiber, may reduce risk of developing COPD.

diet; dietary fiber; pulmonary disease, chronic obstructive; sex

Abbreviations: CI, confidence interval; COPD, chronic obstructive pulmonary disease; HPFS, Health Professionals Follow-up Study; NHS, Nurses' Health Study; RR, relative risk.

Chronic obstructive pulmonary disease (COPD) is the fourth leading cause of mortality in the United States and in Europe (1). With the increase in cigarette smoking in developing countries, COPD is expected to become the third leading cause of death worldwide by 2020. Over the last decade, there has been growing interest in the identification of foods or nutrients with antioxidant or antiinflammatory properties that affect the level of lung function or COPD symptoms (2). Most of these epidemiologic studies were cross-sectional, but the few longitudinal studies have reported a negative association between fruit, vegetable, and vitamin C intakes and lung function decline. Using an overall approach to assess diet, we recently reported in large cohorts of US women (3) and men (4) that a ''prudent'' dietary pattern (i.e,, with ample intakes of fruits, vegetables, fish, whole grains) was associated with a decreased risk of newly diagnosed COPD, whereas a ''Western'' diet (i.e,, with ample intakes of cured and red meats, desserts, refined grains, French fries) was associated with an increased risk of newly diagnosed COPD. We also demonstrated that frequent consumption of cured meat (one item of the Western diet) was associated with an increased risk of COPD (5, 6). However, no other specific foods or nutrients were investigated in relation to respiratory diseases.

Despite the antiinflammatory and antioxidant properties of fiber (7), little is known about its relation to lung function and COPD. The paucity of data is striking in comparison to the extensive scientific literature on the relation of dietary fiber to cardiovascular diseases (8), diabetes (9), and cancer (10). A recent study found that a high whole-grain food intake was associated with a lower risk for respiratory disease mortality (11). Dietary fiber intake also was reported to be associated with a reduced incidence of cough with phlegm (12) and with a higher level of lung function and a lower prevalence of COPD (13).

We therefore investigated prospectively the association between dietary fiber intake and risk of newly diagnosed COPD in 2 large prospective US cohorts.

## MATERIALS AND METHODS

### Overview

The Nurses' Health Study (NHS) began in 1976 when 121,700 female nurses aged 30–55 years and living in 11 US states responded to a mailed health questionnaire (14). The Health Professionals Follow-up Study (HPFS) began in 1986 when 51,529 US health professionals aged 40–75 years answered a detailed mailed questionnaire that included a diet survey and items on lifestyle practice and medical history. In both cohorts, follow-up questionnaires were sent every 2 years thereafter to update information on lifestyle factors and to ask about newly diagnosed medical conditions. Participants also completed a food frequency questionnaire in 1984 for NHS and at baseline in 1986 for HPFS. Similar food frequency questionnaires were sent every 2–4 years thereafter. The institutional review board approved the NHS and the HPFS protocols, and written consent was obtained from all subjects. The study is being conducted according to the ethical guidelines of Brigham and Women's Hospital, Boston, Massachusetts.

Participants without a completed food frequency questionnaire at baseline were excluded from the analysis. Likewise, we excluded participants with unreasonably high (>3,500 kcal/day for women and >4,200 kcal/day for men) or low (<500 kcal/day for women and <800 kcal/day for men) intakes and those who had left more than 70 items blank. Women and men who reported diagnosed asthma or COPD at baseline also were excluded from the present analysis. The final baseline population included 71,365 women and 40,215 men.

### Assessment of dietary intake

Dietary intake information was collected by a food frequency questionnaire designed to assess average food intake over the previous 12 months. Standard portion sizes were listed with each food. For each food item, participants indicated their average frequency of consumption over the past year in terms of the specified serving size by checking 1 of 9 frequency categories ranging from "almost never" to "≥6 times/day."

Nutrient intakes were computed by multiplying the frequency response by the nutrient content of the specified portion sizes. Food composition values were obtained from the Harvard University Food Composition Database, which was derived from US Department of Agriculture sources and supplemented with information from the manufacturer. In the US Department of Agriculture database, dietary fiber was determined by enzymatic-gravimetric methods 985.29 and 991.43 of the Association of Official Analytical Chemists (15). We considered total fiber, cereal fiber, fruit fiber, and vegetable fiber intakes. All the dietary factors were adjusted for total energy by using the residual method (16).

Fiber intakes were identified from each food frequency questionnaire administrated in 1984, 1986, 1990, 1994, and 1998 in the NHS and in 1986, 1990, and 1994 in the HPFS. To reduce measurement error and to represent long-term dietary intake, the cumulative average of dietary fiber was calculated and then divided into quintiles. The cumulative average incorporated repeated measures of diet. For example, by using this method in the NHS, the 1984 total fiber intake was used to predict newly diagnosed COPD in 1984–1986, an average of the 1984 and 1986 total fiber intake was used to predict COPD in 1986–1990, and so forth.

### Assessment of respiratory phenotypes

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

Self-reported COPD was defined by the affirmative response to physician-diagnosed chronic bronchitis or emphysema and by the report of a diagnostic test at diagnosis (i.e., pulmonary function testing, chest radiograph, or chest computed tomography). Among women, 749 cases of newly diagnosed COPD were reported between 1984 and 2000 and, among men, 83 cases of newly diagnosed COPD were reported between 1986 and 1998.

This epidemiologic definition was validated in a random sample of the Nurses' Health Study (17). We obtained participants' medical records, and a physician reviewed them in a blinded fashion. The diagnosis of COPD was confirmed in 80% of 218 cases who meet this case definition and in 88% of cases who met this definition and denied a physician's diagnosis of asthma. Results of pulmonary function testing were available in the medical records of 71% of confirmed cases; the mean forced expiratory volume in 1 second was 50% of predicted in this group.

### Assessment of other variables

Information on smoking status, assessed every 2 years by self-reported questionnaires, included categories of never, former, and current smokers. Among ever smokers, the amount of tobacco smoke was available by pack-years of smoking. We used updated variables for smoking and pack-years (i.e., that smoking status in 1984 was used to predict newly diagnosed COPD in 1984–1986; smoking status in 1986, to predict COPD in 1986–1998; and so forth). Total calorie intake was estimated through the food frequency questionnaire and expressed as kilocalories per day (kcal/day). Home residence was categorized into 6 US regions (New England, Mid-Atlantic, East North Central, South Atlantic, West South Central, Pacific), and the physician's examination in the previous 2 years was categorized in 3 responses (no visit, screening visit, symptom-related visit).

**Table 1.** Age-standardized Baseline Characteristics of the Women From the Nurses' Health Study (1984–2000, $n = 71,365$) and of the Men From the Health Professionals Follow-up Study (1986–1998, $n = 40,215$), According to Quintiles of Total Fiber Intake

| | Women ($n$ = 71,365) | | | | | | Men ($n$ = 40,215) | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Quintile 1 | Quintile 2 | Quintile 3 | Quintile 4 | Quintile 5 | *P* Value | Quintile 1 | Quintile 2 | Quintile 3 | Quintile 4 | Quintile 5 | *P* Value |
| No. | 13,987 | 14,291 | 14,537 | 14,383 | 14,167 | | 8,210 | 7,899 | 8,127 | 8,051 | 7,928 | |
| Age, years (mean (SD)) | 49.2 (7.0) | 49.6 (7.1) | 50.2 (7.1) | 50.8 (7.1) | 51.8 (7.1) | <0.001 | 51.4 (9.1) | 52.1 (9.2) | 52.7 (9.3) | 53.0 (9.4) | 53.7 (9.5) | <0.001 |
| Smoking habits, % | | | | | | | | | | | | |
| Never smokers | 37 | 42 | 45 | 48 | 52 | | 43 | 46 | 48 | 51 | 54 | |
| Former smokers | 37 | 39 | 40 | 40 | 39 | <0.001 | 42 | 43 | 43 | 43 | 41 | <0.001 |
| Current smokers | 26 | 19 | 15 | 12 | 9 | | 15 | 11 | 9 | 6 | 5 | |
| Pack-years among ever smokers[a,b] | 27 | 24 | 22 | 20 | 18 | <0.001 | 23 | 21 | 20 | 19 | 17 | <0.001 |
| Body mass index, kg/m$^2$ | 24.9 | 25.0 | 25.0 | 25.0 | 24.8 | <0.001 | 25.7 | 25.6 | 25.4 | 25.3 | 25.1 | <0.001 |
| US region, % | | | | | | | | | | | | |
| New England | 15 | 15 | 15 | 14 | 13 | | 22 | 22 | 21 | 20 | 21 | |
| Mid-Atlantic | 44 | 43 | 43 | 43 | 44 | | 16 | 16 | 17 | 17 | 16 | |
| East North Central | 19 | 20 | 19 | 18 | 18 | <0.001 | 20 | 20 | 19 | 21 | 21 | <0.001 |
| South Atlantic | 6 | 6 | 6 | 6 | 6 | | 35 | 35 | 36 | 35 | 35 | |
| West South Central | 5 | 5 | 5 | 5 | 5 | | 1 | 1 | 1 | 1 | 1 | |
| Pacific | 11 | 11 | 12 | 14 | 14 | | 5 | 5 | 6 | 6 | 6 | |
| Physician examination, % | | | | | | | | | | | | |
| No physician visits | 15 | 12 | 11 | 11 | 10 | | 24 | 22 | 21 | 20 | 19 | |
| Screening visits | 17 | 17 | 17 | 18 | 18 | <0.001 | 15 | 16 | 16 | 17 | 17 | <0.001 |
| Symptom-related visits | 68 | 70 | 71 | 71 | 72 | | 61 | 62 | 63 | 64 | 64 | |
| Physical activity, MET-hours/week[c] | 11.0 | 12.6 | 13.7 | 15.2 | 18.9 | <0.001 | 23.0 | 23.9 | 24.3 | 26.1 | 31.3 | <0.001 |
| Total energy, kcal/day | 1,311 | 1,564 | 1,731 | 1,914 | 2,185 | <0.001 | 1,493 | 1,775 | 1,968 | 2,180 | 2,533 | <0.001 |
| Diabetes, % | 3.0 | 3.1 | 3.6 | 3.6 | 3.9 | <0.001 | 2.6 | 3.0 | 3.3 | 3.4 | 3.7 | <0.001 |
| Dietary intake | | | | | | | | | | | | |
| Total fiber, g/day | 10.2 | 13.9 | 16.8 | 20.1 | 26.6 | <0.001 | 11.3 | 15.9 | 19.5 | 23.8 | 33.3 | <0.001 |
| Cereal fiber | 2.5 | 3.6 | 4.4 | 5.3 | 7.0 | <0.001 | 3.0 | 4.4 | 5.5 | 6.8 | 9.5 | <0.001 |
| Fruit fiber | 1.8 | 2.7 | 3.5 | 4.4 | 6.3 | <0.001 | 2.0 | 3.0 | 3.9 | 5.0 | 7.5 | <0.001 |
| Vegetable fiber | 4.0 | 5.3 | 6.2 | 7.4 | 9.9 | <0.001 | 3.9 | 5.3 | 6.4 | 7.8 | 10.9 | <0.001 |
| Omega-3, g/day | 0.10 | 0.10 | 0.10 | 0.11 | 0.11 | <0.001 | 0.14 | 0.14 | 0.14 | 0.14 | 0.15 | <0.001 |
| Cured meat, servings/day | 0.28 | 0.31 | 0.32 | 0.33 | 0.31 | <0.001 | 0.34 | 0.37 | 0.37 | 0.37 | 0.34 | <0.001 |

Abbreviations: MET, metabolic equivalent; SD, standard deviation.

[a] Age-adjusted mean (all such values).

[b] No. of packs smoked per day × no. of years smoked, among past and current smokers.

[c] MET-hours/week are the sum of the average time per week spent in each activity × the MET value of each activity.

**Table 2.** Association Between Quintiles of the Cumulative Average of Fiber Intake and Newly Diagnosed Chronic Obstructive Pulmonary Disease in Women and Men, Nurses' Health Study (1984–2000) and Health Professionals Follow-up Study (1986–1998) ($n = 111{,}580$)

| | Quintile of Intake | | | | | $P_{trend}$ |
|---|---|---|---|---|---|---|
| | Quintile 1 | Quintile 2 | Quintile 3 | Quintile 4 | Quintile 5 | |
| Total fiber | | | | | | |
| Median, g/day | 11.2 | 15.0 | 18.2 | 22.0 | 28.4 | |
| No. of cases | 234 | 182 | 153 | 156 | 107 | |
| No. of person-years | 154,421 | 157,000 | 158,251 | 157,270 | 155,614 | |
| Multivariate RR (95% CI)[a] | 1.00 | 0.72 (0.59, 0.87) | 0.57 (0.47, 0.70) | 0.56 (0.46, 0.68) | 0.36 (0.29, 0.45) | <0.001 |
| Multivariate RR (95% CI)[b] | 1.00 | 0.80 (0.65, 0.98) | 0.70 (0.56, 0.88) | 0.75 (0.59, 0.95) | 0.55 (0.42, 0.74) | <0.001 |
| Multivariate RR (95% CI)[c] | 1.00 | 0.80 (0.65, 0.99) | 0.72 (0.57, 0.90) | 0.79 (0.62, 1.01) | 0.60 (0.45, 0.80) | 0.002 |
| Multivariate RR (95% CI)[d] | 1.00 | 0.82 (0.67, 1.01) | 0.76 (0.60, 0.95) | 0.85 (0.66, 1.09) | 0.67 (0.50, 0.90) | 0.03 |
| Cereal fiber | | | | | | |
| Median, g/day | 2.2 | 3.5 | 4.7 | 6.2 | 9.0 | |
| No. of cases | 230 | 195 | 150 | 145 | 112 | |
| No. of person-years | 153,150 | 156,321 | 157,597 | 157,597 | 157,984 | |
| Multivariate RR (95% CI)[a] | 1.00 | 0.84 (0.69, 1.01) | 0.63 (0.51, 0.77) | 0.59 (0.48, 0.72) | 0.42 (0.33, 0.52) | <0.001 |
| Multivariate RR (95% CI)[b] | 1.00 | 0.99 (0.81, 1.20) | 0.84 (0.68, 1.05) | 0.86 (0.69, 1.09) | 0.71 (0.55, 0.92) | 0.007 |
| Multivariate RR (95% CI)[c] | 1.00 | 0.99 (0.81, 1.21) | 0.85 (0.68, 1.06) | 0.87 (0.69, 1.09) | 0.72 (0.56, 0.93) | 0.008 |
| Multivariate RR (95% CI)[d] | 1.00 | 0.99 (0.82, 1.21) | 0.86 (0.69, 1.08) | 0.90 (0.72, 1.14) | 0.77 (0.59, 0.99) | 0.04 |
| Fruit fiber | | | | | | |
| Median, g/day | 1.4 | 2.6 | 3.7 | 5.1 | 7.6 | |
| No. of cases | 264 | 170 | 152 | 147 | 99 | |
| No. of person-years | 154,559 | 157,843 | 158,025 | 157,378 | 154,751 | |
| Multivariate RR (95% CI)[a] | 1.00 | 0.55 (0.45, 0.67) | 0.45 (0.37, 0.55) | 0.40 (0.33, 0.49) | 0.25 (0.20, 0.31) | <0.001 |
| Multivariate RR (95% CI)[b] | 1.00 | 0.82 (0.67, 0.99) | 0.82 (0.67, 1.01) | 0.88 (0.71, 1.08) | 0.63 (0.49, 0.81) | 0.003 |
| Multivariate RR (95% CI)[c] | 1.00 | 0.83 (0.68, 1.01) | 0.86 (0.70, 1.05) | 0.93 (0.75, 1.16) | 0.68 (0.52, 0.87) | 0.02 |
| Multivariate RR (95% CI)[d] | 1.00 | 0.86 (0.70, 1.05) | 0.91 (0.74, 1.13) | 1.02 (0.82, 1.28) | 0.77 (0.59, 1.01) | 0.31 |
| Vegetable fiber | | | | | | |
| Median, g/day | 3.5 | 5.0 | 6.2 | 7.8 | 10.7 | |
| No. of cases | 206 | 154 | 176 | 157 | 139 | |
| No. of person-years | 154,603 | 157,742 | 158,033 | 157,186 | 154,992 | |
| Multivariate RR (95% CI)[a] | 1.00 | 0.71 (0.58, 0.88) | 0.79 (0.65, 0.97) | 0.70 (0.57, 0.86) | 0.60 (0.49, 0.75) | <0.001 |
| Multivariate RR (95% CI)[b] | 1.00 | 0.76 (0.61, 0.94) | 0.88 (0.71, 1.08) | 0.81 (0.65, 1.01) | 0.74 (0.58, 0.93) | 0.04 |
| Multivariate RR (95% CI)[c] | 1.00 | 0.77 (0.62, 0.95) | 0.89 (0.73, 1.10) | 0.85 (0.68, 1.06) | 0.81 (0.64, 1.03) | 0.22 |
| Multivariate RR (95% CI)[d] | 1.00 | 0.79 (0.63, 0.97) | 0.94 (0.76, 1.16) | 0.92 (0.73, 1.15) | 0.92 (0.71, 1.18) | 0.89 |

Abbreviations: CI, confidence interval; RR, relative risk.

[a] Adjusted for age and sex.

[b] Adjusted for age, sex, smoking status, pack-years, pack-years$^2$, and energy intake.

[c] Adjusted for age, sex, smoking status, pack-years, pack-years$^2$, energy intake, US region, physician visits, body mass index, and physical activity.

[d] Adjusted for age, sex, smoking status, pack-years, pack-years, energy intake, US region, physician visits, body mass index, physical activity, diabetes, omega-3 polyunsaturated fatty acid intake (from foods and supplements), cured meat intake, and other sources of fiber (total fiber intake not adjusted for the specific fiber types).

**Table 3.** Association Between Quintiles of the Cumulative Average of Fiber Intake and Newly Diagnosed Chronic Obstructive Pulmonary Disease in Women and Men Among Former Smokers ($n = 51{,}652$) and Current Smokers ($n = 32{,}353$), Nurses' Health Study (1984–2000) and Health Professionals Follow-up Study (1986–1998)

| | Quintile of Intake | | | | | $P_{trend}$ |
|---|---|---|---|---|---|---|
| | Quintile 1 | Quintile 2 | Quintile 3 | Quintile 4 | Quintile 5 | |
| *Former smokers* | | | | | | |
| Total fiber | | | | | | |
| Median, g/day | 11.3 | 15.1 | 18.3 | 22.0 | 28.4 | |
| No. of cases | 49 | 45 | 48 | 40 | 44 | |
| No. of person-years | 57,235 | 61,659 | 62,775 | 62,015 | 60,314 | |
| Multivariate RR (95% CI)[a] | 1.00 | 0.74 (0.48, 1.13) | 0.74 (0.48, 1.15) | 0.56 (0.35, 0.91) | 0.60 (0.36, 0.99) | 0.03 |
| Multivariate RR (95% CI)[b] | 1.00 | 0.76 (0.50, 1.16) | 0.78 (0.50, 1.21) | 0.61 (0.37, 1.00) | 0.68 (0.40, 1.16) | 0.11 |
| Cereal fiber | | | | | | |
| Median, g/day | 2.2 | 3.5 | 4.7 | 6.2 | 9.0 | |
| No. of cases | 50 | 53 | 37 | 42 | 44 | |
| No. of person-years | 58,278 | 60,803 | 62,282 | 61,553 | 61,082 | |
| Multivariate RR (95% CI)[a] | 1.00 | 1.03 (0.69, 1.54) | 0.68 (0.44, 1.07) | 0.76 (0.48, 1.18) | 0.73 (0.46, 1.14) | 0.07 |
| Multivariate RR (95% CI)[b] | 1.00 | 1.04 (0.69, 1.54) | 0.71 (0.46, 1.12) | 0.81 (0.52, 1.28) | 0.80 (0.51, 1.29) | 0.20 |
| Fruit fiber | | | | | | |
| Median, g/day | 1.4 | 2.6 | 3.7 | 5.1 | 7.6 | |
| No. of cases | 47 | 47 | 44 | 51 | 37 | |
| No. of person-years | 56,217 | 61,520 | 62,604 | 62,612 | 61,045 | |
| Multivariate RR (95% CI)[a] | 1.00 | 0.95 (0.63, 1.43) | 0.84 (0.55, 1.28) | 0.94 (0.62, 1.43) | 0.64 (0.40, 1.01) | 0.09 |
| Multivariate RR (95% CI)[b] | 1.00 | 0.98 (0.65, 1.48) | 0.91 (0.59, 1.39) | 1.05 (0.68, 1.61) | 0.75 (0.46, 1.23) | 0.41 |
| Vegetable fiber | | | | | | |
| Median, g/day | 3.5 | 5.0 | 6.2 | 7.8 | 10.6 | |
| No. of cases | 49 | 42 | 49 | 38 | 48 | |
| No. of person-years | 56,095 | 61,292 | 62,338 | 62,683 | 61,590 | |
| Multivariate RR (95% CI)[a] | 1.00 | 0.76 (0.50, 1.15) | 0.87 (0.58, 1.31) | 0.65 (0.42, 1.01) | 0.82 (0.53, 1.28) | 0.31 |
| Multivariate RR (95% CI)[b] | 1.00 | 0.78 (0.51, 1.19) | 0.92 (0.59, 1.40) | 0.72 (0.45, 1.14) | 0.95 (0.59, 1.54) | 0.77 |

**Table continues**

Body mass index and physical activity (18) were assessed every 2 years by self-reported questionnaires.

### Statistical analysis

All analyses were conducted by using SAS, version 9, software (SAS Institute, Inc., Cary, North Carolina) and included the chi-squared test, analysis of variance, and Cox proportional hazard regression models. Data from the NHS and the HPFS were merged together. Models were adjusted for age, sex, smoking status, pack-years, pack-years$^2$, and energy intake and then for 4 variables (US region, visits to physicians, body mass index, and physical activity). We intensively adjusted for smoking (smoking status, pack-years, pack-years$^2$), because it is the main risk factor for COPD and because smokers tend to have a different diet than nonsmokers do (19). We also adjusted for energy intake to better focus on the specific food, as opposed to the overall energy intake (16). To take into account geographic disparities in COPD and diet across the United States, we also adjusted for US region, and the variable—visits to physicians—was used in the model as a marker of healthy lifestyle. The adjustment for body mass index and physical activity was motivated by the strong interrelations among diet, body mass index, and physical activity. Furthermore, low body mass index is highly related to COPD (20), and it has been reported that physical activity is associated with lower risk of COPD (21). Similarly to Kan et al. (13), we further examined 8 other potential confounders (diabetes, glycemic index, micronutrients from foods and supplements (carotenoids; vitamins C, D, and E; and omega-3 polyunsaturated fatty acid), and cured meat intake) and found that results did

**Table 3.** Continued

| | Quintile of Intake | | | | | $P_{trend}$ |
|---|---|---|---|---|---|---|
| | Quintile 1 | Quintile 2 | Quintile 3 | Quintile 4 | Quintile 5 | |
| | | | *Current smokers* | | | |
| Total fiber | | | | | | |
| Median, g/day | 10.8 | 14.9 | 18.1 | 22.0 | 28.7 | |
| No. of cases | 168 | 123 | 86 | 90 | 41 | |
| No. of person-years | 39,819 | 30,031 | 25,014 | 20,443 | 16,942 | |
| Multivariate RR (95% CI)[a] | 1.00 | 0.84 (0.66, 1.08) | 0.70 (0.52, 0.93) | 0.91 (0.67, 1.23) | 0.56 (0.38, 0.85) | 0.03 |
| Multivariate RR (95% CI)[b] | 1.00 | 0.85 (0.66, 1.08) | 0.70 (0.54, 0.97) | 0.96 (0.69, 1.29) | 0.60 (0.40, 0.94) | 0.09 |
| Cereal fiber | | | | | | |
| Median, g/day | 2.1 | 3.4 | 4.6 | 6.1 | 9.0 | |
| No. of cases | 162 | 126 | 94 | 84 | 42 | |
| No. of person-years | 40,488 | 30,423 | 24,541 | 20,469 | 16,328 | |
| Multivariate RR (95% CI)[a] | 1.00 | 1.02 (0.80, 1.30) | 0.94 (0.72, 1.24) | 0.98 (0.73, 1.30) | 0.63 (0.44, 0.91) | 0.05 |
| Multivariate RR (95% CI)[b] | 1.00 | 1.02 (0.79, 1.30) | 0.95 (0.73, 1.26) | 0.99 (0.76, 1.36) | 0.66 (0.46, 0.94) | 0.09 |
| Fruit fiber | | | | | | |
| Median, g/day | 1.2 | 2.5 | 3.7 | 5.0 | 7.6 | |
| No. of cases | 200 | 114 | 90 | 68 | 36 | |
| No. of person-years | 44,676 | 29,369 | 23,304 | 19,006 | 15,894 | |
| Multivariate RR (95% CI)[a] | 1.00 | 0.88 (0.69, 1.11) | 0.93 (0.72, 1.21) | 0.94 (0.70, 1.25) | 0.65 (0.45, 0.95) | 0.09 |
| Multivariate RR (95% CI)[b] | 1.00 | 0.90 (0.71, 1.14) | 0.98 (0.75, 1.27) | 1.00 (0.74, 1.35) | 0.72 (0.49, 1.06) | 0.33 |
| Vegetable fiber | | | | | | |
| Median, g/day | 3.4 | 4.9 | 6.2 | 7.7 | 10.8 | |
| No. of cases | 133 | 97 | 107 | 101 | 70 | |
| No. of person-years | 32,290 | 28,263 | 25,770 | 23,385 | 22,541 | |
| Multivariate RR (95% CI)[a] | 1.00 | 0.80 (0.61, 1.04) | 0.93 (0.72, 1.21) | 1.02 (0.78, 1.34) | 0.82 (0.60, 1.13) | 0.74 |
| Multivariate RR (95% CI)[b] | 1.00 | 0.81 (0.62, 1.06) | 0.97 (0.75, 1.27) | 1.09 (0.82, 1.45) | 0.92 (0.66, 1.28) | 0.68 |

Abbreviations: CI, confidence interval; RR, relative risk.

[a] Adjusted for age, sex, pack-years, pack-years$^2$, energy intake, US region, physician visits, body mass index, and physical activity.

[b] Adjusted for age, sex, pack-years, pack-years$^2$, energy intake, US region, physician visits, body mass index, physical activity, omega-3 polyunsaturated fatty acid intake (from foods and supplements), cured meat intake, and other sources of fiber (total fiber intake not adjusted for the specific fiber types).

not differ in models with all of these factors (data not shown). Accordingly, to create a more parsimonious model, we further adjusted our model for only diabetes and intakes of omega-3 polyunsaturated fatty acid (foods and supplements) and cured meat. Models for specific fiber types (i.e., cereal, fruit, and vegetables) were adjusted for other sources of fiber intakes.

Residual confounding by smoking remains an important issue in all studies of diet and respiratory diseases. Accordingly, major analyses were repeated among former smokers and current smokers (there were too few cases to permit a meaningful analysis among never smokers only). We formally tested the interaction between fiber intake and smoking status. We also stratified the analyses according to sex and tested for the interaction. Finally, for total fiber intake only, an additional model was performed: Log relative risks from the 2 cohorts (female, male) were pooled in a fixed-effects model, and we tested for heterogeneity.

## RESULTS

Participants with the highest intake of fiber were less often smokers and more physically active, and they reported a higher total energy intake, compared with those with the lowest intake of fiber (Table 1). The intake of specific fiber types (cereal, fruit, and vegetable) was correlated in both women and men: cereal and fruit fibers ($r = 0.30$ in women, 0.25 in men); cereal and vegetable fibers ($r = 0.25$ in women, 0.24 in men); and fruit and vegetable fibers ($r = 0.42$ in women, 0.38 in men).

## Total fiber intake and newly diagnosed COPD

Total fiber intake was inversely associated with newly diagnosed COPD, both in the age- and sex-adjusted model and in the multivariate model (Table 2). Further adjustments for diabetes and for omega-3 and cured meat intakes led to similar results. The pooled relative risk of newly diagnosed COPD supported this result (for the highest vs. the lowest intake, relative risk (RR) = 0.69, 95% confidence interval (CI): 0.35, 1.20; $P_{trend} = 0.14$). The test for heterogeneity of relative risk of newly diagnosed COPD in men versus women was not significant ($P = 0.72$).

In the multivariable model, cured meat remained significantly associated with COPD (for the highest vs. the lowest intake, RR = 1.34, 95% CI: 1.05, 1.72; $P_{trend} = 0.004$), and a borderline significant association was reported with omega-3 intake (for the highest vs. the lowest intake, RR = 0.82, 95% CI: 0.64, 1.05; $P_{trend} = 0.10$).

Because of the potential overlap between the diagnosis of COPD and asthma, we also restricted analyses to ever smokers. The risk of newly diagnosed COPD decreased with increased intake of total fiber, but the trend was borderline significant (Table 3).

We also examined whether sex modified the association between fiber intake and the risk of COPD. In women, after adjustment for confounders, the total fiber intake was negatively associated with newly diagnosed COPD (for the highest vs. the lowest intake, RR = 0.62, 95% CI: 0.46, 0.85; $P_{trend} = 0.01$). Further adjustments for diabetes and for omega-3 and cured meat intakes led to similar results ($P_{trend} = 0.04$). In this multivariate model, only cured meat remained positively associated with COPD (for the highest vs. the lowest intake, RR = 1.21, 95% CI: 0.95, 1.55; $P_{trend} = 0.04$).

In men, after adjustment for confounders, the risk of newly diagnosed COPD decreased with the intake of total fiber (for the highest vs. the lowest intake, RR = 0.46, 95% CI: 0.19, 1.09; $P_{trend} = 0.05$). Further adjustments for diabetes and omega-3 and cured meat intakes led to a nonsignificant association (for the highest vs. the lowest intake, RR = 0.64, 95% CI: 0.26, 1.59; $P_{trend} = 0.26$). The loss of statistical significance appeared to be due to adjustment for cured meat intake; cured meat was strongly associated with newly diagnosed COPD (for the highest vs. the lowest intake, RR = 3.00, 95% CI: 1.27, 7.09; $P_{trend} = 0.001$). The formal test of interaction between fiber intake and sex was not statistically significant ($P = 0.29$).

## Specific sources of fiber intake and newly diagnosed COPD

Cereal fiber contributed 27% of the total fiber intake. The risk of newly diagnosed COPD decreased with the intake of cereal fiber, even after adjustment for confounders and after further adjustment for diabetes and for omega-3, cured meat, fruit fiber, and vegetable fiber intakes (Table 2). In this model, among all the intakes of foods and nutrients, only cured meat intake was significantly associated with the risk of COPD (for the highest vs. the lowest intake, RR = 1.32, 95% CI: 1.05, 1.68; $P_{trend} = 0.004$) and, with borderline significance, omega-3 intake (for the highest vs. the lowest intake, RR = 0.81, 95% CI: 0.64, 1.03; $P_{trend} = 0.09$). When the analyses were stratified according to smoking status, the risk of newly diagnosed COPD decreased with increased intake of cereal fiber among both former smokers and current smokers, but the association was borderline significant only in current smokers (Table 3). When stratified according to sex, the association between cereal fiber intake and newly diagnosed COPD was significant only among women (for the highest vs. the lowest intake, women: RR = 0.74, 95% CI: 0.55, 1.00; $P_{trend} = 0.04$; men: RR = 0.53, 95% CI: 0.24, 1.20; $P_{trend} = 0.17$).

Fruit fiber contributed 22% of the total fiber intake. After adjustment for confounders, the risk of newly diagnosed COPD decreased with an increased intake of fruit fiber (Table 2). Further adjustment for diabetes and for omega-3, cured meat, cereal fiber, and vegetable fiber intakes led to a nonsignificant association. The loss of statistical significance was mostly due to the adjustment for cured meat and cereal fiber intakes. In the final model, we found a significant positive association between the risk of COPD and cured meat intake ($P_{trend} = 0.004$) and cereal fiber intake ($P_{trend} = 0.02$). Stratification according to smoking or according to sex showed no significant association between fruit fiber intake and newly diagnosed COPD.

Vegetable fiber contributed 35% of the total fiber intake. After multivariate adjustment, the intake of vegetable fiber was not associated with newly diagnosed COPD (Table 2). Further adjustments for diabetes and for omega-3 polyunsaturated fatty acid, cured meat, cereal fiber, and fruit fiber intakes led to similar results. When the analyses were stratified according to smoking, no associations were observed among former smokers and current smokers. The stratification according to sex yielded similar results (data not shown).

## DISCUSSION

In 2 large cohorts of US women and men, we found that participants with a higher total fiber intake had a lower risk of newly diagnosed COPD, even after adjustment for many potential confounders. The potentially beneficial effect was independent of other dietary factors, such as omega-3 and cured meat. Only cereal fiber was significantly associated with newly diagnosed COPD.

Many studies have examined antioxidants (or foods rich in antioxidants such as fruits and vegetables) in relation to lung function or COPD (2). The main epidemiologic evidence in support of an antioxidant–COPD association suggests that vitamin C and fruits and vegetables have beneficial associations with lung function, in both cross-sectional and longitudinal analyses. Relatively little attention has been paid to other foods or nutrients except for cured meats, which appear to have a deleterious effect on COPD risk (5, 6, 22).

Two studies have investigated the relation of a novel antioxidant, dietary fiber, to COPD or COPD symptoms (12, 13). Butler et al. (12) reported that nonstarch polysaccharides, a major component of dietary fiber, had an independent, inverse association with the incidence of cough with phlegm in 63,257 Chinese Singaporean women and men. In the Atherosclerosis Risk in Communities Study of 11,897 US women and men, Kan et al. (13) investigated the association between dietary fiber and respiratory phenotypes, using both a cross-sectional design (i.e., level of lung function and COPD prevalence) and a longitudinal design (i.e., mean changes of lung function). In the cross-sectional analysis, they reported a negative association of dietary fiber intake from all sources and from cereal and fruits with the level of lung function and the prevalence of COPD; in the longitudinal analysis (only 3 years apart), they reported a significant inverse association of decline in lung function with cereal fiber but not with total or fruit fiber.

We now report a significant, independent association between total fiber intake and the risk of COPD, particularly in women. Gender influences the epidemiology, diagnosis, and presentation of COPD, in addition to physiologic and psychologic impairments (23). In the study of Butler et al. (12), results were adjusted for sex by statistical modeling; stratified results were not reported. Kan et al. (13) formally tested the interaction between sex and total fiber intake on the level of lung function, and they did not find a statistically significant interaction. As our formal test for interaction between fiber intake and sex was not statistically significant, it supports the likelihood that the difference we observed between men and women might be due to chance. We faced a statistical power issue in men because the number of cases was much lower in men compared with women; the confidence interval for men actually included a strong inverse association. In men, we initially found a borderline significant negative association between the risk of newly diagnosed COPD with total fiber and cereal fiber intakes, associations that became nonsignificant after adjustment for cured meat. In women, we found independent effects of cured meat intake and fiber intake on COPD risk. In earlier work by our group, a very strong association was reported between cured meat intake and the risk of newly diagnosed COPD in men, with a relative risk for daily consumers of similar magnitude to ever smoking (6); in women, the magnitude of the association was smaller but also highly significant (5).

COPD is an oxidant- and nitrosant-related disease (24) with characteristic airway inflammation. Along those lines, a recent study found that the mortality risk of individuals with inflammatory respiratory diseases was significantly lower for those who reported the highest intake of whole-grain foods (11). The biologic explanation for a potential benefit of fiber intake is related to both its antioxidant and antiinflammatory properties. Even if the exact mechanism between dietary fiber and inflammation is unclear (7), it has been reported in epidemiologic data that fiber intake is associated with both a lower level of C-reactive protein and various proinflammatory cytokines, such as interleukins 6 and18 and tumor necrosis factor $\alpha$ (25–27), and a higher level of the antiinflammatory cytokine adiponectin (27, 28). Moreover, we cannot exclude that our findings are not an effect of fiber per se, but that they are due to other constituents of whole grains, including lignans.

Our primary findings for cereal fiber are consistent with the longitudinal finding of Kan et al. (13). Together, these data support the hypothesis that fiber from cereal, or another constituent of whole grains, may have physiologic effects that are more beneficial to the respiratory system than fiber from fruits or vegetables. Identification of the predominant mechanism for the beneficial effects of dietary fiber on COPD risk will require further study (7).

The study has few potential limitations. First, newly diagnosed COPD was defined by a self-reported physician's diagnosis of COPD, and no lung function results were available. Nevertheless the questionnaire-based definition of newly diagnosed COPD was validated in a subset of the Nurses' Health Study (17). Second, we acknowledge that the association between fiber intake and newly diagnosed COPD may be due, in part, to residual confounding by cigarette smoking. To minimize this possibility, we adjusted multivariate models to multiple time-varying measures of tobacco exposure (smoking habits, pack-years, and pack-years$^2$) that were assessed biennially since 1976, and analyses were stratified according to smoking status. Finally, we note the difficulty of studying the health effects of any specific nutrient given the complex interrelations among intakes of different components of diet. Our fiber–COPD findings merit replication in other populations, preferably from cohorts with higher intake of fiber and different patterns of dietary intake.

In summary, the intake of fiber, and particularly cereal fiber, was negatively associated with the risk of newly diagnosed COPD in women. Similar, but weaker, associations were seen among men. Our results support the current dietary guidelines that recommend that Americans increase their daily consumption of whole grains (29). Besides potential prevention benefits for cardiovascular diseases, diabetes, and cancer, fiber or another constituent of whole grains might also be involved through antiinflammatory effects, in the pathogenesis of COPD. For COPD prevention, the most important public health message remains smoking cessation, but our data suggest that diet, another modifiable risk factor, might also influence COPD risk.

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