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## **Prospective study of dietary patterns and chronic obstructive pulmonary disease among US men**

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## ABSTRACT

**Background:** Many foods are associated with chronic obstructive pulmonary disease (COPD) symptoms or lung function. Because foods are consumed together and nutrients may interact, dietary patterns are an alternative way to characterize diet. Our objective was to assess the relation between dietary patterns and newly diagnosed COPD in men.

**Methods:** Data were collected from a large prospective cohort of US men (Health Professionals Follow-up Study). Using principal component analysis, two dietary patterns were identified: a prudent pattern (high intake of fruits, vegetables, fish and whole grain products) and a Western pattern (high intake of refined grains, cured and red meats, desserts and French fries). Dietary patterns were categorized into quintiles and Cox proportional hazards models were adjusted for age, smoking, pack-years, (pack-years)<sup>2</sup>, race/ethnicity, physician visits, US region, body mass index, physical activity, multivitamin use and energy intake.

**Results:** Between 1986 and 1998, we identified 111 self-reported cases of newly diagnosed COPD among 42,917 men. The prudent pattern was inversely associated (RR for highest vs. lowest quintile [95%CI] = 0.50 [0.25-0.98], p for trend = 0.02) with the risk of newly diagnosed COPD. By contrast, the Western pattern was positively associated (RR for highest vs. lowest quintile [95%CI] = 4.56 [1.95-10.69], p for trend < 0.001) with the risk of newly diagnosed COPD.

**Conclusions:** In men, a diet rich in fruits, vegetables and fish may reduce risk of COPD, whereas a diet rich in refined grains, cured and red meats, desserts and French fries may increase risk of COPD.

(246 words)

## **INTRODUCTION**

Currently, chronic obstructive pulmonary disease (COPD) is the fourth leading cause of mortality in Europe and in the United States.[1] With the increase in cigarette smoking in developing countries, COPD is expected to become the third leading cause of death worldwide by 2020.[2] Cigarette smoking is the most important risk factor for COPD in developed nations,[3] but not all smokers develop COPD.[4] This simple observation suggests that genetic and environmental factors also are involved.

Among environmental factors, changes in diet have been evoked to explain the large increase of COPD. [5] Several epidemiological studies have suggested that intake of fruit and other dietary antioxidants are associated with higher level of lung function [6-8] or with lower decline in FEV<sub>1</sub> or in COPD symptoms. [9-12] Some cross-sectional studies have also suggested that a high fish or omega-3 fatty acid intake were associated with higher lung function and lower COPD symptoms,[13, 14] but the only prospective study did not supported this result. [9]

However, all of these studies focused on individual nutrients or foods. Because foods are consumed together and nutrients may interact together, it has been proposed to assess overall diet instead of the individual components. [15] This approach has been used to investigate the role of diet in several chronic diseases. [16, 17] Although one recent study examined the relation between dietary patterns and respiratory phenotypes,[18] the relation between dietary patterns and newly diagnosed COPD among men remained unknown. Previously, two majors dietary patterns were derived in the Health Professionals Follow-up Study and related to coronary heart disease. [19] The objective of the present analysis is to assess the relation between these dietary patterns and the risk of newly diagnosed COPD in a prospective cohort of more than 40,000 US men.

## **MATERIALS AND METHODS**

### **Study population**

The Health Professionals Follow-up Study (HPFS), a prospective cohort study, began in 1986 when 51,529 US health professionals aged 40 to 75 years answered a detailed mailed questionnaire that included a diet survey and items on lifestyle practice and medical history. Follow-up questionnaires were sent every two years thereafter to update information on smoking habits, physical activity, weight, and other risk factors and to ask about newly diagnosed medical conditions. Dietary intake data were collected in 1986, and every 4 years thereafter with a 131-item food frequency questionnaire (FFQ). The study is being conducted according to the ethical guidelines of Brigham and Women's Hospital (Boston, USA).

Men who did not satisfy a reported daily energy intake between 3.3 and 17.6 MJ (800 and 4200 kcal) or who left blank >70 of a total of 131 food items on the diet questionnaire were excluded. Men reporting a history of ever asthma or COPD at

baseline were also excluded from the present analysis. The final baseline population included 42,917 men.

### **Assessment of dietary patterns**

To prepare for factor analysis, food items from the FFQ were grouped into 40 predefined foods groups in 1986 and in 42 foods groups in 1990 and 1994 (see appendix 1) as previously described. [19] Dietary patterns were identified from FFQs administered in 1986, 1990 and 1994 using principal component analysis. [20] We conducted the analyses using the FACTOR procedure in SAS. The factors were rotated by an orthogonal transformation to achieve simpler structure with greater interpretability and the number of factors to retain was determined using the diagram of eigenvalues. The factor score for each pattern was calculated by summing intakes of food groups weighted by their factor loadings. Factor scores were standardized to having a mean of 0 and standard deviation of 1. Factor loadings represent correlation coefficients between the food groups and the particular pattern, with positive loadings representing positive correlations and negative loadings representing inverse correlations. Each man received a factor score for each identified pattern. The resulting factor scores for the Western and prudent dietary patterns were therefore standardized and not correlated with each other. Men with a high intake of the prudent diet might also have a high intake of the Western diet, in others words men with a Western diet and men with a prudent diet are not necessarily two distinct clusters of individuals.

To reduce measurement errors and to represent long-term intake, dietary patterns using all available FFQ were generated and averages of pattern scores were calculated. The present analysis is based on the quintiles of the cumulative average of pattern scores. The cumulative average incorporated repeated measures of diet. With this approach, the 1986 dietary pattern consumption was used to predict newly-diagnosed COPD in 1986-1990, an average of the 1986 and 1990 dietary pattern consumption, to predict COPD in 1990-1994 and the average of the 1986, 1990 and 1994 dietary pattern consumption, to predict COPD from 1994 to 1998.

### **Assessment of respiratory phenotypes**

Because the HPFS includes a large numbers of subjects dispersed throughout the US and is conducted by mail, the diagnosis of COPD was assessed by questionnaire and did not include spirometry. 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 (pulmonary function testing, chest radiograph, or chest computed tomography). Between 1986 and 1998, 111 cases of newly diagnosed COPD were reported. This epidemiologic definition was validated in a random sample of another cohort of health professionals, the Nurses' Health Study. [21] Using the exact same questions, the authors 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 88% of cases who met this definition and denied a physician diagnosis of asthma. Results of pulmonary function testing were

available in the medical records of 71% of confirmed cases; the mean FEV<sub>1</sub> in this group was 50 % of predicted.

Asthma was also self-reported and was defined by a doctor diagnosis of asthma and the use of medication for asthma within the past 12 months. Between 1986 and 1998, 212 new cases of adult-onset asthma were reported.

### **Assessment of others variables**

Information on smoking status was collected every 2 years and categorized into never smokers, ex smokers and current smokers. We further characterized smokers using their lifetime pack-years of smoking and (pack- years)<sup>2</sup>; prior analyses have demonstrated that including both measures optimally controls for the association between smoking and COPD risk. Race/ethnicity was categorized in two classes (white, non-white), physician exam was categorized in three classes (no visit, screening, symptoms) and US region was categorized in three classes (East South Central, Mountain and others regions). Body mass index (BMI), physical activity and multivitamin use were assessed every two years by self-reported questionnaires. BMI was calculated as weight/height<sup>2</sup> (kg/m<sup>2</sup>) and was categorized into seven classes: ≤ 20.0, 20.0-22.4, 22.5-24.9, 25.0-27.4, 27.5-29.9, 30.0-34.9, ≥ 35.0 kg/m<sup>2</sup>. Men also reported duration of several leisure-time physical activity including walking, bicycle, swimming or tennis. Physical activity was calculated in metabolic equivalent per weeks (METs), where one metabolic equivalent was equal to the energy expended at the basal metabolic rate or at rest. [22] Total energy intake was calculated from the food frequency questionnaire, expressed in kilocalorie per day (kcal/d). Job title for each man was recorded: dentist, pharmacist, optometrist, osteopathic physician, podiatrist and veterinarian. Assessment of cardiovascular diseases included angina, myocardial infarction, coronary artery surgery, transient ischemic attack, stroke, or peripheral arterial disease.

### **Statistical analysis**

Statistical analyses included Chi-squared, analysis of variance, linear regression and Cox proportional hazard regression models. Cox proportional hazards models were adjusted for age, smoking status, pack-years, (pack-years)<sup>2</sup>, race/ethnicity, physician visits, US region, body mass index, physical activity, multivitamin use and energy intake. All analyses were conducted using SAS software, version 9 (Cary, NC, USA).

## **RESULTS**

### **Assessment of dietary patterns**

Using principal component analysis, two distinct major dietary patterns were identified at baseline. The first pattern was heavily loaded by a high intake of fruits, vegetables, fish, poultry and whole grain products. The second pattern was heavily loaded by a high consumption of refined grains, cured and red meats, desserts and sweets, French fries, eggs and high-fat dairy products. According to previous studies regarding dietary patterns in this population, the first pattern was labeled the 'prudent' pattern and the second pattern was labeled the 'Western' pattern. Similar dietary patterns were identified using FFQ from 1990 and 1994.

The characteristics of the population according to the quintile of both prudent and Western patterns are presented in table 1. Compared with men with the lowest intake of prudent diet score (the lowest quintile), men with the highest intake of prudent diet (the highest quintile) were more physically active, less likely to be current smokers and took more multivitamin supplements. Men with the highest intake of prudent diet consumed more polyunsaturated fat, more proteins and more carbohydrates, but less saturated fat and trans fatty acids. As expected, the consumption of fruits, vegetables, whole grains and fish was higher among men with the highest intake of prudent diet.

At baseline, 46% of the population was never smokers, 41% were ex smokers and only 9% of men were current smokers. Among ex smokers (n=17,585), 70% had quit smoking at least 10 years before; only 9.5% has quit in the last two years.

Compared with men with the lowest intake of Western diet, men with the highest intake of Western diet had a higher BMI, were less physically active, were more likely to smoke and took less multivitamin supplements. Men with the highest intake of Western diet consumed more saturated fat and trans fatty acids, but less carbohydrates and proteins. As expected, the consumption of cured meat, red meat and desserts and sweet, was higher among men with the highest intake of prudent diet.

**Table 1** Age standardized baseline characteristics by quintiles of 1986 pattern score

	Quintiles for the prudent pattern			Quintiles for the Western pattern		
	Q <sub>1</sub> Small intake of prudent diet	Q <sub>3</sub> Medium intake of prudent diet	Q <sub>5</sub> High intake of prudent diet	Q <sub>1</sub> Small intake of Western diet	Q <sub>3</sub> Medium intake of Western diet	Q <sub>5</sub> High intake of Western diet
Current smokers (%)	16	7	5	5	8	14
Smoking (pack-years)	15.8	11.4	9.2	9.6	11.6	15.1
White race/ethnicity (%)	90	91	91	88	91	93
No physician visits (%)	29	23	19	18	23	28
US region (%)						
East South central	5	4	4	3	4	6
Mountain	7	8	8	6	8	8
Others regions	88	88	89	91	87	86
Body mass index (kg/m <sup>2</sup> )	25.6	25.5	25.2	25.0	25.5	25.9
Physical activity (METs/week)*	22	25	32	29	26	23
Multivitamin use (%)	19	20	21	21	20	18
Total energy (kcal)	1622	1954	2432	1467	1899	2710
Food and nutrient consumption						
Total vegetables (servings/day)	1.4	2.6	5.2	3.1	2.8	3.0
Whole grains products (servings/day)	0.5	1.0	1.9	1.0	1.1	1.2
Fruits (servings/day)	0.9	1.5	2.8	2.2	1.8	1.7
Fish (servings/day)	0.2	0.4	0.6	0.5	0.4	0.3
Desserts and sweets (servings/day)	1.0	1.1	1.0	0.4	1.0	1.8
Cured meats (servings/day)	0.4	0.4	0.3	0.1	0.3	0.7
Red meats (servings/day)	0.6	0.6	0.6	0.2	0.6	1.1
Saturated fat (g)	28.0	24.6	20.3	19.9	25.0	27.6
Monounsaturated fat (g)	30.0	27.5	23.7	22.9	27.7	30.2



Polyunsaturated fat (g)	12.9	13.4	13.2	12.8	13.2	13.6
Trans fat (g)	3.4	2.9	2.2	2.0	2.9	3.4
Total carbohydrates (g)	215	235	257	255	233	221
Total proteins (g)	84.6	92.9	99.5	96.6	91.8	90.0

\* METs: metabolic equivalent.

### **Dietary patterns and COPD**

The prudent pattern was inversely associated with the risk of newly diagnosed COPD after adjustment for age and total energy intake (table 2). This association remained statistically significant after adjustment for smoking (smoking, pack-year, pack-year<sup>2</sup>) and further adjustment for 7 potential confounders (race/ethnicity, physician visits, US region, body mass index, physical activity, multivitamin use and energy intake), led to similar result (table 2). Further adjustment for job title also led to similar result: RR for highest vs. lowest quintile (95%CI) was 0.48 (0.24-0.94), with p for trend = 0.02. Further adjustment for cardiovascular disease led to a borderline significant negative association: RR for highest vs. lowest quintile (95%CI) was 0.56 (0.28-1.13), with p for trend = 0.06.

By contrast, the Western pattern was positively and significantly associated with the risk of newly diagnosed COPD after taking age and total energy intake into account. Further adjustment for smoking and 7 potential confounders continued to demonstrate a strong positive association. Further adjustment for job title also led to similar result: RR for highest vs. lowest quintile (95%CI) was 4.61 (1.97-10.81), with p for trend <0.001. Further adjustment for cardiovascular disease also led to similar results: RR for highest vs. lowest quintile (95%CI) was 3.72 (0.59-8.71), with p for trend < 0.001.

When the population was restricted to men without cancer or cardiovascular disease at baseline (n=35,286), similar associations were found: for prudent pattern the RR for highest vs. lowest quintile (95%CI) was 0.48 (0.23-1.01), with p for trend = 0.04. By contrast, for the Western pattern the RR for highest vs. lowest quintile (95%CI) was 3.46 (1.38-8.67), with p for trend <0.001.

### **Dietary patterns and asthma**

Although the primary outcome of this study was newly diagnosed COPD, but due to the potential overlap between the diagnoses of COPD and asthma, it was interesting to assess the relation between dietary patterns with incident asthma in this cohort of men (table 3). In contrast with the risk of newly diagnosed COPD, no association was found between the prudent and the Western patterns with the risk of adult-onset asthma.

**Table 2** Association between quintiles of the cumulative average patterns and newly diagnosed COPD

	Quintile of intake					p for trend
	Q <sub>1</sub>	Q <sub>2</sub>	Q <sub>3</sub>	Q <sub>4</sub>	Q <sub>5</sub>	
<b>PRUDENT PATTERN</b>						
	Small intake of prudent diet		Medium intake of prudent diet		High intake of prudent diet	
No. of cases	32	28	18	17	16	
Person-years	50003	50105	49669	48830	48227	
RR (95% CI) – adjustment 1*	1.00	0.60 (0.36-1.02)	0.40 (0.22-0.70)	0.30 (0.17-0.55)	0.20 (0.11-0.39)	<0.001
RR (95% CI) – adjustment 2†	1.00	0.82 (0.48-1.39)	0.65 (0.36-1.15)	0.59 (0.32-1.09)	0.47 (0.24-0.92)	0.02
RR (95% CI) – adjustment 3‡	1.00	0.83 (0.49-1.42)	0.64 (0.36-1.15)	0.60 (0.32-1.11)	0.50 (0.25-0.98)	0.02
<b>WESTERN PATTERN</b>						
	Small intake of Western diet		Medium intake of Western diet		High intake of Western diet	
No. of cases	12	9	16	29	45	
Person-years	48958	49353	49663	49592	49268	
RR (95% CI) – adjustment 1*	1.00	1.29 (0.56-2.96)	1.62 (0.70-3.78)	3.94 (1.76-8.79)	10.49 (4.62-23.84)	<0.001
RR (95% CI) – adjustment 2†	1.00	1.12 (0.49-2.58)	1.23 (0.52-2.86)	2.47 (1.11-5.52)	5.07 (2.21-11.66)	<0.001
RR (95% CI) – adjustment 3‡	1.00	1.09 (0.48-2.50)	1.15 (0.49-2.69)	2.30 (1.02-5.18)	4.56 (1.95-10.69)	<0.001

RR denotes relative risk; CI, confidence interval.

\*Multivariate RRs have been adjusted for age and energy intake

†Multivariate RRs have been adjusted for age, energy intake, smoking status, pack-years, pack-years<sup>2</sup>.

‡Multivariate RRs have been adjusted for age, energy intake, smoking status, pack-years, pack-years<sup>2</sup>, race/ethnicity, physician visits, US region, body mass index, physical activity and multivitamin use.

**Table 3** Association between quintiles of the cumulative average patterns and adult onset asthma.

	Quintile of intake					p for trend
	Q <sub>1</sub>	Q <sub>2</sub>	Q <sub>3</sub>	Q <sub>4</sub>	Q <sub>5</sub>	
<b>PRUDENT PATTERN</b>						
	Small intake of prudent diet		Medium intake of prudent diet		High intake of prudent diet	
No. of cases	44	45	44	43	36	
Person-years	49895	50003	49606	48745	48126	
RR (95% CI) – adjustment 1*	1.00	1.37 (0.88-2.12)	1.25 (0.79-1.96)	1.12 (0.70-1.79)	1.06 (0.64-1.73)	0.80
RR (95% CI) – adjustment 2†	1.00	1.29 (0.83-2.01)	1.14 (0.72-1.79)	1.00 (0.62-1.61)	0.93 (0.56-1.54)	0.42
RR (95% CI) – adjustment 3‡	1.00	1.29 (0.83-2.00)	1.13 (0.72-1.79)	0.99 (0.61-1.59)	0.91 (0.55-1.51)	0.37
<b>WESTERN PATTERN</b>						
	Small intake of Western diet		Medium intake of Western diet		High intake of Western diet	
No. of cases	30	42	46	50	44	
Person-years	48864	49358	49639	49480	49034	
RR (95% CI) – adjustment 1*	1.00	1.07 (0.67-1.72)	1.44 (0.90-2.28)	1.11 (0.67-1.85)	1.24 (0.71-2.14)	0.49
RR (95% CI) – adjustment 2†	1.00	1.07 (0.67-1.72)	1.45 (0.91-2.31)	1.13 (0.68-1.89)	1.29 (0.74-2.25)	0.40
RR (95% CI) – adjustment 3‡	1.00	1.06 (0.66-1.71)	1.45 (0.91-2.31)	1.12 (0.67-1.88)	1.28 (0.72-2.25)	0.43

RR denotes relative risk; CI, confidence interval.

\* Multivariate RRs have been adjusted for age, smoking status, pack-years, (pack-years)<sup>2</sup>.

† Multivariate RRs have been adjusted for age, smoking status, pack-years, (pack-years)<sup>2</sup>, race/ethnicity, physician visits, US region, body mass index, physical activity, multivitamin use and energy intake.

## DISCUSSION

In this large, prospective cohort of US men, two distinct dietary patterns were identified using principal component analysis: the prudent pattern, loaded by a high consumption of fruits, vegetables, fish and whole grains and the Western pattern, loaded by a high intake of refined grains, cured and red meats, desserts and sweets and French fries. During 12 years of follow-up, the risk of newly diagnosed COPD decreased as the prudent pattern score increased, whereas the risk of newly diagnosed COPD increased as the Western pattern score increased.

Studies on the association of individual foods and nutrients and COPD have suggested a beneficial effect of antioxidants, particularly vitamin C, and to a lesser extent vitamin E on COPD or FEV<sub>1</sub> level.[5] However, there is no clear association between one particular food and COPD. Data from the  $\beta$ -carotene and Retinol Efficacy Trial (CARET) conducted in the US including 18,341 heavy smokers and asbestos workers also indicated that vitamin A supplementation has no effect on the rate of decline of lung function in smokers and former smokers.[22] Data from the  $\alpha$ -tocopherol and  $\beta$ -carotene Cancer Prevention Study (ATBC Study) conducted in Finland including 29,133 heavy-smoking men aged 50 to 69 years showed no reduction in COPD symptoms in those receiving beta-carotene or alpha-tocopherol supplements.[23] Preliminary results from the Feasibility of Retinoids in the Treatment of Emphysema (FORTE Study), a multi-center clinical trial conducted in US and including around 150 patients with emphysema, showed no change in respiratory symptoms, lung function testing, and CT scan lung density after supplementation with retinoic acid.[24] Although the effect of any individual nutrient in reducing the risk of COPD may be too small to detect, as suggested by these negative results, when several nutrients are consumed together, the cumulative effect may be sufficient for detection. Indeed, considering diet by an overall approach rather than by specific foods or nutrients may suggest a more comprehensive approach to disease prevention.

In this context, dietary patterns provide an overview of diet and are a good way to assess the relation between diet and newly diagnosed COPD. Dietary patterns have been investigated in relation to several diseases such as cardiovascular diseases,[19] breast cancer,[16] or diabetes [17] but few studies have examined the relationship between dietary patterns and respiratory diseases. Butler et al. identified two patterns in 52,325 adult Chinese Singaporeans, men and women, aged 45 to 74 years old: one 'vegetable, fruit, soy' pattern and one 'meat-dim sum' pattern, corresponding to a high intake of chicken, pork, fish, rice and noodle dishes, and preserved foods.[18] The 'meat-dim sum' pattern was associated with an increase risk of incident cough with phlegm. The second study was performed by our group in the Nurses' Health Study.[unpublished data] Briefly, we identified two dietary patterns among 71,871 women, aged 30 to 55 years old in 1976: a prudent pattern highly loaded by intake of fruits, vegetables, fish and whole grain products, and a Western pattern highly loaded by intake of refined grains, processed and red meats, desserts and French fries. We found that the prudent pattern was associated with a decrease risk of newly diagnosed COPD between 1984 and 2000, and by contrast, that the Western pattern was associated with an increased risk of newly diagnosed COPD.

Although the diet and lifestyle of Chinese Singaporeans are different from those in US people, these findings are consistent with those from the female nurses and from the current study of male health professionals. All three studies suggest a deleterious effect of a diet rich in meat, starchy foods and high-fat dairy products on COPD. The Western diet is highly loaded by processed meats, which one of the most important compound is nitrites. Nitrites generate reactive nitrogen species that provoke nitrosative stress, which may contribute to the progressive deterioration of pulmonary function.[25] The Western diet also was loaded by a high intake of foods with a high glycemic index (refined grains, desserts, sweets, ...). It has been suggested that hyperglycemia was related to an impaired lung function,[26] which remains the main measurement for diagnosis of COPD.[27] Furthermore, both hyperglycemia and COPD are positively related to inflammation,[28, 29] even if the causal association between COPD and the systemic inflammation remains unclear.[30] As several foods (cured meat, refined grains,...) from the Western diet might be related to COPD, the Western pattern offers a good way to summarize the possible effects of these diverse but highly correlated foods.

The finding of the prudent pattern (loaded by fruits and vegetables) being associated with a decrease risk of newly diagnosed COPD is consistent with prior epidemiological literature suggesting a beneficial effect of antioxidants, particularly vitamin C, and to a lesser extent vitamin E on COPD or FEV<sub>1</sub> level.[5] Butler et al. also reported a weak association between their fruits-vegetables-soy pattern and cough with phlegm,[19] which disappeared after adjustment for nonstarch polysaccharide. Nonstarch polysaccharide is a major component of dietary fiber and of some noncitrus fruits. In our study, whole grains products are included in the prudent pattern. Although fiber and whole grain consumptions have not been studied much in relation with COPD, Butler et al. reported in this population of Singaporean Chinese that a diet high in fiber may reduce the incidence of cough with phlegm.[31] In a cross-sectional study, Tabak et al. reported a positive association between whole grain consumption and prevalent COPD in 13,651 men from the MORGEN study.[32] The prudent pattern also was loaded by a high intake of fish, one of the main sources of omega-3 PUFA, but results are still inconsistent across studies,[5] and the only published prospective study observed no relation between intake of omega-3 and the incidence of chronic non-specific lung disease.[9]

Principal component analysis to derive dietary patterns involves several arbitrary decisions on the selection of included variables, the construction of the food groups, the number of retained factors, the method of rotation, and the labels of the factors.[33] In this cohort of men, multiple sensitivity analyses were performed to assess the reproducibility and the robustness of these dietary patterns.[17] Similar patterns were identified after using the maximum likelihood method instead of the principal component method to extract initial factors, after using an oblique rotation instead of an orthogonal one, after retaining three patterns instead of two and even after deriving dietary patterns based on the 131 individual food items rather than from the predefined food groups.[17]

Besides these statistical considerations, our study has other potential limitations. First, we acknowledge that the association between dietary patterns and newly diagnosed COPD may be due, in part, to a residual confounding by cigarette smoking. To minimize this possibility, multivariate models were adjusted with multiple measures of tobacco exposure - smoking habits, pack-years and (pack-years)<sup>2</sup>, but residual confounding effect

by smoking remains an issue. Furthermore, we were not able to adjust for environmental tobacco smoke (ETS), which remains an important risk factor for COPD.[34] Nevertheless, analyses were adjusted for ETS in the Nurses' Health Study and it did not change the result.[20] Secondly, newly diagnosed COPD was defined by a self-reported physician-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 a similar population of female health professionals.[21] The low rate of COPD in this population is probably due to the low smoking rates among health professionals. The main source of misclassification was a misdiagnosis with asthma. Yet our findings for asthma diagnosis were null. While we acknowledge the potential for some misclassifications, these data allowed us to investigate the relationship between dietary patterns and COPD in a very large population, with repeated measurements of both diet and COPD. Finally, due to the relatively small number of cases (n=111), it was not possible to perform stratified analyses according to smoking status or to body mass index. Body mass index is considered a marker a low-grade systemic inflammation and we would have liked to examine possible effect modification by this factor. Recently, Celli et al. have suggested that BMI is an important issue regarding the severity of COPD [35] and in the Nurses' Health Study, we reported a significant interaction between BMI and the Western pattern. The association between the Western pattern and the risk of newly diagnosed COPD was stronger in lean ( $BMI \leq 20 \text{ kg/m}^2$ ) than in others women, even if the mechanism for the observed interaction requires further study.

In summary, we report the first study on dietary patterns in relation to the risk of newly diagnosed COPD in men. We identified two major dietary patterns, the prudent and the Western patterns and found that both are associated with risk of newly diagnosed COPD. The prudent pattern was negatively associated with the risk of newly diagnosed COPD, whereas the Western pattern was positively associated with the risk of newly diagnosed COPD. Temporal changes in dietary patterns may contribute to ongoing increases in COPD.

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## **COMPETING INTERESTS**

RV, TTF, FBH, WW: None declared

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## Appendix 1 Food groupings for factor analysis

<b>Foods or food groups</b>	<b>Food items</b>
Processed meats	Hot dogs, processed meats, bacon
Red meats	Hamburger, beef, pork, lamb
Organ meats	Liver
Fish	Canned tuna, dark meat fish, oily fish, shrimp
Poultry	Chicken or turkey with or without skin
Eggs	Eggs
Butter	Butter
Margarine	Margarine
Low-fat dairy	Skim milk, yogurt, sherbet, cottage cheese
High-fat dairy	Whole milk, cream, sour cream, cream cheese, ice-cream, other cheese
Liquor	Liquor
Wine	White wine, red wine
Beer	Beer
Tea	Tea
Coffee	Regular coffee, decaffeinated coffee
Fruit	Raisins, avocado, orange, grapefruit, banana, cantaloupe, water melon, apple, strawberry, blueberry, peach, apricots, plums
Fruit juice	Orange juice, apple juice, grapefruit juice, other juice
Cruciferous vegetables	Broccoli, cabbage, kale, cauliflower, Brussels sprouts
Yellow vegetables	Carrots, yellow squash, yam
Tomatoes	Tomatoes, tomato juice, tomato sauce
Leafy vegetables	Raw spinach, cooked spinach, iceberg lettuce, romaine or leaf lettuce
Legumes	Tofu, string bean, peas, beans or lentils
Other vegetables	Corn, mixed vegetables, eggplant, celery, mushroom, beets, alfalfa sprouts
Potatoes	Potatoes
Fries	French fries
Whole grains	Dark breads, oatbran, brown rice, wheat germ, oats, cooked cereal, whole grain ready-to-eat cereals, other grains
Refined grains	White bread, white rice, English muffins, pasta, pancake, refined grain ready-to-eat cereals
Snacks	Potato chips, popcorn, crackers
Nuts	Peanut butter, nuts
Sugar beverages	Cola, caffeine-free cola, fruit punch, other carbonated beverages
Low-calorie beverages	Diet cola, diet caffeine-free cola, other diet carbonated beverages
Desserts/sweets	Chocolate bars or pieces, candy bars, cookies, brownies, doughnuts, cake, pie, sweet roll, coffee cake, pastry
Garlic	Garlic
Condiments	Jam, mustard, pepper, salt, chili sauce, coffee, whitener
Salad dressings	Oil and vinegar type dressings
Cream soups	Chowder/cream soups
Mayonnaise	Mayonnaise type salad dressings
Pizza	Pizza
Olive oil*	Olive oil
Added salt*	Added salt

\* These particular items were available only on 1990 and 1994 FFQs.