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Abstract

Cured meats are high in nitrites. Nitrites generate reactive nitrogen species that may cause damage to the lung. The objective is to assess the relation between frequent consumption of cured meats and the risk of newly diagnosed chronic obstructive pulmonary disease (COPD). Between 1986 and 1998, we identified 111 self-reported cases of newly diagnosed COPD among 42,915 men from the Health Professionals Follow-up Study. The cumulative average intake of cured meats consumption (processed meats, bacon, hot dogs) was calculated from food frequency questionnaires administrated in 1986, 1990 and 1994, and divided according to servings per week (never/almost never, <1 serving/week, 1–3 serving/week, 4–6 serving/week, at least once/day). After adjustment for age, smoking status, pack-years, pack-years2, energy intake, race/ethnicity, US region, body mass index and physical activity, the consumption of cured meats was positively associated with the risk of newly diagnosed COPD: RR for highest vs. lowest intake = 2.64 (95% confidence interval, 1.39 – 5.00), p for trend = 0.002. In contrast to these findings, the consumption of cured meats was not associated with the risk of adult-onset asthma. These data suggest that cured meat may worsen the adverse effects of smoking on risk of COPD.

MESH Keywords Adult ; Aged ; Body Mass Index ; Chi-Square Distribution ; Diet ; statistics & numerical data ; Food Preservation ; Humans ; Life Style ; Male ; Meat Products ; Middle Aged ; Nitrites ; administration & dosage ; toxicity ; Phenotype ; Proportional Hazards Models ; Prospective Studies ; Pulmonary Disease ; Chronic Obstructive ; epidemiology ; Questionnaires ; Risk Factors ; United States ; epidemiology

Author Keywords meat ; chronic obstructive pulmonary disease ; nitrites ; men ; diet

Cured meats contain various compounds added to meat products as preservatives and color fixatives1, among which the most important are nitrites. Nitrites generate reactive nitrogen species that can amplify inflammatory processes in the airways and lung parenchyma causing DNA damage, inhibition of mitochondrial respiration and nitrosative stress3. The long-term persistence of nitrosative stress may contribute to the progressive deterioration of pulmonary function and may be implicated in the pathogenesis of chronic obstructive pulmonary disease (COPD)4.

Currently, COPD is the fourth leading cause of mortality in Europe and in the United States5. With the increase in cigarette smoking in developing countries, COPD is expected to become the third leading cause of death worldwide by 20206. Cigarette smoking is the most important risk factor for COPD in developed nations7, but not all smokers develop COPD8 - an observation that suggests that others factors also are involved. In the last decade, there has been a growing interest to identify foods related to the level of lung function or COPD symptoms 9. Most investigations have focused on foods with antioxidant properties, and not foods with a potential deleterious effect.

Two recent studies have tested the hypothesis that frequent consumption of cured meats increases the risk of COPD: a cross-sectional study of more than 7,000 men and women10, and a longitudinal study of more than 71,000 women11. Both reported a positive association between the frequent consumption of cured meats and an increased risk of COPD. Gender differences in the manifestations and diagnosis of obstructive airway disease over the human life span12, as well as gender differences in food choices and energy intake13 provide a compelling rationale to study the relation between cured meat and COPD among men as well. We therefore examined the association between cured meats consumption and risk of newly diagnosed COPD in a prospective cohort of more than 40,000 men.

MATERIALS AND METHODS

Study population

The Health Professionals Follow-up Study, a prospective cohort study, began in 1986 when 51,529 US health professionals (dentists, optometrists, pharmacists, podiatrists, and veterinarians) 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 ascertain newly diagnosed medical conditions. Dietary intake data were collected in 1986, and every four years thereafter with a 131-item food frequency questionnaire. 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 megajoules (800 and 4200 kilocalories) or who left blank more than 70 of a total of 131 food items on the diet questionnaire were excluded. We further excluded 232 men with confirmed COPD at baseline or missing date of diagnoses, 1,834 with reported asthma, and 272 with unconfirmed COPD at baseline or during the follow-up. The final baseline population included 42,915 men.

Consumption of cured meats

Cured meats consumption was defined as the total consumption of processed meats, bacon and hot dogs, which were asked as three separate questions: "how often on average you have used the amount specified during the past year: 1) processed meats, e.g. sausage, salami, bologna, … (slice); 2) bacon (2 slices); 3) hot dogs (1)". 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/d." The selected frequency category for each food item was converted to a daily intake. Cured meats consumption was identified from food frequency questionnaires administrated in 1986, 1990 and 1994. To reduce measurement errors and to represent long-term dietary intake, the cumulative average of cured meats consumption was calculated, and then divided into five categories according to the number of servings per week: never/almost never, <1 serving/week, 1–3 serving/week, 4–6 serving/week, and at least once/day. The cumulative average incorporated repeated measures of diet14. With this approach, the 1986 cured meat consumption was used to predict newly-diagnosed COPD in 1986–1990, an average of the 1986 and 1990 cured meat consumption, to predict COPD in 1990–1994 and the average of the 1986, 1990 and 1994 cured meat consumption, to predict COPD from 1994 to 1998. The individual associations with processed meats, bacon and hot dogs were also investigated in relation with newly diagnosed COPD. The cumulative average was calculated for each one of these cured meats, and then divided into three categories according to the number of servings per week (never/almost never, <1 serving/week, and at least once/week).

Assessment of respiratory phenotypes

Because the Health Professionals Follow-up Study includes many participants dispersed throughout the US and is conducted by mail, the diagnosis of COPD was assessed by questionnaire and did not include spirometry. Supplemental questionnaires were sent in 1998 and 2000 to all participants who reported chronic bronchitis or emphysema on the biennial questionnaires. Self-reported COPD was defined by the affirmative response to physician-diagnosed chronic bronchitis or emphysema on the biennial questionnaires, confirmation of chronic bronchitis, emphysema or COPD on the supplemental COPD questionnaire, plus report of a diagnostic test at diagnosis (pulmonary function testing, chest radiograph, or chest computed tomography). This epidemiologic definition was validated in a random sample of another cohort of health professionals15. Between 1986 and 1998, 111 cases of newly diagnosed COPD that were reported met these criteria.

Asthma was also self-reported and was defined by a new physician diagnosis of asthma on the biennial questionnaires, confirmation on the supplemental asthma questionnaire, plus use of medication for asthma in the twelve months preceding the supplemental questionnaire. Between 1986 and 1998, 212 new cases of adult-onset asthma were reported.

Assessment of others variables

Total calorie intake was estimated through the food frequency questionnaire, expressed in kilocalorie per day (kcal/d). Information on smoking status included the categories never smokers, ex smokers, and current smokers. We further characterized smokers using their lifetime pack-years of smoking and pack- years square (pack-years2); prior analyses have demonstrated that including both measures optimally controls for the association between smoking and COPD risk. Data on race/ethnicity and region also were collected. Race/ethnicity was categorized in two classes (white, non-white), 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/height2 (kg/m^2) and was categorized into four classes: ≤ 20.0, 20.0–24.9, 25.0–29.9, ≥ 30.0 kg/m^2. Men also reported physical activity, including a variety of activities such as walking, bicycle, swimming or tennis. Physical activity was measured in metabolic equivalent-hours per weeks (METs), where one metabolic equivalent was equal to the energy expended at the basal metabolic rate or at rest.

Previously, in this cohort of men, a strong association between dietary patterns and the risk of newly diagnosed COPD was reported16. The "prudent pattern" was loaded by a high consumption of fruits, vegetables, fish and whole grains and was negatively associated with newly diagnosed COPD, whereas the “western pattern” was loaded by a high intake of refined grains, cured and red meats, desserts and sweets and French fries and was positively associated with newly diagnosed COPD. Because cured meats are a food group included in the western pattern, we derived a new western pattern without contribution from cured meats, and we termed this the “modified western pattern”.

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 and energy intake and then for seven variables (smoking status, pack-years, pack-years2, race/ethnicity, US region, BMI and physical activity). We intensively adjusted for smoking (smoking status, pack-years, pack-years2) because it is the main risk factor for COPD and because smokers tend to have a different diet than non smokers17. We also adjusted for race/ethnicity because death rates from COPD are rising faster in African Americans than in whites18 and because diet is highly related to racial/ethnic identity. To take into account geographical disparities in COPD and diet across the US, we also adjusted for US region. The adjustment for BMI and physical activity was motivated by the strong interrelationships between diet, BMI and physical activity. Furthermore, low BMI is highly related to COPD19 and it has been reported that physical activity is associated with lower risk of COPD20.

In a subsequent analysis, we also adjusted for the prudent dietary pattern and the “modified western pattern” to better assess the individual effect of cured meat intake and to control for the other potential deleterious effect of the Western diet. All analyses were conducted using SAS software, version 9 (Cary, NC, USA).

RESULTS

The characteristics of the cohort, according to the consumption of cured meats, are presented in table 1. Compared with men eating the most cured meats (≥1 serving/day), men with the lowest intake of cured meats (never/almost never) were more physically active, less likely to be current smokers and had a lower BMI. Men with the highest consumption of cured meats were more likely to eat processed meats than to eat bacon or hot dogs. At baseline, 27% of men reported that they never ate processed meat, while 51% ate less than one serving per week and 22% ate at least one serving per week. The comparable analysis for bacon yielded 38% never, 50% less than one serving per week, and 12% at least one serving per week. Likewise, the results for hot dogs were 44% never, 51% less than once per week, and 5% at least once per week. The consumption of cured meats was positively associated with the risk of newly diagnosed COPD in age-adjusted analysis (RR for highest vs. lowest consumption of cured meats [95%CI] was 4.09 [2.32–7.22], with p for trend < 0.001), and even after adjustment for age and energy intake (Table 2). After controlling for smoking status, pack-years and pack-years2, the positive association between cured meats and the risk of newly diagnosed COPD remained. Further adjustments for race/ethnicity, US region, BMI and physical activity revealed the same significant positive association (table 2). Further adjustment for the prudent diet led to similar results: RR for highest vs. lowest consumption of cured meats [95%CI] was 2.43 [1.26–4.68], with p for trend = 0.006. Adjustment for the “modified western pattern” led to a borderline significant association: RR for highest vs. lowest consumption of cured meats [95%CI] was 1.88 [0.96–3.69], with p for trend = 0.06. The “modified western pattern” remained highly related to the risk of newly diagnosed COPD after adjustment for cured meats (RR for highest vs. lowest quintile of the “modified western pattern” [95%CI] was 4.49 [1.67–12.07], with p for trend = 0.001).

When the population was restricted to men without cancer or cardiovascular disease at baseline (n=35,284), similar associations were found. The consumption of cured meats was positively associated with the risk of newly diagnosed COPD after adjustment for age and energy intake: RR for highest vs. lowest consumption of cured meats (95%CI) was 3.56 (1.46–8.66), with p for trend < 0.001. Further adjustment for smoking status, pack-years, pack-years2, race/ethnicity, US region, BMI and physical activity led to similar result the RR for highest vs. lowest consumption of cured meats [95%CI] was 1.81 [0.88–4.76], with p for trend = 0.01.

Of the three individual cured meats foods (processed meats, bacon, hot dogs), only the consumption of processed meats was significantly associated with the risk of newly diagnosed COPD (RR for highest vs. lowest consumption of processed meats [95%CI] was 1.93 [1.13–3.28], with p for trend = 0.02). A significant association was found for the consumption of bacon (RR for highest vs. lowest consumption of bacon [95 %CI] was 1.79 [0.99–3.22], with p for trend = 0.03) and no relation was found for hot dogs consumption (p for trend = 0.43).

On average over the study period, among the 111 cases of COPD, about 86% reported a history of cigarette smoking. Considering different time periods, the cases occurring between 1990 and 1992 (n=12) had the highest proportion of smokers: 67% were smokers and 12% were ex smokers. Considering “ever smoker” (n=96 cases), the age-adjusted RR [95% CI] for ever smokers vs. never smokers was 3.90 [2.26–6.72], p < 0.001. Because smoking is the main risk factor for COPD, we conducted additional analyses excluding never smokers. This analysis was performed among 27,755 men with a history of cigarette smoking (96 cases) and we found that the consumption of cured meats was strongly and positively associated with the risk of newly diagnosed COPD (table 3).

To examine whether smoking status modifies the relationship between cured meat consumption and COPD risk, we conducted multivariate analyses stratified according to smoking status (table 4). We combined the two highest categories of cured meats consumption because of the small number of cases. After adjustment for age, energy intake, smoking status, pack-years and pack-years2, the relative risk comparing the highest vs. the lowest categories of cured meat consumption was 2.39 [95% CI, 0.91–6.27], with p for trend = 0.07 in past smokers and was 2.69 [95% CI, 1.11–6.56], with p for trend = 0.03 in current smokers.

Although the primary outcome of this study was newly diagnosed COPD, we also examined the relation between cured meats with adult-onset asthma, due to the potential overlap between the diagnoses of COPD and asthma (table 5). In contrast with the risk of newly diagnosed COPD, no association was found between the consumption of cured meats and the risk of adult-onset asthma.

DISCUSSION

In this large prospective cohort of US men during 12 years of follow-up, the risk of newly diagnosed COPD increased with a greater consumption of cured meats after adjustment for many important confounders. Among the individual cured meats, consumption of processed meats was significantly associated with the risk of newly diagnosed COPD and a borderline significant association was found for bacon. In contrast to the COPD findings, there was no association between consumption of cured meats and risk of adult-onset asthma.

The sodium salts of nitrate (NaNO3) and nitrite (NaNO2) are used in the curing and preserving of processed meats. They are used for three purposes: to preserve color, especially the pink color for hot dogs and other cured meats; to enhance flavor by inhibiting rancidity; and to protect against bacterial growth2. Regulations controlling the use of curing agents were established in the USA in 1926, and the same rules are in effect at present, with slight modification. The critical feature of these rules is that a maximum use level of sodium nitrite is defined: no more than one-quarter ounce (7.1 g) may be used per 100 pounds (45.4 kg) of meat. Bacon has been a focus of special attention. Because it is so widely consumed and the risk of infection with anaerobic Clostridium botulinum is relatively high2, the regulations were changed for bacon with ingoing nitrite targeted at 200 ppm. A similar regulation was applied to other cured meats, such as ham, sausages and corned beef.

In an inflammatory microenvironment, exaggerated production of NO in the presence of "oxidative stress" may produce the formation of strong oxidizing reactive nitrogen species, such as peroxynitrite, leading to nitration which provoke DNA damage, inhibition of mitochondrial respiration, protein dysfunction and cell damage ("nitrosative stress")21, 22. Reactive nitrogen species have been implicated in the pathogenesis of COPD4. The level of nitrotyrosine immunoreactivity, a marker or production of reactive nitrogen species, was higher in COPD patients than in healthy subjects23 and correlated with the level of obstruction in COPD patients24, suggesting that nitrosative stress might be involved both in the risk of COPD and in the progression of the disease. These findings are also consistent with animal studies reporting that rats drinking water enriched with sodium nitrite for two-years, developed pulmonary emphysema25.

The hypothesis that frequent consumption of cured meats might be associated with increased risk of COPD was first tested in a cross-sectional study of 7,432 men and women in the Third National Health and Nutrition Examination Survey10. Jiang et al. reported that frequent consumption of cured meats was associated with low lung function (forced expiratory volume in one second - FEV_1) and with an increased risk of COPD. To address a possible reverse causation due to the cross-sectional design, Jiang et al. then tested the association in a longitudinal study from 1984 to 2000 of more than 71,000 US women11. The longitudinal analysis supported the hypothesis that frequent consumption of cured meats was positively associated with the risk of newly diagnosed COPD in women.

Prior epidemiological studies suggested a beneficial association between foods rich in antioxidants and COPD status or FEV_1 level9. Most of these epidemiological studies are cross- sectional26–29, but the few longitudinal studies also have reported a negative association between intake of fruits, vegetables and vitamin C and the decline of FEV_1 30–32. Previously, it was reported in this male cohort a strong association between the prudent dietary pattern and the risk of newly diagnosed COPD16. Adjustment for this "protective" diet did not affect our finding of a strong, independent, positive association between cured meat consumption and COPD risk. It also was previously reported a strong positive association between the western dietary pattern and COPD risk16. Because the western pattern was highly loaded by the cured meats food group, a new pattern was derived in the present analysis to exclude this food group. The association between cured meat and the risk of newly diagnosed COPD remained, although with wider confidence intervals and marginal significance, after taking into account the "modified western pattern". The Western pattern was also loaded by refined grains, red meats, desserts and sweets and French fries and among all these food groups, only cured meats increased the risk of COPD. We also note that the "modified western pattern" remained strongly associated with the risk of newly diagnosed COPD after adjustment for cured meats and that both the "modified western diet" and cured meat contributed independently to the risk of COPD.

The study has several potential limitations. First, we acknowledge that the association between cured meats 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-years2) and despite the small numbers of cases, stratified analysis according to smoking status yielded comparable results. Nevertheless, residual confounding effect by smoking remains an issue. Furthermore, we were not able to adjust for environmental tobacco smoke, which remains an important risk factor for COPD33. Nevertheless, adjustment of cured meats and COPD analyses in the Nurses' Health Study for environmental tobacco smoke did not attenuate the association11.

Secondly, newly diagnosed COPD was defined by a self-reported physician-diagnosis of COPD and no lung function results were available. Nevertheless, validation of an identical, questionnaire-based definition of newly diagnosed COPD in a similar study of female health professionals showed that 80% of a random sample of cases meeting this definition had medical record documentation of COPD, and the mean FEV_1 among those with available spirometry reports was 50 percent of predicted15. In addition, since the main source of misclassification of COPD reported by health professionals was misdiagnosis with asthma, we examined the association of cured meats and the risk of adult-onset asthma. The complete lack of association of cured meat intake with asthma suggests that our findings are unlikely to be due to misclassification with asthma. While we acknowledge the potential for some misclassifications, the HPFS data allowed us to investigate the relationship between cured meats and COPD in a very large population, with repeated measurements of both diet and COPD status.

Even if diet is assessed every four years with accurate food frequency questionnaires, we lacked a specific measure of nitrite intake to more specifically examine the biological mechanism that we believe explains our results. However, cured meats contain thousands of biologically active phytochemicals other than nitrites and it remains possible that they too might be involved in the increase risk of COPD. For example, cured meats are rich in sodium and experimental studies suggest that a high intake of sodium may increase bronchial hyperresponsiveness, although the association with other respiratory endpoints such as medication use and lung function was not consistent34.

In summary, the consumption of cured meats was positively associated with the risk of newly diagnosed COPD. Although several compounds may be responsible for this finding, we believe that nitrites provide a very plausible biological mechanism. Because of emerging evidence regarding the deleterious effect of cured meats in other diseases (e.g., cancer35 and diabetes36), we recommended reduce daily intake of cured meats. For COPD prevention, the most important public health message remains smoking cessation but our data suggest that diet, another modifiable risk factor, might influence COPD risk. Future studies of actual levels of nitrite intake and COPD risk would be useful, as well as the examination of this novel association in other datasets.

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Abbreviations

BMI: body mass index

CI: confidence interval

COPD: chronic obstructive pulmonary disease

FEV_1 : forced expiratory volume in one second

g/day: gram per day

HPFS: Health Professionals Follow-up Study

kcal/day: kilocalories per day

kg/m^2 : kilogram by meter square

METs/week: metabolic equivalents per week

Pack-years^2 : pack-years square

RR: relative risk

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Table 1

Age-standardized baseline characteristics in 42,915 men, according to consumption of cured meats in 1986, Health Professionals Follow-up Study, USA, 1986–1998.

	Frequency of cured meats consumption				
	Never/almost never (n=6,580)	**<l/week (n=10,828)**	**1–3 /week (n=9,369)**	**4–6 /week (n=7,819)**	**1/day (n=8,31**
Cured meats consumption*					
Processed meats (servings/week)	0.0	0.3	0.7	1.6	3.5
Bacon (servings/week)	0.0	0.2	0.6	1.0	2.3
Hot dogs (servings/week)	0.0	0.2	0.5	0.6	1.2
Total energy (kcal)*	1763	1814	1936	2062	2364
Smoking habits (%)					
Never smokers	52	48	45	44	41
Ex- smokers	40	41	42	41	42
Current smokers	4	7	9	11	14
Pack- years of smoking	8.8	10.6	12.3	13.0	14.8
White race/ethnicity (%)	89	91	91	92	92
US region (%)					
ES central	2	3	4	5	6
Mountain	7	7	8	8	7
Others regions	90	89	88	87	87
Body mass index (kg/m^2)*	24.5	25.3	25.6	25.8	26.0
Physical activity (METs/week)* †	32.0	25.8	25.2	23.4	23.1
Antioxidant foods consumption*					
Total vegetables (servings/day)	3.4	2.9	2.7	2.8	2.9
Fruits (servings/day)	2.2	1.7	1.5	1.4	1.4
Fish (servings/day)	0.5	0.4	0.4	0.3	0.3

* Age-adjusted mean

† METs: metabolic equivalent.

Table 2

Association between consumption of the cumulative average of cured meats and newly diagnosed COPD, Health Professionals Follow-up Study, USA, 1986–1998, n=42,915 men

	Frequency of cured meats consumption					
	Never/almost never	**< 1 serving/week**	**1–3 serving/week**	**4–6 serving/week**	**1 serving/day**	**p for tr**
No. of cases	10	19	15	20	47	
Person-years	37806	62212	54112	44899	47793	
RR (95% CI) – adjustment 1*	1.00	1.34 (0.73–2.43)	1.12 (0.55–2.29)	2.00 (1.04–3.81)	3.86 (2.13–6.97)	<0.001
RR (95 % CI) – adjustment 2†	1.00	1.43 (0.78–2.62)	1.10 (0.54–2.27)	1.79 (0.93–3.46)	3.06 (1.66–5.60)	<0.001
RR (95 % CI) – adjustment 3‡	1.00	1.29 (0.69–2.42)	0.97 (0.46–2.04)	1.57 (0.79–3.11)	2.64 (1.39–5.00)	0.002

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^2.

‡ Multivariate RRs have been adjusted for age, energy intake, smoking status, pack-years, pack-years^2, race/ethnicity, US region, body mass index and physical activity.

Table 3

Association between consumption of the cumulative average of cured meats and newly diagnosed COPD in ex and current smokers, Health Professionals Follow-up Study, USA, 1986–1998, n=27,755

	Frequency of cured meats consumption					
	Never/almost never	**< 1 serving/week**	**1–3 serving/week**	**4–6 serving/week**	**1 serving/day**	**p for trend**
No. of cases	12	23	12	18	31	
Person-years	39832	39600	24576	20638	20038	
RR (95% CI) – adjustment 1*	1.00	1.99 (0.98–4.04)	1.76 (0.79–3.96)	3.06 (1.45–6.44)	5.54 (2.76–11.13)	<0.001
RR (95 % CI) – adjustment 2†	1.00	2.04 (1.00–4.19)	1.62 (0.71–3.67)–	2.62 (1.23–5.57)	4.30 (2.11–8.78)	<0.001
RR (95 % CI) – adjustment 3‡	1.00	1.88 (0.89–3.97)	1.45 (0.61–3.41)	2.32 (1.05–5.14)	3.78 (1.77–8.08)	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 (ex or current smokers), pack-years, pack-years^2.

‡ Multivariate RRs have been adjusted for age, energy intake, smoking status (ex or current smokers), pack-years, pack-years^2, race/ethnicity, US region, body mass index and physical activity.

Table 4

Association between consumption of the cumulative average of cured meats and newly diagnosed COPD according to smoking, Health Professionals Follow-up Study, USA, 1986–1998.

	Frequency of cured meats consumption			
	Never/almost never	**< 1 serving/week**	**1 serving/week**	**p for trend**
IN EX SMOKERS				
No. of cases	5	12	30	
Person-years	21936	28434	47362	
RR (95% CI) – adjustment 1*	1.00	2.00 (0.70–5.70)	2.85 (1.09–7.45)	0.03
RR (95 % CI) – adjustment 2†	1.00	1.88 (0.66–5.35)	2.39 (0.91–6.27)	0.07
IN CURRENT SMOKERS				
No. of cases	7	11	31	
Person-years	17896	11166	17890	
RR (95% CI) – adjustment 1*	1.00	2.49 (0.92–6.76)	4.93 (2.07–11.76)	<0.001
RR (95 % CI) – adjustment 2†	1.00	2.06 (0.76–5.58)	2.69 (1.11–6.56)	0.03

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, pack-years and pack-years^2.

Table 5

Association between consumption of the cumulative average of cured meats and adult onset asthma in men, Health Professionals Follow-up Study, USA, 1986–1998.

	Frequency of cured meats consumption					
	Never/almost never	**< 1 serving/week**	**1–3 serving/week**	**4–6 serving/week**	**1 serving/day**	**p for tr**
No. of cases	28	50	47	49	38	
Person-years	37768	62127	54151	44761	47556	
RR (95% CI) – adjustment 1*	1.00	1.26 (0.86–1.85)	1.30 (0.85–1.99)	1.30 (0.82–2.04)	1.07 (0.65–1.77)	0.63
RR (95 % CI) – adjustment 2†	1.00	1.17 (0.80–1.72)	1.20 (0.78–1.84)	1.21 (0.77–1.92)	1.02 (0.61–1.69)	0.80
RR (95 % CI) – adjustment 3‡	1.00	1.11 (0.76–1.72)	1.18 (0.79–1.82)	1.19 (0.81–1.87)	0.99 (0.60–1.69)	0.88

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^2.

‡ Multivariate RRs have been adjusted for age, energy intake, smoking status, pack-years, pack-years^2, race/ethnicity, US region, body mass index and physical activity.