



Association between processed meat intake and asthma symptoms in the French NutriNet-Santé cohort

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Abstract

Purpose Processed meat intake may adversely affect lung health, but data on asthma remains sparse. The magnitude of the processed meat–asthma association may also depend on other unhealthy behaviors. We investigated the association between processed meat intake and the asthma symptom score, and the combined role of unhealthy weight, smoking, low diet quality, and high processed meat intake on the asthma score.

Methods In 2017, 35,380 participants to the NutriNet-Santé cohort answered a detailed respiratory web-questionnaire. Asthma was defined by the asthma symptom score (sum of 5 questions; continuous variable). Based on repeated 24-h dietary records collected on a dedicated website, processed meat consumption was classified as 0, < 2, 2–5, > 5 servings/week. We examined the combined role of body mass index (BMI) (< 25 vs. ≥ 25 kg/m²), smoking (never vs. ever), diet quality score (highest vs. lowest), and processed meat (≤ 5 vs. > 5 servings/week) on the asthma symptom score.

Results Participants were aged 54 on average (women: 75%, smokers: 49%, BMI ≥ 25: 32%, ≥ 1 asthma symptoms: 27%). After adjustment for confounders, processed meat intake was positively and significantly associated with asthma symptom score: odds ratios (ORs) (95% CI) for > 5 vs. 0 servings/week were 1.15 (1.04–1.27) in women; 1.23 (1.01–1.50) in men. Compared to participants with 0 unhealthy behaviors, ORs for the asthma symptom score among participants with the 4 combined unhealthy behaviors were 2.18 (1.91–2.48) in women; 2.70 (2.10–3.45) in men.

Conclusion High processed meat consumption was associated with higher asthma symptoms, and combining overweight/obesity, smoking, low diet quality, with high processed meat intake was strongly associated with asthma symptoms.

Keywords Processed meat · Asthma symptom score · Obesity · Smoking · Unhealthy diet

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Introduction

Recently, sufficient evidences have led the World Health Organization (WHO) to classify processed meat, an important component of Western diet, as carcinogenic to humans [1]. Actually, high processed meat consumption has been associated with increased risk of all-cause mortality [2] and is a risk factor for several major chronic diseases such as type 2 diabetes [3], coronary heart disease [3] or stroke [4].

Regarding lung health, processed meat intake has been associated with a likely increased risk of lung cancer [5], decline of lung function [6] and chronic obstructive pulmonary diseases (COPD) [7–10]. However, in two studies conducted in the USA among women [8] and men [7] which reported a positive association between processed meat intake with the risk of COPD, no significant association was found with the risk of asthma based on a dichotomous

definition of asthma. Recently, a study conducted in France reported positive association between high processed meat intake with the asthma symptom score [11]. The asthma symptom score, proposed as a continuous measure of asthma, was found to be particularly relevant to investigate in epidemiological studies the diet-asthma association [12, 13]. Processed meat contains many compounds such as salt, nitrite or other products which are used for the purposes of preservation, flavor and color. Although the role of processed meat in the pathogenesis of asthma remains unclear, plausible mechanisms involving potential role of high nitrite level, advanced glycation end products and salt have been proposed [8]. Nitrite, especially, can generate reactive nitrogen species that could increase or lead to oxidative and nitrosative stress. The latter can amplify inflammatory process in the airways, and may contribute to progressive deterioration of pulmonary function and asthma pathogenesis [14].

The association between processed meat and asthma may also depend on other important and potentially modifiable factors—reported to be associated with lung health and, in particular, with asthma—which influence the pulmonary oxidant/antioxidant balance and inflammation, such as obesity [15], smoking [16] or unhealthy diet [17–19]. It is now admitted that obesity is a likely risk factors for asthma [15]. Previous studies have reported that smoking was associated with asthma and particularly with worsening of asthma symptom [16]. More recently, association between unhealthy diet and asthma has also been reported [17–19], and we previously reported that healthier diet behaviors were associated with less asthma symptoms [20]. A recent study has reported an independent direct effect of processed meat intake on asthma symptoms, and that only 14% of this association was mediated by body mass index (BMI) [11]. Thus, it is reasonable to posit that processed meat intake may have an independent effect on asthma. To our knowledge, these concepts have not been yet examined and the combined impact of “unhealthy behaviors” (e.g., unhealthy weight, smoking, unhealthy diet, and high processed meat intake) on asthma has not been investigated before.

In the present study, we aimed to investigate in a large French cohort of adults, the association between processed meat intake with the asthma symptom score, and to further investigate the combined effect of unhealthy behaviors on the asthma symptom score.

Methods

Study population

Participants were taken from a sample of volunteers from the NutriNet-Santé study, a large web-based prospective observational cohort launched in France in May 2009 including

more than 160,000 participants (aged older than 18 years). Methods and aims of the NutriNet-Santé study have been extensively described elsewhere [21]. Briefly, its main objective is to investigate the relationship between nutrition and health as well of determinants of dietary behaviors and nutritional status. At enrolment, participants completed a set of questionnaires. During the follow-up, participants received monthly automated emails informing that new questionnaires are available in the secured platform. All participants provided electronic informed consent and all procedures were approved by the Institutional Review Board of the French Institute for Health and Medical Research and the French Institutional Ethics Committee. The NutriNet-Santé Study is registered in ClinicalTrials.gov (NCT03335644).

Dietary data collection

Participants were invited to complete three nonconsecutive self-administered web-based 24-h dietary records randomly distributed within a two-week period at baseline and every 6 months. Self-administered web-based 24-h dietary records has been validated against urinary [22] and plasma biomarkers [23] and against interview by a trained dietitian. In the present study, we included participants who completed at least three 24-h dietary records since their inclusion till 2 years of follow-up, independently of when they were conducted. They reported all foods and beverages consumed throughout the day and the place of each eating occasion were systematically recorded. Portion size for each foods and beverages were estimated using validated photographs [24] and participants can also directly enter the quantity consumed in grams or volume. Daily dietary intake was calculated as the average of at least three 24-h dietary records. Nutrients intakes were estimated using the NutriNet-Santé food composition table, which includes more than 3000 different items [25].

Processed meat included ham, sausage and dried sausage, pâtés, terrines and rillettes. According to participant's consumption frequency of processed meat and to its distribution, we categorized processed meat into four classes: never (0 serving/week; non-exposed group), < 2 servings/week, 2–5 servings/week, and > 5 servings/week. One serving of processed meat corresponds to 50 grams.

The nutritional quality of the diet was assessed by the Alternative Healthy Eating Index 2010 (AHEI-2010), which was designed to target food choices and macronutrient sources associated with reduced chronic disease risk [26] and for which we previously reported in the NutriNet-Santé cohort a negative and significant association with the asthma symptom score [20]. Scoring criteria for the AHEI-2010 have been described elsewhere [26]. Briefly, the AHEI-2010 includes 11 components: six components for which the highest intake was supposed to be ideal, one component

for which moderate intake was supposed to be ideal, and four components for which avoidance or lowest intake was supposed to be ideal. Each component is given a minimal score of 0 and a maximal score of 10, with intermediate values scored proportionally, and all the component scores are summed to obtain a total AHEI-2010 score which ranges from 0 to 110. To account for the overall remaining effect of diet (besides processed meat), we computed a modified AHEI-2010 including all the items except for processed meat and *trans*-fat (not available in the food composition table); therefore, the highest value was 90. The modified AHEI-2010 was divided into sex-specific tertiles.

The respiratory survey in the NutriNet-Santé cohort

To improve the respiratory characterization in the cohort, a non-mandatory detailed questionnaire on respiratory health based on international standardized recommendations with adapted questions from the European Community Respiratory Health Survey (ECRHS) [27] and the French EGEA study [28] was proposed in April 2016 to all the active participants ($n=121,568$). As June 2017, the survey was filled-in by 40,152 adults. Respondents ($n=40,152$) were significantly older as compared to non-respondents ($n=81,416$). After adjustment for age, they were also more likely never smokers, had a higher educational level, were more physically active, and less likely to be obese [20]. Ever asthma was defined by at least one positive answer to the question “Have you ever had asthma?” in main questionnaires or by a positive answer to “Have you ever had an asthma attack?” or “Have you ever had an attack of shortness of breath at rest with wheezing” in the respiratory survey.

We used the asthma symptom score [12, 13] which has been proposed previously as a continuous measure of asthma and widely used over the last 10 years in epidemiological studies [18, 29–32]. It is a validated score, ranging from 0 to 5, based on the number of respiratory symptoms during the past 12 months.

Allergic rhinitis was defined as a positive answer to “Have you ever had allergic rhinitis?” or “Have you ever had hay fever?”. Information about family history of asthma was also collected (yes/no).

Covariates assessment

At baseline, participants answered to validated self-administered questionnaires [33] to collect data on sociodemographic characteristics, lifestyle, physical activity and anthropometric measurements. Educational level was classified in four groups (<13 , 14, 15–16, ≥ 17 years), and smoking status in three groups (never smokers, ex-smokers, current smokers). Among ever smokers, pack-years were calculated to estimate the amount of tobacco smoke. BMI

was calculated as weight (kg)/height² (in m²) and categorized according to the WHO classification (<18.5 , 18.5–24, 25–29, ≥ 30 kg/m²) [34]. Self-reported leisure-time physical activity was estimated using the French short form of the International Physical Activity Questionnaire (IPAQ) [35] and classified in three intensity [vigorous (≥ 60 min/day), moderate (30–59 min/day), low (<30 min/day)].

Statistical analysis

Among the 40,152 participants who filled in the questionnaire on respiratory health, we excluded those with less than three dietary records till their 2 years of follow-up ($n=2122$) and dietary underreporting participants identified on the basis of the method proposed by Black et al. [36], using Schofield equations for estimating resting metabolic rates [37] ($n=2650$). The final sample included 35,380 participants (26,640 women and 8740 men).

Since processed meat intake is usually higher in men than in women, analyses were conducted separately among women and men. As previously done for this score, negative binomial regression models, which allows for extra-Poisson variation, were used to evaluate associations between processed meat intake (0, <2 , 2–5, >5 servings/week) with the asthma symptom score, coded as a continuous variable. Main models were adjusted for age, smoking status, pack-years in smokers, educational level, leisure-time physical activity, overall nutritional quality of diet (sex-specific tertiles of the modified AHEI-2010), total daily energy, allergic rhinitis and family history of asthma. As diet affects BMI, and obesity is a likely risk factor for asthma, BMI might be a potential mediator in the diet-asthma association; therefore, main models were not adjusted for BMI. Tests for linear trends were performed using the independent variable as an ordinal quantitative variable. We also performed a sensitivity analysis among participants who never reported asthma from their inclusion in the NutriNet-Santé cohort till their answer to the specific respiratory survey (a likely free of asthma population). Finally, we further investigated the association between processed meat consumption and asthma prevalence, defined by a positive answer to “Have you ever had asthma?”

To study the combined role of unhealthy behaviors on the asthma symptom score, we first formally tested the interaction between processed meat with BMI, smoking and healthy diet; all these interactions were statistically significant ($p<0.001$). We then created a score by dichotomizing BMI into BMI <25 vs. ≥ 25 kg/m², smoking into never smokers vs. ever smokers, overall diet quality into the highest tertile (healthier diet) vs. tertiles 2 and 1 (less healthy diet), and processed meat into lowest (<5 servings/week) vs. highest intake (≥ 5 servings/week). Summing up these values led to a score of “unhealthy behaviors” ranging

from 0 (e.g., no unhealthy behaviors) to 4. Participants with no unhealthy behaviors were taken as reference. Negative binomial regressions adjusted for age, pack-years (among ever smokers), educational level, leisure-time physical activity, total daily energy, allergic rhinitis and family history of asthma, were performed to evaluate the association between the number of unhealthy behaviors and the asthma symptom score. Finally, we also performed a sensitivity analysis among never smokers only.

Missing data for covariates were handled by multiple imputations ($n = 10$) according to a Markov chain Monte Carlo approach [38].

We used SAS software version 9.4 (SAS Institute, Cary, NC, USA) to analyze the data and statistical significance was set at $p < 0.05$.

Results

Baseline characteristics of participants according to processed meat intake are presented in Table 1 for women ($n = 26,640$) and Table 2 for men ($n = 8740$). Both among women and men, participants with the highest intake of processed meat (> 5 servings/week) were more likely to be current smokers, had a lower educational level, were less physical active, more likely to be obese, and to report higher total daily energy intake and higher sodium consumption, as compared to participants who never ate processed meat (0 serving/week).

Processed meat intake and the asthma symptom score

About 27% of the participants reported at least one asthma symptom (women 28.1%; men 24.9%) in the last 12 months.

In the age-adjusted model, higher intake of processed meat was positively and significantly associated with asthma symptoms both among women and men (Table 3). After adjustment for smoking, pack-years (among ever smokers), educational level, leisure-time physical activity, total daily energy, allergic rhinitis, family history of asthma and the modified AHEI-2010, the association decreased but remained statistically significant: odds-ratio (OR) (95% CI) for participants with the highest processed meat intake (> 5 servings/week) vs. participants who never ate processed meat were 1.15 (1.04–1.27) in women and 1.23 (1.01–1.50) in men.

When restricting analyses to participants without ever asthma ($n = 24,159$ women and 8069 men), the magnitude of the association decreased especially after adjustment for the overall nutritional diet quality, but was still positive (OR for participants with the highest processed meat intake (> 5

servings/week) vs. participants who never ate processed meat were 1.08 in women and 1.09 in men).

Finally, when using a dichotomous definition of asthma, we still observed a positive and significant association between higher consumption of processed meat and ever asthma (Supplementary Table 1).

Combined effect of BMI, smoking, overall diet quality and processed meat on the asthma symptom score

Among women, 12% reported no unhealthy behaviors, 34% reported only 1 unhealthy behavior, 33% two unhealthy behaviors, 17% three unhealthy behaviors, and 4% reported the four unhealthy behaviors. Among men, the corresponding figures were 2%, 7%, 78%, 9% and 4%. Among women who reported only 1 unhealthy behavior, 27% reported “obesity/overweight”, 46% “smoking”, 65% “unhealthy diet” and 29% “high processed meat intake”. In men, 44% reported “obesity/overweight”, 58% “smoking”, 71% “unhealthy diet” and 45% “high processed meat intake”.

In the age-adjusted model, both among women and men, the score of unhealthy behaviors was positively and significantly associated with the asthma symptom score (Table 4). After controlling for potential confounders, we reported similar associations: OR (95%) for participants with the four combined unhealthy behaviors were 2.18 (1.91–2.48) in women and 2.70 (2.10–3.45), as compared to participants with no unhealthy behaviors. Overall, the asthma symptom score was positively associated with increasing number of unhealthy behaviors with a statistically significant linear trend. When restricting analyses to never smokers only, we still observed a positive and significant association between number of unhealthy behaviors and the asthma symptom score both among women and men (Supplementary Table 2).

Discussion

In this large cohort of French women and men, we observed that processed meat intake was positively and significantly associated with a higher asthma symptom score. This association remained even after adjustment for potential confounders. Furthermore, we reported a strong positive association of unhealthy behaviors, combining the effect of overweight/obesity, smoking, low diet quality, and high processed meat intake, on the asthma symptom score.

Few studies have been conducted on the association between processed meat and asthma. Our results are in contrast with two studies conducted in the USA among women [8] and men [7], which reported significant association between high processed meat intake and COPD but not with asthma. Therefore, they used doctor-diagnosed asthma,

Table 1 Characteristics of the participants before imputation, according to processed meat intake, among women ($n=26,640$) from the Nutri-Net-Santé cohort

	Women ($n=26,640$)				<i>p</i> value
	0 s/w ($n=2052$)	< 2 s/w ($n=6030$)	2–5 s/w ($n=10,817$)	> 5 s/w ($n=7741$)	
Age (years), mean (sd)	52.1 (14.7)	54.0 (13.7)	52.9 (13.6)	51.2 (13.3)	<0.001
Smoking, <i>n</i> (%)					<0.001
Never smokers	1102 (53.7)	3379 (56.0)	5942 (54.9)	4038 (52.2)	
Former smokers	690 (33.6)	2026 (33.6)	3626 (33.5)	2621 (33.8)	
Current smokers	260 (12.7)	625 (10.4)	1249 (11.6)	1081 (14.0)	
Missing	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.01)	
Pack years among ever smokers, mean (sd)	11.8 (12.6)	10.8 (12.2)	11.1 (12.5)	11.9 (13.7)	0.01
Educational level, <i>n</i> (%)					<0.0001
≤ 13	297 (14.5)	960 (15.9)	1870 (17.3)	1450 (18.7)	
14	324 (15.8)	887 (14.7)	1717 (15.9)	1311 (16.9)	
15–16	669 (32.6)	1917 (31.8)	3582 (33.0)	2520 (32.6)	
≥ 17	747 (36.4)	2220 (36.8)	3566 (33.0)	2410 (31.1)	
Missing	15 (0.7)	46 (0.8)	82 (0.8)	50 (0.7)	
Leisure-time physical activity, <i>n</i> (%)					0.01
High	665 (32.4)	1844 (30.6)	3099 (28.7)	2015 (26.0)	
Moderate	830 (40.4)	2398 (39.7)	4330 (39.9)	2988 (38.6)	
Low	328 (16.0)	1073 (17.8)	2138 (19.8)	1778 (23.0)	
Missing	229 (11.2)	715 (11.9)	1250 (11.6)	960 (12.4)	
Total daily energy, mean (sd)	1685 (414)	1697 (359)	1766 (354)	1887 (398)	
Body mass index (kg/m^2), mean (sd)	22.4 (4.1)	22.8 (3.9)	23.4 (4.2)	24.5 (5.1)	<0.0001
Body mass index (kg/m^2), <i>n</i> (%)					<0.0001
< 18.5	247 (12.0)	429 (7.1)	569 (5.3)	287 (3.7)	
18.5–24.9	1389 (67.7)	4241 (70.3)	7238 (66.8)	4672 (60.4)	
25.0–29.9	272 (13.3)	979 (16.2)	2086 (19.3)	1666 (21.5)	
≥ 30.0	113 (5.5)	309 (5.2)	800 (7.4)	1007 (13.0)	
Missing	31 (1.5)	72 (1.2)	124 (1.2)	109 (1.4)	
Allergic rhinitis, <i>n</i> (%)	823 (40.1)	2531 (42.0)	4533 (41.9)	3334 (43.1)	0.24
Family history of asthma, <i>n</i> (%)	206 (10.0)	625 (10.4)	1116 (10.3)	803 (10.4)	0.46
Asthma symptom score ^a					<0.0001
Mean (sd)	0.37 (0.74)	0.38 (0.78)	0.42 (0.81)	0.47 (0.88)	
0, <i>n</i> (%)	1519 (74.0)	4467 (74.0)	7810 (72.2)	5395 (69.7)	
1, <i>n</i> (%)	380 (18.5)	1152 (18.5)	2058 (19.0)	1584 (20.5)	
2–5, <i>n</i> (%)	153 (7.5)	450 (7.5)	949 (8.8)	762 (9.8)	
Ever asthma ^b , <i>n</i> (%)	214 (10.4)	658 (10.9)	1221 (11.3)	1004 (13.0)	<0.0001
Modified AHEI-2010 ^c , mean (sd)	59.2 (12.2)	56.4 (11.2)	53.1 (10.7)	49.6 (10.8)	<0.0001
Foods/nutrients intake, mean (sd)					
Processed meat (serving/day)	0.0 (0.0)	0.2 (0.1)	0.5 (0.1)	1.1 (0.4)	<0.0001
Fish (serving/day)	0.32 (0.3)	0.33 (0.3)	0.31 (0.3)	0.27 (0.3)	<0.0001
Whole grain cereals (serving/day)	1.0 (1.1)	0.7 (0.7)	0.6 (0.7)	0.6 (0.6)	<0.0001
Fruits (serving/day)	3.0 (2.4)	2.7 (1.7)	2.5 (1.5)	2.4 (1.6)	<0.0001
Vegetables (serving/day)	3.5 (1.9)	3.0 (1.3)	2.8 (1.2)	2.7 (1.3)	<0.0001
Total fiber (g/day)	23.6 (9.5)	20.1 (6.5)	19 (5.7)	18.6 (5.5)	<0.0001
Sodium (g/day)	2.2 (0.8)	2.3 (0.7)	2.6 (0.6)	3.0 (0.7)	<0.0001
Vitamin C (mg/day)	127 (80)	115 (58)	113 (52)	113 (63)	<0.0001
Total fat (g/day)	70 (24)	72 (20)	76 (19)	84 (23)	<0.0001
N-3 fatty acids (g/day)	1.6 (0.9)	1.4 (0.7)	1.3 (0.6)	1.3 (0.6)	<0.0001

s/w serving/week

^aNumber of respiratory symptoms during the past 12 months: (1) breathless while wheezing, (2) woken up with chest tightness, (3) attack of shortness of breath at rest, (4) attack of shortness of breath after exercise, and (5) woken by attack of shortness of breath. Each item is scored from 0 to 1, and the total asthma symptom score ranges from 0 to 5

^bDefined by at least one positive answer to the question “Have you ever had asthma?” in main questionnaires (baseline, or follow-up), and by a

Table 1 (continued)

positive answer to “Have you ever had an asthma attack?” or “Have you ever had an attack of shortness of breath at rest with wheezing” in the respiratory survey

^cAHEI-2010 without processed meat and *trans-fat*

which rather considered asthma as a dichotomous trait than a complex disease with clinical phenotypic heterogeneity and temporal phenotypic variability. However, we also observed significant association between processed meat intake and prevalence of asthma. Furthermore, our findings are consistent with results from a study conducted in France that used the asthma symptom score as a continuous definition of asthma, which reported positive association between high processed meat intake and worsening asthma symptoms [11]. It has been shown that use of scores based on asthma symptoms such as the asthma symptom score could improve the identification of risk factors and, our results are consistent with the study using the asthma symptom score to define asthma as a chronic disease that exists as a continuum [12]. In addition, being a multi-categorical measure, the asthma symptom score provides more power to investigate risk factors for asthma compared with dichotomous definition of asthma [12].

A number of potential mechanisms have been proposed to explain the association between processed meat intake and asthma. The first was the high nitrite intake from processed meat. Indeed, nitrites generate reactive nitrogen species in the respiratory tract that may cause damage, producing amplification of inflammatory processes in the airways, and lung parenchyma causing DNA damage, inhibition of mitochondrial respiration, protein dysfunction, through oxidative and nitrosative damage [6, 39]. A second potential mechanism is that advanced glycation end products, which were reported to be associated with generation of pro-inflammatory cytokines such as TNF- α , can also increase or induce oxidative stress, and are also abundant in processed meat [6, 40]. Third, the association could also be partly explained by the high level of salt in processed meat. It has been reported that high salt consumption was a potential risk for lung inflammation through specific activation state in macrophages [41]. Finally, association of processed meat intake with plasma levels of biomarkers related to inflammation such as C-reactive protein have also been reported [42], suggesting that processed meat intake by influencing systemic inflammation could potentially play a role in asthma. However, further studies are warranted to better understand potential mechanisms involved in the processed meat–asthma association.

In the present study, we also observed that the asthma symptom score increased with the number of unhealthy risk factors. To our knowledge, no study has investigated the impact of multiple risk factors, including modifiable

dietary and lifestyle factors, on asthma. However, several studies have investigated the association between combined lifestyle factors with other chronic diseases [43, 44], and overall, in line with our results, they reported that adherence to a healthy lifestyle, characterized mainly by non-smoking, healthy diet, healthy weight or high physical activity, was of major importance for preventing cardiovascular diseases [43] or cancer [44].

The key strengths of our study are the large sample size which allowed to account for several potential confounders and to perform stratified analyses. Furthermore, regarding processed meat, we had sufficient contrast concerning level of consumption between groups and we could have isolated participants who did not eat processed meat as the non-exposed group. However, and consistent with our findings, it has been previously reported that non-consumption of processed meat or meat in general was also associated with other protective lifestyle behaviors [45] which suggested that the non-exposed group is a lower-risk group. In addition, we used validated tools to assess asthma symptoms and dietary data were assessed by repeated 24 h dietary records (at least three) which reflect usual dietary behaviors of participants. Nonetheless, our study has several potential limitations. First, associations that have been identified may be difficult to interpret due to the cross-sectional collection of the respiratory data. Second, our results should be extrapolated with caution because participants from the NutriNet-Santé cohort are all volunteers involved in a long-term study investigating the association between nutrition and health and could have overall more health-conscious and higher socio-professional and educational level. Third, we used self-reported questionnaires to gather data which are inherently prone to biases and should also be interpreted with caution. However, self-reported questionnaires are frequently used in population studies for epidemiological purposes, and, validation studies performed in the NutriNet-Santé cohort have supported the accuracy of self-reports as a measure of diet [22, 23] and anthropometric data [33]. Fourth, concerns have been raised about potential confounding by overall diet. Thus, in our analyses we adjusted for overall nutritional diet quality using a modified version of AHEI-2010 without processed meat. Even though we controlled for several potential and known cofounders, our results might still be explained by some leftover confounding. eFifth, potential asthma-COPD overlap might also partly contribute to explain the association. However, we adjusted for smoking status and

Table 2 Characteristics of the participants, before imputation, according to processed meat intake, among men ($n=8740$) from the NutriNet-Santé cohort

	Men ($n=8740$)				<i>p</i> value
	0 s/w ($n=559$)	< 2 s/w ($n=1359$)	2–5 s/w ($n=2905$)	> 5 s/w ($n=3917$)	
Age (years), mean (sd)	58.2 (14.5)	60.5 (13.3)	60.1 (13.4)	58.4 (13.3)	<0.001
Smoking, <i>n</i> (%)					<0.001
Never smokers	274 (49.0)	595 (43.8)	1211 (41.7)	1526 (39.0)	
Former smokers	234 (41.9)	630 (46.4)	1395 (48.0)	1877 (47.9)	
Current smokers	51 (9.1)	134 (9.8)	299 (10.3)	514 (13.1)	
Missing	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
Pack years among ever smokers, mean (sd)	14.9 (16.6)	15.9 (15.9)	15.7 (15.7)	18.1 (16.7)	<0.0001
Educational level, <i>n</i> (%)					<0.0001
≤ 13	85 (15.2)	302 (22.2)	723 (24.9)	1057 (27.0)	
14	64 (11.5)	168 (12.4)	334 (11.5)	501 (12.8)	
15–16	137 (24.5)	280 (20.6)	689 (23.7)	960 (24.5)	
≥ 17	268 (47.9)	601 (44.2)	1147 (39.5)	1383 (35.3)	
Missing	5 (0.9)	8 (0.6)	12 (0.4)	16 (0.4)	
Leisure-time physical activity, <i>n</i> (%)					<0.0001
High	233 (41.7)	513 (37.7)	1145 (39.4)	1520 (38.8)	
Moderate	219 (39.2)	505 (37.2)	1009 (34.7)	1222 (31.2)	
Low	75 (13.4)	215 (15.8)	470 (16.2)	788 (20.1)	
Missing	32 (5.7)	126 (9.3)	281 (9.7)	387 (9.9)	
Total daily energy, mean (sd)	2091 (524)	2125 (450)	2194 (446)	2380 (500)	
Body mass index (kg/m^2), mean (sd)	23.7 (3.4)	24.1 (3.2)	24.8 (3.4)	25.7 (4.0)	<0.0001
Body mass index (kg/m^2), <i>n</i> (%)					<0.0001
< 18.5	14 (2.5)	17 (1.3)	26 (0.9)	27 (0.7)	
18.5–24.9	370 (66.1)	890 (65.4)	1684 (57.9)	1855 (47.3)	
25.0–29.9	148 (26.5)	389 (28.6)	991 (34.1)	1548 (39.5)	
≥ 30.0	26 (4.7)	62 (4.6)	202 (7.0)	485 (12.4)	
Missing	1 (0.2)	1 (0.1)	2 (0.1)	2 (0.1)	
Allergic rhinitis, <i>n</i> (%)	177 (31.7)	409 (30.1)	873 (30.1)	1146 (29.3)	0.02
Family history of asthma, <i>n</i> (%)	42 (7.5)	105 (7.7)	214 (7.4)	278 (7.1)	0.77
Asthma symptom score ^a					<0.0001
Mean (sd)	0.31 (0.70)	0.33 (0.72)	0.35 (0.79)	0.43 (0.83)	
0, <i>n</i> (%)	432 (77.2)	1057 (77.7)	2253 (77.5)	2821 (72.0)	
1, <i>n</i> (%)	97 (17.4)	206 (15.2)	424 (14.6)	747 (19.1)	
2–5, <i>n</i> (%)	30 (5.4)	96 (7.1)	228 (7.9)	349 (8.9)	
Ever asthma ^b , <i>n</i> (%)	38 (6.8)	125 (9.2)	258 (8.9)	421 (10.8)	0.001
Modified AHEI-2010 ^c , mean (sd)	59.6 (12.9)	55.9 (12)	52.3 (11.1)	48.1 (11.4)	<0.0001
Foods/nutrients intake, mean (sd)					
Processed meat (serving/day)	0.0 (0.0)	0.2 (0.1)	0.5 (0.1)	1.3 (0.5)	<0.0001
Fish (serving/day)	0.39 (0.4)	0.42 (0.3)	0.38 (0.3)	0.34 (0.3)	<0.0001
Whole grain cereals (serving/day)	1.4 (1.6)	1 (1.1)	0.8 (1)	0.7 (0.9)	<0.0001
Fruits (serving/day)	3.7 (3)	3.1 (2)	3 (1.9)	2.7 (1.9)	<0.0001
Vegetables (serving/day)	3.8 (2.1)	3.2 (1.5)	2.9 (1.3)	2.8 (1.3)	<0.0001
Total fiber (g/day)	29.4 (12.2)	24.5 (8.3)	22.8 (7.1)	22 (6.9)	<0.0001
Sodium (g/day)	2.7 (1.0)	2.9 (0.8)	3.1 (0.8)	3.7 (1.0)	<0.0001
Vitamin C (mg/day)	146 (84)	131 (80)	123 (58)	123 (63)	<0.0001
Total fat (g/day)	83 (28)	84 (24)	88 (23)	101 (27)	<0.0001
N-3 fatty acids (g/day)	1.9 (1.2)	1.7 (1)	1.6 (0.7)	1.6 (0.7)	<0.0001

s/w serving/week

^aNumber of respiratory symptoms during the past 12 months: (1) breathless while wheezing, (2) woken up with chest tightness, (3) attack of shortness of breath at rest, (4) attack of shortness of breath after exercise, and (5) woken by attack of shortness of breath. Each item is scored from 0 to 1, and the total asthma symptom score ranges from 0 to 5

^bDefined by at least one positive answer to the question “Have you ever had asthma?” in main questionnaires (baseline, or follow-up), and by a

Table 2 (continued)

positive answer to “Have you ever had an asthma attack?” or “Have you ever had an attack of shortness of breath at rest with wheezing” in the respiratory survey

^cAHEI-2010 without processed meat and *trans-fat*

Table 3 Associations between processed meat intake and asthma symptom score (continuous variable) among women and men from the NutriNet-Santé cohort ($n = 35,380$)

	Processed meat intake				<i>p</i> for trend
	0 serving/week	< 2 servings/week	2–5 servings/week	> 5 servings/week	
Women (<i>n</i> = 26,640)					
<i>n</i>	2052	6030	10,817	7741	
Asthma symptom score ≥ 1, <i>n</i>	533	1602	3007	2346	
OR (95% CI) ^a	1.00 (ref)	1.03 (0.93–1.14)	1.12 (1.02–1.24)	1.26 (1.14–1.39)	< 0.0001
OR (95% CI) ^b	1.00 (ref)	1.01 (0.92–1.12)	1.06 (0.97–1.17)	1.15 (1.04–1.27)	0.0001
Men (<i>n</i> = 8740)					
<i>n</i>	559	1359	2905	3917	
Asthma symptom score ≥ 1, <i>n</i>	127	302	652	1096	
OR (95% CI) ^a	1.00 (ref)	1.03 (0.83–1.29)	1.11 (0.91–1.36)	1.35 (1.11–1.64)	< 0.0001
OR (95% CI) ^b	1.00 (ref)	1.02 (0.83–1.27)	1.05 (0.86–1.28)	1.23 (1.01–1.50)	0.001

^aModels were adjusted for age

^bModels were further adjusted for smoking, pack-years (among ever smokers), educational level, leisure-time physical activity, total daily energy, allergic rhinitis, family history of asthma and the modified AHEI-2010

Table 4 Combined association of body mass index, smoking, nutritional quality of diet (AHEI-2010 without processed meat and *trans fat*) and processed meat consumption on asthma symptom score among women and men from the NutriNet-Santé cohort ($n = 35,380$)

	Number of “unhealthy behaviors”					<i>p</i> for trend
	0	1	2	3	4	
Women (<i>n</i> = 26,640)						
<i>n</i>	3109	9019	8883	4633	996	
Asthma symptom score ≥ 1, <i>n</i>	637	2211	2608	1563	430	
OR (95% CI) ^a	1.00 (ref)	1.26 (1.15–1.38)	1.57 (1.44–1.72)	1.87 (1.70–2.05)	2.60 (2.28–2.96)	<0.0001
OR (95% CI) ^b	1.00 (ref)	1.21 (1.11–1.32)	1.44 (1.32–1.58)	1.65 (1.50–1.82)	2.18 (1.91–2.48)	<0.0001
Men (<i>n</i> = 8740)						
<i>n</i>	613	1845	2753	2384	1145	
Asthma symptom score ≥ 1, <i>n</i>	79	341	635	713	409	
OR (95% CI) ^a	1.00 (ref)	1.51 (1.19–1.92)	1.95 (1.56–2.46)	2.58 (2.06–3.25)	3.22 (2.53–4.09)	<0.0001
OR (95% CI) ^b	1.00 (ref)	1.41 (1.11–1.78)	1.78 (1.42–2.23)	2.28 (1.81–2.87)	2.70 (2.10–3.45)	<0.0001

^aModels were adjusted for age

^bModels were further adjusted for pack-years (among ever smokers), educational level, leisure-time physical activity, total daily energy, allergic rhinitis and family history of asthma

pack-years among ever smokers, and the stratified analysis according to smoking yielded comparable results in never smokers. Finally, we acknowledge that the “combined unhealthy behaviors” score we used was created by the simple sum of the individual factor, which might not be optimal because it allocates the same weight to each component of the score [46].

In conclusion, high processed meat intake was associated with higher asthma symptoms and may worsen the adverse effects of obesity, smoking and unhealthy diet on asthma. Our results lent further support to the potential deleterious effect of processed meat intake in asthma and complement recent data suggesting the importance of processed meat consumption in lung health. In agreement with the recent

French dietary guidelines which recommended no more than 150 g of processed meat per week [47], our results reinforce the need of public health efforts in encouraging the population to embrace healthier lifestyle behaviors with a limited consumption of processed meat.

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Author contributions RMA, PG and RV designed and conducted the research; SH, MT, NDP, AM, EKG, PG and RV provided essential reagents or provided essential materials; RMA and RV analysed data or performed statistical analysis; RMA, PG and RV wrote the manuscript and had primary responsibility for final content; RMA, SH, MT, NDP, MA, EKG, PG and RV were involved in interpreting the results and editing the manuscript for important intellectual content; all authors read and approved the final manuscript.

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Compliance with ethical standards

Conflict of interest No conflicts of interest to declare.

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Online Supplementary Material

Association between processed meat intake and asthma symptoms in the French

NutriNet-Santé cohort

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Table 1. Associations between processed meat intake and ever asthma among women and men from the NutriNet-Santé cohort (n=35,380)

	Processed meat intake				p for trend
	0 serving/week	< 2 servings/week	2-5 servings/week	> 5 servings/week	
Women (n=26,640)					
n	2,052	6,030	10,817	7,741	
No. of cases	161	513	973	786	
OR (95% CI) ^a	1.00 (ref)	1.21 (0.93-1.35)	1.18 (0.99-1.40)	1.32 (1.10-1.57)	0.004
OR (95% CI) ^b	1.00 (ref)	1.06 (0.88-1.29)	1.10 (0.92-1.32)	1.21 (1.01-1.46)	0.01
Men (n= 8,740)					
n	559	1,359	2,905	3,917	
No. of cases	31	96	197	338	
OR (95% CI) ^a	1.00 (ref)	1.38 (0.90-2.10)	1.31 (0.88-1.93)	1.63 (1.12-1.98)	0.004
OR (95% CI) ^b	1.00 (ref)	1.41 (0.92-2.17)	1.32 (0.88-1.98)	1.70 (1.14-2.54)	0.01

^a Models were adjusted for age.

^b Models were further adjusted for smoking, pack-years (among ever smokers), educational level, leisure-time physical activity, total daily energy, allergic rhinitis, family history of asthma and the modified AHEI-2010.

Table 2. Combined association of body mass index, nutritional quality of diet (AHEI-2010 without processed meat and trans fat) and processed meat consumption on asthma symptom score among never smoker women and men from the NutriNet-Santé cohort (n=18,067)

	Number of “unhealthy behaviors”				p for trend
	0	1	2	3	
Women (n=14,461)					
n	3,109	6,359	3,906	1,087	
Asthma symptom score ≥ 1, n	637	1,542	1,183	405	
OR (95% CI) ^a	1.00 (ref)	1.26 (1.15-1.38)	1.57 (1.44-1.72)	1.87 (1.70-2.05)	<0.0001
OR (95% CI) ^b	1.00 (ref)	1.21 (1.11-1.32)	1.44 (1.32-1.58)	1.65 (1.50-1.82)	<0.0001
Men (n=3,606)					
n	613	1,241	1,231	521	
Asthma symptom score ≥ 1, n	79	236	268	139	
OR (95% CI) ^a	1.00 (ref)	1.51 (1.19-1.92)	1.95 (1.56-2.46)	2.58 (2.06-3.25)	<0.0001
OR (95% CI) ^b	1.00 (ref)	1.41 (1.11-1.78)	1.78 (1.42-2.23)	2.28 (1.81-2.87)	<0.0001

^a Models were adjusted for age.

^b Models were further adjusted for educational level, leisure-time physical activity, total daily energy, allergic rhinitis and family history of asthma.