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Dietary patterns and asthma in the E3N study

Raphaëlle Varraso [*,#], Francine Kauffmann [*,#], Bénédicte Leynaert [¶], Nicole Le Moual [*,#], Marie Christine Boutron-Ruault [#,§,+], Françoise Clavel-Chapelon [#,§,+], Isabelle Romieu [§,‡]

AFFILIATIONS:

[*] Inserm, U780, Epidemiology and Biostatistics, Villejuif, France;

[#] Univ Paris-Sud, IFR69, Villejuif, France;

[¶] Inserm, U700, Paris, France;

[§] Inserm, ERI20, Villejuif, France;

[+] Institut Gustave Roussy, Villejuif, France ;

[‡] Instituto Nacional de Salud Publica, Cuernavaca Morelos, Mexico.

Corresponding author: Isabelle Romieu, Instituto Nacional de Salud Publica, 655 Avenida Universidad, Col. Santa Maria Ahuacatitlán, 62508, Cuernavaca, Morelos, México. Tel: 52-777-101-2935. Fax: 52-777-311 1148. Email: iromieu@correo.insp.mx

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ABSTRACT

The aim was to determine dietary patterns and investigate their associations with incident asthma, current asthma and frequent asthma exacerbations.

Dietary habits and asthma data were collected from the large E3N study (French women, mostly teachers). Of 54,672 women followed-up in 2003, 2,634 reported ever adulthood asthma, 1,063 current asthma, 206 frequent asthma attacks (≥ 1/week), and 628 asthma-onset between 1993 and 2003. Using principal component analysis, three dietary patterns were identified: 'prudent' pattern (fruits and vegetables), 'Western' pattern (pizza/salty pies, dessert and cured meats) and 'nuts and wine' pattern. Pattern scores were categorized into tertiles and the incidence and prevalence of asthma compared between tertiles.

After adjustment for confounders, no association of dietary patterns was observed with incident, ever or current asthma. The 'Western' pattern was associated with an increased risk of reporting frequent asthma attacks (OR for highest vs. lowest tertile [95% CI]=1.79 [1.11-3.73], p for trend=0.01). Increasing scores of the 'nuts and wine' pattern were associated with a decreased risk of reporting frequent asthma attacks (OR for highest vs. lowest tertile [95% CI]=0.65 [0.31,0.96], p for trend=0.02).

Results suggest that overall diet could be involved in frequent asthma exacerbations, one aspect of asthma severity.

(197 words)

INTRODUCTION

Studying dietary patterns instead of specific foods or nutrients is a new approach in nutritional epidemiology to assess the effects of overall diet [1]. Usually determined by factor analysis, dietary patterns have been used to investigate the role of diet in several chronic diseases,[2-5] but still rarely with respiratory diseases [6-8]. Studies on the association of individual foods and nutrients and asthma are inconclusive [9, 10]; an overall approach based on dietary patterns could provide some insight on the combination of foods that might be beneficial or detrimental to asthma prevalence and severity.

Recently, an association between dietary patterns and newly diagnosed COPD was reported in both a large cohort of men and women in the US [7,8]. A "prudent" pattern (high intake of fruits, vegetables, fish and whole grain products) was associated with a decreased risk, whereas a “Western” pattern (high intake of refined grains, cured and red meats, desserts and French fries) was associated with an increased risk. In contrast, no clear association was observed between the dietary patterns and the risk of asthma onset in the two cohorts. However, the severity of asthma was not investigated. Furthermore, these studies were conducted in the US and cultural factors, varying by countries, influence behaviour and attitudes regarding food choices.

The purpose of the present study was to determine dietary patterns in a large population of French women and to investigate the relationship of these patterns with asthma prevalence and incidence in adulthood, and with frequent asthma attacks, an important component of asthma severity.

MATERIALS AND METHODS

Study population

The E3N study is a prospective investigation of major chronic diseases among members from the Mutuelle Générale de l'Education Nationale, a national health insurance plan covering mostly teachers. Briefly, half a million women aged 40-65 years in 1990, residing in continental France and insured by the Mutuelle Générale de l'Education Nationale were invited to participate. Twenty percent agreed to participate by filling in the first questionnaire and the consent form. Included women were fairly representative of the population insured by the health insurance plan regarding age and geographic region. The general characteristics of this population have been reported elsewhere [11]. Briefly, the mean age of the women was 48.9 years, they were well educated (> 80% completed secondary school) and two third of them were never smokers. Follow-up questionnaires were sent every two years thereafter. In 1993, a validated dietary history questionnaire was sent to women [12]. This questionnaire also included a simple question regarding asthma. More detailed questions were included in the follow-up questionnaire administered in 2003 [13]. Part of the E3N cohort is also included in the European Prospective Investigation on Cancer (EPIC). Both dietary questionnaire and detailed asthma data were available for 56,881 women.

Asthma assessment

In 1993, asthma status was assessed using the simple question: ''Have you ever had asthma attacks?". The age at the first attack was also recorded. In 2003, asthma was defined as recommended by the American Thoracic Society (ATS) by the following questions: "Have you ever had asthma attacks?" and if yes "Was this diagnosis confirmed by a doctor?" [13]. For asthmatic women, age at the first attack, current asthma (in the last twelve months), frequency of attacks in the last twelve months ($\geq$ 1/day, $\geq$ 1/week, $\geq$ 1/month, < 1/month), and current use of inhaled steroids and/or inhaled bronchodilators at least three times a week were

recorded in 2003. Frequent asthma attacks were defined by a report of at least one attack of asthma per week in the last twelve months, regardless of any medication. In addition, women were considered to have adult-onset asthma between 1993 and 2003 if they i) did not report asthma attack ever in the baseline questionnaire, and ii) met the ATS criteria for asthma definition at follow-up, with a coherent reported age of asthma-onset (time of first attack between 1993 and 2003). Questionnaires were self-completed and returned by mail and no lung function test was performed.

Dietary patterns

Dietary patterns were developed using factor analysis [1]. We conducted the analyses using the Factor Procedure in SAS. The factors were rotated by an orthogonal transformation (Varimax rotation function in SAS) to achieve simpler structure with greater interpretability. The number of factors to retain was determined using the diagram of eigenvalues, the Scree plot. Foods that loaded at 0.40 or greater were considered to be making a contribution to the factor, although the value for meaningful factor loading is arbitrary. The factor score for each pattern was constructed by summing up observed intakes of the component food items weighted by the factor loading. Food items were grouped a priori in 56 separate food groups (see appendix) and dietary patterns were described from these food groups. To assess the sensitivity of dietary patterns due to the a priori grouping of foods, principal component analysis was also performed from the 208 food items.

Assessment of other variables

Total energy intake was estimated in 1993 through the diet questionnaire and expressed in kilocalories per day (kcal/day). Because our population was mostly composed of

teachers, years of education were used as a proxy for socio-economic status. Hay fever ever was classified as either present or absent. Dietary supplementation were investigated in 2003 (not available in 1993). Women reported the use of calcium (15.5%), fluoride (1.0%), iron (3.1%), magnesium (15.2%), phytoestrogens (soy) (5.3%), other minerals/trace-elements (9.9%), vitamin A (3.9%), vitamin B (5.1%), vitamin C (7.6%), vitamin D (6.0%), vitamin E (7.0%), folic acid (1.0%), beta carotene (3.1%) and other vitamins (2.2%). Women taking supplements might be more likely to modify their diet in relation to their disease; in the E3N study, they have been found to have a different life style and dietary habits compared to non-users [14, 15].

Body mass index, physical activity, smoking status and menopausal status were investigated in 1993 and in each follow-up questionnaires. Body mass index (BMI) was calculated based on the height and weight and was used as a continuous and categorical variable. Physical activity was measured in Metabolic Equivalents per week (METs/week) [16]. Information on tobacco consumption included the categories never, past, and current smoker. Women were classified as premenopausal, postmenopausal or peri menopausal.

Statistical analysis

Women with extreme values (in the bottom or top one percent) of the ratio between energy intake and required energy (calculated after taking age, weight and height into account) were excluded (n=1,009). Among asthmatic women (n=3,834), 1,200 were excluded because they reported asthma diagnosis during childhood (≤ 16 years) without current asthma. The present analysis is based on 54,672 women (2,634 with asthma ever in adulthood and 52,038 non asthmatics).

For the cross-sectional analysis, the associations between respiratory phenotypes and diet were investigated using logistic regression models, adjusting for potential confounding factors including age, total energy intake, BMI, physical activity, smoking status, menopausal status, education and dietary supplementation. In order to assess the association both between dietary behaviour as a whole, and non supplemented diet itself, analyses were performed both in all women and in those who did not use supplementation. Analyses were both adjusted and stratified for inhaled steroid use. Dietary patterns and food intake were categorized in tertiles. Odds ratios (OR) were determined using the lowest tertile as the reference. For the longitudinal analysis, relative risk (RR) for asthma onset were estimated using Cox proportional hazards models, with age as the time scale. Potential confounding variables included BMI, physical activity, smoking status and menopausal status treated as time-dependent variables, and total energy intake, dietary supplementation and education. All analyses were conducted using the SAS statistical software.

RESULTS

Assessment of dietary patterns

Three major dietary patterns were identified (table 1). The first factor was loaded heavily with fruits and vegetables. The second factor was loaded heavily with pizza/salty pies, dessert, cured meats and pasta. The third factor was loaded heavily with nuts and seeds, salty biscuits, olives, wine, and fortified wine (see annex 1 for food grouping). Factors were labelled 'prudent', 'Western', and 'nuts and wine' patterns respectively. The principal component analysis performed on the 208 foods without *a priori* grouping gave similar results.

Dietary patterns and asthma prevalence and incidence in adulthood

Among women reporting asthma ever in adulthood (n=2,634), 1,063 women reported current asthma (40.5 %) at follow-up, of whom 206 (19.4%) reported frequent attacks. Current asthmatics (n=1,063 women) had a larger body mass index, were more often ex-smokers, reported more hay fever and used more frequently dietary supplements than non asthmatics (table 2).

Women taking supplements (n=20,203) were significantly older (mean (SD): 53.3 years (6.7) vs. 52.3 (6.4)), were more physically active (mean (SD): 40.1 METs/week (25.6) vs. 38.8 (25.7)) and reported a higher BMI (mean (SD): 23.0 kg/m^2 (3.2) vs. 22.4 kg/m^2 (2.9)) than women without supplement intake (n=33,263). Women with supplement intake reported also more hay fever (16.6% vs. 12.1%) and ever asthma (5.3% vs. 4.5%), ate more fruits, vegetables, fish and olive oil, and less processed meats and desserts than women without supplement intake. Similar results were found after adjustment for age.

No statistically significant association was found between dietary patterns and ever adulthood asthma among all women, and among women without supplement intake (data not shown). Similarly, no association was found between dietary patterns and current asthma (table 3).

The only respiratory phenotype that we were able to analyse prospectively in this cohort was ever asthma. Between 1993 and 2003, we identified 628 incident cases of asthma. No relationship between dietary patterns and the risk of adult-onset asthma was observed, either among all women or among women without supplement intake (table 4).

Dietary pattern and the frequency of asthma attacks

Among all current asthmatics, those reporting at least one asthma attack per week were significantly older (mean (SD): 54.5 years (6.9) vs. 51.8 (6.3), $p<0.001$) and had a higher education level than asthmatics with less than one attack per week, even after adjustment for age. Among women with at least one attack per week (n=206), 45% used inhaled steroids vs. 28.5% among those with less than one attack per week (n=786). Among current asthmatics, the use of multivitamin supplements was similar in women with at least one attack per week (42.7%) and in those with less than one attack per week (43.2%).

The 'nuts and wine' pattern was negatively and significantly associated with the risk of frequent asthma attacks both among all current asthmatics (p for trend=0.01) and in the subgroup of non supplement users (p for trend p=0.03, table 5). The risk of frequent asthma attacks increased significantly over tertiles of the 'Western' pattern only among asthmatics without supplement intake (p for trend=0.02). No association was found between the 'prudent' pattern and frequent asthma attacks both in women with and without supplement intake. Further adjustment for inhaled steroids did not modify the results. We further stratified

according to the use of inhaled steroids and found similar results both among women with and without current use of inhaled steroids.

Due to the potential overlap between the diagnosis of chronic obstructive pulmonary diseases (COPD) and asthma, we also performed analyses restricted to never smokers. Among never smoker women, the 'nuts and wine' pattern remained negatively and significantly associated with the risk of frequent asthma attacks (OR for highest vs. lowest tertile [95%CI]=0.49 [0.25-0.98], p for trend=0.02). In never smoker asthmatics without supplement intake, a borderline significant association was found between the 'Western' diet and the risk of frequent asthma attacks (OR for highest vs. lowest tertile [95%CI]=2.36 [0.89-6.26], p for trend=0.07).

Intake of individual foods and the frequency of asthma attacks

The five individual foods or foods groups with the highest loading factor for the 'nuts and wine' and for the 'Western' patterns were studied to determine their association with the frequency of asthma attacks.

Of the five individual foods or food groups with the highest loading factor for the 'nuts and wine' pattern (nuts and seeds, salty biscuits/aperitif biscuits, wine, olives and fortified wines), the risk of frequent attacks was lower in women with the highest consumption of nuts and seeds (>5.3 g/day) than in women with the lowest consumption (≤1.0 g/day), both in all current asthmatics (OR for highest vs. lowest tertile [95%CI]=0.64 [0.41-0.99], p for trend=0.03) and in current asthmatics without supplement intake (OR for highest vs. lowest tertile [95%CI]=0.55 (0.30-1.01), p for trend=0.04). Among current asthmatics, the risk of frequent asthma attacks was lower among women with the highest consumption of wine (>89.4 g/day) than in women with the lowest consumption (≤13.6 g/day) (OR for highest vs.

lowest tertile [95%CI]=0.60 (0.38-0.94), p for trend=0.05). No association was observed for the other food groups of this pattern.

Of the five individual foods or food groups with the highest loading factor for the 'Western' pattern (onion/garlic, dough and pastry, cream desserts, ice cream and processed meats), no specific food was associated with frequent asthma attacks.

DISCUSSION

Three distinct dietary patterns were identified in a large cohort of French adult women: a "prudent" pattern, a "Western" pattern and a "nuts and wine" pattern. No association was observed between these dietary patterns and adult-onset asthma, ever asthma in adulthood, and current asthma. In contrast, significant associations were observed with the frequency of asthma attacks. The highest tertile of the 'nuts and wine' pattern was associated with a decreased risk of frequent asthma attacks in asthmatic women. The highest tertile of the 'Western' pattern was associated with an increased risk of frequent asthma attacks only among asthmatic women without supplement intake. No association was observed with the 'prudent' pattern.

Similar dietary patterns have been identified in other populations [2-4, 6; 17]. There is a consistency across studies to identify a 'prudent' pattern and a 'Western' pattern, whereas the 'drinker' pattern was mostly identified in European surveys [3; 17]. Recently, with different food groups and a larger sample of the E3N cohort, four dietary patterns close to our patterns were identified: 'healthy' (vegetables, fruit, yoghurt, sea products, and olive oil), 'Western' (potatoes, pizzas/pies, sandwiches, sweets, cakes, cheese, cereal products, processed meat, eggs, and butter), 'drinker' (sandwiches, snacks, processed meat, and alcoholic beverages) and 'meat eaters' (meat, poultry, and margarine) [18].

Only three recent studies used dietary patterns to assess diet in relation with respiratory phenotypes [6-8]. Our results regarding adult-onset asthma are consistent with these studies. No significant association between dietary patterns and incident asthma was observed in 52,325 men and women adult Chinese Singaporeans, aged 45 to 74 years. Two patterns were evidenced in this cohort: a 'vegetable, fruit, soy' pattern and a 'meat-dim sum' pattern (chicken, pork, fish, rice and noodle dishes, and preserved foods). In the US, no

association was reported between the risk of adult-onset asthma and dietary patterns in 42,917 men aged 40 to 75 years from the Health Professionals Follow-up Study (HPFS) [7]. In 72,043 US women aged 30 to 55 years from the Nurses' Health Study (NHS), the Western pattern was not associated with adult-onset asthma but a borderline and positive association was reported between the prudent diet and adult-onset asthma [8]. To our knowledge, our study is the first to observe a relationship between a Western diet and the risk of frequent asthma attacks. In the study among the Chinese Singaporeans, the 'meat-dim sum' pattern was associated with an increased risk of incident cough with phlegm, and both in the NHS and in the HPFS, the Western pattern was associated with an increase of COPD. We did not find any association between dietary patterns and the prevalence and incidence of asthma. Therefore, one may wonder whether the same mechanisms as those underlying the association between diet and COPD could be involved also in the association between diet and asthma severity, whereas dietary factors would act differently on the risk of asthma onset. Previous studies have mostly focused on the potentially protective effects of antioxidants [10], but recently, it was reported both in a longitudinal survey [19] and in a cross-sectional survey with FEV_1 measurement [20], that frequent consumption of cured meats was associated with higher prevalence and incidence of COPD. In our study, no specific food from the Western pattern was associated with frequent asthma attacks, suggesting the deleterious role of the overall diet rather than of one specific food. In the NHS, the Western pattern, which is similar to ours, was positively correlated with concentrations of CRP and IL-6, two markers of systemic inflammation [21]. Further studies are needed to better understand the association between Western diet, inflammation and asthma severity.

We also reported an inverse association between the 'nuts and wine' pattern and the frequency of asthma attacks. Regarding the specific foods from this pattern, we reported an inverse association between frequent asthma attacks with both nuts/seeds and wine. We

wondered whether the negative association between nuts and seeds with asthma attacks might be explained by a protective effect of vitamin E. However, the contribution to the total vitamin E intake from nuts and seeds in this population was estimated to be only 3.3% (the fifth highest contribution of the total vitamin E). The borderline significant negative association between moderate wine consumption and frequent asthma attacks that we observed is consistent with the inverse association of red wine intake with asthma severity assessed by a quality of life scale in an English population [22]. Wine is an important source of flavonoids, which could plausibly reduce asthma inflammation through antioxidant, antiallergic and antiinflammatory properties [23]. Besides flavonoids, alcohol itself may have a modest bronchodilator effect and likely relaxes bronchial smooth muscle [24]. Nevertheless, reverse causation cannot be excluded. Sensitized asthmatics might avoid the intake of nuts as well as the intake of wine, alcoholic drinks, and especially red wine, being perceived by a large number of asthmatics to trigger their asthma [24]. Replication of our findings in studies with information on potential nuts and wine avoidance is warranted to support the hypothesis of a protective effect in asthma. In our study, the effect of diet was stronger among women without supplement intake. It is possible that vitamin/mineral supplementation masks the effect of foods or that adjustment for supplement could not adequately control for differences in lifestyle and other characteristics of women using supplementation.

Dietary patterns have several advantages over focusing on nutrients and foods to assess the association between diet and disease, in particular for diseases like asthma, for which no individual dietary factor has shown any consistent and strong effect. The factor analysis approach involves several arbitrary decisions, including the construction of the food groups, the number of factors to extract and the method of rotation, and even the labelling of the components [1]. We also performed a principal component analysis with individual foods

and beverages, without grouping them *a priori*. This sensitivity analysis showed a high consistency and reproducibility of our patterns.

The distinction between asthma and chronic obstructive pulmonary diseases is not easy in the elderly. In the E3N study, asthma was only assessed by questionnaire and self reported asthma might have included chronic obstructive pulmonary disease. Therefore, we conducted an analysis restricted to never smokers, who are unlikely to have chronic obstructive pulmonary disease. Results remained similar supporting the hypothesis that dietary patterns relate to the frequency of asthma attacks. The severity of asthma is difficult to assess in epidemiological studies [25] and there is a general consensus now emerging that asthma is unlikely to be a single disease, but different overlapping phenotypes [26]. It was recently shown that quantitative scores combining clinical items and treatment had good ability to detect risk factors by reducing misclassification of the disease status [27, 28] . The new GINA recommendations (2006) have evolved from severity to control and underlined the importance of asthma treatment [29]. Further, it was recently recommended not to use anymore asthma severity for clinical features off-treatment [30]. In the E3N study, few data regarding treatments were available and we were not able to build a reliable score combining both frequency of asthma attacks and treatment. However, further adjustment and even stratification on the use of inhaled steroids did not modify our findings.

For current asthma and frequent asthma attacks, the cross-sectional nature of the analysis limits the interpretation, given that women with asthma might have modified their dietary pattern towards a healthier pattern or have avoided some foods because of their symptoms. However, our longitudinal finding for adulthood asthma was similar to the cross-sectional one. Furthermore, longitudinal studies performed in cohorts of adults have shown reasonable tracking of diet [31] and a reasonable reproducibility and validity of the major

dietary patterns defined by factor analysis with data from an FFQ has been reported over 8 years [32]. Regarding the generalization of our findings, we need to be cautious as women from the E3N study might be more health-conscious than the general population (i.e. less smokers, with a highest intake of fruits and vegetables, more physically active). Confirmation of these findings in other populations, particularly among men, is warranted.

In summary, we report in French women that the 'Western' pattern was positively associated with frequent asthma attacks, while the 'nuts and wine' pattern was negatively associated with frequent asthma attacks. Further studies are needed to improve the understanding of the complex association between diet and asthma.

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COMPETING INTERESTS

No competing interest.

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Table 1 Factor-loading matrix for the major factors (dietary patterns), (n=54,672 women), E3N Study-France*

	Factor 1 (Prudent pattern)	Factor 2 (Western pattern)	Factor 3 (Nuts and wine pattern)
Fruity vegetables	0.89		
Root vegetables	0.85		
Cabbages	0.79		
Mushrooms	0.73		
Grain and peas	0.72		
Leafy vegetables (except cabbages)	0.71		
Stalk vegetables	0.70		
Fruits with beta carotene	0.61		
Fruits with citric	0.60		
Condiments and sauces	0.42	0.32	
Red meat	0.34		
Poultry	0.33		
Blue-fish	0.32		
Onion, garlic		0.73	
Dough and pastry		0.70	
Cream desserts		0.62	
Ice cream		0.60	
Processed meats		0.55	0.33
Cakes, pies, pastries		0.45	

Pasta, rice, grain	0.40	
Potatoes and other tubers	0.31	
Egg	0.30	
Nuts and seeds		0.58
Salty biscuits, aperitif biscuits		0.56
Wine		0.48
Olives		0.45
Fortified wines		0.40
Cocktails, punches		0.36
Crustaceans, mollusks		0.35
Spirits		0.35

* Diet was assessed in 1993. Factor loadings represent the correlation between factor scores and intake of food groups. Foods or foods groups with factor loadings < 0.30 for both factors were excluded. Absolute values < 0.30 were not listed in the table for simplicity; those with loadings of 0.40 or greater are underlined. Factors loadings presented are those resulted from the orthogonal rotation.

By construction, the dietary patterns were independent and women with a high score on the "nuts and wine" pattern could also have a high score on the "prudent" and/or "Western" pattern. In this analysis, 10.9% of the women were in the highest tertile both for the "prudent" and the "Western" diet, 11.5% in the highest tertile both for the "prudent" and the "nuts and wine" pattern and 12.5% in the highest tertile both for the "Western" and the "nuts and wine" pattern.

Table 2 Baseline characteristics of the population according to current asthma (n=53,101), E3N Study-France

	Current asthma (n=1,063)	No asthma (n=52,038)	p*
Age (years)	52.5 ± 6.5 †	52.7 ± 6.5	0.3
Caloric intake (kilocalories/day)	2190 ± 602	2176 ± 569	0.4
Physical activity (metabolic equivalent/week)	45.8 ± 30.0	46.4 ± 30.2	0.6
Body mass index (kg/m^2)	24.8 ± 4.6	23.8 ± 3.6	<0.001
Body mass index (kg/m^2) (%)			
< 20	9.7	11.5	
20 – 24.9	49.2	58.5	<0.001
25 – 29.9	29.5	24.0	
≥ 30	11.6	6.0	
Tobacco consumption (%)			
Never smokers	51.3	56.4	
Ex smokers	38.6	34.0	0.003
Current smokers	10.1	9.6	
Menopausal status (%)			
Premenopause	5.6	4.6	
Postmenopause	94.4	95.3	0.3
Perimenopause	0.0	0.1	
Education (number of years of school) (%)			
≤12 years	11.7	10.7	

14 years	48.3	51.9	0.15
16 years	20.4	19.0	
17 years	19.6	18.4	
Multivitamin supplement use (%) ‡	43.0	37.2	<0.001
Hay fever ever (%)	27.8	5.1	<0.001
Use of bronchodilators (%)	48.3	0.8	<0.001
Use of inhaled steroids (%)	31.9	1.2	<0.001

* t tests were used for continuous variables and chi-square tests were used for categorical variables.

† Mean ± SD (all such variables).

‡ Includes used of calcium, fluorine, iron, magnesium, phytoestrogens (soy), other minerals/trace-elements, vitamin A, vitamin B, vitamin C, vitamin D, vitamin E, folic acid, beta carotene, other vitamins. Recorded in 2003.

Table 3 Dietary patterns and current asthma (n=53,101 women), E3N study - France

	Low intake (tertile 1)	Moderate intake (tertile 2)	High intake (tertile 3)	*p* for trend*
Prudent pattern				
All women				
No. of current asthmatics / no. of non asthmatics	363/17129	328/17234	372/17675	
Multivariate OR (95% CI) †	1.00	0.94 (0.80-1.1)	1.02 (0.87-1.20)	0.7
Women without multivitamin supplement use in 2003				
No. of current asthmatics / no. of non asthmatics	207/10968	200/11014	199/10675	
Multivariate OR (95% CI) ‡	1.00	1.06 (0.86-1.32)	1.10 (0.89-1.36)	0.4
Western pattern				
All women				
No. of current asthmatics / no. of non asthmatics	347/17183	334/17220	382/17635	
Multivariate OR (95% CI) †	1.00	0.88 (0.70-1.10)	0.98 (0.76-1.26)	0.9
Women without multivitamin supplement use in 2003				

No. of current asthmatics / no. of non asthmatics	203/10808	192/10991	211/10858	
Multivariate OR (95% CI) ‡	1.00	0.94 (0.79-1.11)	1.02 (0.84-1.23)	0.9
Nuts and wine pattern				
All women				
No. of current asthmatics / no. of non asthmatics	354/17163	316/17232	393/17643	
Multivariate OR (95% CI) †	1.00	0.84 (0.71-0.99)	0.93 (0.79-1.10)	0.4
Women without multivitamin supplement use in 2003				
No. of current asthmatics / no. of non asthmatics	199/10449	179/11027	228/11181	
Multivariate OR (95% CI) ‡	1.00	0.84 (0.68-1.05)	0.94 (0.76-1.17)	0.6

OR, odds ratio; CI, confidence interval. The reference category is based on the lowest category of intake. Diet was assessed in 1993 and current asthma in 2003.

* Based on each intake category and modelling these as continuous variables in a logistic regression.

† Logistic regressions adjusted for age, caloric intake, body mass index, tobacco consumption, physical activity, menopausal status, education and multivitamin supplements use.

‡ Logistic regressions adjusted for age, caloric intake, body mass index, tobacco consumption, physical activity, education and menopausal status.

Table 4 Dietary patterns and adult-onset asthma (n=52,666 women), E3N study - France

	Low intake (tertile 1)	Moderate intake (tertile 2)	High intake (tertile 3)	*p* for trend*
Prudent pattern				
All women				
No. of incident asthma / at risk	208/17,301	202/17,405	218/17,332	
Multivariate RR (95% CI) †	1.00	0.97 (0.80-1.18)	0.98 (0.81-1.19)	0.8
Women without multivitamin supplement use in 2003				
No. of incident asthma / at risk	131/10,968	124/11,014	136/10,675	
Multivariate RR (95% CI) ‡	1.00	0.96 (0.75-1.22)	0.98 (0.78-1.24)	0.9
Western pattern				
All women				
No. of incident asthma / at risk	223/17,354	182/17,387	223/17,297	
Multivariate RR (95% CI) †	1.00	0.86 (0.62-1.14)	0.95 (0.77-1.26)	0.4

Women without multivitamin supplement use in 2003				
No. of incident asthma / at risk	137/10,808	116/10,991	138/10,858	
Multivariate RR (95% CI) ‡	1.00	0.80 (0.62-1.04)	0.92 (0.69-1.22)	0.5
Nuts and wine pattern				
All women				
No. of incident asthma / at risk	189/17,337	201/17,406	238/17,295	
Multivariate RR (95% CI) †	1.00	0.96 (0.78-1.17)	1.01 (0.82-1.23)	0.9
Women without multivitamin supplement use in 2003				
No. of incident asthma / at risk	118/10,449	125/11,027	148/11,181	
Multivariate RR (95% CI) ‡	1.00	0.92 (0.72-1.19)	0.98 (0.75-1.26)	0.9

RR, relative risk; CI, confidence interval. The reference category is based on the lowest category of intake. Diet was assessed in 1993 and adult-onset between 1993 and 2003.

* Based on each intake category and modelling these as continuous variables in a Cox model.

† Cox models adjusted for caloric intake, body mass index, tobacco consumption, physical activity, menopausal status, education and multivitamin supplements use.

‡ Cox models adjusted for caloric intake, body mass index, tobacco consumption, physical activity, education and menopausal status.

Table 5 Dietary patterns and frequent asthma attacks in asthmatic women (n=992 women), E3N study - France

	Low intake (tertile 1)	Moderate intake (tertile 2)	High intake (tertile 3)	*p* for trend *
Prudent pattern				
All women				
No. of asthmatics with frequent asthma attacks / no. of asthmatics with non frequent asthma attacks	81/260	49/257	76/269	
Multivariate OR (95% CI) †	1.00	0.65 (0.43-0.97)	0.89 (0.61-1.31)	0.5
Multivariate OR (95% CI) ‡	1.00	0.60 (0.37-0.98)	1.01 (0.65-1.57)	0.9
Women without multivitamin supplement use in 2003				
No. of asthmatics with frequent asthma attacks / no. of asthmatics with non frequent asthma attacks	48/145	28/160	37/148	
Multivariate OR (95% CI) †	1.00	0.59 (0.35-1.00)	0.84 (0.50-1.39)	0.4
Multivariate OR (95% CI) §	1.00	0.46 (0.24-0.89)	0.79 (0.44-1.44)	0.5

Western pattern				
All women				
No. of asthmatics with frequent asthma attacks / no. of asthmatics with non frequent asthma attacks	67/256	62/253	77/277	
Multivariate OR (95% CI) †	1.00	0.91 (0.60-1.38)	1.12 (0.71-1.77)	0.6
Multivariate OR (95% CI) ‡	1.00	1.10 (0.68-1.80)	1.08 (0.62-1.87)	0.8
Women without multivitamin supplement use in 2003				
No. of asthmatics with frequent asthma attacks / no. of asthmatics with non frequent asthma attacks	37/154	31/142	45/157	
Multivariate OR (95% CI) †	1.00	1.25 (0.94-1.85)	1.56 (1.01-2.83)	0.03
Multivariate OR (95% CI) §	1.00	1.45 (0.96-2.83)	1.79 (1.11-3.73)	0.01
Nuts and wine pattern				
All women				
No. of asthmatics with frequent asthma attacks / no. of asthmatics with non frequent asthma attacks	82/251	63/231	61/304	

Multivariate OR (95% CI) †	1.00	0.88 (0.60-1.29)	0.61 (0.42-0.91)	0.01
Multivariate OR (95% CI) ‡	1.00	0.78 (0.52-1.44)	0.65 (0.31-0.96)	0.02
Women without multivitamin supplement use in 2003				
No. of asthmatics with frequent asthma attacks / no. of asthmatics with non frequent asthma attacks	45/139	38/129	30/185	
Multivariate OR (95% CI) †	1.00	0.93 (0.56-1.54)	0.51 (0.30-0.87)	0.01
Multivariate OR (95% CI) §	1.00	0.87 (0.44-1.42)	0.58 (0.27-0.95)	0.03

OR, odds ratio; CI, confidence interval. The reference category is based on the lowest category of intake. Diet was assessed in 1993 and the frequency of asthma attacks in 2003. Among the 992 current asthmatics, 206 had frequent asthma attacks and 786 had no frequent asthma attacks.

* Based on each intake category and modelling these as continuous variables in a logistic regression.

† Logistic regressions adjusted for age, caloric intake and body mass index.

‡ Logistic regressions adjusted for age, caloric intake, body mass index, tobacco consumption, physical activity, menopausal status, education and multivitamin supplements use.

§ Logistic regressions adjusted for age, caloric intake, body mass index, tobacco consumption, physical activity, education and menopausal status.

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Annex 1 Food groupings for factor analysis

Foods or food groups	**Food items**
Potatoes and other tubers	Potato salad, potatoes deep fried, smashed potatoes
Leafy vegetables (except cabbages)	Green salad, endives as salad, chicory, spinach
Fruiting vegetables	Artichoke, tomatoes as salad, avocado, cucumber, tomato (pizza, salty pie, salty pancake), cooked tomatoes, green beans, egg plants, bell pepper, zucchini
Root vegetables	Grated carrots, radish, beetroot, celeriac, cooked carrots, salsify
Cabbages	Cauliflower as salad, white or red cabbage raw, Brussels sprouts, cauliflower, cabbage
Mushrooms	Mushrooms (pizza, salty pie, salty pancake), mushrooms
Grain and pod vegetables	Maize as salad, peas
Onion, garlic	Onions (pizza, salty pie, salty pancake), onions (sandwich, hamburger)
Stalk vegetables	Leek as salad, leek (pizza, salty pie, salty pancake), celery, beet, fennel
Legumes	Lentils as salad, legumes
Fruits with citric	Orange, grapefruit, mandarin, kiwi
Fruits with beta carotene	Peach, melon, apricot
Other fruits	Fresh fruits unspecified, apple, pear, banana, pineapple, strawberries or raspberries, cherry, raisins, plums, compote-fruits-fruits on syrup
Nuts and seeds	Nuts and seeds
Olives	Olives
Milk	Milk non-specified, whole milk, skimmed milk, half-skimmed milk, sweetened concentrated milk
Milk beverages	Chocolate drink
Yoghurts	Yoghurt, ordinary yoghurt, ordinary yoghurt 0%, ordinary yoghurt sweetened, flavoured yoghurt, flavoured yoghurt 0%, flavoured yoghurt light
Cottage cheese	Cottage cheese, ordinary cottage cheese, cottage cheese 0%, cottage cheese 10-20%, cottage cheese 30-40%, flavoured cottage cheese 0%, flavoured cottage cheese 10-20%, flavoured cottage cheese 30-40%
Cheese	Non-specified cheese, camembert-St Marcellin-Brie-munster-…, Soft cheeses, blue cheese-…, Gruyere-…, Cantal-…, Goat cheeses, other cheeses, low-fat cheeses, mozzarella (pizza, salty pie, salty pancake), gruyere (pizza, salty pie, salty pancake), gruyere (sandwich, hamburger)
Cream desserts	Cream dessert, Cream dessert with rice
Cream	Sour cream (pizza, salty pie, salty pancake), plain sour cream, sour cream (15%)
Pasta, rice, grain	Pasta-couscous, rice non-specified, normal rice, whole rice
Bread	Non specified bread, white bread, bread whole-flour, white bread slices, biscotti, unleavened bread, crackers, toasted bread, WASA, small toasted bread, hamburger bread, white bread (sandwich, hamburger)
Breakfast cereals	Breakfast cereals
Salty biscuits, aperitif biscuits	Salted biscuits
Dough and pastry	Pizza dough, puff pastry
Red meat	Non-specified red meats, beef, beef 15% fat (sandwich,

	hamburger), pork, lamb, veal, horse
Poultry	Poultry, rabbit
Processed meats	Sausage, pate, potted meat, cooked ham (pizza, salty pie, salty pancake), smoked lard (pizza, salty pie, salty pancake), sausages-blood sausage-andouillette, cooked harm (hamburger, sandwich)
Offal	Liver, other offal
Crustaceans, molluscs	Sea fruits
Blue-fish	Canned fish, fresh sardines, mackerel fresh, fresh salmon
Whitefish	Fish non specified, hake, julienne, dab, haddock, sole, Pollock, whiting, codfish, trout, other fish
Egg	Boiled eggs, fried eggs-scrambled eggs, egg (pizza, salty pie, salty pancake)
Vegetal oils	Peanut oil, sunflower oil, olive oil, corn oil
Butter	Butter, low-fat butter
Margarines	Normal margarine, low-fat margarine
Other animal fats	Duck fat, other fat
Chocolate	Candy bars, chocolate bars
Sweets	Sweets
Ice cream	Ice cream
Cakes, pies, pastries	Croissant-brioche, cakes, pancake (pizza, salty pie, salty pancake), cream cakes, fruit pie
Dry cakes, biscuits	Dry biscuits
Fruits juice	Fruits juice
Carbonated/soft/isotonic	Soft drinks, sweetened soft drinks, light soft drinks
Coffee and tea	Chicory, coffee, tea
Waters	Tap water, mineral water, non specified water
Wine	Wine or champagne
Fortified wines	Muscat, Porto, Vermouth
Beer, cider	Non specified beer, beer, special beer, cider
Spirits	Whisky, Gin, Vodka, digestive
Aniseed drinks	Alcohol with anis
Cocktails, punches	Punch, aperitif made of cassis liqueur and white wine
Condiments and sauces	Mayonnaise, non specified salad dressing, commercial plain salad dressing, commercial low-fat salad dressing, home-made salad dressing with peanut oil, home-made salad dressing with olive oil, home-made salad dressing with corn oil, home-made salad dressing with sunflower oil, home-made salad dressing with Cole seed oil, home-made salad dressing with soybean oil, Béchamel sauce (pizza, salty pie, salty pancake), ketchup (sandwich, hamburger), béchamel sauce (sandwich, hamburger)
Soups	Soups