ERJ Express. Published on June 9, 2011 as doi: 10.1183/09031936.00115010

Farming in childhood, diet in adulthood and asthma history

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Running head: farm, diet and asthma

Words count: 3,149

ABSTRACT

The decrease in the number of children living on traditional farms in France during early childhood and changes in diet could both play a role in the increase of asthma prevalence over the last decades. This article aims to assess i) the association of farming lifestyle in childhood and asthma ii) whether diet in adulthood modifies the association between farming lifestyle in childhood and adult-onset asthma.

In the French E3N study (54,018 women, 43-68 years), three indicators of farming lifestyle were defined: one using individual data (having farmer parents), and two using ecological data (born in a rural area, exposure to cattle).

All farming lifestyle indicators were related with childhood- (<16 years), and adult-onset asthma: OR (95% CI) for farmer parents were 0.54 (0.42-0.70), 0.72 (0.62-0.84) respectively, and with diet in adulthood, in particular with a high fruit and a low wine intakes. The association between farmer parents and adult-onset asthma was not modified by diet in adulthood.

Results extend previous observations in younger cohorts on the protective role of contact with livestock and farming lifestyle on asthma, in particular during childhood.

182 words

Keywords: asthma; dietary patterns; farmer parents; lifestyle; livestock exposure

INTRODUCTION

Increasing evidence for the role of early life events on chronic diseases in adults has led to the development of life course epidemiology with conceptual models incorporating pathways between biological and social factors for both the onset and progression of disease in adult life (1,2). Asthma provides an example with potential biological pathways to explain both an association with farming lifestyle (3), and with diet (4). Optimal immunological maturation has been proposed to explain the protective effect on allergies of contact with livestock in the farming environment (5,6). Studies in adolescents and in adults have shown that the effect of a farming environment in childhood persists as a protective effect into adult life (7,8). Diet is also hypothesized to influence chronic respiratory diseases in adults, through various biological mechanisms, such as modifying the antioxidant protection (4,9-10).

A decrease in traditional farming and changes in diet are part of the changing environment and lifestyle, which could explain the increase in asthma prevalence over the last decades (11,12). Diet is an essential aspect of lifestyle, with specificities between countries and social groups due to cultural, social and environmental factors. Foods that are commonly and easily grown in a specific region, frequently become a part of the local cuisine. The social context in which a child's eating patterns develop is important because the local environment serves as a model for the developing child (13). In this context, a farming lifestyle in childhood may influence dietary habits in adulthood, but to date, there have been no systematic studies.

No study has yet examined asthma in childhood and in adulthood, taking simultaneously into account, the farming environment in childhood and diet in adulthood. Farming lifestyle and contact with livestock have rarely been assessed retrospectively, although this is possible through agricultural census and residential history (14,15). In the E3N study (18), a large study of women born between 1925 and 1950, before major changes in traditional farming in France, we assessed 1) the association between farming lifestyle in

childhood and asthma prevalence, with three indicators of farming lifestyle (having parents who were farmers, being born in a rural area, being exposed to livestock); 2) whether diet in adulthood modified the association between farming lifestyle in childhood and adult-onset asthma.

MATERIALS AND METHODS

Study population

The E3N study (Etude Epidémiologique des Femmes de la Mutuelle Générale de l'Education Nationale) 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 (18). This study began in 1990 and included 98,995 women aged 40 to 65 years. Follow-up questionnaires were sent every two years thereafter. In 1993, a validated dietary history questionnaire was sent to the women. Part of the E3N cohort was then included in the European Prospective Investigation on Cancer. Standardized questions on asthma and data on farming lifestyle during childhood were included in the seventh follow-up questionnaire in 2003. For each questionnaire, the response rate was close to 85%.

Farming lifestyle

Three farming lifestyle indicators were defined, one using individual data and two using ecological data. Women were asked in 2003 whether they lived on a farm during childhood, continuously for at least 3 months, and if yes, whether their parents were farmers. The first indicator of farming lifestyle was 'farmer parents'.

Using data from the General Agricultural Census, the commune at birth was categorized as rural when the number of inhabitants was fewer than 5,000 (to have a sensitive definition of rural). The second indicator of farming lifestyle was 'birth in a rural area'.

The literature on farming hypothesizes that the endotoxin which results from contact with livestock, cattle in particular, protects from allergic asthma (19). Ecological scores were built in several steps. First, appropriate area and reference periods were chosen in an interdisciplinary research frame with geographers (19). France is divided into geographical areas with various units: 22 regions, 96 Departments, 3,644 cantons, and 36,600 communes.

An in-depth analysis of farming activities in two contrasted regions (Aquitaine, a vineyard region with Bordeaux wine, and Normandy, a bovine region with Camembert production) was performed with the General Agricultural Census (GAC) for both 1955 (close to the year of birth of the women) and 1970 (the first computerized GAC). This analysis showed that the 1970 census was adequate to estimate the bovine density score in 1955 (high correlation between the two scores), and that appropriate assessment was obtained by grouping communes with fewer than 1,000 inhabitants from the same canton.

A 'bovine score' was built based on the 1970 GAC for all French communes by combining the number of cattle per inhabitant and the size of the birth commune (table 1). Because 76% of the communes with ≥ 5,000 inhabitants had fewer than 0.1 cattle per inhabitant, for women not born in rural communes we allocated a bovine density score of 0. Therefore, the bovine density score varied from 0 to 3. The coherence was assessed both by geographical distribution with the expected agricultural heterogeneity within France (supplementary data, figure 1), and by the association of this score with the percentage of women who reported living on a farm (supplementary data, figure 2). Similar scores were constructed for pigs, poultry, goats, and sheep, and with different categories for the number of livestock per inhabitant (supplementary data, methods).

In order to investigate the specific contributions of the different exposures (farmer parents, birth in a rural area, the bovine density score) in relation to asthma risk, we assessed different combinations of exposures (farmer parents with exposure to cattle, and farmer parents with being born in a rural area).

Nutritional factor assessment

Dietary patterns were developed using principal component analysis (16). Briefly, foods items were grouped a priori into 56 separate food groups and, as previously described, three dietary patterns were obtained from these food groups: a Prudent pattern (high intake

of fruits and vegetables), a Western pattern (high intake of pizza/salty pies, dessert, cured meats and pasta) and a Nuts and Wine pattern (high intake of nuts and seeds, salty biscuits, olives, wine and fortified wine) (9). Each score of dietary pattern was categorized into tertiles (tertile 1: the lowest score, tertile 3: the highest score). Total energy intake was estimated in 1993 through the dietary questionnaire and expressed in kilocalories per day (kcal/day). Physical activity was assessed in 1993 and measured in Metabolic Equivalents per week (METs/week). Body mass index (BMI) was calculated on the height and weight reported in 2003 and was used as a continuous and as a categorical variable (<20, 20-24.9, 25-29.9, ≥30 kg/m^2).

Asthma assessment

Asthma, assessed by questionnaire, was investigated in 2003 and was defined as recommended by the American Thoracic Society: "Have you ever had asthma attacks?" and if yes “Was this diagnosis confirmed by a doctor?”. For asthmatic women, age at the first attack and frequency of attacks in the last twelve months (≥1/day, ≥1/week, ≥1/month, <1/month) were recorded. We defined childhood asthma as <16 years and early childhood asthma ≤4 years. The overall prevalence of childhood asthma was 1.6% and of adult onset asthma, 3.2%. Frequent asthma attacks were defined by a report of ≥1 attack/week in the last twelve months (9). As the study was done by mail questionnaire, there was no lung function test.

Statistical analysis

Out of the 98,995 women included in the E3N study, 74,525 completed both the 1993 and the 2003 questionnaires. Among the 74,525 women, 19,542 were excluded because they had missing data for asthma (n=17,646) or for information on farmer parents (n=1,896). Among the remaining, 965 additional women with extreme values of the ratio between

energy intake and required energy were excluded. The present analysis is based on 54,018 women (supplementary data, figure 3). Among the 44,977 women that we excluded from the present analysis, the prevalence of ever asthma (using all the information available from the second follow-up questionnaire till the sixth follow-up questionnaire) was 6.0%, and when we look specifically to the 20,507 women that we excluded from the analyses (who responded to the 1993 and the 2003 questionnaire but who had missing data), this prevalence was 5.6%. These two prevalence were quit similar to the one reported in the present analysis (6.5%). Among the 44,977 women that we excluded, we have information regarding the size of the birth commune for 40,272 of them: 35.8% were born in a rural place (<5,000 inhabitants). This prevalence was similar to the one reported in women included (35.7%). Therefore, farming background and asthma were not overrepresented in the 44,977 women not included in the analyses. The comparison of women included (n=54,018) and excluded due to missing data (n=20,507) is presented in the supplementary data, table 1. Briefly, women included did not differ significantly from women excluded regarding the three indicators of farming lifestyle and asthma history (childhood and adult-onset), but excluded women were older, less educated, had a higher BMI, were more often current smokers and took less supplement.

The strategy of analysis included two steps (figure 1). First, we assessed the association between farming lifestyle in childhood with childhood and adult-onset asthma. These associations were investigated using logistic regression models, both univariable and adjusted for potential mediators. For childhood asthma, models were adjusted for age, education level and pets in childhood. For adult onset asthma, we further adjusted for smoking and nutritional factors, i.e., BMI, physical activity, and diet (dietary patterns and total energy intake). Then, we assessed whether the association between farmer parents in childhood and adult onset asthma was modified by diet in adulthood. We formulated two hypotheses: 1) growing up on a farm protects against adult-onset asthma in women with a diet in adulthood rich in fruit and vegetables (Prudent diet), i.e., sources of antioxidants

(biological aspects) but also a proxy for a healthy lifestyle (social aspects), but not in women with a low intake of fruit and vegetables. This hypothesis is a favour of a cumulative protective effect of both growing up on a farm and of a diet rich in fruit and vegetables; (the same hypothesis is made for the Nuts and Wine pattern); 2) growing up on a farm protects against adult-onset asthma in women with a diet in adulthood low in prepared meals, desserts and cured meats (Western diet), but not in women with a high intake of Western diet, i.e., sources of nitrites, trans fat, lipids (biological aspects) but also a proxy for an unhealthy lifestyle. This hypothesis reflects that the protective effect of growing up in a farm may be nullified by the high intake of Western diet.

Because approximately one third of the women were born during the Second World War and because living conditions on farms might have been quite different before, during and after the war, we stratified our analyses according to the year of birth (n=17,961 born before the war, i.e., between 1925 and 1938; n=18,651 born during the war, i.e., between 1939 and 1945; and n=17,406 born after the war, i.e., between 1946 and 1950). All analyses used SAS statistical software, version 9.1.

RESULTS

Farming lifestyle in the population

Twelve percent of women had farmer parents during childhood (table 2). Among women without farmer parents (n=47,482), 11 percent (n=5,284) had lived on a farm for at least three months continuously, during childhood. Women with farmer parents had more pets during childhood, were more often never smokers and had a lower level of education than women without farmer parents. Regarding nutritional factors, women with farmer parents were more often overweight, had a higher total energy intake, took fewer supplements, and consumed more fruit and less salty pies/pizza, cream desserts, processed meat, nuts and seeds and wine, than women without farmer parents. For the dietary patterns, having farmer parents during childhood was associated with a higher score of the Prudent pattern and a lower score of the Nuts and Wine pattern in adulthood. No association was found with the Western pattern. Similar results were found after adjustments for age and total calorie intake.

Farming lifestyle in childhood, dietary habits in adulthood and asthma history

The three indicators of farming lifestyle were related with a history of early childhood (≤4 years), childhood (<16 years), and adult-onset of asthma, whereas no association was observed between frequent asthma attacks and farming lifestyle (table 3), in univariable and in adjusted models.

A history of asthma in childhood was negatively related with having a parent farmer (table 3), especially for early childhood asthma: odds ratio (OR) for farmer parents adjusted for age, education level and pets in childhood=0.55, 95% confidence interval (CI): 0.41-0.75, P<0.001. Similar results were observed for adult-onset of asthma, even if the strength of the association was weaker.

Being born in a rural commune was associated with a lower risk of childhood and early childhood asthma (OR for rural place adjusted for age, education level and pets in childhood=0.83, 95% CI: 0.70-0.99, *P*=0.04). Similar results were observed for adult-onset of asthma, with an odds ratio closer to 1.

Among women without missing data for the bovine density score (n=48,328), a negative and significant trend was found between a history of childhood asthma and early childhood asthma: for the highest bovine density score vs. the lowest score, OR adjusted for age, education level and pets in childhood=0.51, 95%CI: 0.32-0.83, and P_{trend} =0.02. Similar results were reported for adult-onset of asthma even if the strength of the association was weaker.

Regarding combined exposure to farmer parents and exposure to cattle (high vs. low bovine density score), having farmer parents was more crucial in relation to childhood asthma than exposure to cattle: OR adjusted for age, education level and pets in childhood were: 0.50, 95%CI: 0.36-0.70; 0.77, 95%CI: 0.59-1.00; 0.61, 95%CI: 0.42-0.89, respectively for “farmer parents and low bovine density score”, for “no farmer parents and high bovine density”, and for “farmer parents and high bovine density”, as compared to “no farmer parents and low bovine density score”. Regarding combined exposure to farmer parents and rural area at birth, having farmer parents was more crucial in relation to childhood asthma than being born in a rural area: OR adjusted for age, education level and pets in childhood were: 0.84, 95%CI: 0.72-0.99; 0.51, 95%CI: 0.30-0.87; 0.53, 95%CI: 0.40-0.72, respectively for “rural place at birth and no farmer parents”, for “non rural place at birth and farmer parents”, and for “rural place at birth and farmer parents”, as compared to “no rural place at birth and no farmer parents”. Similar results were reported for adult-onset asthma.

Analyses were also stratified according to period of birth (before, during or after the war). For both childhood and adult-onset asthma, the association between farmer parents and asthma history significantly persisted whatever the period of birth (OR [95% CI] were 0.68 [0.51-0.91], 0.79 [0.62-1.00], 0.67 [0.51-0.89]; respectively among women born before,

during and after the war; p for interaction between farmer parents and period of birth was 0.52), but for childhood asthma, was stronger among women born after the war (OR [95% CI] were 0.62 [0.38-1.00] , 0.68 [0.46-1.00], 0.34 [0.21-0.57]; respectively among women born before, during and after the war; p for interaction between farmer parents and period of birth (before and during vs. after the war) was 0.04).

In each tertile of each dietary pattern (Prudent, Western, and Nuts and Wine), we report a strong negative and significant association between farmer parents and adult onset asthma (figure 2). Other indicators of farming lifestyle (i.e., birth in a rural area and the bovine density score) led to similar results: diet in adulthood did not modify the association between farming lifestyle and adult onset asthma.

DISCUSSION

Evidence regarding the role in respiratory diseases, of farming-related conditions in childhood and dietary patterns in adulthood, has been increasing. This is the first study to evaluate both factors, in a large cohort of French women. We proposed a construction of a bovine density score based on ecological data. The association of farming with childhood asthma was confirmed, whatever the indicator considered: the womens' report on having farmer parents, as well as based on the ecological indicators of being born in a rural commune or the bovine density in this commune. We also report a strong association between farming conditions in childhood and adult onset asthma, an association not mediated by diet, BMI, smoking and physical activity in adulthood, suggesting a long-term beneficial effect of exposure independent of others environmental factors or behaviors in adulthood. When we combined the three indicators, having farmer parents was more crucial in relation to childhood asthma than exposure to cattle or being born in a rural area. Our interpretation is that personal exposure reported by having farmer parent corresponds to a higher level of exposure than exposure assessed by ecological data. We observed an association between farming lifestyle during childhood and dietary habits in adulthood. Farming lifestyle in childhood therefore predicts dietary habits, which have already been shown to be related with asthma and to COPD risk, and is an important mediator to consider in the assessment of the role of diet in respiratory diseases. In the present study, the association between farming lifestyle in childhood and adult onset asthma was not modified by dietary habits in adulthood.

Limitations were the lack of lung function data, that childhood asthma was only reported retrospectively, the limited information on early events and no information on diet before adulthood. We cannot exclude the possibility that an asthma diagnosis was more common in urban than in rural areas, for the same symptoms. However, the comparison of included and excluded women regarding asthma and farming lifestyle indicators showed no significant differences. Our results should be generalized with caution as women from the E3N study are more educated than the general population and therefore, might be more

health-conscious (i.e. fewer smokers, with a highest intake of fruit and vegetables, more physically active). However, the strengths of the study are the availability of a large sample of women born before major changes in agriculture, which took place in the fifties, the social homogeneity of the population, combined with a wide geographical distribution over France.

Feasibility and validation of ecological indicators of contact with livestock

Retrospective indicators of contact with livestock were built using aggregated data. We showed the feasibility of the approach and a high correlation with information from the questionnaire (farmer parents and having lived on a farm during childhood). It is of particular interest in agricultural countries, such as France, with wide geographical heterogeneity (with farms for cereals and wine without livestock, or with regions with specific livestock well identified by their cheese production). As differential roles of cattle, sheep, and poultry have been proposed (20), it would have been of interest to study in depth the potential role of other livestock, but it was not possible due to sample size issues.

The retrospective evaluation of potential early contact with livestock was possible through the questionnaire (farmer parents) and by ecological scores using agricultural census for the place of birth. This ecological approach used could be easily adapted in other countries. Further, the construction of ecological indicators of rural lifestyle over the lifespan might be useful in a variety of settings (pesticide usage for example). The use of aggregated data could be exploited more, isolated and/or in conjugation with individuals indices (21). It is a way to decrease the misclassification Berkson error (occurs where the same approximate exposure is used for many subjects), as emphasized in numerous theoretical reports (22). However, disadvantages include the aspect of ecological fallacy regarding wrong interpretation at the individual level.

Farming and dietary habits: a story of food preferences, availability and social factors

Factors influencing food choice are not only based on individual preferences, but are constrained by circumstances that are social, cultural and economical. Several studies have

reported a clear difference between social classes in food and nutrient intake; low-income groups in particular, have a greater tendency to consume unbalanced diets and have a low intake of fruit and vegetables (23). Numerous studies have investigated relationships between socio-demographic characteristics, lifestyle and dietary patterns (24-26), but few have reported the effect of urban/rural living in adulthood on diet (25, 26).

The social context in which a child's eating pattern develops is important because the eating behavior of people in the environment serves as a model for the developing child (13). In that context, a farming lifestyle probably influences later food preferences, due to different food availability in rural areas, and it was related with a healthier behavior regarding the intake of fruit and vegetables.

Farming lifestyle is also related with cultural behavior, as drinking alcohol was not socially acceptable among women, especially 60 years ago. In our study, women without farmer parents in childhood, drank more wine in adulthood than women with farmer parents in childhood. Two surveys have investigated the association between diet with urban/rural residence in adulthood, and they also reported that alcohol intake, especially wine, increased with urbanization (25, 26).

Interestingly, we also observed a stronger association between farmer parents and childhood asthma among women born post war, as compared to women born before or during the war. It can be speculated that women born post war were likely a more homogenous group regarding exposure to farming during childhood than those born during the war who experienced variable conditions (such as deprivation), or before the war who experienced changes regard to the war period.

Farming, diet and asthma

According to the hygiene hypothesis, the decrease in early contacts with infectious agents, in particular through contacts with livestock, could explain the increase in prevalence of asthma and allergies, and several studies have been conducted regarding farming lifestyle and asthma (6). Our results on childhood asthma and farming lifestyle are consistent with

previous studies (6). The lower prevalence of adult onset asthma in women born in a rural environment is consistent with the hypothesis of a beneficial effect of continuous exposure, independently of others environmental factors or behaviors in adulthood (28-32).

In studies conducted in children on the farming hypothesis, the role of diet has been evoked as a potential mediator in relation to changing lifestyle (i.e. changes in diet with urban living) (7, 33, 34) and as a direct immunological mechanism (8,35). In our study, we investigated whether diet in adulthood might modify the association between farming lifestyle in childhood and adult onset asthma, and we report no modifying effect of diet habits.

This study combined prospective and retrospective data to assess the effect of environment and lifestyle at various times over the life span. Results from this large French survey further supports the hypothesis of contact with livestock and of a farming lifestyle on the lower asthma prevalence, in particular in childhood.

Acknowledgements

We wish to thank all the participants of the E3N study and Lyan Hoang, Maryvonne Niravong and Marie Fangon for invaluable assistance with the implementation of the study. We also thank Beverley Balkau.

Competing interests

No competing interest.

Funding

This work was supported by AFSSET - APR2003, ATC-Environment and Health 2003. The E3N study is supported by the Mutuelle Générale de l'Education Nationale (MGEN), the European Community, the French League against Cancer (LNCC), the Gustave Roussy Institute (IGR), the National Institute for Health and Medical Research (Inserm) and General Councils of France.

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Table 1 Construction of the bovine density score according to the size of the birth commune and to the number of cattle in the commune. Data from the 1970 General Agricultural Census, France.

		Number of inhabitants in the birth commune	
		≥ 5,000	< 5,000[c]
		0 (not rural)[b]	
Number of cattle per inhabitant in the birth commune[a]	<1		1 (low)
	1		2 (medium)
	≥2		3 (high)

[a] For communes with fewer than 1,000 inhabitants, the number of cattle per inhabitant was from the canton of birth, with small communes aggregated.

For example, a woman born in a commune where a) the number of inhabitants was between 1,000 and 4,999; b) and the number of cattle per inhabitant was more than 2, the bovine density score was classified in category 3.

[b] Among the 1,448 places with ≥ 5,000 inhabitants, 15.1% of the communes had 0 cattle per inhabitants, 61.0% had ≤ 0.1 cattle per inhabitants (mean=0.029), 22.8% had ≤ 1 cattle per inhabitants (mean=0.252), and only 1.2% had more than 1 cattle per inhabitants (mean=1.394). More than 76% of the place with ≥ 5,000 inhabitants had less than 0.1 cattle per inhabitants, and 99% had less than 1 cattle per inhabitants. Therefore, for women not born in rural communes, we allocated a bovine density score of 0.

[c] The cut off of 5,000 inhabitants was chosen to have a sensitive definition of “rural”.

Table 2 Characteristics of the population according to farmer parents, E3N study, France (n=54,018 women)

	No farmer parents (n=47,482)	Farmer parents (n=6,536)	*P value*
Age, years (mean (SD))[a]	61.4 (6.4)	61.3 (6.3)	0.37
Have lived on a farm during at least 3 months continuously, (%)	11.1	100.0	<0.001
Born in a rural area (<5,000 inhabitants), (%)	29.5	78.9	<0.001
Bovine density score, place of birth, (%)			
0	70.6	21.2	
1	20.0	38.4	<0.001
2	5.8	22.9	
3	3.6	17.5	
Pets in childhood, %[a]			
No pets	44.3	9.0	
Cats only	18.1	7.3	
Dogs only	13.7	8.5	<0.001
Cats and dogs	19.6	70.2	
Missing	4.3	5.0	
Tobacco consumption, %[b]			
Never smokers	54.9	65.1	
Past smokers	31.2	26.0	<0.001
Current smokers	13.8	8.9	
Menopausal status, %[a]			
Premenopause	4.6	5.2	0.09

Postmenopause	95.4	94.7	
Perimenopause	0.1	0.1	
Education, number of years of school (%)			
≤ 11	9.9	14.7	
12-14	50.4	61.9	<0.001
15-16	19.8	14.3	
≥ 17	19.9	9.1	
Physical activity, metabolic equivalent / week (mean (SD))[b]	40.1 (27.7)	39.5 (27.4)	0.10
Body mass index, kg/m^2, (mean (SD))[b,c]	22.8 (3.2)	23.0 (3.1)	<0.001
Body mass index, kg/m^2 (%)[b,c]			
< 20	13.4	11.8	
20-24.9	56.2	57.8	
25-29.9	14.1	15.0	<0.001
≥ 30	2.8	2.9	
Missing	13.5	12.5	
Total energy intake, kilocalories/day (mean (SD))[b]	2175 (571)	2193 (558)	0.01
Supplement use, %[a,d]	37.7	36.0	0.01
Food groups intake, g/day (mean (SD))[b]			
Fruit	256.7 (165.1)	287.8 (175.0)	<0.001
Vegetables	226.8 (150.5)	224.8 (144.2)	0.29

Red meat	49.1 (37.1)	48.5 (36.5)	0.20
Salty pies/pizza	3.3 (3.5)	2.9 (3.1)	<0.001
Cream desserts	19.8 (27.8)	19.0 (25.5)	0.02
Processed meat	30.8 (22.9)	29.1 (21.2)	<0.001
Nuts and seeds	5.7 (5.5)	5.2 (8.0)	<0.001
Wine	95.2 (134.5)	72.8 (105.5)	<0.001
Prudent diet pattern, %			
Tertile 1 (lowest score)	32.0	31.3	
Tertile 2	34.2	33.1	0.03
Tertile 3 (highest score)	33.8	35.5	
Western diet pattern, %			
Tertile 1 (lowest score)	32.3	31.1	
Tertile 2	34.0	36.2	0.77
Tertile 3 (highest score)	33.7	32.7	

Nuts and Wine diet pattern, %			
Tertile 1 (lowest score)	32.2	40.1	
Tertile 2	33.2	34.7	<0.001
Tertile 3 (highest score)	34.6	25.1	

Abbreviations: SD, standard deviation

[a] Recorded in 2003.

[b] Recorded in 1993.

[c] Body mass index: weight (in kilograms)/height^2 (in meters).

[d] Includes 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.

Table 3 Asthma prevalence in childhood and adulthood according to farming lifestyle, E3N study, France (n=54,018 women)

	Childhood asthma < 16 years			Adult onset asthma			Frequent asthma attacks in adulthood		
	Prevalence (%)	Crude OR (95% CI)	Adjusted OR (95%CI)[a]	Prevalence (%)	Crude OR (95% CI)	Adjusted OR (95%CI)[b]	Prevalence (%)	Crude OR (95% CI)	Adjusted OR (95%CI)[b]
Parents									
Not farmers	2.2	1.00	1.00	4.4	1.00	1.00	20.5	1.00	1.00
Farmer s	1.1	0.51 (0.41-0.66)	0.54 (0.42-0.70)	3.5	0.79 (0.69-0.91)	0.72 (0.62-0.84)	19.2	0.93 (0.51-1.66)	0.95 (0.48-1.88)
P		<0.001	<0.001		<0.001	<0.001		0.80	0.88
Rural place at birth									
No (≥ 5,000 inhabitants)	2.3	1.00	1.00	4.4	1.00	1.00	20.7	1.00	1.00
Yes (< 5,000 inhabitants)	1.7	0.73 (0.64-0.84)	0.79 (0.68-0.92)	4.0	0.90 (0.82-0.99)	0.87 (0.78-0.96)	22.0	1.08 (0.76-1.55)	1.12 (0.74-1.68)

P		<0.001	0.002		0.04	0.007		0.67	0.59
Bovine density score at place of birth [c]									
0	2.3	1.00	1.00	4.4	1.00	1.00	20.6	1.00	1.00
1	1.8	0.78	0.84	4.2	0.97	0.93	23.1	1.16	1.16
		(0.66-0.92)	(0.70-0.99)		(0.87-1.08)	(0.83-1.05)		(0.77-1.74)	(0.72-1.83)
2	1.6	0.69	0.74	3.3	0.75	0.74	19.5	0.93	1.08
		(0.52-0.90)	(0.56-0.98)		(0.62-0.90)	(0.60-0.89)		(0.42-2.07)	(0.47-2.50)
3	1.4	0.62	0.69	3.8	0.86	0.78	19.5	0.93	1.01
		(0.44-0.88)	(0.49-0.98)		(0.69-1.06)	(0.63-0.98)		(0.42-2.07)	(0.43-2.36)
P_{trend}		<0.001	0.002		0.006	<0.001		0.96	0.78

Abbreviations: CI, confidence interval; OR, odds ratio.

[a] Adjusted for age, education level and pets in childhood.

[b] Adjusted for age, education level, pets in childhood, smoking, body mass index, physical activity, dietary patterns and total energy intake

[c] 0: not rural, 1: low bovine density score, 2: medium bovine density score, 3: high bovine density score (see methods).

Figure 1 Study design and conceptual framework

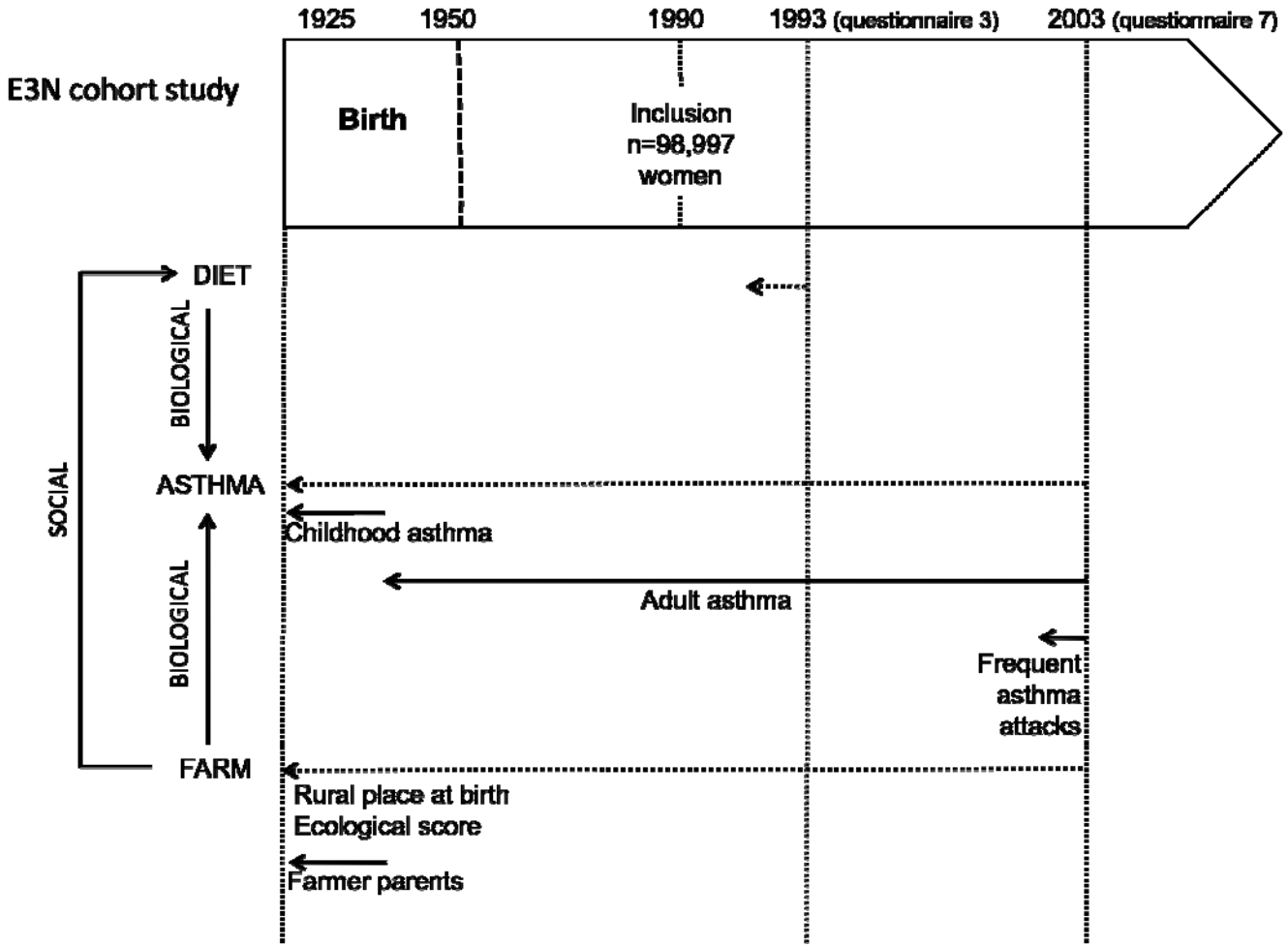
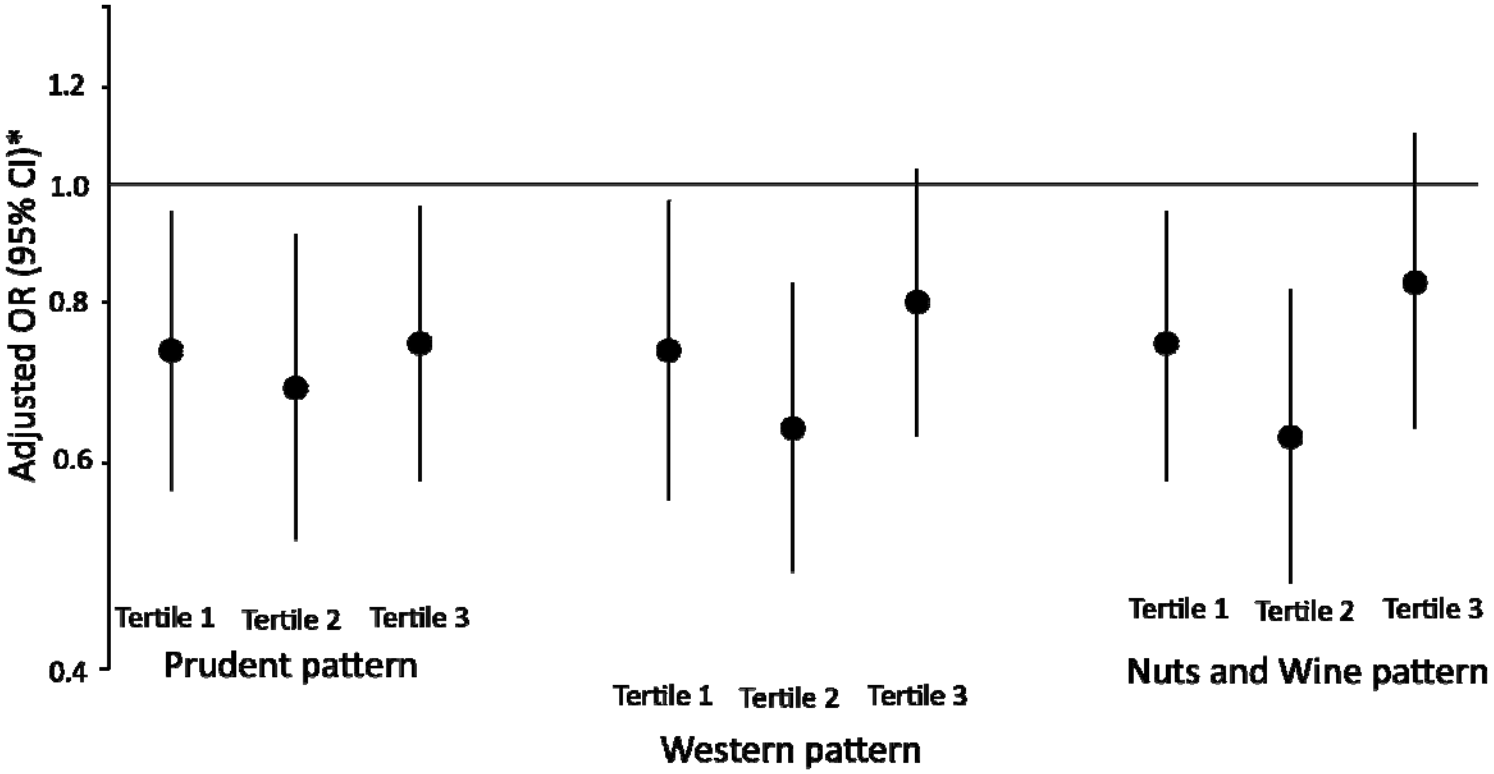


Figure 2 Association between farmer parents and adult onset asthma, according to tertiles of dietary patterns, E3N study, France (n=54,018 women)



* Adjusted for age, education level, pets in childhood, smoking, body mass index, physical activity, total energy intake and the two others dietary patterns