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Body Mass Index, Change in Body Silhouette, and Risk of Asthma in the E3N Cohort Study

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To evaluate the impact of body mass index (BMI) (weight (kg)/height (m)^2) and change in body silhouette on asthma risk, the authors investigated a cohort of women participating in the E3N Cohort Study in France from 1990 to 1993. The authors identified 372 incident cases of asthma among 67,229 women aged 40–65 years at baseline. Data were analyzed using proportional hazard models to determine the risk of asthma incidence in relation to BMI and body silhouette. Reported BMI at baseline was related to the incidence of asthma, with a significantly increased risk corresponding to increasing BMI quintiles (test for trend: $p < 0.001$). Compared with a BMI of 20–21.4 (second quintile), women with a BMI ≥27 had double the risk of incident asthma after adjustment for potentially confounding factors (multivariate relative risk = 2.02, 95% confidence interval: 1.38, 2.98). Increase in body mass between menarche and the start of the follow-up study was significantly related to asthma risk (for an increase of two silhouettes, relative risk = 1.66, 95% confidence interval: 1.18, 2.32). The authors conclude that a high BMI is significantly related to the risk of asthma incidence and that an increase in body silhouette between menarche and adulthood is related to the incidence of asthma later in life.

asthma; body mass index; cohort studies; weight gain; women

Abbreviations: BMI, body mass index; CI, confidence interval; RR, relative risk.

The great increase in the prevalence of asthma observed in most developed countries in recent years (1, 2) has suggested that environmental factors may be responsible for part of the increase. The possible importance of a more sedentary lifestyle has been discussed (3). In some western countries, secular trends of increased asthma prevalence have been accompanied by a similar increase in the prevalence of obesity (2–4). Crater and Platts-Mills (5) recently proposed that the increasing incidence of asthma in westernized countries might in fact be related to the increased prevalence of obesity. Although this observation was made primarily in children (6–11), recent studies have reported an association between body mass index (BMI) (weight (kg)/height (m)^2) and asthma prevalence in adult men and women (12, 13), as well as an increase in asthma incidence corresponding to weight gain in women (14–16). However, none of the previous studies focused on the relation between asthma incidence in adulthood and corpulence earlier in life, particularly during puberty and early adulthood. The fact that weight gain is only associated with asthma incidence in women and the observation that asthma incidence tends to decrease after menopause (17) point toward an endocrine factor, such as the endogenous synthesis of estrogen.

To evaluate the impact of BMI on asthma risk, we used data from the E3N cohort, a cohort of French women assembled in 1990. We estimated the relations of current BMI, body silhouette at different points in life, and changes in weight and body silhouette with self-reported asthma, accounting for factors that are determinants of BMI, such as dietary intake and energy expenditure (18, 19), and that might confound the association.

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MATERIALS AND METHODS

Study population

The E3N Cohort Study (Etude Epidémiologique auprès de Femmes de l'Education Nationale) is a prospective investigation of major chronic diseases in a cohort of members of the Mutuelle Générale de l'Education Nationale, a French national health insurance plan covering mostly teachers. The study started in 1990 when half a million women aged 40–65 years were invited to participate. The consent form clearly stated that the study was planned to last at least 10 years. Approximately 100,000 women agreed to participate, corresponding to a response rate of 20 percent, and returned the first questionnaire (Q_1). The general characteristics of this population have been reported elsewhere (20). Follow-up questionnaires were sent every 2 years thereafter.

In 1993, a dietary history questionnaire (Q_3) was sent to the women. This questionnaire has been described elsewhere and has been validated with 24-hour recalls spread out over 1 year (21). A total of 75,508 women returned the dietary history questionnaire. Among them, 3,777 women were excluded because they had not completed the second questionnaire (Q_2), and 1,346 were excluded because the figures they reported on the food questionnaire were determined to be unrealistic using the ratio of energy intake to energy requirements. In addition, we further excluded women who reported having prevalent asthma at baseline or who could not provide the date of diagnosis (n = 3,156).

Body mass index

BMI was calculated on the basis of the height and weight reported in the questionnaire administered at baseline. BMI was used as a continuous and categorical variable with the following decile cutpoints: ≤19.26, 19.27–20.08, 20.09–20.70, 20.71–21.33, 21.34–21.94, 21.95–22.65, 22.66–23.44, 23.45–24.46, 24.47–26.26, and >26.26. In our population, 4.4 percent of subjects had a BMI under 18.5 (underweight); only 7.2 percent had a BMI exceeding 27, and 2.5 percent had a BMI exceeding 30. We also conducted the analysis using quintile cutpoints, dividing the last quintile into two categories: <20.20, 20.20–21.41, 21.42–22.68, 22.69–24.61, 24.62–26.99, and ≥27. Results were very similar; consequently, we present only the results using this last distribution. As a reference category, we used women in the second quintile of the distribution (BMIs of 20.20–21.41, considered normal).

Change in weight was calculated as the difference between weight reported at baseline (Q_1) and weight reported on the third questionnaire (Q_3). This variable was used as a categorical variable in the analysis, with the following cutpoints: loss of >5 kg, loss of 1–5 kg, no change or change of ±1 kg, gain of 1–5 kg, and gain of >5 kg. We also used the silhouettes the women identified on the baseline questionnaire providing information on their figure at different ages (at approximately age 8 years, at menarche, at age 20–25 years, at age 35–40 years, and at the time of completion of the questionnaire) (22). The eight silhouettes in the questionnaire (figure 1) were considered as categorical variables ranked from 1 (the leanest silhouette) to 5 and over, with the four largest silhouettes being grouped together. If a woman indicated two silhouettes, the largest figure was considered. The actual classification of a woman's perceived figure was validated against anthropometric measurements, and good correlation was observed (correlation coefficient = 0.78). Changes in silhouette between different ages in life and baseline were categorized as a decrease of one silhouette, no change, an increase of one silhouette, or an increase of two or more silhouettes.

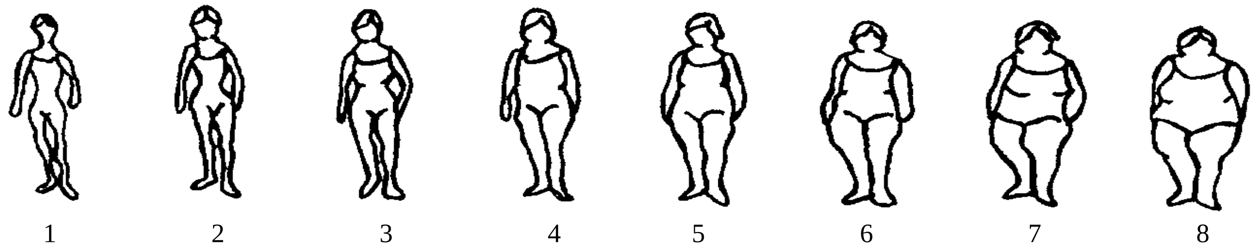

FIGURE 1. Body silhouettes used on the baseline questionnaire to assess body mass at various ages (as first proposed by Sörensen et al. (22)), E3N Cohort Study, France, 1990–1993. The sihouettes are represented by figure drawings ranked from 1 to 8, corresponding to increasing body size (from the leanest to the largest). Women reported the drawing that reflected their perceived body size at a specific age (at approximately age 8 years, at menarche, at age 20–25 years, at age 35–40 years, and at the time of completion of the questionnaire). Because few women reported having a silhouette larger than 5, the eight silhouettes were further ranked from 1 to ≥5, with the four largest silhouettes being grouped together.

Other information

Information on tobacco smoking was reported on all questionnaires and included the categories never smoker, past smoker, usual smoker, and occasional smoker. Women in the last two categories were regrouped as current smokers. Women also reported their current exercise activity, and we calculated their energy expenditure by multiplying the duration of daily activities and leisure physical activities by the estimated metabolic energy spent, based on the values proposed by James and Schofield (23). This variable was then categorized into quartiles of physical activity. Menopausal status was also obtained by the questionnaire, and women were classified as premenopausal, postmenopausal, or perimenopausal. In addition, we obtained information on the use of oral contraceptives and hormone replacement therapy. These variables were classified as "ever having used" and "never having used."

Definition of an incident case of asthma

Our definition of asthma was based on the presence of an affirmative answer to the question "Did you have an asthma attack?" and age at the time of the first attack. Women were considered to have incident asthma if they stated on the baseline questionnaire that they had never had an asthma attack and they reported having an asthma attack between baseline and one of the two following questionnaires (over 3 years). In addition, the date of the first asthma attack needed to be specified and included in the 3-year follow-up period. Women who stated that they had ever had an asthma attack prior to baseline were excluded from the analysis. Among 67,229 women, 372 incident cases of asthma were identified.

Statistical analysis

The general characteristics of the women included in the present analysis were compared with those of the women excluded (see "Study population"). These characteristics were similar in both groups (table 1), except for allergy, which was more frequent among women who were excluded from the analysis.

We then studied the association between new cases of asthma over the 3 years of follow-up and different variables, including BMI, weight gain, and body silhouette at different ages, using Cox proportional hazards models (24). Results were adjusted for potentially confounding factors, including age, socioeconomic status, total caloric intake, intake of antioxidant vitamins (vitamin C, vitamin E, β-carotene), physical activity, smoking status, use of oral contraceptives and hormonal replacement therapy, and menopausal status. We also included an indicator variable for women who reported using dietary supplements, given that we did not have information on the exact composition of these supplements (vitamins and minerals).

Because neither socioeconomic variables nor the nutritional data, except total caloric intake, were significantly related to the incidence of asthma, these variables were not included in our final model. Similarly, use of oral contraceptives and use of hormone replacement therapy did not confound the association between BMI and asthma risk and were not included in our final analyses. To evaluate the impact of change in weight, in addition to the variables noted above, we adjusted for BMI at baseline. Similarly, to determine the impact of change in body silhouette on asthma risk between different ages (index age) and baseline, we additionally adjusted for silhouette at the index age. All analyses were conducted using SAS, version 8 (SAS Institute, Inc., Cary, North Carolina).

RESULTS

During the 3 years of observation, from 1990 to 1993, 372 incident cases of asthma were identified, corresponding to a cumulative incidence of 0.55 percent. At baseline, 34.3 percent of women were less than 45 years of age, 23.8 percent were between 45 and 50 years of age, 19.4 percent were between 51 and 55 years of age, and 22.5 percent were over 55 years of age. The mean BMI at baseline was 22.55 (standard deviation 3.1). The mean total caloric intake was 2,142 kcal/day (standard deviation 626.4). With regard to smoking, 64.30 percent of the women had never smoked, 22.4 percent were ex-smokers, and 11.3 percent were current smokers. Regarding menopausal status, 63.3 percent of the women were premenopausal, 29.2 percent were postmenopausal, and 7.5 percent were perimenopausal.

TABLE 1. Distribution of characteristics between women included in the analysis and women who were excluded, E3N Cohort Study, France, 1990–1993

Variable	Women included in the analysis (%) (n = 67,229)	Women excluded from the analysis (%) (n = 8,279)
Age (years)		
<45	34.3	40.1
45–50	23.8	21.8
51–55	19.4	17.7
56–60	13.7	12.4
>60	8.8	8.0
Physical activity*		
Quartile 1	25.7	22.5
Quartile 2	25.3	22.1
Quartile 3	24.2	20.6
Quartile 4	24.7	22.9
Missing data	0.0	11.9
Caloric intake (kcal/day)		
<1,650	19.3	26.3
1,650–1,948	20.2	16.0
1,949–2,225	20.4	16.3
2,226–2,596	20.4	15.9
>2,596	19.7	25.5
Body mass index†		
<20.20	21.0	18.1
20.20–21.41	19.9	15.6
21.42–22.68	19.7	15.8
22.69–24.61	20.0	16.8
24.62–26.99	11.0	10.6
≥27	7.2	8.8
Unknown	1.2	14.2
Tobacco consumption		
Never smoker	64.3	55.4
Ex-smoker	22.4	20.6
Current smoker	11.3	10.4
Unknown	2.0	13.6
Menopausal status		
Premenopausal	63.3	54.3
Postmenopausal	29.2	26.8
Perimenopausal	7.5	18.9
Education		
Less than high school	11.1	12.3
High school +2 years	49.2	40.9
From high school +2 years to high school +4 years	18.1	15.4
High school +≥5 years		
Unknown	17.6	15.4
	4.0	16.0
Allergy‡		
Yes	24.8	42.9
No	75.2	57.1

* Energy expenditure was calculated by multiplying the duration of daily activities and leisure physical activities by the estimated metabolic energy spent, based on the values proposed by James and Schofield (23). The variable was then categorized into quartiles of physical activity.
† Weight (kg)/height $(m)^2$.
‡ Allergy was defined as allergic rhinitis, eczema, or other allergic problems.

Table 2 presents the characteristics of the population at baseline according to asthma status. Asthma incidence varied with age, being significantly higher in the younger age group. No difference in incidence was observed with level of physical activity. Women in the lowest and highest quintiles of caloric intake had a higher incidence of asthma. Asthma incidence was lowest among never smokers and postmenopausal women.

TABLE 2. Baseline characteristics of the population according to asthma status, E3N Cohort Study, France, 1990–1993

Variable	No. of incident asthma cases (n = 372)	No. in total study population (n = 67,229)	Cumulative incidence of asthma (%)	Crude *p* value
Age (years)				
<45	168	23,053	0.73	<0.001
45–50	88	16,018	0.55	
51–55	54	13,026	0.41	
56–60	34	9,184	0.37	
>60	28	5,948	0.47	
Physical activity*				
Quartile 1	97	17,289	0.56	0.86
Quartile 2	87	17,021	0.51	
Quartile 3	93	16,289	0.57	
Quartile 4	95	16,630	0.57	
Caloric intake (kcal/day)				
<1,650	81	12,986	0.62	0.02
1,650–1,948	56	13,579	0.41	
1,949–2,225	171	13,701	0.52	
2,226–2,596	72	13,741	0.52	
>2,596	92	13,222	0.70	
Body mass index†				
<20.20	71	14,137	0.50	0.0003
20.20–21.41	60	13,351	0.45	
21.42–22.68	76	13,224	0.57	
22.69–24.61	71	13,444	0.53	
24.62–26.99	47	7,405	0.63	
≥27	43	4,848	0.89	
Missing data	4	820		
Tobacco consumption				
Never smoker	211	43,238	0.49	0.02
Ex-smoker	99	15,084	0.66	
Current smoker	53	7,584	0.70	
Missing data	9	1,323		
Menopausal status				
Premenopausal	259	42,536	0.61	0.004
Perimenopausal	31	5,031	0.62	
Postmenopausal	82	19,662	0.41	

* Energy expenditure was calculated by multiplying the duration of daily activities and leisure physical activities by the estimated metabolic energy spent, based on the values proposed by James and Schofield (23). The variable was then categorized into quartiles of physical activity.

† Weight (kg)/height $(m)_2$.

BMI at baseline was significantly related to the risk of incident asthma. Women in the fifth quintile of BMI (BMI >24.61) had an increased risk of asthma compared with women in the second quintile (BMI 20.20–21.41) (age-adjusted relative risk (RR) = 1.79, 95 percent confidence interval (CI): 1.29, 2.49). When we recategorized the last quintile into women with BMIs of 20.61–26.99 and women with BMIs ≥27, we observed the largest risk for women with BMIs ≥27 (age-adjusted RR = 2.15, 95 percent CI: 1.45, 3.20), with a positive trend with increasing BMI level (*p* <0.0001). Similar results were observed after adjustment for age, activity, total caloric intake, smoking status, menopausal status, and use of nutritional supplements (table 3).When we stratified the data by menopausal status, we observed a large risk among postmenopausal women (comparing women with BMIs of 20.20–21.41 (second quintile) with women with BMIs of 24.61–26.99, age-adjusted RR = 2.61, 95 percent CI: 1.07, 6.35; for BMIs ≥27, age-adjusted RR = 2.90, 95 percent CI 1.14, 7.38).

TABLE 3. Relative risk of incident asthma according to body mass index at baseline and change in weight, E3N Cohort Study, France, 1990–1993

Variable	No. of incident asthma cases	No. in total study population	Age-adjusted RR*	95% CI*	Multivariate RR†	95% CI
Body mass index‡						
<20.20	71	14,137	1.09	0.77, 1.53	0.93	0.66, 1.31
20.20–21.41	60	13,351	1.00		1.00	
21.42–22.68	76	13,224	1.31	0.94, 1.84	1.22	0.88, 1.69
22.69–24.61	71	13,444	1.26	0.89, 1.77	1.18	0.84, 1.64
24.62–26.99	47	7,405	1.55	1.06, 2.28	1.46	1.01, 2.12
≥27	43	4,848	2.15	1.45, 3.20	2.02	1.38, 2.98
Missing data	4	820				
p for trend			<0.0001		<0.0001	
Weight change during follow-up						
Loss of 1–5 kg	54	8,026	1.51	1.10, 2.07	1.37	0.99, 1.89
No loss (±1 kg)	135	29,860	1.00			
Gain of 1–5 kg	123	21,405	1.20	0.94, 1.54	1.00	
Gain of >5 kg	35	4,030	1.67	1.15, 2.42	1.17	0.91, 1.50
Missing data	25	3,808			1.49	1.02, 2.18

* RR, relative risk; CI, confidence interval.
† Adjusted for age, total caloric intake, physical activity, smoking status, and menopausal status. The relative risk for weight change during follow-up was adjusted for age, body mass index at baseline, total caloric intake, physical activity, smoking status, menopausal status, and use of nutritional supplements.
‡ Weight (kg)/height (m)^2.

Because a high body mass could give rise to transient respiratory obstruction that might appear symptomatic of asthma but be due to other mechanisms, we conducted a stratified analysis based on responses to the question, "Do you have dyspnea or difficulty breathing when you walk with a person of your age at a normal pace?". We observed that the association between BMI and incident asthma was present mostly in women who did not report dyspnea or difficulty breathing (data not shown).

When considering weight change during follow-up, we observed a J-shaped relation. Taking as the reference category a change of ±1 kg, we observed that women who lost weight (1–5 kg) and women who gained weight (>5 kg) had increased risks of asthma (52 percent and 69 percent, respectively). Adjustment for the variables mentioned above and BMI at baseline decreased the association slightly, but a similar pattern was observed as in the age-adjusted estimates (table 3).

A larger silhouette at menarche was related to a lower risk of incident asthma later in life. Women who had the largest figures at menarche (see figure 1, silhouette 4 or higher) had a 38.9 percent decreased risk of incident asthma later in life as compared with women with the thinnest silhouette (multivariate RR = 0.72, 95 percent CI: 0.52, 0.99) (table 4). In contrast, silhouette at age 35 years and silhouette at baseline were both positively related to asthma incidence. When compared with the thinnest silhouettes (see figure 1, silhouettes 1 and 2), women who had the largest silhouettes (see figure 1, silhouette 5 or higher) at age 35 years had a 60 percent increased risk of incident asthma (multivariate RR = 1.60, 95 percent CI: 1.09, 2.36). This risk reached 82 percent for the women who were largest at baseline (multivariate RR = 1.82, 95 percent CI: 1.28, 2.59) (table 4).

Change in body silhouette over time was related to the risk of asthma later in life (figure 2). Women who gained two or more silhouettes (approximately ≥10 kg) between menarche and baseline had a 66 percent increased risk of asthma when compared with women who did not change silhouette, after adjustment for age and body silhouette at menarche, as well as total caloric intake, physical activity, smoking habits, menopausal status, and use of nutritional supplements (multivariate RR = 1.66, 95 percent CI: 1.18, 2.32; test for trend: $p < 0.001$). Similarly, an 89 percent increased risk of asthma was observed for women who gained two or more silhouettes between the age of 20 years and baseline (multivariate RR = 1.89, 95 percent CI: 1.37, 2.60; test for trend: $p < 0.001$).

TABLE 4. Relative risk of incident asthma according to body silhouette* at different ages, E3N Cohort Study, France, 1990–1993

Variable	No. of incident asthma cases	No. in total study population	Age-adjusted RR†	95% CI†	Multivariate RR‡	95% CI
Silhouette at menarche						
1	87	14,210	1.00		1.00	
2	125	20,828	0.96	0.73, 1.26	0.96	0.73, 1.26
3	78	15,671	0.78	0.53, 1.06	0.78	0.57, 1.06
≥4	65	13,983	0.73	0.53, 1.00	0.72	0.52, 0.99
Missing data	17	2,537				
p for trend			0.02		0.018	
Silhouette at age 20–25 years						
1	31	6,560	1.00		1.00	
2	175	27,190	1.33	0.91, 1.95	1.33	0.91, 1.95
3	94	22,265	0.87	0.58, 1.30	0.87	0.59, 1.30
≥4	57	9,315	1.28	0.83, 1.98	1.28	0.82, 1.98
Missing data	15	1,899				
p for trend			NS†		NS	
Silhouette at age 35–40 years						
1 and 2	111	20,912	1.00		1.00	
3	150	27,916	1.02	0.78, 1.28	1.02	0.80, 1.30
4	63	12,311	0.96	0.70, 1.31	0.98	0.72, 1.34
≥5	34	4,091	1.57	1.07, 2.31	1.60	1.09, 2.36
Missing data	14	1,999				
p for trend			0.12		0.09	
Silhouette at baseline						
1 and 2	64	11,866	1.00		1.00	
3	134	25,129	1.14	0.85–1.53	1.16	0.86–1.56
4	94	17,490	1.22	0.88–1.68	1.26	0.91–1.73
≥5	65	8,723	1.77	1.25–2.51	1.82	1.28–2.59
Missing data	15	2,521				
p for trend			0.002		0.001	

* See figure 1 for illustration of silhouettes 1–8.

† RR, relative risk; CI, confidence interval; NS, not significant.

‡ Adjusted for age, total caloric intake, physical activity, smoking status, menopausal status, and use of nutritional supplements.

When we restricted the analysis to women who had a BMI of 20–24 (“normal”) at menarche or around 20 years of age, results remained similar, suggesting that our estimates were not driven by women with high BMIs who gained additional weight.

DISCUSSION

In this large prospective study of French women, BMI was strongly related to the risk of adult onset of asthma, even after adjustment for potentially confounding factors. Weight change during follow-up was associated with a J-shaped relation with asthma risk. Increase in body silhouette after menarche was strongly associated with adult onset of asthma.

Our results agree with recent reports. Chen et al. (16), in Canada, observed a significant association between baseline BMI and asthma incidence in women but not in men. Similarly, Shaheen et al. (12), in a British cohort, found that overweight and obese women aged 26 years were 51 percent and 84 percent more likely to be asthmatic, respectively, than women of normal weight. Low birth weight was significantly related to asthma, but no relation was observed between BMI at age 10 years and adult asthma (12). In a study conducted in China, Celedon et al. (13) reported that being underweight and being overweight were both related to asthma in adult women. Two follow-up studies also supported the hypothesis that weight change as well as baseline BMI is associated with asthma in adult women. In a study carried out among nurses in the United States, Camargo et al. (14) reported that BMI was a strong predictor of adult onset of asthma and that weight gained after age 18 years significantly increased the risk of developing asthma during the 4-year follow-up period. Similarly, Beckett et al. (15) reported that incident asthma was associated with highest and lowest baseline BMI and change in BMI over a 10-year follow-up period, in a J-shaped curve in females but not in males. Our results support the findings of these studies but further suggest that weight gain prior to adulthood might increase the risk of asthma later in life.

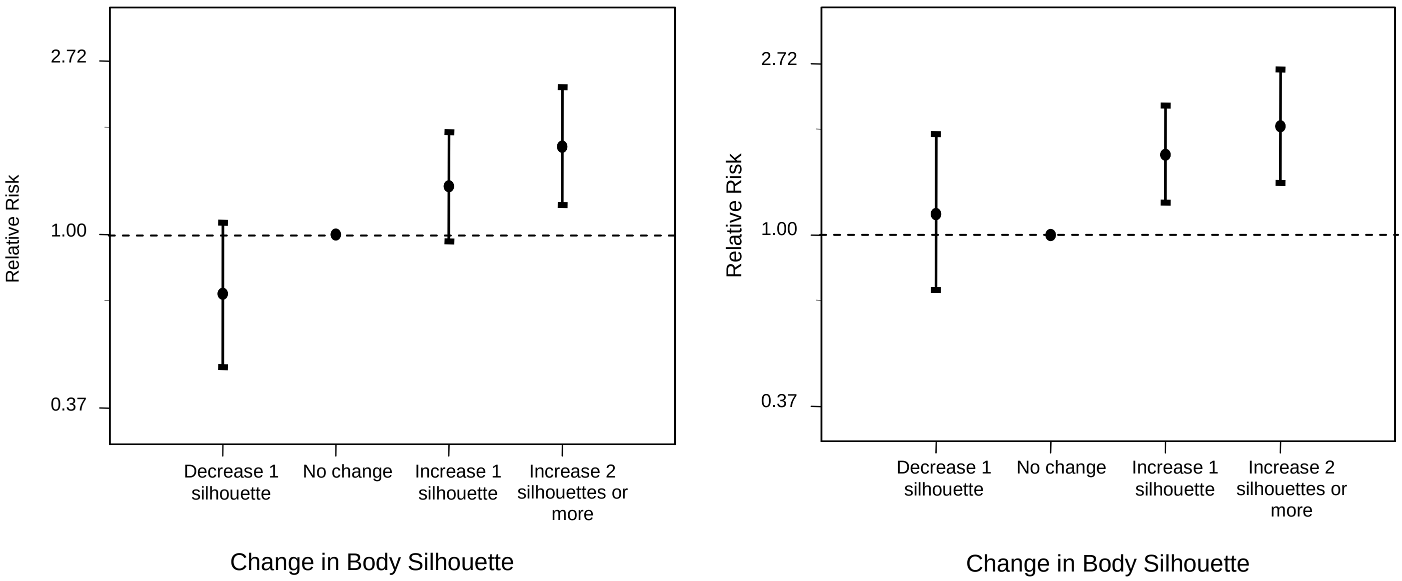

FIGURE 2. Relative risk of asthma incidence among adult women according to change in body silhouette between menarche and baseline (left) and between age 20 years and baseline (right), E3N Cohort Study, France, 1990–1993. Point estimates (circles) and 95% confidence intervals (bars) are presented on a $\log_e$ scale. Relative risks were adjusted for age, total caloric intake, physical activity, smoking status, menopausal status, use of vitamin supplements, and body silhouettes at menarche and age 20 years, respectively.

The fact that the relation between BMI and asthma prevalence and incidence is restricted to women and persists after adjustment for potentially confounding factors such as physical activity and dietary intake suggests that other factors may play a role in the causal pathway**.** The association between BMI and asthma observed in prevalence studies can be interpreted in two ways. On the one hand, a larger BMI might contribute to the increase in symptoms among subjects with subclinical disease (12); on the other hand, asthma might lead to less activity, resulting in weight gain. This latter hypothesis is not supported by the data of Beckett et al. (15), who did not observe changes in asthma incidence with levels of or changes in physical activity among young adults.

The association of adult onset of asthma with change in weight among women suggests that female hormones may play a major role. Asthma is more frequent in girls after menarche, while the reverse is observed before menarche (25). Female hormones have been shown to have a direct effect on the airway, to alter β-2-adrenergic responsiveness (26), and to increase the production of prostaglandins (27) and the production of interleukin-4 and interleukin-13 by blood mononuclear cells (28). In addition, adipose tissue is considered to be one of the major sources of extraglandular estrogen produced by aromatization of androgen precursors (29), leading to elevated levels of circulating estrogens in obese subjects and early menarche (30). Estrogens could also act in synergy with leptin, an adipocyte-secreted hormone that reflects the amount of energy stored in adipose tissue and is positively correlated with percentage of body fat and BMI (30). Estrogens have been found to increase levels of leptin in animals and humans (31), and higher levels of leptin have been observed in women than in men (32). Leptin receptors have been observed in the airways and lung cells, and leptin has been shown to have stimulatory effects on the proliferation of both types of cells (33).

In accordance with the role of female sex hormones is the observation that a larger silhouette at menarche might decrease the risk of asthma incidence, as observed in hormone-dependent diseases such as breast cancer (34), and that weight gain after menarche might play an important role, which also suggests that the timing of weight gain needs to be considered. It is noteworthy that in our population, silhouette at menarche was inversely related to age at menarche ($p < 0.01$), which supports the validity of the women's reports of their perceived silhouette at menarche. The observation that hormone replacement therapy was not associated with incidence of asthma and that it did not modify the association between overweight and incident asthma might be related to the possibility that extra glandular production of estrogen among overweight, postmenopausal women might be more important than oral estrogens. Although our data are suggestive of a hormonal role, they are too limited to provide a clear understanding of the mechanism whereby excess adipose tissue may affect the risk of asthma. Some authors have suggested that another possible link between asthma and obesity is the low sympathetic tone observed in both diseases (35, 36).

Several issues must be addressed for interpretation of our results. Participants in the E3N Cohort Study were mainly female teachers with a high level of education and health consciousness (20). Analyses of risk factors for other diseases such as breast cancer have resulted in the identification of known risk factors, which increases confidence in the questionnaire information (20). In addition, several validation studies have been performed in this population, and the information has proven to be reliable (37, 38). A validation study conducted to determine the accuracy of the reported anthropometric measurements and perceived body silhouettes showed that the correlation between self-reported and external measurements was greater than 0.80 and that the correlation between BMI measured by technicians and the self-reported silhouette was 0.78 (39). The use of recall to evaluate body shape has been used in previous studies and found to be reliable (39–42), and silhouettes might provide a good ranking of past corpulence and change in corpulescence over time. In a recent study conducted among adult women (mean age 42 years), Must et al. (42) reported that BMI percentile at menarche was well correlated with recalled body size at menarche over a recall time interval ranging from 23 years to 33 years. Because the occurrence of the first menstrual period is usually a disrupting event, the ability to recall one's circumstances at menarche appears to be good. These authors also observed a systematic bias in reporting, with the thinnest girls overestimating their body size and the normal and heavier girls underestimating theirs (42). Such a pattern was also observed among adult women in the validation study conducted in our population (39). However, this type of bias will tend to underestimate the association between body silhouette and incident asthma.

In our study, we observed mean-BMI rounded values of 18, 20, 22, 24, and 27 for the five categories of self-reported silhouette at baseline, and an increase of one body silhouette corresponded approximately to a gain of 5–6 kg. BMI, a weight-stature index, has been shown to correlate well with body fatness ($r = 0.5$–0.8) (43, 44) and has been widely used to evaluate the association between body fatness and diseases (44). Although other indicators of fatness have been used, BMI is still the most frequently used index, and it therefore allows comparison between studies.

Information on body silhouette and BMI at baseline was provided before the occurrence of asthma, and therefore bias is an unlikely explanation for our results. Moreover, participants had agreed to participate in a study on cancer risk factors, and the occurrence of asthma was recorded among a variety of other endpoints. In addition, we were able to adjust our estimates for total caloric intake and physical activity, which are determinants of BMI and body silhouette and which might confound the association with asthma occurrence (45).

Our definition of asthma was based on self-reported asthma attacks and the given date of the first attack. Although this information was not validated by a physician who diagnosed asthma and prescribed medication, we believe that both the occurrence of a new asthma attack and a known date for the first attack provide confidence for the validity of the information. In addition, the incidence of asthma followed the age pattern previously described (17). Some asthmatics may have denied asthma "attacks" which they perceived only as severe episodes, and therefore they would have been included as nonasthmatic in our study. Given the low incidence of asthma in our study, this number is likely to have been small in comparison with our total population, and therefore this should not have substantially altered our results. Furthermore, this would probably underestimate the strength of the association. In addition, some adults may have had childhood asthma which remitted and relapsed and was mistaken for new "adult-onset" asthma. This would also probably tend to underestimate the association, given that the misclassification of cases would most probably have been random; therefore, our estimates are likely to be conservative.

Our results could be biased if fatter women systematically reported more asthma attacks or if asthma was diagnosed more often among fatter individuals. However, results of the stratified analysis according to reported dyspnea or difficulty breathing do not support this hypothesis. In addition, change in weight was associated with a J-shaped pattern of asthma risk, which does not support the hypothesis that asthma might be more frequently diagnosed in fatter individuals. Such a J-shaped pattern has been observed in other studies (15), but there is no clear explanation for it.

Finally, our study included only women. Therefore, it precludes comparison of the effects of BMI on the incidence of asthma between genders. Our cohort was mainly composed of teachers who had an intermediate to advanced level of education; 50 percent had had 4 additional years of study after finishing high school. However, our sample was fairly representative of the population insured by the health insurance plan (20). Although our results might not be easily generalized for the entire population of French women, this homogeneity in our sample decreased the risk of uncontrolled confounding, particularly through occupational exposure.

In summary, for a cohort of middle-aged women, we observed that asthma incidence over a 3-year follow-up period was significantly related to BMI at baseline and that change in weight during the period of observation was related to a J-shaped pattern of asthma risk. In addition, women whose body mass changed by more than two silhouettes (corresponding to approximately 10 kg) between menarche and the start of follow-up were at increased risk of asthma later in life, which suggests that long-term exposure to high levels of female hormones might play a role in the incidence of the disease. Further research is needed to clarify the interrelation between obesity, female hormones, and adult onset of asthma.

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