

## Prevalence of asthma and mean levels of air pollution: results from the French PAARC survey

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**ABSTRACT:** Among the possible explanations for the recent increase in the prevalence of asthma in several countries, air pollution is one of the foremost public health concerns.

Data from the "Pollution Atmosphérique et Affections Respiratoires Chroniques" (PAARC) survey collected in 24 areas of seven French towns during 1974–1976 were reanalysed to assess the relationship between the prevalence of asthma and the following air pollutants: sulphur dioxide (specific (SO<sub>2</sub>) and acidimetric methods), total suspended particles (TSP), black smoke (BS), nitrogen dioxide and nitric oxide. Correlation coefficients between annual mean levels of pollution and prevalence of asthma in the different areas were first calculated. Random-effects models were then estimated.

Of the 20,310 adults aged 25–59 yrs, 1,291 (6.4%) were found to be asthmatics as well as 195 (6.1%) of the 3,193 children aged 5–9 yrs. A geographical correlation between asthma and annual mean level of SO<sub>2</sub> (ranging 17–85 µg·m<sup>-3</sup>) was found (r=0.45, p=0.01) in adults. No relationship was found in children. After controlling for age, educational level, smoking, and geographical clustering with a multivariate random-effects model, the relationship remained significant in adults for SO<sub>2</sub> (odds ratio for a 50 µg·m<sup>-3</sup> increase=1.24, confidence interval 1.08–1.44, p=0.0035). It also remained significant when taking into account only the people reporting their last asthma attack occurring after settling in the study area.

These results are consistent with the known short-term effects of SO<sub>2</sub> in asthma and demonstrate the necessity for further studies on delayed effects of air pollution in respiratory diseases.

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As a result of difficulties in diagnostic establishment, differences in prevalence between population groups according to sex, race or age, and variability in study patterns, knowledge of the epidemiology of asthma still remains incomplete. This has become particularly acute and worrying over the last few years, as an increase in both asthma morbidity and mortality has been suggested by several studies in industrialized countries [1, 2]. No clear explanation of this can be proposed. That environmental agents can induce asthma in some circumstances is now well known, for example in occupational asthma, epidemics due to soybean dust [3], and environmental tobacco smoke in children [4]. Thus, research on asthma can no longer avoid the environmental hypothesis.

Because most of the population in urban areas are exposed to air pollution, and because there are ways to reduce pollutant levels, the role of air pollution in the natural history of asthma has become a great concern for public health. For 20 yrs, numerous epidemiological studies in the field of air pollution have been carried out, but most have dealt with acute health effects, and only a few deal with asthma. Panel studies have found relationships between peaks in air pollutants and the frequency of asthmatic symptoms collected on daily diaries [5–7], or of

emergency hospital admissions [8–14]. Therefore, only a few studies have investigated the long-term effects on asthma of moderate, but continuous, levels of air pollution. The results of these studies cannot lead to definitive conclusions because: some are based on age-specific groups such as children [15–17] or young adults [18], some study pollution in a general way and others study specific pollutants [18–20], some do not measure individual confounders [16], some consider asthmatic symptoms [15, 16, 20] and others bronchial hyperresponsiveness [19] or wheezing [21], and finally, some have found an association with asthma [15, 16, 20] while others have not [17, 18].

The present study takes material from the "Pollution Atmosphérique et Affections Respiratoires Chroniques" (PAARC) survey conducted in seven French towns from 1974 to 1976 to investigate the effects of air pollution on chronic respiratory diseases [22]. Among adults of both sexes, the air concentration of SO<sub>2</sub> was associated with the prevalence of lower respiratory symptoms; among children, it was associated with the prevalence of upper respiratory symptoms. In both adults and children, the higher the SO<sub>2</sub> pollution, the lower the forced expiratory volume in one second [23]. In the initial analysis, only

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chronic cough, phlegm and bronchitis were considered. In a later analysis, a relationship was found between occupational exposure and prevalence of respiratory symptoms, including wheezing and asthma in adults [24]. The aim of the present study was to search for a relationship between annual mean levels of air pollutants measured in the PAARC study and the prevalence of asthma in the exposed populations.

### Materials and methods

The detailed protocol of the French cooperative study PAARC has been published elsewhere [22]. Its main characteristics are summarized below.

#### *Study population*

*Geographical areas definition.* In seven French cities (Bordeaux, Lille, Lyons, Mantes-la-Jolie, Marseilles, Toulouse and Rouen), 24 areas were defined, *i.e.* 2–4 areas per town. These areas, situated within a 500 m radius of a pollution monitoring station, were selected in order to provide a large scale of pollutant measures and a large variety of pollutants. They corresponded to ~1,000 inhabitants each. Uniformity of pollution in different points of the areas was checked before the beginning of the study.

*Population definition.* To be included in the PAARC study, people had to be either 6–10-yr-old or 25–59-yr-old. The family household had to be French, to have lived in the area for  $\geq 3$  yrs, and to belong to one of the following socio-occupational classes: self-employed (shopkeepers, craftsmen), managers, administrators, professionals, intermediate, employees, employed workers, or personal service workers. Manual workers were not included because of potential occupational exposures whose effects could be greater than those expected from air pollution.

*Selection procedure.* After an information letter was delivered to the inhabitants of the 24 study areas, an investigator came and visited the household in order to complete a standardized "first questionnaire". Three attempts were made when people were absent from home. The "first questionnaire" was to determine if the household could be included in the study. If the household satisfied the conditions, the investigators visited the people again who filled in the medical "second questionnaire".

A census was made of ~55,000 households in the 24 study areas, 47,000 (85%) of which could be visited. Among them, 13,673 households (28.2%) were eligible according to the inclusion criteria, corresponding to 20,310 adults and 3,193 children who filled in the medical questionnaire.

#### *Pollutants*

Pollutants were selected according to the epidemiological knowledge available in the 1970s and according to the measuring methods available. Sulphur dioxide (spe-

cific (SO<sub>2</sub>) and acidimetric methods), total suspended particles (TSP; gravimetric method), and black smoke (BS; reflectometry), nitrogen dioxide (colorimetric analyser) and nitric oxide (colorimetric analyser) were retained. Detailed measuring procedures were drawn up and handed out to all laboratories. Measurements were performed every day for 3 yrs (1974–1976). Annual means calculated on the whole 3-yr period were used.

#### *Health measurement and other variables*

From September 1974 to June 1976, investigators visited the eligible households. Two questionnaires were used: one for adults, derived from the "Communauté, Européenne du Charbon et de l'Acier" questionnaire, and one for children which included questions taken from the World Health Organization questionnaire on the long-term effects of air pollution on children's health. In both questionnaires, identification data, past and present respiratory symptoms, and respiratory risk factors were collected. Asthmatics were defined as those responding positively either to a diagnostic question "Have you ever had asthma?" or to a symptomatic question "Have you ever had attacks of breathlessness associated with wheezing?". Prevalence of asthma was the rate of adults in the population of the study corresponding to this definition in 1974–1976. Ages of onset and the last attack of asthma were determined by the following questions "How old were you on the first attack?", and "How old were you on the last attack?". For children, questions were as follows: "Has he (she) ever had attacks of wheezy breath?", "Has he (she) attacks of wheezy breath every day or night?", "Has he (she) ever had attacks of asthma?", "When was the first attack?", and "When was the last attack?". Asthmatic children were defined only as the ones who experienced asthma attacks and the prevalence of asthma was the rate of children in the population of the study corresponding to this definition in 1974–1976.

Socio-occupational classes were defined according to the Institut National de la Statistique et des Etudes Economiques (INSEE) criteria: self-employed (I), managers, administrators and professionals (II), intermediate (III), employees (IV), and others (V).

Detailed information on smoking habits was collected, and the current status in 1974–1976 was used. People who had not smoked a single cigarette per day for a whole year were considered as nonsmokers. People who had stopped smoking for at least one month were considered as previous smokers. Others were smokers.

#### *Analysis*

Description of subjects and pollutants and analysis were performed with BMDP statistical software, version 7.0 (BMDP Statistical Software, Inc., Cork Technology Park, Cork, Ireland). Chi-squared and analysis of variance (ANOVA) were used to compare descriptive characteristics of asthmatic people between areas. The  $\alpha$ -risk was 5%.

Geographical correlations between the prevalence of asthma and annual mean levels of each pollutant were calculated and tested with the Spearman's rank correlation

test in order to take into account the clustering of subjects in the 24 areas.

Logistic regression was used to test for an effect of each pollutant on the prevalence of asthma with and without individual confounders. Random effects were used in all univariate models and kept when necessary in the multivariate analysis to avoid bias due to geographical clustering of the data [25]. Indeed, a correlation between the data of a given area could exist, because a number of parameters associated with the area (*e.g.* meteorological conditions, healthcare, *etc.*) could also be associated with asthma and, in part, explain the relationship. Ignoring this potential correlation in data, the variance of estimated parameters would be underestimated and a falsely significant relationship could be found. It was therefore necessary to add to the equation of the model a term whose variance was that of the "area effect" or "random-effect". As the random-effect attached to areas included the one attached to the city (since the areas were within the cities) and because the initial idea was to obtain contrast between areas, a random-effect attached to areas rather than one attached to cities was added to the model. If the random effect was low, its variance tended to zero and a fixed effects logistic regression model could be used. To test if the random effect was significant, the parameter  $\sqrt{D1-D2}$  was estimated, where D1 is the deviance of the random-effects model and D2 the deviance of fixed effects logistic regression model. A 5% significance threshold was used.

## Results

Table 1 presents the sociodemographic characteristics of the population. Slightly more young males than young females were recruited (51.0 *versus* 49.0%), and more females than males in adults aged 25–59 yrs (55.3 *versus* 44.7%). The sex ratio was not statistically different in adults ( $p=0.09$ ) or in children ( $p=0.17$ ) in the 24 areas.

Most of the adults had been living in the area for  $\geq 10$  yrs. One adult out of four had even been living there for  $\geq 15$  yrs. The households with primary, secondary and university level education were approximately in the same proportions.

Differences in the annual mean levels of pollutants were observed not only between areas but also according to the various pollutants. The distribution of these annual levels is summarized in figure 1. TSP showed the largest distribution with mean annual values ranging 45–243  $\mu\text{g}\cdot\text{m}^{-3}$ . On the contrary, the mean annual values of  $\text{NO}_2$  only ranged 13–61  $\mu\text{g}\cdot\text{m}^{-3}$ . The areas with highest or lowest values were not the same according to the various pollutants. In general, most polluted areas were located in the towns of Southern France (Marseilles, Toulouse).

Data on asthma were available for 20,168 adults (99.3%) and 3,122 children (97.8%). Of the children, 195 (6.2%) were asthmatics according to the author's definition. This prevalence differed with sex (7.5% in young males and 4.9% in young females;  $p=0.002$ ), but not with age ( $p=0.9$ ). Among adults, 1,291 (6.4%) were asthmatics. The prevalence of asthma in males was 6.7% and in females 6.2% ( $p=0.1$ ).

For 990 (76.5%) of the asthmatic adults, dates of the first and last attacks were available together with the date of

Table 1. – Sociodemographic characteristics of the population

	Adults (n=20310) %	Children (n=3193) %
Sex		
Female	55.3	49.0
Male	44.7	51.0
Age yrs		
6		18.5
7–8		38.6
9–10		42.9
25–34	26.4	
35–44	28.0	
45–49	17.4	
50–59	28.2	
Length of residence yrs		
$\leq 6$		49.4
$> 6$		50.6
$< 10$	56.1	
$\geq 10$	43.9	
Educational level*		
Primary	35.2	27.9
Secondary	31.6	50.3
University	33.2	21.8

\*: for children the educational level is of the family household.

arrival in the area. It was then possible to distinguish five groups from the combination of the characteristics of the asthma history: whether asthma started before arriving in the area, whether attacks occurred whilst living in the area, whether attacks were still present in the 12 months before the interview. Definitions and distributions of the five groups according to  $\text{SO}_2$  level are presented in table 2.

Table 3 presents the main characteristics of the asthmatic adults compared to the nonasthmatics. Missing data for these characteristics were not numerous, as all were available for 19,747 adults (97.2%). There were more asthmatics in males than females but with no statistical difference ( $p=0.11$ ). The proportion of asthmatics differed with educational level ( $p=0.04$ ): there were more subjects with secondary level education in asthmatics than in nonasthmatics. Asthmatics and nonasthmatics did not differ for socio-occupational class ( $p=0.19$ ). Smoking habits

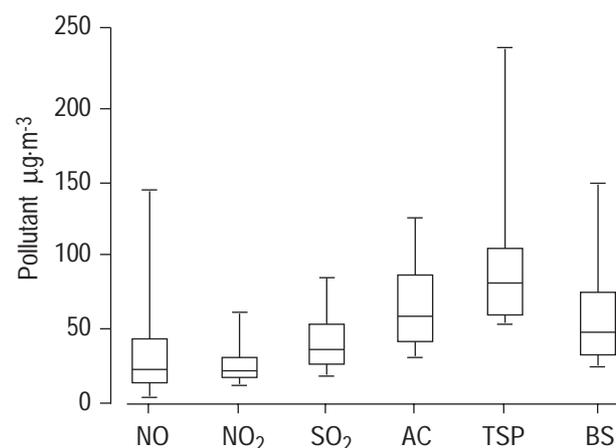


Fig. 1. – Distribution of the pollutant measures (mean annual levels of daily measurements) in the 24 areas. The box plots represent median, first and third quartiles and the vertical bars the range. AC: acidimetric method for  $\text{SO}_2$ ; TSP: total suspended particles; BS: black smoke.

Table 2. – Distribution of the asthma history pattern in adults according to the mean annual SO<sub>2</sub> level

	Mean annual level of SO <sub>2</sub> µg·m <sup>-3</sup>					
	<30		30–50		≥50	
	n	%	n	%	n	%
Group 1	76	1.5	166	2.1	133	1.9
Group 2	21	0.4	41	0.5	37	0.5
Group 3	54	1.1	111	1.4	83	1.2
Group 4	29	0.6	25	0.3	40	0.6
Group 5	56	1.1	46	0.6	72	1.1
Total	236	4.7	389	4.9	365	5.3

Group 1: Asthma starting and finishing before arrival in the area; Group 2: asthma starting before arrival in the area, present whilst living in the area, but finishing 12 months or more before the interview; Group 3: asthma starting before arrival in the area and still present in the 12 months before the interview; Group 4: asthma starting after arrival in the area and still present in the 12 months before the interview; Group 5: asthma starting after arrival in the area and finishing 12 months or more before the interview.

differed in the two groups. Nonasthmatics were more frequently never smokers, and asthmatics were more frequently exsmokers. Asthmatics were significantly older than nonasthmatics (p=0.001) and had been living in the area for a longer period (p=0.01).

*Univariate analysis*

The prevalence of asthma in children differed between the 24 areas (p<10<sup>-9</sup>) from 1.5% in area 1 in Lille to 12.3% in area 2 in Bordeaux. The prevalence of asthma in adults was significantly different between the 24 areas (p=0.001), ranging 2.9% in area 1 in Lille to 8.9% in area 4 in Lyons. This area in Lille seemed aberrant. It concerned only 4% of the population and 2% of the asthmatics of the study. However, excluding this value did not change the results. No evident explanation can be proposed for this result.

Table 3. – Variables associated with asthma in adults

	Asthmatics		Nonasthmatics		p-value
	n	%	n	%	
Sex					
Male	604	46.8	8394	44.5	0.11
Female	687	53.2	10483	55.5	
Educational level					
Primary	458	36.2	6543	35.2	0.04
Secondary	360	28.4	5906	31.8	
Higher	449	35.4	6134	33.0	
Socio-occupational class					
Self-employed	170	13.2	2267	12.1	0.19
Managers, administrators, professionals	211	16.4	2924	15.6	
Intermediate	275	21.4	4012	21.4	
Employees	354	27.5	4960	26.6	
Others	277	21.5	4556	24.3	
Smoking habits					
Never smokers	642	50.2	9879	52.6	0.004
Previous smokers	171	13.4	1968	10.5	
Current smokers	465	36.4	6938	36.9	
Age* yrs	43.2±0.5		42.1±0.1		0.001
Residence duration* yrs	11.6±0.5		11.4±0.1		0.01

\*: presented as means±sd.

The only significant geographical correlation between prevalence of asthma and mean annual level of pollutants was observed for SO<sub>2</sub> in adults (r=0.45, p=0.03) (fig. 2). For other pollutants in adults, the correlation coefficients ranged 0.07 (NO<sub>2</sub>) to 0.24 (BS). In children, all the correlation coefficients were <0.30. When considering males and females separately, this geographical correlation remained significant in males (p=0.03) and was at the limit of significance in females (p=0.06).

Univariate logistic regressions with random effects were presented for each pollutant in adults and children for an increase of 50 µg·m<sup>-3</sup> (table 4). Only SO<sub>2</sub> (specific method) was associated with asthma in adults (p=0.001). The odds ratio (OR) (95% confidence intervals (CI)) for an increase of 50 µg·m<sup>-3</sup> in SO<sub>2</sub> was 1.26 (1.04–1.53). The random effect was significant (p=0.005). This justified the use of this type of model in further analyses. No association was found between asthma and any pollutant.

*Multivariate analysis in adults*

As age, educational level and smoking were associated to asthma in the univariate analysis, they were subsequently included in a multivariate regression model where the dependent variable was asthma (yes/no). Age was ordered in four classes (25–34, 35–44, 45–49, 50–59 yrs), educational level in three classes (primary, secondary, higher), and smoking in three classes (nonsmoker, previous smokers, current smokers). Reference classes for these variables were "25–34" for age, "primary" for educational level and "nonsmokers". Sex was also forced into the initial model. Length of residence in the area was not introduced into the model because of its high correlation with age. When taking into account these confounders, the random effect in the model was no more significant, and the fixed effect models could be performed.

Sex did not contribute significantly (p=0.56) to the explanation of the association between asthma and SO<sub>2</sub>, and

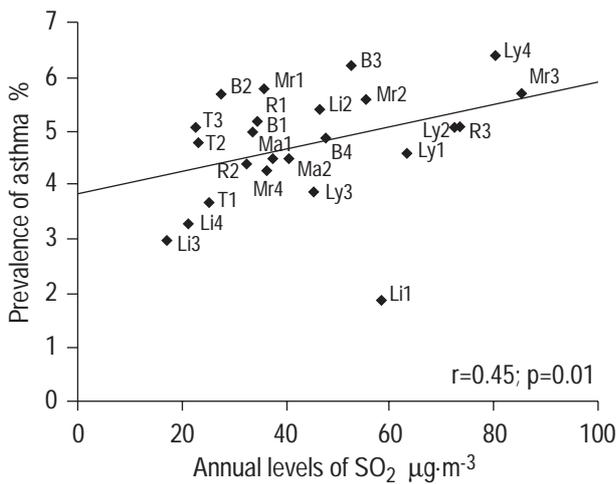


Fig. 2. – Geographic correlation between the prevalence of asthma in adults and the mean annual levels of  $\text{SO}_2$  in the 24 areas. B: Bordeaux; Li: Lille; Ly: Lyons; Ma: Mantes; Mr: Marseilles; R: Rouen; T: Toulouse. 1–4: area number in each town.

could be removed without significant variation of the deviance of the model. On the other hand, even if the  $p$ -value exceeded 0.05, removing educational level from the model led to a significant variation of the deviance of the model. Therefore age, smoking and educational level were left in the final model (table 5). The OR (95% CI) for an increase of  $50 \mu\text{g}\cdot\text{m}^{-3}$  in  $\text{SO}_2$  was 1.24 (1.08–1.44) ( $p=0.0035$ ).

The same analysis performed in the restricted group of 615 asthmatic adults (groups 2–5 in table 2) who reported their last attack occurring after settling in the study area provided similar results: the only significant relationship was between asthma and  $\text{SO}_2$  (OR=1.24 (1.02–1.51),  $p=0.03$ ), even when adjusting for smoking, age and educational level (OR=1.23 (1.01–1.51),  $p=0.04$ ). When considering separately the 700 asthmatics with a first attack of asthma occurring after settling in the area, a significant association with asthma was also found and it remained significant when taking into account smoking, educational level and age (OR=1.25 (1.009–1.54),  $p=0.04$ ). For the group of asthmatics declaring asthma in the past 12 months, no significant association was found ( $p=0.22$ ).

### Discussion

In this re-analysis of the PAARC survey data, a significant relationship was found between the mean annual levels of  $\text{SO}_2$  and the prevalence of asthma in exposed

adults. This association remained significant when adjusting for age, smoking habits and educational level, and when taking into account the effect of the geographical clustering of the data. Furthermore, when restricting the analysis to individuals reporting that they had experienced attacks since settling in the area, the relationship remained significant.

Data of the PAARC study were cross-sectionally collected: air pollution levels and health outcomes were assessed simultaneously in 1974–1976. The sequence in asthma history (first and last attacks) and in settling in the area could be described retrospectively to attempt a longitudinal look to the cross-sectionally collected data. As no clear difference in asthma history pattern distribution according to  $\text{SO}_2$  level in the area was shown, this analysis did not allow us to address whether air pollution triggers or could cause asthma.

Selection bias in the PAARC survey is assumed not to be very important on the grounds that subjects came from the general population and that the procedure for inclusion was closely systematized. The proportion of eligible subjects in the study areas who could not be reached was rather limited, and estimated at ~15%, without big differences within areas. Yet it is not possible to exclude a specific selection bias occurring before and independently of the study pattern: it could be that asthmatics select the area of their residence according to the level of air pollution. They might avoid living in highly polluted areas because they feel uncomfortable or are advised to do so. Should that arise, the prevalence of asthmatics in the polluted areas would be underestimated in this study. This point does not question the relationship that was found but can nevertheless be discussed for pollutants which were not found to be related to asthma in this analysis ( $\text{NO}$ ,  $\text{NO}_2$ , BS, TSP).

Asthma considered in this study is based on self-reported symptoms or history. People with asthma restricted to childhood or with rare attacks might ignore or forget to report their disease. On the other hand, people might incorrectly name some other respiratory symptoms as asthma. However, the asthma definition used in the present study is the one commonly used in epidemiological studies.

This analysis is based on the triple hypothesis that the air pollution measured at the monitoring stations is homogeneous during time, within space, and between individuals. The measurements are assumed to be good reflections of past exposure to pollutants for each individual in the study. Admittedly, one of the inclusion criteria was that the household should have been living in the area for

Table 4. – Univariate analysis of the association between asthma and various pollutants in adults and children by correlation coefficients and regression models with random effects

	Adults				Children			
	r	OR	95% CI	p-value	r	OR	95% CI	p-value
NO	0.22	1.03	0.94–1.13	0.36	0.11	1.10	0.92–1.31	0.32
$\text{NO}_2$	0.07	1.05	0.73–1.52	0.75	0.17	1.47	0.75–2.89	0.28
$\text{SO}_2$	0.45	1.26	1.04–1.53	0.001	0.11	1.08	0.68–1.72	0.61
$\text{SO}_2$ acidimetric methods	0.19	1.06	0.92–1.21	0.28	-0.23	0.82	0.61–1.08	0.20
TSP	0.10	1.01	0.92–1.11	0.77	-0.05	0.99	0.81–1.20	0.96
BS	0.24	1.07	0.96–1.20	0.11	0.11	1.08	0.85–1.38	0.46

OR: Odds ratio for an increase of  $50 \mu\text{g}\cdot\text{m}^{-3}$  in the pollutant; CI: confidence interval; TSP: total suspended particles; BS: black smoke.

Table 5. – Final logistic regression model, assessing the association between asthma and SO<sub>2</sub>

Variables	n	OR	95% CI	p-value
SO <sub>2</sub>	19747	1.24*	1.08–1.44	0.0035
Age yrs				
25–34	5258	1.00		
35–44	5523	1.28	1.08–1.50	0.003
45–49	3415	1.29	1.08–1.55	0.006
50–59	5551	1.30	1.11–1.53	0.001
Educational level				
Primary	6960	1.00		
Secondary	6235	0.90	0.78–1.04	0.14
Higher	6552	1.08	0.94–1.25	0.26
Smoking				
Nonsmokers	10337	1.00		
Exsmokers	2111	1.32	1.11–1.58	0.003
Current smokers	7299	1.04	0.92–1.18	0.56

OR: odds ratio; CI: confidence interval. \*: For an increase of 50 µg·m<sup>-3</sup>.

≥3 yrs. However, the level of pollution in the same area has surely changed in the meantime. It is therefore assumed that the changes were fairly similar in the 24 areas, so the resulting errors might not be systematic and might not indicate an effect where there is none. Homogeneity between individuals is a second assumption. Children and elderly people, females and males, people working outside or inside, and sporting and sedentary people, are undoubtedly not all exposed to the same levels of pollutants. Individual exposure measurements or estimations would provide better evaluation [26, 27]. In most epidemiological studies, especially long-term studies on numerous populations such as the PAARC survey, personal measurements are not feasible. In fact, all these approximations should make it more difficult to detect an effect, as they do not question the association that was found between SO<sub>2</sub> and asthma in adults but rather those that were not found.

Some factors were not taken into account: pollens, meteorological variables, and other air pollutants such as ozone. The meteorological influence has been studied by several authors in its association with respiratory symptoms, with controversial findings [6, 8, 28, 29]. Geographically dependent factors should vary within areas and should represent a random effect attached to the areas in the present models. Such a random effect has been estimated and was not significant. This result indicates that factors such as weather conditions or pollens or other geographically dependent factors did not play a major role in this analysis, and are not likely to explain the association between asthma and SO<sub>2</sub>.

In children, no association between asthma and any pollutant was found. Several explanations for the lack of association in children can be suggested. Compared to the 20,310 adults, the number of children (n=3,193) is quite small and might not be sufficient to find a significant association for a moderate risk. Other determinants of asthma in children might have a greater influence (e.g. upper airway infections) and might overlap the effects of air pollution. The effects of air pollution on the respiratory tract might be cumulative and require a certain latency period which cannot be observed in children aged 6–10 yrs. The role of exposure during early childhood rather

than current ambient pollution could also be of primary concern [19].

The results in adults are consistent with experimental studies of exposure to SO<sub>2</sub>, which show an irritant action of SO<sub>2</sub> on the respiratory (bronchial) tract [30, 31]. Asthmatics have also been found to be more sensitive to SO<sub>2</sub> [12, 32]. It is unlikely that air pollution increases the prevalence of atopic status, but rather that it enhances the development of acute clinical symptoms among already sensitized subjects [16].

Recent epidemiological studies tend to give a greater role to pollutants such as fine particles [33] or ozone [11, 34–37] than to SO<sub>2</sub> in the association with respiratory disorders. However, it has been suggested that SO<sub>2</sub> could be a sensitive surrogate for other pollutants [38]. In the years 1974–1976, measures of pollutants such as ozone or fine particles were not available. It is possible that SO<sub>2</sub> in the present study is just a sensitive indicator of air pollution. Such an uncertainty cannot be easily eliminated as air pollution is a complex mixture [39]. Reviewing the literature on urban air toxicity and asthma, LEIKAUF *et al.* [38] rank the following pollutants from strongest to weakest as follows: particles with a 50% cut-off aerodynamic diameter of 2.5 µm (PM<sub>2.5</sub>) > particles with a 50% cut-off aerodynamic diameter of 10 µm (PM<sub>10</sub>) > SO<sub>x</sub> > H<sup>+</sup> > O<sub>3</sub> > NO<sub>x</sub>, according to the strength of association with mortality. This classification does not allow the specific role of each pollutant to be estimated, but it shows that SO<sub>2</sub> is a pollutant of great concern in epidemiological studies, or for its own effects, or for its sensitivity in indicating the effects of other pollutants.

As preventive measures towards industrial pollution have been undertaken, levels of pollutants have decreased in most French towns since the PAARC study (1974–1976). It must be pointed out that even if they were higher than at present, the levels of the pollutants in the present study were already below the EU (European Union) threshold of 50 µg·m<sup>-3</sup> of SO<sub>2</sub> in two-thirds of the areas.

In conclusion, in this evaluation of the data of the "Pollution Atmosphérique et Affections Respiratoires Chroniques" survey, a significant relationship was found between the mean annual level of SO<sub>2</sub> and the prevalence of asthma in adults aged 25–59 yrs. These results go further than a simple geographical analysis as they are based on individual health data and confounders and take into account the geographical clustering of the data. Even if SO<sub>2</sub> is considered to be only a marker for air pollution, this study strengthens the hypothesis of the role of low but continuous exposure to air pollutants in the natural history of asthma.

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