

Long-term exposure to proximity air pollution and asthma and allergies in urban children.

ONLINE SUPPLEMENT

MATERIAL AND METHODS

Skin prick tests (SPT)

A detailed description of the protocol used to perform SPT and to calculate the wheal size was provided elsewhere [1]. To sum up: children were tested with the following aeroallergens: mixed grass pollens (*Dactylis glomerata*, *Lolium perenne*, *Festuca pratensis*, *Poa pratensis*, and *Phleum pratense*), mixed tree pollens (*Betula verrucosa*, *Alnus glutinosa*, *Carpinus betulus*, and *Corylus avellana*), mites (*Dermatophagoïdes pteronyssinus* and *Dermatophagoïdes farinae*), moulds (*Alternaria tenuis*), cockroach (*Blatta germanica*), and cat fur (Stallergènes laboratories, France). Histamine (10 mg.mL^{-1}) was used as a positive control and glycerine was a negative control. Tests were performed on the volar surface of the forearm using a standard template. The wheal size after 15 min was calculated as the mean of the longest diameter and its perpendicular diameter. SPT positivity was defined as a wheal ≥ 3 mm and greater than the negative control.

The run test

The detailed methods implemented during the run test were precisely presented elsewhere [2-4]. To sum up: Before undergoing the run test, children were advised to avoid β_2 -agonist or anticholinergic inhaler for 4 h, and oral medications (β_2 -agonist, theophylline, or anti-muscarinic agents) for 8 h. Children who had all the same taken β_2 -agonist or anticholinergic inhaler for 4 h, and oral medications (β_2 -agonist, theophylline, or anti-muscarinic agents) for 8 h were asked to withhold medication before returning for testing later in the day, or next day if possible. When possible, children who reported a respiratory tract infection during the previous 3 weeks were rescheduled. Baseline peak expiratory flow (PEF) was measured three times immediately before the run test with a Mini-Wright peak flow meter in accordance with the recommendations of the American Thoracic Society [5]. The maximum of this set of readings prior the run test was retained and compared to predicted value assessed using the child's height and the abacus built through the curve of Godfrey [6]. All the children, whose PEF before exercise attained at least 70% of the predicted value, were invited to undergo the run test unless they reported that they had heart disease or epilepsy, or were taking a β_2 -blocker. After baseline lung function was measured, children underwent a 6 min period of running (1 min slow, 4 fast, 1 very fast). For all children, measurements of PEF were made at 5, 10 and 15 min following the run test. The maximum of this second set of readings was used to calculate the percentage decrease in PEF after exercise compared to the retained baseline PEF. Pulse rate was measured for 15 s before and immediately after completion of the run, as an indicator of exercise intensity. If the heart rate after the run increased of less than 20% of the baseline heart rate, children were excluded from the analysis. If a child presented any respiratory symptom after the run test, the physician examined him at first, and second, a β_2 -agonist with inhalation chamber was administered in order to ensure the reversibility of the bronchospasm.

Health outcomes

- Past year asthma, rhinoconjunctivitis, and eczema.

These three outcomes, which referred to reported symptoms in the last twelve months, were assessed using the replies to the ISAAC questions.

Past year asthma was built using the combination of the following two questions: 'Has your child had wheezing or whistling in the chest in the last 12 months?' and 'Has your child ever

had asthma?'. Past year rhinoconjunctivitis was defined as having affirmative answers to the following two questions: 'In the past 12 months, has your child had a problem with sneezing, or a runny, or blocked nose when he/she did not have a cold or the flu?' and 'In the past 12 months, has this nose problem been accompanied by itchy-watery eyes?'. 'In the last 12 months, has your child ever had an itchy rash which was coming and going for at least six months at any time?' was used to assess past year eczema.

- Lifetime asthma, allergic rhinitis, and eczema.

Using ISAAC core questions, lifetime asthma was assessed from the question 'Has your child ever had asthma?', lifetime allergic rhinitis from at least one affirmative answer to the following questions 'Has your child ever had hayfever?' or 'Has your child ever had other types of AR?' and lifetime eczema from the question 'Has your child ever had eczema?'.

Participation rate

81% of the children (7781/9615) accepted to participate in the study. Completed valid data on both clinical examination and questionnaire were available for 69% of the children (6683/9615). Protocol completion rate among the children having accepted to participate ranged from 79% (Créteil) to 98% (Strasbourg). The 1098 = 7781 - 6683 children having accepted to participate to only one part of the study (questionnaire or clinical examination) were excluded from the study, because missing data were too numerous for these children. Population characteristics of these 1098 children excluded from the study were compared to those of the 6683 children with completed valid data. The 1098 children excluded from the study did not differ significantly from the others in terms of the recorded characteristics, but in 7 factors. They were older ($p < 0.0001$), fatter ($p = 0.0041$) and higher ($p = 0.0146$) than the 6683 children with completed valid data. They had also a higher number of siblings ($p = 0.0015$). They had less frequently a family history of allergies ($p = 0.0007$). Their parents were less frequently native of Metropolitan France ($p < 0.0001$) and had less frequently attended high school and university ($p < 0.0001$)."

These differences are not surprising, in so far as it is well-known that subjects with a higher level of education accept more often to participate in epidemiological study than subjects with a lower level of education [7]. Parents who were not native of Metropolitan France may have refused their child to participate to one part of the study, because they had difficulties to read French. Their child are more likely to have repeated a grade, thus they are older (and consequently higher and fatter) than the other children.

The STREET 5 software

Calculations of urban air pollutants concentrations by the STREET 5 software at the 108 schools attended by the study children are precisely presented elsewhere [8].

To sum up: to apply STREET, 108 street segments were selected, one for each school. In most cases, the street next to the school with the greatest traffic density was selected and modelled with STREET. Otherwise, in cases where another street had a greater traffic density than that of the adjacent streets (up to a distance of 300 m around the school) and where no building screened the school from the street in question, that street was retained in accordance with French Air Quality Monitoring Networks criteria [9].

Emissions of benzene, volatile organic compounds (VOC), sulphur dioxide (SO₂), particles with aerodynamic diameter $\leq 10 \mu\text{m}$ (PM₁₀), nitrogen dioxide (NO₂), nitrogen oxides (NO_x), and carbon monoxide (CO) were calculated automatically by STREET as a function of input traffic conditions, the breakdown of the French motor vehicle fleet into each of the main vehicle classes for a given year (between 1995 and 2025) [10], as well as a suitable and updated database of vehicle emission rates, based on the IMPACT 2 software developed by the French Agency for Environment and Energy Management [11].

To calculate annual mean concentrations of urban air pollutants, STREET adds to input background concentrations a local component of air pollution, assessed as follows. Local component of air pollution was estimated by STREET by combining the results of emissions previously obtained with standard concentrations corresponding to the configuration meteorology/street topography input by the user. These standard concentrations are included in a database, incorporated in STREET, of over 100 000 annual mean concentrations calculated using the advanced Eulerian dispersion model, WINMISKAM4.2 [12, 13]. Thus, principal model inputs included: background concentrations of air pollutants, traffic density, proportion of main vehicle classes, average speed, percentage of gridlocks, direction and slope of the street, number of traffic lines, geometry of the buildings (situation, height, type, and density), quality of the roads surface, wind speed and direction, and precipitation.

Selection of the adjustment factors

These factors (except age included *a priori*) were selected, among about 40 pre-selected potential confounders or modifiers, and included into the marginal models, because they were associated with at least one health outcome in the crude analyses (Chi-squared test, $P < 0.25$) and changed at least one pollutant's effect estimated by $> 10\%$ when included in the multivariate marginal models. To study potential effect modifiers, we tested interactions between each covariate and the pollutant, and we conducted stratified analyses. The definitions of the variables "potential sources of indoor pollution at home" have been published elsewhere [14] and are summarized below.

- Smoking at home was defined as any current exposure to cigarettes, pipes, or cigars at home.
- Exposure to mould or dampness was defined as the current presence of damp or mould stains at home.
- Exposure to natural gas was defined as natural gas used for heating, for cooking, or for water-heater at home (except in cellar or in garage).
- Exposure to pets was defined as the presence of furry or feathered pets (dogs, cats, rodents, ferret, or polecat) at home.

RESULTS

Correlation between the pollutants concentrations calculated by STREET at the 108 schools

All modelled concentrations were significantly correlated with each other ($P < 0.001$) (Table 1). Benzene and VOC were the most correlated ($r = 0.95$) followed by benzene and CO ($r = 0.94$) and VOC and CO ($r = 0.93$). SO_2 was the pollutant the least correlated with the other air pollutants ($r = 0.51$ with NO_x , $r = 0.54$ with VOC, and $r = 0.58$ with NO_2).

Distribution of concentrations, according to the community, showing data for each school separately

For each pollutant, a graph shows the distribution of the concentrations according to the community. Each dot represents the concentration assessed at one school of each of the 6 communities (Figure 1).

Univariate associations between potential confounders or modifiers and pollution exposure

Children with older siblings were exposed to lower concentrations of PM_{10} ($P = 0.04$) and NO_2 ($P = 0.01$) compared with the others. A higher parental education was associated with lower levels of benzene ($P < 0.001$), VOC ($P < 0.001$), SO_2 ($P < 0.001$), PM_{10} ($P < 0.001$), NO_x ($P < 0.001$), and CO ($P < 0.001$). Children with at least one parent with an ethnic origin other than Metropolitan France were exposed to higher levels of NO_x ($P < 0.001$), NO_2 ($P < 0.001$), and CO ($P < 0.001$). Natural gas used at home was related to higher levels of COV ($P < 0.001$) and PM_{10} ($P < 0.001$). Pets at home were associated with lower levels of all the modelled air pollutants ($P < 0.001$). No other significant relationships were observed between potential confounders and pollution exposure.

Comparison of the prevalence of the health outcomes between the study population and the children excluded from the analysis.

When comparing the study population with the children excluded from the analysis, differences observed for health outcomes were not significant (Table 2).

Univariate associations between potential confounders or modifiers and health outcomes

Health outcomes, except EIA, were related to sex (Table 3) and were, as expected, more prevalent in children with a family history of allergy (Table 4) ($P < 0.001$). A higher parental education was related to a higher prevalence of past year rhinoconjunctivitis ($P = 0.005$) and lifetime eczema ($P < 0.001$) (Table 5). Mother's ethnic origin was related to lifetime allergic rhinitis ($P = 0.003$) and lifetime eczema ($P = 0.001$) (Table 6). Smoking at home was associated with a higher prevalence of past year eczema (14.0 versus 11.9; $P = 0.03$), mould or damp stains at home with a higher prevalence of EIA (10.8 versus 8.4; $P = 0.03$), past year rhinoconjunctivitis (15.1 versus 11.6; $P = 0.007$), lifetime allergic rhinitis (24.3 versus 19.4; $P = 0.002$), and past year eczema (15.7 versus 12.3; $P = 0.009$), natural gas used at home with a higher prevalence of sensitisation to pollens (28.9 versus 21.8; $P < 0.001$), and pets at home with a lower prevalence of EIA (7.4 versus 10.2; $P = 0.002$), lifetime allergic rhinitis (18.5 versus 23.1; $P = 0.004$), and sensitisation to pollens (25.1 versus 29.9; $P < 0.001$) (Table 7) [14]. No significant relationships were observed between older siblings and health outcomes (Table 8).

Associations between air pollutants exposure and health outcomes: three additional analyses

We assessed effect modification by sex, family history of allergy, exposure to smoking at home and allergic sensitisation by modelling the interaction of the potential effect modifier with pollutant concentrations and by examining the effects of exposure by strata on potential modifiers. There were no significant interactions of any potential modifier with exposure indicator for any of the seven air pollutants. Even if no significant interaction between

potential modifiers and the pollutants were detected, stratified analyses showed that: (1) the odds ratios for sensitisation to pollens were substantially higher in girls than in boys, whereas the odds ratios for EIA, **asthma (past year and lifetime)** were higher in boys than in girls (Table 9). (2) The odds ratios for EIA, eczema (past year and lifetime), lifetime allergic rhinitis, and sensitisation to pollens were slightly higher in children without family history of allergy (Table 10). (3) The odds ratios for EIA, **asthma (past year and lifetime), sensitisation to pollens, lifetime allergic rhinitis and past year eczema** were slightly higher in children additionally exposed to smoking at home (Table 11). (4) **The odds ratios for EIA, asthma (past year and lifetime) and lifetime eczema were slightly higher in children with allergic sensitisation (Table 12).**

To take into account the two different hierarchical levels (within a same school, within schools in the same community) in which the children were grouped, we also implemented a multi-level model using SAS PROC MIXED and the GLIMMIX macro with two random effects representing respectively the variance component between communities and the variance between schools nested in communities simultaneously [15]. The results concerning the random effects suggested that there was neither significant school-effect nor significant community-effect. **Indeed, adding random slopes for the air pollutant, varying across schools and across communities did not significantly improve the model. These random slopes did not significantly differ from 0.**

A single-stage logistic regression model was also implemented and yielded positive associations between pollutants and health outcomes with similar odds ratios and similar or slightly smaller confidence intervals.

Table 1: The correlation matrix of the pollutants concentrations calculated by STREET at the 108 schools.

Pearson coefficients (r)	Benzene	VOC	CO	NO ₂	NO _x	PM ₁₀	SO ₂
Benzene	1.00	0.95*	0.94*	0.70*	0.79*	0.84*	0.70*
VOC		1.00	0.93*	0.67*	0.83*	0.82*	0.54*
CO			1.00	0.81*	0.88*	0.83*	0.60*
NO ₂				1.00	0.89*	0.85*	0.58*
NO _x					1.00	0.91*	0.51*
PM ₁₀						1.00	0.70*
SO ₂							1.00

VOC = volatile organic compounds; SO₂ = sulphur dioxide; PM₁₀ = particles with aerodynamic diameter ≤ 10 μm; NO₂ = nitrogen dioxide; NO_x= nitrogen oxides; CO = carbon monoxide.

* p<0.0001.

Table 2: Comparison of the prevalence rate (%) of health outcomes between children residing at their current address for at least three years and children excluded from the analyses because they have resided at their current address for less than three years.

Health outcomes	Children residing at their current address for at least three years N=4907	Children excluded from the analyses N=1776	P-value
During the clinical examination			
EIA	8.8	8.4	0.6291
Sensitisation to pollens	12.3	12.3	0.9698
Past year			
Asthma	5.3	5.2	0.8895
Rhinoconjunctivitis	12.2	11.0	0.2367
Eczema	12.8	11.5	0.1629
Lifetime			
Asthma	9.8	10.1	0.7139
Allergic rhinitis	20.1	19.7	0.6988
Eczema	26.1	24.2	0.1288

EIA= exercised-induced asthma

Table 3: Prevalence of health outcomes according to sex (N=4907).

Health outcome	All N=4907	Boys N=2449	Girls N=2458	OR (95%CI)
	Prevalence rate (%)			
During the clinical examination				
EIA	8.8	9.1	8.5	0.92 (0.75-1.13)
Sensitisation to pollen	12.3	14.7	9.9 [§]	0.64 (0.54-0.77)
Past year				
Asthma	5.3	6.9	3.8 [§]	0.53 (0.40-0.71)
Rhinoconjunctivitis	12.2	13.6	10.7 [§]	0.76 (0.64-0.92)
Eczema	12.8	10.7	14.9 [§]	1.46 (1.23-1.74)
Lifetime				
Asthma	9.8	12.5	7.1 [§]	0.54 (0.44-0.65)
Allergic rhinitis	20.1	22.7	17.7 [§]	0.73 (0.63-0.85)
Eczema	26.1	24.7	27.4 [*]	1.15 (1.01-1.31)

EIA= exercised-induced asthma; OR= odds ratio; CI= confidence interval.

Odds-ratios and 95% confidence interval were calculated using boys as reference category.

* p<0.05; † p<0.01; § p<0.001.

Table 4: Prevalence of health outcomes according to family history of allergy (N=4907).

Health outcome	All N=4907	No family history of allergy N=3088	Family history of allergy N=1819	OR (95%CI)
	Prevalence rate (%)			
During the clinical examination				
EIA	8.8	8.5	9.4	1.12 (0.91-1.39)
Sensitisation to pollen	12.3	10.2	15.8	1.65 (1.38-1.97) [§]
Past year				
Asthma	5.3	3.1	9.5	3.31 (2.51-4.38) [§]
Rhinoconjunctivitis	12.2	7.8	19.9	2.93 (2.43-3.53) [§]
Eczema	12.8	9.5	18.4	2.16 (1.81-2.57) [§]
Lifetime				
Asthma	9.8	6.8	14.7	2.36 (1.95-2.86) [§]
Allergic rhinitis	20.1	14.2	30.2	2.62 (2.26-3.03) [§]
Eczema	26.1	20.0	36.1	2.25 (1.97-2.57) [§]

EIA= exercised-induced asthma; OR= odds ratio; CI= confidence interval.

Odds-ratios and 95% confidence interval were calculated using no family history of allergy as reference category.

A child had a family history of allergy if his/her father or his/her mother had ever suffered from asthma, allergic rhinitis, or eczema.

* p<0.05; ‡ p<0.01; § p<0.001.

Table 5: Prevalence of health outcomes according to parental education (N=4907).

Health outcome	All N=4907	Primary or secondary N=2322	High School or university N=2226	OR (95%CI)
	Prevalence rate (%)			
During the clinical examination				
EIA	8.8	8.3	9.9	1.21 (0.98-1.49)
Sensitisation to pollen	12.3	11.3	12.8	1.15 (0.96-1.39)
Past year				
Asthma	5.3	4.9	6.0	1.23 (0.93-1.63)
Rhinoconjunctivitis	12.2	10.8	13.7	1.31 (1.08-1.59) [‡]
Eczema	12.8	12.4	13.7	1.12 (0.93-1.33)
Lifetime				
Asthma	9.8	9.7	9.8	1.02 (0.83-1.24)
Allergic rhinitis	20.1	19.9	20.4	1.03 (0.89-1.20)
Eczema	26.1	23.5	29.6	1.37 (1.20-1.57) [§]

EIA= exercised-induced asthma; OR= odds ratio; CI= confidence interval.

Odds-ratios and 95% confidence interval were calculated using “Primary or secondary” as reference category.

Parental education was defined as the highest achieved educational level of either parent.

* p<0.05; ‡ p<0.01; § p<0.001.

Table 6: Prevalence of health outcomes according to mother's ethnic origin (N=4907).

Health outcome	Prevalence rate (%)							P-value *	
	Metropolitan France N=3637	French overseas depatments N=154	South Europe N=189	Morocco, Algeria, Tunisia N=387	Sub- Saharan Africa N=122	Asia N=136	Other N=142		
During the clinical examination									
EIA	8.4	12.3	10.7	9.3	12.3	11.5	7.5	0.5912	
Sensitisation to pollen	12.5	15.0	12.8	8.9	7.8	12.0	16.0	0.2184	
Past year									
Asthma	5.4	1.5	7.0	5.4	8.6	4.1	4.0	0.2609	
Rhinoconjunctivitis	12.3	15.8	7.9	12.6	9.3	15.3	9.2	0.2876	
Eczema	13.1	16.2	10.3	12.2	9.8	10.2	12.5	0.5894	
Lifetime									
Asthma	9.9	4.8	10.6	10.2	11.0	8.1	7.1	0.3987	
Allergic rhinitis	19.6	33.1	15.7	18.5	24.1	23.2	22.0	0.0026 [‡]	
Eczema	27.7	24.1	23.5	18.7	10.7	18.9	22.9	0.0013 [‡]	

EIA= exercised-induced asthma

* ANOVA (Fischer's test)

[‡] p<0.01.

Table 7: Univariate associations between potential sources of indoor pollution at home and health outcomes (N=4907).

Health outcomes	Potential sources of indoor pollution at home OR (95% CI)			
	Smoking	Pets	Mould or dampness	Gas
During the clinical examination				
EIA	1.06 (0.86-1.30)	0.71 (0.58-0.88) [‡]	1.33 (1.03-1.71) [*]	1.29 (0.96-1.71)
Sensitisation to pollen	0.98 (0.82-1.17)	0.77 (0.65-0.93) [‡]	1.02 (0.81-1.29)	1.54 (1.19-2.00) [‡]
Past year				
Asthma	0.97 (0.74-1.28)	0.76 (0.58-1.01)	1.19 (0.84-1.68)	1.06 (0.74-1.52)
Rhinoconjunctivitis	0.98 (0.81-1.18)	0.93 (0.77-1.12)	1.36 (1.08-1.72) [‡]	1.00 (0.79-1.28)
Eczema	1.21 (1.02-1.43) [*]	1.10 (0.92-1.31)	1.33 (1.07-1.64) [‡]	0.90 (0.72-1.12)
Lifetime				
Asthma	1.17 (0.97-1.41)	0.83 (0.68-1.01)	1.17 (0.92-1.49)	1.20 (0.92-1.56)
Allergic rhinitis	0.95 (0.82-1.10)	0.80 (0.69-0.93) [§]	1.33 (1.11-1.60) [‡]	1.16 (0.96-1.41)
Eczema	0.93 (0.82-1.07)	1.01 (0.88-1.15)	1.00 (0.84-1.19)	0.80 (0.67-0.94) [‡]

EIA= exercised-induced asthma; OR= odds ratio; CI= confidence interval.

Odds-ratios and 95% confidence interval were calculated using no smoking at home or no pets at home or no mould or dampness at home or no natural gas used at home as reference category.

* p<0.05; [‡] p<0.01; [§] p<0.001.

Table 8: Prevalence of health outcomes according to older siblings (N=4907).

Health outcome	All N=4907	No older siblings N=2644	Older siblings N=2258	OR (95%CI)
	Prevalence rate (%)			
During the clinical examination				
EIA	8.8	8.1	9.6	1.19 (0.97-1.46)
Sensitisation to pollen	12.3	12.6	11.9	0.94 (0.79-1.12)
Past year				
Asthma	5.3	5.6	5.0	0.88 (0.68-1.16)
Rhinoconjunctivitis	12.2	12.9	11.3	0.86 (0.72-1.03)
Eczema	12.8	12.7	12.8	1.01 (0.86-1.20)
Lifetime				
Asthma	9.8	10.1	9.3	0.91 (0.76-1.11)
Allergic rhinitis	20.1	20.8	19.4	0.92 (0.80-1.06)
Eczema	26.1	26.2	25.8	0.98 (0.86-1.12)

EIA= exercised-induced asthma; OR= odds ratio; CI= confidence interval.

Odds-ratios and 95% confidence interval were calculated using no family history of allergy as reference category.

A child had older siblings if he/she had at least one brother/sister older than him/her.

* p<0.05; ‡ p<0.01; § p<0.001.

Table 9: Associations between exposure to air pollutants and health outcomes according to sex (N=4907).

Pollutants	Exercise-induced asthma OR (95%CI)		Past year asthma OR (95%CI)		Lifetime asthma OR (95%CI)	
	Boys N=2449	Girls N=2458	Boys N=2449	Girls N=2458	Boys N=2449	Girls N=2458
Benzene	1.50 (1.10-2.03) [‡]	1.35 (1.01-1.83) [*]	1.39 (0.94-2.05)	1.33 (0.82-2.14)	1.23 (0.93-1.62)	1.37 (0.96-1.95)
VOC	1.38 (1.03-1.85) [*]	1.07 (0.84-1.47)	1.29 (0.88-1.89)	1.19 (0.74-1.92)	1.26 (0.96-1.66)	1.11 (0.78-1.57)
SO ₂	1.91 (1.33-2.64) [‡]	1.39 (1.01-1.85) [*]	1.63 (1.10-2.41) [*]	1.20 (0.74-1.93)	1.43 (1.08-1.88) [*]	1.06 (0.75-1.50)
PM ₁₀	1.39 (1.02-1.77) [*]	1.16 (0.87-1.63)	1.41 (0.96-2.07)	1.24 (0.77-1.99)	1.34 (1.02-1.77) [*]	1.23 (0.87-1.74)
NO ₂	1.05 (0.78-1.40)	0.85 (0.52-1.12)	1.12 (0.76-1.65)	0.89 (0.55-1.45)	1.14 (0.86-1.16)	0.84 (0.59-1.20)
NO _x	1.37 (1.03-1.81) [*]	1.06 (0.81-1.54)	1.26 (0.85-1.86)	1.32 (0.82-2.14)	1.21 (0.92-1.60)	1.05 (0.74-1.48)
CO	1.36 (1.04-1.76) [*]	1.11 (0.82-1.62)	1.33 (0.90-1.97)	1.36 (0.84-2.21)	1.30 (0.98-1.71)	1.11 (0.79-1.58)
Pollutants	Sensitisation to pollens OR (95%CI)		Past year rhinoconjunctivitis OR (95%CI)		Lifetime allergic rhinitis OR (95%CI)	
	Boys N=2449	Girls N=2458	Boys N=2449	Girls N=2458	Boys N=2449	Girls N=2458
Benzene	1.16 (0.91-1.49)	1.29 (0.97-1.65)	1.09 (0.85-1.40)	0.99 (0.75-1.30)	1.14 (0.93-1.38)	1.16 (0.93-1.44)
VOC	1.17 (0.89-1.51)	1.17 (0.91-1.59)	1.07 (0.83-1.37)	1.06 (0.80-1.39)	1.15 (0.94-1.39)	1.09 (0.88-1.35)
SO ₂	1.01 (0.78-1.19)	1.08 (0.79-1.41)	1.15 (0.90-1.48)	0.96 (0.73-1.26)	1.23 (1.01-1.50) [*]	1.02 (0.82-1.26)
PM ₁₀	1.16 (0.91-1.44)	1.51 (1.11-2.05) [‡]	1.15 (0.90-1.47)	1.00 (0.76-1.32)	1.16 (0.96-1.42)	1.20 (0.97-1.49)
NO ₂	0.93 (0.71-1.17)	1.29 (0.97-1.68)	1.20 (0.94-1.54)	0.86 (0.66-1.13)	1.12 (0.92-1.37)	1.09 (0.88-1.35)
NO _x	0.94 (0.72-1.19)	1.06 (0.74-1.35)	1.16 (0.90-1.48)	0.99 (0.76-1.31)	1.15 (0.95-1.41)	1.05 (0.85-1.30)
CO	0.92 (0.71-1.22)	1.05 (0.79-1.42)	1.07 (0.83-1.37)	1.06 (0.80-1.39)	1.08 (0.89-1.32)	1.11 (0.89-1.37)
Pollutants	Past year eczema OR (95%CI)		Lifetime eczema OR (95%CI)			
	Boys N=2449	Girls N=2458	Boys N=2449	Girls N=2458		
Benzene	1.28 (0.98-1.66)	1.13 (0.90-1.42)	1.08 (0.87-1.33)	1.10 (0.90-1.34)		
VOC	1.09 (0.84-1.42)	1.23 (0.97-1.55)	1.03 (0.84-1.27)	1.10 (0.90-1.34)		
SO ₂	1.16 (0.89-1.51)	1.01 (0.80-1.27)	0.94 (0.76-1.16)	0.93 (0.76-1.14)		
PM ₁₀	1.28 (0.98-1.66)	1.16 (0.92-1.46)	1.17 (0.95-1.44)	1.12 (0.91-1.36)		
NO ₂	1.23 (0.94-1.59)	1.18 (0.94-1.49)	1.23 (0.99-1.51)	1.21 (0.99-1.49)		
NO _x	1.21 (0.93-1.58)	1.19 (0.94-1.50)	1.15 (0.93-1.42)	1.09 (0.89-1.33)		
CO	1.22 (0.94-1.59)	1.18 (0.94-1.49)	1.21 (0.98-1.49)	1.08 (0.88-1.32)		

OR= odds ratio; CI= confidence interval; VOC = volatile organic compounds; SO₂ = sulphur dioxide; PM₁₀ = particles with aerodynamic diameter ≤ 10 μm; NO₂ = nitrogen dioxide; NO_x= nitrogen oxides; CO = carbon monoxide.

Values are odds-ratios and 95% confidence interval obtained with a marginal model adjusted for age, older siblings, family history of allergy, parental education, mother's ethnic origin, smoking at home, mould or dampness at home, natural gas used for heating, for cooking, or for water-heater at home, and pets at home, with an exchangeable working correlation structure using the community as a stratum.

Odds ratios were calculated, per an increment for the interquartile range (1.1 μg.m⁻³ for benzene; 25.2 μg.m⁻³ for VOC; 5 μg.m⁻³ for SO₂; 10.5 μg.m⁻³ for PM₁₀; 18.5 μg.m⁻³ for NO₂; 52.1 μg.m⁻³ for NO_x; 199 μg.m⁻³ for CO), among the children residing at their current address for at least three years (N=4907).

* p<0.05; ‡ p<0.01; § p<0.001.

Table 10: Associations between exposure to air pollutants and health outcomes according to family history of allergy (N=4907).

Pollutants	Exercise-induced asthma OR (95%CI)		Past year asthma OR (95%CI)		Lifetime asthma OR (95%CI)	
	No family history of allergy N=3088	Family history of allergy N=1819	No family history of allergy N=3088	Family history of allergy N=1819	No family history of allergy N=3088	Family history of allergy N=1819
Benzene	1.58 (1.17-2.12) [‡]	1.32 (0.93-1.87)	1.51 (0.91-2.51)	1.27 (0.87-1.84)	1.41 (1.01-1.96) [*]	1.17 (0.88-1.56)
VOC	1.28 (0.95-1.71)	1.28 (0.90-1.82)	1.43 (0.87-2.37)	1.14 (0.78-1.65)	1.17 (0.84-1.61)	1.21 (0.91-1.60)
SO ₂	1.82 (1.34-2.46) [§]	1.56 (1.09-2.23) [*]	1.52 (0.92-2.53)	1.36 (0.93-1.98)	1.30 (0.94-1.81)	1.23 (0.93-1.64)
PM ₁₀	1.35 (1.01-1.81) [*]	1.29 (0.91-1.83)	1.40 (0.85-2.30)	1.28 (0.88-1.85)	1.34 (0.97-1.86)	1.24 (0.93-1.65)
NO ₂	0.83 (0.62-1.12)	1.17 (0.82-1.66)	0.92 (0.56-1.51)	1.08 (0.74-1.57)	1.06 (0.76-1.47)	0.98 (0.74-1.31)
NO _x	1.35 (1.01-1.82) [*]	1.18 (0.83-1.67)	1.25 (0.76-2.07)	1.29 (0.89-1.89)	1.03 (0.74-1.44)	1.24 (0.93-1.65)
CO	1.38 (1.02-1.86) [*]	1.17 (0.82-1.66)	1.36 (0.82-2.26)	1.32 (0.90-1.93)	1.08 (0.78-1.50)	1.33 (1.00-1.78)
Pollutants	Sensitisation to pollens OR (95%CI)		Past year rhinoconjunctivitis OR (95%CI)		Lifetime allergic rhinitis OR (95%CI)	
	N=3088	N=1819	N=3088	N=1819	N=3088	N=1819
Benzene	1.26 (0.98-1.68)	1.09 (0.82-1.47)	0.97 (0.74-1.29)	1.06 (0.83-1.37)	1.25 (1.00-1.51) [*]	1.02 (0.82-1.35)
VOC	1.33 (1.01-1.72) [*]	0.98 (0.73-1.28)	0.99 (0.75-1.30)	1.10 (0.86-1.42)	1.19 (0.95-1.48)	0.98 (0.76-1.26)
SO ₂	1.08 (0.85-1.44)	1.01 (0.75-1.32)	1.08 (0.82-1.43)	1.01 (0.79-1.30)	1.16 (0.90-1.45)	1.10 (0.86-1.37)
PM ₁₀	1.48 (1.09-1.87) [*]	1.12 (0.83-1.50)	1.07 (0.81-1.42)	1.06 (0.83-1.36)	1.33 (1.08-1.64) [‡]	1.09 (0.88-1.36)
NO ₂	1.11 (0.82-1.43)	0.97 (0.72-1.26)	0.93 (0.70-1.22)	1.13 (0.88-1.46)	1.17 (0.97-1.52)	1.05 (0.83-1.29)
NO _x	0.95 (0.74-1.26)	1.02 (0.77-1.34)	0.91 (0.69-1.20)	1.23 (0.96-1.59)	1.11 (0.90-1.39)	1.07 (0.85-1.32)
CO	1.01 (0.75-1.32)	0.91 (0.68-1.19)	0.92 (0.70-1.22)	1.20 (0.93-1.55)	1.09 (0.88-1.38)	1.02 (0.80-1.26)
Pollutants	Past year eczema OR (95%CI)		Lifetime eczema OR (95%CI)			
	N=3088	N=1819	N=3088	N=1819		
Benzene	1.21 (0.96-1.59)	0.98 (0.76-1.28)	1.14 (0.97-1.41)	0.88 (0.72-1.09)		
VOC	1.19 (0.94-1.56)	1.02 (0.79-1.32)	1.18 (0.96-1.39)	0.98 (0.80-1.16)		
SO ₂	0.85 (0.62-1.14)	1.00 (0.77-1.31)	0.99 (0.79-1.22)	0.91 (0.75-1.11)		
PM ₁₀	1.25 (0.97-1.63)	1.03 (0.80-1.34)	1.21 (1.02-1.46) [*]	1.04 (0.87-1.32)		
NO ₂	1.41 (1.06-1.82) [*]	0.85 (0.71-1.17)	1.25 (1.01-1.52) [*]	1.09 (0.86-1.33)		
NO _x	1.33 (1.02-1.71) [*]	0.92 (0.74-1.21)	1.19 (1.03-1.43) [*]	0.99 (0.79-1.22)		
CO	1.36 (1.01-1.75) [*]	0.88 (0.72-1.19)	1.22 (1.01-1.48) [*]	1.02 (0.83-1.29)		

OR= odds ratio; CI= confidence interval; VOC = volatile organic compounds; SO₂ = sulphur dioxide; PM₁₀ = particles with aerodynamic diameter ≤ 10 µm; NO₂ = nitrogen dioxide; NO_x= nitrogen oxides; CO = carbon monoxide.

Values are odds-ratios and 95% confidence interval obtained with a marginal model adjusted for age, sex, older siblings, parental education, mother's ethnic origin, smoking at home, mould or dampness at home, natural gas used for heating, for cooking, or for water-heater at home, and pets at home, with an exchangeable working correlation structure using the community as a stratum.

Odds ratios were calculated, per an increment for the interquartile range (1.1 µg.m⁻³ for benzene; 25.2 µg.m⁻³ for VOC; 5 µg.m⁻³ for SO₂; 10.5 µg.m⁻³ for PM₁₀; 18.5 µg.m⁻³ for NO₂; 52.1 µg.m⁻³ for NO_x; 199 µg.m⁻³ for CO), among the children residing at their current address for at least three years (N=4907).

* p<0.05; ‡ p<0.01; § p<0.001.

Table 11: Associations between exposure to air pollutants and health outcomes according to smoking at home (N=4907).

Pollutants	Exercise-induced asthma OR (95%CI)		Past year asthma OR (95%CI)		Lifetime asthma OR (95%CI)	
	No smoking at home N=2769	Smoking at home N=2138	No smoking at home N=2769	Smoking at home N=2138	No smoking at home N=2769	Smoking at home N=2138
Benzene	1.24 (0.97-1.71)	1.52 (1.09-2.07) [‡]	1.24 (0.79-1.93)	1.45 (0.97-2.19)	1.14 (0.87-1.48)	1.20 (0.91-1.59)
VOC	1.02 (0.76-1.43)	1.51 (1.04-2.13) [*]	1.24 (0.79-1.93)	1.23 (0.82-1.84)	0.97 (0.75-1.26)	1.35 (1.02-1.79) [*]
SO ₂	1.37 (1.02-1.90) [*]	1.79 (1.25-2.65) [§]	1.33 (0.85-2.07)	1.51 (0.99-2.29)	1.16 (0.89-1.51)	1.26 (0.95-1.67)
PM ₁₀	1.18 (0.85-1.54)	1.46 (1.03-1.98) [*]	1.09 (0.70-1.70)	1.54 (1.03-2.32) [*]	1.19 (0.92-1.55)	1.26 (0.95-1.66)
NO ₂	0.98 (0.72-1.34)	0.96 (0.70-1.30)	0.88 (0.56-1.38)	1.12 (0.75-1.69)	1.05 (0.81-1.36)	1.02 (0.77-1.34)
NO _x	1.15 (0.81-1.57)	1.38 (0.98-1.89)	1.05 (0.67-1.65)	1.49 (0.98-2.27)	1.16 (0.89-1.51)	1.12 (0.84-1.47)
CO	1.19 (0.83-1.59)	1.40 (1.00-1.95) [*]	1.11 (0.71-1.73)	1.55 (1.02-2.36) [*]	1.20 (0.92-1.56)	1.14 (0.86-1.51)
Pollutants	Sensitisation to pollens OR (95%CI)		Past year rhinoconjunctivitis OR (95%CI)		Lifetime allergic rhinitis OR (95%CI)	
	N=2769	N=2138	N=2769	N=2138	N=2769	N=2138
Benzene	0.96 (0.71-1.29)	1.51 (1.15-1.99) [‡]	1.13 (0.89-1.44)	0.93 (0.70-1.23)	0.94 (0.74-1.21)	1.38 (1.11-1.72) [‡]
VOC	1.07 (0.80-1.44)	1.31 (1.00-1.71) [*]	1.05 (0.82-1.34)	1.06 (0.80-1.41)	0.94 (0.73-1.20)	1.25 (1.00-1.55) [*]
SO ₂	0.87 (0.65-1.16)	1.24 (0.95-1.62)	1.11 (0.87-1.41)	0.99 (0.74-1.31)	1.08 (0.84-1.38)	1.21 (0.97-1.51)
PM ₁₀	1.19 (0.88-1.59)	1.53 (1.17-2.00) [‡]	1.15 (0.90-1.47)	0.98 (0.74-1.30)	1.01 (0.79-1.29)	1.40 (1.13-1.74) [‡]
NO ₂	1.04 (0.77-1.40)	1.12 (0.86-1.46)	1.01 (0.79-1.28)	1.07 (0.81-1.42)	1.05 (0.82-1.34)	1.18 (0.95-1.47)
NO _x	0.88 (0.65-1.18)	1.08 (0.83-1.41)	1.11 (0.87-1.42)	1.03 (0.78-1.36)	1.05 (0.82-1.34)	1.12 (0.90-1.39)
CO	0.91 (0.68-1.23)	1.08 (0.83-1.41)	1.11 (0.87-1.41)	1.00 (0.76-1.33)	1.07 (0.83-1.37)	1.10 (0.88-1.36)
Pollutants	Past year eczema OR (95%CI)		Lifetime eczema OR (95%CI)			
	N=2769	N=2138	N=2769	N=2138		
Benzene	1.14 (0.90-1.45)	1.28 (0.99-1.65)	1.03 (0.85-1.26)	1.19 (1.00-1.41)		
VOC	1.10 (0.87-1.39)	1.29 (1.00-1.66) [*]	1.09 (0.89-1.32)	1.09 (0.91-1.29)		
SO ₂	1.09 (0.86-1.38)	1.07 (0.83-1.38)	1.01 (0.83-1.23)	0.90 (0.75-1.07)		
PM ₁₀	1.16 (0.92-1.48)	1.29 (1.00-1.66)	1.08 (0.88-1.31)	1.15 (0.97-1.37)		
NO ₂	1.18 (0.93-1.50)	1.24 (0.96-1.60)	1.07 (0.88-1.31)	1.28 (1.07-1.52) [‡]		
NO _x	1.16 (0.91-1.47)	1.28 (1.00-1.65)	1.04 (0.86-1.27)	1.23 (1.03-1.47) [*]		
CO	1.15 (0.90-1.46)	1.29 (1.00-1.67) [*]	1.05 (0.86-1.28)	1.25 (1.05-1.49) [*]		

OR= odds ratio; CI= confidence interval; VOC = volatile organic compounds; SO₂ = sulphur dioxide; PM₁₀ = particles with aerodynamic diameter ≤ 10 µm; NO₂ = nitrogen dioxide; NO_x= nitrogen oxides; CO = carbon monoxide.

Values are odds-ratios and 95% confidence interval obtained with a marginal model adjusted for age, sex, older siblings, family history of allergy, parental education, mother's ethnic origin, mould or dampness at home, natural gas used for heating, for cooking, or for water-heater at home, and pets at home, with an exchangeable working correlation structure using the community as a stratum.

Odds ratios were calculated, per an increment for the interquartile range (1.1 µg.m⁻³ for benzene; 25.2 µg.m⁻³ for VOC; 5 µg.m⁻³ for SO₂; 10.5 µg.m⁻³ for PM₁₀; 18.5 µg.m⁻³ for NO₂; 52.1 µg.m⁻³ for NO_x; 199 µg.m⁻³ for CO), among the children residing at their current address for at least three years (N=4907).

* p<0.05; ‡ p<0.01; § p<0.001.

Table 12: Associations between exposure to air pollutants and health outcomes according to allergic sensitisation (N=4907).

Pollutants	Exercise-induced asthma OR (95%CI)		Past year asthma OR (95%CI)		Lifetime asthma OR (95%CI)	
	No allergic sensitisation N=3302	Allergic sensitisation N=1250	No allergic sensitisation N=3302	Allergic sensitisation N=1250	No allergic sensitisation N=3302	Allergic sensitisation N=1250
Benzene	1.31 (0.94-1.81)	1.61 (1.23-2.10) [§]	1.18 (0.83-1.67)	1.67 (1.06-2.61) [*]	1.12 (0.85-1.48)	1.37 (1.03-1.83) [*]
VOC	1.26 (0.91-1.75)	1.37 (1.05-1.78) [*]	1.05 (0.74-1.48)	1.70 (1.09-2.67) [*]	1.12 (0.85-1.48)	1.16 (0.88-1.54)
SO ₂	1.32 (1.16-2.27) [‡]	1.74 (1.32-2.28) [§]	1.22 (0.85-1.73)	1.55 (0.99-2.44) [†]	1.10 (0.84-1.46)	1.41 (1.06-1.89) [*]
PM ₁₀	1.30 (0.94-1.81)	1.42 (1.09-1.85) [‡]	1.18 (0.83-1.67)	1.64 (1.05-2.57) [*]	1.19 (0.90-1.57)	1.35 (1.01-1.79) [*]
NO ₂	1.14 (0.83-1.58)	1.07 (0.82-1.39)	1.05 (0.74-1.49)	1.15 (0.75-1.78)	1.01 (0.77-1.33)	1.04 (0.79-1.38)
NO _x	1.18 (0.85-1.63)	1.52 (1.16-1.98) [‡]	1.24 (0.87-1.76)	1.53 (0.98-2.38) [†]	1.02 (0.77-1.35)	1.23 (0.92-1.63)
CO	1.19 (0.86-1.65)	1.52 (1.16-1.99) [‡]	1.27 (0.89-1.81)	1.60 (1.02-2.51) [*]	1.11 (0.84-1.47)	1.26 (0.94-1.68)
Pollutants	Past year rhinoconjunctivitis OR (95%CI)		Lifetime allergic rhinitis OR (95%CI)		Past year eczema OR (95%CI)	
	N=3302	N=1250	N=3302	N=1250	N=3302	N=1250
Benzene	0.97 (0.73-1.29)	1.11 (0.85-1.44)	1.20 (0.97-1.48)	1.08 (0.87-1.34)	1.13 (0.88-1.45)	1.17 (0.91-1.51)
VOC	1.02 (0.77-1.35)	1.03 (0.79-1.33)	1.21 (0.98-1.54)	0.96 (0.78-1.19)	1.12 (0.87-1.44)	1.19 (0.93-1.53)
SO ₂	1.01 (0.77-1.34)	1.09 (0.84-1.42)	1.12 (0.90-1.38)	1.14 (0.92-1.41)	0.98 (0.76-1.26)	1.07 (0.83-1.37)
PM ₁₀	1.03 (0.78-1.37)	1.13 (0.87-1.47)	1.22 (0.99-1.60)	1.09 (0.88-1.35)	1.31 (1.02-1.69) [*]	1.09 (0.85-1.39)
NO ₂	0.95 (0.72-1.26)	1.22 (0.94-1.58)	1.16 (0.94-1.43)	1.07 (0.86-1.32)	1.20 (0.93-1.55)	1.19 (0.93-1.53)
NO _x	1.02 (0.77-1.35)	1.11 (0.85-1.44)	1.16 (0.94-1.43)	1.03 (0.83-1.28)	1.14 (0.89-1.47)	1.24 (0.96-1.60)
CO	1.06 (0.80-1.40)	1.08 (0.83-1.40)	1.15 (0.93-1.43)	1.04 (0.84-1.29)	1.13 (0.88-1.46)	1.24 (0.96-1.60)
Pollutants	Lifetime eczema OR (95%CI)					
	N=3302	N=1250				
Benzene	1.08 (0.87-1.34)	1.20 (0.97-1.48)				
VOC	0.96 (0.78-1.19)	1.25 (1.01-1.54) [*]				
SO ₂	1.14 (0.92-1.41)	1.12 (0.90-1.38)				
PM ₁₀	1.09 (0.88-1.35)	1.29 (1.05-1.60) [*]				
NO ₂	1.07 (0.86-1.32)	1.16 (0.94-1.43)				
NO _x	1.03 (0.83-1.28)	1.16 (0.94-1.43)				
CO	1.04 (0.84-1.29)	1.15 (0.93-1.43)				

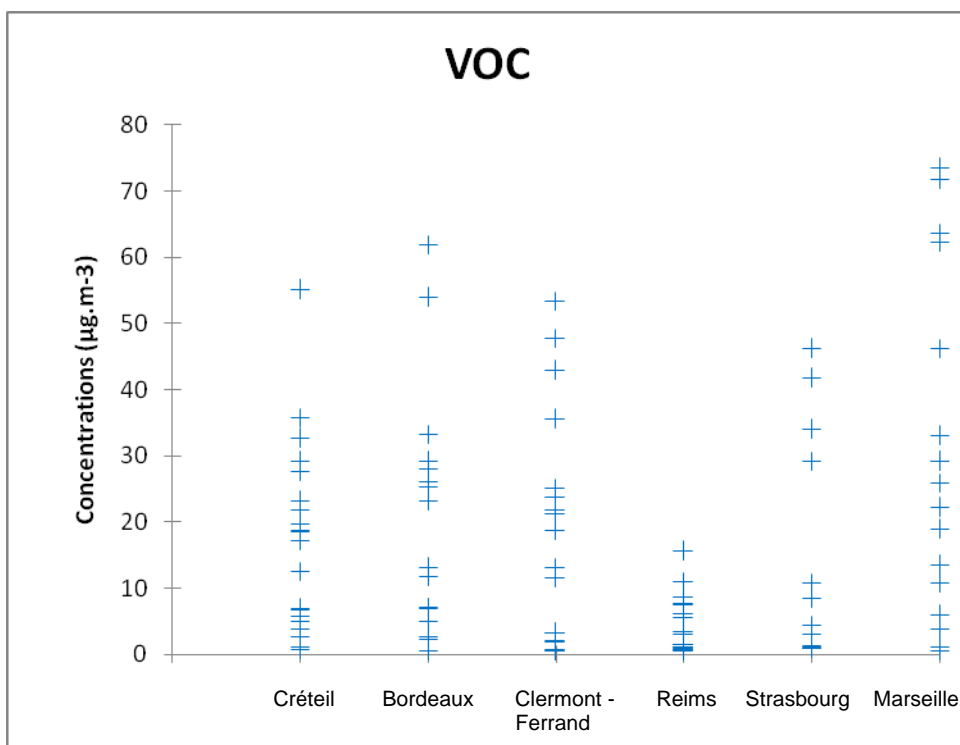
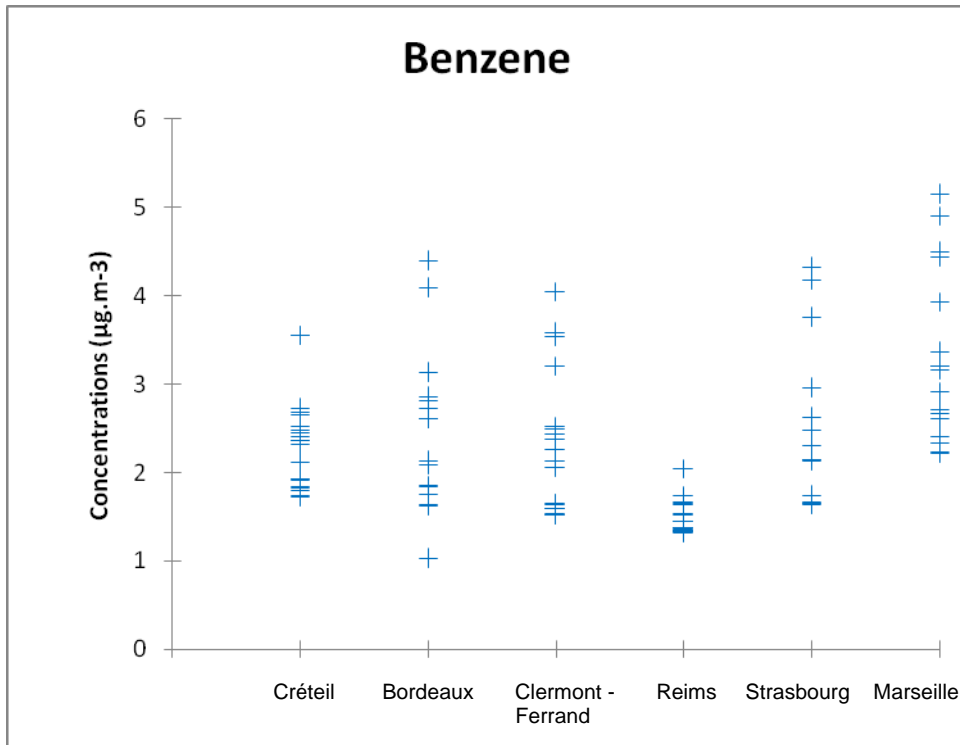
OR= odds ratio; CI= confidence interval; VOC = volatile organic compounds; SO₂ = sulphur dioxide; PM₁₀ = particles with aerodynamic diameter ≤ 10 µm; NO₂ = nitrogen dioxide; NO_x= nitrogen oxides; CO = carbon monoxide.

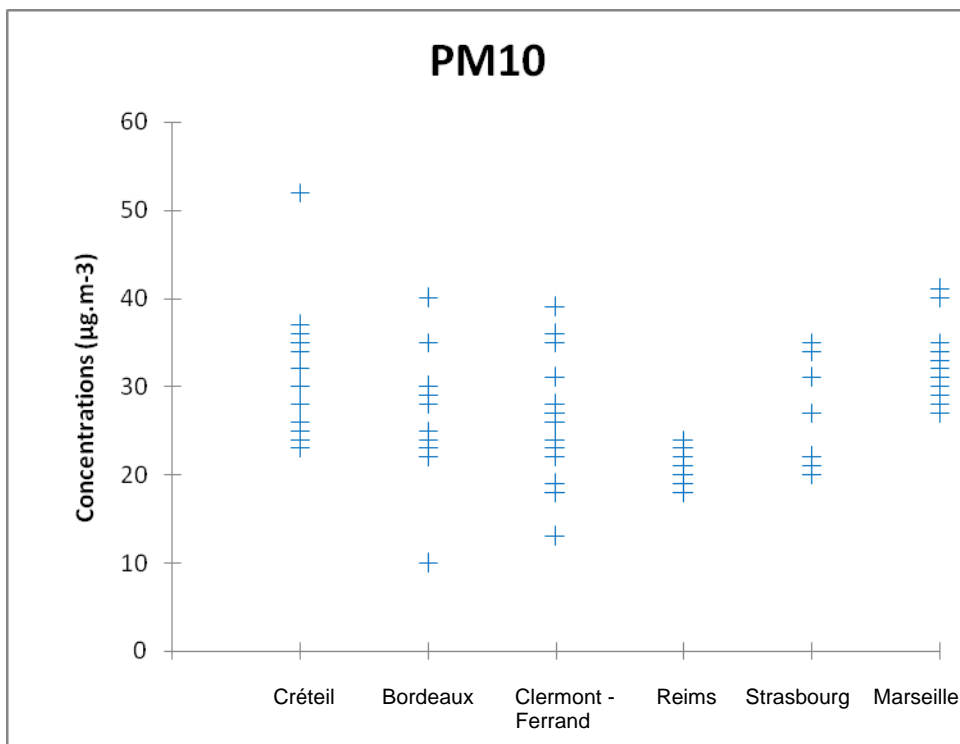
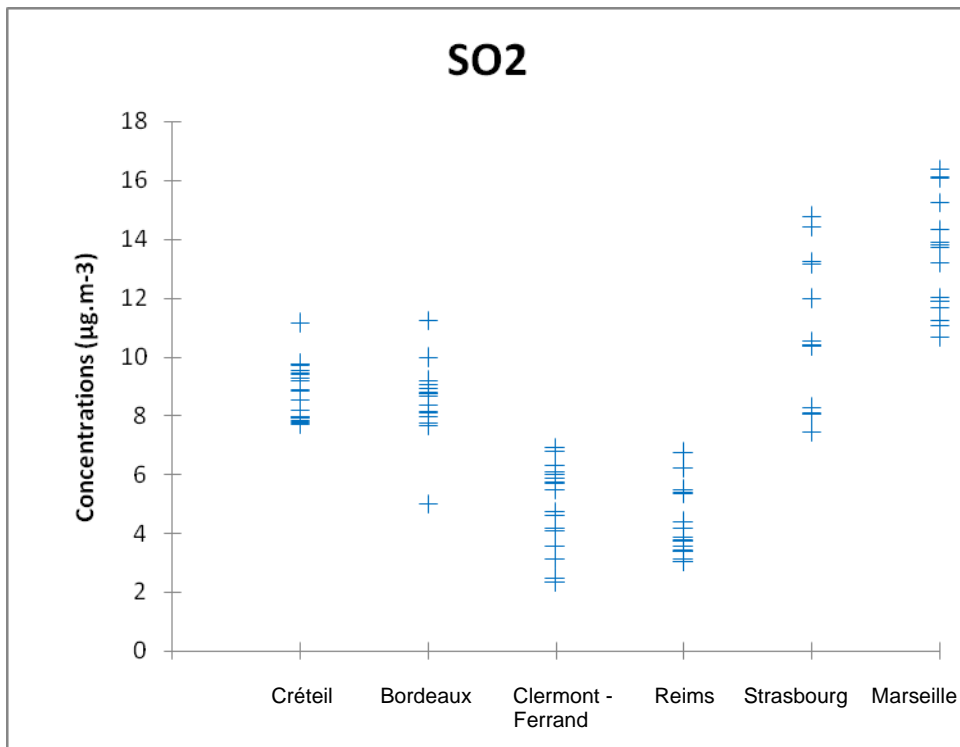
Values are odds-ratios and 95% confidence interval obtained with a marginal model adjusted for age, sex, older siblings, family history of allergy, parental education, mother's ethnic origin, smoking at home, mould or dampness at home, natural gas used for heating, for cooking, or for water-heater at home, and pets at home, with an exchangeable working correlation structure using the community as a stratum.

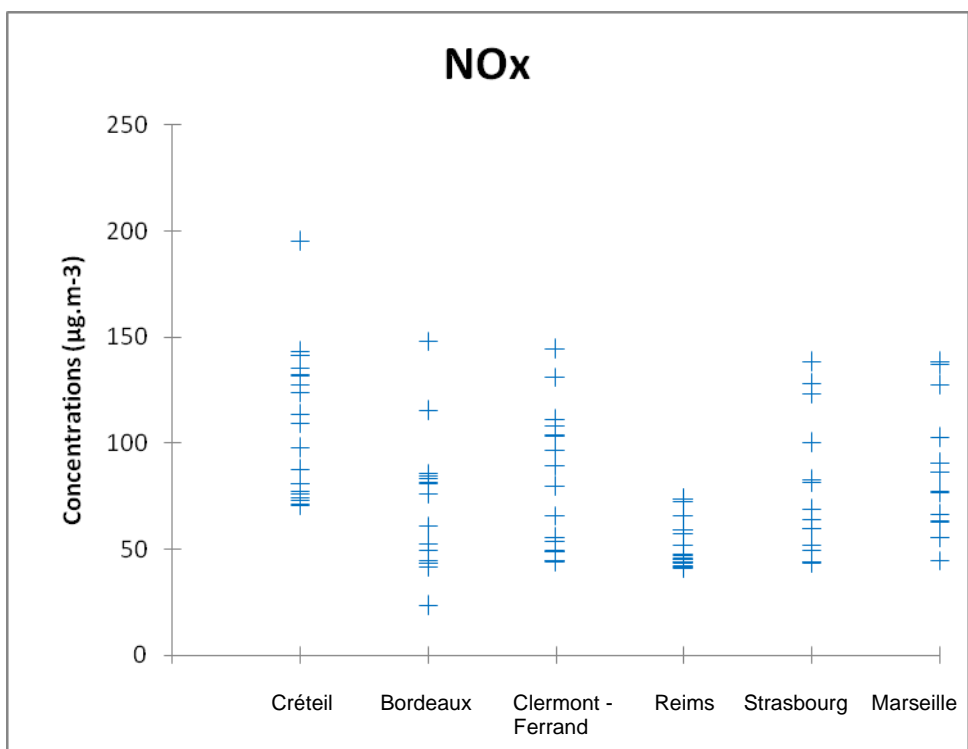
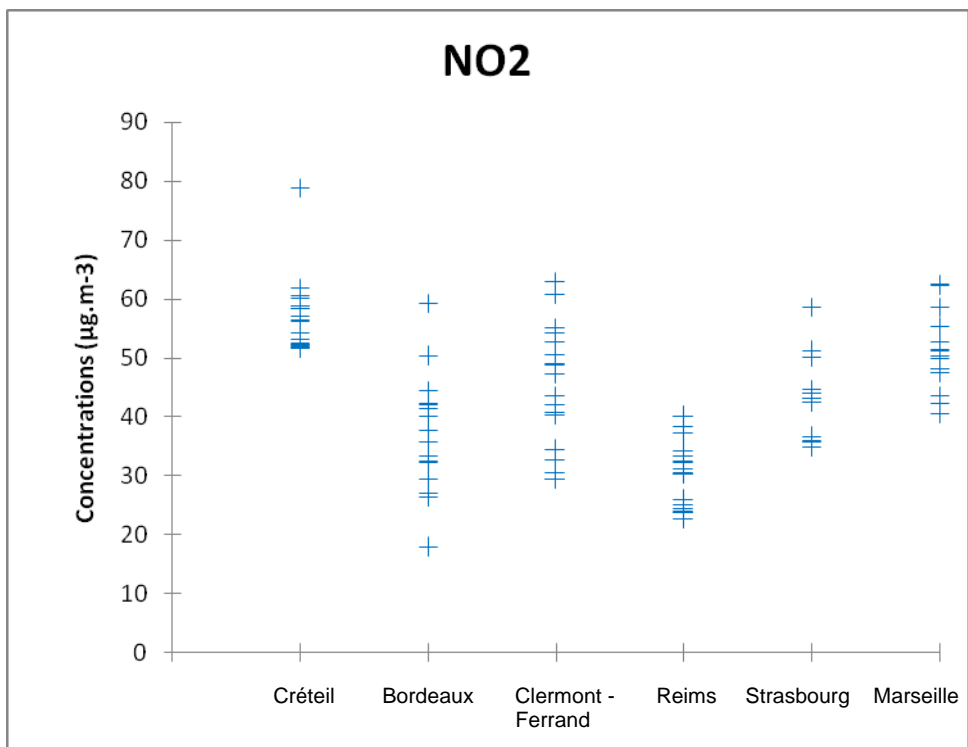
Odds ratios were calculated, per an increment for the interquartile range (1.1 µg.m⁻³ for benzene; 25.2 µg.m⁻³ for VOC; 5 µg.m⁻³ for SO₂; 10.5 µg.m⁻³ for PM₁₀; 18.5 µg.m⁻³ for NO₂; 52.1 µg.m⁻³ for NO_x; 199 µg.m⁻³ for CO), among the children residing at their current address for at least three years (N=4907).

* p<0.05; † p<0.01; § p<0.001.

Figure 1: Concentrations of air pollutants ($\mu\text{g}\cdot\text{m}^{-3}$) calculated by STREET 5 for each school according to the communities in the French Six Cities Study.







The concentration calculated at each school is indicated by a cross.
 108 schools were selected: 21 in Créteil, 16 in Bordeaux, 18 in Clermont-Ferrand, 21 in Reims, 15 in Strasbourg and 17 in Marseille.

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