

Manuscript ID thoraxjnl-2011-200391: "Poor air quality in classrooms related to current asthma and rhinitis in primary schoolchildren. The French 6 Cities Study."

Online data supplement

Detailed methods

Protocol

According to the protocol inspired from the second phase of the International Study of Asthma and Allergy in Childhood (ISAAC), a simple random sample of at least 10 schools had to be chosen from a complete sampling frame of all schools in a defined geographical area (the ISAAC centre). The exact number of schools had to be determined by the required sample size, i.e. 1500 children. The school years studied were those in which the majority of children were aged 10 years 0 months to 10 years 11 months at the start of the fieldwork, which corresponds to the classrooms of CM1 ("Cours Moyen 1") (attended in general by schoolchildren aged 9 years in average) and CM2 ("Cours Moyen 2") (10 years in average) in France. In each selected school, all the CM1 and CM2 classrooms were retained for the survey. In each selected classroom, all the children were invited to participate in the survey. The protocol has been presented elsewhere in detail. [7-8] The timetable of the school visits for air quality assessment and simultaneous medical examination of the children was randomly chosen. However, data collection was avoided during summer, end-of-the-term vacations and week-ends in order to reduce exposure misclassification. Teachers and school personnels were asked not to modify the activities.

Parents gave their written consent to the participation of their child in the survey and filled an enriched version of the questionnaire used in phase II of the International Study of Asthma and Allergies in Childhood (ISAAC). Children were invited to undergo a medical examination including: 1) skin prick tests (SPT) to common aeroallergens (*Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*, cat fur, *Alternaria tenuis*, *Blatta germanica*, mixed grass, *Betulaceae* pollens, cod, milk and peanut (Stallergènes laboratories, France) and positive and negative controls). SPT positivity was defined as a wheal at least 3 mm greater than that of the negative control for any of the allergens 15 minutes after pricking; and 2) exercise-induced bronchial asthma (EIA). EIA was defined using a peak flow (PF) according to the standardised protocol of the run test meter as follows: $PEF_{in} - PEF_{fin} / PEF_{in} \geq 10\%$ [9-11] Children were asked to stop antihistamines, ventolin (salbutamol, albuterol...) and corticosteroids 48 hours before the tests. However, most asthmatics did not stop their treatment as shown by information collected on the day of examination.

Statistical analysis

p-trend values in the figures presenting the associations between exposure to air pollutants in tertiles and health outcomes were assessed using GEE models.

Results

"Between" and "within" school variability of the measured indoor pollutants

The estimation of 'within' and 'between' school measured indoor pollutant variability was done using a linear mixed model for longitudinal data (Verbeke). The SAS MIXED procedure was employed for the purpose:

- The Restricted Maximum Likelihood (REML) method was used for estimating covariance parameters.
- The SUBJECT parameter was equal to the schools (nested within cities), representing the clusters in the data.

- A compound symmetry (or exchangeability) type of covariance matrix structure was considered.
- The statistical significance of the random-intercept was performed by a mixture of χ^2 (0:1) distribution, obtained by halving the P value corresponding to the -2Loglikelihood Ratio Statistic (LRT) difference between the model without and with random-intercept, akin to a unilateral P value (due to the fact, that the random-effect variance can have 'boundary problems' as suggested in the reference). As a precaution NOBOUND option was also used for a potential negative variance component, but it was not necessary finally. In this case, the random-intercepts were always very significant tallying with the Wald test statistic (obtained by COVTEST option).
- Degrees of freedom were estimated by Kenward-Roger method.

The estimated "between" and "within" school variability of the measured indoor pollutants is included in the table below where the "classrooms" variance (first row) is the "WITHIN" school variance whereas the "schools" variance (second row) is the "BETWEEN" school variance. Very heterogeneous variabilities according to the type of air pollutants that are consistent with pollutants' characteristics and geographical variations were observed.

Variance Parameter Estimates for the Measured Indoor Pollutants.

Variance (SE)	Pollutants				
	PM _{2.5}	NO ₂	Formaldehyde	Acetaldehyde	Acrolein
Classrooms	13.04 (0.94)***	27.13 (1.86)***	183.52 (12.47)***	17.00 (1.16)***	2.55 (0.19)***
Schools	36.88 (5.48)***	107.26 (15.54)***	58.96 (13.52)***	9.26 (1.77)***	3.08 (0.53)***

SE: standard error.

Two-sided P values: * $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$.

Reference

Verbeke G, Molenberghs G. Linear Mixed Models for Longitudinal Data, Springer-Verlag ed., NY, USA, 2000.