Increased asthma and respiratory symptoms in children exposed to petrochemical pollution

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Background: Epidemiologic studies show statistical associations between levels of air pollutants and respiratory outcomes.
Objective: We sought to determine the effects of exposure to petrochemical pollution on the respiratory health of children.
Methods: Children aged 6 to 12 years living close to the petrochemical plants in La Plata, Argentina (n = 282), were compared with those living in a region with exposure to heavy traffic (n = 270) or in 2 relatively nonpolluted areas (n = 639). Parents answered a validated questionnaire providing health and demographic data. A random sample (n = 181) had lung function measured. Particulate matter and outdoor and indoor volatile organic compound levels were measured during 4-week study periods and reported as overall means for each study area.
Results: Children living near the petrochemical plant had more asthma (24.8% vs 10.1% to 11.5%), more asthma exacerbations (6.7 vs 2.9-3.6 per year), more respiratory symptoms (current wheeze, dyspnea, nocturnal cough, and rhinitis), and lower lung function (>13% decrease in FEV_1 percent predicted) than those living in other regions. Length of residence in the area was a significant risk factor, but age, sex, body mass index, proximity to busy roads and other nonpetrochemical industries, length of breast-feeding, and socioeconomic and demographic characteristics of children or their families were not.
Conclusion: Exposure to particulate matter and volatile organic compounds arising from petrochemical plants but not from high traffic density was associated ith worse respiratory health in children. (J Allergy Clin Immunol 2009;123:632-8.)

Key words: *Air pollution, asthma, lung function testing, particulate matter, volatile organic compounds*

Abbreviations used
ETS: Environmental tobacco smoke
FEF_{25-75}: Forced expiratory flow over the middle 50% of the FVC
FVC: Forced vital capacity
PAH: Polyaromatic hydrocarbon
PM: Particulate matter
OR: Odds ratio
VOC: Volatile organic compound

The prevalence of asthma and other respiratory disorders in childhood has increased considerably over recent decades, and the influence of exposure to air pollutants has attracted considerable interest. Epidemiologic studies suggest that chronic exposure to traffic-related pollutants, photochemical pollutants, and particulate matter (PM) have adverse effects on lung growth and pulmonary function and increase respiratory morbidity and mortality in children,[1-7] especially in heavily polluted cities in developing countries.[8]

Most studies have concentrated on the health effects of outdoor air pollutants, especially PM and traffic-related pollutants.[1-8] Volatile organic compounds (VOCs) have been shown to increase the risk of asthma[9-11] and to be associated with higher levels of the inflammatory marker nitric oxide in the exhaled breath[12] of young children.

La Plata, Argentina, is located next to the national main oil refinery, with 6 associated petrochemical plants that produce diverse compounds, such as aromatics, aliphatic solvents, polypropylene, and petroleum coke.[13-16] The inner-city area is also subjected to heavy traffic. Previous studies have shown higher levels of PM (PM_{10}, $PM_{2.5}$, and $PM_{0.5}$), polyaromatic hydrocarbons (PAHs), and VOCs in the regions next to petrochemical plants than in other parts of the city.[13-16] In particular, the concentrations of hexane, cycloalkane, and aromatic compounds, such as benzene, toluene, and xylenes, were much higher in the industrial region.[15-17]

The aim of the present study was to investigate the effect of exposure to PM and VOCs on the respiratory health of children aged 6 to 12 years. Children living in an area close to the petrochemical plants were studied and compared with those living in a region with exposure to heavy traffic or in 2 relatively nonpolluted regions. We hypothesized that exposure to petrochemical pollutants would have more severe consequences on the respiratory health of children living near the petrochemical plants when compared with children living in other areas of the city.

METHODS

Study location

The study was conducted during 2005-2006 in La Plata, Argentina, a city of 702,449 inhabitants located next to Argentina's main oil refinery (total crude oil distillation capacity, 38,000 m^3/d). Six petrochemical plants in the region produce diverse compounds, such as aromatics (benzene, toluene, and

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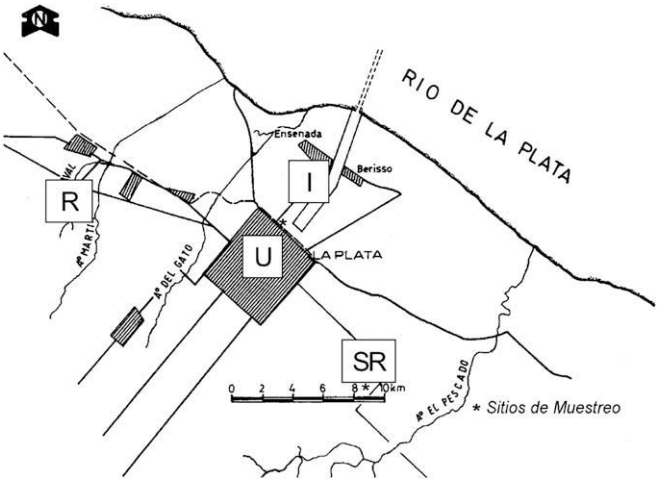

FIG 1. Study locations in La Plata, Argentina. The petrochemical industry (industrial *[I]*) is located to the northeast of the main city region (urban *[U]*). Two relatively nonpolluted areas, semirural *(SR)* and residential *(R)*, are also shown. The *shaded regions* show where municipal pollution-monitoring stations were located.

xylenes), aliphatic solvents (n-pentane, n-hexane, and n-heptane), polypropylene, polybutene, maleic anhydride, cyclohexane, methanol, methyl tertiary butyl ether, and petroleum coke. This industrial complex is located approximately 10 km north-northeast of the main urban sector of the city. Prevailing wind directions blow emissions from the refinery and the petrochemical complex across the urban area.[14-17] The inner city of La Plata is influenced by heavy traffic, with 301,448 vehicles registered in the region, 91% of them in La Plata city. In addition, diesel engines in the public transport system are significant sources of PM and PAHs. The region is characterized by a humid temperate climate. Prevailing winds blow emissions from the refinery and the petrochemical complex across the urban area.[18-20] Four specific areas were chosen for the study: "industrial," next to the petrochemical complex; "urban," an inner urban area with a heavy vehicular traffic; and 2 relatively nonpolluted areas, "semirural" and "residential" (Fig 1). Because there were socioeconomic differences between the 2 polluted regions (industrial and urban), 2 control regions (semirural and residential) were used. The living standards in the residential and urban regions were similar and higher than those in the industrial and semirural regions by using scales appropriate for Argentina (www.indec.mecon.ar; www.siempro.gov.au; and www.melnik.com.ar/espanol/arginfo/nse.htm).

Study participants

Children (n = 1212) of either sex aged 6 to 12 years living in one of the study regions were recruited. Children from industrial (n = 290), urban (n = 263), semirural (n = 303), and residential (n = 327) regions were included in the study. Families of children attending school in the study regions were contacted, and a preliminary survey was distributed. Participation in the study was voluntary; the proportion of students whose parents consented was 94%, 77%, 84.5%, and 97.7% from the industrial, urban, semirural, and residential regions, respectively. *A priori* exclusion criteria were the presence of a chronic disease other than asthma (eg, cystic fibrosis), bronchopulmonary dysplasia, cardiac disease, gastroesophageal reflux requiring treatment, or having received oral steroids for any reason within the past month; however, no child was excluded based on these criteria.

The Human Ethics Committee of La Plata Children's Hospital approved the study, and parents provided written consent for their child's participation.

Study procedures

Questionnaires. Health and demographic information was obtained from parents by using a questionnaire modified from the International Study on Asthma and Allergies in Children,[21] which was translated into Spanish and validated in a pilot study.[22] Additional data collected included children's medical histories, asthma severity and known triggers, allergic status, medical management, family structure and demographics, and potential indoor exposures. Asthma was defined as "doctor-diagnosed asthma" and according to the International Study on Asthma and Allergies in Children definition.[21]

Lung function testing. A randomly selected group of 181 children had lung function measured by means of standard spirometry.[23] Parents of 67% (815/1212) of the children consented to this part of the study. Children were then chosen randomly by the technician, who was blind to questionnaire data. This group included 52 (28.7%) children from industrial, 37 (20.4%) from urban, 63 (34.4%) from semirural, and 30 (16.4%) from residential regions. Lung function was measured in the afternoon (1–5 PM) according to American Thoracic Society guidelines. A portable spirometer (Datospir 120A; Sibelmed, Barcelona, Spain) coupled with computerized data acquisition software was used. The following variables were obtained from the best of 3 reproducible forced expiratory maneuvers: forced vital capacity (FVC), FEV_1, peak expiratory flow, forced expiratory flow over the middle 50% of the FVC (FEF_{25-75}), flow at 75% of expired volume, and FEV_1/FVC ratio. Spirometry was repeated after inhaling 200 μg of salbutamol, and the bronchodilator response (percentage change in FEV_1) was recorded.

TABLE I. VOCs measured

Alkanes	Cycloalkanes	Aromatic compounds
Hexane	Cyclohexane	Benzene
	Methylcyclohexane	Toluene
		m-Xylene
		p-Xylene
		o-Xylene

Air sampling and chemical analysis

PM. Sampling was conducted in 4-week periods during the winter months of 2005 and 2006 by using high-volume collectors consisting of a cascade impactor with a 10-μm inlet (Sierra; Wedding and Associates, Henderson, Nev), which enabled particles to be separated into 6 fractions according to their median aerodynamic diameters: fraction 1, 10 to 7.2 μm; fraction 2, 7.2 to 3 μm; fraction 3, 3 to 1.5 μm; fraction 4, 1.5 to 0.95 μm; fraction 5, 0.95 to 0.49 μm; and fraction 6, less than 0.49 μm. For the purposes of this study, PM_{10} incorporated all fractions, $PM_{2.5}$ included particles in fractions 3 to 6, and $PM_{0.5}$ referred to fraction 6. Particle concentrations were determined by using gravimetric methods. Sampling in all areas was undertaken at the same time. Data were available from 1 monitoring station per geographic region and are reported as the average daily concentration for the sample period.

VOCs. Sampling was conducted in 4-week periods during the winter months of 2005 and 2006 by using passive samplers (3M OVM 3500; 3M, St Pul, Minn) in schools and children's homes in representative areas of the 4 study regions. A sampling period of 4 weeks was used because integrative sampling provides a better estimate of human exposure than shorter periods. Eight compounds were selected for monitoring based on previous studies in this region (Table I).[15,17]

VOCs were desorbed from the charcoal pads of the passive samplers by using 1.5 mL of carbon disulfide with low benzene (Merck, Whitehouse Station, NJ) containing 1% methanol and analyzed by using a Varian gas chromatograph (Varian, Inc., Palo Alto, Calif) with a flame ionization detector and electron capture detectors equipped with a Zebron ZB-624 column (60 m column length, 0.32 mm ID, 1.0-μm film thickness). The oven temperature increased from 43°C to 200°C at a rate of 2.5°C · min^{-1}. The injector temperature was held at 250°C. The detection limits of the assays were between 0.18 and 0.41 $\mu g/m^3$.

Statistical analysis

Data were analyzed by using multivariate techniques with SPSS version 11.5 (SPSS, Inc, Chicago, Ill) and Statistica 7.0 (StatSoft, Inc, Tulsa, Okla)

TABLE II. Pollutant concentrations in the study regions

Pollutant concentration ($\mu g/m^3$)	Industrial		Urban		Semirural		Residential	
	Median	25th–75th Percentile	Median	25th–75th Percentile	Median	25th–75th Percentile	Median	25th–75th Percentile
PM_{10}	33.8*	18.9–67.5	26.9*	22.4–40.5	10.6	2.7–11.0	NA	NA
$PM_{2.5}$	15.4*	1.0–25.7	19.0*	1.38–18.5	6.1	0.1–4.9	NA	NA
$PM_{0.5}$	9.1*	8.6–25.7	14.2*	12.9–18.5	4.0	0.9–4.9	NA	NA
Outdoor VOCs								
Hexane	38.3*	33.7–39.4	15.1*	12.5–20.3	2.7	1.8–3.5	3.5	2.7–3.7
Cyclohexane	8.9*	7.9–9.3	1.9*	1.6–2.0	0.6	0.5–0.6	1.1	0.8–1.3
Methylcyclohexane	3.8*	3.3–5.2	1.3*	1.3–1.4	0.6	0.4–0.6	0.6	0.5–0.7
Benzene	19.3*	16.1–21.1	2.9	2.1–3.5	1.9	1.8–2.0	3.1	2.6–3.9
Toluene	19.1*	12.3–23.2	9.3*	7.7–9.6	3.8	3.4–4.3	5.4	3.8–7.0
m-Xylene	1.3	0.9–1.5	0.9	0.8–0.9	1.3	0.6–2.6	0.7	0.6–0.7
o- Xylene	1.5*	0.9–3.2	2.1*	1.3–2.7	0.5	0.4–0.7	0.2	0.1–0.2
p-Xylene	6.8*	2.1–16.8	6.5*	5.0–8.9	2.1	1.5–26	3.9	3.5–7.2
Total VOCs	102.1*	88.0–122.4	45.8*	39.8–46.4	13.6	10.6–16.5	25.3	20.7–25.5

NA, Particulate levels not available for residential area.
*Significantly higher than control regions ($P < .05$), Mann-Whitney *U* test.

software. Multiple linear and logistic regressions (where independent variables were quantitative) were used to analyze the lung function and questionnaire data. Likely confounders, including age, sex, environmental tobacco smoke (ETS), living close to busy roads (<50 m) or other nonpetrochemical industries, time of residence in the study area, home environment (eg, use of solid fuel for cooking and heating, presence of visible mold, and overcrowding [>3 per room]), length of exclusive breast-feeding, and family socioeconomic and demographic data were stepwise included in the models considering their significance. The resulting effects are reported as odds ratios (ORs) with CIs and were calculated either for the geographic regions or for the concentrations of specific VOCs. The latter show the increase in the chance for a disease with an increase in concentration by 1 $\mu g/m^3$.

A nonparametric method (Mann-Whitney *U* test) was used to compare the levels of pollution (PM fractions and VOCs). For the prevalence rates (π), we calculated the lower and upper confidence limits according to the following formula:

$$\pi_{1/u} = \pi \mp u_{a/2}\sqrt{\pi(1-\pi)/n} \mp 1/2n.$$

This formula takes account of the sample size (n) and assumes a binomial distribution of the cases. The latter fact is only approximately valid because some overdispersion is inevitable as a result of the heterogeneity of the subpopulations.[24]

A pooled analysis was conducted by using the χ^2 test comparing asthmatic with nonasthmatic subjects to further explore the relations between pollution exposure and respiratory outcomes. ANOVA was also used to examine the relationship between asthma and lung function.

RESULTS

Pollutant levels

The concentrations of PM_{10}, $PM_{2.5}$, and $PM_{0.5}$ were higher in the industrial and urban areas than in the semirural control area (Table II), with no differences between the 2 polluted regions (Table II). Concentrations of VOCs were also higher in both polluted regions than in the 2 relatively nonpolluted regions (Table II). The concentrations of hexane, cyclohexane, benzene, and toluene were particularly high in the industrial region. The total concentration of the VOCs analyzed was 4-fold higher in the industrial area and twice as high in the urban region than in the 2 relatively nonpolluted regions.

Demographics

There were no significant differences in the demographic characteristics of children recruited from the different geographic regions (Table III).

Effect of pollutant exposure on respiratory health

The higher levels of pollutants in the industrial region were associated with an increased prevalence of adverse respiratory health outcomes. Children living in the industrial region, the area exposed to petrochemical pollutants, had a substantially greater prevalence of asthma ($P < .001$), more asthma exacerbations ($P < .001$), and more respiratory symptoms ($P < .001$, Table IV). The increased risks for adverse respiratory outcomes for children living in the industrial region compared with those living in other areas were as follows: asthma (OR, 2.76; 95% CI, 1.96-3.89); asthma exacerbations (OR, 1.88; 95% CI, 1.25-1.83); wheezing (OR, 1.93; 95% CI, 1.39-2.67); chest tightness (OR, 1.77; 95% CI, 1.23-2.55); dyspnea (OR, 1.72; 95% CI, 1.19-2.48); nocturnal cough (OR, 1.76; 95% CI, 1.29-2.41); and rhinitis (OR, 1.87; 95% CI, 1.12-3.12). As a group, children living in the urban region reported more allergies (OR, 2.4; 95% CI, 1.1-5.1) and more eczema (OR, 1.4; 95% CI, 1.0-2.4) but not more respiratory symptoms than children living in the control regions.

Lung function was also lower in children living in the industrial region, with substantial and significant deficits seen in FVC ($P < .01$), FEV_1 ($P < .001$), FEV_1/FVC ratio ($P < .001$), and FEF_{25-75} ($P < .001$, Table IV). This deficit is shown for FEV_1 in Fig 2. Although the children from the industrial area had greater percentage changes in FEV_1 after bronchodilator, this did not reach statistical significance ($P = .051$).

Combining data from all geographic regions showed that children exposed to higher levels of pollutants had lower lung function. Inverse associations (Pearson correlations) were found between FEV_1, FEV_1/FVC ratio, and FEF_{25-75} and PM_{10} (-0.408, $P < .001$; -0.661, $P < .001$; and -0.498, $P < 0.001$, respectively), $PM_{2.5}$ (-0.414, $P < .001$; -0.672, $P < .001$; and -0.499, $P < .001$, respectively), and ultrafine particles (-0.396, $P < .001$; -0.639 $P < .001$; and -0.494, $P < .001$,

TABLE III. Demographic characteristics of the study cohort by geographic region

Characteristic	Industrial	Urban	Semirural	Residential
No. recruited	290	263	303	327
Age (y), mean (SD)	8.0 (1.8)	8 (1.4)	8 (1.6)	8 (1.5)
Sex (% male)	53	56	55	52
BMI, mean (SD)	18 (3)	19 (3)	17 (3)	18 (3)
Length of residence in region (y), mean (SD)	6 (2.5)	6 (3)	6 (2.6)	6 (2.4)
Exclusive breast-feeding (mo), mean (SD)	4.5 (2)	3.7 (2)	3.7 (2)	4 (2)
ETS exposure (%)				
Current	35.8	38.2	33.7	29.5
Pregnancy	14.5	19.3	15.8	18.4
First year	19.9	21.5	20.5	19.3
0-3 y	29.4	30.7	28.6	25.4
Family history (prevalence)				
Asthma (%), (SD)	8.9 (1.7)	6.5 (1.5)	9.6 (1.7)	8.5 (1.5)
Rhinitis (%), (SD)	6.2 (1.4)	12.1 (2.0)	3.6 (1.1)	2.1 (0.8)
Chronic bronchitis (%), (SD)	9.3 (1.7)	4.1 (1.2)	3.6 (1.1)	6.4 (1.4)

BMI, Body mass index.

TABLE IV. Prevalence of adverse respiratory outcomes for each geographic region (n = 181)

Respiratory outcome	Industrial	Urban	Semirural	Residential
Asthma (%)	24.8*	11.5	10.1	10.5
Asthma exacerbations†	6.7 (2.5)	3.6 (2.8)	2.9 (1.3)	3.1 (2.7)
Symptoms (%)				
Current wheeze	27.9*	15.6	13.9	13.5
Dyspnea	20.4*	12.2	11.8	11.4
Nocturnal cough	32.4*	19.7	18.9	13.7
Rhinitis	16.9*	13.7	11.2	9.9
Lung function‡				
FVC (% predicted)	107.4 (15.7)	112.7 (18.4)	112.1 (14.2)	114.1 (20.1)
FEV_1 (% predicted)	91.4 (12.5)*	105.9 (15.6)	104.4 (12.0)	107.8 (14.7)
FEV_1/FVC (%)	80.4 (7.6)*	93.1 (3.8)	92.2 (4.2)	91.6 (3.0)
FEF_{25-75} (L/s; % predicted)	96.8 (26.8)*	117.8 (16.3)	122.0 (17.0)	137.9 (28.4)
BDR (%)	7.9 (9.8)	4.5 (5.2)	5.7 (7.6)	3.0 (4.1)

BDR, Bronchodilator response; change in FEV_1 (percentage) after albuterol inhalation.
*Significantly different from control regions ($P < .001$).
†Asthma exacerbations are mean numbers (SDs) of exacerbations in the previous 12 months per child.
‡Lung function data are presented as group means (SDs).

respectively). The influence of living near the industrial complex, total VOCs, benzene, and hexane on lung function are shown in Table V. Living in proximity to a busy road had no detectable effect on lung function (data not shown). On grouped data, the time of residence was associated with lower lung function, with FEF_{25-75} decreasing 1.85% per year of residence (Pearson correlation: −0.271, $P < .01$). *Post-hoc* analyses showed that this effect was significant for children living in the industrial region when compared with those living in the relatively nonpolluted regions.

The influence of exposure to air pollution on adverse respiratory outcomes was not affected by age, sex, body mass index, the proximity to busy roads and other nonpetrochemical industries and garbage, the presence of pets or cockroaches in the houses, length of exclusive breast-feeding, family history of asthma or allergies, and socioeconomic and demographic characteristics of the children or their families. Exposure to ETS was not an independent predictor of lung function, and no interactions between exposure to pollutants and ETS were found.

DISCUSSION

The data from the present study demonstrate that living in an area of the city of La Plata, Argentina with higher levels of PM and VOCs in the ambient environment was associated with worse respiratory health in children aged 6 to 12 years. This effect was predominantly seen in children living in an industrial region exposed to pollutants from the main petrochemical complex. Children living in this area had a higher prevalence of asthma and asthma-like symptoms and a greater number of acute exacerbations of asthma than children living in less polluted regions of the city. The data also show evidence of airway obstruction that is related to both pollutant levels and the length of time the children have lived in the polluted area.

Before considering the implications of the results presented here, several technical aspects of the study need to be acknowledged. The pollution data were analyzed as the daily average of a 7-day period rather than as peak levels or the number of days exceeding a particular level. In addition, no lags between exposure and health outcome were included. This approach

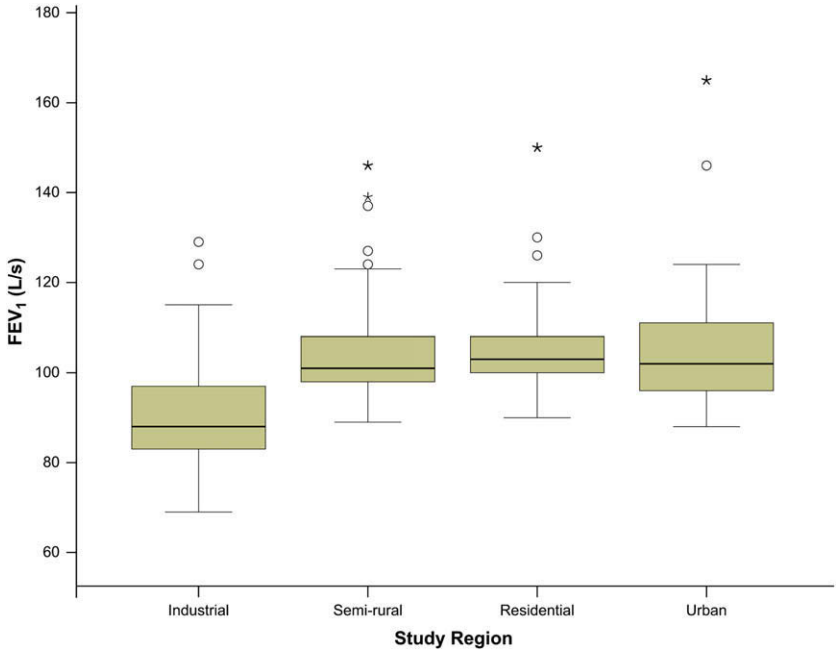

FIG 2. Lung function, expressed as FEV_1 (percent predicted) in children living in the different geographic regions. *Box plots* show the median and interquartile ranges, with outliers shown as *symbols*.

TABLE V. Effect of VOC concentration and living environment on parameters of lung function

Lung function		Living near industrial complex (<1 km)	Total VOC ($\mu g/m^3$)	Benzene ($\mu g/m^3$)	Hexane ($\mu g/m^3$)
	Lowest quartile*	OR‡ (95% CI)	OR§ (95% CI)	OR (95% CI)	OR (95% CI)
FEV_1 (% predicted)	<92%	32.2 (10.6–98.01)	1.03 (1.02-10.5)	1.19 (1.17–3.10)	1.09 (1.06–1.13)
FVC (% predicted)	<99%	3.7 (1.4–9.2)	1.01 (1.00-1.02)	1.07 (1.02–1.23)	1.03 (1.01–1.06)
FEV_1/FVC (%)	<86%	74.4 (19.6–281)	1.05 (1.03-1.07)	1.26 (1.17–1.37)	1.13 (1.08–1.18)
FEF_{25-75} (% predicted)	<101%	46.8 (13.4–163)	1.04 (1.03-1.06)	1.22 (1.14-1.31)	1.11 (1.07–1.15)
	Highest quartile†				
BDR (% change in FEV_1)	>9%	3.94 (1.5–10.2)	ND	1.07 (1.02-1.13)	ND

ORs (95% CIs) for having lung function in the lowest quartile and bronchodilator responsiveness in the highest quartile are shown.
ND, Not detectable.
*Upper limit of lowest quartile of lung function.
†Lower limit of higher quartile.
‡Multivariate analysis (ORs and 95% CIs) adjusted for sex, age, ETS, and familiar diseases (bronchitis and asthma).
§Increase in risk per microgram per cubic meter of total VOCs, benzene, or hexane.

assesses the long-term effects of cumulative exposure to pollutants rather than the acute effects of short-term exposure. This approach is consistent with that of the World Health Organization[25] and the US Environmental Protection Agency.[26] We primarily assessed long-term health consequences, including asthma, number of asthma exacerbations in the past 12 months, and respiratory symptoms occurring in the past 12 months, based on questionnaire and lung function results. The fact that the time the child resided in the polluted area was a significant factor in producing the adverse health outcome demonstrates that our use of mean daily average pollution levels is valid for the health outcomes we have studied. In addition, we have conducted a cross-sectional study and can thus only report statistical associations between pollutant exposures and health outcomes.

The analyses of the adverse effects of VOCs on respiratory health have been conducted by using total outdoor VOC levels, as used in previous studies.[15,17,27] Children in the present study were exposed to a complex mixture of VOCs, as is generally the case. Individual pollutants are frequently measured and studied in isolation; however, exposure to individual pollutants in isolation is uncommon, and exposures to mixtures are more usual. The individual components of pollutant mixtures might have additive, synergistic, or antagonistic effects, and interpreting them in isolation is difficult. In the present study we have examined the effects of the individual VOC and found that although there were significant effects of individual VOCs on lung function, using the total level of outdoor VOCs provided the most comprehensive description of the effects of exposure to VOCs on lung function. In addition, the levels of many of the individual VOCs were highly

correlated, reducing our ability to assess the health effects of individual compounds.

In the present study we were not able to measure the lung function of all children. The sample we did measure was chosen randomly, and the lung function technicians were blind to the region in which the children lived. The sample measuring lung function was representative of the total study population, with no significant differences in any of the demographic variables measured. Thus we are confident that lung function data presented here can be generalized to all children living in the study region.

The data in the present study are consistent with those from other studies of the health effects of ambient pollution in Latin America, where pollutant levels are often higher than in Western communities. Exposure to higher levels of PM have been shown to be associated with an increased rate of hospital admission for respiratory and cardiovascular diseases, especially acute asthma, in children and adults in Sao Paulo, Brazil.[18] Mexican children aged 5 to 17 years who were exposed to higher levels of pollutants, including PM_{10}, O_3, NO_2, SO_2, and CO, had abnormal chest x-ray findings and lower lung function when compared with children living in less polluted regions.[28] Similar data have also been published from Europe[29] and North America,[30] demonstrating that these problems are not restricted to children living in developing countries, although the magnitude of the effects might be greater.

Although epidemiologic studies, including the present study, have demonstrated adverse effects on respiratory health from exposure to pollutants, including PM, O_3, and VOCs, the mechanisms by which these effects occur are not clear. PM enters the lungs and is taken up by resident macrophages. Kulkarni et al[3] demonstrated a direct relationship between the density of PM in alveolar macrophages in induced sputum from children and lower lung function. They reported that for each increase of 1 μm^2 in macrophage carbon content, decreases in FVC of 13%, FEV_1 of 17%, and FEF_{25-75} of 34.7%, when expressed as a percentage of predicted lung function, were seen. Although these data are not directly comparable with those shown in the present study, they are consistent with the lower lung function seen in children living in the region exposed to petrochemical pollution in the present study.

Data from the present study suggest that it is not simply a matter of the level of particulate exposure that is important but that the source of the particles might also be important. Children living in the inner-city area were exposed to similar levels of particulates as those living in the industrial area close to the petrochemical plant; however, the source of the particles was likely different. In the urban region the source of PM was probably the heavy traffic density, whereas in the industrial region the petrochemical plant was probably responsible. Lung function in children living in the urban region was not different from that seen in those living in the relatively nonpolluted areas (semirural and residential regions). PM in the air consists of a carbon core with various compounds adsorbed onto the surface. Although we were not able to determine the characteristics of the compounds adsorbed onto the surface of the particles in the present study, it is reasonable to expect that these might be different in particles originating from petrochemical refineries and from traffic-related sources. We have previously shown that higher levels of PAHs were associated with particles in the industrial region than in the urban or control areas.[16] Whether the carbonaceous core or the adsorbed chemicals are primarily responsible for the respiratory consequences of particulate expose is not known; however, it is likely that both contribute.

Adverse health effects of exposure to VOCs have been previously documented in children, although again the mechanism or mechanisms involved is not clear. Exposure to the VOC formaldehyde in indoor air was associated with increased levels of nitric oxide in the exhaled breath of healthy children with no respiratory disease.[12] In studies conducted in Perth, Australia, a city considered to have relatively clean air, young children living in homes with higher levels of formaldehyde were more likely to demonstrate allergic sensitization to aeroallergens and to have asthma,[10,11] with the risk of asthma increasing by 3% for every 10 $\mu g/m^3$ increase in formaldehyde in the indoor air.[10] Previous studies conducted in La Plata have shown that the levels of VOCs in both indoor and outdoor air were higher in the industrial region.[15,17]

In the present study children living in areas with higher levels of PM and VOCs had lower lung function, a higher prevalence of asthma, more asthma exacerbations, and more respiratory symptoms. Misclassification of asthma is always a concern in epidemiologic studies; however, we do not believe that misclassification can explain the increase in asthma seen in the industrial region. The proportion of children with asthma and atopy in the present study was similar to those previously reported in Argentina.[22] In addition, the length of residence in the more polluted region was a significant determinant of the adverse respiratory consequences. Although a cross-sectional study cannot establish a causal relationship between pollution exposure and increased asthma prevalence, our data are consistent with this notion.

In summary, the data from the present study show that living in areas with higher levels of pollutants, both PM and VOCs, was associated with an increased prevalence of asthma, more asthma exacerbations, more respiratory symptoms, and lower lung function in Argentinean children. These effects were primarily seen in children living in an area subject to pollution from petrochemical plants and suggest that the source of the pollution might be an important determinant of the adverse consequences on respiratory health.

Clinical implications: Clinicians might need to take into account the source of air pollution when considering potential health effects in children.

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