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Effect of air pollution on lung function in schoolchildren in Rio de Janeiro, Brazil

ABSTRACT

OBJECTIVE: To assess the association between daily exposure to air pollution and lung function in school children.

METHODS: Panel study with a random sample of 118 students (between 6 and 15 years of age), enrolled in a public school of the city of Rio de Janeiro, state of Rio de Janeiro, and living within 2 km of the study site. Data on students' characteristics were obtained with a questionnaire, including the International Study of Asthma and Allergies in Childhood – ISAAC. Daily peak expiratory flow measurements were taken to measure lung function. Daily data on PM10, SO_2, O_3, NO_2 and CO levels, temperature and humidity were provided by a portable monitor. Repeated measurements of lung function were associated with pollutant levels with a multilevel model adjusted for time trend, temperature, air humidity, exposure to smoking at home, presence of asthma, height, sex, weight and age of children.

RESULTS: Mean peak expiratory flow was 243.5 l/m (sd=58.9). The lowest mean peak expiratory flow was 124 l/m, and the highest, 450 l/m. For the 10 µg/m³ increase in PM10, there was a 0.34 l/min decrease in mean peak flow on the third day. For the 10 µg/m³ increase in NO_2, there was a decrease between 0.23 l/min and 0.28 l/min in mean peak flow after exposure. CO and SO_2 effects on students' peak flow were not statistically significant. O_3 showed a protective result: an increase in 10 µg/m³ of O_3 would be associated, after a day of exposure, with a 0.2 l/min increase in mean lung function.

CONCLUSIONS: Even within acceptable levels most of the time, air pollution, especially PM10 and NO_2, was associated with a decrease in lung function in children living in the city of Rio de Janeiro.

DESCRIPTORS: Air Pollution, adverse effects. Child. Respiratory Function Tests. Inhalation Exposure. Respiratory Tract Diseases, prevention & control.

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INTRODUCTION

Harmful effects of air pollution on human health have been observed not only in the mortality in general and due to respiratory and cardiovascular diseases, but also in the morbidity, including increases in respiratory symptoms and decreases in lung function.[5]

In Brazil, time-series studies have assessed the impact of pollutants on population health.[8,17,18] A study performed in the two largest Brazilian cities, Rio de Janeiro and São Paulo,[8] found that air pollution was associated with both respiratory and cardiovascular health. The number of hospitalizations due to respiratory diseases

in children rose as a result of increases in pollution: 1.8% in Rio de Janeiro and 6.7% in São Paulo for $10\mu g/m^3$ increases in PM10 (particulate material with up to 10 micrometers in diameter); yet in São Paulo, 6.7% for $10\mu g/m^3$ increases in SO_2 (sulfur dioxide) and 1.7% for 1ppm increases in CO (carbon monoxide). Air pollution was also associated with prevalence of asthma in children, in a study performed in the cities of Duque de Caxias and Seropédica, state of Rio de Janeiro.[15]

Among international studies, one investigation in rural Holland found a reduction in lung function during two weeks after a pollution episode, when SO_2 and particulate material levels rose, affecting 1,000 children aged between six and 12 years.[2] In Austria, 975 children were followed for three years, when a reduction in lung function, associated with an increase in PM10, SO_2, NO_2 (nitrogen dioxide) and O_3 (ozone) levels, was observed.[11] These studies indicate that the impact of air pollution on asthmatic children, expressed in school absenteeism and higher number of hospitalizations, seems to be more serious among those with lower socioeconomic level.[9]

Time-series studies have been employed to support arguments aimed at reducing exposure limits or showing health impacts with pollution levels well below the limits recommended by the Resolution Nº 3/90 of the *Conselho Nacional do Meio Ambiente – CONAMA* (National Environmental Council).[a]

Participants in the panel studies have their lung function assessed with a daily measurement of peak expiratory flow, asthma episodes and number of nebulizations. These studies are frequently performed to estimate acute effects of air pollution on susceptible populations, such as children[1] and asthmatic adults.[25]

Exposure to air pollution can be measured individually with portable personal monitors or by a station located near the study site. In the latter case, it is assumed that individuals live in the same location where air monitoring is performed. Thus, situations in which susceptible population samples remain in the same place for relatively long periods of time are used. In this manner, both exposure to air pollution and respiratory or cardiac symptoms, or yet lung function indicators, can be more accurately assessed.[3]

This study aimed to investigate the association between daily exposure to air pollution and lung function in schoolchildren.

METHODS

This study was performed in the Complexo de Manguinhos, located in the city of Rio de Janeiro, Southeastern Brazil, in 2004. This area has some fixed and mobile sources with high potential for air pollution, among which is an avenue with intense flow of heavy vehicles (Avenida Brasil), Manguinhos refinery, Caju garbage and transferring station, in addition to several other small factories. A sample of 120 children from one public school was selected, of which ten students from 12 classes were randomly chosen. These children, aged between six and 15 years, were considered to belong to low-income families and living within 2 km of the study site. A panel study was performed, whose main characteristic is its longitudinal dimension, with daily measurements of exposure to pollutants and peak expiratory flow in children during three months. Children were submitted to daily tests for six weeks in a row, in May, June, September and October of 2004. These were performed in the morning, between 9:00am and 12:00pm, from Mondays to Fridays.

Information on students was obtained with the application of a questionnaire, weight and height measurements and peak expiratory flow tests. Questionnaire was answered by those responsible for the children, and included eight questions from the International Study of Asthma and Allergies in Childhood (ISAAC) protocol, used to assess the severity and diagnosis of asthma.[24] Starting with the standardization of the research instruments (written questionnaire), they were validated by a pilot study, in several countries, and by Solé et al,[21] in Brazil, confirming its applicability and reproducibility. After this phase, ISAAC began to be performed in several parts of the world and it has been validated, until now, for the 6-to-7-year and 13-to-14-year age groups.

The test was performed under technical supervision and followed by a pediatrician and a pneumologist. A portable Mini-Write Peak Flow Meter® (Clement Clare, London, UK) was employed. Children were instructed to breathe in deeply, place the peak flow meter on their mouth and then blow quickly and strongly. They would blow three times, values would then be noted down, and the highest value would be selected for analysis.

Lung function in children was assessed with a peak flow test. This test aims to measure the maximum expiratory flow, which represents the highest peak flow value found after forced expiration, measured in liters per minute.

Information on air quality was obtained with a mobile pollutant monitoring unit from the Rio de Janeiro City Department of Environment, at the study site. Data on PM10, SO_2, O_3, NO_2 and CO were used as daily air pollution indicators for children under the same exposure conditions. Meteorological conditions were

obtained with measuring devices located at the Galeão Airport. Minimum, mean and maximum temperatures and relative air humidity were used.

Considering the structure of a panel study or repeated measurements, a time series of about 120 peak expiratory flow observations was associated with each child.

The statistical analysis approach consisted in exploring the data's natural hierarchy. Repeated lung function measurements were analyzed with a Gaussian multilevel model, where the first and second level units were the days with pulmonary assessments and the children, respectively. Main exposure variables were the daily levels of PM10, SO_2, O_3, NO_2 and CO pollutants. Daily meteorological conditions and child individual characteristics, such as weight, height, sex, age, presence of asthma, and exposure to smoking, were considered as confounding variables. The variable "air pollution exposure" and the meteorological factors were designated to first level units, whereas child individual characteristics were considered as second level variables.

The mean time trajectory of peak flow measurements was adjusted using a third-degree polynomial curve (parametric spline), which admitted that each child had their own individual trajectory adjusted (random effects in the polynomial curve parameters). This strategy was employed so that modeling of the observed child lung function levels took into consideration child growth during the study period, as well as the learning of measurement device use.

It was assumed that both the exposure to pollution and meteorological conditions could have had lagged effects on lung function trajectories. Thus, indicators were created from simple lags and cumulative indices (moving averages) of the same day and previous days for pollutants and meteorological factors. Part of the analysis aimed to determine which meteorological factor indicators, among all those available, best fit the data. Using the daily measured median time series of model residues that considered adjustment by trend (parametric spline), dose-response graphical models (daily residue series as previously described versus meteorological indicator series) and significance and/or goodness-of-fit tests of models, based on inclusion of indicators, were used to select temperature and humidity indicators. When there were doubts about the most suitable indicator, the final choice was made according to the Akaike's information criterion (AIC).

The dose-response pattern observed between each meteorological indicator, selected in the previous step, and lung function, was adjusted in a way similar to that previously described for the time trajectory (parametric), admitting, if necessary, that children could have their own dose-response curves adjusted (random effects).

With this approach, the absence of observations on certain days (eventual absence of children in school) does not compromise the estimation process of model parameters. However, due to the data's temporal nature, self-correlation patterns were adequately adjusted. There are different procedures to estimate self-correlation and also to diagnose adjusted models, in terms of the presence of self-correlation residues. Some of these procedures were applied to guarantee the correct identification and modeling of self-correlation and the pattern of partial self-correlation function of median daily series and residue averages from the model adjusted by trend, temperature and humidity was analyzed.

The effects of pollution on daily variations in the students' peak expiratory flow trajectory were estimated after controlling for factors associated to both their lung function and pollution levels. The base model consisted of these confounding factors, which included the time trend, temperature, relative air humidity and the following students' characteristics: age, height, smoking in the family and asthma. This base model was diagnosed according to the presence of outliers, normality, and correct specification, among other things. When the model was considered adequate, it was used in the following phases to estimate effects of interest.

After determining the base model, the effect of air pollution on lung function could be estimated for each pollutant, and each lag was incorporated into the basic model, one at a time. The effects of pollutants on lung function levels were estimated both on average and individually (random effects).

This study was approved by the Research Ethics Committee of the Universidade Estadual do Rio de Janeiro. Consent from parents and teachers was obtained to adjust the project to the school's educational guidance norms.

RESULTS

A total of 118 children were assessed (two children were excluded from the study, due to their change of schools) with mean age of 9.14 years (sd=1.84), mean height of 1.36 meters (sd=0.12) and mean weight of 32 kg (sd=10.7). Half of the students were female. Out of the 118 children, 18.4% were asthmatic, and 49.1% lived in a home with smokers.

Mean peak expiratory flow was 243.5 l/min (sd=58.9). The lowest mean peak expiratory flow was 124 l/min and the highest was 450 l/min. On average, students had peak flow measured for 78 days, varying from nine to 122 days. Random missing values were assumed on the days students were absent from school and discarded from the analysis. This procedure considered students' absences as random missing data, assuming these absences were not caused by the association between air pollution and health. In the

case of students changing schools during their period of study, this change of schools was also considered not to be associated with air pollution levels.

Daily mean levels of air pollutants in the Complexo de Manguinhos, during the study period, surpassed the maximum limits established by the *CONAMA* resolution Nº 003/1990 (horizontal line in the graphs) for PM10 and O_3, and did not surpass these limits for CO, NO_2 and SO_2, as observed on Table 1 and Figure 1.

Data on pollutants were missing on some days, especially for SO_2. For PM10, the mean in the period was 84.7 µg/m³ (sd=29.5) and the highest mean concentration on one day was 199 µg/m³. CO varied between 0.1 and 3 ppm, whereas NO_2 varied between 35 and 216 µg/m³.

Average temperature was 26ºC (sd=3.1) and relative air humidity varied between 50% and 96%, with a mean of 73.6% (sd=9.2).

PM10 was associated with a decrease in students' peak expiratory flow. Increases of 10 µg/m³ in PM10 on a certain day caused a decrease in peak flow, varying between 0.32 l/min and 0.52 l/min, depending on the lag. An increase of 10 µg/m³ in PM10, for example, led to a 0.34 l/min decrease in mean lung function in children, three days later (Table 2 and Figure 2).

The rise in PM10 levels corresponding to the difference between the group of 10% most polluted days (90 percentile of PM10 distribution) and the group of 10% least polluted days (10 percentile of PM10 distribution) was associated with a decrease of 2.42 l/min in mean peak expiratory flow. This value represented a reduction of about 1% in children's mean lung function at a certain moment (Table 2).

CO and SO_2 effects on students' peak flow were not statistically significant. There was also a trend towards a decrease in students' peak expiratory flow when CO and SO_2 levels rose. SO_2 effects must be interpreted with caution, due to the great amount of missing data for this pollutant in the study period (Table 2 and Figure 2).

O_3 showed a significant protective effect; a 10 µg/m³ increase in O_3 was associated with a 0.2 l/min increase in mean peak expiratory flow, one day later. In contrast, considering the three-day lag, there was a reduction in mean peak expiratory flow, though not significant (Table 2 and Figure 3).

NO_2 was significantly associated with a decrease in students' peak expiratory flow. Increases of 10 µg/m³ in NO_2, on a certain day were associated with a decrease from 0.23 l/min to 0.28 l/min in mean lung function, two and three days later, respectively. There was also an increase in local levels of NO_2 corresponding to the difference between the least polluted day of the 10% most polluted days (90 percentile of NO_2 distribution) and the most polluted day of the 10% least polluted days (10 percentile of NO_2 distribution) associated with a reduction of 3.66 l/min in mean peak expiratory flow. This value represented a decrease of about 1.5% in students' lung function. In this case, the mean peak expiratory flow would have dropped about 0.22 l/min for a 10 µg/m³ increase in the moving average levels of three days of NO_2 (Table 2 and Figure 2).

DISCUSSION

Air pollution was associated with a reduction in students' lung function in the short term. Specific increases in PM10 and NO_2 levels were associated with decreases in lung function. In contrast, CO, SO_2 e O_3 levels were not associated with reductions in students' lung function.

Similar effects were obtained in panel studies from other regions.[22] A systematic review study with children to investigate air pollution effects concluded that, according to a classic meta-analysis model, children's peak flow levels would decrease 0.012 l/min (95% CI

Table 1. Distribution of pollutants and meteorological variables. City of Rio de Janeiro, Southeast Brazil 2004.

Variable	n	% missing	mean	sd	min	p10	p50	p90	max
Air pollutant									
PM10 (µg/m³)	210	2.33	84.68	29.47	41.0	53.0	78.5	123.1	199.0
CO (ppm)	186	13.49	0.97	0.63	0.1	0.3	0.8	1.8	3.0
SO₂ (µg/m³)	104	51.63	18.59	17.89	0.0	5.0	13.5	40.7	96.0
O₃ (µg/m³)	187	13.02	81.08	37.67	12.0	35.6	79.4	129.3	192.0
NO₂ (µg/m³)	171	20.47	92.50	35.30	35.0	58.0	86.0	140.0	216.0
Meteorological characteristic									
Minimum temperature (ºC)	215	0.00	21.68	2.39	14.4	18.7	21.6	25.1	27.1
Average temperature (ºC)	215	0.00	25.96	3.11	19.5	21.7	25.9	30.1	33.6
Maximum temperature (ºC)	215	0.00	31.59	4.65	21.4	25.0	31.6	37.8	43.0
Relative air humidity (%)	215	0.00	73.57	9.18	50.0	61.0	74.0	84.0	96.0
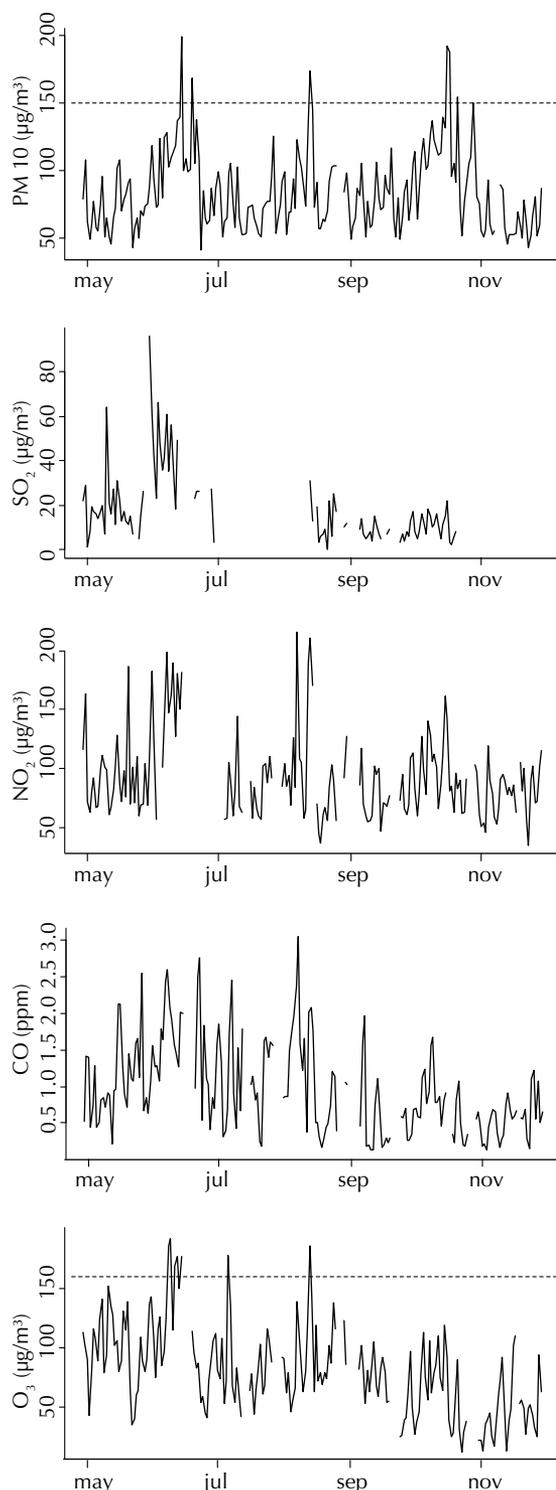
Figure 1. Distribution of pollution by PM 10, CO, SO$_2$, O$_3$ and NO$_2$ in the period studied. Rio de Janeiro, Southeast Brazil, 2004.

−0.017; −0.008)[22] on average for a 10 μg/m³ increase in PM10 levels. When considering a random coefficient model, the mean effect was −0.033 l/min (95% CI

−0.047; −0.019), very similar to that observed in this panel study, −0.034 l/min (95% CI −0.053; −0.012), for the same PM10 increase and a two-day lag.

In 2001, a study with children aged between seven and nine years, in the city of São Paulo, Southeast Brazil, observed associations with several pollutants.[4] Even though no pollutants could be singled out as the main cause of the harmful effects on child health, for an interquartile variation in PM10 concentration, there was a 1.05% reduction in peak expiratory flow, a result comparable to that found in this study. Other international studies have shown a correlation between the 10 μg/m³ increase in PM10 and the reduction of more than 10% in peak flow for the same day.[14,15,16]

Nitrogen dioxide (NO$_2$) is a strong respiratory irritant produced by different fixed and moving pollutant sources. In this study, it was associated with reductions in students' lung function. This result is corroborated by other panel studies in children with distinct outcomes, such as cough and respiratory symptoms.[12] In contrast, among children younger than 18 months of age, this association between exposure to NO$_2$ and respiratory problems was not observed.[19] Different results show that other studies need to assess the impact of NO$_2$ on child lung function.

Carbon monoxide (CO), sulfur dioxide (SO$_2$) and ozone (O$_3$) were not associated with harmful effects on child lung function in this study. However, peak expiratory flow decreasing trends associated with increases in levels of pollutants, such as CO and SO$_2$, were identified.[13] Studies on CO have shown its impact, correlated with the increase in adult arterial pressure[20] and child symptoms.[10]

Contrary to what was expected, the increase in ozone levels was associated with an increase in child lung function. Absenteeism may partly explain this result, due to the reduction in mean lung function on the second and third days after exposure, although not significant. In other words, the hypothesis is that more sensitive children are absent on the first day after exposure, returning on the following days. Further analysis using a logistic regression model for absenteeism related to pollutants levels may help understand these findings.

Results of this study diverge from those of some studies,[8] and agree with others.[6] Ozone was associated with a reduction in lung function in Swiss children after physical exercise and in those who remained outdoors for a longer time.[7]

Conflicting information about O$_3$ could be related to the methods used in different studies, the low ozone levels, or even the negative correlation between ozone and other pollutants, such as PM10 and NO$_2$.

Table 2. Estimated reductions in child peak expiratory flow (in l/min) for increases in pollutants***** and increases according to least and most polluted days******. Rio de Janeiro, Southeast Brazil, 2004.

| Pollutant	coef	(95% CI)		coef(10-90)	(95% CI)		p-value
PM10 (µg/m³)							
1-day lag	-0.11	-0.319;	0.106	-0.74	-2.234;	0.745	0.327
2-day lag	-0.32	-0.526;	- 0.120	-2.26	-3.685;	- 0.838	0.002
3-day lag	-0.35	-0.555;	- 0.136	-2.42	-3.889;	- 0.954	0.001
2-day mean	-0.34	-0.605;	- 0.078	-2.40	-4.242;	- 0.549	0.011
3-day mean	-0.52	-0.824;	- 0.211	-3.63	-5.776;	- 1.478	0.001
CO (ppm)							
1-day lag	-0.37	-1.316;	0.585	-0.58	-2.085;	0.927	0.451
2-day lag	-0.82	-1.702;	0.070	-1.29	-2.698;	0.110	0.071
3-day lag	-0.48	-1.483;	0.515	-0.77	-2.351;	0.816	0.342
2-day mean	-0.65	-1.838;	0.545	-1.02	-2.913;	0.863	0.287
3-day mean	-0.87	-2.383;	0.640	-1.38	-3.777;	1.015	0.259
SO$_2$ (µg/m³)							
1-day lag	-0.28	-0.942;	0.380	-1.00	-3.362;	1.355	0.404
2-day lag	-0.38	-0.986;	0.235	-1.34	-3.519;	0.841	0.229
3-day lag	0.13	-0.427;	0.688	0.47	-1.523;	2.456	0.646
2-day mean	-0.69	-1.439;	0.066	-2.45	-5.138;	0.236	0.074
3-day mean	-0.56	-1.293;	0.175	-2.00	-4.616;	0.625	0.136
O$_3$ (µg/m³)							
1-day lag	0.21	0.016;	0.395	1.92	0.145;	3.695	0.034
2-day lag	-0.11	-0.273;	0.049	-1.05	-2.554;	0.460	0.173
3-day lag	-0.16	-0.330;	0.006	-1.51	-3.088;	0.059	0.059
2-day mean	0.02	-0.186;	0.233	0.22	-1.738;	2.183	0.824
3-day mean	-0.08	-0.314;	0.159	-0.73	-2.941;	1.487	0.520
NO$_2$ (µg/m³)							
1-day lag	0.01	-0.153;	0.165	0.05	-1.251;	1.353	0.939
2-day lag	-0.28	-0.447;	- 0.118	-2.31	-3.663;	- 0.966	0.001
3-day lag	-0.23	-0.400;	- 0.065	-1.91	-3.282;	- 0.531	0.007
2-day mean	-0.16	-0.357;	0.037	-1.31	-2.926;	0.305	0.112
3-day mean	-0.22	-0.444;	0.001	-1.82	-3.641;	0.007	0.051

* Increase in 10 units for all pollutants, except for CO: 1 unit.
** Corresponding to the difference between the least polluted day of the 10% most polluted days and the most polluted day of the 10% least polluted days.

Lack of data when measuring pollutants is one of the limitations of this study. In contrast, the following are among the advantages of this study: daily follow-up of children, daily monitoring of exposure to pollution near the place of residence and study, and use of multidisciplinary team with the collaboration of municipal, state and federal institutions.

Another advantage was the use of a multilevel model and adjustment for confounding variables, enabling the estimation of pollution effects on lung function. Several statistical models can be employed to analyze repeated measurements similar to the ones found in this study, which used a multilevel model with two hierarchical levels. The first level has each student's

peak expiratory flow repeated measures (outcome), the air pollutants (main exposures) and time-related confounding factors (time and meteorological indicators). Growth experienced by each child in the study period influences their lung function. However, due to age and genetic factors, it could be hypothesized that each child has their own growth curve. Thus, the growth pattern was specifically modeled for each child, using random effect models in the lung function time trajectory. The second hierarchical level has the students' characteristics that can either explain or change the association between outcome and main exposures, such as age, height, weight, presence of respiratory disease (asthma, for example) and passive smoking.
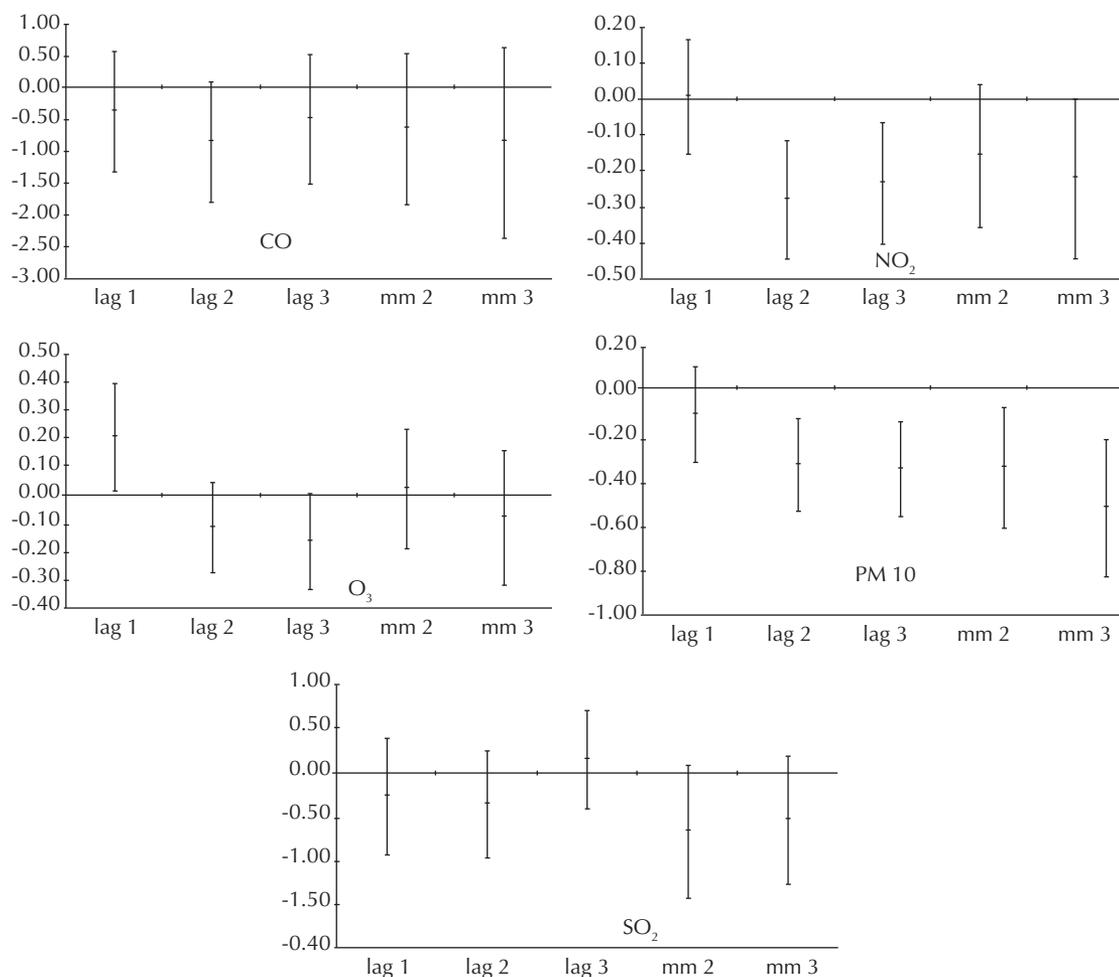
Figure 2. Estimated reductions in child peak expiratory flow (in l/min) and confidence intervals for increases of 10 units in pollutants (except for CO: 1 unit). Rio de Janeiro, Southeast Brazil, 2004.

Air pollutants exposure limits have been the subject of discussion in different countries. The 2005 report by the World Health Organization (WHO)[23] established new guidelines on air quality and reduction of current limits of human exposure. Even though there are many scientific publications on air pollution effects on population health and distinct methods used to measure these effects,[3] questions about the effective impact of different pollutants still remain. Panel studies can contribute to a better understanding of the effects and risks of air pollution on human health.

Panel studies allowed us to investigate in more detail the impact of specific air pollutants on child lung function. The methodology applied here can be reproduced in other regions and also allows factors that may interfere with lung function to be better controlled for.

Further studies on the impact of air pollution on population health from different regions may contribute to the application of better and local methods of air pollution control.

ACKNOWLEDGEMENTS

REFERENCES

1. Bates DV. The effects of air pollution on children. *Environ Health Perspect*. 1995;103 (Suppl 6):49-53. DOI: 10.2307/3432345

2. Brunekreef B, Lumens M, Hoek G, Hofschreuder P, Fischer P, Biersteker K. Pulmonary function changes associated with an air pollution episode in January 1987.*JAPCA*.1989;39(11):1444-7.

3. Castro HA, Gouveia N, Escamilla-Cejudo, José A. Questões metodológicas para a investigação dos efeitos da poluição do ar na saúde. *Rev Bras Epidemiol*. 2003;6(2):135-49. DOI: 10.1590/S1415-790X2003000200007

4. Correia JEM. Poluição atmosférica urbana e fluxo expiratório de pico (peak flow) em crianças de 7 a 9 anos na cidade de São Paulo, SP. Dissertação de mestrado: Faculdade de Saúde Pública-USP. São Paulo; 2001. 215 p.

5. Curtis L, Rea W, Smith-Willis P, Fenyves E, Pan Y. Adverse health effects of outdoor air pollutants. *Environ Int*. 2006;32(6):815-30. DOI: 10.1016/j.envint.2006.03.012

6. Frischer T, Studnicka M, Gartner C, Tauber E, Horak F, Veiter A, et al. Lung function growth and ambient ozone. A three years population study in school-children. *Am J Respir Crit Care Med*. 1999;160(2):390-6.

7. Gauderman WJ, McConnell R, Gilliland F, London S, Thomas D, Avol E, et al. Association between air pollution and lung function growth in Southern California children. *Am J Respir Crit Care Med*. 2000;162(4 Pt 1):1383-90.

8. Gouveia N, Mendonça GAS, Leon AP, Correia JEM, Junger WL, Freitas CU, et al. Poluição do ar e efeitos na saúde nas populações de duas grandes metrópoles brasileiras. *Epidemiol Serv Saude*. 2003;12(1):29-40.

9. Halfon N, Newacheck PW. Childhood asthma and poverty: differential impacts and utilization of health services. *Pediatrics*. 1993;91(1):56-61.

10. Hirsch T, Weiland SK, von Mutius E, Safeca AF, Gräfe H, Csaplovics E, et al. Inner city air pollution and respiratory health and atopy in children. *Eur Respir J*. 1999;14(3):669-77. DOI: 10.1034/j.1399-3003.1999.14c29.x

11. Horak F, Studnicka M, Gartner C, Spengler JD, Tauber E, Urbanek R, et al. Particulate matter and lung function growth in children: a 3-yr follow-up study in Austrian school children. *Eur Respir J*. 2002;19(5):838-45. DOI: 10.1183/09031936.02.00512001

12. Mukala K, Pekkanen J, Tiittanen P, Alm S, Salonen RO, Tuomisto J. Personally measured weekly exposure to NO2 and respiratory health among preschool children. *Eur Respir J*. 1999;13(6):1411-7.

13. Medley AJ, Wong CM, Thach TQ, Ma S, Lam TH, Anderson HR. Cardiorespiratory and all-cause mortality after restrictions on sulfur content of fuel in Hong Kong: an intervention study. *Lancet*. 2002;360(9346):1646-52. DOI: 10.1016/S0140-6736(02)11612-6

14. Pope CA III, Dockery DW. Acute health effects of PM10 pollution on symptomatic and asymptomatic children. *Am Rev Respir Dis* 1992;145(5):1123-8.

15. Rios JLM, Boechat JL, Sant'Anna CC, França AT. Atmospheric pollution and the prevalence of asthma: study among schoolchildren of two areas in Rio de Janeiro, Brazil. *Ann Allergy Asthma Immunol*. 2004;92(6):629-34.

16. Roemer W, Hoek G, Brunekreef B. Effect of ambient winter air pollution on respiratory health of children with chronic respiratory symptoms. *Am Rev Respir Dis*. 1993;147(1):118-24.

17. Rutishauser M, Ackermann U, Braun Ch, Gnehm HP, Wanner HU. Significant association between outdoor NO2 and respiratory symptoms in preschool children. *Lung*. 1990;168 (Suppl):347-52. DOI: 10.1007/BF02718151

18. Saldiva PH, Lichtenfels AJ, Paiva PS, Barone IA, Martins MA, Massad E, et al. Association between air pollution and mortality due to respiratory diseases in children in São Paulo, Brazil: a preliminary report. *Environ Res*. 1994;65(2):218-25. DOI: 10.1006/enrs.1994.1033

19. Samet JM, Lambert WE, Skipper BJ, Cushing AH, Hunt WC, Young SA, et al. Nitrogen dioxide and respiratory illnesses in infants. *Am Rev Respir Dis*. 1993;148(5):1258-65.

20. Santos UP, Braga AL, Giorgi DM, Pereira LA, Grupi CJ, Lin CA, et al. Effects of air pollution on blood pressure and heart rate variability: a panel study of vehicular traffic controllers in the city of São Paulo, Brazil. *Eur Heart J*. 2005;26(2):193-200. DOI: 10.1093/eurheartj/ehi035

21. Solé D, Vanna AT, Yamada E, Rizzo MC, Naspitz CK. International study of asthma and allergies in childhood (ISAAC) written questionnaire: validation of the asthma component among Brazilian children. *J Invest Allergol Clin Immunol*. 1998;8(6):376-82.

22. Ward DJ, Ayres JG. Particulate air pollution and panel studies in children: a systematic review. *Occup Environ Med*. 2004;61(4):e13. DOI: 10.1136/oem.2003.007088

23. World Health Organization. WHO air quality guidelines global update 2005: Report. Copenhagen; 2005.

24. Worldwide variation in prevalence of symptoms of asthma, allergic rhinoconjuntivitis, and atopic eczema: ISAAC. *Lancet*. 1998;351(9111):1225-32. DOI: 10.1016/S0140-6736(97)07302-9

25. Wichmann HE, Heinrich J. Health effects of high level exposure to traditional pollutants in East Germany--review and ongoing research. *Environ Health Perspect*. 1995;103 (Suppl 2):29-35. DOI: 10.2307/3432446