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Association between fine particulate matter and the peak expiratory flow of schoolchildren in the Brazilian subequatorial Amazon: A panel study ☆

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ABSTRACT

Background: Exposure to high levels of particulate matter with an aerodynamic diameter less than 2.5 μm ($PM_{2.5}$) resulting from biomass burning is frequent in the subequatorial Amazon region.
Objective: To investigate whether or not current exposure to $PM_{2.5}$ in the Brazilian Amazon has adverse effects on the daily peak expiratory flow (PEF) of schoolchildren.
Methods: The study design consisted of a panel comprising 309 children aged 6 to 15 years from the same school. PEF was measured daily, except weekends and holidays, from August to December 2006. Each child contributed to the study up to 67 daily measurements. All together there were 19115 PEF measures. Participation rate was 90%. Daily measurements of $PM_{2.5}$, temperature, and humidity as well as passive smoking, and subject features were regarded in the statistical analysis. Various exposures of $PM_{2.5}$ were considered throughout the analysis, among them 24-hour, 12-hour, 6-hour, and 5-hour means. To account for subject responses to confounders, mixed effects models were applied. The effects were evaluated considering air pollution levels on the current day or at 1- or 2-day lags and the averages of 0–1-day lags, 1–2-day lags and 0-, 1-, and 2-day lags.
Results: The 24-hour $PM_{2.5}$ means ranged from 6.39 to 99.91 μg/m^3. The adjusted models for the entire group of children revealed adverse effects. For instance, for an increase of 10 μg/m^3 in $PM_{2.5,}$ the reduction in the PEF average varied between 0.26 l/min (95% Confidence Interval (CI): −0.49; −0.04) and 0.38 l/min (95% CI: −0.71; −0.04). Restricted to the subgroup of non-asthmatic children, classified as such according to the International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire, there was a reduction in the PEF ranging from 0.38 l/min (95% CI: −0.63; −0.13) to 0.53 l/min (95% CI: −0.90; −0.16) for an increase of 10 μg/m^3 in $PM_{2.5}$. There was no significant effect in the asthmatic group. When stratified by time of the day children were at school, the concurrent effects of air pollution on PEF were not significant, whereas the 6-hour exposure from 0 am to 5:30 am was significant for both morning and afternoon groups. Finally, the 24-hour mean lagged effect was only significant for the afternoon group of children. For an increase of 10 μg/m^3 in $PM_{2.5,}$ there was a reduction in the PEF that ranged from 0.41 l/min (95% CI: −0.76; −0.06) to 0.49 l/min (95% CI: −0.91; −0.07).
Conclusion: Exposure to current levels of $PM_{2.5}$ in the Brazilian Amazon was associated with reductions in the lung function of schoolchildren. The adverse effects were more consistent in non-asthmatic children and with respect to the 6-hour mean from 0 am to 5.30 am.

1. Introduction

Recent reports and literature reviews have established that atmospheric pollution presents an important health risk (HEI, 2003; U.S EPA, 2004; Ward and Ayres, 2004; WHO, 2005; Pope and Dockery, 2006; Grigg, 2009; Weinmayr et al., 2010). The most vulnerable populations are children, the elderly, and those with respiratory conditions such as asthma and other chronic

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obstructive pulmonary diseases (WHO, 2005). The effects of air pollution exposure are characterized by health problems ranging from a reduction in pulmonary function to increases in the mortality rate, primarily due to cardiorespiratory illnesses (WHO, 2005; Pope and Dockery, 2006).

The respiratory capacity increases from childhood up to the onset of adulthood, during which a process of decline begins (Gotschi et al., 2008). Several studies have demonstrated that exposure to atmospheric pollution not only causes a reduction in expiratory volume (Castro et al., 2009) but also affects the growth of pulmonary function in children (Gauderman et al., 2000). Studies focusing on the effects of air pollution on pulmonary function predominantly relies on Peak Expiratory Flow (PEF) and Forced Expiratory Volume measurements (SBPT, 2001; Ward and Ayres, 2004; Trenga et al., 2006).

The Amazon region is marked by seasonal dry and rainy periods, typically from June to October and from November to May, respectively. This region has been marked by regular forest burnings that usually occur during the dry season when both humidity and precipitation are low. In this region, environmental air pollution studies have been conducted since 1992 (Artaxo et al., 1994; Hacon et al., 1995). High concentrations of inhalable particles measured in the region during the dry season generally range from 400 to 600 $\mu g/m^3$ and are caused by intense anthropogenic biomass burning activity (Pauliquevis et al., 2007). Most of the particles are fine or ultrafine, and they can remain in the atmosphere for approximately a week (Reid et al., 2005). Most of the forest fires occur in multiple sites that are somewhat far apart whilst the resulting smoke may be transported far away.

Even though the air quality of the Amazon region has been assessed by several research groups, few have addressed its health effects. All together nine states form the Brazilian Amazon region, which houses approximately 25 million inhabitants (IBGE., 2010). A great part of the population in this region has been enduring seasonal biomass burning over the last couple of decades, primarily as a result of the agricultural and cattle breeding expansion. This subregion of the Brazilian Amazon is known as Arc of Deforestation, and it houses 40% of the total population. More recently, the State of Mato Grosso, located in the center-west of the country, has become the leader in total burned areas. However, several studies have demonstrated that particulate matter found anywhere in Mato Grosso State may come from neighboring countries, such as Bolivia or from the others states of the Brazilian Amazon (Freitas et al., 2005; Martin et al., 2010).

To our knowledge, the first assessments of the health effects of biomass burning in the Amazon region were published fairly recently. Rosa et al. (2008) analyzed hospital admissions due to respiratory diseases among children living in an Amazon municipality between 2000 and 2005. Another study investigated the association between daily concentrations of particulate matter with an aerodynamic diameter less than 2.5 μm ($PM_{2.5}$) and daily counts of emergency room visits due to respiratory symptoms (Mascarenhas et al., 2008). An additional study restricted to Mato Grosso State and based on counts of respiratory hospital admissions as well as mortality indicators for children, revealed the two worst-ranked municipalities, namely Alta Floresta and Tangará da Serra (Ignotti et al., 2007).

The latter motivated a series of three repeated measures studies to investigate whether or not current levels of $PM_{2.5}$ have adverse effects on the respiratory health of schoolchildren. Because the burnings occur in the dry season, and the amount of burning varies yearly, the three studies spanned different years and locations, including Alta Floresta and Tangará da Serra. This article reports the findings of the Alta Floresta study.

2. Material and methods

2.1. Study setting and design

The study was held in the municipality of Alta Floresta, situated in the extreme North of Mato Grosso State, Brazil, in the subequatorial Amazon (Fig. 1). According to the latest Brazilian Census (http://www.ibge.gov.br/home/estatistica/populacao/censo2010/calendario.shtm, last accessed August 4th, 2011), Alta Floresta has 49,164 inhabitants and a population density of 5.34 inhabitants per km^2. Approximately 18% (8981 inhabitants) are 6 to 15 years old. Its main economic activities include cattle breeding, dairy production, and agribusiness, particularly timber

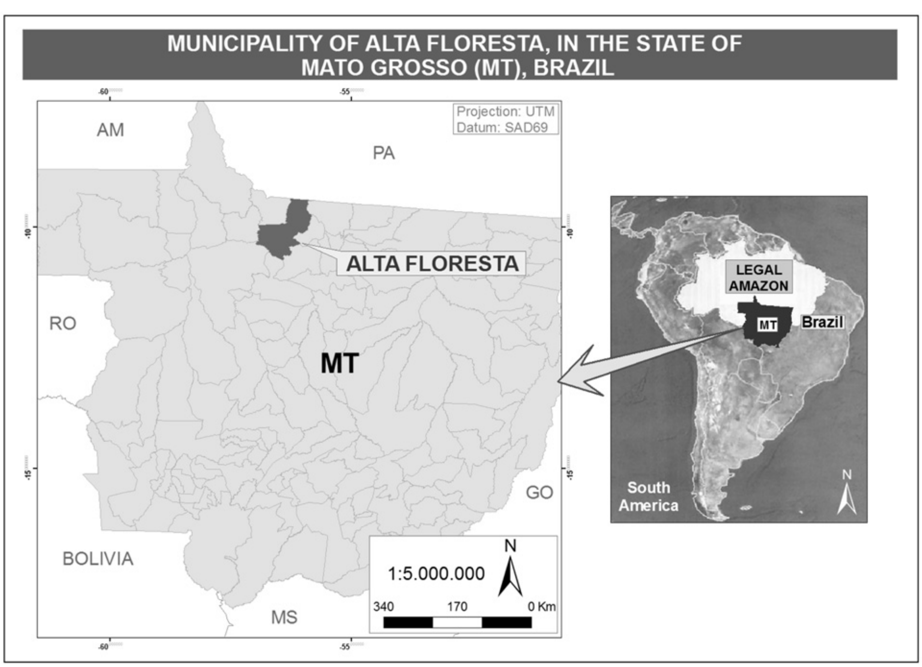

Fig. 1. Geographical location of the municipality of Alta Floresta, Mato Grosso State.

exploitation. Biomass burning from local and distant sources is the main source of air pollution, to which only a small number of vehicles in the city contribute. In August 2006, Alta Floresta harbored 17,290 vehicles, corresponding to only 0.3% of the São Paulo city fleet (Chiarelli et al., 2011).

The study design consisted of a panel based on a random sample of schoolchildren, who were followed up daily for 4 months. The outcome variable was the daily measure of PEF, and the exposure variable was the daily level of $PM_{2.5}$ measured at the school.

The study took place in the largest public school in Alta Floresta. In 2006, this school had more than 1000 registered students. It is located in a wide and open area that lacks physical barriers to circulating air. Additionally, the school best represents the social, economic, and cultural features of the region.

All children attending public schools in Brazil either study in the morning or in the afternoon. At the study school, classes started at 7:00 am (morning group) or 12:30 (afternoon group) daily and finished at 12:00 and 17:30, respectively. Furthermore, younger children usually attend school in the afternoon and older children in the morning. All 1st, 2nd, and 3rd grade pupils attended the school in the afternoon, whereas 7th and 8th grade pupils attended in the morning. Students in the remaining grades attended either in the morning or afternoon.

2.2. Subjects and duration of the study

Children were selected to the sample by randomly following the school schedule, i.e. according to the proportion of pupils per classroom. This randomization ensured proportional representation of both gender and all age groups between 6 to 15 years. The study sample comprised 309 schoolchildren and lasted from the middle of the dry season until the beginning of the rainy season (August 14 to December 3, 2006). Ethical approval was obtained from the Oswaldo Cruz Foundation Ethics Committee. A consent form to participate in the study was signed by the children's parents.

2.3. Data

PEF measures were taken daily for approximately 4 months, excluding weekends and holidays. When a subject was absent from school for any reason, the measure was taken in his or her home, which significantly reduced the amount of missing data. Data collection depended on the time of the day subjects were at school. Data was collected so as to minimize disruption of regular school activities. The device employed in the study was the Mini-Wright Peak Flow Meter, and each subject was assigned a single device. The protocol described by the American Thoracic Society (1995) was adopted throughout the study. Biology undergraduate students collected the data after careful training and supervision by a senior pneumologist and an experienced spirometry technician, who both frequently performed PEF exams in children and teenagers. During the entire study period, the spirometry technician supervised the data collection daily.

Respiratory symptoms, such as coughing, itchy ears, itchy throat, running nose, watery eyes, and the seeking of medical help were recorded in a diary to be filled out weekly at home by parents or another guardian of the subject. Symptoms were recorded together with the day of their occurrence. Other individual covariates, such as weight and height, were measured at the onset of the study using a Welmy anthropometric mechanical scale, with 150 kg maximum capacity. Furthermore, the standard questionnaire related to phase I of the "*International Study of Asthma and Allergies in Childhood*" – ISAAC methodology – was answered by each subject's guardian/parent, thus allowing for the stratification of the sample into asthmatics and non-asthmatics (ISAAC Steering Committee, 2006). Teenagers scoring greater than or equal to 6 were regarded as asthmatics, whereas children that scored greater than or equal to 5 were considered asthmatic.

$PM_{2.5}$ concentrations were measured using a Tapered Element Oscillating Microbalance (TEOM) device, with a time resolution of 30 min. It was operated at the lowest possible inlet temperature to avoid losing volatile aerosol. Parallel measurements of TEOM and gravimetric mass were collected for two months, and a strong correlation among the measurements (correlation coefficient$=$0.86) was observed. The device was located in the schoolyard during the entire study period. The closest main road is located 4 km away from the school, and only small industries that do not emit air pollutants are present in the city. The study $PM_{2.5}$ monitor likely captured the amount of pollutants most people endure during the yearly season of forest fires, which we will expound on further in the Section 4.

Average daily readings of meteorological variables, specifically relative humidity and temperature, were obtained from the local airport, which is located 4 km from the school. These data were provided by the Brazilian airport authority.

2.4. Data analysis

The outcome variable of the study was the maximum of the three PEF measures taken sequentially every day for each subject. The exposure variable for the same day was the average $PM_{2.5}$ value calculated either for morning or afternoon and assigned to each subject accordingly. For the morning group the readings were taken between 7:00 am and noon whereas for the afternoon group they were between 12:30 pm and 5:30 pm. For single-day, lagged short-term exposures, we considered the 24-hour mean of the previous day (lag 1) and the day before (lag 2). Cumulative exposures were defined as follows: (i) the average 24-hour mean of the previous two days (lag 1–2), (ii) the average 24-hour mean of the same day and the previous one (lag 0–1), and (iii) the average 24-hour mean of the same day and the two previous days (lag 0–2). Respiratory symptoms, height, weight, age, gender, and asthma status as set by ISAAC for each child as well as average daily temperature and humidity were also added to the database.

Over the 4 months, some subjects in the age groups may grow extensively, whereas others may not. Similarly, the effects of temperature and humidity on the PEF levels vary across subjects, particularly the latter because temperature levels are high and almost unchanging during the dry season in the Amazon, whereas humidity levels are rather low but varying. These features, along with the subjects' age, gender, occurrence of respiratory infections contribute to the PEF mean level over time. Therefore, these parameters must be taken into account in the modeling. Mixed models allow fitting both fixed and random effects; thus, they are appropriate for the data analysis required in this study. The R library *nlme* (Pinheiro et al., 2011) not only fits nonlinear and linear mixed effects models but also allows for the modeling of the intra-subject variability, including autocorrelation.

We approached the fitting of the long-term time trend of the outcome using 4 distinct shapes: a cubic parametric spline based on a single knot, a quadratic parametric spline with two equally spaced knots or only one knot, and a quadratic polynomial of the time variable (see Snijders and Bosker, 1999, chapter 12). Under the four approaches, the time variable was centered in the middle of the study period and the polynomial coefficients were supposedly random and normally distributed over the sample of subjects. This assumption was later verified. Similarly, the effects of temperature and humidity were accessed based on the same type of polynomials; however, we also examined the possibility of lagged effects. In contrast, to account for between-subject variability, individual covariates, such as height, weight, age, gender, asthma status, and passive smoking, were regarded with fixed effects. Finally, the use of medication and air pollution levels are time-varying covariates, and thus, these may have fixed or random effects on PEF levels. In this study, the use of medication was tested with regards to its random effect, whereas we only examined the overall fixed effect for air pollution.

To complete the model specification, our modeling allowed for heteroskedasticity of the outcome variable across subjects under a common autocorrelation coefficient of lag 1 (AR(1)). The variance function comprised the following time-invariant covariates: height categorized in three groups, asthma status, and gender. Inclusion of these covariates in the variance function attempts to explain variability among sets of repeated PEF measures within subjects. The option *weights* from the library *nlme* was used with this purpose.

Furthermore, the statistical analysis was stratified according to asthma status or time of the day children were at school. Also, to further evaluate effect modification between morning and afternoon groups of children, exposure to $PM_{2.5}$ was refined into a sequence of 6-hour and 12-hour periods. For the 6-hour $PM_{2.5}$ exposure the average of 30-min measures between 0 am and 5:30 am, 6 am and 11:30 am, 12 am and 5:30 pm, and 6 pm and 11:30 pm were obtained. For the 12-hour $PM_{2.5}$ exposure the averages between 0 am and 11:30 am and between 12 am and 11:30 pm were obtained.

Finally, to evaluate the robustness of the air pollution effects findings, we performed a set of sensitivity analyses, wherein the same models were readjusted disregarding outliers (defined as those observations for which the absolute value of the standardized residual was greater than 4) and restricting the analysis to the first half of the study period, when $PM_{2.5}$ levels were somewhat higher, while excluding outliers. In all modeling circumstances, residual diagnostics were accessed with respect to their main expected properties, particularly the assumption of normality of the random effects. Moreover, the Akaike Information Criterion (AIC) and the log-likelihood ratio test were frequently examined to compare non-nested and nested models, respectively, whereas the issue of multicollinearity of the fixed effects was evaluated via its variance-covariance matrix.

3. Results

Given the available resources to carry out the study and our willingness to include as many schoolchildren as possible, 309 subjects were selected at random, mimicking the distribution of schoolchildren per class. Of the 309 students, 28 subjects did not answer the ISAAC questionnaire, which is a crucial covariate in the study, so they were excluded from the statistical analysis. An additional subject dropped out during the first week of the study. To minimize effects caused by PEF exam learning processes, the first week of data collection was disregarded; thus, the total number of study days was 67. Taken together, the PEF measures, asthma status, and most of the other covariates were available for 280 schoolchildren, 279 of whom participated for the full study period; a single subject dropped out after 51 days; thus the participation rate was 90%. Even though most absenteeism was avoided by collecting data at the subjects' homes when they did not attend classes on a given day, 13% of the measurements were missing for several reasons, including school activities that caused classes to be suspended as well as schoolchildren that were neither found at home nor at school.

Table 1 summarizes the statistics of individual characteristics (age, weight, height, asthma, passive smoking), PEF measurements, weather variables (daily mean temperature and daily mean humidity), and 24-hour $PM_{2.5}$ averages. The average age of the 280 study subjects was approximately 10.4 years old. With regards to physical characteristics, the average weight was 34.6 kg (minimum 17; maximum 72 kg), and the average height was 1.42 m (minimum 1.09; maximum 1.75 m). The sample was gender-balanced: 48.6% were boys. According to the ISAAC scores, 20% of the subjects ($n=56$) were classified asthmatic (27 girls and 29 boys). Passive smoking at home was reported by 35.4% of the subjects ($n=99$). PEF measures ranged between 140 l/m and 570 l/m, whereas the overall mean of the study period was 282.1 l/m (Table 1). Morning and afternoon periods were evenly represented. Of the total, 138 subjects attended school in the morning and 142 in the afternoon.

Daily time series of relative humidity and temperature, and 24-hour $PM_{2.5}$ averages are presented in Fig. 2. The overall mean daily temperature in the period was 26.5 °C, (minimum 20.9 °C; maximum 28.8 °C), whereas the overall mean daily relative humidity was 70% (minimum 30%; maximum 93%). The daily average of $PM_{2.5}$, restricted to the morning or afternoon, varied from 3.34 to 120.78 $\mu g/m^3$ whereas the overall mean for the period was 23.06 $\mu g/m^3$ (Table 1). Finally, the overall mean of the 24-hour averages was 24.35 $\mu g/m^3$ (minimum 6.39 $\mu g/m^3$; maximum 99.91 $\mu g/m^3$). Further, in approximately 37% of the study period, the 24-hour average was higher than 25 $\mu g/m^3$. The highest $PM_{2.5}$ values occurred in August and September, concurrent with the lowest humidity levels. In October and November, humidity levels increased, and $PM_{2.5}$ levels decreased. Temperature levels varied slightly during the study period.

Regarding the covariates related to respiratory symptoms, a cough occurred in 7% of the study days, a runny nose in 5.2%, a headache in 4.8%, and watery eyes in 2.7%. The seeking of medical care occurred in 0.5% of the study days, whereas the use of medication was reported by the subjects in 5% of the study days.

Table 1
Summary statistics of weather variables, $PM_{2.5}$, peak expiratory flow measurements, and children's individual characteristics. Alta Floresta-MT, Brazil, 2006.

Variables					Percentiles					
	n	**% missing**	**Mean (standard deviation)**	**Minimum**	**10**	**25**	**50**	**75**	**90**	**Maximum**
Average daily temperature (°C)	112	0.0	26.5 (1.44)	20.9	24.6	25.8	26.7	27.6	28.0	28.8
Average daily humidity (%)	112	0.0	70.1 (16.2)	30	46.1	56	77	83	87	93
Average daily $PM_{2.5}$ ($\mu g/m^3$)	108	4.0	24.34 (19.25)	6.39	8.56	11.95	16.77	30.12	44.08	99.91
Peak Flow (l/m)	19115	43.7[a]	286.4 (73.7)	75	190	230	290	340	380	580
Age	309	0.0	10.3 (2.31)	6	7	8	10	12	13	15
Height (cm)	309	0.0	141.7 (13.6)	109	124	131	141	153	159	175
Weight (kg)	309	0.0	34.6 (10.6)	17	22	27	33	41	48	73
Asthmatic	281	9.0	20.0[b]							

[a] Includes holidays and weekends and actual missing values.
[b] Percentage of children with asthma according to ISAAC criteria.

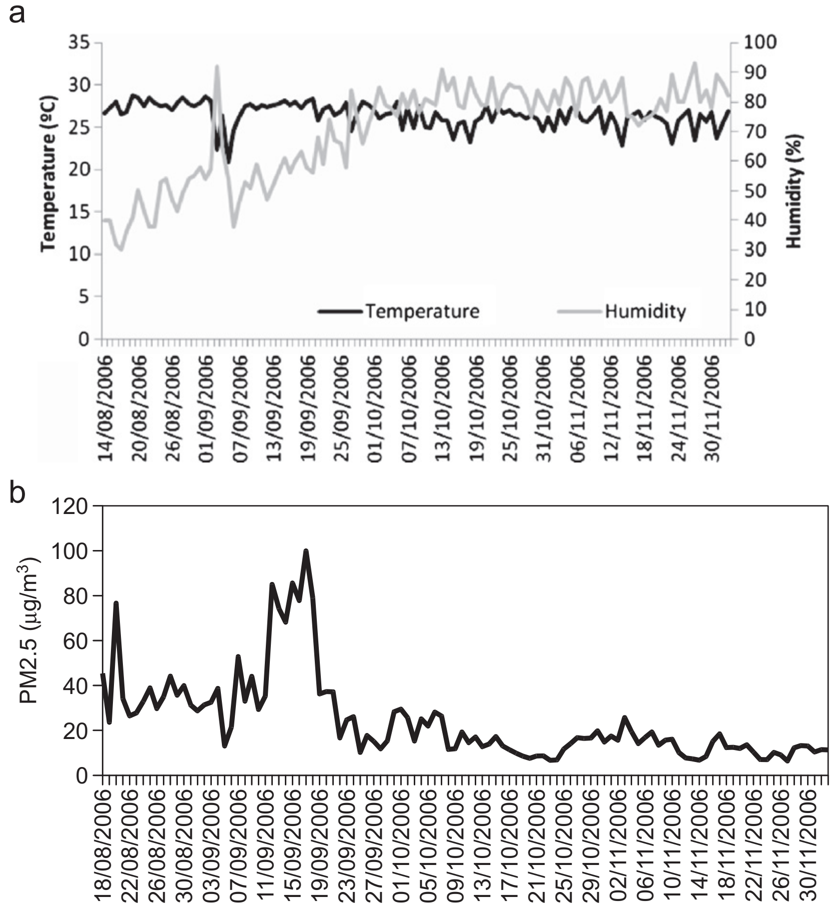

Fig. 2. Daily temperature, humidity and $PM_{2.5}$ readings. Alta Floresta, MT, Brazil —2006.

However, this information was not specific, and we do not know what type of medication was taken.

Table 2 displays results of the main modeling together with those of the sensitivity analyses for all study subjects, only for asthmatics, only for non-asthmatics, only for the morning group and only for the afternoon group. Based on the statistical significance and the adequacy of residual diagnostics, the core model specification consisted of long-term trends adjusted by quadratic polynomials with random effects, temperature and humidity lagged by two days and adjusted by quadratic polynomials with random effects to account for weather, time-invariant covariates height, age, gender, and asthma status with fixed effects to account for between-subject variability, an AR(1) specification to account for autocorrelation and twelve different subject-error variances according to the subject status with respect to asthma, gender, and height. The latter was categorized into three groups whilst for gender girls were the reference category. Symptoms such as cough, itchy ears, itchy throat, running nose, and watery eyes were not included in the modeling since exposure to air pollution may lead to both lower PEF and increased symptoms.

The modeling revealed some significant adverse effects and some non-significant effects. Firstly, in the analysis for all children for an increase of 10 $\mu g/m^3$ in $PM_{2.5}$, the effects were as follows: (i) for same-day exposure, there was an average reduction of 0.26 l/min (95% CI: -0.49; -0.04) in the PEF; (ii) for lag 0-1, there was an average reduction of 0.37 l/min (95% CI: -0.68; -0.07) in the PEF; (iii) for lag 0–2, there was an average reduction of 0.38 l/min (95% CI: -0.71; -0.04); and (iv) no effects were found for exposure to lag 1, lag 2 and lag 1–2 of $PM_{2.5}$.

To test whether asthma status based on ISAAC is an effect modifier, an interaction term between this covariate and exposure to $PM_{2.5}$ was evaluated in the model for all children. The main effect of $PM_{2.5}$ as well as its interaction with asthma were significant on the same day, lag 0–1, and lag 0–2. For instance, the effect of $PM_{2.5}$ was equal to -0.40 (95% CI: -0.64; -0.16) and the interaction effect was 0.72 (95% CI: 0.20; 1.25) for the same day exposure. Thus, the effect of $PM_{2.5}$ restricted to the asthmatics is equal to 0.31 (95% CI: -0.17; 0.79). Such a large effect difference between asthmatics and non-asthmatics is worthy of stratification.

When stratified by asthma status, no significant $PM_{2.5}$ effects were observed for the group of asthmatics, however, for the group of non-asthmatics for an increase of 10 $\mu g/m^3$ in $PM_{2.5}$ there was a reduction of 0.38 l/min (95% CI: -0.63; -0.13) on the same day exposure, a reduction of 0.50 l/min (95% CI: -0.84; -0.16) for lag 0–1 and a reduction of 0.53 l/min (95% CI: -0.90; -0.16) for lag 0–2. The effects of lag 1, lag 2, and lag 1–2 were not significant.

The results stratified by time of the day revealed significant adverse effects of $PM_{2.5}$ on PEF only for the afternoon group of children. There was an average reduction of 0.41 l/min (95% CI: -0.76; -0.06) for lag 1 and a reduction of 0.49 l/min (95% CI: -0.91; -0.07) for the cumulative exposure lag 0–1, both for an increase of 10 $\mu g/m^3$ in $PM_{2.5}$. The effects of same-day exposure, lag 2, lag 1–2, and lag 0–2 were not significant.

To investigate further differences in effect between the morning and afternoon groups, more specific exposures were examined. In the morning, for an increase of 10 $\mu g/m^3$ in $PM_{2.5}$ there was a reduction of 0.36 l/min (95% CI: -0.66; -0.06) for the exposure between 0 am and 5:30 am and a reduction of

Table 2
Estimated changes in peak expiratory flow (in l/min) for an increase of 10 μg/m^3 $PM_{2.5}$, for the total group of all children, only asthmatics, only non-asthmatics, only morning group, and only afternoon group. Alta Floresta-MT, Brazil—2006.

Models	Full [a] Change in PEF [d] (95% CI)		Sensitivity Analysis 1 [b] Change in PEF [d] (95% CI)		Sensitivity Analysis 2 [c] Change in PEF [d] (95% CI)	
All children (n=280)						
Same day	−0.26	(−0.49 to −0.04)	−0.34	(−0.56 to −0.12)	−0.29	(−0.52 to −0.07)
lag 1	−0.21	(−0.46 to 0.05)	−0.24	(−0.48 to 0.01)	−0.03	(−0.28 to 0.23)
lag 2	−0.13	(−0.37 to 0.12)	−0.12	(−0.35 to 0.12)	−0.01	(−0.26 to 0.25)
lag 0–1	−0.37	(−0.68 to −0.07)	−0.44	(−0.73 to −0.14)	−0.31	(−0.62 to 0.01)
lag 1–2	−0.24	(−0.53 to 0.06)	−0.25	(−0.54 to 0.04)	−0.02	(−0.34 to 0.29)
lag 0–2	−0.38	(−0.71 to −0.04)	−0.43	(−0.75 to −0.10)	−0.27	(−0.63 to 0.09)
Only asthmatics (n=56)						
Same day	0.22	(−0.29 to 0.73)	−0.18	(−0.66 to 0.31)	−0.06	(−0.55 to 0.43)
lag 1	−0.14	(−0.72 to 0.45)	−0.22	(−0.78 to 0.34)	−0.12	(−0.67 to 0.43)
lag 2	0.25	(−0.30 to 0.80)	0.25	(−0.27 to 0.76)	0.39	(−0.15 to 0.94)
lag 0–1	0.13	(−0.58 to 0.83)	−0.19	(−0.85 to 0.47)	−0.12	(−0.79 to 0.55)
lag 1–2	0.10	(−0.58 to 0.79)	0.04	(−0.60 to 0.68)	0.21	(−0.46 to 0.88)
lag 0–2	0.27	(−0.51 to 1.04)	0.01	(−0.71 to 0.73)	0.15	(−0.60 to 0.90)
Only non-asthmatics (n=224)						
Same day	−0.38	(−0.63 to −0.13)	−0.38	(−0.62 to −0.14)	−0.35	(−0.60 to −0.10)
lag 1	−0.23	(−0.52 to 0.05)	−0.24	(−0.52 to 0.03)	0.01	(−0.28 to 0.30)
lag 2	−0.22	(−0.49 to 0.05)	−0.21	(−0.47 to 0.05)	−0.10	(−0.39 to 0.19)
lag 0–1	−0.50	(−0.84 to −0.16)	−0.51	(−0.83 to −0.18)	−0.34	(−0.70 to 0.01)
lag 1–2	−0.32	(−0.65 to 0.01)	−0.33	(−0.65 to 0.00)	−0.07	(−0.43 to 0.29)
lag 0–2	−0.53	(−0.90 to −0.16)	−0.54	(−0.90 to −0.18)	−0.36	(−0.77 to 0.04)
Only morning group[e] (n=138)						
Same day	−0.27	(−0.59 to 0.06)	−0.36	(−0.68 to −0.05)	−0.21	(−0.55 to 0.13)
lag 1	0.06	(−0.31 to 0.43)	−0.03	(−0.38 to 0.32)	0.17	(−0.20 to 0.55)
lag 2	−0.22	(−0.56 to 0.13)	−0.19	(−0.52 to 0.14)	−0.15	(−0.52 to 0.22)
lag 0–1	−0.19	(−0.63 to 0.25)	−0.32	(−0.74 to 0.10)	−0.10	(−0.56 to 0.37)
lag 1–2	−0.12	(−0.55 to 0.31)	−0.16	(−0.57 to 0.25)	0.01	(−0.45 to 0.48)
lag 0–2	−0.29	(−0.77 to 0.19)	−0.38	(−0.84 to 0.09)	−0.19	(−0.72 to 0.34)
Only afternoon group[e] (n=142)						
Same day	−0.28	(−0.58 to 0.02)	−0.35	(−0.64 to −0.06)	−0.35	(−0.65 to −0.06)
lag 1	−0.41	(−0.76 to −0.06)	−0.40	(−0.74 to −0.06)	−0.16	(−0.50 to 0.18)
lag 2	−0.03	(−0.36 to 0.30)	−0.04	(−0.36 to 0.29)	0.13	(−0.21 to 0.47)
lag 0–1	−0.49	(−0.91 to −0.07)	−0.52	(−0.93 to −0.11)	−0.44	(−0.85 to -0.02)
lag 1–2	−0.30	(−0.71 to 0.11)	−0.30	(−0.70 to 0.10)	−0.03	(−0.45 to 0.39)
lag 0–2	−0.41	(−0.87 to 0.05)	−0.44	(−0.88 to 0.01)	−0.29	(−0.76 to 0.18)

[a] Using all data and adjusted for long-term trend (quadratic curve), temperature (quadratic curve), humidity (quadratic curve), height, age, asthma status, gender, and exposure variability.
[b] Using data without outliers above 4 and adjusted for long-term trend (quadratic curve), temperature (quadratic curve), humidity (quadratic curve), height, age, asthma status, gender, and exposure variability.
[c] Using data until September 30th without outliers above 4 and adjusted for long-term trend (linear), temperature (linear), height, age, asthma status, gender, and exposure variability.
[d] Estimated changes in peak expiratory flow (in l/min) for an increase of 10 μg/m^3 in $PM_{2.5}$.
[e] Only Morning Group: only children attending school in the morning; Only Afternoon Group: only children attending school in the afternoon.

0.40 l/min (95% CI: −0.75; −0.04) for the exposure between 0 and 11:30 am. In the afternoon, for an increase of 10 μg/m^3 in $PM_{2.5}$ there was a reduction of 0.37 l/min (95% CI: −0.67; −0.08) for the exposure between 0 and 5:30 am and a reduction of 0.31 l/min (95% CI: −0.65: 0.02) for the 12-hour exposure between 0 am and 11:30 am.

A chi-square test was applied to assess the association between time of the day (morning or afternoon) and age groups. Significant differences existed (chi-square=125.8; p-value$<$0.001). Variable age was combined into three categories: (i) 6 to 9 years of age (37%); (ii) 10 to 12 years of age (41%); and (iii) 13 to 15 years of age (22%). Of those who studied in the afternoon, 63% were 6 to 9 years of age, 36% were 10 to 12 years of age, and 1% were 13 to 15 years of age.

To assess the role of passive smoking, this covariate was regarded in the core model, alone and interacting with exposure to $PM_{2.5}$ on the same day. Similarly, the potential role of the use of medication as an effect modifier was investigated by adding a triple interaction comprising this covariate, asthma status and exposure to $PM_{2.5}$ on the same day (all main effects and double interactions were also included in the model). None of these analyses demonstrated significant effects.

The first sensitivity analysis that discarded observations identified as outliers enhanced the effect of $PM_{2.5}$ on PEF for all children, whereas there were no major changes on the results of the asthmatic and non-asthmatic groups (see Table 2). However, using the same analysis, there were significant effects of same-day exposure to $PM_{2.5}$ for both groups defined by the morning and afternoon groups. For the morning group, an increase of 10 μg/m^3 of same-day $PM_{2.5}$ was associated with a reduction of 0.36 l/min (95% CI: −0.68; −0.05) in the PEF levels. A similar point estimate (−0.35 l/min, 95% CI: −0.64; −0.06) was found for the afternoon group.

Proceeding with the sensitivity analysis, the panel data set was restricted to all of the days up to September 30th and excluded outliers. As the study period was shorter than the previous one, all of the modeling steps had to be reexamined. The adjustment for the long-term trend changed to linear with a random effect, while temperature, also lagged by two days, was adjusted linearly plus a random effect. The humidity was removed from the model because its fixed effect was highly co-linear with that of temperature, resulting in slightly unstable model estimates. As a result of the change in the time period and as a consequence of the core model specification, the effect of $PM_{2.5}$ was significant for all children, the non-asthmatic group, and the group of subjects attending school in the afternoon on the same-day exposure. For an increase of 10 $\mu g/m^3$ in $PM_{2.5,}$ there was a reduction of 0.29 l/min (95% CI: −0.52; −0.07) in the PEF levels for all children. See Table 2 for further results.

For all adjusted models the effects of the time-invariant covariates gender, age and height were positive and statistically significant whilst asthma status had a negative and highly significant effect.

4. Discussion

In this study daily PEF measurements were associated negatively with exposure to $PM_{2.5}$ yielded by biomass burning in the Amazon region. The study was based on a large sample of schoolchildren. A statistically significant reduction on PEF measures, ranging from 0.26 l/min (95% CI: −0.49; −0.04) to 0.38 l/min (95% CI: −0.71; −0.04), was observed based on the sample as a whole. Although lagged health effects have also been identified, the strongest associations were observed for the current day of exposure. The effects were stronger following stratification of the study group, with reductions for the non-asthmatics, ranging from 0.38 l/min (95% CI: −0.63; −0.13) to 0.53 l/min (95% CI: −0.90; −0.16), and for the group of children attending school in the afternoon, ranging from 0.41 l/min (95% CI: −0.76; −0.06) to 0.49 l/min (95% CI: −0.91; −0.07). Surprisingly, no significant effects of exposure to air pollution were observed for the asthmatic group. Reductions in the PEF due to an exposure to air pollution are subclinical effects; however, these reductions may have implications on lung function growth (Gauderman et al., 2000).

Most of the biomass burning in the Brazilian Amazon occurs overnight; thus the effects of 6-hour and 12-hour exposures previous to children being at school were investigated more closely. This analysis lead to the conclusion that exposure between 0 am and 5:30 am is more deleterious and statistically significant for both morning and afternoon groups of children, as opposed to what had been found for the exposure during the time children were at school. Such a finding may be somehow used by local health care workers in order to promote health in their communities.

Almost all children (88%) from 6 to 9 years of age studied in the afternoon. This could explain most of the significant effects observed for the afternoon, whereby younger children are more vulnerable to the effects of air pollution exposure because their lungs are not fully developed (Bateson and Schwartz, 2008).

The results of this study can be extrapolated to the population of children and teenagers living in other parts of the Arc of Deforestation because exposure to $PM_{2.5}$ and other characteristics related to schoolchildren in the Amazon region are similar. The similarities among Amazonian cities in terms of sources and properties of aerosol particles are discussed in Martin et al., 2010. Because the study was undertaken in a single municipal public school, the variability of socioeconomic differences was small. Children attending public schools in Brazil come from similar socioeconomic backgrounds, particularly those who live in the Amazon region, but this is not the case for private schools. Nevertheless, Hancox et al. (2004) and Laurent et al. (2008) have confirmed the absence of socioeconomic factors related to pulmonary function affected by atmospheric pollution.

Recent epidemiological studies of the Brazilian Amazon have identified associations between exposure to air pollution and respiratory endpoints. Mascarenhas et al. (2008) observed an increase in the number of emergency treatments for respiratory illnesses during the dry season in the municipality of Rio Branco, located to the west of the Arc of Deforestation. In 2007, two epidemiological investigations were undertaken, using the ISAAC methodology—phase I with 100% of the children and adolescents in the municipalities of Alta Floresta and Tangará da Serra, both in the state of Mato Grosso. In both studies, the ISAAC questionnaire was provided to children aged 6, 7, 13 and 14. The results demonstrated a high prevalence of asthma in both locations compared with similar studies conducted in Brazil and Latin America (Rosa et al., 2009; Col Farias, 2009). According to Ignotti et al. (2010), exposure to $PM_{2.5}$ from biomass burning increased respiratory disease hospitalizations in children and the elderly living in the municipality of Alta Floresta. Moreover, Carmo et al. (2010) observed that a 10 $\mu g/m^3$ increase in the level of $PM_{2.5}$ was associated with increases in outpatient consultations due to respiratory diseases in children.

Summary estimates of effect were presented in Ward and Ayres (2004) and Weinmayr et al. (2010). Both works presented a systematic review of panel studies that investigated short-term effects of air pollution exposure in pulmonary function. Ward and Ayres (2004) demonstrated that for each increase of 1$\mu g/m^3$ in $PM_{2.5}$, the pooled effect estimate for the PEF based on a random effect model was −0.144 l/min (95% CI: −0.243; −0.044). Weinmayr et al., 2010 reported that for each increase of 10 $\mu g/m^3$ in PM_{10}, the authors observed a borderline significant decrease in PEF of −0.082 l/min (95% IC: −0.214; 0.050).

Other panel studies in Brazil have used PM_{10} as a measure of exposure in large urban centers. Castro et al. (2009) observed results similar to those of this study, with a PEF reduction of 0.34 l/min for each increment of 10 $\mu g/m^3$ in $PM_{10,}$ working with the same age group in Rio de Janeiro city. Correia (2001) verified a decrease of 1.05% in the PEF for an increase of an interquartile range in PM_{10} concentration in a panel study with children between 7 and 9 years of age in São Paulo city.

In the present study, no significant effect was found in the group of asthmatic children when analyzed separately, which could be explained by asthmatic subjects taking medication when they perceived air quality was deteriorating. Unfortunately, only general intake of medication, not specific medication, was recorded in this study. To investigate the effect of medication intake, we analyzed the triple interaction of asthma status, the use of medication and $PM_{2.5}$ levels, but significant effects were not observed. Other studies have demonstrated contradictory results on the effects of atmospheric pollution on asthmatics. According to Lagorio et al. (2006), exposure to $PM_{2.5}$ increased the risk of respiratory crises and, therefore, reduction in pulmonary function. Conversely, Trenga et al. (2006) observed a reduction in pulmonary function in asthmatic children not using medication when exposed to $PM_{2.5}$ and an attenuated reduction when the group used an anti-inflammatory drug. According to those authors, asthmatics who are taking inflammatory medication may be less sensitive to the effects of $PM_{2.5}$ and other pollutants than those who are not taking any medication. Peters et al. (1997) and Delfino et al. (2002) have verified reduced effects of exposure to atmospheric pollution in asthmatic children and adolescents using medication. Blomberg (2000) also observed that anti-inflammatory drugs reduced the inflammatory effect of pollutants.

This study did not record information about the type of medication was taken by the subjects nor the reasons for school absenteeism. These could be limitations of the study. Another limitation involves the asthma diagnosis based on the ISAAC questionnaire because all of the individuals varied in age from 6 to 15 years. The ISAAC methodology is validated only for 6- to 7-year-olds and for adolescents between 13 and 14 years (Solé et al., 1998). In addition, it does not provide a gold-standard method for a diagnostic definition of asthma. These limitations may account for a lack of observable significant effects in the asthmatic group.

In contrast, the strengths of the study are its large sample, the range of ages from 6 to 15 years old, and the long follow-up period. Concerning the quality of the PEF measurements, for each subject and each sitting, we calculated half the range (maximum minus minimum, divided by two) of the three flow measurements followed by the calculation of the proportion of days in which this value was greater than 20 l/min. These proportions varied from 0 to 0.40, with average equal to 0.13 (standard deviation equal to 0.08), and median equal to 0.12. On the modeling aspects, we investigated many possibilities for long-term trend fitting and for the fitting of meteorological variables. Furthermore, a sensitivity analysis was performed, and the results demonstrated significant effects of $PM_{2.5}$ on PEF when restricting data to high dry months (August and September) and discarding observations identified as outliers.

5. Conclusions

Exposure to current levels of fine particulate matter in the Amazon region released by biomass burning was associated with reductions in the lung function of schoolchildren. The adverse effects were more consistent in non-asthmatic children and with respect to the 6-hour mean from 0 am to 5:30 am.

Long-term studies should be undertaken to extensively evaluate the limits and subclinical effects of exposure to $PM_{2.5,}$ thus contributing to the establishment of standards for this type of exposure in the area of the Arc of Deforestation.

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The authors declare no competing interest.

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