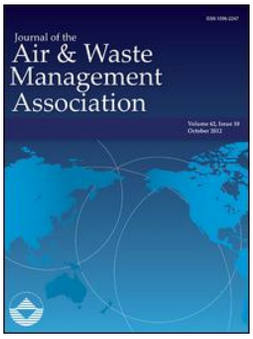

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Association between Levels of Fine Particulate and Emergency Visits for Pneumonia and other Respiratory Illnesses among Children in Santiago, Chile

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ABSTRACT

Recent evidence has implicated the fine fraction of particulate as the major contributor to the increase in mortality and morbidity related to particulate ambient levels. We therefore evaluated the impact of daily variation of ambient $PM_{2.5}$ and other pollutants on the number of daily respiratory-related emergency visits (REVs) to a large pediatric hospital of Santiago, Chile. The study was conducted from February 1995 to August 1996. Four monitoring stations from the network of Santiago provided air pollution data. The $PM_{2.5}$ 24-hr average ranged from 10 to 111 $\mu g/m^3$ during September to April (warm months) and from 10 to 156 $\mu g/m^3$ during May to August (cold months). Other contaminants (ozone (O_3), nitrogen dioxide (NO_2), and sulfur dioxide (SO_2)) were, in general, low during the study period. The increase in REVs was significantly related to PM_{10} and $PM_{2.5}$ ambient levels, with the relationship between $PM_{2.5}$ levels and the number of REVs the stronger. During the cold months, an increase of 45 $\mu g/m^3$ in the $PM_{2.5}$ 24-hr average was related to a 2.7% increase in the number of REVs (95% CI, 1.1–4.4%) with a two-day lag, and to an increase of 6.7% (95% CI, 1.7–12.0%) in the number of visits for pneumonia with a three-day lag. SO_2 and NO_2 were also related to REVs. We conclude that urban air pollutant mixture, particularly fine particulates, adversely affect the respiratory health of children residing in Santiago.

IMPLICATIONS

Particulate matter (PM) has been implicated as a major contributor to the increase in morbidity and mortality. However, there is controversy regarding which particulate fraction may be the most harmful for health. This has important implications in relation to monitoring and control strategies. In this study, we evaluate the health impact of different particulate fractions and other air pollutants on REVs in a population of children highly exposed to PM primarily from vehicle exhaust, particularly diesel exhaust. Although it is difficult to separate the health effect of specific air pollutants because of correlation in the air pollutant mixture, our data suggest that PM is related to the risk of pneumonia and other respiratory illnesses in children and that the fine fraction may be the most toxic. Lower respiratory illnesses present an important health and economic burden in many countries and control strategies should focus on reducing fine particulate emission, particularly from diesel exhaust.

INTRODUCTION

Recent evidence has implicated the fine fraction of particulate matter (PM) as the major contributor to the increase in mortality and morbidity associated with particulate ambient levels.[1] Data on emergency visits (EVs) have been used to examine the effects of a variety of air pollutants, including particulate, ozone (O_3), sulfur dioxide (SO_2), nitrogen dioxide (NO_2), sulfate, and hydrogen sulfide.[2–6] To date, however, few studies have been able to determine the impact of fine PM on the number of respiratory-related emergency visits (REVs) given that monitoring of PM equal or smaller than 2.5 μm in diameter ($PM_{2.5}$) was not mandatory in the United States or Europe. As health end points, EVs have the advantage of reflecting adverse health event of clear clinical significance, which at the same time is more frequent in occurrence than deaths or hospital admissions and may more easily relate to recent exposure.

The metropolitan area of Santiago, Chile, suffers important air pollution problems related in part to its geographic and climatic conditions. Surrounded by hills, this city experiences thermal inversion (with the presence of the subtropical Pacific anticyclone) and weak winds that tend to decrease the dispersion of contaminants, particularly during winter months. Mobile sources are considered the major polluters in Santiago, emitting close to 80% of the contaminants.[7] Concentrations of fine particulates reach high levels, particularly during winter months. Acute respiratory illnesses have become the most common cause of medical visits among children during the cold months and are considered a priority by the health authorities.[8] In 1996, based on data collected through the epidemiological monitoring of healthcare units by the Ministry of Health, the incidence of acute respiratory infections in children less than five years of age was estimated to be 43,398/100,000.[9] In addition to cold climate and high air pollution levels, poor housing conditions are probably responsible for this high rate. The primary objective of this study was to determine the impact of fine particulate ($PM_{2.5}$) and other air pollutants on REVs, particularly visits for pneumonia by a child population heavily exposed to air pollutants.

METHODS

Study Population

This study was carried out in Santiago, a city of approximately 5,300,000 people.[7] The population for this study was composed of children and adolescent under 15 years of age who lived in Santiago and who sought outpatient care at the pediatric emergency clinic of the Hospital Calvo Mackenna (HCM), located in the central eastern area of Santiago. This hospital is one of the major pediatric hospitals that serves people from central and eastern Santiago with medium-to-low socioeconomic levels. The base population is difficult to quantify because, although patients are assigned to specific healthcare units in Santiago, any patient may attend this reference hospital. However, we estimate that it serves a population of approximately 124,200 children under 15 years of age, this population being fairly constant over time.[10]

This hospital is located close to the metropolitan monitoring network. To obtain better information on the population that was attended at the HCM, we reviewed records and conducted a prospective survey for two weeks in August 1996. Forty-five questionnaires were completed every day by people who brought children to the emergency room. We had the questionnaires filled out at different hours of the day on weekdays and weekends in order to obtain a good representation of the population. In total, we obtained 540 questionnaires. Results showed that in 82% of the cases, children were brought in by their mother. Of the EVs, 36.12% were surgical, 31.3% respiratory-related, and 32.6% related to other pediatric problems. Among the children with REVs, 52.6% reported that symptoms started more than two days prior to the visit, 16.6% two days prior to the visit, 13% less than one day prior to the visit, and 17.2% less than 12 hr prior to the visit.

The study was conducted from February 1, 1995, to August 31, 1996 (578 days). Trained health professionals reviewed and extracted data from daily EV records and categorized the data by the date of the visits, by diagnosis, and by the children's age. The diagnoses made by the attending physician were used to classify the EVs according to the International Classification of Diseases, Ninth Revision (ICD-9) codes. We divided children's EVs into different categories: respiratory-related visits, other medical visits, and surgical visits. We divided respiratory-related visits into two categories: visits for upper respiratory illnesses (URIs) (ICD-9 460–465, 487) and visits for lower respiratory illnesses (LRI) (ICD-9 466, 480–486, 490–494, 496, 519.1, and 033.9). We also studied pneumonia (ICD-9 480–486) separately because of the substantial number of children affected. Nonrespiratory medical visits included visits for all causes that did not fall into one of the above categories.

Data Quality Control

We exercised quality control over the data in three various ways. First, we ascertained the standardization of respiratory diagnosis and treatment given by the emergency clinic pediatricians and observed that all physicians followed the pediatric guidelines established by the Ministry of Health. Second,[11] we audited the quality of the record summary of daily EVs by comparing the data with original medical records (October 15–23, 1996). Errors were observed in less than 2% of the records. In 1% of the records, the diagnosis assigned was not sustained by the medical records, and in 0.04% croup was classified as URI. Third, for 5.2% of the study days selected at random, corresponding to 8,135 medical records, we extracted additional information on patients' residency, health insurance, and prognosis. We observed that diagnoses were missing in 4.4% of the medical records, and that 89.1% of the patients resided in the influence area of the monitors.

Air Pollution

Air pollution data were provided by the air monitoring network of Santiago, Chile. Data from four central stations of the monitoring network of air pollutants

and meteorology (Stations A, B, F, and D) were obtained. Stations measured SO_2, NO_2, O_3, PM_{10}, and $PM_{2.5}$, and Station D measured only O_3, PM_{10}, and $PM_{2.5}$. Particulates (PM_{10} and $PM_{2.5}$) were measured by dichotomous samplers (Sierra Andersen). Meteorological data (temperature, relative humidity, wind speed, and direction) were provided by the "Dirección Meteorológica de Chile."

During cold months, particulates were measured daily. However, during the rest of the year particulates were measured only every two days. For days when particulates were not measured with dichotomous samplers, we used data provided by Tapered Element Oscillating MicroBalance (TEOM, Rupprecht-Patashnick, Albany, NY). During the study period, the correlations between PM_{10} and $PM_{2.5}$ levels measured by dichotomous samplers and TEOM were 0.97 for PM_{10} and 0.92 for $PM_{2.5}$. The correlations of air pollutants levels measured at the four monitoring stations were high: 0.87–0.97 for PM_{10}; 0.91–0.97 for $PM_{2.5}$ (24-hr average); 0.90–0.94 for SO_2 (24-hr average); 0.70–0.88 for NO_2 (24-hr average); and 0.86–0.91 for O_3 (8-hr mobile average). Daily averages were only calculated if the monitors provided 18 or more valid hourly levels. For the analyses, we averaged the air pollutant levels of the four monitoring stations.

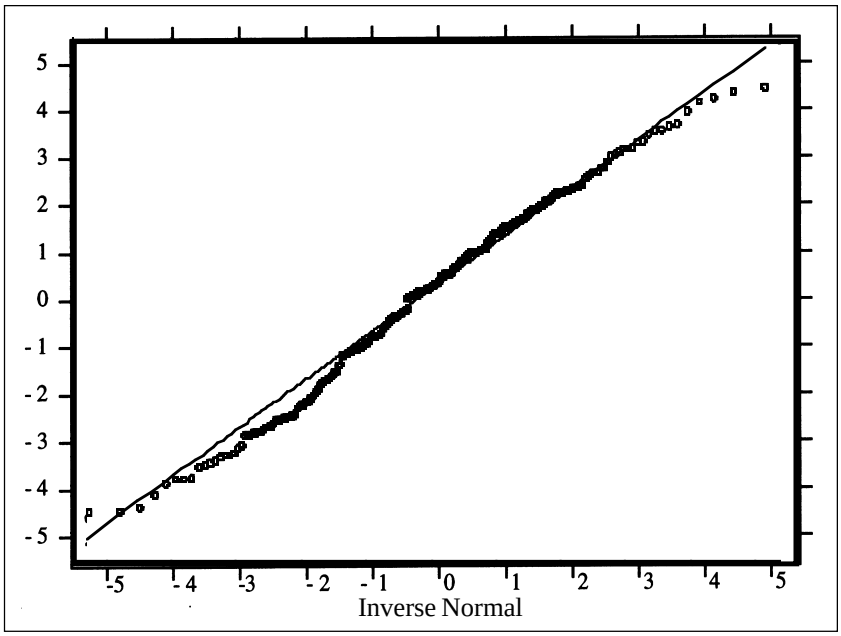

Figure 1. Quantile-quantile plot of the residuals from the regression model of the relation of $PM_{2.5}$ and REVs during cold months: Santiago, Chile, 1995–1996.

Statistical Analysis

We modeled the daily number of EVs at the HCM for respiratory illnesses and studied the relationship between this number and the daily levels of air pollutants. We assumed the conditional distribution of the daily count to be Poisson and used the methodology proposed by Schwartz et al.[12] The outcome variable was smoothed by controlling for long-term and short-term trends that might cause confounding.

We adjusted for the long-term trend by controlling for study months (including dummy variables for months) and conducting separate analyses for warm and cold months. We adjusted for the short trend by fitting a linear, quadratic, third- and fourth-order time trend, temperature (mean daily temperature and second-order temperature), and daily relative humidity. Other calendar features related to daily levels of respiratory admissions were day of the week and influenza epidemic. A major influenza epidemic occurred in Santiago from May 19 to June 18, 1996, during which the number of daily REVs was twice that for the previous month, and for the same dates during 1994 and 1995. We modeled these effects using one dummy variable for weekdays or weekends because we did not observe significant differences in daily visit counts between the weekdays, and one dummy variable to account for the epidemic (only in the "cold months" models).

We checked the goodness of fit of our final model using a quantile-quantile normal plot of the deviance residuals.[13] Figure 1 shows this plot for the relation between $PM_{2.5}$ lag 2 and number of REVs in which the following covariates were used: mean temperature (linear and quadratic term); relative humidity; dummy variables for months, weekdays and weekends and epidemic; and time order 1–4 in addition to $PM_{2.5}$. We observed that the residuals fit a normal line, indicating that the model is adequate for the data. We performed similar tests for the other models and observed a good fit of the data.

We modeled one pollutant at a time exploring different lags (one, two, and three days), and also examined the cumulative effect of each pollutant by averaging its levels over several days. The effects of each air pollutant were examined separately for warm months (September–April) and cold months (May–August). Results are presented separately because of the different patterns observed during these two periods. Air pollutants were included in the models as continuous and categorical variables, defining interquartile ranges based on the distribution of each pollutant. We

considered the following categories of EVs as outcome variables: total respiratory illnesses, URIs, LRIs, and pneumonia. Multipollutant models were fitted, including the pollutant expression that best fit in the single pollutant models (lowest deviance). Because of the high collinearity between pollutants, we also ran multipollutant models including particulate as a continuous variable and one other pollutant as a dichotomous variable, using as a cut-off point the median value of this pollutant during the study period. Finally, we used hockey-stick regression models[14] to estimate the presence of a threshold in the relation of PM and REVs.

RESULTS

Summary statistics for the pollution and meteorological variables are shown in Table 1. Time series of air pollutant data for particulates (PM_{10}, $PM_{2.5}$) and mean temperature and relative humidity are shown in Figure 2. The highest concentrations of particulates

Table 1. Summary statistics for air pollutants (μg/m^3) and meteorological variables.

	Period	Range	Mean	SD	Percentile 5th	50th	95th	Missing Values (%)
PM_{10}(daily average)	Warm	23-170	80.3	26.7	47	75	136	0.6
	Cold	16-270	123.9	52.0	48	119	215	0.0
$PM_{2.5}$(daily average)	Warm	10-111	34.3	16.3	17	30	70	3.3
	Cold	10-156	71.3	31.5	24	67	129	0.0
SO_2(daily average)	Warm	1.9-60.2	14.9	8.8	5.6	13.2	32.0	0.3
	Cold	5.6-92.1	31.8	18.4	9.4	28.2	75.2	0.0
NO_2(daily average)	Warm	37.2-246	97.0	34.6	54.3	91.5	163.0	0.0
	Cold	60.1-397.5	160.2	59.5	74.4	154.4	266.0	0.0
O_3(1 hr max)	Warm	4-168	66.6	25.2	18	68	106	0.0
	Cold	2-120	27.6	20.2	6	22	66	0.0
Temperature (°C)	Warm	8.8-23.7	17.2	3.3	11.6	8.0	21.6	0.0
(daily average)	Cold	2.3-16.1	9.6	2.6	5.6	9.6	14.1	0.0
Relative humidity (%)	Warm	35-94	64.4 1	2.3	44	65	85	0.0
	Cold	36-97	79.5	8.1	66	80	92	0.4

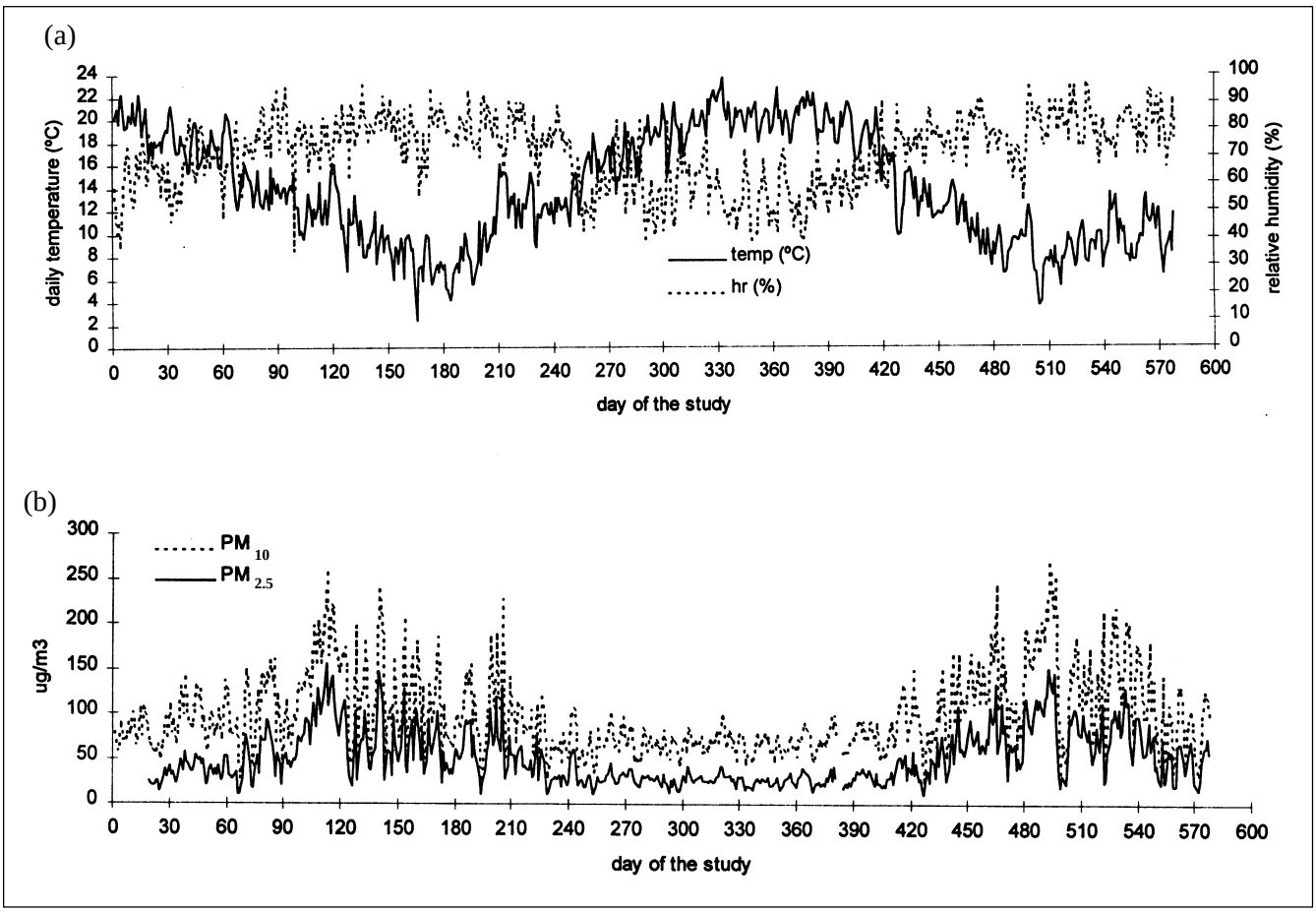

Figure 2. Time-series of climatic and particulate data. Santiago, Chile, 1995-1996: (a) temperature and relative humidity, (b) PM_{10} and $PM_{2.5}$.

were registered during the cold months ranging from 16 to 270 μg/m^3 for PM_{10} and 10 to 156 μg/m^3 for $PM_{2.5}$. The highest concentrations of O_3 were registered during the warm months, ranging from 4 to 168 μg/m^3. SO_2 and NO_2 levels were low during both periods. During the study, PM_{10} ambient levels exceeded the Chilean air pollutant standard (150 μg/m^3 24-hr average) on 81 days. SO_2 and NO_2 ambient levels never exceeded their standards.[14] Table 2 presents the correlation (Pearson) between air pollutants levels and temperature, according to warm and cold months. Particulate levels were highly correlated with SO_2 and NO_2 during the warm and cold months. The correlation between PM_{10} and O_3 levels was higher during the warm months than during the cold months, and $PM_{2.5}$ and O_3 were very weakly correlated. The different particulate fractions (PM_{10}, $PM_{2.5}$, and $PM_{10-2.5}$) were highly correlated (correlation of $PM_{2.5}$ and $PM_{10-2.5}$ were, respectively, 0.84 during the cold months and 0.61 during the warm months).

Table 2. Pairwise correlation coefficients among air pollutants and meteorological variables.

	Temperature	PM_{10}	$PM_{2.5}$	SO_2	NO_2	O_3	Temperature
$PM_{2.5}$	Warm	0.9170[a]					
	Cold	0.9723[a]					
SO_2	Warm	0.6687[a]	0.5764[a]				
	Cold	0.7337[a]	0.6874[a]				
NO_2	Warm	0.7065[a]	0.7008[a]	0.6556[a]			
	Cold	0.8203[a]	0.7960[a]	0.7440[a]			
O_3	Warm	0.1628[a]	0.0603	0.1835[a]	0.1531[a]		
	Cold	0.0853	0.0776	0.1252[a]	0.2158[a]		
Temperature	Warm	-0.1583[a]	-0.3667[a]	-0.1271[a]	-0.3604[a]	0.5216[a]	
	Cold	0.0894	0.0360	0.1960[a]	0.1431[a]	0.3578[a]	
Relative humidity	Warm	0.2174[a]	0.3932[a]	0.0045	0.2034[a]	-0.5632[a]	-0.7076[a]
	Cold	-0.3676[a]	-0.2902	-0.6251[a]	-0.5381[a]	-0.3585[a]	-0.2459[a]

[a]$p < 0.05$.

Time series of counts of hospital admissions for the different respiratory diagnoses are shown in Figure 3. Trend, seasonality and peak during the influenza epidemic during May–August 1996 (study day 456–578) are noticeable features in respiratory series. The number of

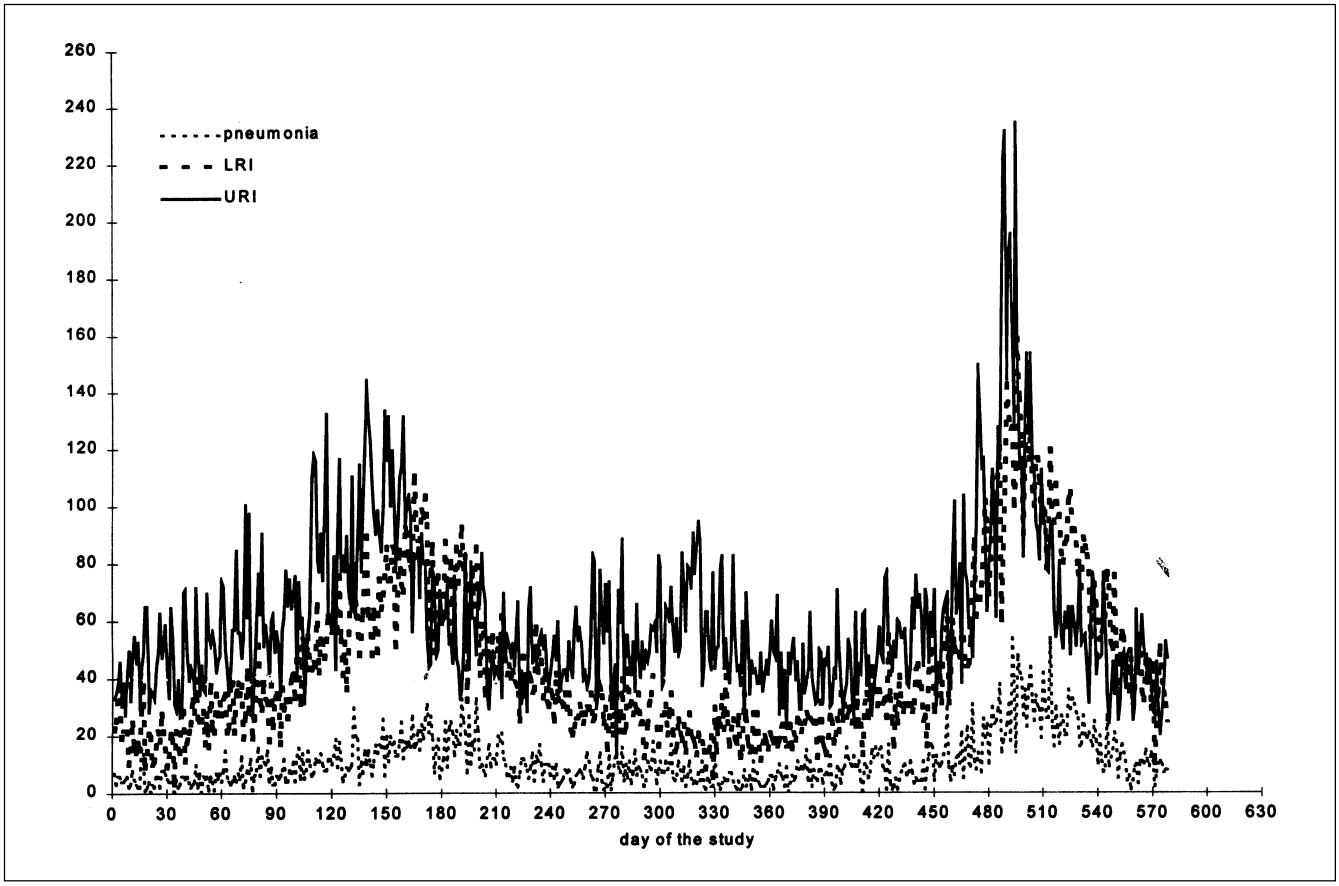

Figure 3. Daily count of REVs, Santiago, Chile, 1995–1996.

Table 3. Daily count of EVs to HCM, February 1995–August 1996, Santiago, Chile.

	Period	Mean	Median	SD	Range
Total visits	Warm	247.0	242	33.5	138-372
	Cold	281.6	277	65.7	105-522
REVs	Warm	77.6	75	18.6	34-130
	Cold	144.6	136	54.9	37-349
LRIs	Warm	27.1	26	9.9	3-62
	Cold	68.3	64	26.3	10-159
URIs	Warm	50.5	49	15.1	12-101
	Cold	76.3	67.5	36.5	20-235
Pneumonia	Warm	6.7	6	4.1	0-21
	Cold	16.8	15	9.7	1-54
Surgical visits	Warm	66.2	64	17.2	22-116
	Cold	59.2	58	15.6	27-102

REVs tended to be higher during the cold months. Summary statistics for the hospital admission variables are shown in Table 3.

Table 4 presents the coefficients of regression models of the relation between air pollutants levels and number of REVs. For each of the pollution variables, effects are presented separately during the cold and warm months. Relative risks (RRs) were calculated for the interquartile ranges of specific air pollutants frequency distribution. The number of REVs was strongly associated with particulate levels. During the cold months, we observed that the effect after a two-day lag was stronger for $PM_{2.5}$ than that for PM_{10} and $PM_{10-2.5}$ (bet = 0.0006 vs. 0.0003 and 0.0004, respectively, for the effect of 1 $\mu g/m^3$). More specifically, a 45-$\mu g/m^3$ increase in the $PM_{2.5}$ 24-hr average was related to a 2.7% increase in REVs (95% CI 1.1–4.4%). With a 30.6-$\mu g/m^3$ increase in the weekly mean $PM_{2.5}$, the increase in REVs was 3.5% (95% CI 1.7–5.4%). SO_2 and NO_2 levels were also related to an increase in REVs. However, given the low levels observed during the study, the effect could be due to the high correlation of the levels of these contaminants with particulate levels. O_3 levels were not related to REVs during the cold months (Table 4). When we studied specific diagnoses, we observed that particulate ambient levels were related to the rates of URI and LRI. The major effect was observed for the number of cases of pneumonia, which increased 6.7% (95% CI 1.7–12.0%) with an increase of 45 $\mu g/m^3$ in $PM_{2.5}$ 24-hr average with a three-day lag. PM_{10}, SO_2, and NO_2 levels were also related to the risk for pneumonia (Table 5).

During the warm months, we also observed a significant association between particulate levels and EVs for pneumonia. A 16–$\mu g/m^3$ increase in $PM_{2.5}$ 24-hr average was related to an 8.9% increase in the risk of pneumonia (95% CI 2.9–15.3%). We also observed a cumulative effect. A 13.1-$\mu g/m^3$ increase in the weekly mean $PM_{2.5}$ levels was related to a 12.5% increase in the risk of pneumonia (95% CI 2.6–23.4%). Other contaminants, SO_2, NO_2, and O_3 were also related to an increase in EVs for pneumonia (Table 5). Because of the high correlation between levels of different air pollutants in our data, multipollutants models are difficult to interpret; however, when two pollutants were included in the same regression model (1) PM ($PM_{10,}$ $PM_{2.5,}$ or $PM_{10-2.5}$) as a continuous variable; (2) another contaminant as a dichotomous variable (SO_2, NO_2, or O_3), as described in the method section, we observed that the regression coefficients of particulates remained similar to those of single pollutant models, while the coefficient of the other pollutant changes sign and loses significance. This suggested that particulates were the most important factor for the health effects observed.

Figure 4 presents the smoothing relationship between the estimated number of EVs for total respiratory illnesses and $PM_{2.5}$ levels with a two-day lag. The curve suggests that $PM_{2.5}$ would affect a susceptible population at low ambient levels and that, after a level-off, the incidence of REVs will increase again. Using "hockey-stick" models[14] with different cut-off points, we observed that 60 $\mu g/m^3$ could be considered as a threshold (high coefficient and lowest deviance) for the acute effect of $PM_{2.5}$ on total respiratory illnesses (Figure 5). A similar pattern was observed for pneumonia.

DISCUSSION

In the present study, increases in levels of particulate pollution (especially of fine particulates) were related to an increase in REVs among children and to an increase in REVs for pneumonia, after controlling for trend, epidemic, and the effect of climatic variables. Levels of other air pollutants (SO_2, NO_2) were also related to the number of REVs; however, because of the high correlation between contaminants in our study, it is difficult to establish their independent health effects. This supports the fact that exposure to air pollution mixture may decrease immune functions and increase the risk for respiratory infections among children.

In Santiago, the major air pollution problem is related to particulates that frequently exceed the current guidelines, in particular during the winter. In our study, during the cold months the mean $PM_{2.5}$ was 71.3 $\mu g/m^3$ and ranged from 10 to 156 $\mu g/m^3$. These fine particulates are mainly coming from vehicular exhaust.[7] Diesel is widely used in Santiago for public transportation. A recent study has shown higher levels of benzo(a) pirene

Table 4. Regression coefficients and RRs for REVs: Santiago, Chile, 1995–1996.

Variables ($\mu g/m^3$)	Coefficients	SE	Interquartile	RR	95% CI	
Cold months						
PM_{10}, lag 2	0.0003	0.0001	76.0	1.0231	1.0060	1.0406
PM_{10}, lag 3	0.0003	0.0001	76.0	1.0232	1.0063	1.0404
PM_{10}, avg 7	0.0006	0.0002	48.3	1.0296	1.0108	1.0488
$PM_{2.5}$, lag 2	0.0006	0.0002	45.0	1.0273	1.0106	1.0443
$PM_{2.5}$, lag 3	0.0005	0.0002	45.0	1.0247	1.0083	1.0414
$PM_{2.5}$, avg 7	0.0011	0.0003	30.6	1.0354	1.0166	1.0544
$PM_{(10-2.5)}$, lag 2	0.0004	0.0003	32.0	1.0133	0.9968	1.0300
$PM_{(10-2.5)}$, lag 3	0.0005	0.0003	32.0	1.0170	1.0007	1.0336
$PM_{(10-2.5)}$, avg 7	0.0009	0.0005	19.9	1.0181	0.9985	1.0381
SO_2, lag 2	0.0009	0.0002	31.46	1.0289	1.0151	1.0428
SO_2, lag 3	0.0012	0.0002	31.46	1.0374	1.0236	1.0513
SO_2, avg 7	0.0010	0.0003	22.88	1.0230	1.0086	1.0377
NO_2, lag 2	0.0007	0.0001	56.40	1.0378	1.0211	1.0549
NO_2, lag 3	0.0005	0.0001	56.40	1.0294	1.0131	1.0460
NO_2, avg 7	0.0005	0.0002	33.84	1.0161	1.0000	1.0325
O_3, lag 2	-0.0002	0.0003	24.00	0.9945	0.9784	1.0108
O_3, lag 3	-0.0004	0.0003	24.00	0.9913	0.9755	1.0073
O_3, avg 7	-0.0010	0.0003	40.00	0.9606	0.9347	0.9872
Warm months						
PM_{10}, lag 2	0.0000	0.0003	29.0	1.0005	0.9831	1.0182
PM_{10}, lag 3	0.0006	0.0003	29.0	1.0183	1.0007	1.0362
PM_{10}, avg 7	0.0003	0.0006	22.0	1.0075	0.9813	1.0343
$PM_{2.5}$, lag 2	-0.0004	0.0005	16.0	0.9942	0.9774	1.0112
$PM_{2.5}$, lag 3	0.0004	0.0005	16.0	1.0068	0.9900	1.0240
$PM_{2.5}$, avg 7	-0.0006	0.0010	13.1	0.9920	0.9655	1.0192
$PM_{(10-2.5)}$, lag 2	0.0005	0.0006	14.0	1.0066	0.9909	1.0225
$PM_{(10-2.5)}$, lag 3	0.0012	0.0006	14.0	1.0170	1.0013	1.0329
$PM_{(10-2.5)}$, avg 7	0.0020	0.0012	12.6	1.0254	0.9963	1.0554
SO_2, lag 2	0.0002	0.0006	14.30	1.0029	0.9860	1.0200
SO_2, lag 3	0.0008	0.0006	14.30	1.0108	0.9937	1.0282
SO_2, avg 7	0.0008	0.0014	12.87	1.0108	0.9756	1.0473
NO_2, lag 2	0.0007	0.0004	30.08	1.0208	0.9992	1.0428
NO_2, lag 3	0.0013	0.0004	30.08	1.0395	1.0181	1.0612
NO_2, avg 7	0.0011	0.0006	22.56	1.0251	0.9964	1.0548
O_3, lag 2	0.0006	0.0003	30.00	1.0188	1.0027	1.0352
O_3, lag 3	0.0005	0.0003	30.00	1.0139	0.9977	1.0303
O_3, avg 7	0.0000	0.0004	26.00	0.9992	0.9810	1.0179

and benzo(ghi) perylene and higher mutagenic activities of particulates in Santiago as compared to Tokyo, Japan.[16] Diesel exhaust has also been related to a decrease in immune response,[17] and this may explain the increase in pneumonia observed among children; although, as previously mentioned, we cannot exclude a combining effect of different pollutants. Particulate air pollution could increase the incidence of REVs by adversely affecting specific and nonspecific host defenses of the respiratory tract against pathogens[18] in particular, by adversely affecting mucociliary clearance and macrophages.[19]

The relationship between particulate exposure and adverse health effects has been observed in many ecological studies; however, few studies could investigate the impact of fine particulate ($PM_{2.5}$) on health and provide data on children's risk for pneumonia. Earlier ecological studies have been summarized,[2,3] and results suggested that a 10-$\mu g/m^3$ increase in the PM_{10} daily mean level was related to a 1–4% increase in EVs. In a study conducted in Utah Valley, UT, a positive association was observed between the number of hospital admissions for pneumonia and pleurisy and monthly mean PM_{10} levels among children 0–17 years of age.[20] A recent study conducted in Montreal reported that an increase of 10 $\mu g/m^3$ in $PM_{2.5}$ level was related to a 9.5% increase in REVs among the elderly. In the same study, the number of REVs was related to the aerosol acidity; 4.0 nmol H+/m^3 led to a 5% increase in the mean number of REVs for children under two years of age, but no association was observed with other contaminants in this age group. However, in the Montreal study $PM_{2.5}$ levels were lower than in our study (mean 18.5 $\mu g/m^3$ vs. 71.3 $\mu g/m^3$).[5] In a study, conducted in Ontario, Burnett et al.[4] reported a 19.1% increase in EVs for respiratory infection among children less than two years of age, the O_3 levels exceeded 50 ppb and sulfate levels exceeded 5.3 $\mu g/m^3$. In this study, particulate data were not available, but the authors mentioned that PM_{10} levels were highly correlated to sulfate levels in the study area. In our study, we observed an increase of 1.4% (95% CI 0.36–2.6%) in ERs for pneumonia for every increase of 10 $\mu g/m^3$ in the $PM_{2.5}$ daily mean levels; however, we did not have data on particle-strong acidity and sulfate levels, and the age range in our study was wider

≤15 years), so the results are difficult to compare. In general, we observed stronger coefficients for models including $PM_{2.5}$ than for models including PM_{10} or $PM_{10-2.5}$, but particulate fractions were highly correlated in our data.

We detected significant effects of copollutants. During the cold months, levels of NO_2 and SO_2 were significantly associated with the number of REVs for URIs and for pneumonia. During the warm months, the NO_2 levels were related to the number of EVs for URIs, and the SO_2 levels to the number of EVs for pneumonia. However, because of the high correlation between the levels of these contaminants and particulates in our study, it is difficult to establish the independent health effect of these contaminants, and regression models may have partially captured the effects of particulates. Based on regression models including particulate and one other pollutant, it seems that PM play the most important role in the health effects observed.

Several factors need to be considered in the interpretation of our results. A major problem inherent to the ecological design is the lack of accurate information on the exposure of the population studied. In our study, we used data from the monitoring network of Santiago, whose monitors are mainly located in the center of the city. Therefore, assigning the network pollutant levels to the population living outside of the area of influence of the monitors would be inadequate. We conducted an audit of 5.2% of the study days (30/578) survey during 12 days of the study, and could determine that more than 90% of the patients treated at the emergency room (ER) of the HCM resided in the area of influence of the monitoring network. This minimized error in the exposure estimates of the participants, although spatial variability within the area of influence of the monitoring network remained an issue. It is also important to mention that exposure to indoor air pollutants was not considered in this study, although during the cold months indoor heating is widely used in Santiago. In a sample of our population, the prevalence of kerosene heating was approximately 50%. In our analysis, we assumed that pollution from indoor sources was constant over time; however, on days with lower temperature, indoor air may have been more polluted because of the use of indoor heating. This could result in a systematic increase in measurement error on days of low temperature and high pollution and an overestimation of the impact of outdoor air pollution on respiratory illnesses. However, we also observed a strong association between pneumonia and air pollutant exposure during the warm months, during which children are not exposed to indoor sources of exposure. Furthermore, the impact of outdoor air pollutants on the risk of pneumonia appeared to be larger during the warm months than the cold months, probably because during warm months exposure assessment was more accurate.

Table 5. Regression coefficients and RRs for URIs and pneumonia EVs: Santiago, Chile, 1995–1996.

Cold Months Variables ($\mu g/m^3$)	Coefficients	SE	Interquartile	RR	95% CI	
URIs						
PM_{10}, lag 2	0.0006	0.0002	76.0	1.0443	1.0206	1.0685
PM_{10}, lag 3	0.0004	0.0002	76.0	1.0310	1.0078	1.0548
PM_{10}, avg 7	0.0009	0.0003	48.3	1.0429	1.0172	1.0693
$PM_{2.5}$, lag 2	0.0010	0.0003	45.0	1.0462	1.0232	1.0697
$PM_{2.5}$, lag 3	0.0007	0.0002	45.0	1.0303	1.0079	1.0533
$PM_{2.5}$, avg 7	0.0016	0.0004	30.6	1.0496	1.0239	1.0758
$PM_{(10-2.5)}$, lag 2	0.0011	0.0004	32.0	1.0343	1.0115	1.0576
$PM_{(10-2.5)}$, lag 3	0.0008	0.0004	32.0	1.0268	1.0041	1.0500
$PM_{(10-2.5)}$, avg 7	0.0015	0.0007	19.9	1.0295	1.0027	1.0571
SO_2, lag 2	0.0018	0.0003	31.46	1.0584	1.0394	1.0778
SO_2, lag 3	0.0016	0.0003	31.46	1.0513	1.0324	1.0706
SO_2, avg 7	0.0014	0.0004	22.88	1.0316	1.0120	1.0515
NO_2, lag 2	0.0010	0.0002	56.40	1.0569	1.0339	1.0803
NO_2, lag 3	0.0006	0.0002	56.40	1.0318	1.0095	1.0545
NO_2, avg 7	0.0005	0.0003	33.84	1.0177	0.9960	1.0399
O_3, lag 2	0.0006	0.0005	24.00	1.0141	0.9921	1.0366
O_3, lag 3	0.0001	0.0005	24.00	1.0028	0.9814	1.0247
O_3, avg 7	0.0000	0.0005	40.00	0.9994	0.9634	1.0368
Pneumonia						
PM_{10}, lag 2	0.0006	0.0003	76.0	1.0475	0.9952	1.1025
PM_{10}, lag 3	0.0010	0.0003	76.0	1.0773	1.0252	1.1320
PM_{10}, avg 7	0.0014	0.0006	48.3	1.0704	1.0119	1.1322
$PM_{2.5}$, lag 2	0.0009	0.0006	45.0	1.0406	0.9899	1.0939
$PM_{2.5}$, lag 3	0.0014	0.0005	45.0	1.0670	1.0165	1.1200
$PM_{2.5}$, avg 7	0.0022	0.0009	30.6	1.0702	1.0123	1.1313
$PM_{(10-2.5)}$, lag 2	0.0014	0.0008	32.0	1.0472	0.9977	1.0991
$PM_{(10-2.5)}$, lag 3	0.0023	0.0007	32.0	1.0760	1.0268	1.1276
$PM_{(10-2.5)}$, avg 7	0.0032	0.0015	19.9	1.0653	1.0050	1.1292
SO_2, lag 2	0.0005	0.0007	31.46	1.0164	0.9757	1.0587
SO_2, lag 3	0.0011	0.0006	31.46	1.0342	0.9938	1.0762
SO_2, avg 7	0.0013	0.0010	22.88	1.0291	0.9850	1.0751
NO_2, lag 2	0.0014	0.0004	56.40	1.0824	1.0300	1.1374
NO_2, lag 3	0.0013	0.0004	56.40	1.0768	1.0273	1.1287
NO_2, avg 7	0.0016	0.0007	33.84	1.0564	1.0062	1.1092
O_3, lag 2	-0.0010	0.0010	24.00	0.9759	0.9290	1.0251
O_3, lag 3	0.0000	0.0010	24.00	0.9998	0.9525	1.0494
O_3, avg 7	-0.0021	0.0011	40.00	0.9205	0.8467	1.0007

Continued on next page.

Table 5 (Continued from previous page). Regression coefficients and RRs for URIs and pneumonia EVs, Santiago, Chile, 1995–1996.

Warm Months Variables ($\mu g/m^3$)	Coefficients	SE	Interquartile	RR	95% CI	
URIs						
PM_{10}, lag 2	-0.0002	0.0004	29.0	0.9939	0.9723	1.0160
PM_{10}, lag 3	0.0007	0.0004	29.0	1.0206	0.9986	1.0431
PM_{10}, avg 7	-0.0003	0.0008	22.0	0.9925	0.9604	1.0256
$PM_{2.5}$, lag 2	-0.0009	0.0007	16.0	0.9862	0.9652	1.0075
$PM_{2.5}$, lag 3	0.0004	0.0007	16.0	1.0064	0.9852	1.0280
$PM_{2.5}$, avg 7	-0.0012	0.0013	13.1	0.9838	0.9510	1.0177
$PM_{(10-2.5)}$, lag 2	0.0003	0.0007	14.0	1.0036	0.9841	1.0235
$PM_{(10-2.5)}$, lag 3	0.0016	0.0007	14.0	1.0221	1.0025	1.0421
$PM_{(10-2.5)}$, avg 7	0.0003	0.0015	12.6	1.0034	0.9681	1.0400
SO_2, lag 2	0.0004	0.0008	14.30	1.0061	0.9850	1.0277
SO_2, lag 3	0.0009	0.0008	14.30	1.0130	0.9916	1.0349
SO_2, avg 7	-0.0014	0.0018	12.87	0.9815	0.9390	1.0260
NO_2, lag 2	0.0005	0.0005	30.08	1.0150	0.9881	1.0426
NO_2, lag 3	0.0014	0.0004	30.08	1.0425	1.0157	1.0699
NO_2, avg 7	-0.0002	0.0008	22.56	0.9944	0.9591	1.0311
O_3, lag 2	0.0006	0.0003	30.00	1.0180	0.9978	1.0387
O_3, lag 3	0.0005	0.0003	30.00	1.0161	0.9956	1.0370
O_3, avg 7	-0.0007	0.0005	26.00	0.9820	0.9592	1.0053
Pneumonia						
PM_{10}, lag 2	0.0031	0.0011	29.0	1.0955	1.0309	1.1641
PM_{10}, lag 3	0.0015	0.0011	29.0	1.0460	0.9853	1.1104
PM_{10}, avg 7	0.0053	0.0021	22.0	1.1243	1.0268	1.2311
$PM_{2.5}$, lag 2	0.0053	0.0018	16.0	1.0893	1.0290	1.1531
$PM_{2.5}$, lag 3	0.0033	0.0018	16.0	1.0546	0.9967	1.1159
$PM_{2.5}$, avg 7	0.0090	0.0036	13.1	1.1250	1.0256	1.2339
$PM_{(10-2.5)}$, lag 2	0.0035	0.0020	14.0	1.0497	0.9947	1.1077
$PM_{(10-2.5)}$, lag 3	0.0005	0.0019	14.0	1.0074	0.9550	1.0627
$PM_{(10-2.5)}$, avg 7	0.0083	0.0040	12.6	1.1101	1.0053	1.2258
SO_2, lag 2	0.0067	0.0020	14.30	1.1010	1.0404	1.1653
SO_2, lag 3	0.0017	0.0021	14.30	1.0248	0.9669	1.0862
SO_2, avg 7	0.0151	0.0048	12.87	1.2151	1.0771	1.3709
NO_2, lag 2	0.0039	0.0012	30.08	1.1232	1.0450	1.2072
NO_2, lag 3	0.0001	0.0012	30.08	1.0029	0.9332	1.0779
NO_2, avg 7	0.0046	0.0022	22.56	1.1084	1.0071	1.2200
O_3, lag 2	0.0030	0.0009	30.00	1.0934	1.0369	1.1529
O_3, lag 3	0.0018	0.0009	30.00	1.0545	0.9994	1.1126
O_3, avg 7	0.0037	0.0012	26.00	1.0997	1.0343	1.1693

Another concern about interpreting the results of epidemiological studies is that the length of the lead-lag relationship of particulate pollution effects differ across studies.[2] These differences may be partially due to disparities in the type of healthcare visits and healthcare delivery systems. To better understand the lag between exposure and effect in our study, we conducted a survey to determine the lag between the first symptoms and the time of the visit to the ER. This survey indicated that for respiratory patients, the median number of days between the onset of the first symptoms and the REV was two to three days for the majority of the patients (70%). This lag corresponded to that observed in our analysis. This observation gives more weight to our results because, in many cases, the pattern of EVs is unknown, and it is therefore difficult to determine the relevant exposure associated with the health effects. While it is not sufficient evidence to infer a causal association, it does suggest that on average, the timing of the air pollution effect is consistent with the temporal pattern of REVs in this population.

One of the major strengths of our study is that the large number of REVs observed on a daily basis gave enough power to examine specific diagnoses. During the cold months, an average of 144.59 respiratory visits per day were observed, reaching a maximum of 349 visits per day. These included a mean of 16.8 and a maximum of 54 visits for pneumonia per day. A total of 61,337 REVs and 6,344 EVs for pneumonia occurred during the study. We also ascertained respiratory diagnoses and treatment by emergency physicians based on the norms of the pediatric guidelines from the Chilean Ministry of Health.[11] We observed that diagnoses were based on medical examinations and complementary exams, including laboratory and X-ray exams when necessary. Therefore, we believe that the diagnoses provided were largely accurate and particularly accurate for pneumonia. We also conducted an audit of the quality of the daily medical records for EVs and found errors in less than 2% of the records reviewed.

Our results suggest that air pollution mixtures observed in large cities are toxic pollutants for children's respiratory tract and are related to an increased risk for respiratory illnesses, in particular pneumonia. It is likely that a large part of the adverse effects observed are related to fine particulate exposure, although our data cannot clearly separate the specific role played by each pollutant. These findings are of large public health relevance given the health and economical burden imposed by these diseases. In Chile, acute respiratory illness is the second leading cause of years of life lost for incapacity, after congenital malformation.[21] Although control measures are being implemented, further studies are needed to better understand the adverse effects that particulate pollution has on human health. Such studies should be

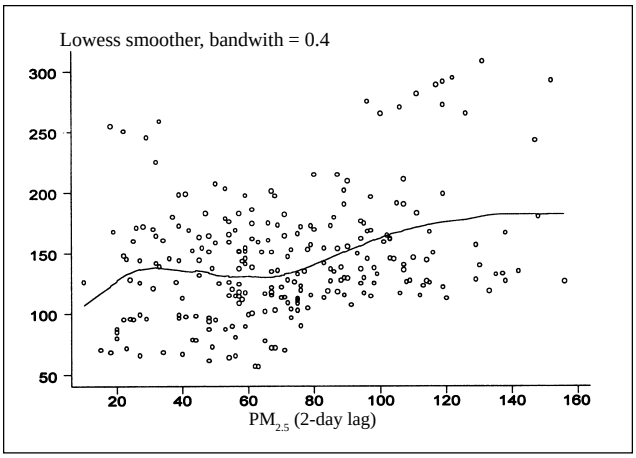

Figure 4. Smooth function (Lowess) of the total number of respiratory-related emergency visits estimated by the regression model versus $PM_{2.5}$ lag 2 (µg/m³): Santiago, Chile, 1995–1996.

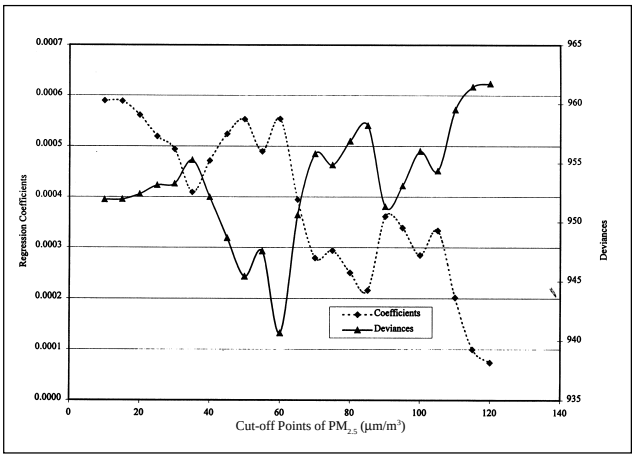

Figure 5. Regression coefficients and deviances from hockey-stick regression models between $PM_{2.5}$ lag 2 and total REVs during cold months: Santiago, Chile, 1995–1996.

conducted prospectively and should evaluate exposure to outdoor and indoor air pollutants and ascertain health outcomes in a standardized manner. The impact of particulate composition on health effects should also be considered.

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