



Gaseous Air Pollutants and Asthma Hospitalization of Children with Low Household Income in Vancouver, British Columbia, Canada

Mei Lin¹, Yue Chen^{1,2}, Paul J. Villeneuve³, Richard T. Burnett^{2,4}, Louise Lemyre⁵, Clyde Hertzman⁶, Kimberlyn M. McGrail⁶, and Daniel Krewski^{1,2}

¹ Department of Epidemiology and Community Medicine, Faculty of Medicine, University of Ottawa, Ottawa, Ontario, Canada.

² McLaughlin Centre for Population Health Risk Assessment, University of Ottawa, Ottawa, Ontario, Canada.

³ Department of Public Health Sciences, University of Toronto, Toronto, Ontario, Canada.

⁴ Safe Environments Directorate, Health Canada, Ottawa, Ontario, Canada.

⁵ School of Psychology, Faculty of Social Sciences, Institute of Population Health, University of Ottawa, Ottawa, Ontario, Canada.

⁶ Centre for Health Services and Policy Research, University of British Columbia, Vancouver, British Columbia, Canada.

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Associations of gaseous air pollutants (including carbon monoxide, sulfur dioxide, nitrogen dioxide, and ozone) with asthma hospitalization, stratified by sex and socioeconomic status, were examined among children 6–12 years of age in Vancouver, British Columbia, Canada, between 1987 and 1998. Relative risks for an exposure increment corresponding to the interquartile range for each gaseous air pollutant were estimated for asthma hospitalization after adjustment for weather conditions, including daily maximum and minimum temperatures as well as average relative humidity. Similar results were obtained by using locally weighted smoothing functions (LOESS) with default convergence criteria and by using natural cubic splines with a more stringent setting. Exposures to nitrogen dioxide were found to be significantly and positively associated with asthma hospitalization for males in the low socioeconomic group but not in the high socioeconomic group. For females, this same pattern of association was observed for exposures to sulfur dioxide. No significantly positive associations were found between carbon monoxide and ozone and asthma hospitalization in either low or high socioeconomic groups.

air pollution; asthma; child; hospitalization; social class

Abbreviations: CI, confidence interval; GAM, generalized additive model; LOESS, locally weighted smoothing function; SES, socioeconomic status.

A number of studies have related gaseous air pollutants to asthma hospitalization or emergency room visits (1–11). However, the findings obtained from these studies are equivocal. Inconsistencies among such studies may be partly due to differences in exposure levels in different study areas and differences in susceptibility to the adverse health effects of ambient air pollution among the populations examined. Questions have recently been raised about the existence of sensitive population subgroups, defined by age, sex, race, or socioeconomic status (SES) (12, 13).

SES is a comprehensive index that refers to a broad range of factors, such as level of social standing, income, education, and living conditions (14, 15). Specific material and social characteristics of people at different socioeconomic

levels may contribute to differences in environmental exposure patterns, health behaviors, and risks of developing certain diseases (16). However, it is still not clear whether people of a lower SES bear a disproportionate burden of the adverse health impacts of air pollution. Two recent studies found a stronger association between exposure to particulate matter and mortality in populations with lower educational and income levels relative to those with higher levels (12, 17), although converse results were observed in Sao Paulo, Brazil (13). Other studies have reported that lower SES is a risk factor for asthma (18–20). However, the potential modifying effect of SES on the relation between air pollution and asthma hospitalization has not been studied extensively. The purpose of the present study was to evaluate the associations

Reprint requests to Dr. Yue Chen, Department of Epidemiology and Community Medicine, University of Ottawa, 451 Smyth Road, Ottawa, Ontario, Canada K1H 8M5 (e-mail: ychen@uottawa.ca).

between gaseous air pollutants and asthma hospitalization stratified by sex and SES among children 6–12 years of age in Vancouver, British Columbia, Canada.

MATERIALS AND METHODS

The present analysis was based on air pollution and asthma hospitalization data from 13 census subdivisions in the Vancouver area between 1987 and 1998. Hospitalization data were obtained from the British Columbia Linked Health Dataset described by Chamberlayne et al. (21). This comprehensive and dynamic database includes all provincial health care records and covers virtually all residents of British Columbia.

Asthma hospitalization data for acute care hospitals were extracted from this person-oriented hospital separation database including separations for inpatient care for children 6–12 years of age admitted in the Vancouver area between 1987 and 1998. We selected this age group for the following reasons. First, children are generally thought to be more susceptible than adults to the adverse health effects of air pollution. Second, the diagnosis of asthma is problematic for infants and young children. Some children under 6 years of age experience transient wheezing, which is frequently resolved as they become older (22). This phenomenon may be partly due to the rapid growth and development of the lungs during infancy and childhood.

We defined asthma hospitalization as an admission for which one of the first five diagnoses was asthma (*International Classification of Diseases*, Ninth Revision, code 493). The data available for each record included age, sex, admission and discharge dates, and SES as measured by census indicators at the local health area level. Hospital admissions outside of the Vancouver area were excluded since they were unlikely to be related to the air pollution levels in this area.

Daily measurements of gaseous air pollutants were available from five to 31 monitoring stations between January 1, 1987, and December 31, 1998. Specifically, daily average pollutant levels were available for carbon monoxide (six stations), sulfur dioxide (four stations), and nitrogen dioxide (30 stations), while daily levels of the maximum 1-hour ozone concentration were obtained from 25 stations. Measurements of fine particulate matter (<2.5 μm in average aerodynamic diameter) and thoracic particulate matter (<10 μm in average aerodynamic diameter) were available only for the period 1995–1998. Daily data on weather conditions, including daily maximum and minimum temperatures and average relative humidity, were obtained from meteorologic monitoring conducted from the Vancouver international airport.

Time-series analysis was used to examine the associations between ambient levels of gaseous air pollutants and asthma hospitalization. The generalized additive model (GAM) (23) was used nonparametrically. To take into account possible overdispersion of daily hospital admission counts, quasi-likelihood estimation was used. Both asthma hospitalization and air pollution display strong temporal trends. The potential confounding effects of these cycles on the association between air pollution and asthma hospitalization were

controlled by including a nonparametric function, a locally weighted smoothing function (LOESS) (24) of day of study with a selected span of 93 days. The smoother is characterized by defining a window of observations with fixed length about a specified day (25). The span is defined as the percentage of data points used as nearest neighbors. The appropriate span was characterized by minimal autocorrelation in the residuals of asthma hospitalization and was examined by Bartlett's test with no significant serial correlation (26). In addition to the LOESS function of days of the study, day-of-week indicator variables and weather conditions were also considered as covariates. On the basis of results from previous studies (27, 28) and smoothing functions of asthma hospitalization and meteorologic data, we added squared terms for each of the weather variables as additional covariates. Relative risks were calculated based on an increment in exposure corresponding to the interquartile range for each gaseous air pollutant. The time-series analysis was run with S-PLUS 2000 Professional Edition for Windows software (29) by using the GAM function.

Recently, concerns have been raised about some nonparametric smoothing functions used in GAMs (30, 31). Ramsay et al. (30) used a simulation analysis to demonstrate that S-PLUS can underestimate the variance of fitted model parameters if concurrency, the nonparametric analogue of multicollinearity, is present in the data. In another simulation study, Dominici et al. (31) found that the default convergence parameters in the GAM function in S-PLUS may overestimate relative risks and produce standard errors that are too small, thereby overestimating the significance of observed associations between air pollution and hospital admission or mortality. It was also found that the upper bias in the relative risk is larger when LOESS smoothers are used compared with the smoothing splines. Dominici et al. further observed that GAMs with stricter convergence criteria can be used to obtain risk estimates closer to the true values used in their simulation studies. To determine whether this was the case for our data, we repeated our analyses with natural cubic splines instead of LOESS functions by using 1,000 iterations and a convergence criterion of 10^{-15} . Natural cubic splines divide the data into a prespecified number of knots. Cubic polynomial regression is carried out within each region defined by these knots (31, 32). We used one knot for every 3 months because Bartlett's test revealed no significant serial correlation in the asthma hospitalization residuals with this choice (26).

The acute effects of air pollution may be immediate or they may occur several days after exposure. We considered a cumulative lag structure, which examines the acute effects of 1-day and multiple-day average air pollution levels ending on the admission date and reduces the effect of the short-term autocorrelation (within 5–7 days) in the environmental variables (27, 33). One- to 7-day exposure averages were considered in this study.

To explore possible differences in air pollution effects due to sex or SES, we conducted separate analyses for males and females and for different categories of SES. In this study, SES was represented by average household income adjusted for household size within each enumeration area defined by

TABLE 1. Distributions of daily concentrations of gaseous air pollutants, weather conditions, and asthma hospitalizations among children 6–12 years of age, Vancouver, British Columbia, Canada, 1987–1998

Variable	Mean (SD)*	Percentile				
		Minimum	25th	50th	75th	Maximum
Air pollution						
CO* (ppm)	0.96 (0.52)	0.23	0.62	0.80	1.12	4.90
SO ₂ * (ppb)	4.77 (2.75)	0	2.75	4.25	6.00	24.00
NO ₂ * (ppb)	18.65 (5.59)	4.28	14.82	17.75	21.36	45.36
O ₃ * (ppb)	28.02 (11.54)	1.93	20.19	27.70	35.00	105.50
Weather conditions						
Relative humidity (%)	73.1 (12.6)	17.0	64.0	72.0	83.0	100.0
Maximum temperature (°C)	14.14 (6.36)	-7.60	9.20	13.80	19.40	31.90
Minimum temperature (°C)	6.99 (5.60)	-14.10	3.20	7.30	11.60	19.90
Asthma hospitalizations						
Total (<i>n</i> = 3,822)	0.87 (1.05)	0	0	1	1	10
Males (<i>n</i> = 2,368)	0.54 (0.80)	0	0	0	1	6
Females (<i>n</i> = 1,454)	0.33 (0.60)	0	0	0	1	5

* SD, standard deviation; CO, carbon monoxide (daily average); SO₂, sulfur dioxide (daily average); NO₂, nitrogen dioxide (daily average); O₃, ozone (daily maximum 1-hour concentration).

the Canadian census. Specifically, SES was obtained from the 1991 census for hospitalizations from 1987 to 1993 and from the 1996 census for those persons admitted between 1994 and 1998. The enumeration area is the smallest standard geographic area for which census data are reported and is enumerated by one census representative. The number of dwellings in an enumeration area may vary from 375 in large urban areas to 125 in rural areas. SES was grouped into two levels: “low” SES was classified as an average income for which percentiles did not exceed the 50th percentile for the Vancouver population, whereas “high” SES was defined as percentiles of more than the median.

RESULTS

Table 1 provides summary statistics for the gaseous air pollutants, weather conditions, and asthma hospitalization. In this study, 3,754 asthma hospitalizations occurred for children 6–12 years of age (2,331 for males and 1,423 for females), with a daily average of 0.87 admissions (0.54 for males and 0.33 for females) in Vancouver between 1987 and 1998. Daily concentrations of gaseous air pollutants in Vancouver were relatively low compared with the maximum acceptable levels given by Canada’s National Ambient Air Quality Objectives (NAAQOs) (34). The daily average levels of carbon monoxide, sulfur dioxide, and nitrogen

TABLE 2. Correlations between daily concentrations of gaseous air pollutants and weather conditions in Vancouver, British Columbia, Canada, 1987–1998

Gaseous air pollutant/ weather condition	Gaseous air pollutant				Weather condition		
	CO*	SO ₂ *	NO ₂ *	O ₃ *	Maximum temperature	Minimum temperature	Relative humidity
CO	1.00	0.67	0.73	-0.35	-0.32	-0.42	0.21
SO ₂		1.00	0.67	-0.10	0.002	-0.18	-0.001
NO ₂			1.00	-0.03	-0.16	-0.34	0.03
O ₃				1.00	0.58	0.43	-0.58
Maximum temperature					1.00	0.91	-0.44
Minimum temperature						1.00	-0.20
Relative humidity							1.00

* CO, carbon monoxide (daily average); SO₂, sulfur dioxide (daily average); NO₂, nitrogen dioxide (daily average); O₃, ozone (daily maximum 1-hour concentration).

TABLE 3. Distribution of asthma hospitalizations by sex and SES* among children 6–12 years of age, Vancouver, British Columbia, Canada, 1987–1998

Sex	SES		Total
	Low	High	
Males	1,271	1,060	2,331
Females	754	669	1,423
Total	2,025	1,729	3,754

* "Low" socioeconomic status (SES) was classified as an average income for which percentiles did not exceed the 50th percentile for the Vancouver population, whereas "high" SES was defined as percentiles of more than the median.

dioxide never exceeded the national guidelines; the maximum values were only 37 percent of the guideline for carbon monoxide (13.1 ppm), 21 percent for sulfur dioxide (115 ppb), and 42 percent for nitrogen dioxide (106 ppb). For only 5 days (0.1 percent) of the total of 4,383 days did levels of maximum 1-hour ozone concentrations exceed the 82-ppb objective.

Table 2 shows the correlations among the gaseous air pollutants and weather conditions. Carbon monoxide, sulfur dioxide, and nitrogen dioxide were positively and highly

correlated with each other, whereas ozone was negatively correlated with carbon monoxide ($r = -0.35$). Weather conditions were related to the gaseous air pollutants, with relatively strong correlations with ozone. Carbon monoxide and nitrogen dioxide were both negatively correlated with temperature, and ozone was positively related to temperature and negatively correlated with relative humidity.

Table 3 shows asthma hospitalizations stratified by sex and SES. There were more asthma admissions of males than of females. We excluded 68 (1.8 percent) children admitted for asthma because SES was missing in subsequent time-series analyses.

Tables 4 and 5 provide estimates of the relative risk of asthma hospitalization in relation to each gaseous air pollutant based on time-series analysis that included LOESS functions with default convergence parameters for males and females separately. Specifically, figures 1, 2, 3, and 4 display relative risk estimates for nitrogen dioxide and sulfur dioxide stratified by SES for males and females, respectively. For males, 1- to 4-day average exposures to nitrogen dioxide (table 4) showed significantly positive effects on asthma hospitalization in the low SES group, with relative risk estimates ranging from 1.13 (95 percent confidence interval (CI): 1.04, 1.23) for 1-day to 1.14 (95 percent CI: 1.02, 1.28) for 4-day averages (as shown in figure 1). Similarly, 4- to 6-day average exposures to sulfur dioxide in females (table 5)

TABLE 4. Adjusted relative risk estimates* and 95% confidence intervals for asthma hospitalization in relation to daily concentrations of gaseous air pollutants in males 6–12 years of age stratified by SES†, Vancouver, British Columbia, Canada, 1987–1998‡

Pollutant (IQR) and SES	Exposure averaging period													
	1 day		2 days		3 days		4 days		5 days		6 days		7 days	
	RR	95% CI§	RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI
CO§ (0.5 ppm)														
Low	1.06	0.99, 1.14	1.03	0.95, 1.12	1.01	0.93, 1.11	0.99	0.90, 1.09	0.96	0.87, 1.06	0.98	0.88, 1.08	0.98	0.88, 1.09
High	1.06	0.98, 1.14	1.06	0.97, 1.15	1.07	0.97, 1.17	1.03	0.93, 1.14	1.01	0.91, 1.12	1.01	0.91, 1.13	1.06	0.94, 1.18
SO ₂ § (3.3 ppb)														
Low	1.02	0.94, 1.10	1.03	0.94, 1.13	1.03	0.93, 1.15	1.01	0.90, 1.13	0.98	0.88, 1.10	0.97	0.86, 1.10	0.98	0.86, 1.12
High	1.03	0.95, 1.12	1.06	0.96, 1.17	1.06	0.95, 1.18	1.04	0.92, 1.17	1.02	0.90, 1.14	1.02	0.89, 1.16	1.05	0.91, 1.21
NO ₂ § (6.5 ppb)														
Low	1.13	1.04, 1.23	1.13	1.02, 1.24	1.14	1.02, 1.27	1.14	1.02, 1.28	1.12	0.99, 1.27	1.12	0.98, 1.28	1.11	0.97, 1.28
High	1.04	0.95, 1.14	1.06	0.95, 1.18	1.06	0.94, 1.19	1.05	0.92, 1.19	1.10	0.96, 1.26	1.07	0.93, 1.23	1.09	0.94, 1.27
O ₃ § (14.8 ppb)														
Low	0.85	0.76, 0.94	0.86	0.77, 0.97	0.86	0.76, 0.98	0.85	0.75, 0.98	0.85	0.74, 0.98	0.84	0.72, 0.96	0.80	0.69, 0.93
High	0.93	0.83, 1.04	0.89	0.78, 1.01	0.81	0.70, 0.93	0.84	0.72, 0.97	0.90	0.77, 1.05	0.93	0.79, 1.09	0.93	0.79, 1.09

* The relative risk (RR) estimates were calculated for an interquartile range (IQR) increment of each gaseous air pollutant, which was calculated based on daily levels. The relative risk estimates were adjusted for daily weather conditions (maximum temperature, minimum temperature, and average relative humidity).

† "Low" socioeconomic status (SES) was classified as an average income for which percentiles did not exceed the 50th percentile for the Vancouver population, whereas "high" SES was defined as percentiles of more than the median.

‡ Time-series analysis was used. Generalized additive models using locally weighted smoothing functions (LOESS) with default convergence criteria in S-PLUS software (MathSoft, Inc., Seattle, Washington).

§ CI, confidence interval; CO, carbon monoxide (daily average); SO₂, sulfur dioxide (daily average); NO₂, nitrogen dioxide (daily average); O₃, ozone (daily maximum 1-hour concentration).

TABLE 5. Adjusted relative risk estimates* and 95% confidence intervals for asthma hospitalization in relation to daily concentrations of gaseous air pollutants in females 6–12 years of age stratified by SES†, Vancouver, British Columbia, Canada, 1987–1998‡

Pollutant (IQR) and SES	Exposure averaging period													
	1 day		2 days		3 days		4 days		5 days		6 days		7 days	
	RR	95% CI§	RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI
CO§ (0.5 ppm)														
Low	1.01	0.92, 1.11	0.98	0.89, 1.10	0.99	0.88, 1.11	1.05	0.93, 1.19	1.07	0.94, 1.21	1.07	0.94, 1.23	1.04	0.91, 1.20
High	1.05	0.94, 1.16	1.02	0.90, 1.15	0.97	0.85, 1.11	0.95	0.83, 1.10	0.93	0.80, 1.08	0.95	0.82, 1.11	1.01	0.87, 1.19
SO ₂ § (3.3 ppb)														
Low	1.05	0.95, 1.16	1.11	0.99, 1.25	1.11	0.97, 1.26	1.18	1.02, 1.36	1.18	1.02, 1.35	1.19	1.01, 1.40	1.15	0.97, 1.36
High	1.07	0.96, 1.19	1.07	0.94, 1.21	1.07	0.93, 1.23	1.02	0.87, 1.19	0.99	0.85, 1.15	0.95	0.80, 1.13	0.98	0.81, 1.17
NO ₂ § (6.5 ppb)														
Low	1.07	0.96, 1.19	1.03	0.91, 1.17	1.04	0.91, 1.20	1.11	0.95, 1.29	1.11	0.94, 1.30	1.08	0.91, 1.28	1.07	0.90, 1.28
High	1.01	0.90, 1.13	0.98	0.85, 1.12	0.98	0.84, 1.13	1.01	0.86, 1.19	0.99	0.83, 1.17	1.03	0.86, 1.24	1.09	0.90, 1.32
O ₃ § (14.8 ppb)														
Low	1.11	0.97, 1.28	1.11	0.96, 1.30	1.08	0.92, 1.28	1.16	0.97, 1.38	1.19	0.99, 1.43	1.15	0.95, 1.39	1.12	0.92, 1.36
High	0.91	0.78, 1.05	0.97	0.82, 1.14	1.05	0.88, 1.25	1.10	0.91, 1.32	1.17	0.96, 1.41	1.18	0.97, 1.45	1.16	0.94, 1.42

* The relative risk (RR) estimates were calculated for an interquartile range (IQR) increment of each gaseous air pollutant, which was calculated based on daily levels. The relative risk estimates were adjusted for daily weather conditions (maximum temperature, minimum temperature, and average relative humidity).

† "Low" socioeconomic status (SES) was classified as an average income for which percentiles did not exceed the 50th percentile for the Vancouver population, whereas "high" SES was defined as percentiles of more than the median.

‡ Time-series analysis was used. Generalized additive models using locally weighted smoothing functions (LOESS) with default convergence criteria in S-PLUS software (MathSoft, Inc., Seattle, Washington).

§ CI, confidence interval; CO, carbon monoxide (daily average); SO₂, sulfur dioxide (daily average); NO₂, nitrogen dioxide (daily average); O₃, ozone (daily maximum 1-hour concentration).

were significantly and positively associated with asthma hospitalization in the low SES group but not in the high SES group; relative risks were 1.18 (95 percent CI: 1.02, 1.36) for a 4-day average and 1.19 (95 percent CI: 1.01, 1.40) for a 6-

day average (as shown in figure 4). Nitrogen dioxide and sulfur dioxide were highly correlated ($r = 0.67$). However, when both sulfur dioxide and nitrogen dioxide were included in the models, the effects of nitrogen dioxide in males and

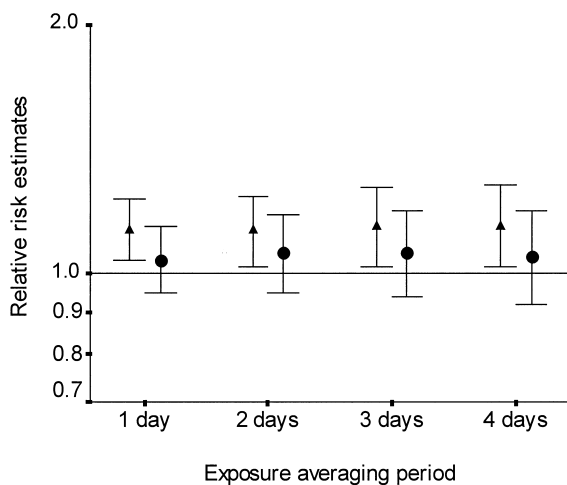


FIGURE 1. Adjusted relative risk estimates and 95% confidence intervals for nitrogen dioxide exposure in males stratified by socioeconomic status, Vancouver, British Columbia, Canada, 1987–1998. Circles, low socioeconomic status; triangles, high socioeconomic status.

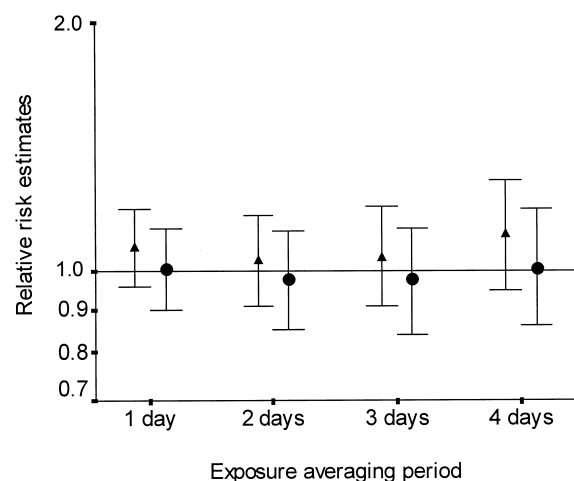


FIGURE 2. Adjusted relative risk estimates and 95% confidence intervals for nitrogen dioxide exposure in females stratified by socioeconomic status, Vancouver, British Columbia, Canada, 1987–1998. Circles, low socioeconomic status; triangles, high socioeconomic status.

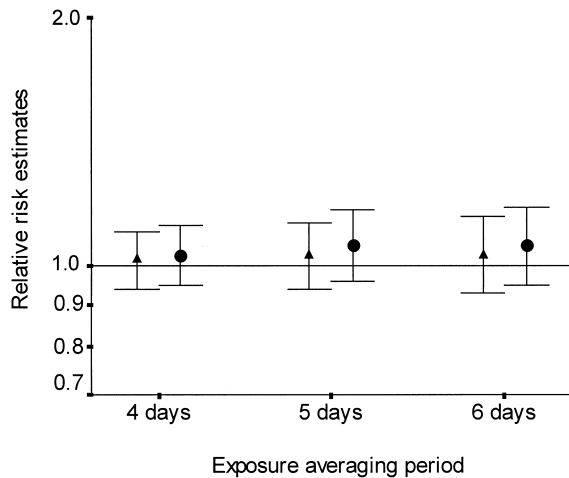


FIGURE 3. Adjusted relative risk estimates and 95% confidence intervals for sulfur dioxide exposure in males stratified by socioeconomic status, Vancouver, British Columbia, Canada, 1987–1998. Circles, low socioeconomic status; triangles, high socioeconomic status.

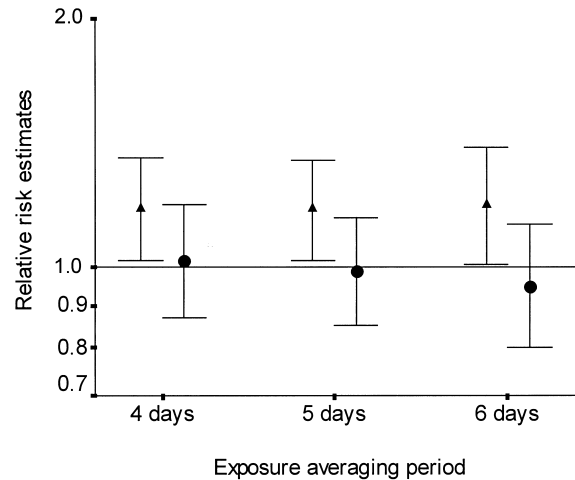


FIGURE 4. Adjusted relative risk estimates and 95% confidence intervals for sulfur dioxide exposure in females stratified by socioeconomic status, Vancouver, British Columbia, Canada, 1987–1998. Circles, low socioeconomic status; triangles, high socioeconomic status.

sulfur dioxide in females in the low SES group remained significant. The relative risk estimates for males were 1.16 (95 percent CI: 1.06, 1.28) for 1-day nitrogen dioxide exposure and 1.18 (95 percent CI: 1.03, 1.34) for 4-day nitrogen dioxide exposure. For sulfur dioxide, the relative risk estimates for females were 1.17 (95 percent CI: 1.00, 1.37) for a 4-day average and 1.19 (95 percent CI: 1.00, 1.42) for a 6-day average. No significant positive effect of either carbon monoxide or ozone on asthma hospitalization was found for males or females in either the low or high SES group.

Use of natural cubic splines with a more stringent convergence rate produced results similar to those in which LOESS functions were used with default settings. However, the standard errors of the model parameters were slightly larger when natural splines were used. As in our first analysis, 1- to 4-day exposures to nitrogen dioxide in males and 4- to 6-day average exposures to sulfur dioxide in females were significantly related to asthma hospitalization in the low SES group but not in the high SES group.

DISCUSSION

In our study, no significantly positive associations of carbon monoxide and ozone with asthma hospitalization were observed for either males or females. However, nitrogen dioxide (males only) and sulfur dioxide (females only) were found to be significantly and positively associated with asthma hospitalization in the low SES group but not in the high SES group.

Previous findings regarding the association between gaseous air pollutants and asthma hospitalization have been inconsistent. One study conducted in Vancouver observed no significant correlation between asthma emergency room visits and levels of sulfur dioxide, nitrogen dioxide, and ozone for children aged 1–14 years (35). However, this study

did not consider potential effects of air pollution exposure at lags of more than 2 days. In addition, a simple correlation study may not be sufficiently sensitive to detect the adverse effects of air pollution at relatively low levels (36). Three other studies have used time-series methods to assess the relation between air pollution and asthma hospital admissions or emergency room visits in Seattle, Washington, an urban area close to Vancouver (2, 28, 37). Air pollutant levels in Seattle were slightly higher than those in Vancouver. Two of these studies (2, 37) found a significant association between carbon monoxide and hospital admissions or emergency room visits for asthma for subjects less than 18 years of age as well as for all ages combined. However, Norris et al. (2) postulated that carbon monoxide could be acting as a surrogate for particulate matter. Carbon monoxide has been commonly thought to be an air pollutant closely associated with adverse effects on the heart. To date, no plausible mechanism has been observed by which carbon monoxide might exacerbate asthma (38). No association with sulfur dioxide was observed in any of these three studies. Only one study assessed the effect of nitrogen dioxide but observed no association with asthma (2). For ozone, two studies reported no effect on emergency room visits for asthma (2, 28), whereas the third reported a significant association between ozone with a 2-day lag and asthma hospitalization in all age groups (37).

A number of studies relating gaseous air pollutants and asthma hospitalization have also been conducted in other urban areas throughout the world. Significant effects were found for carbon monoxide in Toronto, Ontario, Canada (1); for sulfur dioxide exposures in Paris, France (39), and Birmingham, United Kingdom (40); and for nitrogen dioxide in Paris (39) and Sydney, Australia (3). However, other studies have failed to demonstrate a significant effect of sulfur dioxide or nitrogen dioxide on asthma hospitalization

or emergency room visits (2, 5, 6). The effect of ozone on asthma hospitalization and emergency room visits varies considerably, especially at low levels of exposure. One study found a significant relation between ozone and asthma emergency room visits for adults but not children in Saint John, New Brunswick, Canada (5). White et al. (41) observed an association between pediatric asthma visits and ozone concentrations exceeding 110 ppb but found no effect for ozone exposure of less than 110 ppb in Atlanta, Georgia. An effect of ozone on asthma hospitalization was not found in other urban areas such as Amsterdam, the Netherlands (6), and Montreal, Quebec, Canada (42), with relatively low ozone concentrations. In our study, we did not observe a significantly positive effect of ozone on asthma hospitalization. However, we found a significantly negative association between ozone and asthma hospitalization for females. The reasons for no positive effect of ozone remain unclear. The negative effect of ozone found in this study may be in part due to the negative correlations between ozone and other gaseous air pollutants.

To date, there have been no consistent results to support the positive associations of sulfur dioxide and nitrogen dioxide with asthma hospitalization found in our study. There are at least two possible reasons that such associations may be found at the relatively low air pollution levels in Vancouver compared with those in most other urban areas of the world. First, the unique geographic and meteorologic characteristics of Vancouver may contribute to the adverse effects of sulfur dioxide and nitrogen dioxide found in this study. The close proximity to both mountains and ocean is one cause of episodes of air pollution in this area. The surrounding mountains inhibit the dispersion of air pollutants, and the inland wind direction enhances air pollution episodes in this area (43). Temperature inversions, in which cold air underlies warmer air at higher altitudes, are common in Vancouver. Temperature inversions trap air pollutants near the earth's surface and limit ventilation of the area (43). These features prevent self-cleaning of the air and result in protracted periods of exposure to air pollution even if the air pollution levels are not that high. Second, although we found significant positive relations between sulfur dioxide and nitrogen dioxide and asthma hospitalization, the relatively high correlations among these gaseous air pollutants make it difficult to identify a specific pollutant responsible for the observed effect.

One limitation of this study is that potential confounding effects of particulate matter on the association between gaseous air pollutants and asthma hospitalization could not be adequately accessed. The particulate matter data were available for only June 1, 1995, to December 31, 1998, which is only 30 percent of the total days of study for gaseous air pollutants. When data between 1995 and 1998 were used, the effects of nitrogen dioxide and sulfur dioxide on asthma hospitalization were not significant both before and after adjustment for particulate matter because of insufficient statistical power. The relative risks were 1.13 (95 percent CI: 0.82, 1.55) for 4-day nitrogen dioxide exposure in males and 1.17 (95 percent CI: 0.84, 1.63) for 4-day sulfur dioxide exposure in females of low SES when particulate matter less than 10 μm in average aerodynamic diameter and

TABLE 6. Correlations between daily concentrations of gaseous air pollutants and particulate matter in Vancouver, British Columbia, Canada, June 1, 1995–December 31, 1998

Particulate matter	Gaseous air pollutant			
	CO*	SO ₂ *	NO ₂ *	O ₃ *
PM ₁₀ *	0.45	0.60	0.55	0.24
PM _{2.5} *,†	0.22	0.42	0.37	0.29

* CO, carbon monoxide (daily average); SO₂, sulfur dioxide (daily average); NO₂, nitrogen dioxide (daily average); O₃, ozone (daily maximum 1-hour concentration); PM₁₀, daily average thoracic particulate matter <10 μm in average aerodynamic diameter; PM_{2.5}, daily average fine particulate matter <2.5 μm in average aerodynamic diameter.

† For PM_{2.5}, values were missing for 4.8% (63 days) of the total of 1,310 days between June 1, 1995, and December 31, 1998.

particulate matter less than 2.5 μm in average aerodynamic diameter were included in the models. In addition, particulate matter is significantly correlated with gaseous air pollutants (table 6). Separating the effects of gaseous air pollutants from those of particulate matter is always a challenge in environmental epidemiology.

The potential modifying effect of SES on the relation between air pollution and asthma hospitalization has not been well assessed in previous studies. A study conducted in central Los Angeles, California (44), used insurance status as a surrogate for SES and found a stronger association between thoracic particulate matter (<10 μm in average aerodynamic diameter) and asthma hospital admissions of persons enrolling in California's Medicaid program, with eligibility limited mainly to the poor. But no such relation was observed for uninsured persons who were admitted. A few studies have examined the association between air pollution and mortality stratified by SES. A recent reanalysis of the Harvard Six Cities cohort study found a stronger mortality effect for long-term exposure to fine particulate matter in populations with lower educational and income levels compared with those with higher levels (17). Zanobetti and Schwartz (12) also observed slightly higher mortality in relation to exposure to particulate matter less than 10 μm in average aerodynamic diameter among subjects with lower educational attainment in the four largest US cities. Somewhat converse results were found in Sao Paulo, Brazil (13). However, the apparent trend of increasing mortality in relation to particulate matter less than 10 μm in average aerodynamic diameter with increasing SES has not been observed consistently.

Several possible explanations exist for the potential modifying effect of SES observed in our study. In several studies, SES itself has been found to be a risk factor for asthma (18, 19), with the risk of asthma being higher for persons of low SES. Although the pathways linking SES and health are poorly understood, higher SES is associated with a healthier lifestyle, better living conditions, and better health status. SES may affect health through structural and material factors as well as sociobehavioral variables (16). Differential coex-

istence of disadvantageous conditions related to asthma across different socioeconomic levels could contribute to risk modification by SES. Proven viral respiratory infections (45), maternal smoking (46), and exposure to indoor dust mites and cockroach and mouse antigens (18, 47) are closely associated with asthma in children, and these factors exhibit substantial socioeconomic variability. One study found the incidence of acute respiratory infections to be significantly higher in undernourished children of lower SES (48). Another study observed that the odds of being a smoker were larger for respondents of lower socioeconomic standing (49). The possible synergistic effects of these risk factors with air pollution exposure may partly explain the interrelation among SES, air pollution, and asthma hospitalization observed in this study.

Short-term exposures (less than 3 hours) to nitrogen dioxide have been shown to lead to changes in airway responsiveness and lung function in children 5–12 years of age who have preexisting respiratory illnesses (50). The combined effect of smoking and air pollution on airway responsiveness has been demonstrated (51). The combination of aeroallergen and air pollution may lead to enhanced bronchoconstriction (47).

In this study, nitrogen dioxide showed a positive effect on asthma hospitalization of males, while sulfur dioxide displayed a positive effect in females. To date, there has been little convincing evidence to confirm sex differences in the effects of air pollution on asthma hospitalization. A recent study in 12 Southern California communities (52) found that boys and girls responded differently to air pollutants. An association between decreased lung function and increased air pollution was found for females, not for males. Compared with girls, boys have smaller airways relative to their lung volume and may be predisposed to airway obstruction (53). Differences in smooth muscle and vascular functions, the rates of lung growth and decline, and hormonal status between males and females during the prepubertal period may contribute to the complexity of sex differences in asthma risk in relation to air pollution (53). Host factors such as age and sex also influence asthma prevalence and incidence. Susceptibility to various gaseous air pollutants is expected to vary differentially with age and sex. Our study did not provide large-enough power to test such a difference. The sex difference in the nitrogen dioxide effect was not statistically significant ($p > 0.1$). We found a marginal statistical significance ($p = 0.06$) for the sex difference in the effect of 6-day average sulfur dioxide exposure. Further studies are needed to clarify this issue.

In our study, average household income was an ecologic indicator of SES at the enumeration-area level. This measure of SES is helpful to observe more of the community-level/contextual effects, although it is possible that use of such a measure as a proxy for individual SES may attenuate the effects seen (54). Additional indicators of individual-level SES such as education and relative deprivation would help disentangle various pathways (material, behavioral, psychosocial) through which SES may influence the relation between health outcomes and exposures (14, 55). Future research with a larger sample may help to better characterize

the gradient of effect modification of SES measures on the relation between air pollution and asthma hospitalization.

Some concerns exist regarding application of default parameters in S-PLUS software when using generalized additive models that include smoothing functions (30, 31). Dominici et al. (31) found that the default convergence criteria in S-PLUS may not be sufficiently strict to ensure convergence of the backfitting algorithm, leading to overestimations of risk and underestimation of variance of risk estimates. In our study, LOESS functions with default convergence criteria produced results similar to those from natural splines with more stringent convergence criteria, although larger standard errors of the estimated model parameters were observed when natural splines were used. Natural splines produced slightly higher point estimates than LOESS functions did, with the exception of ozone in females; slightly lower point estimates were found when natural splines were used. This finding suggests that LOESS functions may not always lead to overestimation of air pollution health effects in time-series studies. In our study, both approaches demonstrated significant effects of gaseous air pollutants on asthma hospitalization in the low SES group.

In summary, we found significant effects of nitrogen dioxide in males and sulfur dioxide in females on asthma hospitalization in the Vancouver area, a city with moderately low air pollution levels. Such effects tended to be greater in those whose socioeconomic standing was relatively low. Similar results were obtained by using LOESS functions with default convergence criteria and natural cubic splines with more stringent corresponding criteria.

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