

RESEARCH REPORT

Effect of short-term exposure to gaseous pollution on asthma hospitalisation in children: a bi-directional case-crossover analysis

M Lin, Y Chen, R T Burnett, P J Villeneuve, D Krewski

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Study objective: Assess associations between short-term exposure to gaseous pollutants and asthma hospitalisation among boys and girls 6 to 12 years of age.

Design: A bi-directional case-crossover analysis was used. Conditional logistic regression models were fitted to the data for boys and girls separately. Exposures averaged over periods ranging from one to seven days were used to assess the effects of gaseous pollutants on asthma hospitalisation. Estimated relative risks for asthma hospitalisation were calculated for an incremental exposure corresponding to the interquartile range in pollutant levels, adjusted for daily weather conditions and concomitant exposure to particulate matter.

Setting: Toronto, Ontario, Canada.

Participants: A total of 7319 asthma hospitalisations for children 6 to 12 years of age (4629 for boys and 2690 for girls) in Toronto between 1981 and 1993.

Main results: A significant acute effect of carbon monoxide on asthma hospitalisation was found in boys, and sulphur dioxide showed significant effects of prolonged exposure in girls. Nitrogen dioxide was positively associated with asthma admissions in both sexes. The lag time for certain gaseous pollutant effects seemed to be shorter in boys (around two to three days for carbon monoxide and nitrogen dioxide), as compared with girls (about six to seven days for sulphur dioxide and nitrogen dioxide). The effects of gaseous pollutants on asthma hospitalisation remained after adjustment of particulate matter. The data showed no association between ozone and asthma hospitalisation in children.

Conclusions: The study showed positive relations between gaseous pollutants (carbon monoxide, sulphur dioxide, and nitrogen dioxide) at comparatively low levels and asthma hospitalisation in children, using bi-directional case-crossover analyses. Though, the effects of certain specific gaseous pollutants were found to vary in boys and girls.

See end of article for authors' affiliations

Correspondence to:
Dr Y Chen, Department of
Epidemiology and
Community Medicine,
University of Ottawa, 451
Smyth Road, Ottawa,
Ontario, Canada
K1H 8M5;
ychen@uottawa.ca

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Asthma is one of the most prevalent chronic conditions of childhood in Canada and most other developed countries.^{1,2} Exposure to outdoor air pollution is a potential risk factor for the development or exacerbation of asthma. Although ongoing efforts are being made to improve air quality,³ the persistent growth in car ownership continues to threaten the ambient air quality in industrialised countries.⁴ Carbon monoxide (CO), nitrogen dioxide (NO₂), sulphur dioxide (SO₂), and ozone (O₃) represent major constituents of gaseous outdoor pollutants arising from motor vehicles exhaust in most urban areas, including Toronto, Canada.^{4,5}

Although there are numerous studies relating gaseous pollution to asthma hospitalisation or emergency room visits,^{6–17} the results of these studies are not entirely consistent. Almost all of the previous epidemiological studies on the short-term effects of air pollution on asthma and other respiratory conditions have used the time series analysis approach. Some investigators have argued that time series analysis is somewhat model dependent, and thereby hindering comparison of results from different studies.^{18,19} Consequently, alternative analytic approaches may help in clarifying the relation between ambient air pollution and respiratory health.

The case-crossover design developed by Maclure²⁰ has been used to study the effect of air pollution on mortality in recent years.^{21,22} The case-crossover approach has an advantage of using design based rather than model based techniques to control for potential confounding attributable to individual characteristics and time trends in both exposure and health outcomes. Though, few studies used the case-crossover

approach to assess the relation between air pollution and asthma hospitalisation.

In this study, we use bi-directional case-crossover analyses to evaluate the associations between gaseous pollutants and asthma hospitalisations among boys and girls aged 6 to 12 years in Toronto. One to seven day exposure averages were used to assess effects of prolonged exposure to gaseous pollution on asthma hospitalisation. Children are thought to be more susceptible to air pollution because of the rapid growth and development of the lungs and the greater amount of time spent outdoors by children as compared with adults.²³

METHODS

This analysis was based on air pollution and asthma hospitalisation data collected in metropolitan Toronto between 1980 and 1994. The study area had a total population of 2.1 million people in 1980 and 2.4 million in 1994.

Hospitalisation data were obtained from the Ontario Ministry of Health, as described previously by Burnett *et al.*⁶ Subjects 6 to 12 years of age hospitalised for asthma were selected for this analysis for the following reasons. (1) Children are generally thought to be more susceptible to air pollution than adults under 65 years of age. (2) Asthma diagnosis remains unclear in infants and early childhood. Some children under 6 years of age experienced transient wheezing, which is resolved as they became older.²⁴ (3) Asthma diagnosis in puberty remains to be clarified. This may be partially related to hormonal changes.²⁵

We defined asthma hospitalisation as an admission for which the primary diagnosis was asthma (International

Table 1 Distribution of daily concentrations of gaseous air pollutants* in Toronto

Gaseous pollution	Mean	Standard deviation	Centiles				
			Minimum	25th	50th	75th	Maximum
CO (ppm)†	1.18	0.50	0	0.90	1.10	1.40	6.10
SO ₂ (ppb)†	5.36	5.90	0	1.00	4.00	8.00	57.00
NO ₂ (ppb)†	25.24	9.04	3.00	19.00	24.00	30.00	82.00
O ₃ (ppb)‡	30.39	17.87	0	18.00	26.00	38.00	141.00

*CO=carbon monoxide; SO₂=sulphur dioxide; NO₂=nitrogen dioxide; O₃=ozone. †Daily average level. ‡Daily maximum one hour level.

Classification of Diseases, 9th revision, code: 493). The data for each admission included age, sex, and the dates of admission and discharge. There were a total of 7319 asthma hospitalisations for children 6–12 years of age (4629 for boys and 2690 for girls) with a daily average of 1.54 admissions (0.97 for boys and 0.57 for girls) in Toronto between 1981 and 1993.

The environmental data included daily information on particulate matter, gas phase pollutants, and weather conditions from 1980 to 1994. These data were obtained from the Ontario Ministry of Environment and Energy (OMEE) and have been described in greater detail elsewhere.²⁶ In brief, daily measurements of CO, NO₂, SO₂, and O₃ were obtained from four monitoring stations within the study area. Values of fine particulate matter (PM_{2.5}), coarse particulate matter (PM_{10-2.5}), and thoracic particulate matter (PM₁₀) were obtained from a dichotomous sampler running every sixth day during the period from 1984 to 1990. Daily particulate values were predicted based on co-located high volume samplers in downtown Toronto providing daily concentrations of sulphates, total suspended particulates, and coefficient of haze.²⁰ Information on daily maximum, and minimum temperatures and average relative humidity were obtained from the Pearson International Airport in Toronto.²⁶

A bi-directional case-crossover analysis was used to examine the associations between gaseous pollutants and asthma hospitalisation in boys and girls separately. The level of air pollution at the time of asthma hospitalisation for each case (the case period) was compared with levels obtained in a specified period before and after the health event (the control periods). This scheme is helpful in reducing bias caused by time trends both in air pollution exposures and health outcomes as compared with unidirectional approach.^{19, 27} Cases in this analysis included only those children 6–12 years of age who were admitted to a hospital in the study area during the period from 1 January 1981 to 31 December 1993, with asthma as the principal reason for the hospital stay. Both planned admissions and transfers from another institution were excluded from this analysis. As the case-crossover analysis requires asthma hospitalisation data to be matched to environmental data before and after to admission for asthma, only hospitalisation data from 1981 to 1993 were used in this analysis.

The acute effects of environmental exposure may be immediate, or may occur several days subsequent to exposure. Two lag structures have been commonly used in previous studies.^{8, 28} One approach is to examine the effect of exposures on the day before the event. However, as such an approach may lead to unstable estimates because of the existence of short-term autocorrelation (within five to seven days) in environmental variables,^{28, 29} this was not pursued here. Instead, we considered cumulative lag structures, which examined the acute effect of one day to multiple day averages of air pollution ending on the admission date. This approach provided estimates for prolonged exposure effects, which reduce the effect of the short-term autocorrelation. Previous studies have reported that increased asthma hospitalisations are most strongly associated with air pollution on day of admission or within up to four days.^{6, 7, 30} In this study, we calculated one to seven day exposure averages ending on the admission date as case period.

Control periods of two weeks before and after the admission date were used in this analysis. One day to seven day averages ending on the date two weeks before or after the admission date, were calculated for each pollutant, and matched the case periods. In this study, we selected an interval of two weeks between case and control periods to minimise autocorrelation between case and control exposures, as well as to control for seasonal effects. Short-term autocorrelation (within the past five to seven days) in air pollution exposures could be a concern when the interval is too short³¹; seasonal trends could not be controlled when the interval is too long. Using the simulation study, Bateson and Schwartz^{19, 32} suggested that a separation time of seven days between case and control periods could better control for time trends in data, and choosing shorter separation time could reduce bias attributable to time varying factors. In our study, however, the interval of one week between case and control periods could be too close when multi-day exposure effect was examined. A simulation study conducted by Levy *et al*³¹ showed there is little bias (0.4%) when the interval of two weeks (14 days) was used.

Conditional logistic regression models were fitted to the data for boys and girls separately. We calculated odd ratios for each gaseous pollutant in relation to asthma hospitalisation after adjustment for weather conditions, including daily

Table 2 Correlations between daily concentrations of gaseous air pollutants* and particulate matter† and weather conditions in Toronto

Air pollutant	Air pollutant							Weather condition		
	CO‡	SO ₂ ‡	NO ₂ ‡	O ₃ §	PM _{2.5} ‡	PM _{10-2.5} ‡	PM ₁₀ ‡	Maximum temperature	Minimum temperature	Relative humidity‡
CO	1.00	0.37	0.55	-0.16	0.45	0.17	0.38	-0.10	-0.09	0.27
SO ₂		1.00	0.54	-0.01	0.46	0.28	0.44	-0.07	-0.14	0.04
NO ₂			1.00	0.03	0.50	0.38	0.52	-0.01	-0.05	0.09
O ₃				1.00	0.21	0.56	0.44	0.67	0.57	-0.42

*CO=carbon monoxide; SO₂=sulphur dioxide; NO₂=nitrogen dioxide; O₃=ozone. †PM_{2.5}=particulate matter less than 2.5 microns in aerodynamic diameter; PM_{10-2.5}=coarse particulate matter between 2.5 and 10 microns in aerodynamic diameter; PM₁₀=particulate matter less than 10 microns in aerodynamic diameter. ‡Daily average level. §Daily maximum one hour level.

Table 3 Adjusted odds ratios† (ORs) and 95% confidence intervals (CIs) for gaseous pollutants‡ in relation to asthma hospitalisation in boys 6 to 12 years of age, Toronto

Analysis	Exposure averaging period													
	1 day		2 days		3 days		4 days		5 days		6 days		7 days	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Daily average CO (0.5 ppm)														
A§	1.05	1.00 to 1.11	*1.07	1.01 to 1.14	*1.08	1.01 to 1.16	*1.08	1.00 to 1.17	1.07	0.99 to 1.16	1.07	0.98 to 1.17	1.07	0.98 to 1.17
B§	1.05	0.99 to 1.11	*1.08	1.01 to 1.16	*1.09	1.01 to 1.18	*1.10	1.02 to 1.20	1.09	1.00 to 1.18	1.09	0.99 to 1.19	1.09	0.99 to 1.20
Daily average SO ₂ (7 ppb)														
A	1.00	0.95 to 1.05	0.99	0.93 to 1.06	0.98	0.90 to 1.06	0.96	0.87 to 1.05	0.95	0.86 to 1.05	0.93	0.83 to 1.03	0.93	0.83 to 1.04
B	0.98	0.93 to 1.04	0.99	0.91 to 1.06	0.96	0.88 to 1.05	0.95	0.85 to 1.05	0.94	0.84 to 1.06	0.91	0.80 to 1.04	0.91	0.80 to 1.04
Daily average NO ₂ (11 ppb)														
A	1.04	0.99 to 1.10	1.07	1.00 to 1.14	*1.09	1.01 to 1.17	*1.10	1.01 to 1.20	*1.10	1.00 to 1.20	*1.12	1.01 to 1.23	*1.11	1.00 to 1.24
B	1.03	0.97 to 1.10	*1.09	1.01 to 1.18	*1.10	1.01 to 1.21	*1.15	1.04 to 1.27	*1.13	1.01 to 1.26	*1.16	1.03 to 1.31	*1.15	1.01 to 1.30
Daily maximum O ₃ (20 ppb)														
A	0.96	0.88 to 1.04	0.94	0.85 to 1.04	0.93	0.82 to 1.04	0.89	0.79 to 1.02	0.91	0.79 to 1.05	0.90	0.77 to 1.05	0.88	0.75 to 1.04
B	0.95	0.87 to 1.03	0.93	0.84 to 1.03	0.91	0.81 to 1.02	0.88	0.77 to 1.00	0.89	0.77 to 1.03	0.87	0.74 to 1.02	0.85	0.71 to 1.00

*p Value ≤0.05. †The odds ratios were calculated for an interquartile range increment of each gaseous pollutant, which was calculated based on daily levels. ‡CO=carbon monoxide; SO₂=sulphur dioxide; NO₂=nitrogen dioxide; O₃=ozone. §A=odds ratios adjusted for daily weather conditions; B=odds ratios adjusted for particulate matter (PM_{10/2.5} and PM_{2.5}) and daily weather conditions.

Table 4 Adjusted odds ratios† (ORs) and 95% confidence intervals (CIs) for gaseous pollutants‡ in relation to asthma hospitalisation in girls aged 6 to 12 years, Toronto

Analysis	Exposure averaging period													
	1 day		2 days		3 days		4 days		5 days		6 days		7 days	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Daily average CO (0.5 ppm)														
A§	1.00	0.93 to 1.06	1.01	0.94 to 1.10	1.00	0.91 to 1.09	0.98	0.89 to 1.09	1.01	0.91 to 1.13	1.03	0.92 to 1.16	1.04	0.93 to 1.17
B§	1.00	0.93 to 1.07	1.01	0.92 to 1.10	0.99	0.90 to 1.09	0.97	0.87 to 1.08	0.99	0.89 to 1.11	1.02	0.90 to 1.15	1.05	0.93 to 1.20
Daily average SO ₂ (7 ppb)														
A	1.04	0.97 to 1.11	1.04	0.95 to 1.13	1.05	0.95 to 1.16	1.09	0.98 to 1.22	1.13	1.00 to 1.28	*1.17	1.02 to 1.34	*1.20	1.04 to 1.39
B	1.06	0.98 to 1.14	1.03	0.93 to 1.14	1.04	0.92 to 1.17	1.08	0.95 to 1.23	1.12	0.97 to 1.29	*1.18	1.00 to 1.38	*1.28	1.08 to 1.51
Daily average NO ₂ (11 ppb)														
A	0.99	0.92 to 1.06	1.03	0.94 to 1.12	1.07	0.96 to 1.18	1.09	0.97 to 1.21	*1.14	1.02 to 1.28	*1.16	1.02 to 1.31	*1.16	1.02 to 1.32
B	0.99	0.92 to 1.08	1.02	0.92 to 1.12	1.05	0.93 to 1.18	1.07	0.93 to 1.22	1.12	0.98 to 1.29	1.16	1.00 to 1.35	*1.21	1.03 to 1.42
Daily maximum 1-hr O ₃ (20 ppb)														
A	0.86	0.78 to 1.04	0.90	0.78 to 1.02	0.92	0.79 to 1.07	0.95	0.80 to 1.13	1.02	0.84 to 1.23	1.00	0.82 to 1.23	0.93	0.75 to 1.16
B	*0.86	0.78 to 0.96	0.88	0.77 to 1.01	0.89	0.76 to 1.04	0.92	0.77 to 1.10	0.97	0.80 to 1.18	0.95	0.78 to 1.17	0.89	0.72 to 1.12

*p Value ≤0.05. †The odds ratios were calculated for an interquartile range increment of each gaseous pollutant, which was calculated based on daily levels. ‡CO=carbon monoxide; SO₂=sulphur dioxide; NO₂=nitrogen dioxide; O₃=ozone. §A=odds ratios adjusted for daily weather conditions; B=odds ratios adjusted for particulate matter (PM_{10/2.5} and PM_{2.5}) and daily weather conditions.

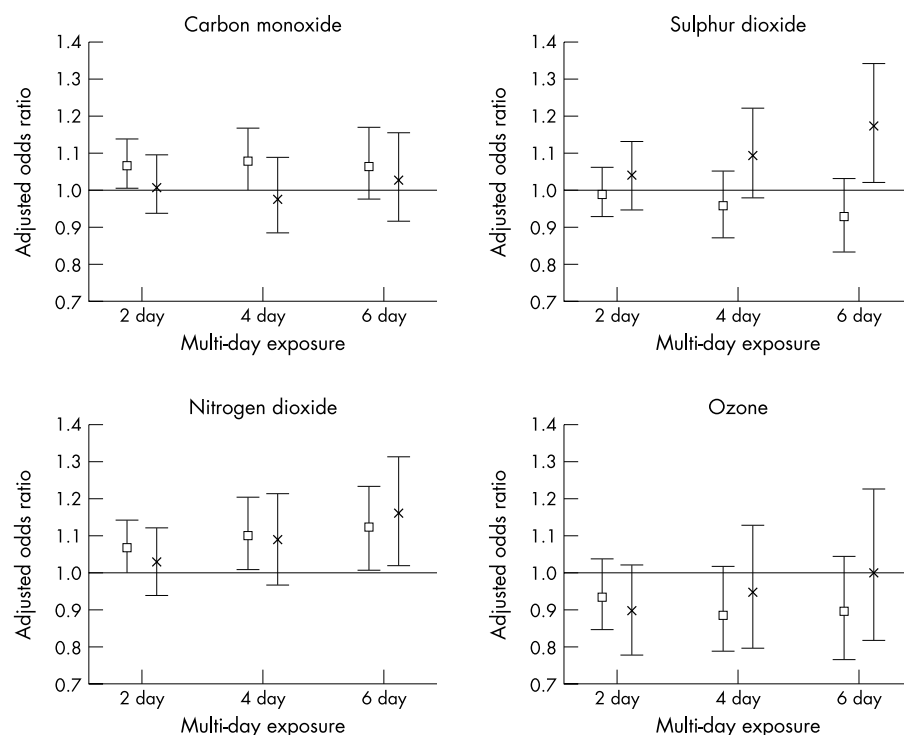


Figure 1 Adjusted odds ratios* and 95% confidence intervals of each gaseous pollutant in relation to asthma hospitalisation in children 6 to 12 years of age, Toronto (squares: boys; crosses, girls). *Odds ratios were adjusted for daily weather conditions. The odds ratios were calculated for an interquartile range increment of each gaseous pollutant (CO: 0.5 ppm; SO₂: 7 ppb; NO₂: 11 ppb; O₃: 20 ppb).

maximum and minimum temperature, and average relative humidity. Based on results from previous studies^{29,30} we added squared terms of each of the weather conditions as additional covariates. Particulate matter was also taken into consideration when examining the relation between gaseous pollution and asthma hospitalisation. As thoracic particulate matter (PM₁₀) is a function of fine (PM_{2.5}) and coarse (PM_{10-2.5}) particulate matter, only fine and coarse particulate matter were considered in the models. Odds ratios were calculated based on an increment in exposure corresponding to the interquartile range of each gaseous pollutant.

RESULTS

Table 1 provides summary statistics for the gaseous air pollutants considered for the period 1980 and 1994. Air pollution levels were comparatively low during the study period. The daily concentrations of CO, SO₂, and NO₂ remained below the Canadian National Ambient Air Quality Objectives (NAAQOs).³³ In particular, the daily one hour maximum level of ozone exceeded the objective of 82 ppb on only 1.7% of the total of 5479 days.

Correlations between gaseous and particulate air pollutants and weather conditions are shown in table 2. Gaseous pollutants were all positively correlated with each other, with the exception of ozone, which was weakly correlated with the other gaseous pollutants, and negatively correlated with CO ($r=-0.16$). The gaseous pollutants were all positively correlated with ambient particulate matter.

Tables 3 and 4 show adjusted odds ratios and their 95% confidence intervals for exposure to each gaseous pollutant in relation to asthma hospitalisation for boys and girls separately. Estimates were calculated for one to seven day average levels of each gaseous pollutant. NO₂ was positively associated with asthma hospitalisation both in boys and girls. However, the lag time for the NO₂ effect seemed to be different in boys and girls. In boys, NO₂ showed no significant effect until three days of accumulated exposure, and seemed to increase slightly with increasing number of days of exposure averaging until six days of accumulation. In girls, only seven day exposure averages of NO₂ consistently showed a significant effect on

asthma hospitalisation, after adjustment for exposure to particulate matter. There was a significantly positive association between CO and asthma hospitalisation in boys, and the lag time for the CO effect seemed to be short. The effect of CO remained significant until four days of averaging. For SO₂, only six and seven day averaging exposures showed a significant effect in girls; these effects were not apparent in boys. O₃ was not found to be associated with asthma hospitalisation in either boys or girls before and after controlling for particulate matter. Figure 1 displays odds ratios and 95% confidence intervals for two, four, and six day averaging exposures to each gaseous pollutant in boys and girls.

DISCUSSION

Time series analyses are frequently used to examine associations between environmental exposure and daily counts of morbidity and mortality.^{6,7,26,30} However, some investigators have argued that time series analysis is somewhat model dependent, and can be sensitive to the length of window used in the locally weighted smoothing function (LOESS),³⁴ lack of standard approach may hinder comparisons of results from different studies.^{18,19}

The case-crossover analysis offers an alternative approach to assess the acute health effects of ambient air pollution. The case-crossover design has the advantage of controlling for confounding factors by design rather than by complex time series modelling. Because this design is an adaptation of the matched case-control study, it can eliminate the effects of potential confounding caused by individual characteristics, such as age, sex, and race. Bi-directional control sampling can control for time trends through the selection of control periods in both directions from the case period. Although the interval between case and control periods in the case-crossover design might be selected, an interval of two weeks seemed to control for seasonal trends and minimise autocorrelation in exposure occurring within the past five to seven days. Using the bi-directional case-crossover design, this study found CO, SO₂, and NO₂ to be positively associated with asthma hospitalisation, although the relations varied in boys and in girls. Some investigators have raised concerns about the possible surrogate role of gaseous pollutants attributable to joint exposure to

Key points

- We used bi-directional case-crossover analyses to assess associations between short-term exposure to gaseous pollutants and asthma hospitalisation in children.
- We found positive relations between gaseous pollutants at comparatively low concentrations and asthma hospitalisation, with an exception of ozone.
- We observed positive effects of CO for boys, SO₂ for girls, and NO₂ for both sexes.

gases and particulate matter.^{9–35} In our study, the effects of gaseous pollutants persisted after adjustment for concomitant exposure to particulate matter.

We found a significant association between CO and asthma hospitalisation in boys using two to four day averaging exposure measures. CO was also found to be associated with asthma hospitalisation in two previous studies conducted in Seattle³⁶ and Toronto.⁶ There has been no plausible mechanism by which CO exacerbates asthma.³⁷ Norris *et al*⁷ postulated that a CO effect could be explained by acting as a surrogate for the effect of particulate matter. However, the CO effect remained significant in boys even after adjustment for particulate matter in this study. Further studies are needed to clarify the mechanism by which CO may exacerbate asthma in different populations.

Six and seven day averaging exposures to SO₂ showed a significant effect on asthma hospitalisation in girls, but not in boys in this study. Some human controlled studies have found that asthmatic children are more sensitive to SO₂ than healthy subjects, with SO₂ concentrations below 250 ppb resulting in temporary breathing impairment and reduced lung function.⁴ Most previous epidemiological studies have not demonstrated a significant effect of SO₂ on asthma hospitalisation or emergency room visits.^{6–8 11 12 17 30} However, SO₂ exposures of 80 ppb or less were found to be related to asthma hospitalisation in some studies.^{13 38 39}

There are several possible explanations for these inconsistent results. Firstly, as SO₂ can only reach the gas exchange region of the lungs after sorption onto fine particles,³ SO₂ effects may not be observed at high concentrations. Secondly, most previous studies did not examine the prolonged exposure effects of SO₂. And thirdly, the effects of SO₂ seem to be age and gender related, which have not been well studied in previous studies.

In our study, we found a significant association between NO₂ and asthma hospitalisation in both boys and girls even after adjustment for the effect of ambient particulate matter. There are several potential mechanisms supporting the association between NO₂ and asthma. NO₂ has a greater airway deposition than O₃, because of its comparatively higher water solubility.⁴⁰ A bronchoconstrictive response in people with asthma is much more susceptible to exposure to NO₂ than SO₂.³ However, there is no convincing epidemiological evidence for an association between ambient NO₂ and hospital admissions for asthma. Significant associations were observed in several studies.^{10 12 13 17 38} However, some other studies failed to link NO₂ exposure to asthma hospitalisation.^{7 8 11 15 16 41} Increased susceptibility to NO₂ in children, different concentrations of NO₂, and the potential cumulative nature of the effects may explain in part the discrepancies between studies.

We did not detect any association between ozone and asthma hospitalisation. Although ozone may produce toxic effects in the small airways, including irritative cough and decreased inspiratory capacity,³⁷ there has been considerable variation in the ozone effect on asthma hospitalisation or emergency room visits, especially at low levels of exposure. Positive associations have been found in Toronto,⁶ Chicago (P V Targonski *et al*, Air and Waste Management Association 88th

Policy implications

- These data suggest that ambient concentrations of CO, SO₂, and NO₂ in urban areas are linked to increased asthma hospitalisation in children 6 to 12 year of age.
- Although the risk of asthma hospitalisation attributable to these pollutants is comparatively small, the population health impact can be appreciable because of the large number of children exposed.
- These results contribute to a growing body of scientific evidence demonstrating associations between ambient air pollution and respiratory health.
- Collectively, these results will inform the development of ambient air quality objectives designed to reduce the population health impact of air pollution.

annual meeting and exhibition, San Antonio, Texas, June 1995), and New Jersey,⁴² but no analyses of children were conducted in these studies. In Saint John, Canada, a significant relation between ozone and asthma emergency room visits was found in adults (>15 years of age), but not in children (≤15 years of age).⁸ Similar results were also found in London.¹⁵ White *et al*⁴³ observed an effect of ozone on paediatric asthma visits in Atlanta, Georgia when ozone concentrations exceeded 110 ppb, but no effect was found at values less than 110 ppb. Other studies found no relations between ozone and asthma hospitalisation, including those conducted in Seattle,⁷ Amsterdam,¹¹ Barcelona,¹² Vancouver,⁴⁴ and Montreal,⁴⁵ where the ozone concentrations were below 110 ppb most of the time. In our study, 99.8% of the total of 5479 days had the ozone concentrations below 110 ppb. We do not know the reasons for the lack of significant effect of ozone on asthma hospitalisation in children 6 to 12 years of age in our study. Delfino *et al*⁴⁶ reported that the ozone effect on respiratory hospitalisation disappeared after adjustment for temperature. Moderate correlations between weather conditions and ozone were found in our study. However, we found no significant ozone effect either with or without controlling for weather conditions. Some studies have suggested that the association between ozone and asthma hospitalisation or emergency room visits differs among age groups.^{8 15 44}

In this study, the gender differences with respect of responses to different gaseous pollutants are of particular interest. Asthma hospitalisation seemed to be more strongly related to CO in boys than in girls, while the SO₂ effect was more pronounced in girls. Although there was a significant association between NO₂ and asthma hospitalisation in both genders, different response patterns were observed. The lag time for manifestation of an NO₂ effect was shorter for boys (about two to three days) than for girls (about six to seven days). These data suggest that boys exhibit prompt response to gaseous pollutants, including CO and NO₂, in terms of asthma hospitalisation. Boys have smaller airways relative to their lung volume than girls, and may consequently be more prone to wheezing in response to specific stimuli.⁴⁷ Asthma is also more common in boys than in girls.^{2 48} In addition to relative airway size, the different responses to gaseous pollutants between boys and girls may also be influenced by differences in smooth muscle and vascular functions, and hormonal status.⁴⁹ Chen *et al* (unpublished data) have demonstrated age and sex related differences in the risk of hospital admission attributable to asthma, with the risk in boys higher than girls; the difference between the sexes disappeared during puberty, and reversed after puberty. Host factors such as age, sex also affect asthma prevalence and incidence. The susceptibility to various gaseous pollutants is expected to vary differentially with age and gender, although there is no convincing evidence yet that could illustrate the sex difference in response to CO, NO₂, and SO₂ in this analysis.

In summary, we found positive relations between gaseous pollutants and asthma hospitalisation in children, using

bi-directional case-crossover analyses. Asthma admissions were related to CO in boys and to SO₂ in girls. NO₂ was related to asthma admission in both sexes. The lag time for induction of significant effects of certain specific gaseous pollutants appeared to be shorter in boys than in girls. In particular, such significant effects were observed for gaseous pollutants at relatively low concentrations, as compared with the values that are considered as "safe" by most of public authorities. Although the effects were small, the overall influence on public health could be substantial. Further efforts to reduce current levels of air pollution are necessary.

Authors' affiliations

M Lin, Y Chen, P J Villeneuve, Department of Epidemiology and Community Medicine, Faculty of Medicine, University of Ottawa, Ottawa, Canada

R T Burnett, Environmental Health Directorate, Health Canada, Ottawa, Ontario, Canada

D Krewski, McLaughlin Center for Population Health Risk Assessment, University of Ottawa, Ottawa, Ontario, Canada

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Conflicts of interest: none.

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