The Influence of Ambient Coarse Particulate Matter on Asthma Hospitalization in Children: Case-Crossover and Time-Series Analyses

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In this study, we used both case-crossover and time-series analyses to assess the associations between size-fractionated particulate matter and asthma hospitalization among children 6–12 years old living in Toronto between 1981 and 1993. Specifically, we used exposures averaged over periods varying from 1 to 7 days to assess the effects of particulate matter on asthma hospitalization. We calculated estimates of the relative risk of asthma hospitalization adjusted for daily weather conditions (maximum and minimum temperatures, and average relative humidity) for an incremental exposure corresponding to the interquartile range in particulate matter. Both bidirectional case-crossover and time-series analyses revealed that coarse particulate matter ($PM_{10–2.5}$) averaged over 5–6 days was significantly associated with asthma hospitalization in both males and females. The magnitude of this effect appeared to increase with increasing number of days of exposure averaging for most models, with the relative risk estimates stabilizing at about 6 days. Using a bidirectional case-crossover analysis, the estimated relative risks were 1.14 [95% confidence interval (CI), 1.02, 1.28] for males and 1.18 (95% CI, 1.02, 1.36) for females, for an increment of 8.4 µg/m^3 in 6-day averages of $PM_{10–2.5}$. The corresponding relative risk estimates were 1.10 and 1.18, respectively, when we used time-series analysis. The effect of $PM_{10–2.5}$ remained positive after adjustment for the effects of the gaseous pollutants carbon monoxide (CO), nitrogen dioxide (NO_2), sulfur dioxide (SO_2), and ozone (O_3). We did not find significant effects of fine particulate matter ($PM_{2.5}$) or of thoracic particulate matter (PM_{10}) on asthma hospitalizations using either of these two analytic approaches. For the most part, relative risk estimates from the unidirectional case-crossover analysis were more pronounced compared with both bidirectional case-crossover and time-series analyses. ***Key words:*** **asthma hospitalization, case-crossover analysis, coarse particulate matter, risk assessment, time-series analysis.** ***Environ Health Perspect*** **110:575–581 (2002). [Online 15 April 2002]**
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Numerous studies have documented that ambient particulate matter is associated with asthma hospitalizations, emergency department visits, respiratory symptoms, and pulmonary function (*1–6*). Most previous studies have focused on fine particulate matter < 2.5 µm in average aerodynamic diameter ($PM_{2.5}$) and thoracic particulate matter < 10 µm in average aerodynamic diameter (PM_{10}) that dominate concentrations of fine particles in most urban areas (*7*). The notion that $PM_{2.5}$ is more relevant to adverse health effects than are coarse particles has been widely accepted in recent years (*3,8*). However, the pathophysiologic mechanism by which particles exert their health effects has not been well established. Most coarse particles are of geologic origin and may include biologic material such as bacteria, pollen, and fungal spores. Although many studies failed to consider the potential health effects of coarse particulate matter (between 2.5 and 10 µm in average aerodynamic diameter; $PM_{10–2.5}$), recent research (*1,9*) has suggested that exclusion of $PM_{10–2.5}$ from consideration could lead to neglect of important health effects. The U.S. Environmental Protection Agency (EPA) (*10*) has noted that $PM_{10–2.5}$ deposited in the upper airways may be more relevant for asthmatic responses and irritation. Toxicologic studies have also found both sulfate and coarse particles (dominated by road dust) caused suppression of alveolar macrophage function in rats (*11*). Coarse particles may also contain endotoxin, a potent inflammatory agent derived from bacteria (*7*). However, little strong evidence supports association between $PM_{10–2.5}$ and asthma hospitalization.

Time-series analysis is widely used to assess the association between air pollution and acute respiratory health outcomes (*4,12–14*). Although time-series analysis has the advantage of controlling for temporal trends in the data, it also has certain disadvantages. Specifically, the results from time-series analysis are model dependent (*15,16*). Further, associations between air pollution and health outcomes identified using time-series analyses can be sensitive to the length of the window selected in the locally weighted smoothing function (LOESS, described below) used to filter the data (*17*). Schwartz et al. (*18*) suggested a potential bias of overfiltering certain patterns of exposure, which should be assessed if cumulative exposure effects are present.

The case-crossover design developed by Maclure (*19*) has been used to study the short-term health effects of air pollution in recent years (*20–22*), in which cases serve as their own controls. This design has the advantage of controlling for potential confounding caused by fixed individual characteristics, including measured and unmeasured variables. The bidirectional case-crossover design proposed by Navidi (*23*) is able to control for time trends in the data through the use of information on the study subjects both before and after the event (*23,24*). Although a number of case-crossover studies have focused on short-term exposure to air pollution and mortality (*20–22*), few have considered hospitalization for asthma.

In the present study, we used unidirectional and bidirectional case-crossover and time-series analyses to evaluate the associations between size-fractionated particulate matter and asthma hospitalizations among children 6–12 years old in Toronto. We used 1- to 7-day exposure averages to assess effects of prolonged exposure to particulate matter on asthma hospitalization.

Materials and Methods

We based the present analysis on air pollution and asthma hospitalization data collected in metropolitan Toronto between 1980 and 1994. The study area had a total population of 2.13 million in 1980 and 2.42 million in 1994.

We obtained hospitalization data from the Ontario Ministry of Health, as described previously by Burnett et al. (*1*). We selected

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subjects 6–12 years old inclusive who were hospitalized for asthma, for the following reasons. First, children are generally thought to be more susceptible to air pollution than are adults younger than 65 years old because children tend to spend more time outdoors and have a higher respiratory rate than do adults, taking in more air per kilogram of body weight. Second, asthma diagnosis remains problematic in infants and early childhood. Some children younger than 6 years old experience transient wheezing, which resolves as they age (*25*). This may be caused partly by the rapid growth and development of the lungs during infancy and childhood.

We defined asthma hospitalization as an admission for which asthma was the primary diagnosis that caused the greatest number of hospital days of stay [International Classification of Diseases, 9th revision, code 493 (*26*)]. We restricted admissions to children who both resided in Toronto and were admitted there. The data for each admission included dates of admission and discharge and age and sex of the individual.

The environmental data included daily information on particulate matter, gas phase pollutants, and weather conditions from 1980 to 1994. We obtained these data from the Ontario Ministry of Environment and Energy; these data have been described in greater detail elsewhere (*27*). In brief, we selected sites for this study that had nearly continuous sampling records for the 1980–1994 period and were not significantly influenced by a local pollution source. Four stations met these criteria for the gaseous pollutants, whereas only one station located in the downtown of Toronto was acceptable for particulate pollutants (*27*). We obtained daily measurements of CO, NO_2, SO_2, and O_3 from four monitoring stations within the study area. Daily values of $PM_{2.5}$, $PM_{10-2.5}$, and PM_{10} were not available for the entire study period (1980–1994). We measured $PM_{2.5}$ and $PM_{10-2.5}$ values from a dichotomous sampler running every 6 days from 1984 to 1990, producing 272 measurements colocated with the central downtown monitoring station. We predicted daily particulate values based on colocated monitors providing daily data on concentrations of sulfates and total suspended particulates (TSPs). We obtained the coefficient of haze (COH) from a high-volume sampler at the downtown site.

We fitted two season-specific linear regression models (one for April–September and another for October–March) for the 272 measurements, and then used the estimated regression parameters in conjunction with the daily values of TSPs, sulfates, and COH to construct a daily time series of the predicted particulate matter (*27*). Sulfates explained 77% of the variation of $PM_{2.5}$, 65% of the variation of PM_{10}, and only 20% of the variation in $PM_{10-2.5}$. In contrast, TSP was a weak predictor of fine particles (r^2 = 0.22), a moderate predictor of thoracic particles (r^2 = 0.50), and a stronger predictor of the coarse fraction (r^2 = 0.63). COH was a weak predictor of all three particulate indices (r^2 = 0.33) (*27*). We obtained information on daily maximum and minimum temperatures and average relative humidity from the Pearson International Airport in Toronto (*27*).

To help interpret the relationship between ambient air pollution and asthma hospitalization, we assumed that the ambient air pollution level from the centrally sited outdoor monitor represented personal outdoor exposure, and that the child's exposure to particles generated indoors was independent of, and uncorrelated with, outdoor ambient particulate matter.

We used case-crossover and time-series analyses to examine the associations between particulate matter and asthma hospitalization in children. For the case-crossover analysis, we compared the level of air pollution at the time of asthma hospitalization for each case (the case period) with a level obtained in a specified period before and/or after the health event (the control period). Cases in this analysis included only those children 6–12 years old who were admitted to a hospital in the study area, with asthma as the principle reason for the hospital stay, 1 January 1981 to 31 December 1993. We excluded both planned admissions and transfers from another institution. Because the case-crossover design requires asthma hospitalization data to be matched to environmental data before and after the health event, we used only hospitalization data from 1981 to 1993 in this analysis.

Previous studies have documented that increased asthma hospitalizations are most strongly associated with air pollution occurring on the day of admission or on multiday averages up to 4 days (*1,4,12*). Here, we calculated 1–7-day exposure averages ending on the admission date.

We used both uni- and bidirectional control schemes in the case-crossover analysis. We selected the 2 weeks before the admission date as the control period for the unidirectional scheme and 2 weeks before and after the admission date for the bidirectional scheme. To match the case period, we also expressed each control period as 1-day or up to 7-day averages for each pollutant ending on the date 2 weeks before or after the admission date. We handled control periods in the same manner as case periods (Figure 1).

We fitted conditional logistic regression models to the data for males and females separately. We calculated odds ratios for each pollutant in relation to asthma hospitalization after adjustment for three weather conditions: daily maximum and minimum temperature and average relative humidity. On the basis of results from previous studies (*12,18*) and locally weighted regression model (LOESS) of smoothing plot of asthma hospitalization and weather conditions, we added squared terms of each of the weather conditions as additional covariates. We calculated the relative risk estimates (odds ratios) based on an increment in exposure corresponding to the interquartile range of each pollutant. We further examined the effects of particulate matter on asthma hospitalization after taking the effects of gaseous pollutants (CO, SO_2, NO_2, and O_3) into consideration.

For time-series analysis, we used the generalized additive model to estimate the relationship between air pollution measures and asthma hospitalization in a nonparametric manner. To take into account possible overdispersion of daily hospital admission

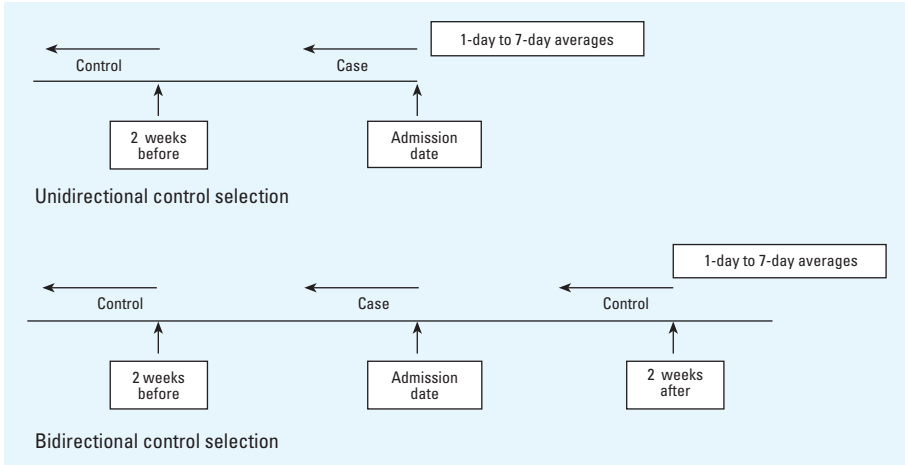

Figure 1. Case-crossover study design.

counts, we used quasi-likelihood estimation. We removed temporal trends as well as seasonal and subseasonal cycles in asthma hospitalizations by using a LOESS nonparametric smoothed function with a span of 93 days (*17*). We characterized the appropriate span by minimal autocorrelation in the residuals and examined them by Bartlett's test (*28*). To achieve comparability with the results from the case-crossover analysis, we used similar strategies for the time-series analysis. In addition to LOESS functions of time, we also considered day-of-week indicator variables and squares of weather conditions as covariates. We considered models with 1- to 7-day averages of each pollutant.

Results

Table 1 provides summary statistics for particulate matter, weather conditions, and asthma hospitalizations. A total of 7,319 asthma hospitalizations occurred for children 6–12 years old (4,629 for males and 2,690 for females) with a daily average of 1.54 (0.97 for boys and 0.57 for girls) in Toronto during the period from 1981 to 1993. Air pollution levels were relatively low during the study period. The level of PM_{10} never exceeded the standard set by the U.S. EPA (*29*), with an average level of PM_{10} being about 20% of the standard of 150 µg/m^3. For $PM_{2.5}$, the concentration exceeded the U.S. 24-hr standard of 65 µg/m^3 on only 9 days of the total of 5,479 days in the study period.

Table 2 shows correlations among particulate matter and weather conditions. $PM_{10–2.5}$ and $PM_{2.5}$ were both highly correlated with PM_{10} (r = 0.87 for $PM_{2.5}$, r = 0.83 for $PM_{10–2.5}$). We found the moderate correlation between $PM_{10–2.5}$ and $PM_{2.5}$ (r = 0.44). Maximum and minimum temperatures were both positively correlated with particulate matter, although to a lesser degree for $PM_{2.5}$ than for $PM_{10–2.5}$ or PM_{10}. Relative humidity was negatively correlated with $PM_{10–2.5}$ (r = –0.35).

Figures 2 and 3 show the time trends in particulate matter and asthma hospitalizations over the study period. On average, the concentrations of PM_{10} and $PM_{2.5}$ decreased over the study period. The levels of $PM_{10–2.5}$ and daily asthma hospitalizations also showed a modest decline.

Tables 3 and 4 show adjusted relative risk estimates and their 95% confidence intervals (CIs) for exposure to particulate matter in relation to asthma hospitalization for males and females separately, using unidirectional case-crossover, bidirectional case-crossover, and time-series analyses. We calculated estimates for 1- to 7-day average levels of particulate matter. In general, we observed stronger associations between particulate matter and asthma hospitalizations in the unidirectional case-crossover analysis compared with the bidirectional case-crossover and time-series analyses, for both males and females. The relative risks estimated from bidirectional case-crossover analysis were similar to those from time-series analysis, but their confidence intervals were wider. Only $PM_{10–2.5}$ with 5- to 6-day averages showed significant associations in both bidirectional case-crossover and time-series analyses for either sex. Figure 4 shows the relative risk estimates and their 95% confidence intervals of $PM_{10–2.5}$ in relation to asthma hospitalization using the three approaches. The magnitude of positive effects was more pronounced with increasing days of exposure averaging (up to 6 days) for most models.

We also examined the effects of PM on asthma hospitalization after taking both weather conditions and gaseous pollutants (CO, SO_2, NO_2, and O_3) into consideration. Table 5 presents the results using 5- and 6-day exposure averages for particular matter. The results were similar after controlling for gaseous pollutants, with the relative risk estimates for $PM_{10–2.5}$ ranging from 1.14 to 1.17 for an interquartile range increment.

The data did not show any significant effects of $PM_{2.5}$ and PM_{10} on asthma hospitalization before and after adjusting for gaseous pollutants when we used bidirectional case-crossover and time-series analyses.

Discussion

In this study, the results from bidirectional case-crossover analyses and time-series analyses were more consistent than those from unidirectional case-crossover analyses. In the case-crossover and time-series analyses, $PM_{10–2.5}$ showed a stronger effect on asthma hospitalization than did $PM_{2.5}$ and PM_{10}. The relative risk estimates based on the unidirectional case-crossover analyses might be overestimated because of the time trends in hospitalization and air pollution.

The case-crossover design can be used to assess transient effects on the risk of acute events (*19*). The conventional case-crossover design uses unidirectional retrospective control sampling. However, recent simulation studies have demonstrated that results

Table 1. Distribution of daily average concentrations of PM, weather conditions, and asthma hospitalizations for children 6–12 years old in Toronto.

Variables	Mean	SD	Percentiles				
			Minimum	25th	50th	75th	Maximum
Air pollution							
$PM_{2.5}$ (µg/m^3)	17.99	8.49	1.22	12.43	16.21	21.71	89.59
$PM_{10–2.5}$ (µg/m^3)	12.17	7.55	0	6.97	10.40	15.42	68.00
PM_{10} (µg/m^3)	30.16	13.61	3.03	21.11	27.17	35.88	116.20
Weather conditions							
Relative humidity (%)	73.47	11.16	35.00	66.00	74.00	81.00	99.00
Maximum temperature (°C)	12.60	11.36	–21.00	3.10	13.00	22.50	37.60
Minimum temperature (°C)	2.54	10.03	–31.30	–3.80	2.60	10.80	24.30
Asthma hospitalizations							
Total (n = 7,319)	1.54	1.51	0	0	1	2	11
Males (n = 4,629)	0.97	1.14	0	0	1	1	11
Females (n = 2,690)	0.57	0.81	0	0	0	1	5

Table 2. Correlations between daily concentrations of PM and gaseous air pollutants and weather conditions in Toronto.

	Air pollutants							Weather conditions		
	$PM_{2.5}$[a]	$PM_{10–2.5}$[a]	PM_{10}[a]	CO[a]	SO_2[a]	NO_2[a]	O_3[b]	Maximum temperature	Minimum temperature	Relative humidity[a]
$PM_{2.5}$	1.00	0.44	0.87	0.45	0.46	0.50	0.21	0.15	0.14	0.22
$PM_{10–2.5}$	—	1.00	0.83	0.17	0.28	0.38	0.56	0.47	0.38	–0.35
PM_{10}	—	—	1.00	0.38	0.44	0.52	0.44	0.36	0.30	–0.06

[a]Daily average level. [b]Daily maximum 1-hr level.

using unidirectional control sampling can be biased when time trends in exposures and outcomes are present, because it may lead to systematically higher or lower exposure levels for control periods than for case periods (*23,24*). Navidi (*23*) proposed a bidirectional case-crossover design, in which control information is assessed both before and after the event to control for the time trends. Bateson and Schwartz (*24*) have reported that the bidirectional case-crossover design can control for different patterns of time trends in exposures and outcomes.

Time-series analysis has been the most popular technique for studying associations between environmental exposure and daily counts of morbidity and mortality over time (*1,4,12–14,27*). Sophisticated modeling techniques have been introduced to control better for the temporal trends, including generalized additive models, in which a nonparametric smooth function of time is used to control for temporal trends in the data. However, some investigators have argued that time-series analysis is somewhat model dependent, requiring decisions on the selection of the length of the window in smoothing, and lacks a standard approach permitting comparisons of results from different studies (*16,24*). Although some recent studies advocated minimizing autocorrelation in the residuals as a principle for the selection of the length of the window (*13,18,24,27,30*), this technique also involves an element of subjectivity. Associations between air pollution and health outcomes using time-series analysis can be sensitive to the length of window (*17*).

Compared with time-series analysis, the case-crossover analysis has the advantage of controlling for confounding factors by design rather than by complex modeling. Because this design is an adaptation of the matched case–control study, it can completely eliminate the effects of potential confounding caused by fixed individual characteristics, such as age, sex, and race. Bidirectional control sampling design can control for time trends through the selection of control periods in both directions from the case period. Variations in season and weather conditions are of less concern because of the shorter interval between the case and control periods. The analytical methods used in the case-crossover design, primarily logistic regression, are similar to those for a matched case–control study and are simpler to apply than are time series methods. However, the selection of the interval between the case and control periods in case-crossover design can be problematic. In this study, which involved an effect assessment of up to 7-day average exposure, we selected an interval of 2 weeks between case and control periods to minimize autocorrelation between case and control exposures and to control for seasonal effects.

Our findings of stronger associations between particulate matter and asthma hospitalizations using the unidirectional case-crossover analysis compared with bidirectional case-crossover analysis and time-series analysis are consistent with those from a simulation study conducted by Bateson and Schwartz (*24*). They found that the effect estimates from bidirectional case-crossover and time-series analyses with control for time trends were close to the true value, whereas the unidirectional case-crossover analysis overestimated the effect when the data contained time trends. The time trends in our data (Figures 2 and 3) may provide an explanation for this bias in the unidirectional case-crossover analysis. The direction of the bias caused by time trend in exposure and outcome data is not clear, however, even in the absence of clear overall time trend in the exposure data. In a simulation study, Navidi (*23*) found underestimation of risk in the unidirectional case-crossover design. The direction of the bias in the unidirectional case-crossover analysis could be related to multiple factors, such as the degree and direction of temporal trends, as well as the interrelationship between time trends in exposure and health outcomes. These issues need to be further explored in simulation studies.

We also observed small differences in point and confidence interval estimates between the bidirectional case-crossover analysis and time-series analysis in this study. The confidence intervals on the relative risk estimates from the bidirectional case-crossover analysis were slightly wider than those from time-series analysis, implying lower statistical power for the bidirectional case-crossover design, as documented previously (*24,31*). The relative risk estimates for $PM_{10–2.5}$ in relation to asthma hospitalization in the bidirectional case-crossover analysis were slightly higher compared with those from time-series analysis, especially for multi-day averages among males. Because of the uncertainty in span selection for the smoothed function, the time-series analysis may filter out some patterns of effects over several days, which may cause potential bias (*18*).

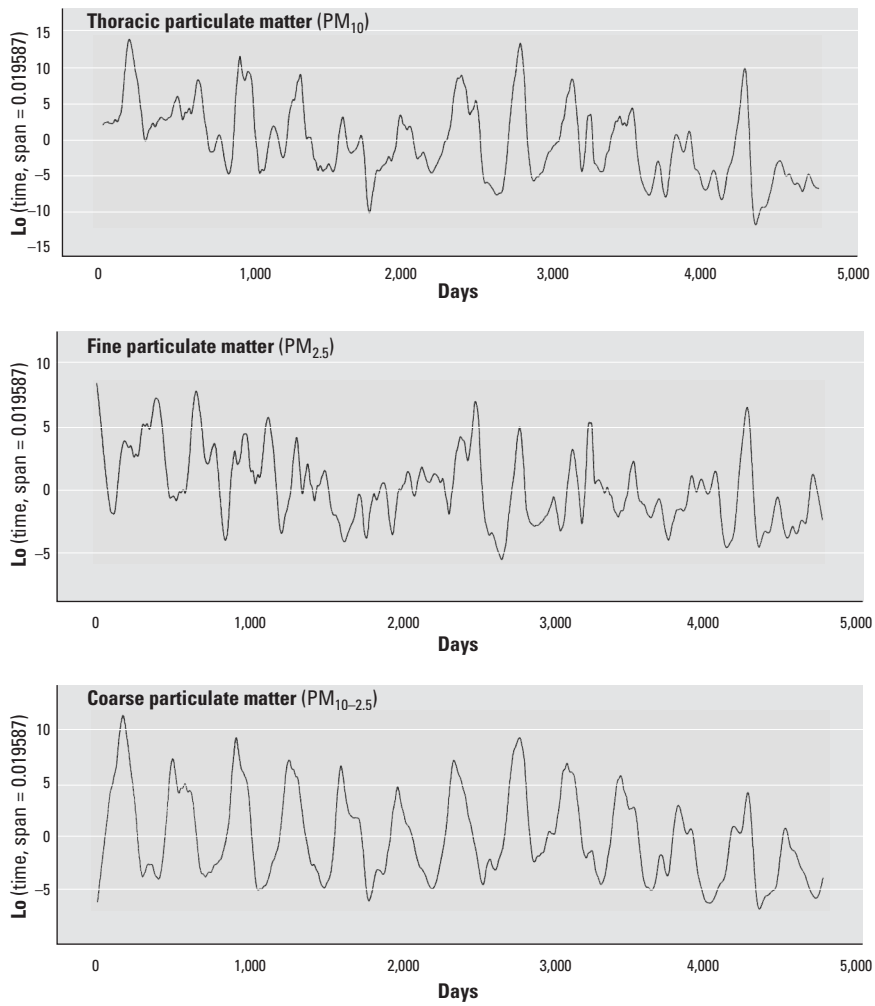

Figure 2. LOESS (Lo) nonparametric smoothed function of particulate matter with a span of 93 days.

The results from both bidirectional case-crossover and time-series analyses have shown that only $PM_{10-2.5}$ with 5- to 6-day averages was significantly associated with asthma hospitalization for both sexes. These results are consistent with previous findings using time-series analysis (*1,32*). One study in Toronto (*1*) found the $PM_{10-2.5}$ fraction to be a better predictor of asthma admissions than the $PM_{2.5}$ and PM_{10} fractions in subjects of all ages. The estimated relative risks for $PM_{10-2.5}$, $PM_{2.5}$, and PM_{10} corresponding to an increase of 10 µg/m^3 with a 3-day averaging were 1.04, 1.01, and 1.01, respectively. The effect of $PM_{10-2.5}$ on asthma hospitalization found in our study was larger than that reported in the study described above (*1*). Possible reasons for this include the following: First, the present analysis included children only, who are more susceptible to environmental exposures. Second, we observed a stronger effect of prolonged period of exposure. Finally, time-series analysis might slightly underestimate the relative risks for multi-day averaged exposure.

Another time-series study relating air pollution and nonelderly asthma hospital admissions in Seattle from 1987 to 1994 (*32*) also found a significant association for $PM_{10-2.5}$ lagged 1 day, with the relative risk estimated to be 1.04 for an increase of 9.3 µg/m^3. In our study, we did not find a clear association between 1–2-day average $PM_{10-2.5}$ and asthma hospitalization. However, we observed a strong relationship, particularly with longer averaging times around 5–6 days. Although the results using different lag structures may not be strictly comparable, the longer lag time identified in our study may be explained in part by the relatively low concentration of $PM_{10-2.5}$ in Toronto compared with that in Seattle (*32*).

Although the relationship between $PM_{10-2.5}$ and asthma hospitalization has not been well documented, $PM_{10-2.5}$ has stronger positive effects on other health outcomes such as mortality from all causes, respiratory diseases, and cardiovascular disease, as well as on hospitalizations for cardiovascular diseases (*9*). Whether respiratory effects of $PM_{2.5}$ are stronger than $PM_{10-2.5}$ has been questioned recently, with Loomis (*9*) suggesting that such a conclusion only applies to lower respiratory symptoms. Burnett et al. (*1*) found that $PM_{10-2.5}$ was a better predictor for asthma hospitalizations and $PM_{2.5}$ was a stronger predictor for respiratory infection.

Because PM_{10} from most urban areas consists primarily of $PM_{2.5}$ (*7*), the magnitude of association for PM_{10} and $PM_{2.5}$ in such areas is most likely to be similar (*1,4,12*). This was the case with our data. We observed similar patterns for the concentration of PM_{10} and $PM_{2.5}$ (Figure 2) but no significant effects of both PM_{10} and $PM_{2.5}$ on asthma hospitalization in both the bidirectional case-crossover and time-series analyses.

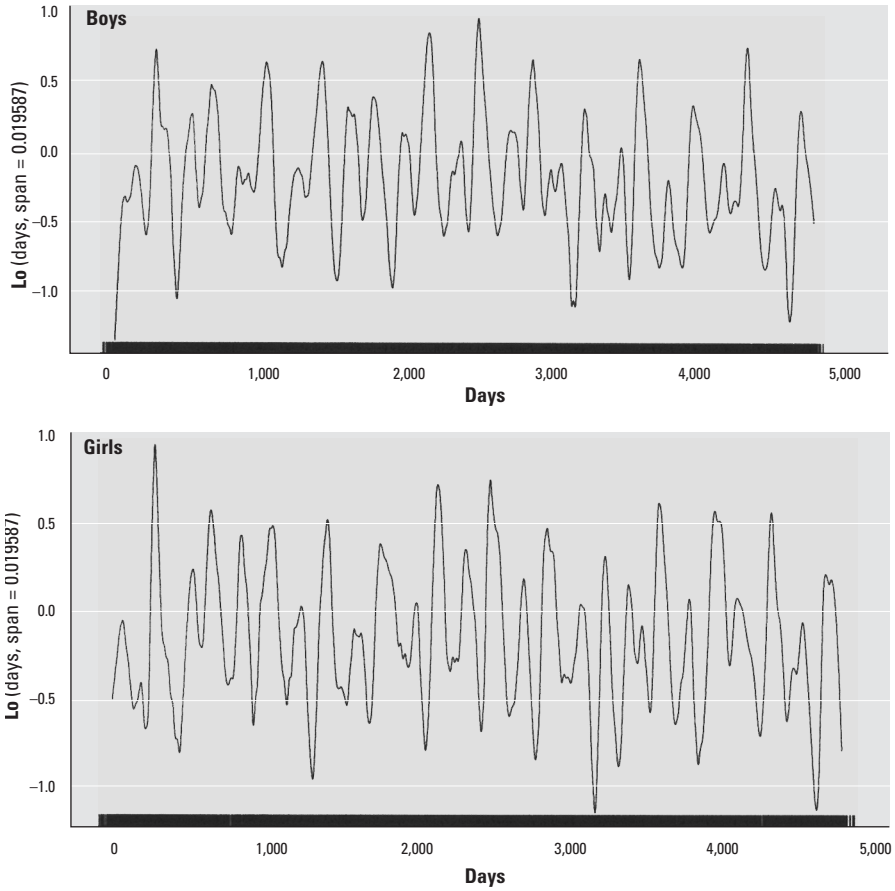

Figure 3. LOESS (Lo) nonparametric smoothed function of daily asthma hospitalizations for boys and girls with a span of 93 days from 1981 to 1993.

Table 3. Adjusted relative risk estimates[a] (RRs) and 95% CIs for PM in relation to asthma hospitalization in boys 6–12 years old in Toronto.

	1 day		2 days		3 days		4 days		5 days		6 days		7 days	
Methods	RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI
$PM_{10-2.5}$ (8.4 µg/m^3)														
UCC	1.08	1.01–1.16	1.08	0.99–1.17	1.09	0.99–1.20	1.11	1.00–1.22	1.13	1.01–1.26	1.16	1.03–1.31	1.18	1.04–1.34
BCC	1.06	1.00–1.14	1.06	0.98–1.14	1.08	0.99–1.18	1.09	0.99–1.20	1.12	1.01–1.24	1.14	1.02–1.28	1.16	1.04–1.31
TS	1.08	1.03–1.12	1.07	1.01–1.13	1.07	1.01–1.13	1.08	1.01–1.15	1.09	1.02–1.16	1.10	1.03–1.18	1.12	1.04–1.20
$PM_{2.5}$ (9.3 µg/m^3)														
UCC	1.09	1.04–1.15	1.09	1.02–1.16	1.11	1.03–1.19	1.09	1.01–1.18	1.10	1.01–1.19	1.10	1.00–1.20	1.10	1.00–1.21
BCC	1.01	0.97–1.06	0.99	0.93–1.05	1.00	0.93–1.06	0.97	0.90–1.04	0.97	0.90–1.05	0.96	0.88–1.04	0.97	0.88–1.05
TS	1.00	0.97–1.04	0.98	0.94–1.02	0.98	0.94–1.03	0.97	0.92–1.02	0.97	0.92–1.02	0.96	0.90–1.01	0.96	0.91–1.02
PM_{10} (14.8 µg/m^3)														
UCC	1.10	1.04–1.17	1.10	1.02–1.17	1.11	1.03–1.20	1.11	1.02–1.20	1.12	1.02–1.22	1.13	1.03–1.24	1.14	1.03–1.26
BCC	1.04	0.98–1.09	1.01	0.95–1.08	1.03	0.96–1.10	1.01	0.93–1.09	1.02	0.94–1.11	1.02	0.93–1.11	1.03	0.94–1.13
TS	1.03	0.99–1.07	1.01	0.96–1.05	1.01	0.97–1.06	1.00	0.95–1.06	1.00	0.95–1.06	1.00	0.94–1.07	1.01	0.95–1.08

Abbreviations: BCC, bidirectional case-crossover analysis; TS, time-series analysis; UCC, unidirectional case-crossover analysis.
[a]RR estimates were calculated for an interquartile range increment of particulate matter, which was calculated based on daily levels, and were adjusted for daily weather conditions (maximum temperature, minimum temperature, and average relative humidity).

Table 4. Adjusted RR estimates[a] and 95% CIs for PM in relation to asthma hospitalization in females ages 6–12 years in Toronto.

Methods	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
$PM_{10-2.5}$ (8.4 µg/m^3)														
UCC	1.07	0.97–1.18	1.16	1.03–1.31	1.27	1.11–1.44	1.33	1.16–1.54	1.41	1.21–1.65	1.46	1.24–1.73	1.44	1.21–1.72
BCC	0.98	0.90–1.07	1.05	0.94–1.16	1.10	0.98–1.24	1.13	1.00–1.28	1.17	1.03–1.34	1.18	1.02–1.36	1.14	0.98–1.33
TS	1.00	0.94–1.06	1.05	0.98–1.13	1.08	1.00–1.16	1.12	1.03–1.22	1.17	1.08–1.28	1.18	1.08–1.30	1.20	1.09–1.31
$PM_{2.5}$ (9.3 µg/m^3)														
UCC	1.06	0.99–1.14	1.11	1.02–1.21	1.16	1.05–1.28	1.20	1.08–1.33	1.24	1.11–1.39	1.26	1.11–1.42	1.22	1.07–1.38
BCC	0.99	0.93–1.06	1.02	0.94–1.09	1.02	0.94–1.11	1.03	0.94–1.13	1.04	0.95–1.15	1.04	0.94–1.15	1.00	0.90–1.11
TS	0.99	0.95–1.04	1.00	0.95–1.06	1.01	0.95–1.06	1.02	0.95–1.08	1.06	0.99–1.13	1.05	0.97–1.12	1.06	0.98–1.13
PM_{10} (14.8 µg/m^3)														
UCC	1.07	0.99–1.16	1.15	1.04–1.26	1.22	1.10–1.35	1.27	1.13–1.43	1.33	1.17–1.50	1.36	1.19–1.55	1.32	1.14–1.51
BCC	0.99	0.92–1.06	1.03	0.95–1.12	1.05	0.95–1.15	1.07	0.97–1.18	1.09	0.98–1.21	1.09	0.97–1.22	1.05	0.93–1.18
TS	0.99	0.94–1.04	1.02	0.96–1.08	1.03	0.97–1.09	1.04	0.97–1.12	1.08	0.99–1.16	1.07	0.98–1.16	1.07	0.98–1.16

Abbreviations: BCC, bidirectional case-crossover analysis; TS, time-series analysis; UCC, unidirectional case-crossover analysis.
[a]RR estimates were calculated for an interquartile range increment of particulate matter, which was calculated based on daily levels, and were adjusted for daily weather conditions (maximum temperature, minimum temperature, and average relative humidity).

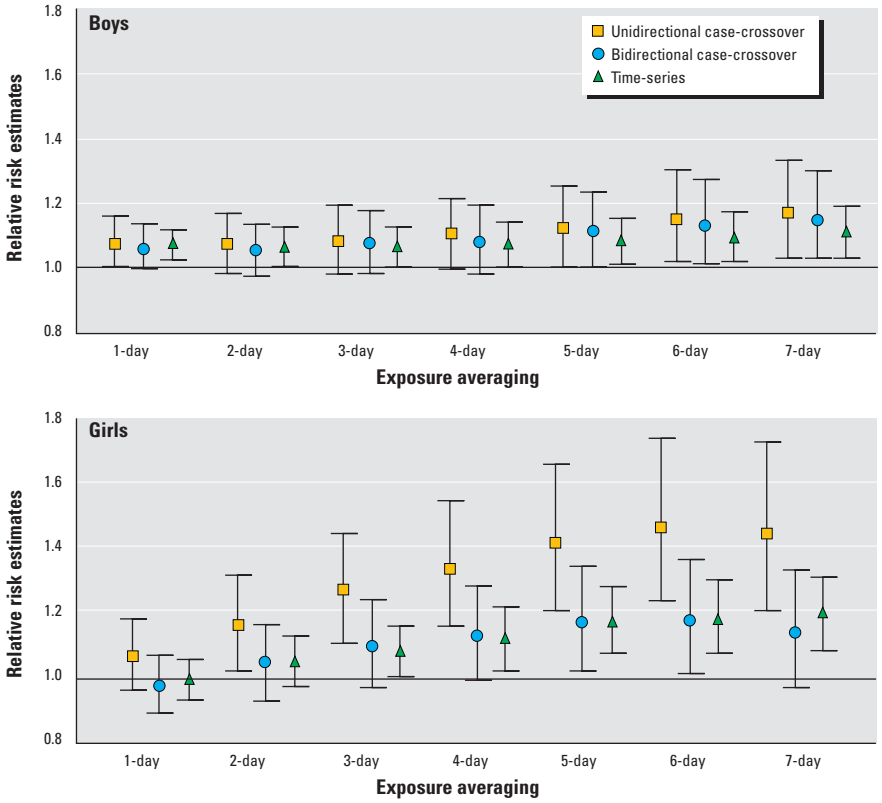

Figure 4. RR estimates and 95% CIs for $PM_{10-2.5}$ for children 6–12 years old, Toronto, 1981–1993, adjusted for weather conditions, using case-crossover and time-series analyses.

Table 5. Adjusted RR estimates[a] and 95% CIs for PM in relation to asthma hospitalization in children 6–12 years old in Toronto, with a consideration of gaseous pollutants.

Methods	5 days		6 days		5 days		6 days	
	RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI
$PM_{10-2.5}$ (8.4 µg/m^3)								
BCC	1.14	1.01–1.28	1.17	1.03–1.33	1.15	0.98–1.35	1.16	0.98–1.38
TS	1.14	1.05–1.23	1.15	1.06–1.25	1.14	1.02–1.26	1.15	1.03–1.29
$PM_{2.5}$ (9.3 µg/m^3)								
BCC	0.94	0.85–1.03	0.92	0.83–1.02	0.96	0.85–1.09	0.93	0.82–1.06
TS	0.96	0.90–1.02	0.94	0.88–1.01	1.01	0.93–1.10	0.98	0.90–1.08
PM_{10} (14.8 µg/m^3)								
BCC	0.99	0.90–1.09	1.01	0.90–1.12	1.02	0.89–1.17	0.99	0.85–1.15
TS	1.03	0.95–1.11	1.02	0.94–1.11	1.05	0.95–1.17	1.03	0.93–1.15

Abbreviations: BCC, bidirectional case-crossover analysis; TS, time-series analysis.
[a]RR estimates were calculated for an interquartile range increment of particulate matter, which was calculated based on daily levels, and were adjusted for daily weather conditions (maximum temperature, minimum temperature, and average relative humidity) and gaseous pollutants (CO, SO_2, NO_2, O_3).

Previous studies have shown no consistent effects of PM_{10} and $PM_{2.5}$ on asthma hospitalization. A study conducted in Sydney, Australia, from 1990 to 1994 (*33*) indicated no significant effects of fine particulate (~$PM_{2.0}$) on asthma hospitalization for both children and adults. Another study from Birmingham, England (*2*), where the maximum level of PM_{10} (130.9 µg/m^3) exceeded the levels found in Toronto (Table 1) and Seattle (*12*) by over 30%, also showed no significant effect of PM_{10} on asthma hospitalization. However, the results from a number of other studies conflict in this regard. Significant effects of PM_{10} and $PM_{2.5}$ were found in Seattle, with estimated relative risks of 1.05 (19 µg/m^3) and 1.04 (11.8 µg/m^3), respectively (*31*). Three time-series analyses conducted in the same area found significant effects of $PM_{2.0}$ and PM_{10} on asthma emergency department visits for children younger than 18 years old (*4*) and adults younger than 65 years old (*12*), and on decreased lung function for elementary school children (*34*). Stronger effects of PM_{10} related to asthma hospitalizations or emergency room visits were found in Utah Valley (*35*) and in Santa Clara County, California (*36*).

Although we have no clear explanations for such a discrepancy regarding the influences of PM_{10} and $PM_{2.5}$ on asthma hospitalizations, reasons may include variability in population characteristics, natural systems, and the complex mixture of fine particles with a different level and composition over time and space. Stronger effects found in Santa Clara County (*36*) and Utah Valley (*35*) are likely related to higher mean and maximum concentrations of PM_{10} compared with those shown in the present study and those in studies from Seattle (*4,12,32*). Also, the degree of correlation between $PM_{2.5}$ and PM_{10} particles and gas pollutants varies from one area to another. One study from Seattle (*4*) showed relatively high correlations between $PM_{2.5}$ and PM_{10}, and CO (r = 0.74) and NO_2 (r = 0.66 for thoracic particles, and r = 0.59 for

fine particles), whereas the correlations in the present study were moderate for CO (r = 0.45 for $PM_{2.5}$ and r = 0.38 for PM_{10}) and even lower for NO_2.

In our study, the magnitude of effects of $PM_{10–2.5}$ appeared to increase with increasing days of exposure averaging up to 6 days for most models. We also found a similar trend in a previous study by Lipsett et al. (*36*). Although allergic asthma is most likely to be an immediate reaction (within 1 hr), asthmatic reactions may also be persistent or have a late onset (*37,38*). The appropriate exposure averaging for each air pollutant has not been established. We found no consistent exposure averaging with largest effects found in previous studies.

In summary, we found a stronger positive effect of $PM_{10–2.5}$ on asthma hospitalizations compared with those of $PM_{2.5}$ and PM_{10} for both sexes, using both bidirectional case-crossover and time-series analyses. Furthermore, the stronger effect of $PM_{10–2.5}$ persisted even after adjustment for the effects of gaseous pollutants (CO, SO_2, NO_2, O_3). We also found a stronger effect of exposure to $PM_{10–2.5}$ averaged up to 6 days for boys and girls in most models. The effects from unidirectional case-crossover analyses may be biased and may overestimate the relative risks because of time trends in the data. We also observed relatively small differences between estimates of relative risks based on the bidirectional case-crossover and time-series analyses.

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