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Effect of short-term exposure to low levels of gaseous pollutants on chronic obstructive pulmonary disease hospitalizations

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Abstract

We examined the associations between gaseous pollutants and hospitalization for chronic obstructive pulmonary diseases (COPD) among elderly people living in Vancouver, British Columbia, Canada, a city in which ambient air pollution levels are relatively low. We regressed the logarithm of daily counts of acute COPD hospitalization during the 5-year period from 1994 to 1998 on the daily mean levels of each pollutant, after accounting for seasonal and subseasonal fluctuations, non-Poisson dispersion, and weather variables. Nitrogen dioxide and carbon monoxide were significantly associated with hospitalization for COPD, and the magnitude of effects was increased slightly with increasing days of exposure averaging, with the relative risk for a 7-day average being 1.11 (95%CI: 1.04, 1.20) and 1.08 (1.02, 1.13) for nitrogen dioxide and carbon monoxide, respectively. There was no significant association between either sulfur dioxide or ozone and COPD hospitalization. The combined relative risk for all four gaseous pollutants on COPD hospitalization was 1.21. The effects of gaseous pollutants on COPD hospitalization were not significant after adjustment for PM_{10}, although its inclusion did not have a marked effect on the point estimates for relative risks. Nitrogen dioxide has a significant impact on COPD hospitalization. Further studies are needed to separate the effects of single pollutants from the combined effects of the complex mixture of air pollutants in urban atmospheres.

Keywords: COPD; Hospitalization; Gaseous pollutants; Particulate; Relative risk

1. Introduction

Chronic obstructive pulmonary diseases (COPD) are a major cause of morbidity and mortality worldwide, and COPD continues to cause a heavy health and economic burden around the world. Deaths due to or associated with COPD have been increasing steadily in the United States over the past 20 years. Exposure to outdoor air pollution is a potential risk factor for development or exacerbation of COPD. Air pollution has been recognized as a trigger for exacerbations of COPD for more than 50 years and has lead to the development of air quality standards in many countries that have resulted in substantially decreased levels of air pollutants derived from the burning of fossil fuels (MacNee and Donaldson, 2000). However, this decrease in the levels of traditional air pollutants was been accompanied by an increase in the levels of other pollutants, such as carbon monoxide (CO), ozone (O_3), and nitrogen dioxide (NO_2), that associated with increased motor vehicle traffic in urban areas (Macfarlane et al., 2000; Thurston and Ito, 1999).

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Few studies have examined the effects of air pollution on people with COPD. Most of them have reported an association between particulate air pollution and COPD (Wordley et al., 1997; Sunyer and Basagana, 2001). However, inconsistent results have been found with gaseous pollutants (Sunyer and Basagana, 2001; Anderson et al., 1997). An European time-series study has suggested that gaseous air pollutants are important determinants of acute hospitalization for respiratory conditions, being at least as important as particulate mass (Fusco et al., 2001). In this study, we employ time-series methods to explore associations between gaseous pollutants and COPD hospitalization among elderly people living in Vancouver, British Columbia (BC), Canada, a city where ambient air pollution levels are relatively low and with the lowest ozone level among 16 Canadian cities (Burnett et al., 1997a).

2. Materials and methods

2.1. Study area

Vancouver is Canada's third-largest city, with an area population of more than 2 million inhabitants. The city, with mild winters and warm summers, is warmed by Pacific Ocean currents and protected by a range of mountains. Vancouver is also the commercial and cultural heart of Canada's West Coast, and has relatively low air pollution levels (Burnett et al., 1997a). The approximately 1 million automobiles in the city are the main source of air pollution.

2.2. Study subjects

The present analysis was based on data from the BC Linked Health Dataset (BCLHD) (Chamberlayne et al., 1998). The BCLHD is housed at and has been developed by the Centre for Health Services and Policy Research at the University of British Columbia. The BCLHD contains data files from a number of different sources. Information about an individual's encounter with the BC health care system may occur as a Medical Services Plan record, a Hospital Separations record, a PharmaCare record, or an incidence of cancer reported to the BC Cancer Agency. The information from each data file in the BCLHD is linkable at the level of the individual. The Hospital Separations file was used in this analysis. Health outcomes were ascertained using primary discharge diagnosis records for residents of the study area between January 1, 1994, and December 31, 1998. Only those considered emergencies or urgent were selected, with an exclusion of planned admissions and transfers from other institutions. Study subjects were adults 65 years of age or older who had acute COPD [International Classification of Disease Codes, Ninth Revision (ICD-9): 490-492, 494, and 496] admissions at hospitals in greater Vancouver, BC during the 5-year period from 1994 to 1998.

2.3. Air pollution and weather data

Gaseous [CO, NO_2, sulfur dioxide (SO_2), and O_3] and thoracic particulate matter (PM_{10}, $<10\,\mu m$ in average aerodynamic diameter) measurements were available on a daily basis throughout the study period. Daily measurements of gaseous air pollutants were available from 5 to 31 monitoring stations between 1994 and 1998. Specifically, daily average pollutant levels were available for carbon monoxide (6 stations), sulfur dioxide (5 stations), nitrogen dioxide (31 stations), and ozone (25 stations). Continuous sampling measures for air gaseous and particulate pollutants had been compiled for the 13 census subdivisions in the greater Vancouver area. Specifically, PM_{10} levels were obtained using a tapered element oscillating microbalance. Only PM_{10} was considered in multiple-pollutant models with gaseous pollutants because the relative risks of COPD hospitalization for $PM_{2.5}$ ($<2.5\,\mu m$ in average aerodynamic diameter) and $PM_{10-2.5}$ (average aerodynamic diameter between 2.5 and $10\,\mu m$) were lower than that for PM_{10} in our recent study (Chen et al., 2004). In the study, Chen et al. conducted a time-series analysis among elderly people 65+ years of age living in Vancouver between June 1995 and March 1999 to assess the association between size-fractioned PM and hospitalization for COPD. Gaseous pollutants were measured daily using fixed-site ambient monitors operated by the Great Vancouver Regional District Air Quality Department (Vedal et al., 2003). CO, NO_2, SO_2, and O_3 were averaged with no missing average values. Average daily concentrations of these pollutants, results across monitors derived by taking a simple daily average for each monitor and then averaging these to obtain a final daily mean value, were used in all analyses. Daily average temperature (°C) and relative humidity were included to adjust for weather conditions. Other meteorological measures, including maximum temperature, minimum temperature, mean wind speed, and temperature change from the previous day, were also available but were not included in final models.

2.4. Statistical analysis

The association between air pollution and COPD was assessed using time-series analysis. Daily counts of COPD admissions were assumed to follow a time-homogeneous Poisson distribution. Quasilikelihood estimation, allowing for over- or underdispersion, was used to model the logarithm of daily counts of COPD admissions as functions of the predictor variables. Recently, Dominici et al. (2002) and Ramsay et al.

(2003) found that the use of nonparametrically smoothed splines or locally weighted regression smoothers in generalized additive models (Hastie and Tibshirani, 1990) may lead to biased estimates of regression coefficients for continuous covariates. As a consequence, we used natural splines to model the effects of continuous covariates in the present analysis. Our time-series model included indicator variables for the day of the week and was adjusted for temporal trends using a natural spline-smoothed representation of day of study. We regressed the natural logarithm of the daily number of admissions on the natural spline for day of study, thus providing an adjustment for seasonal (and sub-seasonal) variation, on a dummy variable to account for annual trends in daily admission, and on natural splines of relevant weather variables that may affect the association between air pollution and respiratory health. For each analysis, we first selected the temporal filter having the number of knots that produced a filtered time series that was consistent with a white noise process, using Bartlett's statistic (Priestly, 1981) to identify the filter with the least amount of serial autocorrelation in residual time series. We examined knots every $f = 15$, 30, 60, 90, and 120 days (knots being study length/f) and found that serial autocorrelation in the residual time series was minimized at $f = 30$ days. The combination of weather variables that minimized the Aikake Information Criterion (Hastie and Tibshirani, 1990) was then determined. All analyses were conducted using S-Plus, Version 6.1.

Since air pollution can induce health effects not only on the day of the exposure but also on subsequent days, the number of admissions on a given day will depend on the effect of pollution on that day as well as the lagged effect of pollution on previous days. We observed a lagged association ranging from the day of the admission to 6 days prior to admission. Consequently, associations between COPD and air pollution were estimated using 1- to 7-day lagged moving averages (lag 0–6). The lagged moving averages were used to access possible cumulative or lagged effects of air pollution. We calculated the relative risk of COPD and 95% confidence limits based on an increment in exposure corresponding to the interquartile range (IQR) of each pollutant of interest. The relative risk for the total effect of several pollutants was determined by exp $(\beta_1^* p_1 + \beta_2^* p_2 + \cdots)$, where β's were the regression coefficients from the time-series model and $p_1, p_2 \ldots$ were IQR of the pollutants.

3. Results

A total of 6027 COPD admissions occurred among the elderly during the 5 years from 1994 to 1998 in greater Vancouver. On average, 3.3 patients were admitted to hospitals daily for COPD, ranging from a minimum of 0 to a maximum of 16 admissions. Table 1 summarizes the means, standard deviations (SDs), medians, minimum, maximum and interquartiles of daily average concentrations of air pollutants, weather conditions, and COPD admissions for the elderly in Vancouver during the study period. In general, air pollution levels in Vancouver were relatively low (Burnett et al., 1997a). Table 2 presents the seasonal variations of air pollutants, weather conditions, and COPD admissions. The mean concentrations of CO, NO_2 and SO_2 were highest in the winter, O_3 in the spring, and PM_{10} in the summer, while COPD admissions were highest in the winter. Table 3 shows the correlations for the mean concentrations of gaseous co-pollutants with PM_{10} and meteorological indicators. CO was strongly correlated with NO_2 ($r = 0.74$), moderately correlated with SO_2 (0.67) and PM_{10} (0.50), and inversely correlated with O_3 (−0.44). O_3 was inversely correlated with NO_2 (−0.10) and SO_2 (−0.12) and positively correlated with PM_{10} (0.19), although these associations were minimal. NO_2 was moderately correlated to SO_2 (0.61) and PM_{10} (0.61).

Table 1
Distribution of daily average concentrations of air pollutants, weather conditions, and COPD admissions for the elderly in Vancouver, BC (1994 to 1998)

	Days of observation	Mean ± SD	Minimum	Median	Maximum	IQR[a]
Air pollutants						
CO (ppm)	1826	0.71 ± 0.28	0.30	0.64	2.48	0.26
O_3 (ppb)	1826	14.08 ± 6.57	1.00	13.76	38.61	9.30
NO_2 (ppb)	1826	17.03 ± 4.48	4.28	16.49	33.89	5.47
SO_2 (ppb)	1826	3.79 ± 2.12	0.75	3.33	22.67	2.75
PM_{10} (μg/m^3)	1826	14.02 ± 6.22	3.79	12.59	52.17	8.27
Weather conditions						
Mean temperature (°C)	1810	10.79 ± 5.83	−9.20	10.60	25.90	9.10
Relative humidity (%)	1825	78.44 ± 10.00	30	79	99	14
COPD admissions	1826	3.30 ± 2.06	0	3	16	2

[a]IQR, interquartile range.

Table 4 shows the relative risk of COPD hospitalization and 95% confidence intervals (95% CI) for exposure to each gaseous pollutant and PM_{10} after the adjustment for weather conditions. Estimates were calculated for an IQR increment of each air pollutant for 1- to 7-day average levels of each pollutant. NO_2, CO, and PM_{10} were all significantly associated with COPD hospitalization. The relative risk of COPD hospitalization based on a 7-day average exposure was 1.11 (95% CI, 1.04, 1.20), 1.08 (1.02, 1.13), and 1.13 (1.05, 1.21) for NO_2, CO, and PM_{10}, respectively. There was no significant association between either SO_2 or O_3 and COPD hospitalization.

The relative risks of COPD hospitalization in two-pollutant models involving gaseous pollutants are given in Table 5. All risk estimates are based on 7-day exposure averages, except for O_3, for which a 4-day exposure average was used. The estimates from CO and NO_2 were stable after an adjustment for either O_3 or SO_2; however, CO and NO_2 estimates were reduced by almost half after an adjustment for the other pollutant. The effects of gaseous pollutants on COPD hospitaliza-

Table 2
Seasonal variations of air pollutants, weather conditions, and COPD admissions for the elderly in Vancouver, BC (1994 to 1998)

	Mean ± SD				*P* value
	Winter (Jan–Mar)	Spring (Apr–Jun)	Summer (Jul–Sep)	Fall (Oct–Dec)	
Air pollutants					
CO (ppm)	0.83 ± 0.35	0.56 ± 0.11	0.65 ± 0.21	0.81 ± 0.29	<0.001
O_3 (ppb)	13.24 ± 6.94	19.42 ± 4.99	13.75 ± 5.08	9.96 ± 5.27	<0.001
NO_2 (ppb)	19.20 ± 4.86	15.36 ± 3.72	16.33 ± 4.57	17.27 ± 3.77	<0.001
SO_2 (ppb)	4.10 ± 2.87	3.40 ± 1.58	4.10 ± 1.79	3.56 ± 1.92	<0.001
PM_{10} ($\mu g/m^3$)	12.73 ± 6.23	14.00 ± 6.07	17.18 ± 5.99	12.14 ± 5.34	<0.001
Weather conditions					
Mean temperature (°C)	5.51 ± 3.40	13.05 ± 3.18	17.45 ± 2.36	6.96 ± 4.10	<0.001
Relative humidity (%)	80.61 ± 11.74	73.94 ± 7.61	74.98 ± 7.91	84.23 ± 8.48	<0.001
COPD admissions	4.37 ± 2.34	3.29 ± 1.92	2.49 ± 1.63	3.07 ± 1.85	<0.001

Table 3
Pearson correlation coefficients for mean concentrations of pollutants and meteorology, the greater Vancouver area, 1994 to 1998

	RH	CO	O_3	NO_2	SO_2	PM_{10}
Temperature (°C)	−0.27	−0.39	0.27	−0.31	−0.03	0.27
Relative humidity (%)		0.32	−0.56	0.09	0.07	−0.24
Pollutant						
CO (ppm)			−0.56	0.73	0.67	0.50
O_3 (ppb)				−0.32	−0.34	−0.09
NO_2 (ppb)					0.61	0.61
SO_2 (ppb)						0.62
PM_{10} ($\mu g/m^3$)						1.00

Table 4
Adjusted relative risk estimates[a] and 95% CI for air pollutants in relation to COPD hospitalizations among the elderly in Vancouver, BC (1994–1998)

Pollutants (IQR[b])	Exposure period						
	1 day	2 days	3 days	4 days	5 days	6 days	7 days
CO (0.3 ppm)	1.03 (1.00, 1.06)	1.04 (1.01, 1.08)	1.05 (1.01, 1.09)	1.05 (1.00, 1.10)	1.06 (1.01, 1.11)	1.07 (1.02, 1.12)	1.08 (1.02, 1.13)
O_3 (9.3 ppb)	1.04 (0.98, 1.10)	1.03 (0.96, 1.11)	1.03 (0.94, 1.13)	1.04 (0.94, 1.14)	1.00 (0.90, 1.10)	0.97 (0.87, 1.07)	0.95 (0.86, 1.06)
NO_2 (5.5 ppb)	1.05 (1.01, 1.09)	1.04 (1.00, 1.10)	1.07 (1.01, 1.13)	1.08 (1.02, 1.15)	1.10 (1.03, 1.17)	1.11 (1.04, 1.19)	1.11 (1.04, 1.20)
SO_2 (2.8 ppb)	1.00 (0.97, 1.04)	1.02 (0.98, 1.06)	1.04 (0.99, 1.08)	1.04 (0.99, 1.09)	1.05 (0.99, 1.11)	1.06 (1.00, 1.13)	1.06 (0.99, 1.13)
PM_{10} (8.3 $\mu g/m^3$)	1.07 (1.03, 1.12)	1.08 (1.03, 1.13)	1.09 (1.03, 1.16)	1.10 (1.03, 1.17)	1.11 (1.04, 1.18)	1.12 (1.05, 1.20)	1.13 (1.05, 1.21)

[a]Relative risk estimates were calculated for an interquartile range increment for each air pollutant, which was adjusted for daily mean temperature and average relative humidity.
[b]IQR, interquartile range.

Table 5
Relative risk estimates[a] (and 95% CI) for COPD hospitalization associated with gaseous pollutants in two-pollutant models

Pollutants (IQR[b])	One-pollutant models	Two-pollutants models					
		Model 1 $CO+O_3$	Model 2 $CO+NO_2$	Model 3 $CO+SO_2$	Model 4 O_3+NO_2	Model 5 O_3+SO_2	Model 6 NO_2+SO_2
CO (0.3 ppm)	1.08 (1.02, 1.13)	1.11 (1.04, 1.18)	1.04 (0.95, 1.14)	1.11 (1.01, 1.22)	—	—	—
O_3 (9.3 ppb)	1.04 (0.94, 1.14)	1.10 (0.99, 1.21)	—	—	1.05 (0.95, 1.16)	1.06 (0.96, 1.17)	—
NO_2 (5.5 ppb)	1.11 (1.04, 1.20)	—	1.07 (0.96, 1.20)	—	1.12 (1.04, 1.20)	—	1.12 (1.02, 1.24)
SO_2 (2.8 ppb)	1.06 (0.99, 1.13)	—	—	0.97 (0.87, 1.07)	—	1.07 (1.00, 1.14)	0.99 (0.91, 1.08)

[a]Relative risk estimates were calculated for an interquartile range increments for each air pollutants, which were adjusted for daily mean temperature and average relative humidity. Seven-day average exposure was used for CO, NO_2, and SO_2, and 4-day average exposure was used for O_3.
[b]IQR, interquartile range.

Table 6
Relative risk estimates[a] (and 95% CI) for COPD hospitalization associated with gaseous pollutants adjusted for PM_{10}

Pollutants (IQR[b])	One-pollutant models	Two-pollutant models				Full model
		Model 1 $CO+PM_{10}$	Model 2 O_3+PM_{10}	Model 3 NO_2+PM_{10}	Model 4 SO_2+PM_{10}	
CO (0.3 ppm)	1.08 (1.02, 1.13)	1.02 (0.93, 1.12)	—	—	—	1.08 (0.96, 1.22)
O_3 (9.3 ppb)	1.04 (0.94, 1.14)	—	1.05 (0.96, 1.16)	—	—	1.07 (0.96, 1.19)
NO_2 (5.5 ppb)	1.11 (1.04, 1.20)	—	—	1.03 (0.90, 1.17)	—	1.01 (0.88, 1.16)
SO_2 (2.8 ppb)	1.06 (0.99, 1.13)	—	—	—	0.97 (0.88, 1.06)	0.94 (0.85, 1.05)
PM_{10} (8.3 μg/m^3)	1.13 (1.05, 1.21)	1.10 (0.99, 1.23)	1.13 (1.05, 1.21)	1.10 (0.97, 1.25)	1.15 (1.05, 1.27)	1.10 (0.85, 1.26)

[a]Relative risk estimates were calculated for an interquartile range increment for each air pollutant, which was adjusted for daily mean temperature and average relative humidity. Seven-day average exposure was used for CO, NO_2, and SO_2, and 4-day average exposure was used for O_3.
[b]IQR, interquartile range.

tion were not significant after the adjustment for PM_{10} (Table 6).

We also coregressed COPD hospitalization simultaneously on CO, O_3, NO_2, and SO_2. The relative risks (95% CI) evaluated at their respective IQRs were 1.10 (0.98, 1.23) for CO, 1.08 (0.97, 1.20) for O_3, 1.06 (0.95, 1.19) for NO_2, and 0.96 (0.86, 1.06) for SO_2. The combined relative risk for these four gaseous pollutants was 1.21. Inclusion of PM_{10} in this multiple regression would result in relative risks of 1.08 (0.96, 1.22) for CO, 1.07 (0.96, 1.19) for O_3, 1.01 (0.88, 1.16) for NO_2, 0.94 (0.85, 1.05) for SO_2, and 1.10 (0.85, 1.26) for PM_{10}. The inclusion of PM_{10} in the multiple-regression models did not have a marked effect on the relative risk estimates for the gaseous pollutants. The combined relative risk for the four gaseous pollutants plus PM_{10} was virtually unchanged at 1.21.

4. Discussion

In this study, NO_2 was the strongest predictor of hospital admissions for COPD among all gaseous pollutants in single-pollutant models. This finding is consistent with recent previous results reported by members of our research team (Lin et al., 2003; Burnett et al., 1999). The attenuation of particulate mass effects by NO_2 in the present study was also seen previously by Moolgavkar and Luebeck (1996) and Burnett et al. (1997b). In a study of air pollution and hospital admissions in Sydney, Australia, COPD was more strongly associated with NO_2 than with particulates (Morgan et al., 1998). Some biologic links between NO_2 and exacerbation of respiratory problems support these findings. Oxidants are not highly soluble and most inhaled gas is retained in the small airways of lungs, particularly in the case of NO_2 (Steenland and Savitz, 1999). NO_2 has a greater airway deposition than O_3 (Evans et al., 1973) and remains a pollutant of current concern (National Research Council, 1998). Morrow et al. (1992) found that patients with COPD were more sensitive to nitrogen dioxide than healthy control subjects in experimental studies. Sunyer et al. (2002) found that nitrogen dioxide was associated with mortality for all causes of death in asthmatic patients with more than one emergency room visit for asthma. The association was particularly strong for respiratory causes. However, other studies have failed to link NO_2 exposure with respiratory admissions (Morrow et al., 1992). Different concentrations and varying susceptibility to NO_2 may explain in part the discrepancies between these studies, along with differences in analysis methods.

Using time-series analysis, we found CO to be significantly associated with COPD hospitalization in single-pollutant models. Several studies have found CO to be associated with asthma admission in children, total respiratory admissions, and hospitalization for cardiovascular diseases (Burnett et al., 1997c, 1999; Morris et al., 1995). In our study, ambient CO was highly correlated with NO_2 and PM_{10}. All three of these pollutants are generated primarily from transportation sources. Both NO_2 and PM_{10} attenuated the risk estimate for CO in two-pollutant models at the same time; CO reduced the risk estimates for both NO_2 and PM_{10}. These results were consistent with those of Burnett et al. (1997c) and Linn et al. (2000). Burnett et al. (1997c) found little evidence of an association between CO and either respiratory or cardiac admissions after adjustment for any other ambient air pollutant. Linn et al. (2000) found that pulmonary disease admissions were more strongly associated with NO_2 and PM_{10} than with CO. Norris et al. (1999) postulated that CO could be acting as a surrogate for particular matter. However, in the studies of Burnett et al. (1997c) and Morris et al. (1995), CO was a stronger predictor of hospitalization rates compared with other gaseous pollutants. The reasons for the discrepancies are not known and it is likely that there are no simple explanations. Many factors may play a role, including changing pollutant concentrations, peak levels, and population characteristics such as SES variables and demographic pyramid, etc. Different biological mechanisms may also exist for different outcomes. We found a marginally significant association between COPD hospitalization and 6-day average SO_2 exposure. Most previous epidemiological studies have not detected a significant effect of SO_2 on respiratory emergency room visits or hospital admissions (Anderson et al., 1997; Burnett et al., 1999). This inconsistent result could be because most previous studies did not examine prolonged exposure to SO_2 and that the SO_2 effect seems to be age and gender related (Lin et al., 2003).

Ozone is a powerful oxidant and toxic air pollutant of which the primary target tissue is the lung; breathing slightly elevated concentrations of ozone results in a range of respiratory symptoms. People with conditions such as asthma and COPD generally experience an exacerbation of their symptoms following exposure to ozone (Mudway and Kelly, 2000). Most previous epidemiological studies have detected a significant effect of O_3 on COPD admissions and respiratory admissions (Anderson et al., 1997; Fusco et al., 2001; Desqueyroux et al., 2002; Tenias et al., 2002). However, no association between O_3 and COPD hospitalization was found in this study. Similar null results have also been found in some other studies (Lin et al., 2003; Morgan et al., 1998). White et al. (1994) observed an effect of ozone on pediatric asthma emergency room visits in Atlanta, GA, USA when ozone concentrations exceeded 110 ppb, but no effect was found at concentrations of less than 110 ppb. Ozone concentrations were all below 110 ppb in the present study throughout the study period. Our results also are supported by an animal study in which concurrent O_3 exposure had no effect on the induction of emphysema by cigarette smoke (March et al., 2002).

There is a stronger correlation between personal and ambient exposures to various air pollutants (Sarnat et al., 2000), and, therefore, we believe that ambient measures are reasonably good indicators for personal exposures. In this study, several air pollutants showed moderate to strong positive correlation with one another. As such, risk estimates for these pollutants were sensitive to adjustment for co-pollutant exposures. The effects of gaseous pollutants on COPD hospitalization disappeared after further adjustment for PM_{10}. The combined relative risk for all four gaseous pollutants (CO, O_3, NO_2, and SO_2) was estimated to be 1.21 and was unchanged by the adjustment for PM_{10}. Similar results were observed by Burnett et al. (1997b). Since one of the main sources of fine particles in most urban environments is the condensation of gases, it is not unexpected that gaseous pollutants should be able to explain variation in health responses beyond that attributable to particle mass alone. However, since the gaseous pollutants were moderately or highly correlated with PM_{10}, it is difficult to separate the individual effects of a single pollutant from the combined effects of the complex mixture of air pollutants found in urban environments.

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