

Air Pollution and Daily Mortality in a City with Low Levels of Pollution

Sverre Vedal,¹ Michael Brauer,^{2,3} Richard White,⁴ and John Petkau⁴

¹Department of Medicine, National Jewish Medical and Research Center, Denver, Colorado, USA; ²Department of Medicine, ³School of Occupational and Environmental Hygiene, and ⁴Department of Statistics, University of British Columbia, Vancouver, British Columbia, Canada

The concentration–response relationship between daily ambient inhalable particle (particulate matter $\leq 10 \mu\text{m}$; PM_{10}) concentrations and daily mortality typically shows no evidence of a threshold concentration below which no relationship is observed. However, the power to assess a relationship at very low concentrations of PM_{10} has been limited in studies to date. The concentrations of PM_{10} and other air pollutants in Vancouver, British Columbia, Canada, from January 1994 through December 1996 were very low: the 50th and 90th percentiles of daily average PM_{10} concentrations were 13 and 23 $\mu\text{g}/\text{m}^3$, respectively, and 27 and 39 ppb, respectively, for 1-hr maximum ozone. Analyses of 3 years of daily pollution (PM_{10} , ozone, sulfur dioxide, nitrogen dioxide, and carbon monoxide) concentrations and mortality counts showed that the dominant associations were between ozone and total mortality and respiratory and cardiovascular mortality in the summer, and between nitrogen dioxide and total mortality in the winter, although some association with PM_{10} may also have been present. We conclude that increases in low concentrations of air pollution are associated with increased daily mortality. These findings may support the notion that no threshold pollutant concentrations are present, but they also raise concern that these effects may not be effects of the measured pollutants themselves, but rather of some other factor(s) present in the air pollution–meteorology mix. **Key words:** air pollution, mortality, nitrogen dioxide, ozone, particulate matter. *Environ Health Perspect* 111:45–51 (2003). [Online 14 November 2002] doi:10.1289/ehp.5276 available via <http://dx.doi.org/>

An association between short-term changes in ambient pollutant concentrations, especially particle concentrations, and daily mortality has been observed in many settings (1,2). These settings have included a range of mean particle concentrations and of particle emission sources and different types and concentrations of other ambient pollutants. When concentration–response relationships between particle concentration and daily mortality have been evaluated, most studies have observed that the relationship is reasonably linear, even down to the lowest concentrations observed in any given study (3–5). One implication of such observations is that no clear threshold concentration can be identified below which no effects of particle pollution are observed.

Conclusions about the linearity of the concentration–response relationship extending down to the lowest observed concentrations should be tempered by the relative scarcity of observations at the lowest, as well as the highest, particle concentrations in most studies. This is reflected in the larger confidence intervals around the fitted relationship typically observed at both low and high concentration extremes (6). Further, error in measuring individual particle exposures due to the use of only a few pollution monitors to reflect individual exposures would be expected to blur any threshold concentration, if one exists. This occurs because some individuals will have true exposures above their “thresholds” when measured exposures are below these thresholds, and some will have true exposures below their “thresholds” when measured

exposures are above these thresholds (7). The observed linearity of the concentration–response relationships may therefore partly be a result of measurement error.

Vancouver, British Columbia, Canada, is a large urban area that has low levels of air pollution relative to other large urban areas (2,8). For example, the mean daily PM_{10} (particulate matter $\leq 10 \mu\text{m}$ in diameter) concentration in Vancouver during 1994–1996 was lower than that reported for any of the 90 cities studied in the National Morbidity and Mortality Air Pollution Study (NMMAPS) (2). A large number of observations are therefore available at very low concentrations of ambient particles and other pollutants, which should enhance the ability to assess effects at the low end of the concentration–response relationship. The presence of an association at these low concentrations would argue in favor of the linearity of the concentration–response relationship extending down to very low concentrations. Conversely, the absence of an association would argue that a threshold concentration is present.

Methods

Mortality data. Vancouver is a metropolitan area with a population of approximately 1.8 million located on the southwest coast of British Columbia. Daily mortality data for the lower mainland of British Columbia, including Vancouver, for the 3-year period January 1994–December 1996 were obtained from the Centre for Health Services and Policy Research at the University of British Columbia, with approval from the British

Columbia Vital Statistics Agency, Ministry of Health Services, and included date of death, underlying cause of death according to the *International Classification of Diseases*, Ninth Revision (ICD-9), local health area of residence and of death, and date of birth. Total deaths were defined as all deaths except those with an underlying cause of trauma or suicide (ICD-9 codes 800–999). Respiratory deaths were defined as all deaths coded with ICD-9 codes of 460–519, and cardiovascular deaths were defined as deaths with ICD-9 codes of 390–459.

Pollution and meteorology data. Mean hourly pollutant concentration data [inhalable particulate matter (PM_{10}), ozone, nitrogen dioxide, sulfur dioxide, and carbon monoxide] were obtained from the Greater Vancouver Regional District for the same 3-year period for which mortality data were available. The pollutant monitoring network spanned the entire region extending from Vancouver proper eastward to Chilliwack, 90 km east of Vancouver. The network for continuous pollutant monitoring included 10 monitoring sites for PM_{10} [using tapered element oscillating microbalance (TEOM) monitors], 19 O_3 monitoring sites, 12 SO_2 sites, 19 NO_2 sites, and 16 CO sites. Mean hourly meteorologic data on temperature (16 sites), relative humidity (7 sites), barometric pressure (7 sites), and rainfall (8 sites) were obtained from Environment Canada and the Greater Vancouver Regional District.

Analysis. We filled in missing hourly data values for each pollutant and each meteorologic variable (except rainfall) separately using the EM algorithm, after preprocessing to remove systematic patterns in the data. Specifically, temporal patterns were first removed from the observed data at each of the available sites using sine and cosine functions with periods of 1, 1/2, 1/3, 1/4, 1/6, 1/12 and 1/24 of a year, as well as indicators for the hour of the day as predictors. We

Address correspondence to S. Vedal, Division of Environmental and Occupational Health Sciences, National Jewish Medical and Research Center, 1400 Jackson Street, Denver, CO 80206 USA. Telephone: (303) 398-1520. Fax: (303) 398-1452. E-mail: vedals@njc.org

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removed any autoregressive (AR) structure in the residuals from this initial fit by fitting an AR model; the AR order was chosen to adequately minimize residual autocorrelation, with fourth-order AR models being adequate for all variables. We then applied the EM algorithm to these residuals from all sites simultaneously to take advantage of any spatial autocorrelation that might be present in the variables. This yields an imputed residual for each missing hourly value, which, when added to the predictions from the temporal and AR fits, provides the filled-in value. The available rainfall data were converted to an indicator (present or absent) for each hour at each site. The estimated probability of rainfall was imputed for missing hourly values of the indicator using a logistic regression separately at each site, incorporating temporal patterns as described above for the other variables.

The estimation procedure for missing data was carried out on the log scale for the pollution variables because their distributions were skewed. To overcome the minor complication of some sites reporting zero readings for some

variables, we added a small positive constant (one-half the smallest nonzero hourly measurement of that variable in the entire data set) to all the observations before the data were log transformed. After exponentiating to transform back to the original scale, we subtracted this same constant from each of the filled-in hourly values.

Because the mortality data were available on a daily basis, all analyses were carried out with daily data. We obtained overall daily values of the pollutants (except O_3) and the meteorologic variables by first averaging the filled-in hourly values across the day at each site and then averaging these site-specific daily average values across the available sites. For O_3 , the maximum hourly value over the day was first determined at each site, and these site-specific maxima were then averaged across the available sites. For rainfall, the overall daily value is the proportion of hours for which rain was recorded.

Because of the marked seasonality of some of the pollutants, we stratified analyses by season. Only two “seasons” were chosen given

the relatively moderate marine climate in Vancouver: summer ranging from May through September, and winter from October through April. We used both Poisson regression and generalized additive models for count data (9) to estimate the effects of the air pollutants on daily mortality. A systematic battery of preliminary analyses were carried out separately on the total, respiratory, and cardiovascular mortality counts in summer and winter to identify appropriate forms to adjust for temporal trends and meteorologic effects. The primary approach taken to removing the temporal trends was to fit a loess smooth. Initially, we explored a wide range of window widths using total mortality, with more detailed exploration subsequently of window widths ranging from 90 to 180 days for all mortality outcomes. Examination of the partial autocorrelation functions suggested a window width of 120 days sufficed to remove almost all of the autocorrelation in the residuals and was therefore used for all subsequent loess-based temporal adjustments. We then explored various combinations of loess smooths of the

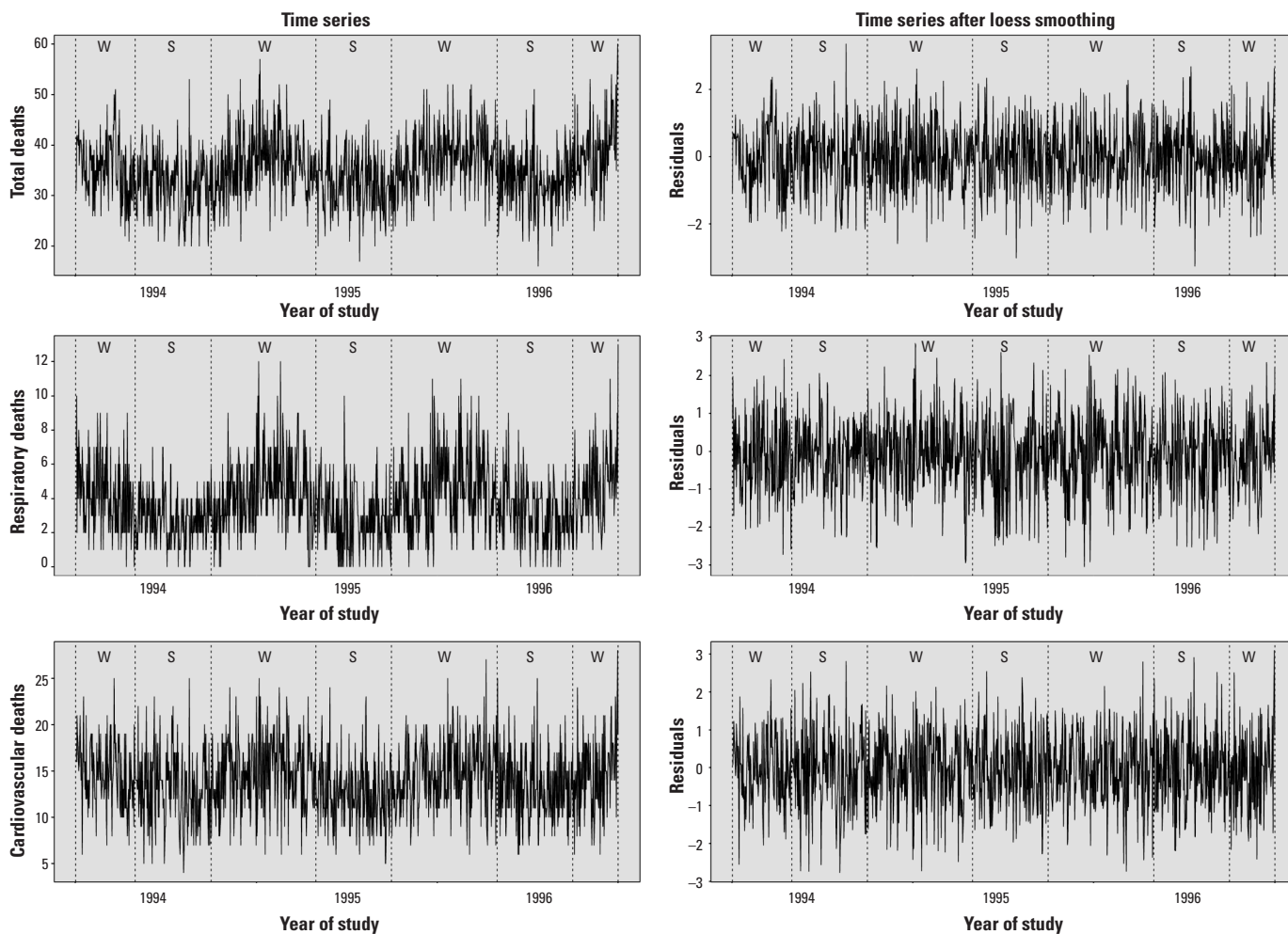


Figure 1. The time series of daily total, respiratory, and cardiovascular deaths from January 1994 through December 1996 show an annual cyclical pattern that is most pronounced for respiratory deaths [dotted lines separate summer (S) from winter (W)]. The corresponding residual time series plots after use of loess smoothing of long-term temporal trends show that no meaningful cyclical patterns persist.

meteorologic variables as additional adjustments. The impact of these adjustments was much more modest than that for the temporal trends in the winter, but comparable in the summer. In each case, there was little to choose among many of the different possible adjustments. Results reported here are for models in which the meteorologic adjustment is a sum of separate loess smooths of temperature, relative humidity, barometric pressure, and rainfall on the same day, each based on the default window width of one-half.

To allow for easy interpretation and significance testing, we then entered linear terms for each pollutant in separate models for day lags ranging from no lag (same day) to 2 days. We examined the simultaneous effects on mortality of two pollutants by fitting models

with linear terms for each of the two pollutants together.

We performed sensitivity analyses to assess the influence on the results of using a different approach to accounting for temporal trends. For these analyses, a linear trend and sine and cosine terms with periods of 1 year, and 6, 4, and 3 months were included in the models instead of a loess smooth to capture the temporal trends. Exploration of various loess smooths of the meteorologic variables indicated that the same sum of separate loess smooths of temperature, relative humidity, barometric pressure, and rainfall on the same day provided adequate adjustment for the meteorologic variables.

We used S-Plus (Insightful Corp., Seattle, WA, USA) for all analyses. Model fits using

loess smooths were based on stringent convergence criteria (10^{-9} for both the local scoring and backfitting algorithms) to eliminate recently identified difficulties with the use of the default convergence criteria in the S-Plus generalized additive models (GAM) module (10). Standard errors for the pollutant effects in these model fits were determined by a Monte Carlo approach (based on 1,000 simulated Poisson data sets for each model fit) to avoid reliance on the potentially inaccurate approximation used to evaluate these standard errors in the S-Plus implementation of GAM (10,11).

Results

Mortality, pollution, and meteorology. Total daily deaths showed an annual cyclical pattern with peaks occurring in the winter (Figure 1). Numbers of daily deaths ranged largely from 30 to 40 per day. Respiratory deaths showed an even more pronounced cyclical pattern, with peaks again occurring in the winter. Cardiovascular deaths also showed an annual cyclical pattern, but this was much less pronounced than for respiratory deaths. After removal of long-term temporal trends using a loess smooth (with a window width of 120 days) separately for summer and winter, residual plots showed that the annual patterns seemed to be adequately removed (Figure 1).

Each of the monitored pollutants and meteorologic variables had some data missing. For PM_{10} , 8.9% of the monitor-hours had missing concentration data. For O_3 , SO_2 , NO_2 , and CO, 4.7%, 6.4%, 6.5%, and 5.0% of the monitor-hours, respectively, were missing. For temperature, humidity, barometric pressure, and rainfall, 5.3%, 12.9%, 14.7%, and 2.7% of the hourly measurements, respectively, were missing. We estimated the missing hourly data using an EM algorithm as detailed in "Methods," with the overall daily values based on the complete set of pollution and meteorologic data, both measured and estimated, used in the analyses.

The overall daily air pollution concentrations and the meteorologic measures exhibited various temporal patterns (Figure 2). Of the pollutants, O_3 , with higher concentrations in summer, and CO, with higher concentrations in winter, exhibited the most seasonal variability. Air pollution concentrations were uniformly low (Table 1). The pollution variables, apart from O_3 , were highly correlated (Table 2). Correlations between pollutants were generally similar for the summer and winter seasons, with the exception of O_3 , for which correlations with other pollutants were negative in winter but positive in summer.

Single-pollutant models. Linear terms for the pollution variables were added singly to the regression models in which separate loess smooths were used to remove the long-term

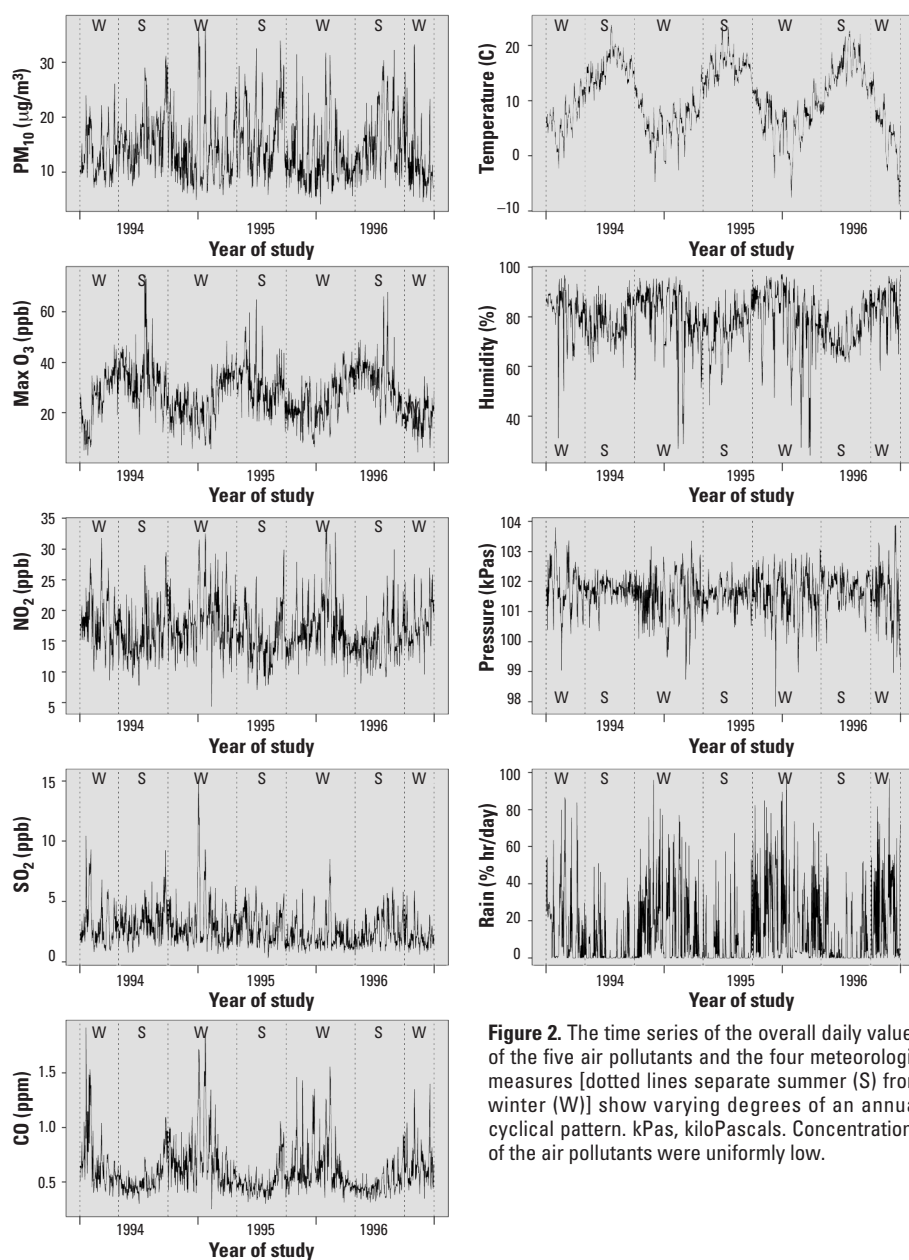


Figure 2. The time series of the overall daily values of the five air pollutants and the four meteorologic measures [dotted lines separate summer (S) from winter (W)] show varying degrees of an annual cyclical pattern. kPas, kiloPascals. Concentrations of the air pollutants were uniformly low.

temporal patterns and adjust for the same day temperature, relative humidity, barometric pressure, and rainfall. Estimated effects for total, respiratory, and cardiovascular deaths by season for a standard deviation change in concentration for each pollutant at lags of 0, 1, and 2 days are presented in Figure 3. In the summer, we observed a statistically significant effect on total deaths only for O₃ at lag 0, and a nearly significant effect ($p < 0.10$) for SO₂ at lag 0. Statistically significant effects on respiratory deaths in the summer were observed for PM₁₀, O₃, and SO₂, but effects of NO₂ and CO were also nearly significant. Effects on cardiovascular deaths were seen only for O₃, and then only for lag 0 ($p < 0.10$). In the winter, we observed significant effects on total deaths for PM₁₀ (lag 2), NO₂ (lag 2), and SO₂ (lag 1). No significant deleterious effects on respiratory deaths were observed. Effects on cardiovascular deaths were observed for NO₂ (lags 1 and 2) and SO₂ (lag 1).

Two-pollutant models. Because pollutant concentrations are often highly correlated, findings from single-pollutant models may be difficult to interpret. We fit models including linear terms for all pollutant lag pairs (lags 0, 1, 2) to attempt to identify independent pollutant effects. We focused attention on those models in which both pollutant effects were observed in the single-pollutant models. In the summer, of the significant effects detected in the single-pollutant models, only the effects of O₃ on total mortality at lag 0 and on respiratory mortality at lag 2 remained statistically significant in all two-pollutant models (Figure 4 shows the estimates of effect from the most relevant two-pollutant models). In the winter, only the effect for NO₂ on total mortality at lag 2 was largely unchanged after the addition of other pollutants (Figure 4). Other effects that were significant in the single-pollutant models were substantially diminished after addition of some of the other pollutants in the two-pollutant models: for example, the greatly diminished effect of PM₁₀ at lag 1 on respiratory mortality in the summer after the addition of O₃, and the greatly diminished effect of SO₂ at lag 1 on total mortality in the winter after the addition of NO₂ (Figure 4).

Sensitivity analyses. As detailed in the "Methods," another approach taken to removing the long-term temporal trends was to fit a linear trend and sine and cosine functions with frequencies ranging from 1 year to 3 months to the mortality series. Residuals from these fits showed that the annual pattern for total, respiratory, and cardiovascular deaths was removed (data not shown). Although, in general, there was little difference in estimates of pollution effect between the two approaches to removing the long-term temporal trends, there were exceptions. For example, Figure 5

illustrates the smaller effect estimates obtained for total mortality in the summer with the sine-cosine function approach. If differences were observed, loess smooth models almost always resulted in larger estimates of pollution effect. However, no qualitative differences in the study findings resulted from the use of the trigonometric function approach rather than loess smoothing for the removal of long-term temporal trends.

Discussion

In Vancouver, where ambient concentrations of all major air pollutants are low relative to other large urban areas (2,8), the principal finding of this 3-year study was that increases in the concentrations of some of the gaseous air pollutants, particularly O₃ in the summer, were associated with increases in daily mortality. For PM₁₀, the only relatively robust effect was for increased respiratory mortality in the summer at lag 1, but even that was sensitive to inclusion of O₃ (at lag 2) in the two-pollutant model.

Estimated effects of ambient particulate matter have been less consistently observed in some more recently reported time-series studies, whereas gaseous pollutant effects have been observed more consistently (12–16). It is not known whether these effects reflect those of the gaseous pollutants themselves, or whether the gaseous pollutants are acting as surrogate markers of pollutant sources that contain more toxic compounds. In Vancouver, given the low concentrations of these pollutants, it seems unlikely that the observed effects are due to the

measured pollutants themselves. The mean concentrations of both PM₁₀ and O₃ (mean 24-hr average was 13.7 ppb) during the 3-year period of the study (1994–1996) were lower than those in any of the 90 cities studied in NMMAPS (2). Further, only one of the cities in NMMAPS in which data on carbon monoxide were available had a lower mean concentration of carbon monoxide than Vancouver. Mean concentrations of NO₂ and SO₂ in Vancouver were lower than 72% and 76% of the cities in NMMAPS, respectively. Because the mean concentrations reported in NMMAPS were trimmed means in which the upper and lower 10th percentiles were excluded, and because the distribution of concentration data is typically skewed to the right, it would be expected that the trimmed means would be lower than those calculated from the complete set of data. If trimmed values had been calculated for Vancouver, mean concentrations relative to the cities included in NMMAPS would have been even lower.

In Vancouver, the most notable effects on mortality were those associated with increases in O₃ concentrations. It is noteworthy that, of the pollutants, O₃ was least strongly correlated with the other pollutants. Two-pollutant models with O₃ also typically had the lowest correlations between pollutant effect estimates; effect estimate correlations may be more relevant because they reflect pollutant correlations after long-term temporal trends and effects of meteorology have been removed. The weaker correlations associated with O₃ may have contributed to the ability

Table 1. Distribution of daily mortality counts and overall daily pollutant and meteorologic measures.

	Min	10%	50%	90%	Max	Mean (SD)
Total mortality	16	27	35	43	60	35.0 (6.6)
Respiratory mortality	0	1	4	7	13	3.8 (2.2)
Cardiovascular mortality	4	9	14	19	28	14.0 (4.0)
PM ₁₀ (µg/m ³)	4.1	7.8	13.1	22.8	37.2	14.4 (5.9)
O ₃ [ppb (1-hr max)]	3.1	14.6	27.3	39.4	75.1	27.4 (10.2)
NO ₂ (ppb)	4.3	11.8	16.1	22.9	33.9	16.9 (4.5)
SO ₂ (ppb)	0.3	1.2	2.4	4.9	15.4	2.8 (1.7)
CO (ppm)	0.3	0.4	0.5	0.9	1.9	0.6 (0.2)
Temperature (°C)	-8.8	2.7	10.1	17.8	24.2	10.2 (6.0)
Relative humidity (%)	24.2	65.4	79.9	91.3	97.3	78.6 (11.1)
Barometric pressure (kPas)	97.4	100.7	101.7	102.4	103.9	101.6 (0.7)
Rainfall (% hours/day)	0	0	2.6	48.1	97.9	14.7 (20.9)

Abbreviations: Max, maximum; Min, minimum; kPas, kiloPascals.

Table 2. Pearson correlations among the overall daily pollutant and meteorologic measures by season.^a

	PM ₁₀	O ₃	SO ₂	NO ₂	CO	Temperature	Humidity	Pressure	Rainfall
PM ₁₀		0.48	0.76	0.84	0.71	0.61	-0.35	0.01	-0.47
O ₃	-0.32		0.44	0.45	0.12	0.41	-0.59	-0.02	-0.33
SO ₂	0.78	-0.41		0.80	0.67	0.59	-0.36	0.13	-0.47
NO ₂	0.73	-0.38	0.68		0.81	0.45	-0.24	-0.01	-0.31
CO	0.76	-0.65	0.83	0.78		0.28	0.12	-0.01	-0.19
Temperature	-0.11	0.28	-0.13	-0.34	-0.29		-0.42	0.00	-0.41
Humidity	-0.38	-0.38	-0.21	-0.21	-0.05	0.21		-0.20	0.55
Pressure	0.40	-0.25	0.35	0.24	0.28	-0.04	-0.21		-0.40
Rainfall	-0.55	-0.02	-0.40	-0.31	-0.31	0.13	0.56	-0.40	

^aSummer (May–September) above diagonal; winter (October–April) below diagonal.

to detect effects of O_3 that were relatively insensitive to effects of other pollutants. The difficulty of disentangling the effects of the other pollutants is not surprising in view of the high correlations among them. Because of concerns regarding the interpretability of estimated effects in models containing several strongly correlated variables, we did not attempt to estimate effects from models that included any more than two pollutant terms.

Findings from a study of the acute mortality effect of short-term increases in PM_{10} concentrations in the 88 largest cities in the United States have recently been reported (2,10) (in only 88 of the 90 cities was an effect for PM_{10} estimated). Because these cities were selected only on the basis of population size and availability of pollution concentration data, and a standardized approach was taken to the analysis, these data provide the most comprehensive picture to date of the consistency of acute PM_{10} effects on mortality. An overall effect of a 0.21% increase in total mortality (at a lag of 1 day) for each $10 \mu\text{g}/\text{m}^3$ increase in

PM_{10} concentration was estimated. However, a substantial degree of heterogeneity of effect across cities was observed, with the estimated effect being zero or negative (that is, a decrease in mortality effect associated with an increase in PM_{10} concentration) in 32 of the 88 cities (36%) in the single-pollutant models. The presence of a positive effect in any given city was not clearly related to the average PM_{10} concentration in that city, although there was a trend for stronger effects to be present in cities with lower PM_{10} concentrations, suggesting that the inability to observe a PM_{10} effect in the 33% of cities was not due to the PM_{10} concentrations being below a certain threshold concentration below which effects were not present.

Based on our single-pollutant models, an effect of PM_{10} was present for respiratory mortality in the summer and for total mortality in the winter. However, these effects were sensitive to the addition of other pollutants in the two-pollutant models. The effects of PM_{10} were present even though the average

daily PM_{10} concentration in Vancouver from 1994 to 1996 ($14.4 \mu\text{g}/\text{m}^3$) was lower than that of any of the 88 American cities during 1987–1994, where average daily PM_{10} concentrations ranged from a low of $15.3 \mu\text{g}/\text{m}^3$ to a high of $53.2 \mu\text{g}/\text{m}^3$ (2). In a recent analysis of the concentration–response relationship in the 20 largest of these U.S. cities (4), the investigators argued that no evidence for a threshold for PM_{10} could be found, at least above a concentration of $15 \mu\text{g}/\text{m}^3$. Similar findings were reported for an analysis of all 88 cities (5). The effects of PM_{10} in this study are consistent with the contention that there is no threshold concentration for PM_{10} , nor for some of the other pollutants.

Because the absence of a concentration–response threshold for most air pollutants seems biologically implausible, consideration should be given to possible reasons that time-series studies seem to be unable to detect such thresholds. First, a “blurring” of a threshold might be expected if the use of ambient pollutant concentrations measured with a few

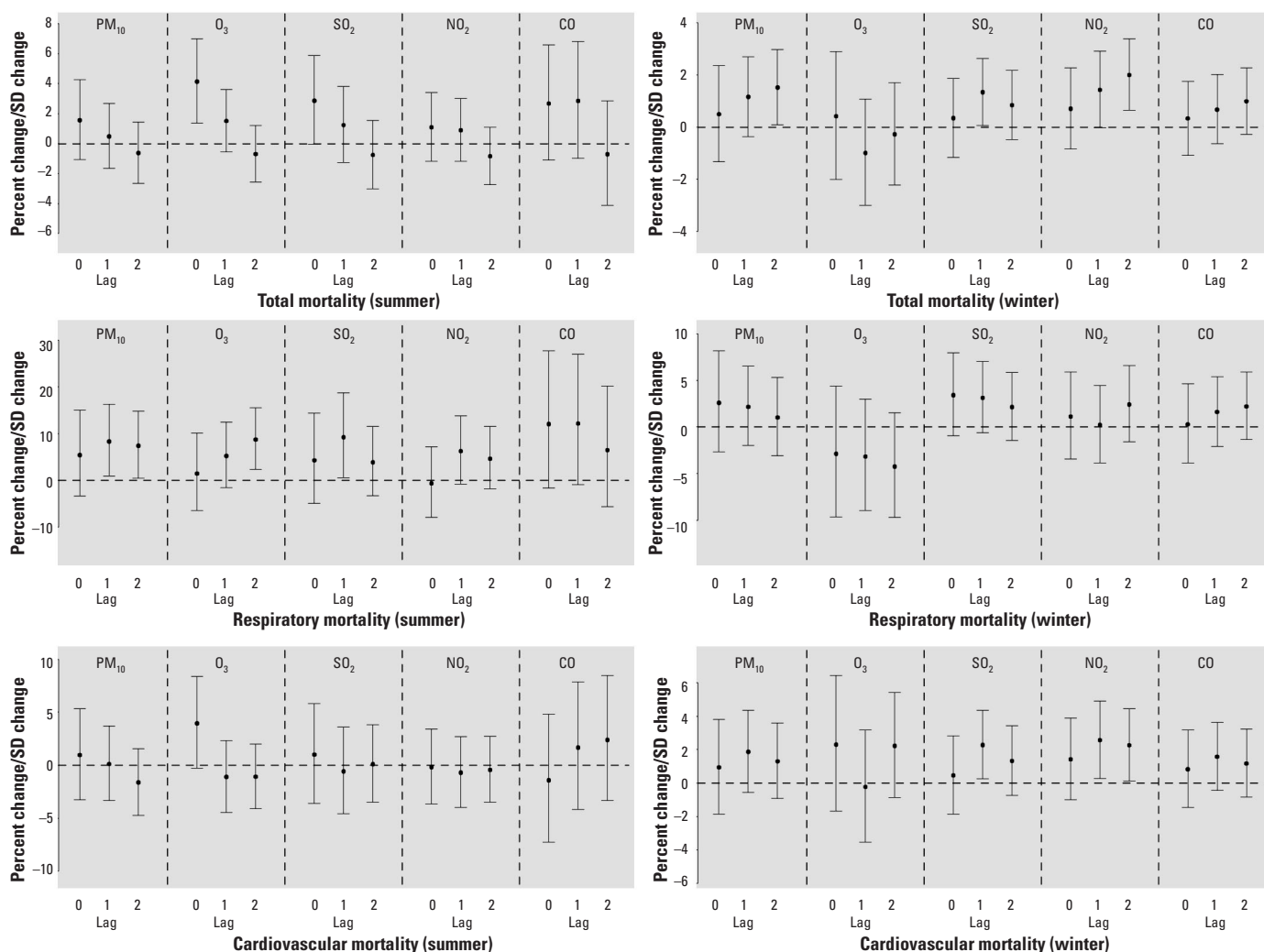


Figure 3. Estimated increases (and 95% confidence intervals) in daily mortality (total, respiratory, and cardiovascular) corresponding to a standard deviation increase in each pollutant from single-pollutant models for three lag periods for summer (May–September) and winter (October–April) periods.

pollution monitors results in error in the measurement of exposure. Such measurement error must be present to some extent. Recent findings of a simulation study based on actual ambient and personal monitoring data suggest that measurement error can have a substantial effect on the ability to detect a threshold (7). Others have not found that measurement error causes any difficulty in identifying a threshold within a meta-analysis context using a collection of cities (3). The detection of effects in Vancouver, where concentrations of all of these pollutants are low, suggests that measurement error may not be solely responsible for the inability to detect threshold concentrations in settings with higher pollutant concentrations.

Second, ambient concentrations of air pollutants may be acting as surrogate measures of exposure to other agents or to specific pollution sources that are in fact responsible for the

observed effects. For example, there is no known mechanism whereby exposure to ambient O₃ might produce adverse cardiac effects, although some have been suggested (17), yet O₃ was associated with cardiac mortality in Vancouver. One could postulate that ambient O₃ concentrations in this setting may be reflecting other pollutants in the photochemical smog mix that might potentially have adverse cardiac effects, although the identity of these agents is not known. No apparent threshold O₃ concentration might therefore be observed if O₃ were acting as such a surrogate measure. Similarly, if PM₁₀ concentrations or concentrations of other pollutants are acting as surrogate measures of another unmeasured toxic pollutant or pollutants, or of specific sources, absence of an apparent threshold for these pollutants could also be observed. It has recently been suggested (18) that in some settings concentrations of

gaseous pollutants may be better measures of exposure to particle pollution than the particle mass concentrations, in which case the apparent gaseous effects merely reflect unmeasured effects of particles. For example, others have also reported an inverse association between O₃ concentrations and mortality in the winter (19) (see Figure 3). It has been proposed that this effect is an example of negative confounding due to the negative correlation between wintertime O₃ and fine PM (20). This seems unlikely in our data given the winter correlation between O₃ and PM₁₀ of -0.32 (Table 2), although the negative correlation with PM_{2.5} could have been stronger. There was little change in the estimate of effect of O₃ on respiratory mortality in the winter in the two-pollutant models (data not shown). We had no data on PM_{2.5} during the 3 years of the study to allow us to specifically address this hypothesis. Additional monitoring in multiple settings is needed to determine whether this is likely.

Third, because meteorology is a strong determinant of air pollutant concentrations in an urban setting, with variation in pollutant emissions being relatively minor, ambient pollutant concentrations might conceivably also be acting as surrogate measures of meteorologic factors. If some of the observed effects of the pollutants are due to meteorology rather than to the pollutants themselves, again, a threshold for the pollutants might not be observable. The addition of daily meteorologic variables to the regression models in this study was aimed at controlling for effects of meteorology in the estimation of air pollutant effects. Alternative approaches to controlling for the effects of meteorology have not significantly affected estimates of pollution effects in other studies (21), suggesting that significant, uncontrolled confounding by meteorology is unlikely. However, when effects of pollutants are detected at low concentrations at which no adverse effects would be expected (that is, no threshold concentrations are detected), and the primary determinant of pollutant concentrations is meteorology, then a case can be made that the pollutant concentrations are

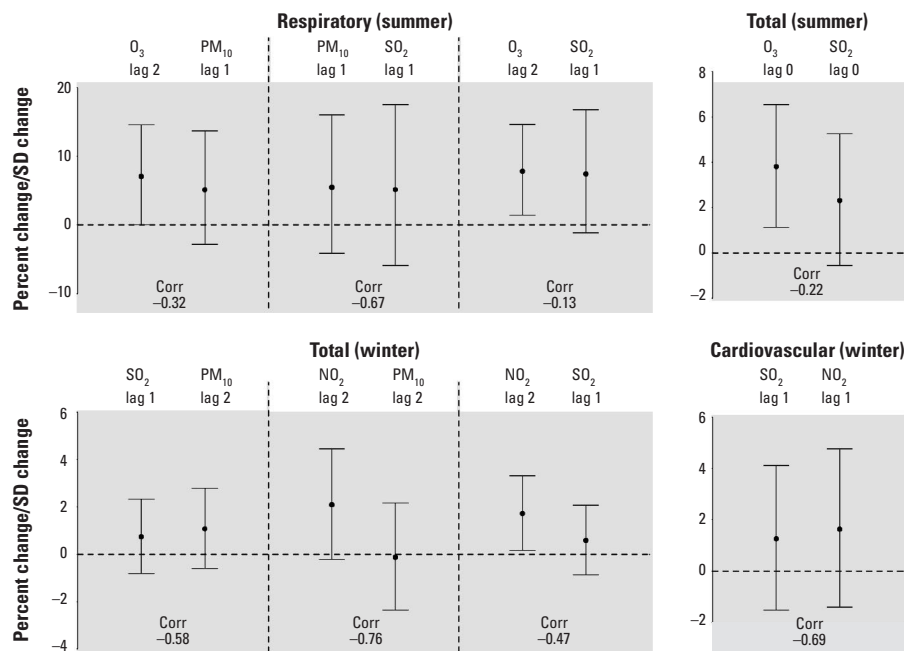


Figure 4. Estimated increases (and 95% confidence intervals) in daily mortality (total, respiratory, and cardiovascular) for a standard deviation increase in each pollutant from selected two-pollutant models. Corr, correlation between the pollutant effect estimates.

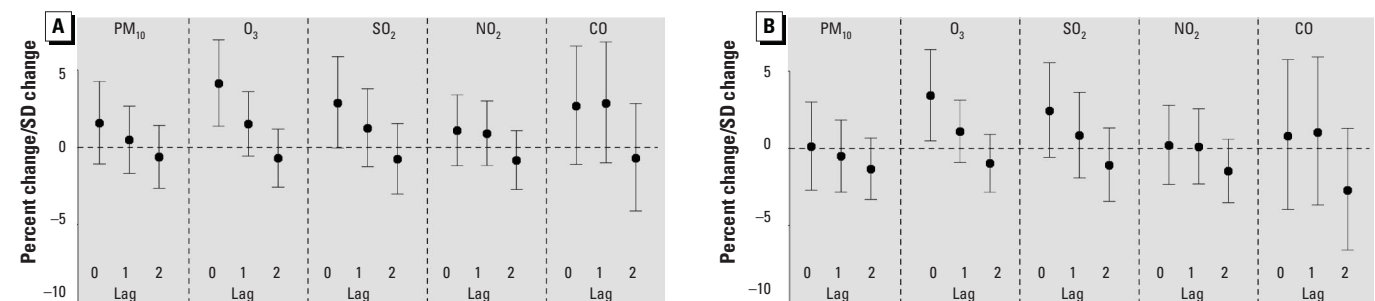


Figure 5. Estimated increases (and 95% confidence intervals) in daily total mortality for a standard deviation increase in pollutant concentration estimated from the single-pollutant models for the summer using (A) loess smoothing or (B) a trigonometric function approach to removing long-term temporal trends. Estimates of effect using the trigonometric functions resulted in smaller estimates of pollution effect in this case.

servicing as better measures of the meteorologic factors influencing mortality than the meteorologic measures themselves (in this case daily temperature, humidity, barometric pressure, and rainfall). Exposure measurement error of the relevant meteorologic factors as measured by pollutant concentrations would also presumably be less than that of the ambient pollutants. Given the multitude of adverse health effects attributed to changes in meteorology (22,23), confounding by meteorology still seems plausible.

Confidence in the study findings can be enhanced by demonstrating that the method of data analysis did not substantially influence the findings. The findings did not exhibit much sensitivity to the approach taken to removing the long-term temporal trends from the data. Findings may have been influenced, however, by the decision to use a seasonally stratified analysis. The decision to stratify the analysis by season was prompted by the obvious annual cycles in much of the time series data (Figures 1 and 2). Rather than attempting to incorporate this seasonal complexity in a single model, an approach that may not succeed in adequately removing all of the seasonal correlations between the time-varying measures (24), it seems justified to stratify by season. A potential disadvantage of stratification is the loss of statistical power and the associated instability of the estimates of effect, but this concern seems relatively unimportant in the current study.

For loess smoothing of the long-term temporal trend, our Monte Carlo estimates of the standard errors of the pollutant effects were typically about 10% larger than those reported by the S-Plus GAM module, though for a few models they were as much as 30% larger. A number of additional pollutant effects would have been judged to be statistically significant based on the smaller standard errors reported by the S-Plus GAM module. The latter should not be used for model fits involving loess smoothing (10,11). For the present context of overdispersed Poisson regression models, the only currently available

alternative for evaluating accurate standard errors is a Monte Carlo approach. This is computationally intensive and time-consuming. This fundamental limitation of the S-Plus GAM module may encourage the use of parametric approaches to smoothing (e.g., natural splines) for which explicit evaluation of exact standard errors of pollutant effects is straightforward even for this context.

In conclusion, assuming that the findings from Vancouver are generalizable to other cities with low pollutant concentrations, increases in air pollutant concentrations, even when concentrations are low, are associated with adverse effects on daily mortality. Although this observation may support the argument that there are no threshold concentrations of air pollution below which adverse effects cannot be detected, it also raises concern that the associations are not reflecting the effects of the measured pollutants, but rather some factor or combination of factors, such as, for example, unmeasured air pollutants or uncontrolled features of meteorology that are correlated with the measured pollutants.

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