Air Pollution and Daily Mortality in Three U.S. Counties

Suresh H. Moolgavkar

Fred Hutchinson Cancer Research Center and Sciences International, Inc, Seattle, Washington, USA

I used generalized additive models to analyze the time-series of daily total nonaccidental and cause-specific (cardiovascular, cerebrovascular, and chronic obstructive pulmonary disease) deaths over the period 1987–1995 in three major U.S. metropolitan areas: Cook County, Los Angeles County, and Maricopa County. In all three counties I had monitoring information on particulate matter ≤ 10 μm (PM_{10}), carbon monoxide, sulfur dioxide, nitrogen dioxide, and ozone. In Los Angeles, monitoring information on particulate matter ≤ 2.5 μm ($PM_{2.5}$) was available as well. I present the results of both single and multi-pollutant analyses. Air pollution was associated with each of the mortality end points. With respect to the individual components of the pollution mix, the results indicate considerable heterogeneity of air pollution effects in the different geographic locations. In general, the gases, particularly CO, but not ozone, were much more strongly associated with mortality than was particulate matter. This association was particularly striking in Los Angeles County. ***Key words:*** **carbon monoxide, cardiovascular disease, cerebrovascular disease, chronic obstructive pulmonary disease, nitrogen dioxide, ozone, particulate matter, sulfur dioxide.** *Environ Health Perspect* **108:777–784 (2000). [Online 12 July 2000]**
http://ehpnet1.niehs.nih.gov/docs/2000/108p777-784moolgavkar/abstract.html

A substantial body of epidemiologic literature indicates that air pollution, even at the generally low concentrations found in contemporary U.S., Canadian, and western European cities, is associated with adverse effects on human health. Reported effects of air pollution include decreased lung function (*1,2*), increased emergency room visits for asthma (*3*), increased hospital admissions (*4,5*) and, most importantly, increased mortality (*6–16*). Although human populations are exposed to a complex mixture of air pollutants that vary in composition with geography and climatic conditions, much of the recent work on air pollution epidemiology has focused on individual components of air pollution, rather than sources of pollution or the entire pollution mix. Because the estimated risks of adverse health effects from exposure are small, it is difficult to investigate the effect of individual components on human health. Therefore, consistency of results from different geographic areas with different climatic conditions and pollution mixes is an important consideration in drawing conclusions regarding the health effects of individual components of air pollution.

In this paper I analyzed the association between air pollution and the time-series of daily deaths in three large U.S. metropolitan areas, Cook County, Illinois, Los Angeles County, California, and Maricopa County, Arizona, with different pollution mixes and climatic conditions. Specifically, I investigated the association between monitored components of air pollution and daily nonaccidental deaths in these three areas over the 9-year period 1987–1995. In addition to total nonaccidental deaths, I also analyzed deaths from cardiovascular disease (CVD), cerebrovascular disease (CrD), and chronic obstructive lung disease and allied conditions (COPD). I undertook the analyses described in this paper to determine whether, when identical methods of analyses over the same period of time are used in different geographic locations, the results for individual components of pollution are consistent. My analyses indicated that, although air pollution was associated with daily mortality in all three metropolitan areas, there was considerable heterogeneity from one location to another. I conclude that, while a direct effect of individual components of air pollution on mortality cannot be ruled out, individual monitored components of air pollution are best thought of as indices of the air pollution mix associated with mortality and that the best index varies from one location to another.

Data and Methods

I obtained daily counts of total mortality, excluding accidents and suicides [i.e., excluding *International Classification of Diseases, Ninth Revision,* (ICD-9), codes 800 and up] in the three counties from data collected by the National Center for Health Statistics (NCHS) over the 9-year period 1987–1995. In addition I extracted the daily counts of deaths due to diseases of the circulatory system (ICD-9 codes 390–448), which I analyzed in two broad subgroups, codes 390–429, dominated by CVD, and codes 430–448, dominated by CrD. Finally, I analyzed deaths from COPD and allied conditions (ICD-9 codes 490–496, which includes asthma, ICD-9 code 493).

I obtained air pollution data for Cook and Maricopa counties from the Aerometric Retrieval System (AIRS) of the U.S. Environmental Protection Agency (Research Triangle Park, NC). The Air Resources Board of the California Environmental Protection Agency (Sacramento, CA) provided the air pollution data for Los Angeles County. In all three counties, daily readings were available for the gaseous criteria pollutants, ozone, sulfur dioxide, nitrogen dioxide, and carbon monoxide. SO_2 and NO_2 readings in Maricopa County were spotty with a number of missing days. In Maricopa and Los Angeles Counties, readings for particulate matter ≤ 10 μm (PM_{10}) were available every sixth day, while in Cook County daily readings for PM_{10} were available. In Los Angeles County, in addition to PM_{10}, every sixth day data were available for particulate matter ≤ 2.5 μm ($PM_{2.5}$). For my analyses, I used the average of daily readings over all monitors in the county for each of the pollutants. I obtained weather-related covariates (temperature and relative humidity) from the monitoring stations at the respective airports.

I analyzed the data using Poisson regression allowing for overdispersion in a generalized additive model (GAM) (*17*). All models included an intercept term, indicator variables for day of week, and a spline smoother (30 degrees of freedom except for sensitivity analyses) for temporal trends. I first investigated the effect of weather related covariates on each of the mortality end points. Specifically, I regressed daily deaths (for each of the mortality end points) against temperature and relative humidity with various lag times from 0 to 5 days. I modeled the effect of temperature and relative humidity on mortality using a spline smoother with 6 degrees of freedom. Once I found the lags for temperature and relative humidity that minimized the deviance, I kept these lags fixed for the subsequent analyses incorporating the effect of the pollutants. In all analyses, missing data were treated as being missing completely at random, and dropped from the analyses.

Once I had determined the optimal model for weather related effects on mortality,

Address correspondence to S.H. Moolgavkar, Fred Hutchinson Cancer Research Center, Division of Public Health Sciences - MP 665, 1100 Fairview Avenue N., Seattle, WA 98109 USA. Telephone: (206) 667-4273; Fax: (206) 667-7004. E-mail: smoolgav@fhcrc.org

I thank E.G. Luebeck for computational support. This work was supported by the American Iron and Steel Institute.

Received 29 February 2000; accepted 11 April 2000.

Table 1. Distribution of key variables in Cook, Los Angeles, and Maricopa counties.

County	Temp (°F)	RH	CO (ppb)	NO_2 (ppb)	O_3 (ppb)	SO_2 (ppb)	PM_{10} (μg/m^3)	$PM_{2.5}$ (μg/m^3)	Deaths from CVD	Deaths from CrD	Deaths from COPD	Total deaths[a]
Cook												
Minimum	– 16	35	224	7	0.2	0.5	3	–	21	1	0	77
1st	35	62	769	20	10	4	25	–	38	7	2	108
Median	51	70	993	25	18	6	35	–	43	9	4	116
3rd	67	80	1,252	30	26	8	47	–	49	11	5	126
Maximum	91	100	3,912	58	67	36	365	–	300	22	13	410
NA	0	0	0	0	0	0	374	–	0	0	0	0
Los Angeles												
Minimum	42	11	237	10	0.6	0	7	4	28	4	0	95
1st	58	67	962	30	14	1	33	15	50	11	4	138
Median	63	77	1,347	38	24	2	44	22	57	14	6	149
3rd	67	82	2,160	48	35	4	59	31	64	17	8	161
Maximum	86	98	5,955	102	77	16	166	86	135	36	21	250
NA	0	0	0	0	0	0	2,638	2,783	0	0	0	0
Maricopa												
Minimum	37	9	269	2	1	0	9	–	3	0	0	16
1st	61	22	875	14	17	0.5	32	–	11	2	1	35
Median	76	31	1240	19	25	2	41	–	13	3	2	40
3rd	89	44	1,849	26	32	4	51	–	17	5	4	47
Maximum	107	94	4,777	56	50	14	252	–	34	12	11	81
NA	0	0	3	1,967	3	796	2,788	–	0	0	0	0

Abbreviations: 1st, first quartile; 3rd, third quartile; Max, maximum; Med, median; Min, minimum; NA, number of days on which data were unavailable; RH, relative humidity; Temp, temperature.
[a]Total nonaccidental deaths.

I examined the association between exposure to a pollutant and daily deaths. Specifically, I entered each pollutant linearly (with a log link function) into the regression and examined lags of between 0 and 5 days. I then investigated the effect of two or more pollutants, each with the same lag. Finally, I undertook limited sensitivity analyses to investigate the effect of the degree of smoothing on the results.

Results

Table 1 shows the distributions of some key variables in the analyses. Table 2 shows the correlations among the pollutants and temperature and relative humidity. The maximum concentration of PM_{10} in Cook County reported in Table 1 is 365 μg/m^3. I was concerned that this high reading reflected an error in my processing of the pollutant data. I was reassured, however, by the fact that the same reading was reported by Styer et al. (*7*) in their analysis of air pollution and mortality in Cook County. There was only one other day during the study period when the concentration of PM_{10} exceeded 150 μg/m^3. Exclusion of these two outliers did not alter the results of my analyses. Table 1 shows that the highest concentrations of both PM_{10} and the gases, particularly CO, were found in Los Angeles.

Table 1 also shows that the maximum number of daily deaths in Chicago over the period of the study was an extraordinary 410, far higher than the number of deaths on any single day in Los Angeles County, which has a considerably larger population. These deaths occurred on 17 July 1995 and were largely attributed to CVD; there were 300 CVD deaths on that day. On closer examination, there were only 4 days over the entire 9 year period of the study on which CVD deaths exceeded 100. These days were 14–17 July 1995, when Cook County experienced a heat wave with average daily temperatures in excess of 85°F. The relative humidity hovered around 65% during these 4 days. The concentrations of the pollutants were not particularly high during those 4 days. A similar 4-day period of average daily temperatures in excess of 85° with relative humidity around 65% also occurred 1–4 August 1988. This period was not marked by unusually high mortality, however. The results of the analyses reported here were not sensitive to the removal of the period 14–17 July 1995.

Season-specific summary statistics (not shown in tables) indicated that the median number of cerebrovascular deaths was more or less constant from season to season in all three counties. Total nonaccidental, CVD, and COPD deaths were highest in winter in all three counties. The gases, with the exception of ozone and, in particular CO, peaked in winter in all three counties. Ozone was

Table 2. Correlations among key variables in Cook, Los Angeles, and Maricopa counties.

County	Temp	RH	PM_{10}	$PM_{2.5}$	CO	NO_2	SO_2	O_3
Cook								
Temp	1.00	–0.14	0.37	NA	–0.08	0.09	–0.02	0.67
RH		1.00	–0.29	NA	0.10	–0.19	–0.26	–0.39
PM_{10}			1.00	NA	0.30	0.49	0.42	0.36
CO					1.00	0.63	0.35	–0.28
NO_2						1.00	0.44	0.02
SO_2							1.00	0.01
O_3								1.00
Los Angeles								
Temp	1.00	0.08	0.18	–0.07	–0.26	0.04	0.00	0.56
RH		1.00	0.06	0.22	–0.33	0.00	–0.29	0.37
PM_{10}			1.00	0.71	0.45	0.70	0.41	0.20
$PM_{2.5}$				1.00	0.58	0.73	0.42	0.04
CO					1.00	0.80	0.78	–0.52
NO_2						1.00	0.74	–0.10
SO_2							1.00	–0.21
O_3								1.00
Maricopa								
Temp	1.00	–0.56	0.11	NA	–0.58	–0.32	–0.31	0.73
RH		1.00	–0.24	NA	0.16	0.01	–0.10	–0.47
PM_{10}			1.00	NA	0.20	0.22	0.11	–0.00
CO					1.00	0.66	0.53	–0.61
NO_2						1.00	0.02	–0.23
SO_2							1.00	–0.37
O_3								1.00

Abbreviations: RH, relative humidity; Temp, temperature.

highest in summer in all three counties. PM_{10} was highest in winter and fall in Los Angeles, in fall in Maricopa, and in summer in Cook.

Figures 1–3 show the results of GAM analyses with total nonaccidental mortality as the end point. These figures show the results of both single- and two-pollutant analyses, with a particulate matter metric as one of the pollutants and one of the gases as the other.

Table 3 shows the estimated percent changes in daily CVD deaths in the three counties for specified increases in pollutants after controlling temporal trends, temperature, relative humidity and day of week. The results for ozone are not shown for Los Angeles and Maricopa Counties because these were either negative or small and highly insignificant in those counties. I obtained similar results for ozone in these two counties when I restricted analyses to the 6-month period April–September. For each of the counties, Table 3 shows the results of single- and multipollutant analyses with lags from 0 to 5 days. For the multipollutant analyses, I chose the gases that appeared to have the strongest association with CVD deaths in single-pollutant analyses and used them along with PM_{10} (and $PM_{2.5}$ in Los Angeles) in the analyses. The table also shows the 95% confidence interval for the estimated change in daily mortality.

Tables 4 and 5 show the percent changes in daily COPD and CrD deaths, respectively, for specified increases in pollutant concentrations after controlling temporal trends, temperature, relative humidity, and day of week. I do not show results for O_3 in Los Angeles and Maricopa because these were either negative or small and insignificant both in full-year analyses and with analyses restricted to the 6-month period April–September. I do not present results of multipollutant analyses of CrD deaths in any of the counties because there was only weak evidence of any association with air pollution, and no evidence of association with particulate matter. For COPD mortality there was no evidence of association with particulate matter in Los Angeles and Maricopa Counties and only weak evidence of association with particulate matter in Cook County. I have, therefore, presented the results of two-pollutant models only for Cook County.

In Los Angeles I could investigate the association between coarse particles, defined as PM_{10}–$PM_{2.5}$, and the various mortality end points. I found no evidence of association between the coarse particles and any of the mortality end points. Even in single-pollutant models, the coefficients for the coarse particles were either negative or, if positive, small and highly insignificant.

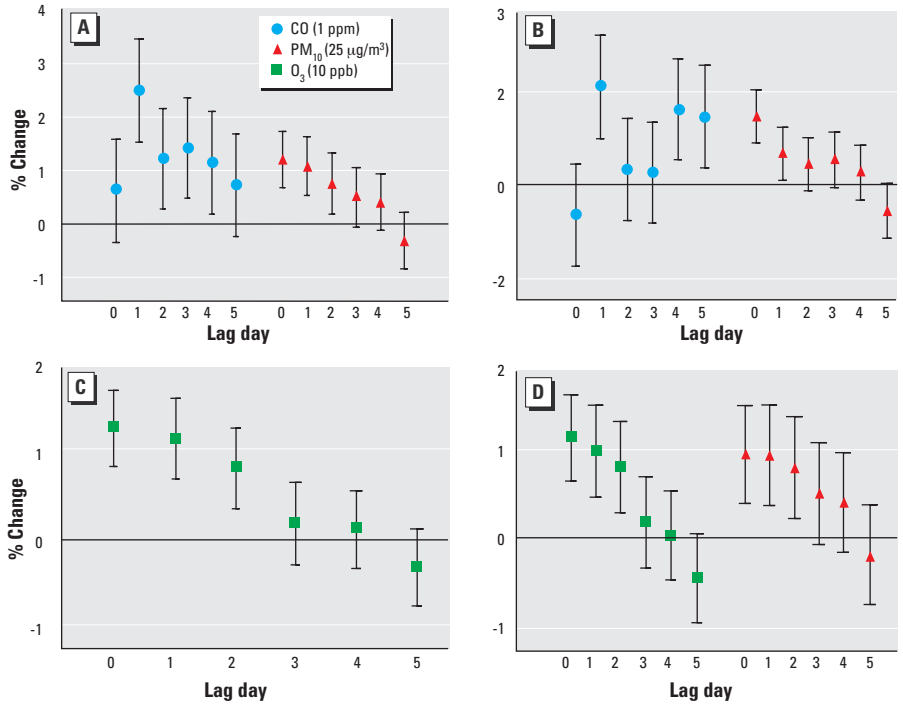

Figure 1. Results of GAM analyses of total mortality in Cook County. (*A*) Single-pollutant model: CO and PM_{10}. (*B*) Joint-pollutant model: CO and PM_{10}. (*C*) Single-pollutant model: O_3. (*D*) Joint-pollutant model: O_3 and PM_{10}. The estimated percent changes (log relative risk × 100) in daily nonaccidental deaths for lags between 0 and 5 days, are shown together with their 95% confidence intervals adjusted for overdispersion. Although the effect estimates are shown for arbitrary increases in pollutant concentrations, they can be converted to increases equal to the interquartile ranges by a simple scaling. The interquartile ranges for the pollutants were PM_{10}, 22 µg/m^3; CO, 0.48 ppm; and O_3, 16 ppb.

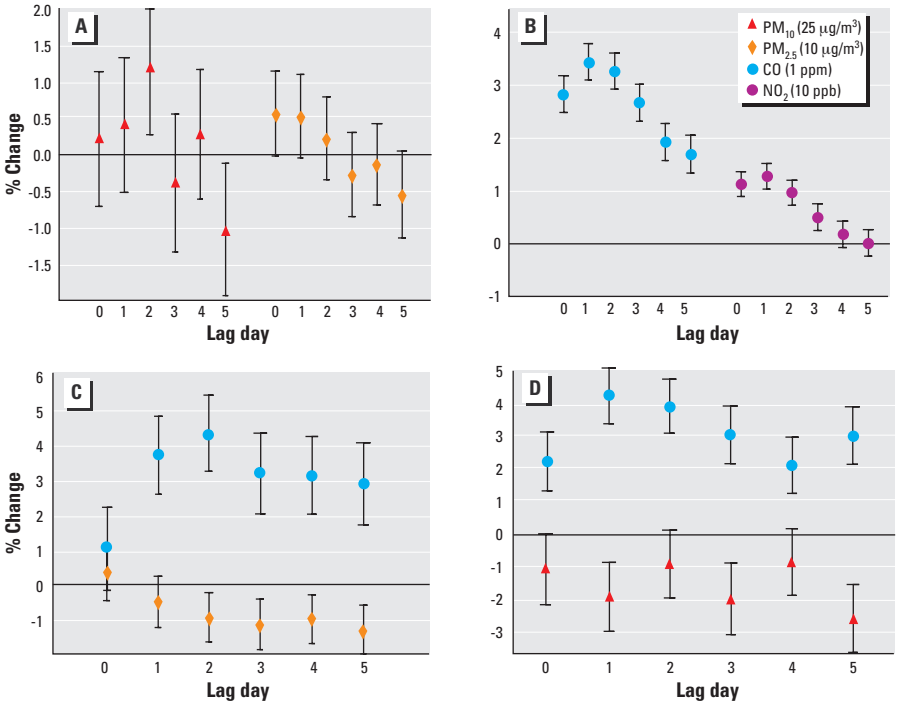

Figure 2. Results of GAM analyses of total mortality in Los Angeles County. (*A*) Single-pollutant model: PM_{10} and $PM_{2.5}$. (*B*) Single-pollutant model:CO and NO_2. (*C*) Joint-pollutant model: CO and $PM_{2.5}$. (*D*) Joint-pollutant model: CO and PM_{10}. The estimated percent changes (log relative risk × 100) in daily nonaccidental deaths, for lags between 0 and 5 days are shown together with their 95% confidence intervals adjusted for overdispersion. Although the effect estimates are shown for arbitrary increases in pollutant concentrations, they can be converted to increases equal to the interquartile ranges by a simple scaling. The interquartile ranges for the pollutants were PM_{10}: 26 µg/m^3; $PM_{2.5}$: 16 µg/m^3; CO: 1.2 ppm; NO_2: 18 ppb.

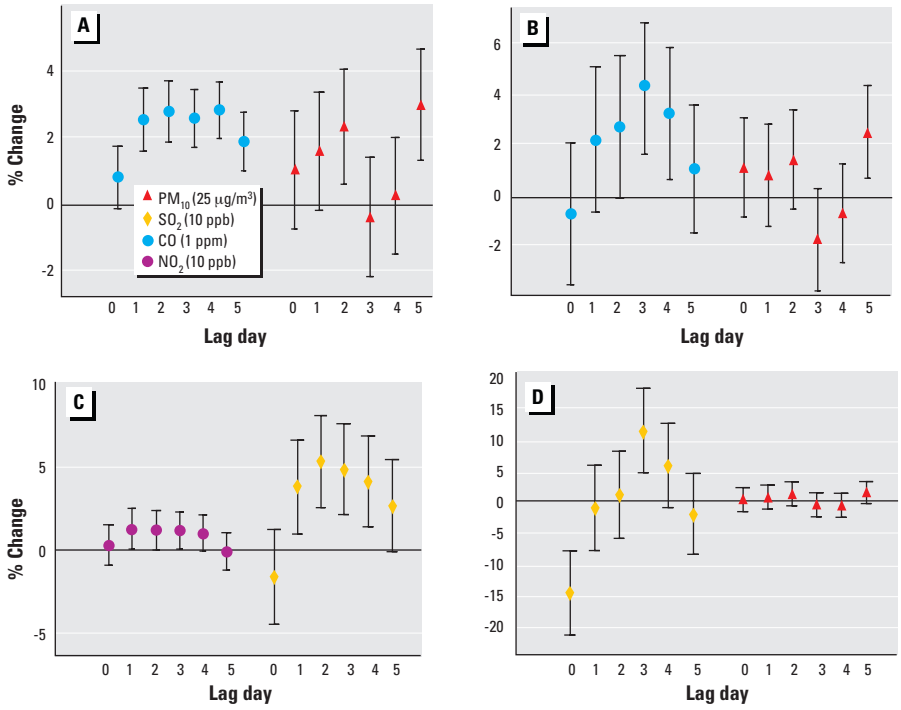

Figure 3. Results of GAM analyses of total mortality in Maricopa County. (*A*) Single-pollutant model: CO and PM_{10}. (*B*) Joint-pollutant model: CO and PM_{10}. (*C*) Single-pollutant model: NO_2 and SO_2. (*D*) Joint-pollutant model: SO_2 and PM_{10}. The estimated percent changes (log relative risk × 100) in daily nonaccidental deaths for lags between 0 and 5 days are shown together with their 95% confidence intervals adjusted for overdispersion. Although the effect estimates are shown for arbitrary increases in pollutant concentrations, they can be converted to increases equal to the interquartile ranges by a simple scaling. The interquartile ranges for the pollutants were PM_{10}, 19 µg/m^3; CO, 0.97 ppm; NO_2, 12 ppb; and SO_2, 3.5 ppb. Such rescaling is particularly important in interpreting the results for NO_2 and SO_2 (C). If not properly interpreted, the data appears to suggest that for lags days 1–4, the toxicity associated with SO_2 is higher than that associated with NO_2. If the estimated risks are scaled to the interquartile ranges, the toxicity associated with these gases is quite similar in Maricopa County.

The results were robust to sensitivity analyses in which I allowed the degrees of freedom of the spline smoothers of temporal trends to vary between 20 and 100.

Discussion

Although a number of pollutants must have been high during the notorious London smog episode of December 1952, subsequent analyses of the increased mortality during the episode considered only particulates and sulfur dioxide (*14,15*). It is generally true that, before the mid-1990s, most epidemiologic studies of air pollution and mortality focused on the particulates and sulfur dioxide, to the exclusion of other pollutants (*13*). These early analyses concluded that particulate matter, rather than sulfur dioxide, was the likely culprit in the excess mortality attributed to air pollution. More recent analyses have reported associations between other pollutants, such as CO (*10,12*) and NO_2 (*13*), and mortality. It is not my intention to summarize the rather substantial epidemiologic literature on air pollution and mortality that has appeared in the last decade. The reported findings from the totality of analyses have been mixed. In single-pollutant models, most analyses have reported associations between various indices of particulate matter and mortality, although some have failed to find an association (*7*). The results of multipollutant analyses have been much more variable. Some studies have reported robust associations between indices of particulate matter and mortality (*10*), but others, particularly those that have appeared since the mid-1990s and considered a number of copollutants, have reported that the effect of the gaseous pollutants dominates that of particulate matter (*11,12*). Interestingly, a large multicity study of air pollution and mortality in Europe (*8*) reported, in contrast to the results from analyses stimulated by the London smog episode, that "sulfur dioxide was more consistently associated with daily mortality than were particles." Conclusions made on the basis of analyses of data from the 1950s may not hold for the mix of pollutants found in contemporary cities. And it is entirely possible that quite different conclusions might have been reached had the focus of attention in the early London studies not been restricted to particulate matter and SO_2.

My intention in this study was to examine the association between all measured components of air pollution and total and cause-specific mortality in three large counties in the United States. My study covered identical periods and used identical analytic strategies in all locations. I also considered longer lags than have been considered in many of the previous studies. In evaluating and interpreting the results of analyses in different locations, it is important to keep in mind that the uncertainties inherent in the analyses go far beyond the sampling variability that is captured by the standard error or the confidence interval. These uncertainties arise from model misspecification, omitted covariates, and, not least, errors in the measurement of covariates considered in the models. Thus, it is important to look for consistency in the overall patterns detected in the analyses. A single statistically significant result may or may not be important depending on the general context in which it is observed. For example, if there is truly an association between some component of air pollution and an adverse health effect, one should expect to see a smooth falling off of effects on both sides of an optimal lag.

Previous publications (*7,13*) have suggested that the association of air pollution with mortality is modified by season. I have not presented season-specific analyses here. With four mortality end points of interest, three geographic locations and five pollutants (six in Los Angeles), season-specific analyses would be a major undertaking. I will consider such analyses in future publications.

I should caution the reader that I have chosen to present the estimates of effects associated with individual pollutants in terms of unit increases in concentration. This procedure makes comparison of effect estimates associated with unit increases easier across different cities, and is, moreover, directly relevant to current standard setting practice. Some investigators have adopted this approach; others have preferred to report effect estimates at the mean concentration or in terms of interquartile changes in pollutant levels, which more faithfully represent actual effects in a given area. Obviously, a simple scaling is all that is required to move from any estimate of effect to any other.

Total mortality. The results for total nonaccidental mortality are shown in Figures 1–3. In Cook County, Figure 1 shows that, in single-pollutant analyses, CO, PM_{10}, and O_3 were all associated with total mortality. All the coefficients for CO were positive and four of the six were significant at the 0.05 level. Similarly, the patterns of estimated changes in mortality for PM_{10} and O_3 suggest that the associations are not spurious. Likewise, I found both NO_2 and SO_2 to be

strongly associated with mortality in single-pollutant analyses. These results are not shown in Figure 1. For NO_2 the strongest association was seen at a lag of 1 day (% change in daily mortality associated with a 10 ppb increase in NO_2 = 1.1, *t*-statistic = 4.5). For SO_2 the strongest association was also seen at a lag of 1 day (% change in daily mortality associated with a 10 ppb increase in SO_2 = 2.4, *t*-statistic = 4.3). In joint analyses with one of the gases (analyses with CO and O_3 in Figure 1), the coefficients of both the gas and PM_{10} were attenuated somewhat, but both continued to be significant for some lags. In three-pollutant models (results not shown), however, the gases dominated and the coefficients for PM_{10} became small and insignificant except at 0 lag. My results for PM_{10} are similar to those reported in an earlier study of air pollution and mortality in Cook County (*7*). That study concluded that, in a single-pollutant model, an increase of 10 μg/m^3 in 3-day mean PM_{10} was associated with 0.54% increase in daily mortality. The authors did not report any joint analyses with other pollutants.

The results for Los Angeles are shown in Figure 2. In single-pollutant analyses, the figure shows that PM_{10}, $PM_{2.5}$, CO, and NO_2 were all associated with total mortality, with the gases showing much stronger associations. I found no association with ozone, even when I restricted analyses to the 6-month period April–September. As can be seen in Table 2, however, ozone is negatively correlated with CO, which is strongly associated with mortality. Surprisingly, even with the generally low levels of SO_2 in Los Angeles County, this gas was strongly associated with mortality (results not shown). The strongest association with SO_2 was seen at a lag of 1 day (% change in daily mortality associated with a 10 ppb increase in SO_2 = 12.1, *t*-statistic = 16.0, which is equivalent to about a 3.6 % increase in daily mortality associated with an increase in SO_2 equal to the interquartile range of 3 ppb). In fact, the association with SO_2, which was stronger, as judged by the *t*-statistic, than the association with NO_2, was highly significant at all lags. In two-pollutant models, with SO_2 as one of the pollutants and either PM_{10} or $PM_{2.5}$ as the other, the coefficients for particulate matter became either negative or small and highly insignificant, whereas those for SO_2 were robust to the simultaneous consideration of either one of the particulate matter metrics. The most plausible explanation of the strong association with SO_2 is that the gas acts as a marker of the relevant pollution mix.

Figure 2 also shows that, in joint analyses of CO with one of the two particulate matter metrics, CO dominated completely. My analyses in this paper are at odds with those reported recently by Kinney et al. (*10*). They concluded that CO and PM_{10} were independently associated with total nonaccidental mortality in Los Angeles County. They found, moreover, that ozone was associated with nonaccidental mortality in single-pollutant analyses. Although their period of study (1985–1990) did not coincide with mine, there is an overlap of 4 years. I am not sure how to explain the discrepancy in our findings. Their analytic strategy and methods of analyses were different from mine. But, I do not believe that these differences in approach can explain the rather discrepant findings. If indeed they do, then one must conclude that results of time-series analyses can be quite sensitive to statistical approaches.

Table 3. Results of GAM analyses of CVD mortality in Cook, Los Angeles, and Maricopa counties.

County	Lag 0	Lag 1	Lag 2	Lag 3	Lag 4	Lag 5
Cook						
Single						
PM_{10}	0.75 (–0.13–1.62)	0.59 (–0.33–1.50)	0.81 (–0.14–1.77)	1.10 (0.18–2.02)	0.65 (–0.25–1.54)	–0.18 (–1.08–0.71)
CO	–1.07 (–2.67–0.54)	1.25 (–0.36–2.87)	1.49 (–0.09–3.07)	1.90 (0.32–3.48)	1.44 (–0.16–3.03)	0.72 (–0.89–2.32)
NO_2	–0.59 (–1.39–0.21)	0.56 (–0.26–1.37)	0.84 (0.02–1.66)	1.03 (0.22–1.84)	0.92 (0.12–1.71)	0.28 (–0.53–1.08)
SO_2	1.94 (0.09–3.79)	2.95 (1.1–4.8)	2.33 (0.47–4.20)	2.23 (0.37–4.09)	2.54 (0.73–4.35)	0.93 (–0.90–2.76)
O_3	1.51 (0.78–2.24)	1.32 (0.55–2.09)	0.65 (–0.11–1.40)	0.23 (–0.56–1.02)	–0.11 (–0.85–0.64)	–0.72 (–1.46–0.01)
SO_2, O_3 and PM_{10}						
SO_2	0.20 (–0.02–0.42)	0.31 (0.08–0.53)	0.20 (–0.02–0.41)	0.04 (–0.19–0.26)	0.14 (–0.09–0.36)	0.10 (–0.12–0.32)
O_3	1.31 (0.49–2.12)	1.41 (0.56–2.25)	0.91 (0.09–1.73)	0.87 (–0.47–1.27)	0.83 (–0.94–0.73)	–0.73 (–1.55–0.09)
PM_{10}	–0.03 (–1.06–1.00)	–0.31 (–1.36–0.75)	0.50 (–0.50–1.51)	0.99 (–0.03–2.02)	0.40 (–0.64–1.43)	–0.18 (–1.22–0.86)
Los Angeles						
Single						
PM_{10}	0.84 (–0.56–2.23)	0.70 (–0.71–2.11)	2.21 (0.81–3.61)	–0.80 (–2.21–0.61)	0.70 (–0.68–2.09)	–1.22 (–2.59–0.14)
$PM_{2.5}$	0.99 (0.10–1.89)	1.03 (0.15–1.91)	0.78 (–0.11–1.67)	–0.30 (–1.20–0.60)	–0.09 (–0.97–0.79)	0.89 (–1.72–0.06)
CO	3.47 (2.94–4.00)	3.93 (3.41–4.46)	4.08 (3.56–4.60)	3.76 (3.24–4.28)	2.91 (2.37–3.44)	2.63 (2.09–3.17)
NO_2	1.22 (0.86–1.58)	1.39 (1.02–1.76)	1.25 (0.89–1.61)	0.88 (0.52–1.24)	0.49 (0.12–0.85)	0.31 (–0.06–0.68)
SO_2	12.40 (10.16–14.64)	14.06 (11.81–16.32)	13.02 (10.77–15.27)	11.21 (8.96–13.45)	7.33 (5.06–9.59)	7.36 (5.08–9.65)
CO and PM_{10}						
CO	2.27 (0.88–3.66)	4.33 (2.96–5.69)	4.72 (3.38–6.05)	4.26 (2.90–5.63)	2.49 (1.10–3.88)	5.93 (4.60–7.27)
PM_{10}	–0.43 (–2.12–1.25)	–1.63 (–3.32–0.05)	–0.28 (–1.93–1.38)	–3.11 (–4.79–⁻1.43)	–0.65 (–2.30–1.01)	–4.46 (–6.06–⁻2.85)
CO and $PM_{2.5}$						
CO	0.43 –1.35–2.20)	2.88 (1.16–4.60)	4.65 (2.93–6.37)	5.93 (4.20–7.65)	3.88 (2.13–5.63)	5.85 (4.12–7.58)
$PM_{2.5}$	0.88 (–0.23–1.99)	0.24 (–0.85–1.33)	–0.50 (–1.61–0.61)	–1.96 (–3.08–⁻0.84)	–1.19 (–2.30–⁻0.09)	–2.50 (–3.60–⁻1.40)
Maricopa						
Single						
PM_{10}	1.38 (–1.69–4.45)	4.33 (1.28–7.37)	2.90 (–0.20–5.99)	1.20 (–1.81–4.20)	1.95 (–0.95–4.84)	4.26 (1.41–7.11)
CO	0.81 (–0.79–2.39)	2.20 (0.61–3.79)	3.05 (1.49–4.61)	3.78 (2.27–5.28)	3.73 (2.27–5.19)	2.25 (0.76–3.72)
NO_2	1.09 (–0.97–3.14)	2.30 (0.22–4.37)	2.27 (0.20–4.34)	2.30 (0.92–5.00)	2.30 (0.98–4.96)	0.54 (–1.45–2.52)
SO_2	–5.51 (–10.33–⁻0.69)	–3.94 (–8.78–0.88)	5.16 (0.34–9.98)	8.70 (3.90–13.49)	6.65 (1.87–11.42)	0.35 (–4.45–5.16)
NO_2 and PM_{10}						
NO_2	–6.77 (–11.90–⁻1.64)	10.13 (4.98–15.27)	6.83 (1.87–11.79)	1.18 (–3.38–5.73)	4.46 (–0.29–9.21)	–3.88 (–9.02–1.26)
PM_{10}	0.15 (–4.10–4.37)	3.61 (–0.56–7.77)	2.97 (–1.10–7.01)	2.15 (–1.58–5.88)	0.93 (–3.11–4.97)	3.56 (–0.57–7.68)

For lags between 0 and 5 days, the estimated percent changes (log relative risk × 100) in daily CVD deaths associated with changes in the pollutants are shown. Results for single- and multipollutant models are reported. See "Materials and Methods" for details. Ninety-five percent confidence intervals adjusted for overdispersion are shown in parentheses. The estimated changes are for increases of 25 μg/m^3 PM_{10}, 10 μg/m^3 $PM_{2.5}$, 1 ppm CO, and 10 ppb NO_2, SO_2, and O_3.

Figure 3 shows the results in Maricopa County. In single-pollutant analyses, PM_{10} and each of the gases was associated with total mortality (with the exception of ozone, which was not associated with mortality even when analyses were restricted to the period April–September). In two-pollutant models, the coefficients for the gases were more robust than those for PM_{10}. As in Los Angeles, I found a strong association of sulfur dioxide with mortality although levels of the gas were quite low.

Cardiovascular disease mortality. The results of analyses of CVD mortality are reported in Table 3. These analyses showed that the association of air pollution with CVD mortality was weaker than the association with total mortality. In Cook County, in single-pollutant analyses, each one of the pollutants was associated with CVD mortality: the coefficients for most of the lags were positive, and some were statistically significant (in that the confidence interval did not include 0). Of the pollutants, SO_2 appeared to be most strongly associated with CVD mortality, followed by NO_2. The association of PM_{10} with CVD mortality was statistically significant at a lag of 3 days. In two-pollutant analyses with one of the gases (not shown), PM_{10} continued to be significantly associated with CVD mortality with a 3-day lag. In joint analyses with ozone and SO_2, however, three of the six coefficients for PM_{10} were negative, and none was statistically significant (Table 3). Thus, in Cook County, these analyses indicate that the gases explained the major fraction of the CVD mortality attributed to air pollution.

As with total nonaccidental mortality, in Los Angeles the gases (with the exception of ozone) completely dominated the association between air pollution and CVD mortality. Ozone was not associated with CVD mortality even when analyses were restricted to the period April–September. Although in single-pollutant analyses both PM_{10} and $PM_{2.5}$ were associated with CVD mortality, the coefficients of these two pollutants were not robust to the inclusion of a gas in the analyses. Results of two-pollutant analyses with CO are shown in Table 3. As in the case of total mortality, there was strong association between SO_2 and CVD mortality.

In Maricopa County, in single-pollutant analyses each of the gases (with the exception of ozone) was associated with CVD mortality, as was PM_{10}. In joint analyses with particulate matter and one of the gases, the coefficients for both were somewhat unstable. The results of two-pollutant analyses with PM_{10} and NO_2 are shown in Table 3. In these analyses, the coefficients of NO_2 were significant at lags of 1 and 2 days, whereas none of the PM_{10} coefficients was significant. However, the NO_2 coefficients were quite different from those estimated from the single-pollutant models indicating that they were unstable, whereas the coefficient for PM_{10} appeared to be robust to the inclusion of NO_2.

Table 4. Results of GAM analyses of COPD mortality in Cook, Los Angeles, and Maricopa counties.

County	Lag 0	Lag 1	Lag 2	Lag 3	Lag 4	Lag 5
Cook						
Single						
PM_{10}	1.16 (–1.25–3.57)	2.40 (–0.04–4.80)	2.66 (0.12–5.20)	0.01 (–2.55–2.57)	1.49 (–0.90–3.89)	–0.34 (–2.76–2.08)
CO	–2.65 (–7.05–1.75)	2.80 (–1.60–7.19)	0.98 (–3.34–5.31)	2.20 (–2.12–6.53)	1.31 (–3.06–5.68)	1.59 (–2.78–5.97)
NO_2	2.11 (–4.31–0.09)	2.24 (0.02–4.47)	1.24 (–1.00–3.49)	1.52 (–0.70–3.73)	0.75 (–1.44–2.93)	–0.55 (–2.75–1.65)
SO_2	–2.14 (–7.21–2.94)	2.16 (–2.90–7.21)	5.81 (0.78–10.83)	5.04 (–0.01–10.08)	1.59 (–3.37–6.56)	–3.00 (–8.02–2.07)
O_3	1.53 (–0.49–3.55)	1.67 (–0.45–3.78)	2.65 (0.50–4.80)	0.23 (–1.94–2.40)	–0.53 (–2.59–1.53)	–2.71 (–4.74–⁻0.67)
O_3 and PM_{10}						
O_3	1.40 (–0.89–3.68)	1.44 (–0.82–3.70)	2.96 (0.68–5.24)	0.96 (–1.30–3.22)	–1.15 (–3.36–1.06)	–2.89 (–5.11–⁻0.67)
PM_{10}	1.09 (–1.43–3.60)	2.03 (–0.43–4.48)	1.51 (–0.95–3.96)	0.57 (–1.97–3.10)	2.16 (–0.30–4.62)	0.29 (–2.20–2.79)
Los Angeles						
Single						
PM_{10}	1.24 (–2.61–5.10)	2.90 (–0.90–6.7)	1.35 (–2.50–5.21)	–4.94 (–8.75–⁻1.13)	0.35 (–3.49–4.19)	–1.19 (–5.08–2.70)
$PM_{2.5}$	–0.76 (–3.20–1.68)	1.06 (–1.39–3.52)	–0.13 (–2.56–2.29)	–3.45 (–5.81–⁻1.09)	–2.00 (–4.47–0.49)	0.12 (–2.30–2.53)
CO	3.78 (2.31–5.25)	5.23 (3.78–6.69)	5.71 (4.26–7.17)	5.42 (3.95–6.89)	4.01 (2.51–5.50)	3.82 (2.31–5.33)
NO_2	1.30 (0.29–2.31)	1.86 (0.83–2.88)	1.70 (0.69–2.71)	1.41 (0.40–2.41)	0.55 (–0.46–1.56)	0.23 (–0.79–1.25)
SO_2	14.49 (8.13–20.85)	19.41 (13.05–25.79)	17.05 (10.71–23.39)	16.27 (9.93–22.60)	12.93 (6.56–19.30)	11.59 (5.50–17.51)
Maricopa						
Single						
PM_{10}	3.96 (–2.51–10.42)	4.04 (–2.55–10.63)	1.47 (–5.79–8.74)	–5.28 (–13.05–2.50)	3.96 (–2.60–10.52)	–3.42 (–10.71–3.87)
CO	1.29 (–2.19–4.76)	4.63 (1.17–8.09)	0.07 (–3.36–3.50)	3.00 (–0.30–6.30)	6.21 (3.02–9.40)	3.27 (0.04–6.50)
NO_2	0.77 (–3.68–5.21)	–0.85 (–5.35–3.65)	1.91 (–2.58–6.39)	4.50 (0.10–8.90)	2.45 (–1.85–6.76)	0.19 (–4.09–4.29)

For lags between 0 and 5 days the estimated percent changes (log relative risk × 100) in daily COPD deaths associated with changes in the pollutants are shown. Results for single- and two-pollutant models are reported. See "Materials and Methods" for details. Ninety-five percent confidence intervals adjusted for overdispersion are shown in parentheses. The estimated changes are for increases of 25 μg/m^3 PM_{10}, 10 μg/m^3 $PM_{2.5}$, 1 ppm CO, and 10 ppb NO_2, SO_2 and O_3.

Chronic obstructive pulmonary disease mortality. The results for COPD mortality are shown in Table 4. In Cook County, in single-pollutant analyses, each of the pollutants showed some association with COPD mortality. Both ozone and PM_{10} were significantly associated with COPD mortality with a lag of 2 days. In joint analyses, however, the coefficient for ozone at a 2-day lag remained stable and statistically significant, whereas the coefficient for PM_{10} was attenuated and became insignificant.

In Los Angeles County, in single-pollutant analyses each of the gases (with the exception of ozone) was associated with COPD mortality. There was no evidence that either PM_{10} or $PM_{2.5}$ was associated with COPD mortality.

In Maricopa County, in single-pollutant analyses, CO and NO_2 were weakly associated with COPD mortality. There was no evidence of any association of the other gases or particulate matter with COPD mortality.

Cerebrovascular disease mortality. The results for CrD mortality are shown in Table 5. I do not show the results of any two-pollutant analyses because there was little evidence of an association between particulate matter and CrD mortality. The most consistent associations were seen in Los Angeles with each of the gases (with the exception of ozone). As in the case of the other end points, strong and consistent associations were seen with CO and SO_2. In Maricopa County, strong associations were seen with CO and weaker associations with NO_2 and SO_2. In Cook County, there was a suggestion of a weak association with CO.

Conclusion

It is clear from the analyses presented here that there was heterogeneity in the association of individual components of air pollution with each of the mortality end points in the three counties. The most consistent

Table 5. Results of GAM analyses of cerebrovascular disease mortality in Cook, Los Angeles, and Maricopa counties.

County	Lag 0	Lag 1	Lag 2	Lag 3	Lag 4	Lag 5
Cook						
Single						
PM_{10}	0.49 (–1.09–2.08)	0.89 (–0.75–2.53)	1.62 (–0.07–3.32)	0.01 (–1.67–1.69)	–1.00 (–2.60–0.65)	–0.54 (–2.14–1.07)
CO	–0.41 (–3.30–2.47)	3.13 (0.23–6.02)	2.12 (–0.73–4.97)	1.00 (–1.85–3.86)	2.50 (–0.36–5.37)	1.88 (–1.00–4.76)
NO_2	0.11 (–1.34–1.55)	1.19 (–0.29–2.66)	0.72 (–0.76–2.21)	0.79 (–0.67–2.25)	0.24 (–1.20–1.68)	0.30 (–1.15–1.74)
SO_2	–0.31 (–3.67–3.01)	1.07 (–2.29–4.44)	1.79 (–1.58–5.17)	0.90 (–2.48–4.28)	0.02 (–3.28–3.33)	–1.31 (–4.63–2.02)
Los Angeles						
Single						
PM_{10}	–2.06 (–4.71–0.58)	–0.55 (–3.15–2.05)	1.02 (–1.65–3.69)	1.45 (–1.17–4.08)	0.02 (–2.68–2.71)	–1.00 (–3.58–1.57)
$PM_{2.5}$	–1.04 (–2.65–0.58)	–0.50 (–2.19–1.19)	0.92 (–0.72–2.56)	1.43 (–0.24–3.10)	–1.34 (–3.10–0.41)	–0.31 (–1.94–1.32)
CO	3.31 (2.32–4.31)	3.88 (2.89–4.87)	3.23 (2.25–4.22)	2.65 (1.66–3.65)	2.11 (1.11–3.12)	2.04 (1.02–3.06)
NO_2	1.38 (0.70–2.06)	1.33 (0.64–2.01)	0.63 (–0.05–1.32)	0.39 (–0.29–1.08)	0.13 (–0.55–0.82)	0.16 (–0.53–0.85)
SO_2	11.26 (7.03–15.49)	12.62 (8.36–16.87)	8.95 (4.69–13.21)	5.87 (1.62–10.12)	5.65 (1.39–9.91)	5.94 (1.63–10.24)
Maricopa						
Single						
PM_{10}	0.40 (–5.28–6.08)	–3.37 (–9.54–2.80)	–1.07 (–6.65–4.51)	–1.60 (–7.35–4.15)	0.90 (–4.73–6.53)	5.30 (0.05–10.55)
CO	0.26 (–2.65–3.16)	3.50 (0.60–6.41)	3.52 (0.66–6.38)	4.61 (1.85–7.37)	4.78 (2.10–7.46)	5.15 (2.45–7.84)
NO_2	3.18 (–0.42–6.79)	3.97 (0.32–7.61)	2.45 (–1.19–6.10)	2.29 (–1.30–5.87)	2.20 (–1.30–5.71)	0.16 (–3.33–3.65)
SO_2	13.34 (4.68–22.00)	20.99 (12.35–29.62)	6.56 (–2.23–15.34)	4.59 (–4.21–13.39)	1.35 (–7.41–10.10)	2.75 (–5.97–11.47)

For lags between 0 and 5 days the estimated percent changes (log relative risk × 100) in daily CrD deaths associated with changes in the pollutants are shown. Results for single-pollutant models are reported. See "Materials and Methods" for details. Ninety-five percent confidence intervals adjusted for overdispersion are shown in parentheses. The estimated changes are for increases of 25 μg/m^3 PM_{10}, 10 μg/m^3 $PM_{2.5}$, 1 ppm CO, and 10 ppb NO_2, SO_2, and O_3.

finding was that some index of air pollution was associated with each of the end points, although the associations with COPD and CrD mortality were weak except in Los Angeles County. The gases, with the exception of ozone, were generally much more strongly associated with the various mortality end points than was particulate matter. Insofar as single-pollutants are concerned, the most striking finding of these analyses is the strong association between CO and total and cause-specific mortality, especially in Los Angeles County. Associations between CO and a number of health end points, including hospital admissions (*5,18*), and mortality (*12*), have been reported in recent papers. In a study of daily mortality in Toronto, Burnett et al. (*12*) reported that once the effect of CO had been taken into account total suspended particulate matter (TSP) contributed only a small amount to the daily mortality. Curiously, they found a stronger effect of TSP than sulfates, PM_{10}, or $PM_{2.5}$. They had no direct measures of PM_{10} and $PM_{2.5}$ in their study, however. Concentrations of these pollutants were imputed from other measurements.

The surprisingly strong association between SO_2 and mortality in Los Angeles is also worthy of note. Not only was this association strong as judged by the *t*-statistic, but also the estimated percentage changes in the end points of interest for a 10-ppb change in SO_2 were surprisingly large. The interquartile range of SO_2 concentrations in Los Angeles was about 3 ppb, and my finding of changes in total mortality of the order of 12% for a 10 ppb change in SO_2 translates into a change of about 3.6% for a change in SO_2 equal to the interquartile range. I believe that the most appropriate interpretation of these findings is not that SO_2 has a direct effect on these end points, but that, even at low levels, fluctuations in SO_2 in Los Angeles County efficiently track changes in the air pollution mix responsible for the effects. The results for SO_2 suggest strongly that components of air pollution cannot be ignored in regression analyses even when levels of these pollutants are low. The idea of control of confounding by restriction has been used in air pollution epidemiology. For example, in a study of mortality in Utah (*6*), it was suggested that SO_2 could be safely ignored because levels were low. The results in Los Angeles show that this reasoning is flawed.

Coherence of effects is often examined in evaluating epidemiologic data on the health consequences of air pollution. Simply stated, this argument says that consistency of effects across a spectrum of health outcomes strengthens the case that association between air pollution and a specific health end point is not spurious. In recent publications (*20,21*) I have examined the association between air pollution and hospital admissions for cardiovascular, cerebrovascular, and chronic obstructive pulmonary disease in Cook, Los Angeles, and Maricopa counties over the time period 1987–1995, which is identical to the time period of this study. The ICD-9 codes I used to define the admissions were identical to the ICD-9 codes used in this paper to define the mortality end points. I also used an identical analytic strategy. A consistent result from these analyses is that the gases are more strongly associated with each of the end points than is particulate matter. The strong association of CO and SO_2 with each of the end points in Los Angeles is also noteworthy.

Human populations, particularly in urban areas, are exposed to a complex air pollution mixture consisting perhaps of thousands of components. We probe this complex mixture by monitoring a half dozen criteria pollutants. Regression analyses using this limited set of pollutants must be interpreted carefully. In the analyses that I have presented here, the recent emphasis on particulate matter appears to be misplaced, and gases, particularly CO, appear to be most consistently associated with total nonaccidental, CVD, CrD, and COPD mortality. However, suggestive results for any single-pollutant must be considered in the context of the entire pollution mix, much of which is not accounted for in analytic models. With respect to the monitored components of air pollution, the most plausible interpretation of a positive association with adverse health effects is that the pollutant is simply an indicator of either a pollution source or, more generally, of the mixture of pollutants that is associated with adverse health effects, although a direct effect of the pollutant cannot be ruled out. Thus, for example, CO may simply be a surrogate for mobile source pollution, although a plausible case can be made for a direct effect of CO on cardiorespiratory end points (*12*). In the face of the heterogeneity of results presented here, attempts at quantitative meta-analyses (*16*) to arrive at a best estimate of risk associated with any single pollutant would appear to be misguided.

References and Notes

1. Ware JH, Ferris BG Jr, Dockery DW, Spengler JD, Stram DO, Speizer FE. Effects of ambient sulfur oxides and suspended particles on respiratory health of preadolescent children. Am Rev Respir Dis 133:834–842 (1986).
2. Dockery DW, Speizer FE, Stram DO, Ware JH, Spengler JD, Ferris BG Jr. Effects of inhalable particles on respiratory health of children. Am Rev Respir Dis 139:587–594 (1989).
3. Schwartz J, Slater D, Larson TV, Pierson WE, Koenig JQ. Particulate air pollution and hospital emergency room visits for asthma in Seattle. Am Rev Respir Dis 147:826–831 (1993).
4. Moolgavkar SH, Luebeck EG, Anderson EL. Air pollution and hospital admissions for respiratory causes in Minneapolis-St. Paul and Birmingham. Epidemiology 8:364–370 (1997).
5. Burnett RT, Dales RE, Brook JR, Raizenne ME, Krewski D. Association between ambient carbon monoxide levels and hospitalizations for congestive heart failure in the elderly in 10 Canadian cities. Epidemiology 8:162–167 (1997).
6. Pope CA III, Schwartz J, Ransom MR. Daily mortality and PM_{10} pollution in Utah valley. Arch Environ Health 47:211–217 (1992).
7. Styer P, McMillan N, Gao F, Davis J, Sacks J. Effect of outdoor airborne particulate matter on daily death counts. Environ Health Perspect 103:490–497 (1995).
8. Zmirou D, Schwartz J, Saez M, Zanobetti A, Wojtyniak B, Touloumi G, Spix C, Ponce de Leon A, Le Moullec Y, Bacharova L, et al. Time-series analysis of air pollution and cause-specific mortality. Epidemiology 9:495–503 (1998).
9. Kinney PL, Ozkaynak H. Association of daily mortality and air pollution in Los Angeles County. Environ Res 54:99–120 (1991).
10. Kinney PL, Ito K, Thurston GD. A sensitivity analysis of mortality/PM associations in Los Angeles. Inhal Toxicol 7:59–69 (1995).
11. Burnett RT, Cakmak S, Brook JR. The effect of the urban air pollution mix on daily mortality rates in 11 Canadian cities. Can J Public Health 89:152–156 (1998).
12. Burnett RT, Cakmak S, Raizenne ME, Stieb D, Vincent R, Krewski D, Brook JR, Philips O, Ozkaynak H. The association between ambient carbon monoxide levels and daily mortality in Toronto, Canada. J Air Waste Manag Assoc 48:689–700 (1998).
13. Moolgavkar SH, Luebeck EG. A critical review of the evidence on particulate air pollution and mortality. Epidemiology 7:420–428 (1996).
14. Mazumdar S, Schimmel H, Higgins ITT. Relation of daily mortality to air pollution: an analysis of 14 London winters, 1958/59–1971/72. Arch Environ Health 37:213–220 (1982).
15. Schwartz J, Marcus A. Mortality and air pollution in London: a time series analysis. Am J Epidemiol 131:185–194 (1990).
16. Schwartz J. Air pollution and daily mortality: a review and meta analysis. Environ Res 64:36–52 (1994).
17. Hastie TJ, Tibshirani RJ. Generalized Additive Models. New York:Chapman and Hall, 1990.
18. Burnett RT, Cakmak S, Brook JR, Krewski D. The role of particulate size and chemistry in the association between summertime ambient air pollution and hospitalization for cardiorespiratory diseases. Environ Health Perspect 105:614–620 (1997).
19. Sheppard L, Levy D, Norris G, Larson TV, Koenig JQ. Effects of ambient air pollution on nonelderly asthma hospital admissions in Seattle, Washington, 1987–1994. Epidemiology 10:23–30 (1999).
20. Moolgavkar SH. Air pollution and hospital admissions for chronic obstructive pulmonary disease in three metropolitan areas in the U.S. Inhal Toxicol (in press).
21. Moolgavkar SH. Air pollution and hospital admissions for diseases of the circulatory system in three U.S. metropolitan areas. J Air Waste Manag Assoc (in press).