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 (PM₁₀), carbon monoxide, sulfur dioxide, nitrogen dioxide, and ozone. In Los Angeles, monitoring information on particulate matter ≤ 2.5 μm (PM₂.₅) 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]

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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. SO₂ and NO₂ readings in Maricopa County were spotty with a number of missing days. In Maricopa and Los Angeles Counties, readings for particulate matter ≤ 10 μm (PM₁₀) were available every sixth day, while in Cook County daily readings for PM₁₀ were available. In Los Angeles County, in addition to PM₁₀, every sixth day data were available for particulate matter ≤ 2.5 μm (PM₂.₅). 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) (1/7). 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,
Table 1. Distribution of key variables in Cook, Los Angeles, and Maricopa counties.

| County  | Temp (°F) | RH | CO (ppb) | NO₂ (ppb) | O₃ (ppb) | SO₂ (ppb) | PM₁₀ (μg/m³) | PM₂₅ (μg/m³) | CVD | Deaths from CVD | Total deaths*
|---------|-----------|----|----------|-----------|----------|-----------|--------------|--------------|-----|----------------|--------------
| Cook    | -16       | 35 | 224      | 7         | 0.2      | 0.5       | 3            | -            | 21  | 1              | 0            | 77           |
| 1st     | 35        | 62 | 789      | 20        | 10       | 4         | 25           | -            | 39  | 7              | 2            | 108          |
| Median  | 51        | 70 | 953      | 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        | 6        | 0         | 7            | 4            | 28  | 4              | 0            | 95           |
| 1st     | 59        | 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 | 1,240    | 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. *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 PM₁₀ in Cook County reported in Table 1 is 365 μg/m³. 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 Stryer 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 PM₁₀ exceeded 150 μg/m³. Exclusion of these two outliers did not alter the results of my analyses. Table 1 shows that the highest concentrations of both PM₁₀ 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°F 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...
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$_{2.5}$–PM$_{10}$, 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$_{10}$.](image1)

![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$_{10}$: 22 μg/m$^3$; CO: 0.48 ppm; and NO$_2$: 16 ppb.)](image2)
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 NO₂ (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, 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 SO₂.

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 ranges 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, PM₉₀, and O₃ 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 PM₉₀ and O₃ suggest that the associations are not spurious. Likewise, I found both NO₂ and SO₂ to be
strongly associated with mortality in single-pollutant analyses. These results are not shown in Figure 1. For NO₃, the strongest association was seen at a lag of 1 day (% change in daily mortality associated with a 10 ppb increase in NO₃ = 1.1; *statistic = 4.5). For SO₂, the strongest association was also seen at a lag of 1 day (% change in daily mortality associated with a 10 ppb increase in SO₂ = 2.4; *statistic = 4.3). In joint analyses with one of the gases (analyses with CO and O₃ in Figure 1), the coefficients of both the gas and PM₁₀ were attenuated somewhat, but both continued to be significant for some lags. In three pollutant models (results not shown), the gases dominated and the coefficients for PM₁₀ became small and insignificant except at 0 lag. My results for PM₁₀ 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 mg/m³ in 3-day mean PM₁₀ was associated with a 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 PM₁₀, PM₁₂, CO, and NO₂ 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 SO₂ in Los Angeles County, this gas was strongly associated with mortality (results not shown). The strongest association with SO₂ was seen at a lag of 1 day (% change in daily mortality associated with a 10 ppb increase in SO₂ = 12.1; *statistic = 16.0, which is equivalent to about a 3.6% increase in daily mortality associated with an increase in SO₂ equal to the interquartile range of 3 ppb). In fact, the association with SO₂, which was stronger, as judged by the *statistic, than the association with NO₂ was highly significant at all lags. In two-pollutant models, with SO₂ as one of the pollutants and either PM₁₀ or PM₁₂ as the other, the coefficients for particulate matter became either negative or small and highly insignificant, whereas those for SO₂ were robust to the simultaneous consideration of either one of the particulate matter metrics. The most plausible explanation of the strong association with SO₂ 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 PM₁₀ 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 their 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     |       |       |       |       |       |       |
| PM₁₀       | 0.75  | 0.59  | 0.81  | 1.10  | 0.65  | -0.18 |
| CO         | -1.07 | 1.25  | 1.49  | 1.90  | 1.44  | 0.72  |
| NO₂        | -0.59 | 0.56  | 0.84  | 1.03  | 0.92  | 0.28  |
| SO₂        | 1.94  | 2.95  | 2.33  | 2.23  | 2.54  | 0.93  |
| O₃         | 0.15  | 1.32  | 0.65  | 0.32  | -0.11 | -0.72 |
| PM₁₀, O₃, and NO₂ | 0.20 | 0.31  | 0.20  | 0.04  | 0.14  | 0.10  |
| Los Angeles|       |       |       |       |       |       |
| Single     |       |       |       |       |       |       |
| PM₁₀       | 0.84  | 0.70  | 2.21  | -0.65 | 0.70  | -1.22 |
| PM₁₂       | 0.99  | 1.03  | 0.78  | -0.20 | -0.09 | 0.49  |
| CO         | 3.47  | 9.33  | 4.08  | 3.76  | 2.91  | 2.63  |
| NO₂        | -0.22 | 1.39  | 1.25  | 0.68  | 0.49  | 0.31  |
| SO₂        | 12.40 | 14.06 | 13.02 | 11.21 | 7.33  | 7.36  |
| CO and PM₁₀|       |       |       |       |       |       |
| PM₁₀       | 2.27  | 4.33  | 4.72  | 4.26  | 2.49  | 5.93  |
| PM₁₂       | -0.43 | -1.53 | -0.20 | 0.11  | -0.65 | -4.46 |
| CO         | 0.43  | 2.88  | 4.65  | 5.93  | 3.88  | 5.85  |
| PM₁₂       | -1.35 | -2.20 | 1.16  | 6.60  | 2.47  | 2.50  |
| Maricopa   |       |       |       |       |       |       |
| Single     |       |       |       |       |       |       |
| PM₁₀       | 1.38  | 4.33  | 2.90  | 1.20  | 1.95  | 4.26  |
| CO         | -0.67 | 2.20  | 3.05  | 3.76  | 3.73  | 2.25  |
| NO₂        | -0.79 | 2.30  | 2.27  | 2.30  | 2.54  | 0.54  |
| SO₂        | 0.97  | -3.14 | 0.22  | -0.20 | 2.95  | -1.96 |
| NO₂        | -5.11 | 9.56  | 8.70  | 6.65  | 0.35  |       |
| PM₁₀       | -10.33 | -0.98 | 2.98  | 3.49  | 1.17  | -4.55 |
| NO₂        | 4.26  | 6.60  | 2.47  | 2.50  | 2.50  | 0.54  |
| NO₂        | -0.79 | 2.30  | 2.27  | 2.30  | 2.54  | 0.54  |
| PM₁₀       | -11.90 | -1.64 | 1.87  | -3.38 | 1.18  | -0.99 |
| PM₁₀       | 0.15  | 3.61  | 2.97  | 2.15  | 0.53  | 3.56  |

For lags 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/m³ PM₁₀, 10 μg/m³ PM₁₂, 1 ppm CO, and 10 ppb NO₂, SO₂, and O₃.

Environmental Health Perspectives • VOLUME 108 | NUMBER 8 | AUGUST 2000

781
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 particular 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$_2$.

**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 NO$_2$. 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

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### 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  | 2.40  | 2.66  | 0.01  | 1.49  | −0.34 |
|           | (−1.25−3.57) | (−0.04−4.80) | (0.12−5.20) | (−2.55−2.57) | (−0.90−3.89) | (−2.76−2.08) |
| SO$_2$    | 2.11  | 2.24  | 1.24  | 1.52  | 0.75  | −0.55 |
|           | (−0.31−4.09) | (0.02−4.47) | (−1.00−3.49) | (−0.70−3.73) | (−1.44−2.93) | (−2.75−1.65) |
| NO$_2$    | 1.53  | 1.67  | 2.65  | 0.23  | −0.53 | −2.71 |
|           | (−0.49−3.55) | (−0.45−3.78) | (0.50−4.80) | (−1.94−2.40) | (−2.59−1.53) | (−4.74−0.67) |
| $O_3$     | 1.40  | 1.44  | 2.96  | 0.96  | −1.15 | −2.89 |
|           | (−0.69−3.68) | (−0.82−3.70) | (0.68−5.24) | (−1.30−3.22) | (−3.36−1.06) | (−5.11−0.67) |
| $O_3$ and PM$_{10}$ | 1.09  | 2.03  | 1.51  | 0.57  | 2.16  | 0.29 |
|           | (−1.43−3.60) | (−0.43−4.48) | (−0.95−3.96) | (−1.97−3.10) | (−0.30−4.62) | (−2.20−2.79) |

For lags at 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$^2$ PM$_{10}$, 10 µg/m$^3$ PM$_{2.5}$, 1 ppm CO, and 10 ppb NO$_2$, SO$_2$ and $O_3$.
The strongly surprising 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$_2$, translated 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 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 an 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.
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