Assessing Confounding, Effect Modification, and Thresholds in the Association between Ambient Particles and Daily Deaths

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I examined the relationship between daily deaths and airborne particles in 10 U.S. cities with varying climatic conditions and seasons in which particle concentrations were high. Airborne particles were associated with significant increases in daily deaths [0.67% increase for a 10 μg/m^3 increase in particles; 95% confidence interval (CI), 0.52–0.81%]. This association was the same in summer and winter. To examine potential confounding by other pollutants, I regressed city- and season-specific effect sizes against the relationship between airborne particles and other pollutants. Controlling for other pollutants did not substantially (or significantly) change the estimated effect of airborne particles. Socioeconomic differences between cities likewise did not modify the effect. The increase in daily deaths that occurred out of hospitals (0.89% per 10 μg/m^3; CI, 0.67–1.10%) was substantially greater than the increase in deaths in hospitals (0.49%; CI, 0.31–0.68%). This is consistent with results previously reported in Philadelphia, Pennsylvania, and suggests that the particle-associated deaths are not just being brought forward by a few days. It is also consistent with recent animal and human studies of the mechanisms of particle toxicity. *Key words*: airborne particles, air pollution, climate mortality. *Environ Health Perspect* 108:563–568 (2000). [Online 3 May 2000]
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Studies on four continents have reported associations between daily concentrations of ambient particles and daily deaths (*1,2*). The magnitude of the regression coefficients varied, but were remarkably similar compared to epidemiologic studies of other exposures. Several arguments have been made to question the relevance of these findings for public health and preventive measures. It has been argued that the deaths are occurring in persons who were already seriously ill and who would have died in a few days anyway. It has been argued that air pollution is responsible for the deaths, but that airborne particles are not the responsible agent; rather, other pollutants confound the particle findings. It has also been argued that the particle associations only exist at higher concentrations, and therefore, most days are below a presumed threshold for effect; hence public health interventions to lower exposure would have no impact on most days.

Two recent papers addressed the first argument by showing that the association between daily deaths and airborne particles persisted after accounting for any short-term displacement of (reduced time until) deaths (*3,4*). In this paper, I address the latter two issues in a multiple-city analysis of particulate air pollution and daily deaths. I also indirectly address the first issue by an analysis stratified by location of death.

Recently, Sunyer et al. (*5*) reported that persons with a previous emergency room visit for chronic obstructive pulnmonary disease (COPD) had a greater risk of air pollution-induced mortality. In general, there is interest in potential effect modifiers for particulate air pollution. Among these are social and economic factors that may represent differences in underlying risk. For example, income has been shown to be a potent predictor of life expectancy. These factors differ among cities in the United States, and these diffferences can be used to explore their role as effect modifiers for the impact of airborne particles.

Methods

Data. I selected 10 U.S. cities with approximately daily PM_{10} (particulate matter ≤ 10 μm) monitoring to provide a reasonable number of locations for a combined analysis. The cities were New Haven, Connecticut; Pittsburgh, Pennsylvania; Birmingham, Alabama; Detroit, Michigan; Canton, Ohio; Chicago, Illinois; Minneapolis–St. Paul, Minnesota; Colorado Springs, Colorado; and Spokane and Seattle, Washington. Daily deaths in the metropolitan county containing each city were extracted from National Center for Health Statistics mortality tapes (*6*) for the years 1986–1993. I also computed separate daily counts of deaths in the hospitals and deaths out of hospitals. Minneapolis and St. Paul were combined and treated as one city. Daily weather data were obtained for the same years, from the nearest airport weather station, and daily concentrations of PM_{10}, sulfur dioxide, ozone, and carbon monoxide were obtained for those years from the U.S. Environmental Protections Agency's Aerometric Information Retrieval System (AIRS) monitoring network (Research Triangle Park, NC). Nitrogen dioxide data were not available in enough of the cities to allow examination of that variable.

Social and economic factors were extracted from the 1990 decennial Census (*7*) for use as potential effect modifiers. The variables used were the unemployment rate, the percentage of the population living below the poverty level, the percentage of the population with a college degree, and the percentage of the population that was nonwhite.

The assignment of PM_{10} exposure raised a number of issues. Many of the locations have more than one monitoring location, but typically only one monitor operates on a daily basis, with the others operating every third or sixth day. If data from all of the monitors were simply averaged, the daily mean would change on days when new monitors were included merely because their annual average differs from the monitoring station that operates on a daily basis.

The variance of PM_{10} measurements also can differ from monitoring location to monitoring location. Day-to-day changes in which monitors are included in the daily average would also result in changes in the day-to-day variation in the exposure measure that do not represent true changes in exposure, but only changes in the sampling of monitors. To remove these influences, I used the following algorithm. The annual mean was computed for each monitor for each year and subtracted from the daily values of that monitor. I then standardized these daily deviances from each monitor's annual average by dividing by the standard deviation for that monitor. The daily standardized deviations for each monitor on each day were averaged, producing a daily averaged standardized deviation. I multiplied this by the standard deviation of all of the centered monitor readings for the entire year and added back in the annual average of all of the monitors. This gave a daily average PM_{10} concentration for each day in each

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city. I then computed the mean of the PM_{10} concentration on the day of death and the day preceding death to use as my exposure index. Most studies have found that a 2-day average is a better predictor of mortality than a single day's exposure. Rather than optimizing in each location, I used the same 2-day average to ensure comparability.

Analytical methods. For each city, a generalized additive Poisson regression was fit (*8,9*), modeling the logarithm of the expected value of daily deaths as a sum of smooth functions of the predictor variables. The generalized additive model allows regressions to include nonparametric smooth functions to model the potential nonlinear dependence of daily admissions on weather and season. It assumes that

$$\log[E(Y)] = \beta_0 = S_1(X_1) + \ldots + S_p(X_p),$$

where Y is the daily count of deaths, $E(Y)$ is the expected value of that count, the X_i are the covariates and the S_i are the smooth (i.e., continuously differentiable) functions. For the S_i I used loess (*10*), a moving regression smoother. This approach is now standard in air pollution time series (*11*). For each covariate, it is necessary to choose a smoothing parameter that determines how smooth the function of that covariate should be. Three classes of predictor variables were used: a smooth function of time to capture seasonal and other long-term trends in the data, weather and day-of-the-week variables to capture shorter term potential confounding, and PM_{10}. The choice of smoothing parameter for each set of variables is described below.

The purpose of the smooth function of time is to remove the basic long-term pattern from the data. Seasonal patterns can vary greatly between Birmingham and Spokane, for example, and a separate smoothing parameter was chosen in each city to reduce the residuals of the regression to "white noise" (*12*) (i.e., remove serial correlation). This approach was used because each death is an independent event, and autocorrelation in residuals indicates there are omitted time-dependent covariates whose variation may confound air pollution. If the autocorrelation is removed, remaining variation in omitted covariates has no systematic temporal pattern, and hence confounding is less likely. This approach has been described previously (*12*). Sometimes it was necessary to incorporate autoregressive terms (*13*) to eliminate serial correlation from the residuals.

The other covariates were temperature, dew point temperature, and barometric pressure on the same day, the previous day's temperature, and day of the week. To allow for city-specific differences, the smoothing parameters for these covariates were also optimized separately in each location. The criterion used was to choose the parameter for each variable that minimized Akaike's Information Criterion (*14*).

PM_{10} was treated as having a linear association with daily mortality in this analysis to facilitate the combination of coefficients across cities. Robust regression was used to reduce sensitivity to outliers in the dependent variable. To reduce sensitivity to outliers in the pollution variable, the baseline analysis was restricted to days when PM_{10} levels were < 150 µg/m^3, the currently enforced ambient standard. This also ensures that the results are unambiguously relevant to questions of revision of those standards.

Assessment of confounding. Confounding is usually assessed by including the potential confounder in the regression. This is a problem for air pollution epidemiology because atmospheric patterns, such as the height of the inversion layer, tend to produce parallel increases and decreases in all air pollutants. This creates considerable collinearity, and hence instability, in the estimated regression coefficients. However, while most pollutants tend to go up and down together within each city, the increase (in micrograms per cubic meter) in one pollutant that accompanies a 1 µg/m^3 increase in another pollutant varies considerably among cities, as this depends on the source term. For example, some cities have very low sulfur fuels, and hence very different slopes in the association between PM_{10} and SO_2 than in cities with high sulfur fuels. In the eastern United States, PM_{10} peaks in the summer, when O_3 levels are high and CO levels are low, whereas in many western U.S. cities, PM_{10} peaks in the winter. This creates considerable variation in the slopes between PM_{10} and the other pollutants, particularly if analyses are stratified by season. This variation is often larger than the variation in within-city correlations among the pollutants, and my approach to confounding takes advantage of this fact. It is based on the observation that if the PM_{10} effect is really due to confounding by another pollutant, I would expect a larger PM_{10} effect in cities or seasons where 1 µg/m^3 PM_{10} is representing more of that other causal pollutant.

In this paper I use a hierarchical modeling approach to take advantage of this variation to assess confounding. In such an approach, the first stage consists of standard regression analyses, producing regression coefficients for the exposure or exposures of interest. In a second stage, those coefficients are regressed against explanatory factors. This approach has been widely used in the social sciences (*15*) and has begun to be applied in epidemiology (*16*). The city-specific Poisson regressions described above are the first stage. The second stage can be used to assess confounding by cooccuring pollutants. Consider, for simplicity, a Gaussian outcome and imagine that X_t is the concentration on day t of the pollutant that is causally associated with the outcome Y_t. Hence

$$Y_t = \beta_0 + \beta_1 X_t + \text{error}. \quad [1]$$

X_t is correlated with another pollutant, Z_t, which is not causally related to Y_t. Therefore I may write

$$X_t = \gamma_0 + \gamma_1 Z_t + \text{error}. \quad [2]$$

What happens if Z_t is used as the exposure variable instead of X_t? Substituting Equation 2 into Equation 1 I have

$$Y_t = \beta_0 + \beta_1\gamma_0 + \beta_1\gamma_1 Z_t + \text{error}. \quad [3]$$

I have confounding by the omitted covariate X_t, and the coefficient of Z_t will be proportional to γ_1, the slope of the association between X_t and Z_t. This can be illustrated by some simple simulations. Figure 1 shows the results of a simulated example where one variable has a true association with the outcome, and the second variable does not but is correlated with the first. The slope between the pollutants varies across different (simulated) cities, which are represented as different points in the figure. Figure 1 shows how the estimated effect size of the noncausal variable varies with γ_1, the slope between the pollutants in each city. The effect size for the noncausal pollutant varies randomly about a line with a zero intercept. The zero intercept follows from Equation 3, where I see that if γ_1 is zero, the expected effect size for the noncausal variable is zero. If I formalize this by performing a regression in the second stage, where, for example, the PM_{10} effect size (in single pollution models) in each town is regressed against the SO_2 to PM_{10} slope in each town, I would expect a zero intercept in the regression if the effect of PM_{10} is all due to confounding. If both pollutants have a

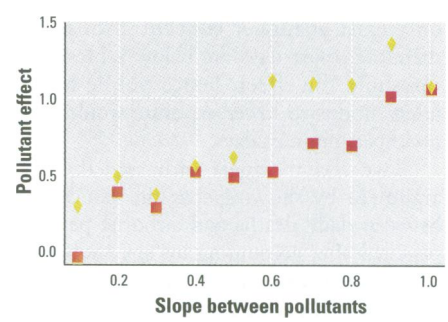

Figure 1. Scatterplot showing the results of a simulation. Plotted are the effect-size estimate for one pollutant as a function of the regression coefficient between it and a confounding pollutant that is causally related to the outcome. The squares show the results when the first pollutant has no causal association with the outcome. The diamonds show the expected results when both pollutants are causally connected to the outcome, but the second pollutant confounds the association with the first.

causal impact on the number of deaths, the effect size for PM_{10} in each city may be overstated in a single-pollutant model. In that case, I would expect a nonzero intercept for PM_{10} but one that is smaller than the average PM_{10} effect size. This is shown by the diamonds in Figure 1. These data points are from a second set of simulations where both exposures were associated with the outcome. In this case, if I perform a second-stage regression, the intercept is an estimate of the effect size I would see for PM_{10} in a city where it is uncorrelated with SO_2, which is to say, the unconfounded PM_{10} effect size. I used this approach to examine confounding.

Of course, the actual models fit to mortality data are log-linear. That is, I assume that

$$E(Y_t) = \lambda_0 exp(\beta Z_t),$$

where λ_0 is the baseline risk before considering pollution. Since the relative risks associated with air pollution are generally < 1.1, $exp(\beta Z_t) \sim 1 + \beta Z_t$, and the results are as before.

More formally, the two-stage approach consists of first fitting regressions of daily deaths against PM_{10} in each location, controlling for season, weather, and day of the week. I assume these estimated coefficients $\hat{\beta}_i$ are normally distributed about some true city-specific coefficient that is proportional to γ_i, plus possibly an effect of PM_{10} net of confounding, that is,

$$\hat{\beta}_i \sim N(\alpha + \delta\gamma_i, \Sigma).$$

In the second stage, I estimate α using a weighted regression, with inverse variance weights.

I have added one further refinement to increase the power of the analysis. In most cities, O_3, CO, and SO_2 show greater differences in their mean level between the indoor-heating season and the warm season than does PM_{10}. This indicates that further variability in the slope between these pollutants and PM_{10} can be obtained by dividing the data in each city into the indoor-heating season (defined as November through April) when CO and SO_2 are high but O_3 is low, and the warm season, when the opposite is true. This increases our ability to determine whether the PM_{10} effect size varies with the slope between PM_{10} and the other pollutants. To accomplish this, the regressions were fit separately in each city in each of the two seasons.

Assessment of effect modification. To test for effect modification, I used social and economic factors in the meta-regression instead of the slopes between pairs of air pollutants. This tests for an interaction term, where, for example, the effect of air pollution increases as the unemployment rate increases. Here our primary interest is in the coefficient of the effect modifier, which tells how much the PM_{10} effect changes for a 1% increase in the unemployment rate, for example.

Assessment of low-level dose–response relationships. If there is a threshold for the effect of PM_{10} on daily deaths, then the observed slope for PM_{10} represents an average of the true slope above the threshold and a slope of zero below the threshold. One unambiguous way to determine whether the effect persists at low PM_{10} concentrations is to limit the analysis to days with low concentrations. I chose a cutoff of 50 μg/m^3, well below the current standard of 150 μg/m^3 for PM_{10}. If a threshold exists above that concentration, I would expect the mean effect estimate in the 10 cities to fall to zero. If there is a threshold < 50 μg/m^3, I would expect the average effect-size estimate to fall because a larger fraction of the days are below the threshold in the restricted analysis than in the analysis that included days up to 150 μg/m^3. I refit the individual city analyses with a restriction limiting the analysis to days < 50 μg/m^3 to test this hypothesis and combined the results using inverse variance weighting.

Location of death analysis. In addition to examining all cause mortality, I computed separate daily counts of deaths occurring in and out of hospitals. This is of interest for several reasons. First, it indirectly addresses the question of whether the time until death is only being reduced by a few days. One would expect people who are on the brink of death to disproportionately die in hospitals because many are in the hospital already. If air pollution primarily affected those people, I would expect its impact on hospital deaths to be larger than on out-of-hospital deaths. Second, the 1952 London smog disaster has been cited as providing biological plausibility to the observed associations at lower concentrations (*17*). If this association is real, one would expect the impact of particulate air pollution on deaths in and out of hospitals to show similar patterns to those observed during the London smog disaster.

Results

Table 1 shows the populations, mean daily deaths, and means of the environmental variables in the 10 study locations. The Census data are shown in Table 2. PM_{10} was only modestly correlated with the weather variables in most of the 10 locations, and the correlations varied considerably, as shown in Table 3. There was considerable variation in the relationship between PM_{10} and the other air pollutants across locations and seasons. The SO_2/PM_{10} coefficients ranged from a low of 0.079 to a high of 1.24. This is more than an order of magnitude, providing enough power to determine if there is a trend to higher PM_{10} slopes in locations where 1 μg/m^3 PM_{10} represents more SO_2. The same was true for the other pollutants, where the O_3/PM_{10} slopes ranged from -0.22 to 1.07 and the CO/PM_{10} slopes ranged from 0.013 to 0.08.

Table 4 shows the estimated effect of a 10 μg/m^3 increase in PM_{10} for all deaths, for deaths out of hospitals, and for deaths in hospitals. PM_{10} was a significant predictor of all-cause mortality [0.67% increase for a 10 μg/m^3 increase in PM_{10}; 95% confidence interval (CI), 0.52–0.81%]. The effect size

Table 1. Characteristics of the study locations.

City	1990 Population	Deaths	PM_{10} (μg/m^3)	Dew point	Temperature (°F)	Pressure (mmHg)
New Haven	804,219	20.4	28.6	40.1	50.5	29.8
Birmingham	651,525	19.1	34.8	51.7	62.4	29.4
Pittsburgh	1,336,449	63.3	36.4	41.2	52.1	28.8
Detroit	2,111,687	59.7	36.9	40.7	50.9	29.3
Canton	367,585	9.9	29.31	41	50.4	28.7
Chicago	5,105,067	133.4	36.5	39.8	50.3	29.3
Minneapolis–St. Paul	1,518,196	32.3	27.5	35.5	46.3	29.1
Colorado Springs	397,014	6	27.1	28.9	48.9	24.0
Spokane	361,364	8.7	40.6	34.2	47.9	27.5
Seattle	1,507,319	29.3	32.5	43.9	52.5	29.6

Table 2. Demographic characteristics of study locations.

City	Percent unemployed	Percent with college degree	Percent below poverty level	Percent nonwhite
New Haven	5.8	24.2	7.9	14
Birmingham	6.5	19.9	16.0	36
Pittsburgh	6.3	22.6	11.5	12
Detroit	12.4	13.7	20.1	43
Canton	7.2	14.3	11.1	8
Chicago	8.0	22.8	14.2	37
Minneapolis–St. Paul	4.8	30.7	9.9	11
Colorado Springs	7.3	25.8	10.4	14
Spokane	7.3	20.6	13.7	5
Seattle	4.1	32.8	8.0	15

was identical in the summer and winter periods. However, the effects of airborne particles were substantially higher for deaths out of the hospital than for deaths in the hospital.

Table 4 also shows the results when restricted to days with PM_{10} < 50 µg/m^3. The slope of airborne particles was larger when restricted to low air pollution days. These results are illustrated graphically in Figure 2.

Table 4 also shows the estimated effect of PM_{10} after controlling for potential confounding by SO_2, O_3, and CO (i.e., the intercept term in the regression of the baseline PM_{10} effect on the coefficient relating PM_{10} to each of the other pollutants). For all three cooccurring pollutants, the effect size after controlling for confounding was not substantially (or statistically significantly) different from the baseline result. This is illustrated in Figure 3. These results indicate that there is no trend to a higher PM_{10} coefficient in cities or seasons with higher slopes between the cooccurring pollutants and PM_{10}. This is illustrated in Figure 4, which shows the effect size for PM_{10} in each city and season plotted against the O_3/PM_{10} coefficient.

Figure 5 shows the estimated effect modification by different measures of social and economic status. It shows how much more of an increase in daily deaths is associated with a 10 µg/m^3 increase in PM_{10} if the city had a 5% higher unemployment rate, an additional 5% of the population living under the poverty level, an additional 5% of the population with college degrees, or an additional 5% of the population nonwhite. These are substantial increases in each of the postulated effect modifiers, but they are associated with no noticeable change in the estimated PM_{10} effect.

Table 3. Correlations between PM_{10} and weather variables.

City	Temperature (°F)	Dew point	Pressure (mmHg)
New Haven	0.05	-0.11	0.11
Birmingham	0.26	0.19	0.19
Pittsburgh	0.45	0.44	0.44
Detroit	0.37	0.38	0.38
Canton	0.42	0.45	0.45
Chicago	0.36	0.32	0.32
Minneapolis[a]	0.29	0.26	0.26
Colorado Springs	-0.34	-0.42	-0.42
Spokane	-0.01	-0.16	-0.16
Seattle	-0.22	-0.29	-0.29

[a]Minneapolis–St.Paul.

Table 4. Estimated effect of a 10-µg/m^3 increase in PM_{10} on daily deaths in the meta-analysis.

Model	Percent increase in deaths	95% CI
Overall	0.67	0.52–0.81
Summer only	0.67	0.48–0.86
Winter only	0.66	0.45–0.87
In hospitals	0.49	0.31–0.68
Out of hospitals	0.89	0.67–1.10
Days < 50 µg/m^3	0.87	0.62–1.12
Confounding by		
SO_2	0.57	0.25–0.90
CO	0.90	0.42–0.97
O_3	0.69	0.53–1.26

Discussion

In an analysis of multiple cities across the United States, PM_{10} was a significant predictor of daily deaths. The association was identical in analyses restricted to the indoor-heating season and the warm months. This is consistent with previously published results (*18*). Given the large differences in the concentrations of cooccurring pollutants between the summer and winter months, this alone is evidence that the particle associations cannot be primarily due to confounding with other pollutants.

The association differed by location of death, with a larger effect on deaths out of hospitals. These results are consistent with previous reports from Philadelphia (*19*) and with the experience in the great London smog episode of 1952 (*17*). This suggests that most of the PM_{10}-associated deaths are not in people who are desperately ill and hence that, in most cases, increased mortality is not a result of time of death simply being reduced by a few days.

A higher risk of death out of the hospital suggests that sudden death is a major component of the air pollution-associated risk and, indeed, "dead on arrival" deaths were most strongly associated with air pollution in the Philadelphia analysis (*16*). Recently, more mechanistic evidence has been developed that supports the notion that airborne particles can be associated with sudden death. A study of subjects with implanted cardiac defibrillators found an increased risk of ventricular tachycardia and ventricular arrhythmia associated with $PM_{2.5}$ (*20*). Arrhythmia is one of the major causes of sudden death. Arrhythmia and sudden death have also been produced in rats by combustion particles (*21*) under experimental conditions where the responses cannot be attributed to cooccurring pollutants. This association is also supported by studies of electrocardiogram changes that are precursors to arrhythmia. Godleski et al (*22*) reported an association between these electrocardiogram changes and exposure to concentrated air particles under experimental conditions in animals with preexisting illnesses. Similar changes have been reported to be associated with airborne particles in three epidemiologic studies using continuous electrocardiogram monitoring in humans (*23–25*). Increases in heart rate have been associated with exposure to airborne particles in studies in Baltimore, Maryland (*25*); Germany and Boston, Massachusetts (*26*); and Utah (*27*).

Another major cause of sudden death is thrombotic processes leading to myocardial infarctions. Here again, recent animal and human studies indicate that airborne particles may be affecting these processes. Exposure to combustion particles has been associated with increased plasma fibrinogen in rats (*28*), and an episode of high particulate air pollution was associated with increased plasma viscosity in a large epidemiology study (*29*). The findings of the present study are therefore consistent with a growing body of more mechanistic research in humans and animals.

There was no trend of higher PM_{10} effect sizes in towns with higher SO_2/PM_{10} slopes, nor in towns with higher O_3/PM_{10}

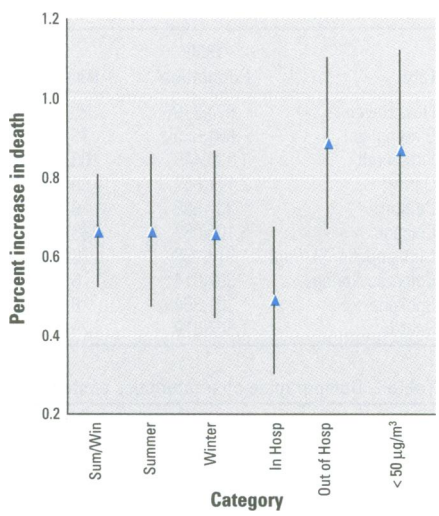

Figure 2. Percent increase in daily deaths associated with a 10-µg/m^3 increase in PM_{10} from six separate analyses. Hosp, hospital. Results are shown for all deaths for summer and winter combined (Sum/Win), summer only, winter only, deaths in hospitals, deaths out of hospitals, and all deaths, but restricted to days when PM_{10} was < 50 µg/m^3.

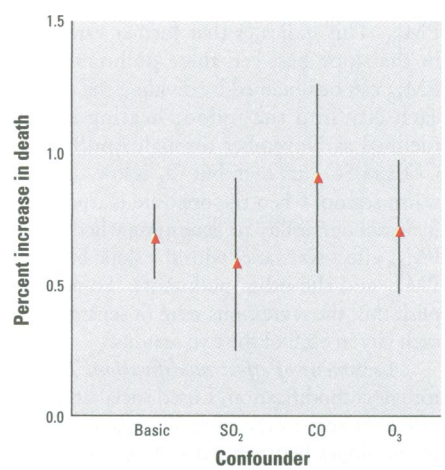

Figure 3. Effect of a 10-µg/m^3 increase in all deaths in the basic analysis and analysis using the intercept term from the meta-regression of the PM_{10} effect size in each city against the relationship between PM_{10} and SO_2, O_3, and CO.

or CO/PM_{10} slopes. This indicates that the PM_{10} effects are not likely to be caused by confounding by other pollutants. These results address the issue of whether the PM_{10} effect is due to the other pollutants: they do not address the question of whether those other pollutants have significant associations with daily deaths as well. This will be addressed in a later study.

Recent animal studies, in which exposure can be controlled and limited to airborne particles, support the finding of an independent particle effect. For example, Zelikoff et al. (*30*) reported that exposure to concentrated air particles after infection with streptococcal pneumonia was associated with a doubling of the area of lung involvement and a doubling of the bacterial burden of rats within 48 hr. Effects of particle exposure on influenza mortality have also been noted (*31*).

The PM_{10} effect was not substantially modified by socioeconomic status measured at the city level, but when the analysis was restricted to days with PM_{10} concentrations < 50 μg/m^3, the effect was greater. These results are inconsistent with a threshold for PM_{10} at any concentrations except those substantially < 50 μg/m^3. Indeed, they suggest that the PM_{10} slope increases at lower concentrations, rather than approaching zero. This tendency for a lower slope at high concentrations has been noted in London (*32*) and in the APHEA study (Air Pollution and Health: a European Approach) (*33*). A study of six U.S. cities recently reported a higher slope for $PM_{2.5}$ when the analysis was restricted to days < 30 μg/m^3 (*34*).

One limitation of studies such as these is the use of outdoor monitoring stations rather than personal exposure monitors. Because the difference between these measurements can be large, some have questioned whether the associations reported in daily time–series studies could be causal. Several recent papers have addressed parts of this issue. Wilson and Suh (*35*) pointed out that outdoor monitors are surrogates for personal exposure to particles of outdoor origin, such as motor vehicle exhaust and sulfates. Current personal monitors measure personal exposure to particles of all sources, including resuspended house dust, environmental tobacco smoke, and cooking aerosols. Hence, personal exposure to particles of outdoor origin are more closely related to outdoor concentrations than some interpretations of personal monitoring data suggest. This has been confirmed by Janssen et al. (*36*), who found median correlations between personal particle monitors in adults and outdoor monitors were much higher after excluding environmental tobacco smoke (ETS) exposure. Janssen et al. (*36*) also highlighted another key issue. Most of the difference between personal PM exposure and outdoor concentrations reflects cross-sectional variations among persons. For time–series studies, it is the longitudinal correlation that matters, and Janssen et al. (*36*) reported considerably higher longitudinal correlations between personal PM exposure and outdoor concentrations, with a median of 0.70 for PM_{10} in the absence of ETS exposure. Finally, two recent articles examined the statistical implications of the measurement error. Schwartz and Levin (*37*) pointed out that most of the difference between personal and central measurements of exposure in the time–series context are Berkson error, and hence do not bias the estimates. Zeger et al. (*38*) have explored the issue in more detail and have shown that the remaining bias is negative—that is, an underestimation of the effect. Hence, measurement error in exposure is an unlikely cause of these associations.

In sum, this study provides evidence that airborne particles influence the number of daily deaths and that these effects are not primarily attributable to other air pollutants. The data show the same pattern of higher relative effect on deaths out of the hospital that was seen in an air pollution episode where causality of the pollution effect is well accepted. That pattern, moreover, is consistent with recent animal and human data on the effects of particles on risk factors for sudden death. Finally, the public health benefit of each incremental reduction of 1 μg/m^3 appears to be higher at the lower air pollution levels that prevail on most days. This suggests that intervention strategies that lower average levels, rather that those that address the few peak days, are the most appropriate. This is an important consideration, as a number of cities (e.g., Mexico City, Mexico; Athens, Greece) have adapted strategies that limit driving or industrial activity on peak pollution days. Such approaches do lower average levels, but are costly and disruptive, and the same effort put into reducing everyday emissions appears likely to produce greater public health benefit.

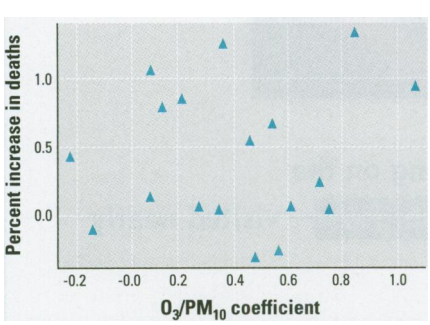

Figure 4. Plot of the PM_{10} effect size in each season in each city versus the regression coefficient relating O_3 to PM_{10} in that season and city.

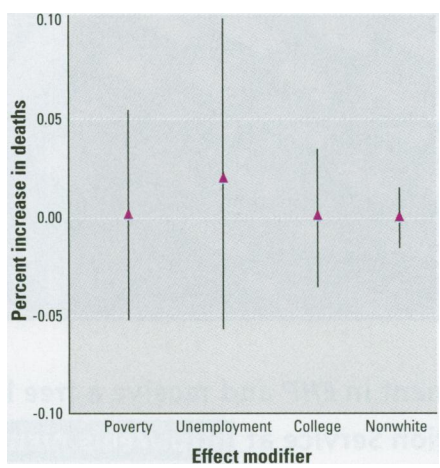

Figure 5. Incremental effect (above the baseline) of 10 μg/m^3 PM_{10} on all deaths associated with a 5% increase in the poverty rate, the unemployment rate, the proportion of the population with a college degree, and the proportion of the population that is nonwhite.

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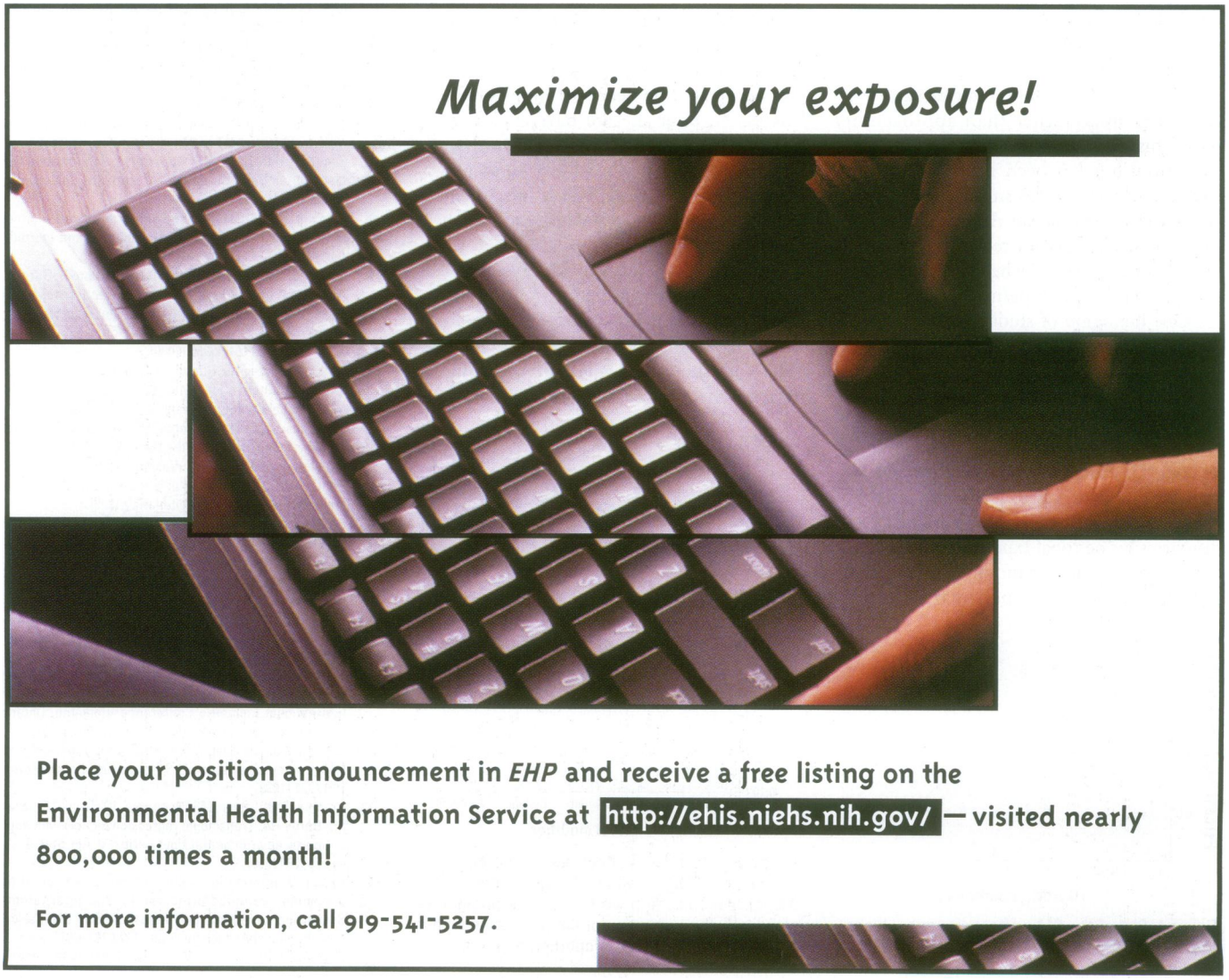
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