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ABSTRACT

Daily data for fine (<2.5 μm) and coarse (2.5–10 μm) particles are available for 1995–1997 from the U.S. Environmental Protection Agency (EPA) research monitor in Phoenix, AZ. Mortality effects on the 65 and over population were studied for both the city of Phoenix and for a region of about 50 mi around Phoenix. Coarse particles in Phoenix are believed to be natural in origin and spatially homogeneous, whereas fine particles are primarily vehicular in origin and concentrated in the city itself. For this reason, it is natural to focus on city mortality data when considering fine particles, and on region mortality data when considering coarse particles, and most of the results reported here correspond to those assignments.

After allowing for seasonality and long-term trend through a nonlinear (B-spline) trend curve, and also for meteorological effects based on temperature and specific humidity, a regression of mortality was performed on PM using several different measures for PM. Based on a linear PM effect, we found a statistically significant coefficient for coarse particles, but not for fine particles, contrary to what is widely believed about the effects of coarse and fine particles. An analysis of nonlinear pollution-mortality relationships, however, suggests that the true picture is more complicated than that. For coarse particles, the evidence for any nonlinear or threshold-based effect is slight. For fine particles, we found evidence of a threshold, most likely with values in the range of 20–25 μg/m³. We also found some evidence of interactions of the PM effects with season and year.

The main effect here is an apparent seasonal interaction in the coarse PM effect. An attempt was made to explain this in terms of seasonal variation in the chemical composition of PM, but this led to another counterintuitive result: the PM effect is highest in spring and summer, when the anthropogenic concentration of coarse PM is lowest as determined by a principal components analysis. There was no evidence of confounding between the fine and coarse PM effects. Although these results are based on one city and should be considered tentative until replicated in other studies, they suggest that the prevailing focus on fine rather than coarse particles may be an oversimplification. The study also shows that consideration of nonlinear effects can lead to real changes of interpretation and raises the possibility of seasonal effects associated with the chemical composition of PM.

IMPLICATIONS

The EPA standard for fine particles introduced in 1997 was based on the widespread belief that the most serious health effects occur for fine rather than coarse particles. The present study shows that coarse particles may still have an effect and, therefore, should not be neglected. It also confirms that fine particles have an effect, but in this analysis, it is only observed above a threshold in the region of 20–25 μg/m³; there appears to be no effect below 15 μg/m³. Since the latter figure is the 1997 EPA standard for long-term average fine PM, the standard may possibly be more stringent than needed. However, the main message of the paper is that more study is needed of the comparative effects of coarse and fine PM, of possible threshold or nonlinear relationships, and of the effect of variations in the chemical composition of PM.

BACKGROUND AND DATA

In 1997, the U.S. Environmental Protection Agency (EPA) introduced a new PM standard based on $PM_{2.5}$ to supplement an earlier standard based on PM_{10}. The new standard was founded on the widely held belief that $PM_{2.5}$ is more directly injurious to human health than is PM_{10}. Nevertheless, although there has been widespread research on the human health effects of PM_{10} based on time-series analysis of daily mortality and morbidity counts,[1–5] there has been comparatively little direct comparison of the epidemiologic effects of fine PM (i.e., $PM_{2.5}$) and coarse PM (PM_{10}–$PM_{2.5}$).

Schwartz et al.[6] compared the effects of fine PM and coarse PM on mortality using data from the Harvard "Six

Cities Study," which involved an average of 8 years of data at each of six cities, using dichotomous sampling data collected every other day. In their study, they reported a consistently stronger effect for fine particles than for coarse particles. They also considered the possibility of the "threshold effect" for fine particles by repeating the analysis but restricting it to days on which the level of $PM_{2.5}$ was below either 25 or 30 $\mu g/m^3$, and they reported that even within those days there was still a statistically significant association between $PM_{2.5}$ and mortality.

However, Lipfert and Wyzga[7] criticized this study, arguing that the difference in results for coarse and fine PM could have resulted from differential measurement errors in the two series. Another study by Schwartz et al.[8] reported that coarse particles did not have an adverse health effect in Spokane, WA, a fact which could very likely be explained by the fact that coarse particles in Spokane are mostly natural dust and, therefore, far less toxic than particles of industrial origin. Despite these studies, overall there has been much less direct epidemiologic comparison of fine and coarse PM than there has been of cases where the two are combined into PM_{10} or TSP (total suspended particulates). Of course, the main reason for this is that daily $PM_{2.5}$ data is available at only a very small number of stations.

The present study makes use of a new data source from Phoenix, AZ. From 1995 to early 1998, the EPA located a research monitoring platform in Phoenix, collecting daily data from DFPSS, tapered element oscillating microbalance (TEOM), and dichotomous samplers, to determine both fine and coarse PM measurement as well as particulate carbon and elemental concentration measurement. These data have been described by the PM Research Monitoring Network Data report for Phoenix, AZ, February 1995–December 1997, produced by the EPA National Exposure Research Laboratory, Research Triangle Park, NC. Based on these data, we have calculated daily fine and coarse PM data by averaging hourly measurements from a TEOM monitor. Although the data contained a small number of negative values, these were not removed, as it seems likely that they result from the method used to calculate hourly concentrations rather than from simple recording error. Because it is common in this field of research to use averages of up to 5 days of PM data as an exposure measure, rather than just single daily readings, we also calculated the k-day running averages, for k = 2, 3, 4, and 5, of coarse and fine PM. In performing this calculation, we followed the convention that if at least one but less than k of the daily readings were available, we calculated a k-day average using all available days. For most of the analysis to follow we used k = 3, and with this convention, we had 1038 available days of fine PM data and 1026 days of coarse PM data.

Climatic data for Phoenix have been downloaded from the Web site of the National Climatic Data Center (NCDC) in Asheville, NC. Although climatic data are also directly available from the EPA report, we preferred to use the NCDC data because of the wider range of variables available. Specifically, we made use of the following data available on a daily basis: daily maximum temperature, daily minimum temperature, and specific humidity, the latter calculated from dew point and pressure. Daily deaths data were obtained from the Arizona Health Services Department. Based on these, we developed two series of daily deaths, one from the city of Phoenix, and the other from a wider region of about 50 mi around Phoenix, which includes other cities such as Scottsdale, Mesa, and Tempe. We refer to this as the "Phoenix region" data set. Both data sets were restricted to residents, which avoids a possible bias due to seasonal influx of temporary residents during the winter.

Some discussion needs to be given of the reasons for considering separate city and regional data. There were good a priori reasons, which the detailed analysis confirms, for expecting fine particles effects to be strongest in the city data and coarse particles effects to be strongest in the regional data. Fine particles in Phoenix are primarily vehicular in origin, spatially heterogeneous, and concentrated in urban areas. We would not expect effects due to downtown traffic to affect people living many miles from the city or in other cities where the PM levels are different from those in Phoenix. In contrast, coarse PM in this region is believed to be primarily of natural origin and spatially homogeneous. We therefore expect the effects of coarse PM to be homogeneous over the region, and from a statistical point of view, we can expect to get more precise estimates if we use a larger data set.

INITIAL DATA ANALYSIS

Previous time-series studies of air pollution and mortality have made clear that there are both meteorological and long-term trend and seasonality effects which must be taken into account. Naturally, we find the same for the current data set.

Figure 1 shows daily deaths for both the city and region, with a scatterplot smoother running through the data points. The latter was obtained using the lowess function in the statistical package S-Plus (MathSoft Inc.; Seattle, WA), with f = 0.05 (this is a parameter controlling the amount of smoothing). This plot shows a strong seasonal pattern and possibly some additional long-term trend.

Figure 2 shows levels of 3-day averages of coarse PM and fine PM, also with a scatterplot smoother. These are shown in preference to 1-day values because the 3-day values are the ones used in the more detailed analysis later in this paper. A strong seasonal effect is clear here as well, and possibly an overall increasing trend.

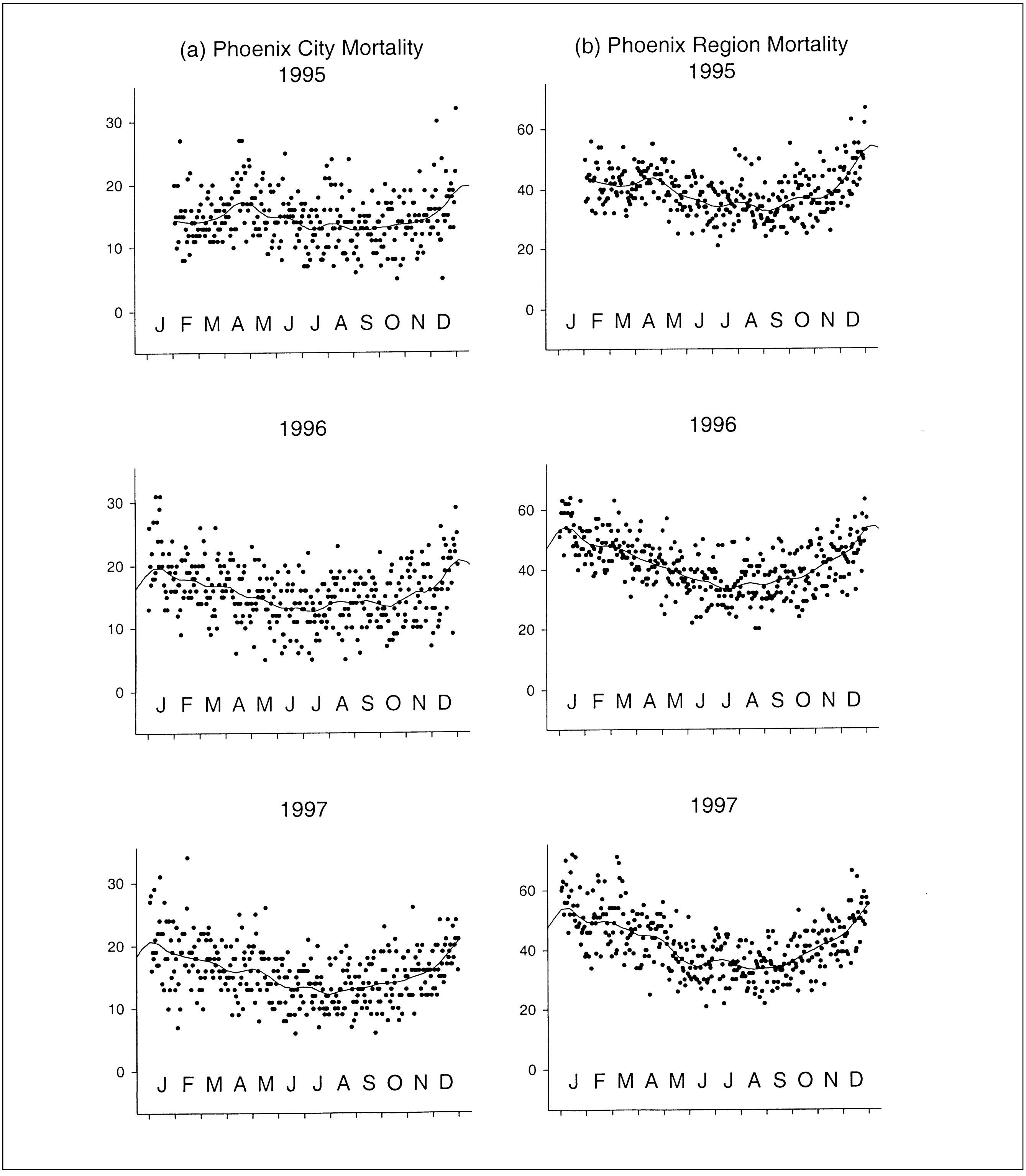

Figure 1. Daily deaths in (a) Phoenix city and (b) Phoenix region for the 3 years of the study, with a fitted smooth curve.

Initial studies of meteorological effects show that both temperature and specific humidity are relevant, but the effects may be nonlinear. With temperatures, some previous studies[4,5] have suggested that a piecewise linear effect, with different slopes on either side of some threshold value, may fit the data better than a polynomial trend, and initial exploratory regression analyses suggested that this might be true here. Specifically, a model where the dependence on daily maximum temperature *tmax* is of the form

$$\begin{cases} b_1 tmax, & \text{if } tmax < u \\ b_1 tmax + b_2 (tmax - u), & \text{if } tmax > u \end{cases} \qquad (1)$$

with $b_1 < 0$, $b_1 + b_2 > 0$ and some threshold u, appears to be a good fit. Exploration of u = 20, 25, 30, and 35 °C

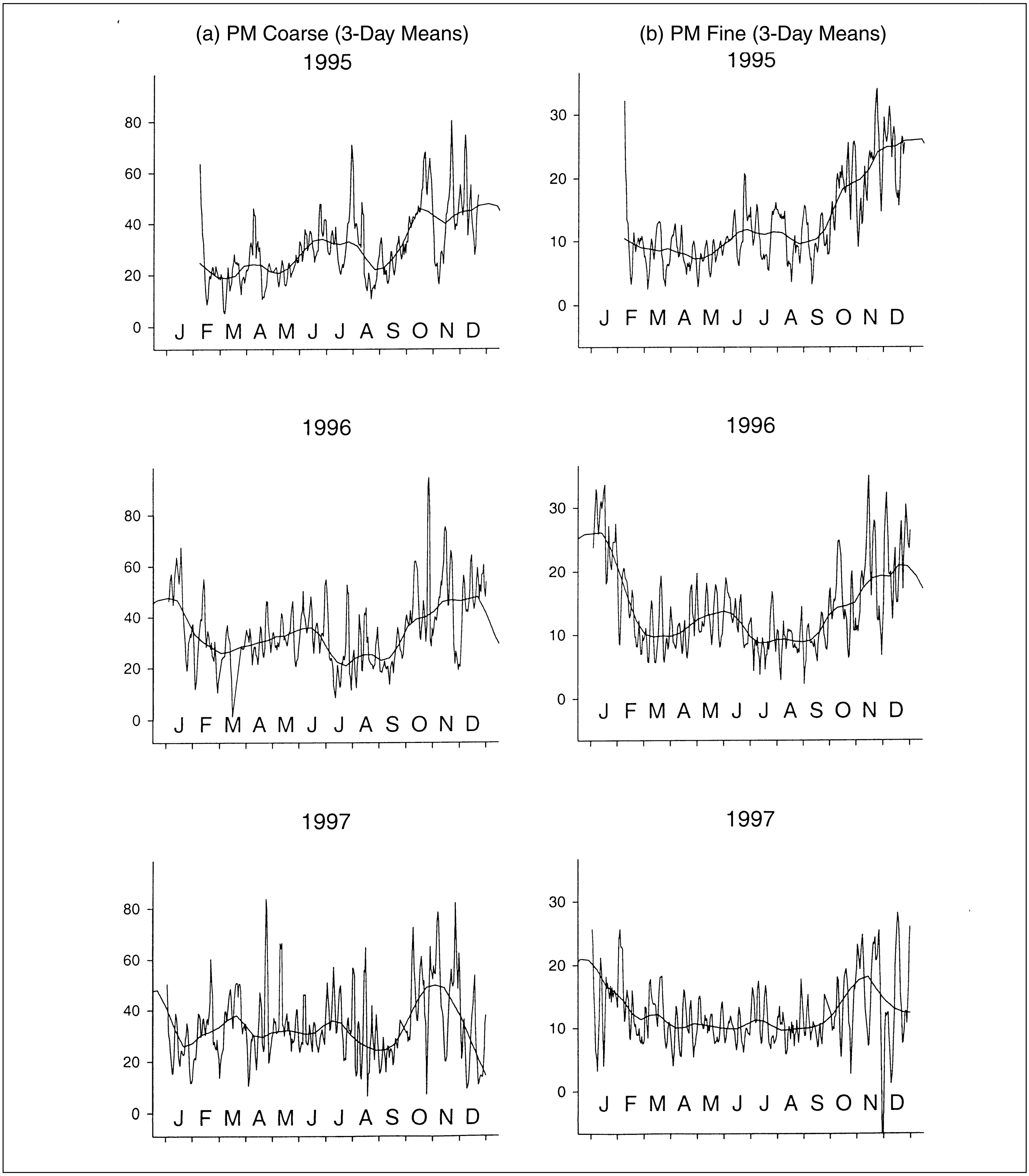

Figure 2. Three-day averages of (a) coarse PM and (b) fine PM (measured in μg/m³), with a fitted smooth curve.

led to u = 30 as the threshold chosen for subsequent analysis. Other variables included were daily minimum temperature, *tmin*; specific humidity, *sh*; and the square of specific humidity, which we denote *shsq*. A complete list of covariates used in the analysis, including both these and the PM-based variables, is contained in Table 1.

In addition, all the variables in Table 1, except *day* and the mortality variables, are also considered in lagged form; for instance, $tmax_m$ means the value of *tmax* lagged m days. We consider m = 0, 1, 2, 3, and 4; $tmax_0$ is today's maximum temperature, $tmax_1$ is yesterday's, and so on.

For the seasonal and long-term trend, it is obvious from Figure 1 that a simple polynomial or piecewise linear

Table 1. Description of variables used in analysis.

day	Number of days (1 = Feb 1, 1995; 1065 = Dec 31, 1997)
mortc	Elderly nonaccidental mortality in city
mortr	Elderly nonaccidental mortality in region
tmax	Daily maximum temperature
tmin	Daily minimum temperature
sh	Daily mean specific humidity
*tg*30	Larger of *tmax*–30 and 0
shsq	Square of *sh*
*p*1*c*	Daily coarse particles level (PM_{10}–$PM_{2.5}$)
*p*2*c*	2-day averages of *p*1*c*
*p*3*c*	3-day averages of *p*1*c*
*p*4*c*	4-day averages of *p*1*c*
*p*5*c*	5-day averages of *p*1*c*
*p*1*f*	Daily fine particles level ($PM_{2.5}$)
*p*2*f*	2-day averages of *p*1*f*
*p*3*f*	3-day averages of *p*1*f*
*p*4*f*	4-day averages of *p*1*f*
*p*5*f*	5-day averages of *p*1*f*

function will not be adequate, and the solution adopted here is a B-spline representation, which represents the estimated function as a continuous sequence of cubic polynomials of the form

$$f(day) = \sum_{k=1}^{K} c_k B\left(\frac{K \times day}{1065} - k + \frac{1}{2}\right) \qquad (2)$$

where $B(\cdot)$ is the B-spline basis function.[4,9] In effect, this represents the trend as a linear combination of K independent functions, with coefficients c_k estimated from the data, and whose smoothness may be controlled by varying the value of K. Note that eq 2 effectively ensures that the "knots" of the B-spline representation, given the value of K, are uniformly distributed throughout the 1065 days for which data are available.

The final "initial data analysis" issue is the form of dependence of mortality on the regression terms. In the present paper, this has been achieved by a linear regression of the square root of daily mortality on the long-term trend, meteorological, and PM-based variables. The choice of a square root transformation was made after a comparison with a logarithmic transformation and with no transformation, using methods similar to Atkinson, section 6.2.[10] The square root transformation was clearly superior to the other two transformations in every comparison made.

To summarize the results of this section, the model adopted is a linear regression in which the dependent variable is the square root of daily mortality in either the city of Phoenix or the Phoenix region, and the linear regression terms are long-term trends modeled by eq 2, together with a subset of the meteorological and PM-based variables in Table 1, lagged from 0 to 4 days.

DETAILS OF REGRESSION ANALYSIS

For the first part of the analysis, several different values of K, ranging from 8 to 48, were tried in eq 2, and for each, meteorological variables from Table 1 (and their lagged values) were selected by backward selection, using hypothesis tests with size 0.1 to decide whether to retain the meteorological variables (in other words, a meteorological variable was retained whenever the p value for that variable was smaller than 0.1). The resulting models were compared by a variety of model selection devices, including *PRESS*, *AIC*, and *BIC*.[11] In general, *PRESS* and *AIC* behave similarly and tend to favor models with larger numbers of parameters, while *BIC* selects models with fewer parameters. This behavior was seen here, as the optimal value of K when selected by *PRESS* or *AIC* was 40 for the regional data and 24 for the city data; when selected by *BIC*, it was 16 and 12, respectively. Although this leaves open the question of which K we should actually use, one point in favor of the smaller K was that the backward selection procedure in that case selected more meteorological variables, and that seemed desirable in principle, so that the resulting model included both meteorological terms and a long-term trend. Therefore, the *BIC* values were adopted for further analysis, with meteorological variables given in Tables 2 and 3. The subsequent results in the paper are not overly sensitive to the precise model chosen at this stage of the analysis, a point we return to later.

After selecting an initial model to represent the long-term trend and meteorological components, different PM variables based on Table 1, together with lagged values, were added to the model one at a time, in an attempt to ascertain what the strongest effect would be. At this point in the analysis, it emerged that, taken as linear terms, those based on coarse PM contributed more statistically significant effects than those based on fine PM. For example, using the regional data, any one of $p1c_0$, $p2c_0$, or $p3c_0$ was statistically significant, with t statistics (ratio of parameter estimate to standard error) of 3.5, 3.6, and 3.2, respectively. For a large data set such as this, the t distribution effectively coincides with a normal distribution, so any t value larger than 2 is statistically significant at level 0.05, and the values quoted here are significant at levels 0.001 or smaller. Results for coarse particles in the city of Phoenix are similar, but with larger standard errors leading to smaller t values; for example, the t value for $p3c_0$ is 2.0. In contrast, no analysis based on fine PM for either the city or the region produced a t statistic larger than 1.2, which is not statistically significant.

At this stage, therefore, our conclusion is that there may be a significant result due to coarse PM, but there is no sign of any due to fine PM.

Table 2. Meteorological variables used in analysis of Phoenix region data. Suffixes denote lags. The model also included a long-term trend based on eq 2, with $K = 24$.

$tmax_1$	$tmin_0$	sh_1	$tg30_1$	$tg30_2$	$shsq_1$	$shsq_3$

Table 3. Meteorological variables used in analysis of Phoenix city data, together with long-term trend based on eq 2 with $K = 16$.

$tmax_2$	$tmin_1$	$tmin_3$	sh_1	$tg30_0$	$shsq_1$

Nonlinear Dependence for Coarse and Fine PM

The picture becomes considerably more complicated, however, if the possibility of a nonlinear PM response is taken into consideration. For most of the following discussion, for reasons explained earlier, we used regional data when looking at coarse PM and city data when looking at fine PM. The results for coarse PM on the city data were similar to those for the regional data, but with much wider confidence bands, making it harder to characterize the form of the relationship. In contrast, it was impossible to find any effect, linear or nonlinear, relating fine PM to regional mortality. As noted already, however, this is only to be expected based on what is known about the sources of PM, so it seems reasonable to concentrate on the city data when looking for fine PM effects.

At this stage of the analysis, it was decided to concentrate on $p3c_0$ and $p3f_0$ (3-day averages with no time lags; in other words, the average of today's, yesterday's, and the day before yesterday's values) as the main PM variables of interest. This decision was based both on the results of the previous section and on general experience of this field of research, which has shown that 2- or 3-day averages of PM very often give a more reliable indication of epidemiologic effects than do single-day values.

There are, however, numerous ways in which we can look for nonlinear effects, and in this section we consider three of them. All models fitted include the same meteorological and long-term trend terms as in the preceding section.

Piecewise Linear Analysis

The first nonlinear method tried was a piecewise linear method, similar to the model adopted in eq 1 for temperature. For each of several possible thresholds, separate linear trends were estimated below and above the threshold, together with 95% confidence intervals. An early example of the idea of looking at separate linear trends below and above a threshold was the paper by Ostro,[12] in which he applied this method to data from London in the 1950s and in 1960.

Figure 3 shows the result of this analysis, in which the response to PM as a piecewise linear function is plotted together with the confidence bands. Plots are shown for coarse PM for the region data and for fine PM for the city data. The results show a contrast between the cases of coarse and fine PM. For coarse PM (left-hand half of the plot), there is no significant change in slope on either side of the threshold, except for threshold 10, which is rather meaningless in view of the shortage of coarse PM data (and very wide confidence bands on the coefficient) below this threshold. In contrast, for fine PM, although there is no significant effect when represented as a linear term, when piecewise linear terms are selected, there are some significant results. In particular, the plots for thresholds 20 and 25 show that for either of these, the fine PM effect above the threshold is statistically significant, though the effect below the threshold is not. The t statistics for the effect above the threshold were 2.4 and 2.7, respectively, for thresholds 20 and 25.

It is possible to give a firmer characterization of the effects in Figure 3 by formally testing the null hypothesis of a linear PM effect against the alternative hypothesis of a piecewise linear effect with threshold as shown. For the five plots based on coarse PM, the p values of the test statistics are all in excess of 0.5, indicating no threshold effect. For the five plots based on fine PM, the p values (top to bottom) are 0.06, 0.05, 0.007, 0.005, and 0.33. For thresholds 20 and 25, in particular, this provides strong evidence that a piecewise linear fit improves on a simple linear fit.

B-Spline Analysis

The second nonlinear method tried was to represent the PM (coarse or fine) effect as a B-spline representation, similar to the formula given in eq 2 for the time-dependent effect. For this analysis, the number of knots was fixed at $K = 4$, which is large enough to display a nonlinear effect if there is one; for a much larger K than that, the randomness in estimating the coefficients of the individual B-spline terms (equivalent to c_k in eq 2) would be so large as to render the results meaningless. The meteorological and long-term trend terms in the model were the same as in the linear analysis.

Results were expressed as relative risks (RR), using the long-term mean PM value as a reference level for which $RR = 1$. This was 13.0 for fine PM and 33.6 for coarse PM. Pointwise 95% confidence bands were computed using the standard errors and covariances of parameter estimates in the regression analysis. Unfortunately, confidence bands computed by this method tend to be very wide,

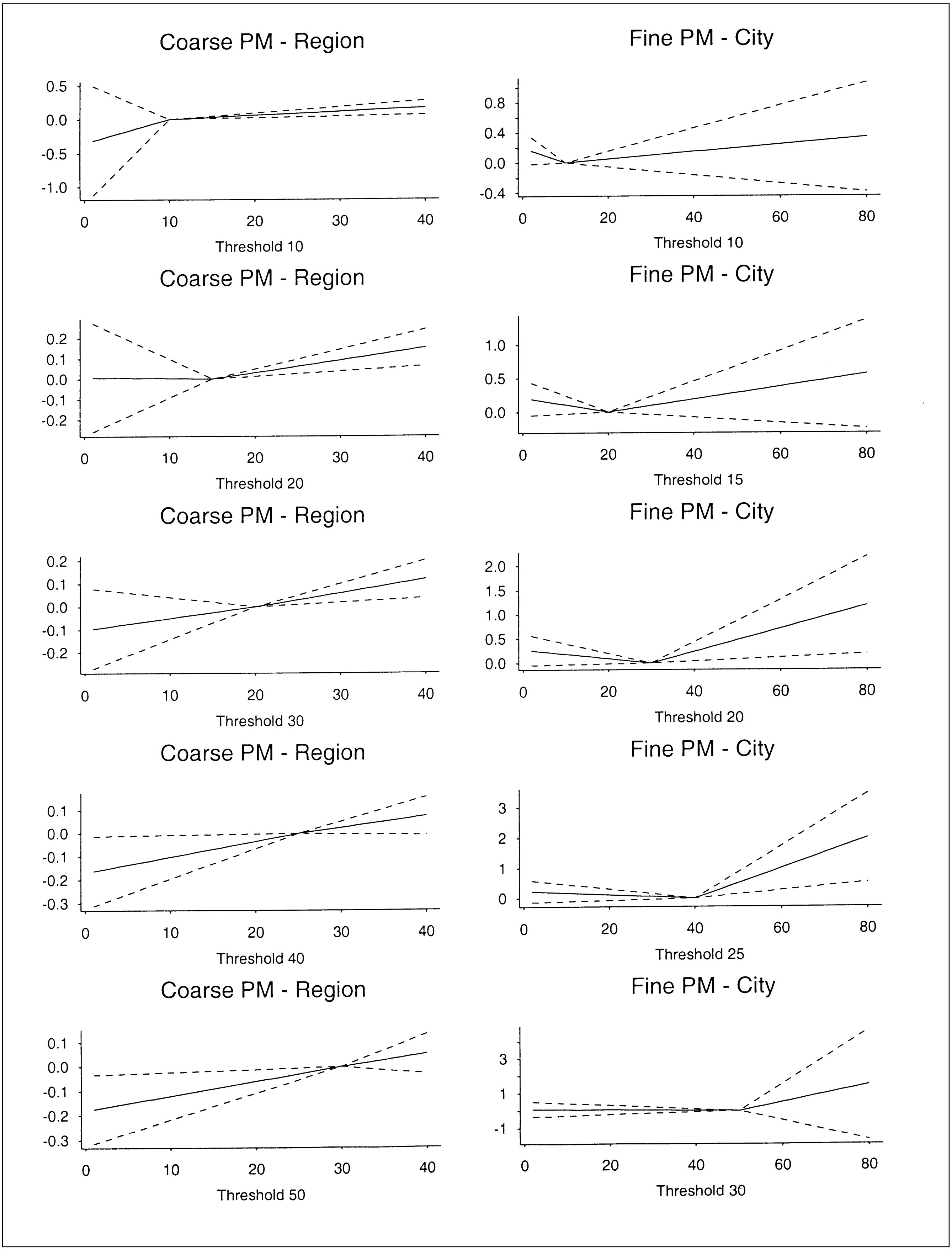

Figure 3. Piecewise linear estimates of the coarse PM effect for the region and the fine PM effect for the city plotted for different thresholds.

but they were included in the plots because they give at least a rough indication of the extent to which various nonlinearities in the plot may be regarded as true effects rather than just artifacts of the data. Figure 4 shows these plots for both coarse (regional data) and fine PM (city data).

In Figure 4a, for coarse PM in the region, it can be seen that the sharpest increase in the nonlinear curve occurs between 20 and 40 μg/m^3, though there also appears to be a second sharp rise over 60 μg/m^3. Overall, however, the results of this plot do not contradict a simple overall linear effect. In contrast, in Figure 4b, for fine PM, there appears to be a clear change in the slope somewhere in the region of 20 μg/m^3, and the accompanying confidence bands show that this is statistically significant. This may be evidence of a threshold effect or at least a significantly nonlinear relationship, which contrasts sharply with our earlier finding of no relationship at all.

Diagnostics for the B-Spline Analysis

A number of the standard regression diagnostics[11] were computed for the fitted models with the B-spline representation for the PM effect. These serve as a check on whether the model is a reasonable fit to the data. Such diagnostics could have been computed for all the models fitted, but we focused on this one because of all the models considered, the one involving a nonlinear PM effect appeared to provide the best overall fit to the data.

One issue raised by our decision to concentrate on linear regression with a square root transformation of deaths was whether this approach copes adequately with the problems of overdispersion and serial correlation that sometimes arise in studies involving Poisson regression.[2] Overdispersion refers to the property that variances of the observed responses are larger than those which would hold if the data were truly independent Poisson counts. In the case of a square root transformation, the variance is very nearly stabilized to a constant value of 0.25. An observed variance larger than that is, therefore, an indication of overdispersion. Other studies typically indicate an overdispersion in the region of 1.05–1.1 (i.e., 5–10% larger than the Poisson variance).

For fine particles, the estimated residual variance was 0.2715. Dividing by 0.25, this therefore corresponds to an overdispersion of 1.09. For coarse particles, the corresponding residual variance is 0.2816, or an overdispersion of 1.13. These results are, therefore, at the high end of the accepted range of overdispersions, which may indicate some additional source of variability that has not been taken into account.

Serial correlations have been calculated based on the studentized residuals. For fine particles, the first three values are 0.034, 0.035, and 0.103. To judge the significance of these, a common rule of thumb is to compare them with $2/N^{0.5}$, where N is the sample size on which the serial correlations are based. In this case, $2/N^{0.5} = 0.062$, which means that the third-order autocorrelation is significant. However, none of the other autocorrelations is significant. The results for the model based on coarse particles fitted to the region data are similar: serial correlations 0.055, 0.037, 0.084, ... so that the third value is again significant, but none of the others are. We do not have a ready explanation for this.

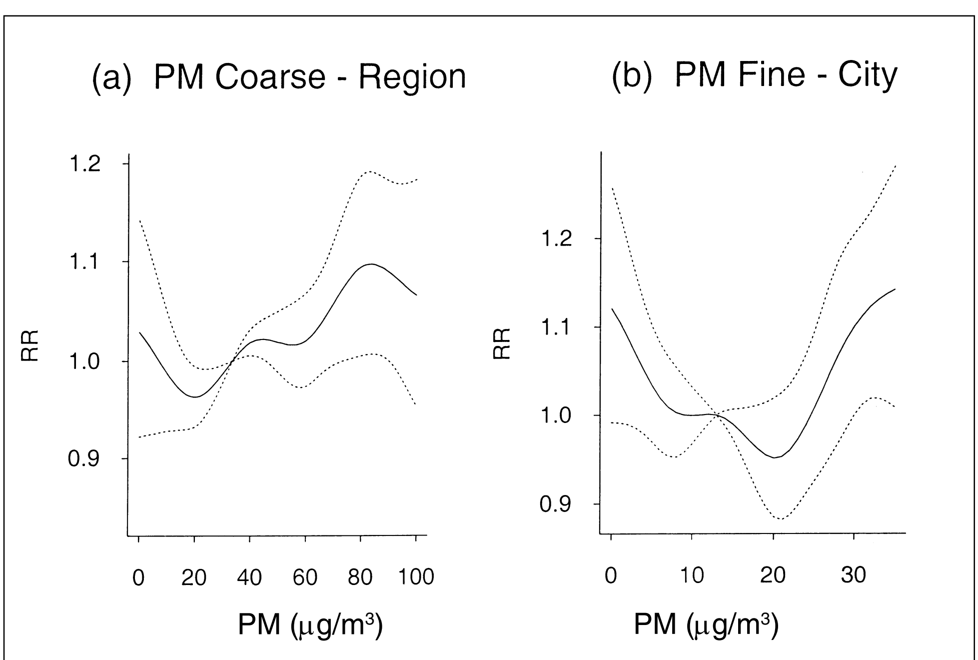

Figure 4. Nonlinear estimates of *RR* (relative to the mean PM variable), together with pointwise 95% confidence bands. (a) Coarse PM effect–regional deaths data. (b) Fine PM effect–city deaths data.

There are also a number of diagnostics aimed at determining whether any of the observations are particularly influential on the final results. There are several of these that tend to work in a similar way, so we concentrated on one, namely, DFFITS.[10,11] According to criteria originally given by Belsley et al.,[13] DFFITS indicates an influential observation at a value $2(p/N)^{0.5}$, where N is the sample size and p is the number of parameters in the model. In the case of the fine particles analysis, p was 0.295, and there were 65 values (out of the 1014 for which DFFITS could be calculated) which exceeded that in absolute value, the largest absolute value being –0.6196. This is a little difficult to interpret, but we have examined whether outlying values of DFFITS correspond to outlying observations of PM, and no clear pattern emerges. The picture for coarse particles is similar, with 55 values of DFFITS exceeding the cut-off value of 0.327, the largest absolute value being –0.5853, but extreme values of DFFITS again do not correspond to extreme values of the PM variable of interest.

Overall, there are a number of features here that might justify further exploration, but none that casts serious doubt on the correctness of the model.

Bayesian Analysis for Threshold Selection

One can take the analysis of the previous section somewhat further by looking specifically for a threshold effect of the form

$$\begin{cases} 0, & \text{if } p \le u \\ b_1(p-u), & \text{if } p > u \end{cases} \qquad (3)$$

where p is a PM variable (coarse or fine) and u is the threshold. The purpose of this section was to see how far we could go toward formally selecting the best value of u to be consistent with the formula in eq 3.

Conditionally on u, the dependence between the vector of responses Y and the matrix of covariates X (which includes long-term trend, meteorology, and PM variables) is a linear model of the form

$$\mathrm{E}\{Y\} = X^{(u)}b^{(u)}, \quad \mathrm{Cov}\{Y\} = v^{(u)}I \qquad (4)$$

in which the matrix of covariates $X^{(u)}$, the regression parameters $b^{(u)}$, and the residual variance $v^{(u)} > 0$ all depend on the threshold parameter u, and I is the identity matrix. If we take a Bayesian point of view, assuming a joint prior density for $(u, b^{(u)}, v^{(u)})$ of the form

$$\pi(u, b^{(u)}, v^{(u)}) \propto \frac{1}{v^{(u)}}, \quad 0 \le u \le u_{\max}, \quad v^{(u)} > 0 \qquad (5)$$

for some upper bound $u_{\max}$ on the permissible values of u, then by combining eqs 4 and 5 and integrating out $b^{(u)}$ and $v^{(u)}$, the marginal density of Y given u is of the form

$$f(Y \mid u) \propto G(u)^{n-q}, \quad 0 \le u \le u_{\max} \qquad (6)$$

Here, n is the number of observations, q is the number of regressors in the linear model eq 4, and $G(u)^2$ is the conventional error sum of squares for the linear regression model eq 4 with u treated as fixed. Bayesian inference for u may, therefore, be based directly on the conditional density in eq 6, renormalizing the probabilities so that the posterior density of u integrates to 1.

In practice, we have assumed u to lie on a discrete grid (10, 11, 12, ..., 35 for fine PM and 0, 2, 4, ..., 70 for coarse PM) and have computed posterior densities by summing the values of eq 6 over this grid, renormalizing so that the overall sum of probabilities is 1. The results are shown in Figure 5. These results may be interpreted as an overall probabilistic statement about the location of the threshold based on the data available.

We have already seen that the strongest evidence for a threshold is in Figure 4b, for fine PM in the city of Phoenix, with less strong evidence in Figure 4a (coarse PM in the region). Results in Figure 5 confirm this, but also give new insights into the strength of evidence for the existence of a threshold.

For coarse PM, Figure 5a shows a peak in the posterior density around 20 μg/m³, but it is not a very strong peak, and the posterior density does not tend to 0 near $u = 0$, which suggests that there may in fact be no threshold at all.

For fine PM, Figure 5b shows a very clear peak in the posterior density near u = 22 μg/m³, with the posterior density near 0 outside the range of 15–30. Although the results have been calculated on the assumption of a uniform prior distribution for u, the general form of this plot (with a much higher posterior density in the range of 15–30 than outside that range) will not be very sensitive to this, provided a prior density is adopted that is consistent with reasonable prior belief over a wide range of values of u. Thus, in this case we deduce strong evidence in favor of the existence of a threshold.

SENSITIVITY ANALYSES

As a check on the sensitivity of the main results in this paper to some of the modeling assumptions made at the beginning, they were repeated with the following changes: (1) the choice of K (number of knots in the B-spline representation) was made by *AIC* rather than *BIC*; (2) the size of the hypothesis tests performed at the backward selection stage was increased from 0.10 to 0.15 (the effect of this will be to include more meteorological variables in the analysis); and (3) the meteorological modeling was confined to temperature-based variables (no humidity), that is, *tmax*, *tmin*, and *tg*30 (see Table 1), together with their lagged values.

We shall not present detailed results of this, but the following are the main conclusions. An *AIC*-based selection of K led to $K = 40$ for the region data and $K = 20$ for the city data. With these changes to the model, both coarse and fine PM effects are a little weaker than those in the preceding analysis, but the qualitative results are the same—there is a significant linear effect for coarse PM in the region and a significant nonlinear effect for fine PM in the city.

We should note, however, that the trend and seasonal variation must not be overmodeled. During the *AIC* analysis for the city data, it was noted that $K = 48$ gives an *AIC* value not very different from the optimal value $K = 20$, but when the fine particles analysis was repeated with this value of K, the results were entirely different, several of the linear coefficients appearing significantly negative. The interpretation of this result would appear to be that local fluctuations of the order of 3 weeks (the interval between knots in this analysis) are short enough to be confounded with the fine particles effect, leading to incorrect estimates for the latter. This serves as a warning against indiscriminate reliance on *AIC* or indeed on any "black box" statistical criterion.

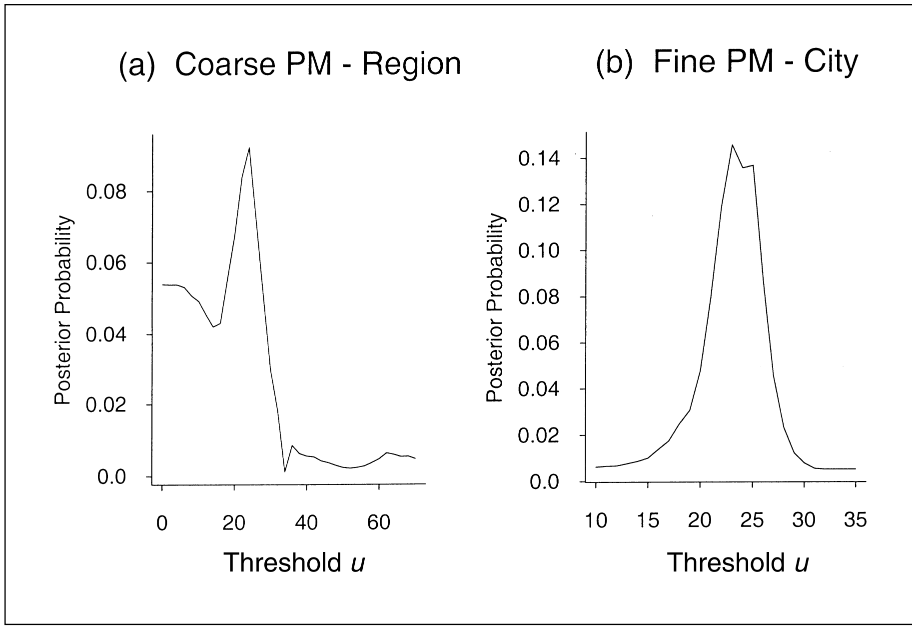

Figure 5. Posterior densities for threshold. (a) Coarse PM effect–regional deaths data. (b) Fine PM effect–city deaths data.

INTERACTIONS

Another question we have considered is the possibility of an interaction between the PM effect and either season or year. If there are different effects in different seasons or years, this could be an indication that the true relationship is more complicated than simple cause and effect.

As an example, a seasonal interaction model for coarse PM was defined as follows. Instead of a single regressor for coarse PM, four variables were defined, one for each season. For example, "winter coarse PM" is the coarse PM value during the winter months (December, January, and February) and 0 for the remainder of the year. Spring, summer, and fall coarse PM values were defined similarly. The main regression analysis of the paper, for the region data, was rerun, producing the results in Table 4. Also shown for comparison are the mean levels of coarse PM for each season.

It can be seen from Table 4 that the coarse PM effect is really only significant during the spring and summer months. It is possible that this could be an artifact of what is really a nonlinear relationship between PM and mortality, but we doubt this because (1) our previous studies showed no sign of this, and (2) it appears that if it were due to a nonlinear relationship, it is the wrong way round—the high PM coefficient occurs during seasons when the mean coarse PM level is low. Below, we offer another explanation for the seasonal variation in the PM coefficient.

The possibility of an interaction by year was suggested by Figure 2, where it can be seen that both coarse and fine PM were unusually low during the first half of 1995. To test whether this had any influence on the results, 4 "years" were defined corresponding to February–June 1995 (year 1), July 1995–June 1996 (year 2), July 1996–June 1997 (year 3), and July–December 1997 (year 4). A year effect was estimated using exactly analogous methodology to that just described for the season effect. In the case of coarse PM, it indeed turns out that the effect is lowest in year 1, but when the overall significance of the coarse PM × year interaction was tested using an F test, it was not significant (p value = 0.07). In contrast, the F test for a seasonal interaction was significant, with a p value of 0.004.

In the case of fine PM, there was again evidence of a seasonal interaction when modeled as a linear effect, but in this case it does appear to be a proxy for the threshold dependence noted earlier in the paper. When the seasonal interaction model was fitted based on a threshold model, with separate effects below and above a threshold of 25 $\mu g/m^3$, the seasonal effect disappeared. A year interaction effect was noted even in the threshold model, with a significant negative coefficient below the threshold in year 1. In this case, an F test for the overall presence of a year interaction effect in the threshold model was significant, with a p value of 0.016. However, this is not as significant as the previously noted seasonal effect for coarse PM, and since it is rather hard to explain a negative dependence between fine PM and mortality, we feel this is much more likely to be an artifact of some kind.

It is not yet known whether there is any natural explanation for the seasonal interaction effect that was found for coarse PM. One possibility is that this effect might be associated with seasonal variations in the chemical composition of PM. In addition to the TEOM data used throughout this paper, we have the air pollution data broken down into 44 chemical elements (excluding carbon) that are constituents of coarse PM. We removed elements that are typically below the detection limit. This analysis was based on about 300 days of data, and the elements used in the study were Al, Si, S, Ci, K, Ca, Ti, Mn, Fe, Cu, Zn, and Pb. A principal components analysis of the constituent elements of coarse PM showed that the crustal elements (Al, Si, K, Ca, Ti, Mn, and Fe) explain 55% of the variation of coarse PM, the anthropogenic elements (Fe, Cu, Zn, and Pb) explain 30%, and the elements of marine origin (Cl [NaCl, Na was not measured]) explain 5%. Table 5 shows a breakdown by season of the means of three principal components corresponding to each of these groups.

The results in Table 5 suggest that the composition of coarse PM differs throughout the year, with the crustal elements highest and the anthropogenic elements lowest in spring and summer. If this were the explanation for the seasonal interaction, however, the implication would be that crustal, rather than anthropogenic, elements were responsible for the PM mortality associations. This result seems counterintuitive and suggests that we do not yet fully understand the seasonal interactions.

A final effect that has been examined is the possibility of confounding between coarse and fine particles. In all models studied before now, coarse and fine particles have been treated separately, with one or the other included, but not both at the same time. If the regression coefficients were to change dramatically when both pollutants were included in the same model, that would further complicate the interpretation of the results. Fortunately, the evidence on this point is that the coefficients do not change very much. To make a specific comparison, piecewise linear effects were fitted for both fine and coarse particles (separately) based on threshold $u = 25$. They were then all included together to examine how the coefficients changed.

In Table 6, regression parameter estimates and their standard errors are shown both for fine and coarse particles, below and above the threshold. As with earlier studies, the results indicate fine particles are the primary pollutant for the city data and coarse particles are the primary pollutant for the region data. Then, however, whichever was the primary pollutant, the other was also included as a co-pollutant, and the coefficient of the primary pollutant was re-estimated in this case. The results are in the last two columns of Table 4. In no case does the estimate for the primary pollutant change significantly as a result of including the co-pollutant.

The last conclusion is reassuring in that it is consistent with fine and coarse particles being essentially separate pollutants having distinct effects. Note, however, that we have not studied possible confounding of either fine or coarse particles with gaseous pollutants such as O_3 or SO_2, and since past studies have suggested confounding between PM and gaseous co-pollutants,[3] it would seem worthwhile to consider that aspect as well.

DISCUSSION

A number of aspects of this analysis raise further points for discussion. The study is based on only 3 years of data at a single site; many other studies are based on either a much longer series or on combining data from many sites.[14] This is a limitation, pointing toward the need for more studies of these issues.

Other recent studies have examined both of the primary issues in this paper, the existence of thresholds and the comparisons of fine and coarse particles. In particular, ours is not the only study to suggest that the effect of coarse particles may be equal to or greater than that of fine particles. For example, Ostro et al.[15] showed in the case of some California data, which are dominated by coarse particles, that there is still a significant effect using PM_{10} as a regressor, which challenges the notion that there is no particulate-based effect in cases where the particles are primarily coarse.[8] Castillejos et al.[16] have compared fine and coarse particles effects in data from Mexico City, finding, as we have here, that the coarse particles effect can by no means be neglected. There are also other recent studies on thresholds. Cakmak et al.[17] have considered the possible effect of measurement error on the estimation of a threshold. Daniels et al.[18] have examined the existence of a threshold in PM_{10} data across the 20 largest cities of the United States, the same database as in Dominici et al.[14] Their preliminary results suggest the absence of a threshold in PM_{10} data for all-cause mortality, though there is clearly a need for more detailed research on the best way to combine data from different cities.

Lipfert and Wyzga[7] discussed the possible role of differential measurement error in the attribution of mortality effects to a single pollutant. Specifically, they argued that the results of Schwartz et al.,[6] which claimed a stronger effect for fine particles,

Table 4. Interactions of coarse PM and season.

Season	Mean Coarse PM	Estimate	Standard Error	*t* Statistic	*p* Value
Winter	33.6	0.0036	0.0023	1.5	0.13
Spring	28.9	0.0139	0.0026	5.3	0.0001
Summer	31.6	0.0063	0.0026	2.4	0.018
Fall	39.3	0.0023	0.0022	1.0	0.3

Table 5. Breakdown by season of mean level of each of the three principal groups of elements (standardized to overall mean 0 for each component).

Season	Crustal	Anthropogenic	Marine
Winter	–0.144	0.503	–0.589
Spring	–0.278	–0.323	0.073
Summer	0.004	–0.483	0.41
Fall	0.245	0.222	0.03

could be the result of fine particles being more accurately measured than coarse particles in the six-cities data set. We have no direct evidence on measurement error in the Phoenix data set, but we have no reason to think that it acts differentially in favor of either coarse or fine particles.

The question of measurement error also arises in the difference between ambient monitor measurements and the personal exposure of individuals. There have been some studies of the effect of imputing personal exposures—for example, Dominici et al.[19] have proposed a mathematical modeling approach to this, but it also appears from their paper that currently available data on personal exposure are quite limited and do not distinguish between fine and coarse particles. Another issue related to this topic is the effect of spatial variation. Lipfert and Wyzga[7] reported on various studies in the eastern United States in which fine particles were more homogeneously distributed than were coarse particles. As noted at the beginning of this paper, we believe that in Phoenix, coarse particles are more homogeneously distributed than are fine particles. Direct data to support this point are limited, but we do have data on fine and coarse particles from the city of Phoenix and from four other locations within the Phoenix region used in this paper. Measuring correlations of logarithms of PM concentration to improve numerical stability of the results, we found that the spatial correlations between the Phoenix downtown site and four other sites in the region (Higley, Tempe, ASU West, and Estrella Park) are, respectively, 0.85, 0.88, 0.93, and 0.76 for coarse PM and 0.64, 0.90, 0.91, and 0.74 for fine PM. Thus, in the case of Higley, the correlation of coarse PM with the Phoenix station is clearly higher than that of fine PM, while for the other three stations, the correlations are about the same for coarse and fine PM. This is, inevitably, inconclusive about whether coarse particles are indeed more homogeneously distributed than fine particles, but the results are qualitatively very different from those reported by Lipfert and Wyzga[7] for Philadelphia, for instance.

Table 6. Interactions of fine and coarse PM.

Primary Pollutant	Estimate With Co-Pollutant	Std. Err. With Co-Pollutant	Estimate Without Co-Pollutant	Std. Err. Without Co-Pollutant
Fine particles, below threshold	–0.006	0.005	–0.010	0.005
Fine particles, above threshold	0.050	0.018	0.042	0.019
Coarse particles, below threshold	0.0003	0.0062	0.0008	0.0003
Coarse particles, above threshold	0.0065	0.0019	0.0068	0.0021

CONCLUSIONS

The original purpose of this study was to compare the effects of coarse and fine PM on mortality in Phoenix. Knowledge of the dominant origins of PM (natural dust for coarse, vehicular emissions for fine) suggested that the effects would be primarily concentrated on the city of Phoenix for fine PM, but would be apparent throughout the region for coarse PM, and this was largely confirmed by the statistical analysis. Linear regressions for coarse and fine PM, taking into account meteorological and trend/seasonal effects, led us to conclude that there is a significant effect for coarse PM but not for fine PM, contrary to the prevailing orthodoxy in this field. The results were rather different, however, when nonlinear effects were taken into consideration.

Three different methods were used to study nonlinear effects: (1) a piecewise linear effect below and above a threshold, (2) a smooth nonlinear effect based on a cubic spline representation, and (3) formal selection of a threshold by Bayesian means. None of the three methods led to any conclusions that contradicted a linear effect for coarse PM, but in the case of fine PM, there was clear evidence for a change of slope somewhere in the region of 20–25 $\mu g/m^3$. The conclusion is that fine PM may indeed have an effect at high levels, but only above the current EPA standard for the long-term mean of 15 $\mu g/m^3$.

Additional analyses suggested there could be significant interactions in the PM effect with season and year. The strongest effect was a seasonal interaction for coarse PM, the effect being significant only in spring and summer. An attempt was made to explain this in terms of the chemical constituents of coarse PM, and it was found that crustal elements of coarse PM were highest and anthropogenic elements lowest in spring and summer. If interpreted causally, however, this result would imply that crustal and not anthropogenic sources of PM are primarily responsible for deaths, which does not seem a very plausible conclusion. A more reassuring conclusion was that there was no evidence of any confounding between fine and coarse PM.

These results, being based on a single city and for a comparatively short time period, cannot be regarded as definitive. Nevertheless, they carry clear implications that contradict those of (very few) previous studies of these kinds of questions, in particular, the paper of Schwartz et al.[6] The story about the comparative effects of coarse and fine PM is by no means concluded, and this paper also shows that it is worthwhile to consider nonlinear or threshold-based effects as well as the possibility of seasonal interaction.

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DISCLAIMER

This paper has not been subjected to the U.S. Environmental Protection Agency's internal peer review system and no endorsement by the Agency should be implied or inferred.

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