

The Temporal Pattern of Respiratory and Heart Disease Mortality in Response to Air Pollution

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Short-term changes in ambient particulate matter with aerodynamic diameters < 10 µm (PM₁₀) have been associated with short-term fluctuations in mortality or morbidity in many studies. In this study, we tested whether those deaths are just advanced by a few days or weeks using a multicity hierarchical modeling approach for all-cause, respiratory, and cardiovascular deaths, for all ages and stratifying by age groups, within the APHEA-2 (Air Pollution and Health: A European Approach) project. We fit a Poisson regression and used an unconstrained distributed lag to model the effect of PM₁₀ exposure on deaths up to 40 days after the exposure. In baseline models using PM₁₀ the day of and day before the death, we found that the overall PM₁₀ effect (per 10 µg/m³) was 0.74% [95% confidence interval (95% CI), -0.17 to 1.66] for respiratory deaths and 0.69% (95% CI, 0.31–1.08) for cardiovascular deaths. In unrestricted distributed lag models, the effect estimates increased to 4.2% (95% CI, 1.08–7.42) for respiratory deaths and to 1.97% (95% CI, 1.38–2.55) for cardiovascular deaths. Our study confirms that most of the effect of air pollution is not simply advanced by a few weeks and that effects persist for more than a month after exposure. The effect size estimate for PM₁₀ doubles when we considered longer-term effects for all deaths and for cardiovascular deaths and becomes five times higher for respiratory deaths. We found similar effects when stratifying by age groups. These larger effects are important for risk assessment. **Key words:** air pollution, heart disease, hierarchical models, lung disease, mortality displacement. *Environ Health Perspect* 111:1188–1193 (2003). doi:10.1289/ehp.5712 available via <http://dx.doi.org/> [Online 6 March 2003]

The association between daily deaths for all causes (Hoek et al. 1997; Ostro et al. 1996; Pope et al. 1995a; Saldiva et al. 1995; Schwartz 1994; Schwartz and Dockery 1992; Touloumi et al. 1994) or cause-specific mortality (Hoek et al. 2001; Ostro et al. 1999b; Rossi et al. 1999; Simpson et al. 2000; Wordley et al. 1997) and airborne particles has been reported in many studies over the last decade, and multicity analyses have confirmed these findings (Biggeri et al. 2001; Katsouyanni et al. 1997, 2001; Samet et al. 2000; Schwartz 2000a; Zanobetti et al. 2000a).

Early studies reported the association between daily deaths and pollution concentrations on the same day or 1–2 days before. Often the “best” lag was chosen in each analysis. This has been criticized as possibly tending to an overestimate of the effect.

However, several studies have demonstrated that air pollution levels, not just for the current day but for several preceding days, affect counts of daily deaths on a given day (Katsouyanni et al. 1990; Kelsall et al. 1997; Schwartz and Dockery 1992). In these studies, multiday averages of pollution are found to be better predictors of daily death counts than is a single day's exposure (even the best

single day), and some have examined the shape, or distribution, of the lagged effect (Schwartz 2000b; Zanobetti et al. 2000a).

Some researchers have speculated that air pollution kills those who would have died in a few days anyway. This could occur if air pollution hastened the deaths of persons who were extremely frail. If air pollution did not simultaneously increase the number of people who become frail, the size of the frail pool would decrease after an air pollution episode. On subsequent days, a smaller frail pool would result in a reduction in daily deaths. Hence, this “harvesting” hypothesis implies a negative correlation between pollution concentrations and daily deaths at longer lags. This harvesting effect has been described previously (Zanobetti et al. 2000b, 2002).

A number of studies have examined this issue using several different methodologies (Schwartz 2000c, 2001; Zeger et al. 1999). All of them reported increased, rather than decreased, effects when longer lags were examined, but only one of them examined the correlation at multiple lags in a multicity hierarchical model.

Among the studies that analyzed the associations between air pollution and cause-specific

mortality (Hoek et al. 2001; Ostro et al. 1999b; Rossi et al. 1999; Simpson et al. 2000; Wordley et al. 1997), Rossi et al. (1999) reported different lags for different causes in Milan, Italy. One possible reason for this is that different causes of death are affected by air pollution with different latency periods. The use of a multicity analysis that cancels out the noise by averaging over many estimates would provide a more reliable estimate of the effect and differences in the lag structure. Recently, Braga et al. (2001) reported differences in the lag structure

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pattern between particulate matter with aerodynamic diameters < 10 μm (PM_{10}) and cause-specific mortality in a multicity hierarchical model. Only one study (Schwartz 2000c) has looked at mortality displacement with regard to cause-specific deaths.

Some studies found an association between airborne particles and mortality by age groups (Bremner et al. 1999; Goldberg et al. 2000; Ostro et al. 1999a; Ponka et al. 1998; Verhoeff et al. 1996), but again, none analyzed the distribution of the effect over time since exposure and whether the mortality displacement is short term.

In our previous study of the APHEA-2 (Air Pollution and Health: A European Approach) project (Zanobetti et al. 2002), we examined mortality displacement between air pollution and all daily deaths. The goal of that analysis was to estimate the dependence of daily deaths on day t on PM_{10} on that day, and up to the previous 40 days using an unconstrained distributed lag model. As a sensitivity analysis, in that study we used a fourth-degree polynomial and a cubic distributed lag model, and all the models showed similar results.

In the present study, within the APHEA-2 project, we examined mortality displacement by age, and we looked at the differences between cardiovascular and respiratory deaths compared with all causes of deaths. Following the same approach as in our previous analysis, we applied a fourth-degree polynomial and unconstrained distributed lag models in a multicity hierarchical framework.

Data and Methods

Health data. The APHEA-2 project was a multicenter study of 30 cities across Europe and adjacent countries (e.g., Istanbul, Turkey, and Tel Aviv, Israel). The goal of the APHEA-2 project was to examine the effects of air pollution on daily mortality. Details on APHEA-2 data have been reported previously (Katsouyanni et al. 2001).

To maximize the power of the study, we chose the largest cities in the project, subject to the constraint that only one city be chosen in each country. The 10 cities selected were Athens, Greece; Budapest, Hungary; Lodz, Poland; London, United Kingdom; Madrid, Spain; Paris, France; Prague, Czech Republic; Rome, Italy; Stockholm, Sweden; and Tel Aviv. Together, they comprise a population of about 28 million people, which is two-thirds of the population in the full study, and represents Northern Europe, Central Europe, and the Mediterranean region.

The data that we analyzed in this study included daily counts of all-cause mortality, excluding deaths from external causes [*International Classification of Disease, 9th Revision (ICD-9)* code > 800], daily counts of

deaths from cardiovascular disease (CVD) (*ICD-9* code 390–429), and daily counts of respiratory mortality (*ICD-9* code 460–519). In all cities, the mortality counts were also divided in the following age groups: 15–64, 65–74, and ≥ 75 years.

The years of study were 1990 through 1997; however, mortality data in most cities were available only through 1995 or 1996.

Air pollution data were available as daily averages of the monitoring stations in each city. Particulate matter was measured as PM_{10} in four cities, as PM_{13} in Paris and PM_{15} in Rome. The Paris data were assumed to be equivalent to PM_{10} in this study. In Rome, Athens, Lodz, and Budapest, the data were converted from other measurements into PM_{10} using city-specific conversion factors. Further details have been published previously (Katsouyanni et al. 2001; Zanobetti et al. 2002).

We first analyzed respiratory and heart mortality; then, we examined deaths from all causes and stratified respiratory and cardiovascular deaths by age groups.

Methods. In the first step of the analysis, generalized additive regression models (Hastie and Tibshirani 1990) were fit in each of the 10 cities, and the models were built following the APHEA-2 methodology. Details on the models for all-cause mortality have been published (Katsouyanni et al. 2001).

Separate models were built in each city because of the substantial variability in seasonal patterns and weather between, for example, Stockholm and Tel Aviv.

In the generalized additive model, the outcome is assumed to depend on a sum of nonparametric smooth functions for each variable. This allows us to better model the nonlinear dependence of daily deaths on weather and season. The model is of the form

$$\log[E(Y_p)] = \alpha_0 + S_1(X_1) + S_i(X_i) + \dots + S_p(X_p),$$

where $E(Y_p)$ is the expected value of the daily count of deaths Y_p , and S_i is the smooth function of the covariate X_i . The covariates we examined were weather, influenza epidemics, holidays, and day of the week. The locally weighted running-line smoother (Cleveland and Devlin 1988) was chosen to estimate the smooth function.

All models controlled for temperature and relative humidity on the same day using nonparametric smooth functions. In addition, we examined nonparametric functions and linear weather variables on the previous day or up to 3 previous days or the average of a few days. We chose the variables that minimized Akaike's Information Criterion (Akaike 1973) for the model. This approach has been used and discussed previously (Katsouyanni et al. 2001; Schwartz 1999; Schwartz et al. 1996).

To remove seasonal and long-term fluctuations, we used a smooth function of time. Seasonal patterns are controlled because there are unmeasured predictors of death, such as diet, which have long-term trends over time and vary seasonally. Because air pollution also shows seasonal variations, and often long-term trends, this creates a potential for confounding. Day-to-day fluctuations in diet are unlikely to be correlated with air pollution.

To model seasonality, we chose the smoothing parameter that minimized the sum of the autocorrelation of the residuals while removing seasonal patterns.

In some models, it was necessary to introduce autoregressive terms to eliminate the remaining serial correlation from the residuals (Brumback et al. 2000). This approach has been used in a number of recent studies (Rossi et al. 1999; Schwartz 1999, 2000a).

Recently several authors have pointed out that there are problems with the implementation of generalized additive models in current statistical packages (Dominici et al. 2002; Ramsay et al. 2003). One is the lax default convergence criterion in generalized additive models in S-PLUS software (MathSoft, Inc., Seattle, WA). A more serious problem is that this program does not properly estimate standard errors. To deal with the underestimation of the parameters' variances, we calculated standard errors for the estimated regression coefficients using the nonparametric bootstrap (Efron and Tibshirani 1993). In particular, we generated 250 bootstrap samples each consisting of n values drawn with replacement from the observed data, where n was the number of observations in each city. The model of interest was run for each generated data set, and the sample standard deviation of the resulting regression coefficients serves as the bootstrap standard error.

We examined the dependence of daily deaths on PM_{10} of that day and of preceding days, up to the previous 40 days, using first an unconstrained distributed lag model and then a fourth-degree polynomial distributed lag model.

If the pollution-related deaths are only being advanced by a few days to a few weeks, we would see this "harvesting" effect expressed by negative associations between air pollution and deaths several days to weeks afterward. The effect of air pollution, net of any such short-term rebound up to 40 days, is the sum of the effect estimates for all 41 days.

For Poisson regression, the unconstrained distributed lag model can be written as

$$\text{Log}[E(Y_t)] = \alpha + \text{covariates} + \beta_0 Z_t + \beta_1 Z_{t-1} + \dots + \beta_q Z_{t-q} \quad [1]$$

The unconstrained distributed lag model is too noisy to provide any information about

the shape of the effect versus lag, but it does give an unbiased estimate of the overall effect, computed as the sum of the β_j . To be able to have an idea of the shape of the curve, it is preferable to constrain the coefficients to vary smoothly with lag number (Almon 1965). A polynomial distributed lag constrains the β_j to follow a polynomial pattern in the lag number; that is,

$$\beta_j = \sum_{k=0}^d \eta_k j^k, \text{ for } j = 0 \dots q, \quad [2]$$

where j is the number of lags and d is the degree of the polynomial.

Too much constraint risks bias, producing a distorted shape, whereas too little constraint produces estimates that are too noisy to be informative.

To fit a fourth-degree polynomial distributed lag model with 40 days of delay, in equation 2 we would have $d = 4$ and $j = 0, \dots, 40$.

In the first stage of the analysis, a separate distributed lag model was fit for each of the 10 cities. The coefficients β_j by lag for the distributed lag model were obtained from equation 2,

and because we used the bootstrap method, we computed the sum of the effect estimates for all 41 days in each city. In the second stage, we combined the city-specific results using inverse variance weighted averages.

In our primary analysis we used an unconstrained distributed lag, because it makes the fewest assumptions. We used the polynomial distributed lag model as a sensitivity analysis because this gives more stable results and also allows us to examine the pattern of the mortality response over time.

To verify whether the longer lags really contribute to the overall pollution effect, we also analyzed the unconstrained distributed lag model with 20 and 30 days of delay.

Results

Table 1 shows, for the 10 cities, the mean and standard deviation of the daily number of total, cardiovascular, and respiratory deaths, in total and for the three age groups. It also shows the mean and standard deviation of the environmental variables. The mean of daily deaths for 15- to 64-year-olds is generally very

low when subdivided by cause. For respiratory mortality, the second age group is also small; therefore, we decided that the cause-specific analysis by age could be done for the two older groups for cardiovascular mortality, and in the oldest age group for respiratory mortality.

Table 2 shows the percentage increase for the combined effect estimates across all of the 10 cities of PM_{10} [per 10 $\mu g/m^3$ and its 95% confidence interval (95% CI)] for the fourth-degree polynomial (sum of the β_j per 10 $\mu g/m^3$), and the unconstrained distributed lag models when stratified by cause of death.

Figures 1 and 2 show plots of the residuals from the unconstrained distributed lag model for Athens and London, respectively, with no residual seasonality in the models.

We found a 4.2% increase (95% CI, 1.08–7.42) in respiratory deaths for a 10 $\mu g/m^3$ increase in PM_{10} concentration using the unconstrained distributed lag model. Similar results, but with tighter confidence intervals, were found with the polynomial distributed lag models. In contrast, the mean of PM_{10} on the same and previous day was associated with only

Table 1. Study period, population, and mean \pm SD of the number of daily deaths and the environmental variables in the 10 cities.

City/age group (years)	Years of study	Mortality			PM_{10} (mg/m ³)	Temperature	Humidity
		Total	CVD	Respiratory			
Athens	1992–1996	72.9 \pm 13.2	35.9 \pm 8.7	4.6 \pm 2.4	42.7 \pm 12.9	17.8 \pm 7.4	61.7 \pm 13.6
15–64	8.3 \pm 3	2.9 \pm 1.7	0.4 \pm 0.6				
65–74	21.3 \pm 5.2	9.3 \pm 3.4	1.1 \pm 1.1				
\geq 75	42.4 \pm 9.6	23.7 \pm 6.7	3.2 \pm 1.9				
Budapest	1992–1995	80 \pm 11.6	40.1 \pm 8	3.1 \pm 2	41 \pm 9.1	12.8 \pm 8.8	70.1 \pm 12.6
15–64	22.1 \pm 4.7	6.8 \pm 2.7	0.6 \pm 0.8				
65–74	19.5 \pm 4.6	9.5 \pm 3.2	0.7 \pm 0.8				
\geq 75	37.6 \pm 7.9	23.7 \pm 6	1.7 \pm 1.4				
Lodz	1990–1996	29.5 \pm 6.3	16.8 \pm 4.6	1.2 \pm 1.1	53.5 \pm 15.5	8.4 \pm 8.4	79 \pm 12.4
15–64	8.9 \pm 3.2	3.7 \pm 2	0.3 \pm 0.5				
65–74	8.1 \pm 3	4.5 \pm 2.2	0.3 \pm 0.6				
\geq 75	12.2 \pm 3.9	8.7 \pm 3.2	0.5 \pm 0.8				
London	1992–1996	168.5 \pm 25.2	71.4 \pm 12.9	29 \pm 11	28.8 \pm 13.7	11.8 \pm 5.4	69.3 \pm 11.3
15–64	28.8 \pm 5.7	9.5 \pm 3.2	2.4 \pm 1.7				
65–74	37 \pm 7.4	15.7 \pm 4.5	4.6 \pm 2.6				
\geq 75	101.7 \pm 18.5	46.1 \pm 9.6	21.8 \pm 8.9				
Madrid	1992–1995	60.8 \pm 11.1	21.7 \pm 6.1	6.1 \pm 3.1	37.8 \pm 17.7	14.5 \pm 7.4	61.8 \pm 16.7
15–64	13.7 \pm 3.9	3.1 \pm 1.8	0.7 \pm 0.9				
65–74	13 \pm 3.8	4 \pm 2.1	1.1 \pm 1.1				
\geq 75	33.4 \pm 7.7	14.6 \pm 4.6	4.2 \pm 2.5				
Paris	1992–1996	123.3 \pm 15.7	37.9 \pm 7.5	9 \pm 3.8	22.5 \pm 11.5	12.1 \pm 6.5	75.6 \pm 12.5
15–64	30.7 \pm 5.7	4.1 \pm 2	0.9 \pm 0.9				
65–74	20.8 \pm 5	5.4 \pm 2.5	1.2 \pm 1.1				
\geq 75	69.9 \pm 11.8	28.3 \pm 6.4	6.9 \pm 3.2				
Prague	1992–1995	38.2 \pm 7.2	22.2 \pm 5.2	1.4 \pm 1.2	76.2 \pm 45.7	11 \pm 8	69.4 \pm 14.1
15–64	7.5 \pm 3	2.8 \pm 1.7	0.3 \pm 0.5				
65–74	10.2 \pm 3.2	5.3 \pm 2.3	0.4 \pm 0.6				
\geq 75	20.1 \pm 5.1	14.1 \pm 4.2	0.7 \pm 0.9				
Rome	1992–1996	56.2 \pm 10.4	23.2 \pm 6.4	3.1 \pm 2	58.7 \pm 17.4	16.8 \pm 6.7	61.6 \pm 11.9
15–64	11.3 \pm 3.6	2.7 \pm 1.7	0.2 \pm 0.5				
65–74	13.4 \pm 4	4.5 \pm 2.3	0.6 \pm 0.8				
\geq 75	30.9 \pm 7.5	16 \pm 5.1	2.2 \pm 1.7				
Stockholm	1994–1996	28.9 \pm 6.1	14 \pm 4.1	2.5 \pm 1.7	15.5 \pm 7.9	7.7 \pm 8.1	71.4 \pm 15.8
15–64	3.7 \pm 2	1 \pm 1.1	0.1 \pm 0.4				
65–74	5.3 \pm 2.4	2.2 \pm 1.6	0.3 \pm 0.6				
\geq 75	19.7 \pm 5.1	10.7 \pm 3.5	2 \pm 1.5				
Tel Aviv	1993–1996	27.4 \pm 6.3	11.5 \pm 4.1	1.4 \pm 1.4	50.3 \pm 57.5	20.6 \pm 5.4	65.6 \pm 11
15–64	4 \pm 2	1 \pm 1.1	0.1 \pm 0.4				
65–74	5.8 \pm 2.5	2.3 \pm 1.5	0.2 \pm 0.5				
\geq 75	17.2 \pm 4.9	8.2 \pm 3.3	1 \pm 1.2				

a 0.74% increase (95% CI, -0.17 to 1.66) in respiratory mortality.

We found a 1.97% (95% CI, 1.38–2.55) increase in CVD deaths using the unconstrained distributed lag model. Again, the results for the polynomial distributed lag models were similar, whereas the results for the mean of lag 0 and 1 of PM₁₀ were lower (0.69% increase, 95% CI, 0.31–1.08).

Overall, the estimated effect of PM₁₀ was doubled for CVD when the lagged effects were considered; the effect was five times larger for respiratory mortality.

Table 3 shows the percentage increase for the combined effect estimates across all of the 10 cities for PM₁₀ (per 10 µg/m³ and its 95% CI) derived by applying the unconstrained distributed lag model with 20, 30, and 40 days of delay. The results show a clear increasing trend with increasing numbers of lags.

Figure 3 shows the estimated effect of PM₁₀ at each lag (and its confidence interval) for CVD deaths. PM₁₀ has a major immediate impact, declining rapidly to near 0 with a lag of 1 week. It then shows a prolonged, slight elevation in risk for the next month.

The pattern for respiratory deaths is quite different, as shown in Figure 4. The estimated

immediate effect of PM₁₀ decreases much more slowly than it does for CVD deaths. It again rises to a second smaller peak about a month later, before decreasing again by lag 40.

We then repeated the same analyses stratifying by age groups. Table 4 shows the results for all the outcomes by age group. Within each age group, we found similar results using the constrained and unconstrained distributed lag models. When looking across the age groups, we found that the risks increase. For example, using the fourth-degree polynomial distributed lag model, we found a -0.25% (95% CI, -0.876 to 0.36) increase in total mortality in the 15- to 64-year-olds, a 0.78% (95% CI, 0.23–1.33) increase in the 65- to 74-year-olds, and a 1.84% (95% CI, 0.92–2.78) increase in the ≥ 75-year-old group.

Applying the fourth-degree polynomial distributed lag model, we found a 2.06% increase (95% CI, 1.05–3.09) in CVD mortality for the 64- to 75-year-olds for a 10 µg/m³ increase in PM₁₀. For the ≥ 75 year group, we obtained a 2.35% (95% CI, 1.42–3.29) increase in CVD deaths. We found a 4.57% (95% CI, 1.25–7.99) increase in respiratory disease for the ≥ 75 year group, which is similar to the results for all ages.

Discussion

Recent discussions of the effects of airborne particles on deaths have distinguished between effects within days of exposure and effects of chronic exposures seen in prospective cohort studies.

In the present study we report an analysis of the effects of PM₁₀ on an intermediate time scale, and the potential for short-term mortality displacement by specific causes of death, by specific age groups, and for age groups by cause in 10 European cities, within the APHEA-2 project. Rather than finding that most of the effect of air pollution is due to “harvesting” individuals on the brink of death anyway, our study shows that the effect size estimate for airborne particles doubles for cardiovascular deaths when we look at the first 40 days after exposure, and increases 5-fold for respiratory deaths. We found a different pattern of mortality risk over time for cardiovascular and respiratory deaths, with the elevation in risk of death after exposure declining more slowly over time for respiratory than cardiovascular deaths. Zelikoff et al. (1999) have shown that exposure to urban particles exacerbates pneumonia. In a broad population of individuals with varying susceptibility, we

Table 2. Results for the combined estimated PM₁₀ effect for the fourth degree and unrestricted models, with 40 days of delay using bootstrap methods.

	CVD		Respiratory disease	
	Percent	95% CI	Percent	95% CI
Mean lag 01	0.69	0.31–1.08	0.74	-0.17–1.66
Distributed lag				
Fourth degree	1.99	1.44–2.54	4.21	1.70–6.79
Unrestricted	1.97	1.38–2.55	4.20	1.08–7.42

Increases are for a 10 µg/m³ increase in PM₁₀.

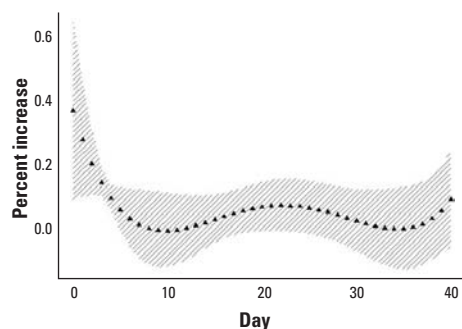


Figure 3. The estimated shape of the association of PM₁₀ for each lag with daily deaths for CVD with a fourth-degree distributed lag model with random effect in 10 cities (percentage increase in deaths for a 10 µg/m³ increase in PM₁₀). The shaded area represents the 95% CIs.

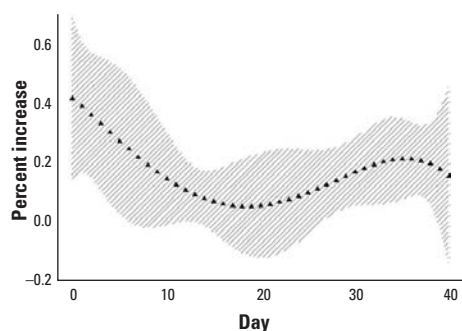


Figure 4. The estimated shape of the association of PM₁₀ for each lag with daily deaths for respiratory disease with a fourth-degree distributed lag model with random effect in 10 cities (percentage increase in deaths for a 10 µg/m³ increase in PM₁₀). The shaded area represents the 95% CIs.

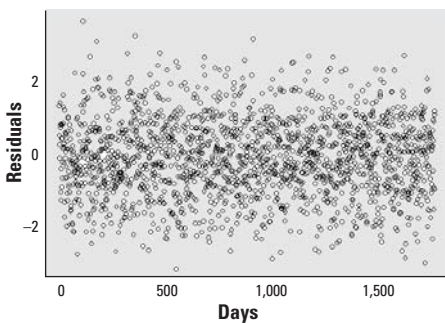


Figure 1. CVD mortality in Athens: plot of the residuals from the unconstrained distributed lag model showing no residual seasonality in the models.

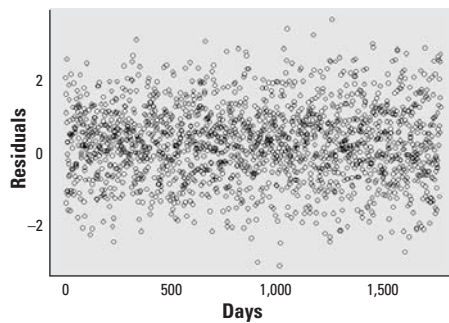


Figure 2. CVD mortality in London: plot of the residuals from the unconstrained distributed lag model showing no seasonality left in the models.

Table 3. Results for the combined estimated PM₁₀ effect for the unrestricted models, with 20, 30, and 40 days of delay, using bootstrap methods.

	CVD		Respiratory disease	
	Percent	95% CI	Percent	95% CI
Unrestricted distributed lag				
20 lags	1.34	0.89–1.79	1.71	-0.65–4.12
30 lags	1.72	1.20–2.25	2.62	0.19–5.11
40 lags	1.97	1.38–2.55	4.20	1.08–7.42

Increases are for a 10 µg/m³ increase in PM₁₀.

Table 4. Results for the combined estimated PM₁₀ effect for the fourth-degree and unrestricted models, with 40 days of delay, by age groups using bootstrap methods.

Distributed lag	15–64 years		65–74 years		≥ 75 years	
	Percent	95% CI	Percent	95% CI	Percent	95% CI
Total mortality						
Fourth degree	–0.25	–0.87–0.36	0.78	0.23–1.33	1.84	0.92–2.78
Unrestricted	–0.01	–0.76–0.75	0.74	0.02–1.45	1.94	1.07–2.81
Cardiovascular mortality						
Fourth degree	—	—	2.06	1.05–3.09	2.35	1.42–3.29
Unrestricted	—	—	1.62	0.54–2.70	2.52	1.57–3.48
Respiratory mortality						
Fourth degree	—	—	—	—	4.57	1.25–7.99
Unrestricted	—	—	—	—	4.52	0.89–8.28

Increases are for a 10 µg/m³ increase in PM₁₀.

would expect a distribution of times until the exacerbation required hospitalization, which might account for this pattern. We also found an increasing PM₁₀ effect with increasing age.

Up to now, no study has examined long distributed lags or short-term mortality displacement for specific ages and causes of death. This study confirms the basic finding of the previous analysis on mortality displacement (Schwartz 2000c, 2001; Zanobetti et al. 2002; Zeger et al. 1999), because we did not find any net short-term harvesting. Rather, our results are consistent with the report of higher risk estimates in cohort studies (Dockery et al. 1993; Pope et al. 1995b), although still smaller in magnitude. However, there may be short-term displacement for some, but this is outweighed by the longer-term effect.

This study provides insight into the shape of the longer-term responses to particulate air pollution. In particular, it suggests that the adverse response to pollution persists to a month or longer after exposure not only for total mortality but also for respiratory and cardiovascular mortality. This was also observed in the 1952 London smog episode (Anderson 1999).

If we focus on assessing the difference in the lag pattern between particulate matter and cause-specific mortality, we can identify two different patterns. For respiratory deaths, the decline in impact of particle exposure over time is noticeably slower than that for cardiovascular deaths. For both causes, there is a small elevation of death risk that persists for about another month. The confidence intervals prevent us from drawing strong conclusions about the shape of the curves.

Based on the biologic plausibility, the differences on the lag structure here observed are admissible. CVD presents an acute response to trigger agents, and both experimental (Godleski 2000) and human (Peters et al. 2000) studies have supported this point. On the other hand, a wider and more lagged structure can be expected for respiratory diseases such as pneumonia and chronic disease, because these events have slower progression.

The APHEA-2 project was one of three large multicity studies of the effects of particulate air pollution that have recently been

reported. The largest study (National Mortality and Morbidity Air Pollution Study) examined 90 U.S. cities (Samet et al. 2000). Because of the limitations of U.S. monitoring networks, results were reported only for 24-hr PM exposure. Those results were quite similar to the main APHEA-2 results (Katsouyanni et al. 2001) but slightly lower. The APHEA-2 main results used the mean of PM exposure over 2 days (Katsouyanni et al. 2001).

Another U.S. study restricted to 10 U.S. cities with daily PM monitoring showed a gradient in effect size when comparing 1-day averages, 2-day averages, and a 5-day distributed lag (Schwartz 2000a).

Our results, taken together with the reports described above, as well as other approaches to the harvesting question, confirm that estimates of the effects of subchronic exposure to air pollution that rely on 24- or 48-hr exposure measures seriously underestimate the impact of particle exposure.

Moreover, because part of the effect appears to involve triggering myocardial infarctions (Peters et al. 2001), the previous literature showing persons surviving for a month after their infarct have a life expectancy measured in years, suggests that deaths associated with air pollution include many that are advanced by a considerable amount.

Together with previous studies, this study suggests that risk assessment based on the short-term associations likely underestimate the number of early deaths that are advanced by a significant amount, and that estimates based on the cohort studies, or studies such as this one, would more accurately assess the public health impact.

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