Daily deaths are associated with combustion particles rather than SO_2 in Philadelphia

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Abstract

***Objectives*—To assess whether the association between SO_2 and daily deaths in Philadelphia during the years 1974–88 is due to its correlation with airborne particles, and vice versa.**

***Methods*— There is a significant variation in the relation between total suspended particulate (TSP) and SO_2 in Philadelphia by year and season. Firstly, 30 separate regressions were fitted for each pollutant in the warm and cold season of each year. These regressions controlled for weather, long term temporal patterns, and day of the week. Then a meta–regression was performed to find whether the effect of SO_2 was due to TSP, or vice versa.**

***Results*—Controlling for TSP, there was no significant association between SO_2 and daily deaths. By contrast, in periods when TSP was less correlated with SO_2, its association with daily deaths was higher. However, all of the association between TSP and daily deaths was explained by its correlation with extinction coefficient, a measurement of the scattering of light by fine particles, which has been shown to be highly correlated with fine combustion particles in Philadelphia.**

***Conclusions*—The association between air pollution and daily deaths in Philadelphia is due to fine combustion particles, and not to SO_2.**

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In 1991 Schwartz and Dockery[1] published a paper reporting that airborne particles, at concentrations that occurred commonly, were associated with daily deaths in Philadelphia, but there was no evidence of a threshold. This paper and other similar reports[2–4] attracted considerable attention, and renewed interest in the study and control of airborne particles.

Although Schwartz and Dockery reported that the association was primarily with particles and not SO_2, a subsequent study sponsored by the steel industry[5] questioned that finding and reported a weaker association with total suspended particulate (TSP). A study funded by the Health Effects Institute replicated the original findings, but reported that the correlation between particles (measured as TSP) and SO_2 in Philadelphia was too high to allow the effects to be separated.[6] Total suspended particulates is a gravimetric measurement of the mass concentration of particles with aerodynamic diameter of 30 μM or less, in the air.

Because of the high correlation between SO_2 and particles in Philadelphia, more recent studies have focused on analyzing data from cities with essentially no correlation between SO_2 and airborne particles—for example, Tucson, AZ, USA[7]—or with exposure to particles in the absence of noticeable SO_2 concentrations—for example, Santa Clara[8] and Spokane[9]. These studies have reported associations with airborne particles.

Because such locations are rare, and because studies in locations without SO_2 cannot tell us whether SO_2 is an independent risk factor, further work on this issue was warranted.

Although SO_2 and TSP remained highly correlated in Philadelphia during the years 1974–88 studied by Samet *et al*,[6] there were changes in the patterns and trends in their concentration that provide an opportunity to separate the two pollutants that has not previously been considered. Specifically, although the concentrations of both pollutants fell during the period, the fall in SO_2 concentrations was greater. Further, although SO_2 concentrations continued to peak in the winter and be lowest in the summer, particulate matter changed from being a winter peaking pollutant to a summer peaking pollutant during the period 1974–88.

One pollutant may confound the association with another when they are highly correlated because a 1 $\mu g/m^3$ increase in, for example, TSP represents some increase in SO_2 as well. Because the amount of increase in one pollutant that is represented by a 1 $\mu g/m^3$ increase in the other changed over time and by season in Philadelphia, the degree of confounding would be expected also to change. I have used this substantial variation to re-examine the roles of each pollutant in predicting daily deaths in Philadelphia.

Data and methods

Daily counts of deaths in the city of Philadelphia for the years 1974–88 were computed from the mortality tapes of the National Centers for Health Statistics. Weather data was extracted from the Earthinfo CD with data from the Philadelphia airport. Air quality data were obtained from the United States Environmental Protection Agency's AIRS monitoring network. More detailed descriptions of the data and the methods for averaging the monitors to compute daily means of all monitors for each pollutant have been published previously.[10]

ASSESSMENT OF INDEPENDENT EFFECTS

By contrast with the earlier studies, I fitted separate regression models for the warm and cold season of each year. The warm season was

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defined as May to the end of October. For each season and year, I separately modelled the effects of SO_2 and TSP, producing 30 estimated coefficients for each pollutant. Each regression controlled for temperature, previous day's temperature, dew point temperature, within season long term trends, and day of the week dummy variables. The details are described below. The reason for this stratified modelling can be seen by considering the following example. Suppose our outcome (Y) is associated causally with pollutants X and Z. Because Z and X are correlated, a regression with Z only may be confounded. We can, however, measure the degree of expected confounding. If

$$Y_t = \beta_0 + \beta_1 X_t + \beta_2 Z_t + \text{error} \quad (1)$$

represents the causal association between Y and both X and Z, and

$$Z_t = \gamma_0 + \gamma_1 X_t + \text{error} \quad (2)$$

represents the association between Z and X, then by substituting the second equation in the first we have

$$Y_t = \beta_0 + \beta_2\gamma_0 + (\beta_1 + \beta_1\gamma_1)X_t + \text{error} \quad (3)$$

We expect confounding, and the confounding we expect to find for X is proportional to γ_1, the slope relating Z to X. By dividing the Philadelphia data into 30 6 month intervals with considerable variation in the value of γ_1 within each interval, we can test whether that pattern is found. This can all be formalised in a hierarchical model. In this model, we assume that the coefficient for X in each interval is

$$\hat{\beta}_i \sim N(\beta_i, \sigma^2) \quad (4)$$

where $\hat{\beta}_i$ is the estimated coefficient in time interval i, β_i is the true coefficient in interval *i*, and

$$\beta_i \sim N(\beta_1 + \gamma_1\beta_2, \delta^2) \quad (5)$$

Hence we can in the second stage regress the estimated coefficients for TSP in each of the 30 time intervals against the coefficient relating SO_2 to TSP in that interval. The intercept term in this regression (β_1 in the formula above) is an estimate of the unconfounded effect of TSP. It can also be interpreted as the slope for TSP when γ_1, its association with SO_2, is zero. A similar analysis will show an estimate of the effect of SO_2 independent of confounding by TSP.

Recent studies[11] have suggested that the effects of particulate air pollution on daily deaths are primarily due to fine combustion particles. If this were true, then we would expect the association between TSP and daily deaths to vary across the 30 periods according to its association with combustion particles. These particles are generally less the 1 μM in aerodynamic diameter, and are very effective at scattering light. Although direct measurements of combustion particles were not available during most of the period, Ozkaynak *et al* used limited data on fine particle concentrations from 1979 to the end of 1981 to show that a humidity corrected extinction coefficient (calculated from airport visibility measurements) is highly correlated with fine particle mass in Philadelphia.[12] The extinction coefficient is proportional to the inverse of the visible range, and visibility is primarily limited by light scattering due to fine particles in the air. Hence I also investigated whether TSP was a substitute for fine particles by using the extinction coefficient as an explanatory variable.

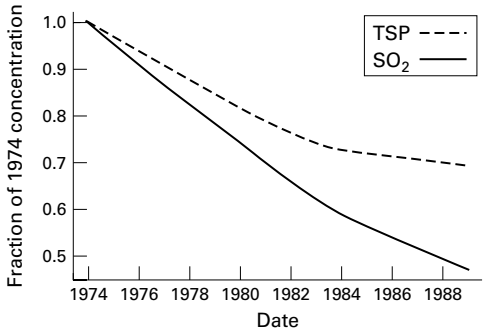

Figure 1 Downward trend in SO_2 and TSP between 1974 and 1988. The concentration in each year is expressed as a fraction of its concentration in 1974. The SO_2 concentrations fell substantially more than the TSP concentrations.

INDIVIDUAL INTERVAL REGRESSIONS

Since their introduction in such studies in 1993,[13] generalised additive models have become the preferred approach for analysing time series of daily mortality counts. In such an approach, we assume:

$$\log(E(Y)) = \beta_0 + f_1(X_1) + f_2(X_2) + \ldots + f_p(X_p)$$

Where Y is the number of daily deaths, E denotes expected value, and $X_1 \ldots X_p$ are the predictor variables. The f_i may be linear functions ($\beta_i X_i$) or be any other smooth function, which is estimated from the data using non-parametric techniques. These are used to model the dependence on temperature and season, which have non-linear associations with daily deaths. This approach has been applied to analyses of mortality and air pollution in Philadelphia in the past[10 14] and produced air pollution coefficients similar to those in the original paper of Schwartz and Dockery.[1] These models were applied in this analysis as well. I used loess[15] as the non-parametric smoothing algorithm. The weather variables were fitted with spans of 0.5, and the within season trend with a span equivalent to 180 days.

Results

Figure 1 shows the downward trend of SO_2 and TSP concentrations during the study period. The drop in SO_2 was more pronounced. Figure 2 shows the seasonal pattern of TSP and SO_2 in 1974 and 1988. The reversal of the seasonal pattern in TSP is evident. Table 1 shows the mean TSP and SO_2 in Philadelphia by year and season. Table 2 shows the slopes between SO_2 and TSP and between TSP and SO_2 for each season of each year. There is considerable variability in these slopes, giving us the ability to detect systematic variations in the mortality associations with variations in these slopes.

The results of the first stage analysis were combined with inverse variance weighting. Both TSP (9.0% increase for a 100 μg/m^3

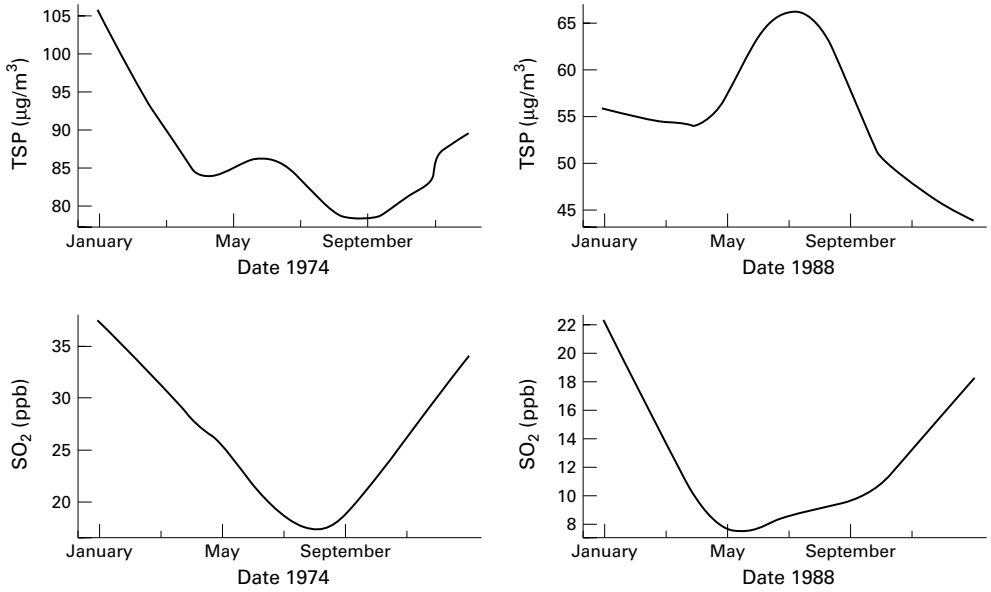

Figure 2 Concentrations of TSP and SO_2 during the course of 1974 and 1988. The TSP concentrations peaked in the winter of 1974, but by 1988 they were peaking in the summer. SO_2 concentrations continued to peak in the winter.

Table 1 Mean TSP and SO_2 by season and year in Philadelphia, 1974–88

	Summer		*Winter*	
Year	*TSP ($\mu g/m^3$)*	*SO_2 (ppb)*	*TSP ($\mu g/m^3$)*	*SO_2 (ppb)*
1974	84	20	93	35
1975	75	17	77	26
1976	78	19	83	25
1977	69	16	77	27
1978	74	17	73	25
1979	77	15	68	21
1980	76	14	59	18
1981	66	14	61	20
1982	64	13	56	20
1983	66	10	52	15
1984	65	10	56	18
1985	62	10	54	17
1986	65	8	53	15
1987	70	9	53	15
1988	64	9	52	17

Table 2 Season and year specific regression slopes between SO_2 and TSP

	Warm		*Cold*	
Year	*TSP/SO_2 slope*	*SO_2/TSP slope*	*TSP/SO_2 slope*	*SO_2/TSP slope*
1974	1.30	0.20	1.12	0.31
1975	1.94	0.24	1.47	0.33
1976	2.13	0.27	1.76	0.26
1977	2.10	0.24	1.54	0.39
1978	1.65	0.29	1.65	0.32
1979	2.53	0.18	1.87	0.26
1980	1.71	0.18	1.44	0.33
1981	1.60	0.20	1.63	0.34
1982	2.47	0.22	1.12	0.37
1983	2.07	0.15	1.93	0.25
1984	3.00	0.17	1.63	0.37
1985	3.10	0.14	1.12	0.21
1986	2.36	0.11	1.43	0.27
1987	2.59	0.12	1.24	0.21
1988	2.15	0.12	1.07	0.43

increase in exposure, 95% CI 5.7%–12.5%) and SO_2 (9.8% increase for a 50 ppb increase in exposure, 95% CI 5.0%–14.8%) were highly significant predictors of daily deaths in Philadelphia. A χ^2 test for heterogeneity of the year and season specific coefficients showed significant heterogeneity for TSP (χ^2=45.6, p<0.03) and marginal heterogeneity for SO_2 (χ^2=38.6, p=0.10).

TSP RESULTS

Table 3 shows the estimated effect of TSP on daily deaths after controlling for the slope relating SO_2 to TSP. That is, it is our estimate of β_1 in equation (5). If the TSP effect were all or substantially due to confounding by SO_2, we would expect a small and insignificant intercept in this second stage regression, and a significant and positive coefficient for the SO_2 slope. In fact, the opposite occurred, as shown in figure 3. The intercept in the regression (β_1) is higher than the coefficient found in the basic meta-analysis, giving us a larger estimated effect for TSP. This indicates that the effects of airborne particles are higher when those particles are less correlated with SO_2. Long range transported sulphate particles are a subcomponent of total airborne particles that is unlikely to be correlated with SO_2, which is locally generated. These sulphates are a substantial fraction of the fine particle aerosol in Philadelphia, which is responsible for scattering light. Table 3 also shows the results of regressing the TSP effect size on daily deaths against the coefficient relating extinction coefficient to TSP in each of the 30 periods. In this case, very different results are found. The intercept term is much smaller than the original meta-analysis, and not significantly different from zero. The association between TSP and daily deaths seems to be due to its representation of fine particle mass.

SO_2 RESULTS

Table 3 shows the results of the meta-regression of the SO_2 effect size estimates on the relation between TSP and SO_2 across the 30 periods. By constrast with the TSP results above, the intercept term in this regression, which represents the unconfounded effect of SO_2, is dramatically diminished by control for the association between the two pollutants, and

Table 3 Estimated relative risk (95% CI) of SO_2 (50 ppb) and TSP (100 μg/m³) in baseline meta-analysis and after control for the other pollutant

	Baseline model	*Controlling for TSP*
SO_2	1.12 (1.08 to 1.16)	1.02 (0.89 to 1.16)
TSP	1.09 (1.06 to 1.13)	1.21 (1.10 to 1.32)
Controlling for visibility		1.01 (0.95 to 1.08)

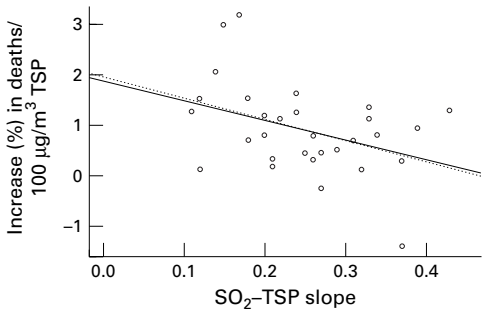

Figure 3 Effect size estimates for TSP in each 6 month study period plotted against the slopes relating SO_2 to TSP in that study period. The solid line shows a least squares fit through the data, whereas the dashed line shows the slope of a weighted least squares regression, with inverse variance weighting. The pattern suggests that TSP slopes are higher in periods when the relation between SO_2 and TSP was weaker.

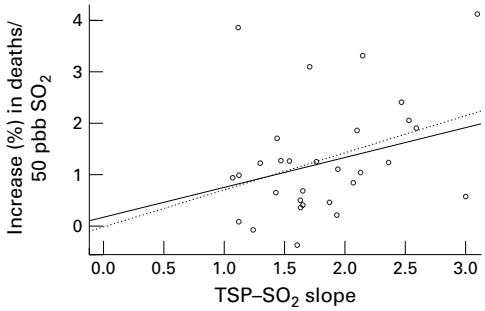

Figure 4 Effect size estimates for SO_2 in each 6 month study period plotted against the slopes relating TSP to SO_2 in that study period. The solid line shows a least squares fit through the data, whereas the dashed line shows the slope of a weighted least squares regression, with inverse variance weighting. The pattern suggests that the SO_2 effect is entirely due to its association with TSP, as the intercept terms for the fitted lines are zero.

is not significantly different from zero (fig 4). Hence, although particles show a stronger association with daily deaths in Philadelphia during periods when their association with SO_2 is weaker, SO_2 seems to have no association with daily deaths in Philadelphia when it is poorly correlated with airborne particles.

Discussion

As in previous analyses in Philadelphia, there was a significant association between both TSP and SO_2 with daily deaths in this analysis. There was evidence of heterogeneity in the association between both pollutants and daily deaths. That is, the coefficients in the 30 half year analyses varied by more than might be expected by chance. Several factors might explain this finding. Firstly, TSP (or SO_2) might be standing for something else and variations in the relation between them and that other factor over the 30 analysis periods might explain the variation in the association with daily deaths.

The principal hypothesis investigated in this paper was that one of these pollutants was substantially standing for the other. For TSP, I found no evidence that it was standing for SO_2. To the contrary, periods when the association between the two pollutants was weaker were periods with larger effect size estimates for TSP. This indicates that variations in particles in Philadelphia that are independent of SO_2 are associated with daily deaths, and that those particles are more toxic than the particles which vary in association with SO_2.

One possible explanation for this finding is long range transported particles. Because they originate elsewhere, and several days earlier, the correlation between such particles and locally generated SO_2 is lower than for locally generated particles. These transported particles are all less than 2.5 μm in aerodynamic diameter, and in the Philadelphia area, are predominantly sulphates and nitrates from the emissions of SO_2 and NO_2 at distant upwind powerplants and industrial facilities.

The suggestion that combustion particles are primarily responsible for the association found is further supported by the analysis looking at the relation between extinction coefficient and TSP as an explanatory variable. As already noted, such fine particles are a major source of impairment of visibility, and the correlation between the extinction coefficient and fine particle mass in Philadelphia is quite high.[12] Periods with a stronger relation between TSP and extinction coefficient did have higher effect sizes for TSP on daily deaths, and as shown in table 3, variations in TSP that were independent of the extinction coefficient were not associated with daily deaths. When combined with the apparent negative confounding of the SO_2 correlation, this indicates a consistent pattern of greater toxicity for such particles.

When we looked at the SO_2 results very different conclusions emerged. The SO_2 association did seem to result primarily from its association with airborne particles. The intercept term of the meta–regression, which shows the estimated SO_2 effect when SO_2 variations are uncorrelated with TSP, is close to zero and far from significant. Overall these findings indicate that SO_2 is not causally associated with daily deaths in Philadelphia.

These findings are consistent with other recent work. For example, Schwartz has just reported that SO_2 did not confound the association between PM_{10} and daily deaths in a hierarchical analysis of data from 10 United States cities.[16]

These results are not entirely surprising. It is hard to imagine how a pollutant that does not get into the lung at these concentrations would be associated with increased deaths from pneumonia and chronic obstructive pulmonary disease, which are lower respiratory illnesses. Yet, in 1961 Speizer *et al*[17] showed that over 90% of inhaled SO_2 was stripped out in the upper airways. Moreover, little of that was absorbed systemically—rather the SO_2 was released back into the air during exhalation.

Shimmel and Murawski[18] decades ago found that the percentage of daily deaths attributable

to air pollution in New York City in regressions between 1963 and 1972 remained constant, whereas SO_2 concentrations fell by 85%, with little accompanying change in airborne particle concentrations. This was accomplished by an almost order of magnitude increase in the size of the SO_2 coefficient, with little change in the coefficient for smoke. They likewise concluded that this was inconsistent with the effect being due to SO_2, but rather suggested confounding by particulate air pollution. The results of this study support that view.

A more recent study in the Netherlands reported similar findings.[19] The SO_2 concentration in the Netherlands fell considerably during the period of study (1986–94). When the analysis was stratified into three periods (1986–8, 1989–91, 1992–4) the regression coefficient for SO_2 increased from the earlier to later period, as the SO_2 concentration fell. This pattern would be expected if SO_2 were merely standing in for something else, which did not change much in concentration, or if the association with SO_2 were non-linear, with higher slopes at lower concentrations.

Non-linear associations with SO_2 have been reported in locations where concentrations can be high— such as Poland—but concentrations were always much lower in the Netherlands. If the higher effect size estimates for SO_2 in later years were due to a non-linear relation, we would also expect to see higher slopes within each period in the parts of the Netherlands that had lower SO_2 concentrations. The authors investigated this, and found that within periods, the slopes were actually lower for SO_2 in the areas with lower concentrations. They therefore concluded that SO_2 was most likely standing in for another factor.

One obvious candidate for that factor is some sub-component of airborne particles. Several studies suggest that the size of airborne particles is related to their toxicity. For example, the particles in the size range 10–30 μm in aerodynamic diameter were shown not to be predictive of mortality,[20] whereas smaller particle size ranges were. Similarly, particles of 2.5–10 μM in aerodiameter have also shown less evidence of toxicity than the smaller particles.[11] If fine combustion particles were the causal factor, we would expect the extinction coefficient to be an important predictor of the TSP mortality relation, as I found.

As in most observational epidemiology studies, the exposure measurements in this study are imperfect. Personal exposure to air pollutants varies greatly from person to person, depending on the ventilation characteristics of their homes as well as activity patterns and other factors. Here it is important to realise that the unit of observation in studies such as this is the day, and not the person. Hence person to person differences in exposure tend to average out. Schwartz and Levin[20] considered this in some detail, and showed that in the context of such time series studies, the differences between the exposure of a single subject on day t and the mean of all personal exposures in the city on that day is a form of Berkson measurement error, which introduces no bias into the regression coefficients. Bias can only come from differences between the mean of all personal exposures on a given day and the ambient monitors on that day, which is small compared with the differences between individual exposures and the population mean. Hence most of the measurement error is of no consequence. Zeger *et al*[21] have carried this approach further, and shown that the remaining bias is towards underestimating the effect of air pollution. Further, in simulation studies, they showed that even in the presence of covariates and other pollutants, the correlations among the pollutants would have to be pathological for the effect size estimate for an air pollutant to be biased upward. It is possible, in the two pollutant model, for one pollutant to be biased downward more than the other. This is an additional advantage of the approach used here, where single pollutant models were fitted, and confounding by other pollutants was considered in a second stage.

These results suggest that the associations reported with SO_2 and daily deaths in Philadelphia and elsewhere are not causal, but are the result of SO_2 being correlated with other combustion pollutants, most likely with combustion particles. By contrast, they strengthen the evidence that the association of daily deaths with combustion particles reported in many studies is not the result of confounding by SO_2, and is likely to be causal.

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1 Schwartz J, Dockery DW. Increased mortality in Philadelphia associated with daily air pollution concentrations. *Am Rev Respir Dis* 1992;**145**:600–4.
2 Katsouyanni K, Touloumi G, Spix C, *et al*. Short term effects of ambient sulphur dioxide and particulate matter on mortality in 12 European cities: results from time series data from the APHEA project. *BMJ* 1997;**314**:1658–1663.
3 Schwartz J. Air pollution and daily mortality in Birmingham, Alabama. *Am J Epidemiol* 1993;**137**:1136–47.
4 Pope CA, Schwartz J, Ransom M. Daily mortality and PM10 pollution in Utah Valley. *Arch Environ Health* 1992; **42**:211–17.
5 Moolgavkar SH, Luebeck EG, Hall TA, *et al*. Air pollution and daily mortality in Philadelphia. *Epidemiology* 1995;**6**: 476–84.
6 Samet JM, Zeger SL, Kelsall JE, *et al*. *Air pollution, weather, and mortality in Philadelphia 1973–88. The phase I.B report of the particle epidemiology evaluation project*. Cambridge, MA: Health Effects Institue, 1997.
7 Schwartz J. Air pollution and hospital admissions for cardiovascular disease in Tucson. *Epidemiology* 1997;**8**: 371–7.
8 Fairley D. The relationship of daily mortality to suspended particulates in Santa Clara County, 1980–6. *Environ Health Perspect* 1990;**89**:159–68.
9 Schwartz J. Air pollution and hospital admissions for respiratory disease. *Epidemiology* 1996;7:20–8.
10 Kelsall JE, Samet JM, Zeger SL, *et al*. Air pollution and mortality in Philadelphia: 1974–88. *Am J Epidemiol* 1997;**146**:750–62.
11 Schwartz J, Dockery DW, Neas LM. Is daily mortality associated specifically with fine particles? *J Air Waste Manage Assoc* 1996;**46**:2–14.
12 Ozkaynak H, Schatz AD, Thurston GD. Relationships between aerosol extinction coefficients derived from airport visual range observations and alternative measures of airborne particle mass. *J Air Pollut Control Assoc* 1989:**35**:1176—85.
13 Schwartz J. Air pollution and daily mortality in Birmingham, Alabama. *Am J Epidemiol* 1993:**137**:1136–47.
14 Schwartz J. Air pollution and daily mortality: a review and meta-analysis. *Environ Res* 1994;**64**:36–52.

15 Cleveland WS, Devlin SJ. Robust locally-weighted regression and smoothing scatterplots. *Journal of the American Statistical Association* 1988;**74**:829–36.
16 Schwartz J. Assessing confounding, effect modification, and thresholds in the association between ambient particles and daily deaths. *Environ Health Perspect* 2000:**108**:563–8.
17 Speizer FE, Frank NR. The uptake and release of SO_2 by the human nose. *Arch Environ Health* 1966 **12**:725–8.
18 Shimmel H, Murawski TJ. The relation of air pollution to mortality. *J Occup Med* 1976;**18**:316–33.
19 Buringh E, Fischer P, Hoek G. Is SO_2 a causative factor for the PM associated mortality risks in The Netherlands? *Inhal Toxicol* (in press).
20 Ozkaynak H, Thurston GD. Associations between 1980 US mortality rates and alternative measures of airborne particle concentration. *Risk Anal* 1987;**7**:449–61.
21 Schwartz J, Levin R. Drinking water turbidity and health. *Epidemiology* 1999:**10**:86–90.
22 Zeger SL, Thomas D, Dominici F, *et al*. Exposure measurement error in time-series studies of air pollution: concepts and consequences. *Environ Health Perspect* 2000;**108**:419–26.