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A derived association between ambient aerosol surface area and excess mortality using historic time series data

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Abstract

Although aerosol mass concentration is widely associated with ill health following inhalation; there is increasing evidence that it is a poor indicator of fine and ultrafine particle toxicity. Research has indicated that biological response to such particles is closely associated with particulate surface area; although no epidemiology data currently exist to validate the association. By applying a simple model to historic mass-based time series data, we have been able to estimate mortality rate as a function of ambient aerosol surface area. Within the simplifying assumptions of the model, a linear association is indicated between mortality rate and surface area concentration for coalescing particles. The analysis also indicates the existence of a threshold aerosol concentration, below which particulate mass and surface area are linearly related. Below this threshold, we suggest that mass concentration measurements may provide a good indicator of health effects, although for high exposures found in the developing world and industry, the model indicates that aerosol exposure may be more appropriately characterized by surface area. Further experimental validation of the model should establish the applicability of derived relationships between aerosol mass and surface area concentration to ambient and occupational exposures.
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Keywords: Aerosol; Exposure; Health effects; Surface area; Computational modeling

1. Introduction

Ambient concentrations of particles are lower in many developed countries today than previously. That such low mass concentrations have damaging effects on health is surprising though repeated, careful epidemiological studies show this to be the case (Katsouyanni et al., 1997; Samet et al., 2000). The most important method demonstrating associations between mass concentrations of pollutants, including particles and effects on health, is the time-series analysis. This method relates daily average concentrations of pollutants, usually monitored at a single site, to daily counts of deaths or hospital admissions. Careful allowance for the effects of confounding factors such as temperature is needed, and separation of the effects from different components in the polluted air mixture has proved difficult. Nevertheless, consistent associations are reported and generally accepted (Department of Health, 1995).

One of the difficulties encountered in trying to establish causality has been the lack of a biologically plausible mechanism of effect (Department of Health, 1995; Department of the Environment Transport and the Regions, 2001). The daily dose is so small that accepted toxicological mechanisms seem insufficient to explain the effects. This has caused researchers to generate new hypotheses and the idea that very small-sized particles could increase aerosol toxicity has been advanced (Oberdörster et al., 1995; Seaton et al., 1995).

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Work by Oberdörster has demonstrated that fresh polytetrafluoroethene (PTFE) particles have unexpected toxicity on a mass basis in rats, and his group and others have shown that for substances including titanium dioxide (TiO_2) and carbon black, a given mass of fine (smaller than 2.5 μm) or ultrafine (smaller than 100 nm) particles is more toxic than an equivalent mass of larger particles (Donaldson et al., 1998; Oberdörster et al., 1995). Why this should be the case was initially obscure, but a range of possible explanations have been suggested, including easier access to the pulmonary interstitium (Ferin et al., 1992), increased potency in triggering inflammatory reactions, and increased capacity to generate oxidant-free radicals (Gilmour et al., 1996; Li et al., 1996). Additionally, an idea has been developed that what matters most is the total surface area of material brought into contact with lung tissue (Brown et al., 2001; Lison et al., 1997; Tran et al., 2000). Chemical composition is important, and even at a specified "surface area dose", different compounds provoke different degrees of reaction (Brown et al., 2001). Recent work has shown that the toxicological effects of particles are not limited to the lung. That the cardiovascular system appears to be an important target (Costa and Dreher, 1997; Pekkanen et al., 2000; Peters et al., 1997a) is supported by both early and recent epidemiological findings (Atkinson et al., 1999; Ministry of Health, 1954; Peters et al., 2001).

One important epidemiological analysis related the effects of current particle concentrations to those extant in London some years ago (Schwartz and Marcus, 1990). A curvilinear relationship between daily mass concentrations of particles (measured using the black smoke (BS) index) and increased risk of death (extra daily deaths) was produced for winters 1958–1972 (Fig. 1). This relationship generated speculation about the reasons for the initial constancy of the line gradient, and its decline at higher concentrations of particles. Numerous ideas were advanced, including the loss of susceptible individuals from the population during earlier days of comparatively longer-lasting, higher concentrations of air pollution and the possibility that people took "evasive action" when pollution levels were especially high. Neither explanation seems entirely satisfactory. It has been proposed that the curvilinear relationship is associated with non-linearity between BS and suspended particulate mass (Schwartz and Marcus, 1990). Although the published data indicate the transformation between BS and suspended particulate mass to be aerosol dependent (Bailey and Clayton, 1982; Lee et al., 1972), there is little to suggest a dependence on mass concentration that would serve to linearize the relationship between BS and mortality.

We advance the hypothesis that particulate mixtures associated with London mortality data differed by the distribution of particle sizes at high and low mass

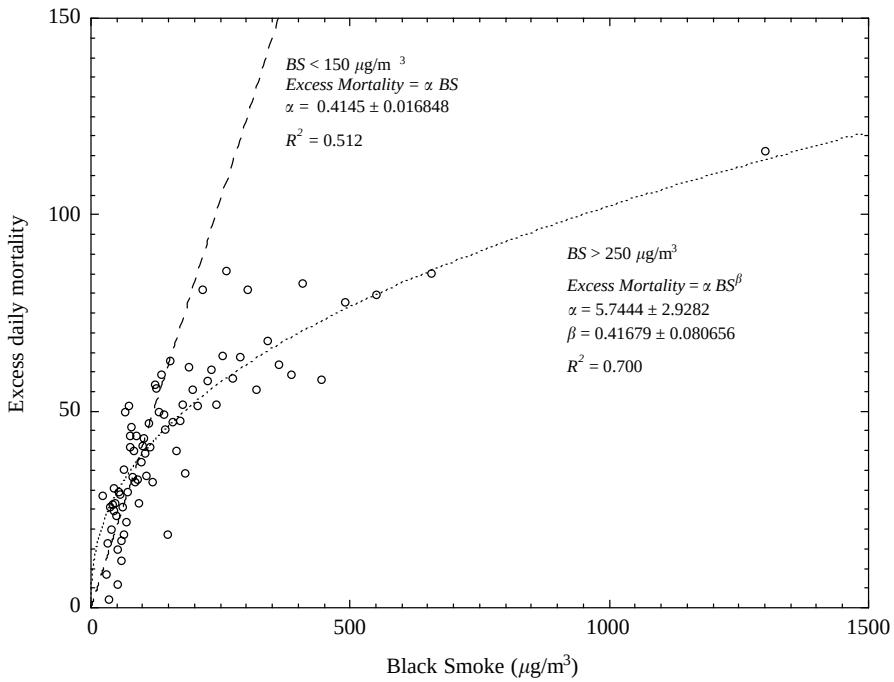

Fig. 1. Estimated excess daily mortality versus BS in London over the winters of 1958–1972 (20). Data below 150 μg/m^3 and above 250 μg/m^3 have been fitted using least-square regression analysis.

concentrations. It seems plausible that at high mass loadings very small particles would disappear rapidly from air through coagulation with larger particles, leading to changes in specific surface area and increasing mass concentration. Recent work showing the dependence of the number of toxicological properties of dusts on total surface area of the applied dose encouraged us to look at the surface area changes of the aerosol as the mass concentration was increased (Peters et al., 2001).

2. Method

In estimating the relationship between particulate surface area and mass associated with London mortality data, we considered the simplest model of ambient particulate generation and evolution. The model was based on aerosol particles characterized by a lognormal size distribution being generated into a fixed volume at a constant rate. We assumed diffusional losses from the volume were matched by the influx from adjacent volumes, leading to coagulation as the dominant mechanism governing evolution of the aerosol size distribution over time. At a critical time (t_{crit}), particle number generation rate would equal coagulation rate within this model. Intuitively below t_{crit} the aerosol size distribution would be relatively constant, leading to a linear relationship between mass and surface area concentration. However, above t_{crit}, coagulation would dominate the development of the size distribution, resulting in a curvilinear relationship between surface area and mass.

To derive the precise nature of the relationship between surface area and mass, we used a computational model based on established coagulation theory. The model was run with and without gravitational settling. Simulations using spherical coalescing particles were run for aerosol generation rates (dn/dt) between 10^3 and 10^{11} particles/m^3 s. Generated aerosol count median diameters (CMDs) were varied between 20 and 200 nm, and generated aerosol geometric standard deviation (σ_g) was varied between 1.1 and 3. The generation of solid, non-coalescing particles was simulated by assuming that particles larger than a defined primary particle diameter (d_p) coagulated to form open-structured fractal-like agglomerates, characterized by the fractal dimension d_f. These simulations were run using an aerosol having a CMD of 50 nm, a σ_g of 1.7, and a generation rate of 10^7 particles/m^3 s. Primary particle diameters between 10 and 100 nm and fractal dimensions between 1.4 and 2 were used, but gravitational settling was not included. For all simulations, the aerosol was generated into a cube 5 m on each side, and a density of 2300 kg/m^3 was assigned to the particles.

Transforming calculated values of surface area (S) and mass concentration (M) to appropriate dimensionless quantities (S' and M') enabled us to identify a generalized function describing the relationship between S' and M'. S and M were initially transformed to S' and M' by normalizing each with the estimated surface area or mass concentration at t_{crit}. This allowed S' and M' to follow a 1:1 relationship below $M' = 1$, irrespective of the parameters describing the generated aerosol. Multiplying S' and M' by the diameter of mean surface to volume ratio within the generated aerosol was found to retain this relationship below $M' = 1$, while allowing the data above $M' = 1$ to converge towards a single function. The resulting transformations used were

$$S' = \frac{S}{\pi d_{\bar{s}}^2}\left(\frac{1}{\bar{K}}\frac{dn}{dt}\right)^{-1/2} e^{-5/2Ln^2\sigma_g},$$

$$M' = \frac{6M}{\pi\rho d_{\bar{m}}^3}\left(\frac{1}{\bar{K}}\frac{dn}{dt}\right)^{-1/2} e^{-5/2Ln^2\sigma_g}. \quad (1)$$

$d_{\bar{s}}$ and $d_{\bar{m}}$ are the diameters of average surface area and mass, respectively in the generated aerosol. $\bar{K}$ is the mean coagulation coefficient of the generated aerosol.

3. Results

Calculated values of S' and M' for coalescing spherical particles are plotted in Fig. 2. Although there is some divergence at high M', the data are easily described by a single function. Inclusion of gravitational settling led to a ceiling on the maximum value of M' attainable, but otherwise had no effect. The 1:1 relationship between S' and M' below $M' = 1$ confirms the assumption that at low mass concentrations coagulation is negligible, leading to a linear relationship between surface area and mass. Above $M' = 10$, the relationship between surface area and mass is described well by the function $S' = \alpha M'^{\beta}$, with $\alpha = 1.3849$ and $\beta = 0.4167$.

Fig. 3 presents the numerical simulation results assuming the formation of fractal-like agglomerates. Above $M' = 1$, S' continues to follow a linear relationship with M' in most cases. At increasingly larger primary particle diameters, a tendency to diverge from the 1:1 relationship is seen around $M' = 1$. However, as M' increases, a linear relationship is re-established. This divergence was primarily driven by simplifying assumptions used to model fractal particle behavior, and is unlikely to represent a physical reality. These results confirm that for $D_f \leqslant 2$, surface area tends to scale linearly with the number of primary particles (Rogak et al., 1993).

4. Discussion

Figs. 2 and 3 define limits on the relationship between S' and M' corresponding to extremes of particle

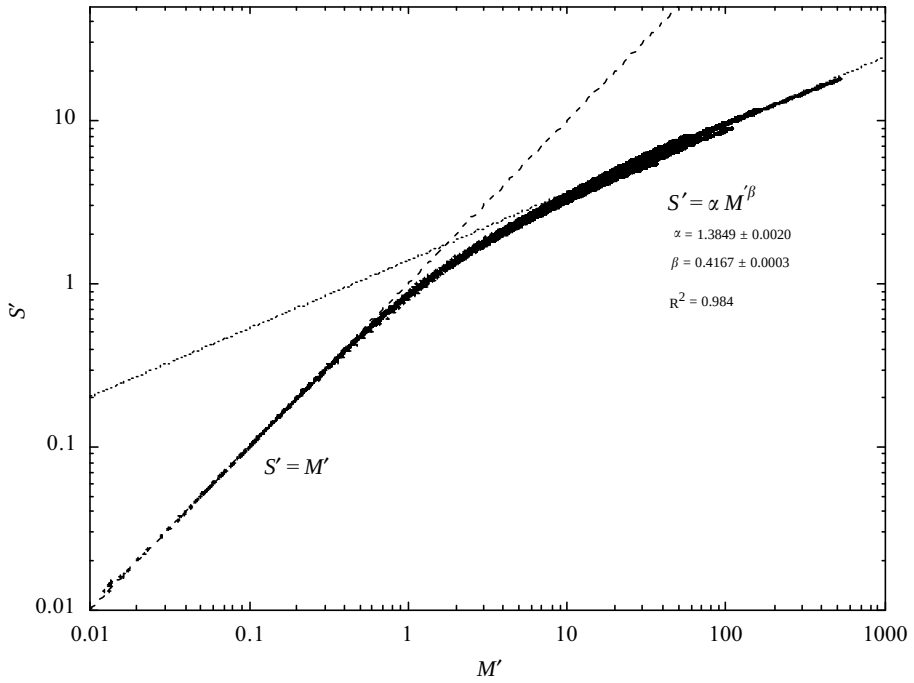

Fig. 2. Plotting S' versus M' for spherical coalescing particles. Data have been evaluated for generated aerosols with $dn/dt = 10^3-10^{11}$ particles/m^3 s, CMD = 20–200 nm and $\sigma_g = 1.1-3$. Data above $M' = 14$ have been fitted using a least-square regression analysis.

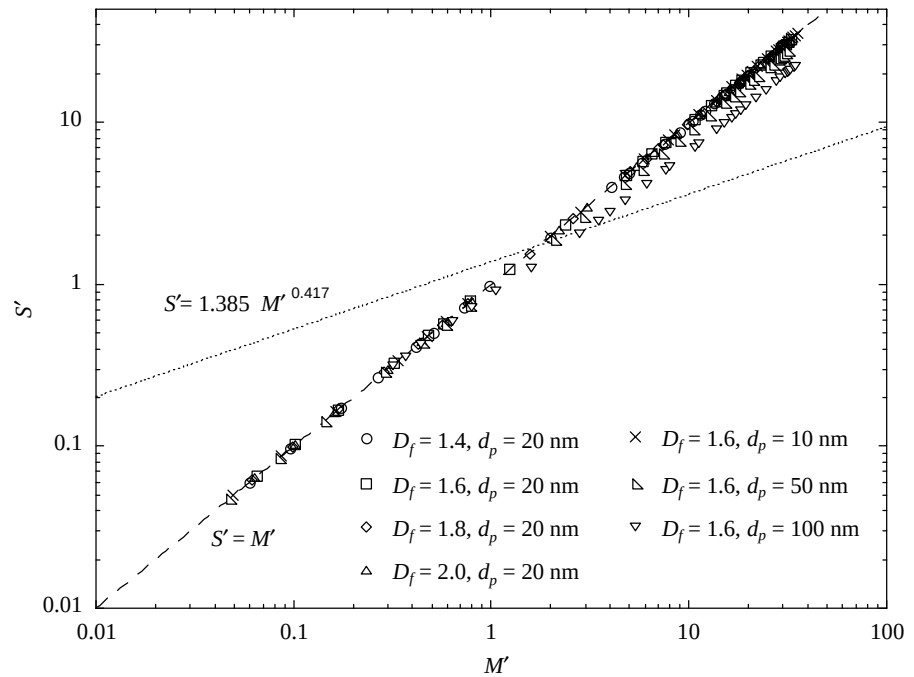

Fig. 3. Plotting S' versus M' for spherical non-coalescing particles ($D_f \leqslant 2$). Data have been evaluated for a generated aerosol with $dn/dt = 10^7$ particles/m^3 s, CMD = 50 nm and $\sigma_g = 1.7$. The function describing S' at high M' for compact particles has been included for comparison.

behavior on coagulation. The relationships between mortality and BS, and S' and M' are remarkably similar if complete coalescence is assumed, indicating that transformation of the Schwartz and Marcus data with appropriate factors could lead to a linear response with respect to particulate surface area. It is unclear whether particles at the time were predominantly fractal-like or compact, although recent images of ambient particles associated with coal combustion indicate that coalescence could have led to the formation of compact particles (Xu et al., 2001).

A critical mass concentration (BS_{crit}) of 90.71 $\mu g/m^3$ can be estimated from Fig. 1 that defines the intersection point between high and low BS exposure regimes. Likewise, a critical dimensionless mass (M'_{crit}) of 1.748 may be estimated that defines the intersection of the lower and upper mass regimes from computational modeling, assuming particle coalescence (Fig. 2). Assuming the model is an appropriate representation of the London aerosol in the winters of 1958–1972 and that BS is equivalent to suspended particulate mass, BS_{crit} and M'_{crit}may be used to estimate dn/dt for an assumed CMD and σ_g:

$$\frac{dn}{dt} = \bar{K}\left(\frac{\pi\rho d_{\bar{m}}^3}{6}\frac{M'_{crit}}{BS_{crit}}e^{5/2Ln^2\sigma_g}\right)^{-2}. \quad (2)$$

Using Eq. (2) and the relationship between S' and M' (Fig. 2), a transformation between BS and S is derivable. This transformation is dependent on the model adequately representing aerosol dynamics when the measurements were made. If aerosol mixing and changes in size distribution occur over a significantly shorter timescale than that governing changes in aerosol generation, the model should provide a close approximation to spatially averaged environmental aerosol dynamics. t_{crit} was found to be inversely proportional to $\sqrt{dn/dt}$ for coalescence on coagulation, with $t_{crit} = 51$ min for $dn/dt = 10^9$ particles/m^3 s (CMD = 50 nm, $\sigma_g = 1.7$). Aerosol generation rate probably followed a diurnal pattern, and thus for generation rates above 10^9 particles/m^3 s, the model should provide a good approximation of changes in aerosol size distribution.

Fig. 4 shows excess mortality against estimated surface area using a range of plausible aerosol parameters. For simplicity, the transformation between BS and surface area was carried out assuming a linear relationship below BS_{crit}, and an exponential relationship above this point. By using a simple model to estimate the relationship between particulate surface area and mass concentration, excess mortality rate data have been transformed from a curvilinear relationship with respect to BS to a linear relationship with respect to estimated surface area. The transformation is highly dependent on assumptions underpinning the model, and it is uncertain how closely the derived surface area values are likely to

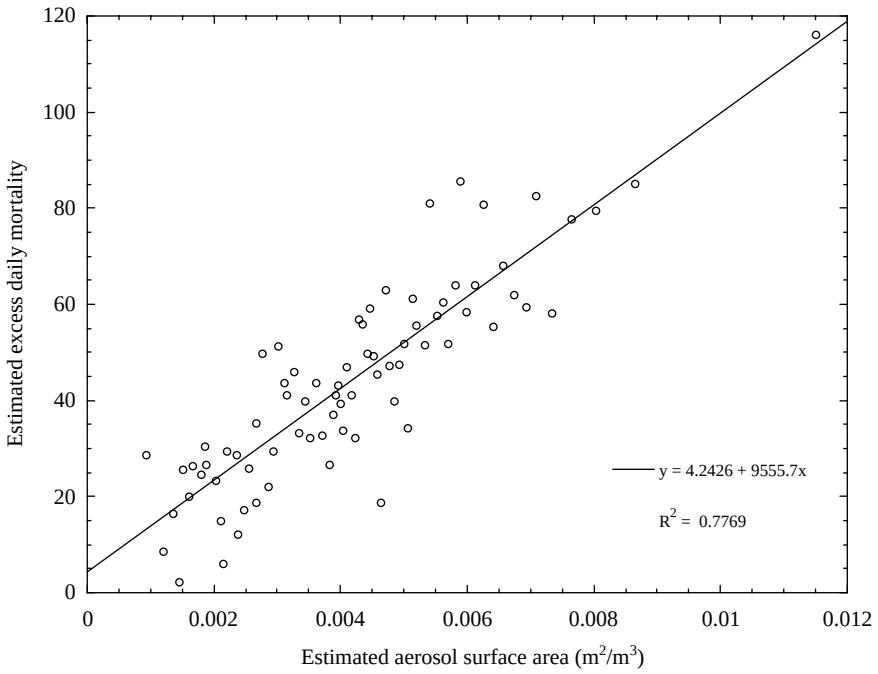

Fig. 4. Estimated excess daily mortality versus estimated particulate surface area in London over the winters of 1958–1972 (Schwartz and Marcus, 1990). The transformation between BS and surface area is based on the midpoints of calculations using CMD between 30 and 50 nm, and σ_g between 1.5 and 1.7. Variation about the midpoint surface area values was $\pm 38\%$.

reflect conditions at the time. However, to our knowledge, time-series data have never before shown excess mortality versus estimated particulate surface area, and we believe that despite the underlying assumptions, the analysis provides a unique, invaluable insight into an association between particles and ill health.

The transformation in Fig. 4 is suggestive of mortality rate being strongly influenced by particulate surface area. This is borne out by toxicology data on low-solubility materials that imply a close association between surface area and biological response (Brown et al., 2001; Lison et al., 1997; Peters et al., 1997b; Tran et al., 2000). Given that the London data span 15 years, over which time the generated aerosol changed in nature, the transformation is even more remarkable and warrants further inspection. Between 1958 and 1971, the mean BS level steadily decreased, indicating a reduction in particle generation rate and/or a reduction in generated particle size (Schwartz and Marcus, 1990). If the size distribution and biological activity (as a function of surface area) of the generated aerosol were constant, the transformation in Fig. 4 would be accounted for, despite variations in generation rate. Large variations in generated particle size distribution would confound the transformation, and it must be concluded, therefore, that either relatively small changes occurred in the key characteristics of particles associated with mortality, or that the transformation is not valid. Schwartz and Marcus noted that curvilinear trends similar to Fig. 1 occurred in individual years throughout the analysis period, supporting the validity of the transformation.

Our assumption that particles coalesced on coagulation implies the presence of a liquid phase. If the particles had been entirely in the liquid phase, no physical grounds would exist for interpreting excess mortality in terms of surface area. A plausible interpretation is that solid-inhaled particles acted as a vector for a liquid component associated with particulate surface—probably present as a liquid condensed on to the particle surface. This hypothesis retains the viability of an association between health effects and particulate surface area, while proposing a causative agent that varies linearly with the surface area of inhaled aerosol.

Below M_{crit} surface area is predicted to follow a linear relationship to mass concentration, allowing suitable exposure measurements and limits to be expressed as particulate mass. At generation rates above 10^7 particles/m^3 s, the model predicts the critical mass concentration to remain above $35\,\mu g/m^3$ (based on a generated aerosol with CMD $= 30$ nm, $\sigma_g = 1.7$ and density $= 2300$ kg/m^3). This threshold is above many PM2.5 levels in the Developed World and provides some insight into the linearity observed between PM2.5 and health effects in a number of studies (Dockery et al., 1993; Schwartz et al., 1996). However, the threshold is substantially lower than mass concentrations found in many industries associated with the generation of fine particles. High generation rates will raise the threshold, and the formation of fractal-like agglomerates in some processes will extend the regime where surface area varies linearly with mass concentration. Nevertheless, our analysis suggests that particulate surface area should be considered as an exposure metric in some industries.

5. Summary

By applying a simple model to historic aerosol exposure–response data, we have demonstrated a linear association between ambient particulate surface area and mortality. This analysis is indicative of a causal relationship between mortality and the surface component of the particulate and supports the hypothesis that an association may exist between health effects and agents condensed on the surface of inhaled particulates. A linear relationship between surface area and PM2.5 concentration is predicted at low mass concentrations, suggesting that PM2.5 may be a suitable indicator of health effects for many environmental exposures. However, our results indicate that at the higher concentrations associated with some workplaces and developing countries, particulate surface area may provide a more appropriate metric for aerosol exposure.

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