Particulate air pollution

David V Bates

Professor Emeritus of Medicine, University of British Columbia, Vancouver, Canada

Introductory article

Particulate air pollution as a predictor of mortality in a prospective study of US adults

CA Pope III, MJ Thun, Mohan M Namboodiri, DW Dockery, JS Evans, FE Speizer, CW Heath Jr

Time-series, cross-sectional, and prospective cohort studies have observed associations between mortality and particulate air pollution but have been limited by ecologic design or small numbers of subjects or study areas. The present study evaluates effects of particulate air pollution on mortality using data from a large cohort drawn from many study areas. We linked ambient air pollution data from 151 U.S. metropolitan areas in 1980 with individual risk factors on 552 138 adults who resided in these areas when enrolled in a prospective study in 1982. Deaths were ascertained through December, 1989. Exposure to sulfate and fine particulate air pollution, which is primarily from fossil fuel combustion, was estimated from national data bases. The relationships of air pollution to all-cause, lung cancer, and cardiopulmonary mortality were examined using multivariate analysis which controlled for smoking, education, and other risk factors. Although small compared with cigarette smoking, an association between mortality and particulate air pollution was observed. Adjusted relative risk ratios (and 95% confidence intervals) of all-cause mortality for the most polluted areas compared with the least polluted equaled 1·15 (1·09 to 1·22) and 1·17 (1·09 to 1·26) when using sulfate and fine particulate measures respectively. Particulate air pollution was associated with cardiopulmonary and lung cancer mortality but not with mortality due to other causes. Increased mortality is associated with sulfate and fine particulate air pollution at levels commonly found in U.S. cities. The increase in risk is not attributable to tobacco smoking, although other unmeasured correlates of pollution cannot be excluded with certainty. (*Am J Respir Crit Care Med* 1995;**151**:669–74).

This remarkable analysis of a cohort of over half a million US adults found significant associations between lifetime exposures to sulphate aerosols and fine particles, as judged by community air pollution data, and some causes of mortality. It reinforced earlier findings of significant associations, on a daily basis, between exposures to fine particles and mortality, and showed that cardiopulmonary and lung cancer mortality were significantly related to particulate air pollutants.

Major concern about the association between particulate air pollution and adverse health impacts can be dated from Dockery and Pope's review of the emerging work in 1994.[1] They showed that there was a consistent relationship in time-series studies between measurements of particulate load (particularly of particles less than 10 μm in diameter, known as PM_{10}s), and daily mortality, excluding accidents and suicides. This was true of places with different climates and with different levels of other pollutants such as sulphur dioxide (SO_2). They also summarised a body of work which indicated that PM_{10} levels were associated with various morbidity indices including hospital admissions for pneumonia, worsening asthma (as shown in panel studies and in hospital emergency visits), and decrements in lung function in children. The consistency and coherence of these data suggested that there was a causal relationship with PM_{10} levels.

In the review which follows some of the questions raised by this work are discussed. From the fact that a recent British review of particulate air pollution was 132 pages long,[2] and the criteria document of the US Environmental Protection Agency (EPA)[3] (which is not yet in its final form) will probably be at least four times longer than that, the reader will conclude that what follows necessarily compresses a great deal of information.

Time series studies of daily mortality

The North American cities that have been studied include Philadelphia, Birmingham, Detroit, Cincinnati, Los Angeles, St Louis, Chicago, and New York. Data are similar from London, Athens, Erfurt, Amsterdam, Milan, Santiago in Chile, and Sao Paulo in Brazil. In general, a 10 $\mu g/m^3$ increase in the PM_{10} level is associated with an average 0·7% increase in mortality. The data from Philadelphia[4] are representative of these studies and, as can be seen from fig 1, the risk is higher

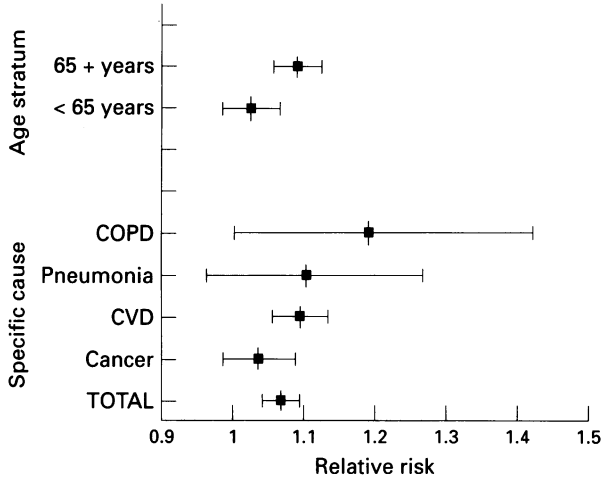

Figure 1 Relative risk of mortality in Philadelphia associated with an increase in total suspended particulate (TSP) concentration of 100 μg/m³ after controlling by regression for year of study, time trend, and weather variables. The results shown are for all cause mortality, age stratified mortality, and cause-specific mortality. Note the increased risks of death from chronic obstructive pulmonary disease (COPD) and pneumonia. However, these account for only about one tenth as many deaths as cardiovascular disease (CVD). Numerically the 10% increase in a relative risk for cardiovascular disease for a 100 μg/m³ increase in particulate pollution is important in deriving the overall relationship. Reproduced from Schwartz and Dockery[4] with permission.

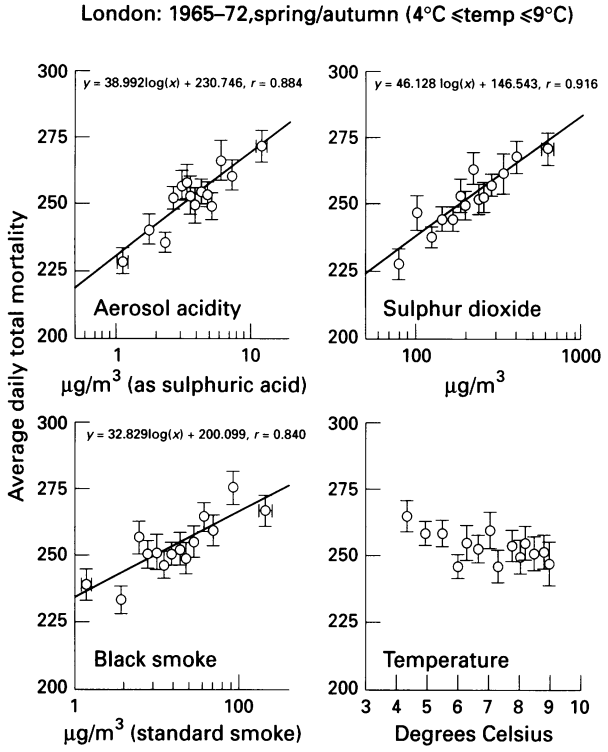

Figure 2 By aggregating data from the spring and autumn, the variation in temperature is minimised. Note the strong associations of aerosol acidity, sulphur dioxide, and black smoke with the average daily mortality. The data are for a six year period (1965–72) when smoke levels had been greatly reduced from levels in the 1950s.[42] Reproduced from Lippmann and Ito[11] with permission.

in those over the age of 65 than in those younger and involves both respiratory causes of death and cardiovascular deaths, which are generally about 10 times more numerous. In five cities, if only the elderly are considered, there is a mean increase of 1·04% in mortality per 10 μg/m³ increase in the PM_{10} level.

When the number of deaths per day is very large – as in Sao Paulo, for instance, with a population of 13 million people – it can be shown that the relationship is present in all seasons of the year in people over the age of 65 and that the association with the PM_{10} level is independent of other pollutants.[5] In all of these studies there is no evidence of a threshold, the relationship between mortality and PM_{10} level being monotonic – that is, a straight line relationship.

It is the consistency of these results which is impressive. Moreover, the consistency of the associations across a large variety of sources of particles suggests that the combustion processes in general are responsible for the observed associations.

Statistical methodology

Not surprisingly, all of these data generated a "rapid response" since the implications of them were not difficult to grasp. The first question therefore was whether the complex statistical methodology that was required was sound. The Health Effects Institute in Boston (funded equally by the US EPA and the automobile industry) asked the investigators to make their databanks available and then commissioned an epidemiologist and a biostatistician (both distinguished contributors to their fields) to re-analyse the data. Their report[6] confirmed the validity of the data and the robustness of the results to alternative statistical methods.

There is still room for discussion on the influence of the model chosen, however, and when small datasets are used,[7,8] or even with larger ones, the magnitude of the association will be sensitive to the choice of model. However, even those who were initially sceptical of the work have now conceded that the association is robust. Lipfert and Wyzga[9] recently wrote that: "Consistent positive associations between mortality and various measures of air pollution have been shown within each of two fundamentally different types of regression studies and in many variations within these basic types. This is extremely unlikely to have occurred by chance." The strongest association appears to be with the mean level of PM_{10} on the concurrent day and the day before,[5] or with a mean of the previous four days. In a number of the studies it has been shown that the regression relationship is not due to "influential outliers" in the datasets.

Weather as a confounder

There is a general agreement that the handling of the weather variables represents a critical issue.[8] Deaths among the elderly increase as winter approaches, and both mortality and morbidity from pneumonia reach their maxima in January and February in the northern hemisphere. Emergency visits to hospital for respiratory diseases are also at their maximum in these months.[10] If the number of observations is large enough, the four seasons can be treated separately as was done in the Sao Paulo study;[5] the influence of temperature variations can be handled by aggregating seasons with a small temperature variation. This was the technique used by Lippmann and Ito in a recent re-analysis of the London data.[11] Figure 2 from their paper shows the associations of daily mortality versus air pollution for the spring and autumn periods combined. The strong association of particulate pollution (here measured as "black smoke") and of SO_2 with daily mortality is evident. In most industrial settings there is a strong correlation between

SO_2 and particulate measures (in central Birmingham the correlation coefficient was 0·73[2]). If numerous weather variables are included (and some analyses have included as many as 28), the calculated effect of variation in PM_{10} levels on mortality can be significantly reduced. Dockery and Schwartz recently described such analyses as representing significant overmodelling.[12]

In any analysis of a specific location it will be impossible to rule out residual confounding by weather or some unmeasured covariate. However, the association between PM_{10} levels and daily mortality has been observed in places with very different climates, and this constitutes the strongest evidence that the level of PM_{10}s rather than climate is the main determinant of the association.

PM_{10} and morbidity indices

No pollutant is likely to be responsible only for an increase in mortality, although it has been argued that the population impacted may be in some way "special". The "coherence" between mortality as an outcome and other indices of effects therefore becomes important in the evaluation of the significance of the overall data.[13] PM_{10} levels have been shown to be strongly associated with hospital admissions for pneumonia in the elderly,[14] with an increase in emergency visits for asthma,[15] with increased bronchodilator use and reduced lung function in children with respiratory symptoms[16] and, in association with other pollutants, with reduced lung function in normal children.[17] The relationship of PM_{10} levels to hospital admissions for pneumonia in the elderly is especially significant and, in a review of data from five US cities, there was a 5–9% increase in pneumonia admissions for a 50 $\mu g/m^3$ increase in PM_{10} level.[14] Considering all respiratory admissions rather than just pneumonia, and including six different regions, there was a 5–12% increase for the same increment of PM_{10} levels.[14] For the chronic obstructive lung disease category the increase in risk was 7–25% for six regions including Barcelona in Spain.

In an analysis of a very large databank from 168 hospitals over a six year period, Burnett *et al*[18] in Canada found that "a 13% $\mu g/m^3$ increase in sulphates recorded on the day before admission (the 95th percentile) was associated with a 3·7% increase in respiratory admissions and a 2·8% increase in cardiac admissions". Both of these increases were highly significant. The association between sulphates (a constituent of PM_{10}s) and cardiovascular hospital admissions was especially important as, prior to this report, the only association of cardiovascular causes had been with mortality (fig 1). These data have been supported by a similar analysis from Detroit[19] in which the daily admissions for ischaemic heart disease were significantly associated with PM_{10} levels but not with sulphur dioxide, carbon monoxide, or ozone. Heart failure admissions were also associated with PM_{10}s but also with carbon monoxide levels.

It may be concluded that the "coherence" requirement has been adequately met; indeed, the morbidity data are now stronger than they were at the time of Dockery and Pope's original review,[1] and the mortality data have been considerably extended.

Longitudinal cohort studies

One of the difficulties in interpreting time-series data is that it can always be argued that the excess mortality only indicates an advancement of the date of death by one or two days. This might occur because of the acute vulnerability of a particular population. A fall in mortality would then follow an episode of a few days duration in which mortality had been increased. This phenomenon is known as "harvesting" (an objectionable term). Although this almost certainly occurs to some extent, two prospective longitudinal studies have indicated that increased particulate pollution is associated with a more meaningful reduction in survival.

The first of these was a 16 year follow up study of a population in six US cities.[20] The cohort was aged between 25 and 75 years when the study began and numbered 8111 adults. Occupational factors and, more particularly, a detailed smoking history were both known. The adjusted mortality ratio for the most polluted of the cities compared with the least polluted was 1·26, and air pollution was positively associated with deaths from lung cancer and cardiopulmonary disease, but not with deaths from other causes. Survival decreased monotonically with particulate pollution concentrations across the six cities. The relationship was as strong for aerosol sulphates (which constitute a major fraction of the $PM_{2·5}$ component) as for PM_{10}s.

The other longitudinal study[21] (reported in the introductory article) involved a cohort of 552 138 adults analysed with respect to sulphates, and a subgroup of 295 223 analysed with respect to PM_{10}s. The cohort had been recruited 17 years earlier in a prospective study for the US Cancer Society. Smoking exposure was accurately known and occupational factors could be accounted for. Risk ratios were adjusted for age, sex, race, cigarette smoking, exposure to passive cigarette smoke, body mass index, alcohol consumption, education, and occupational exposures. The expected effects of smoking were seen, but sulphate exposure (on the basis of measured community levels) was associated with a 36% increase in lung cancer and a 26% increase in other cardiopulmonary causes of death. Exposure to fine particles (PM_{10}s) was associated significantly with cardiopulmonary deaths (31% increase) but not significantly with lung cancer.

Both these studies therefore indicate that long term exposure to increased levels of sulphates or fine particles has a significant effect on long term survival. Thus, the association of increased mortality with particulate pollution in the time-series studies must be more than a "harvesting" phenomenon.

Additional evidence has been provided from a 14 year prospective study of a cohort of 3914 non-smoking Seventh Day Adventists in California.[22] The relative risks of developing chronic respiratory symptoms and of increased severity of airway obstructive disease and asthma were shown to be associated significantly with their calculated PM_{10} exposure levels.

PM_{10}, $PM_{2·5}$, and $PM_{1·0}$

The rapidly accumulating evidence of adverse impacts associated with PM_{10}s has led to a great deal of work to define the nature of particles in different environments. A detailed summary of present knowledge was presented in the UK report on non-biological particles.[2] A very brief summary of some points that might be important in relation to health impacts is shown in the box.

In the light of the consistency of the epidemiological data, it has been suggested that the most harmful components of current PM_{10} pollution are likely to be derived from combustion processes. The fact that smaller particles are likely to be responsible for the adverse health

effects was shown by the observation that hospital admissions in Toronto for acute respiratory disease in the summer were associated with PM_{10}s and with total suspended particulates (TSP), but there was no association with TSP minus PM_{10}[26] indicating that it was the smaller particles that were important.

Another important variable is the relationship between personal exposures and data from area monitors. Balogh *et al*[27] measured particle exposures at the kerbside using rapid response nephelometers and showed that a pedestrian would receive a short burst of up to 45 μg/m³ of particles of <2·5 μm in size as a diesel bus went past (fig 3). Such events must be commonplace and it is very likely that those in city traffic are commonly exposed to short bursts of particle concentrations higher than would be recorded by an averaging ambient monitor. It is perhaps for this reason that personal PM_{10} exposures, measured by monitors carried by the subject, generally show that exposures are higher in aggregate than would be indicated by ambient monitors.

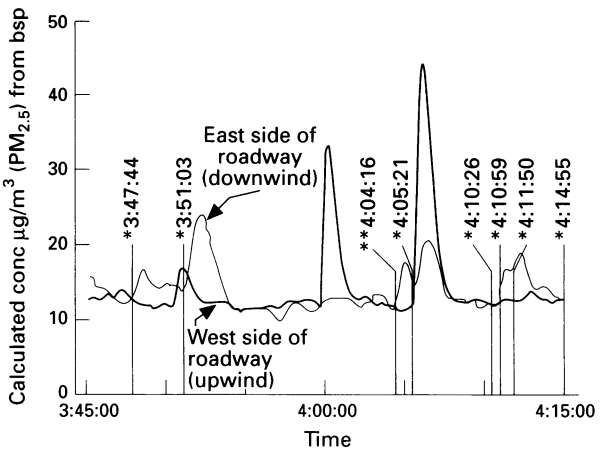

*Figure 3 Recordings made with fast response integrating nephelometers on either side of a paved road on the campus of the University of Washington in Seattle. When one bus passed the location at 4·04:16 there was a peak of $PM_{2·5}$ with a concentration reaching about 45 μg/m³. Calculations based on these observations suggest that a diesel bus with a low exhaust emits 50 times more $PM_{2·5}$ than an automobile. *Time bus passed sampling location; **time diesel bus passed sampling location. Reproduced with permission from Balogh et al.*[27]

Sulphur dioxide (SO_2), sulphates, and acidity

As noted above, SO_2 and PM_{10}s are often highly correlated. In the Philadelphia dataset, re-analysed in the Health Effects Institute report,[6] it was still uncertain whether SO_2 was or was not contributing to the mortality associated with PM_{10}s even after applying the most sophisticated statistical techniques available. Schwartz[14] has pointed out that "in communities with high correlations between outdoor particle concentrations, the outdoor SO_2 concentrations are likely to be a better proxy for personal particle exposure than for personal SO_2 exposure". This might account for the observation in Beijing that SO_2 is more closely related to mortality[28] and decrements in FEV_1 in non-smoking women[29] than is measured particulate pollution. Thus, in cities where the PM_{10} level might be much influenced by crustal dust (presuming that this is less toxic than combustion particles), SO_2 might be a better proxy for relevant PM_{10}

1. Particles less than 10 μm in diameter (PM_{10}s) are sometimes referred to as "inhalable". Alveolar deposition rises from about 10% at 5 μm to 30% at 0·1 μm and 50% at 0·05 μm.
2. Clean air contains as few as 200 particles/cm³ less than 10 μm in size. Particles in cities are not uncommonly at concentrations of 50 000 particles/cm³ and may rise as high as 100 000 particles/cm³. PM_{10} is a mass rather than a number concentration and is measured in terms of μg/m³. In the USA, where PM_{10} levels have been routinely measured for the last six years, mean annual values range from about 18 μg/m³ in more remote areas to 50 μg/m³ in other locations. The highest values are recorded predominantly in cities in California where particles derived from the earth's crust may make a meaningful contribution. The second highest mean 24 hour PM_{10} values (an index used by the US Environmental Protection Agency) range from a high of over 300 in Philadelphia county to more common values of 110–180 μg/m³ in 50 other locations. In these areas crustal particles exert little influence.
3. Assuming a concentration of 1000/cm³ of 0·05 μm particles, which would represent relatively clean air, the total number of particles deposited in the lung in a day would be 296×10^6 – that is, about 270 particles per alveolus in the human lung. Seaton and his colleagues[23] calculated that, at levels of particulate pollution recently recorded in Birmingham, "each lung acinus could receive some 30 million particles and each alveolus about 1500 particles every 24 hours, about 50% of which would be deposited".
4. Particles less than 1 μm in size are present indoors and outdoors at about the same concentration. This could be important since it implies that clinically significant exposure to particles of this size might be encountered by vulnerable people even without venturing out of doors.
5. The composition of the fine particle fraction is very complex. Most fine particles are formed by photochemical reactions of gases. These fine particles have a relatively high surface area and a wide variety of organic compounds are absorbed onto them. Analyses of Los Angeles air, for example,[24] shows that ammonium ions, aliphatic carbons, carbonyl carbons, and organonitrates are always present in submicrometer particles. Nitrate ions are present only in fractions larger than 5 μm. Sulphate ions appear to be present in all size fractions, even those down to 0·05–0·075 μm in size.
6. It must be assumed that the composition of PM_{10}s varies in the same locality at different times, and there must be significant spatial differences between PM_{10} composition in different cities and regions. In some locations wind blown dust may account for 50% of the PM_{10}s (this was thought to be the case in Leeds on one occasion).[21] In general, particles less than 1 μm are the result of combustion, with vehicles constituting the major emission source in most cities. It has been advocated that routine measurements in future should be of $PM_{2·5}$s which are less affected by windblown dust than PM_{10}s and a better indicator of combustion particle pollution.
7. Very fine particle fumes (of Teflon) have been shown by Oberdorster *et al*[25] to be very toxic to rats.

exposure than measurements such as TSPs which are heavily influenced by larger particles. The correlations observed between SO_2 levels and various health outcomes – for example, in Vancouver[10] – might in reality have been indicating a PM_{10} effect.

The case of sulphates is more complex. These are part of the PM_{10} fraction – indeed, sulphate can be detected even in the smallest particles, as referenced above. Much of the data, including that from the six cities longitudinal study,[20] shows as strong a relationship to sulphate aerosol as to PM_{10}. Furthermore, in many regions sulphate is strongly correlated with tropospheric ozone in the summer[30] hence, by inference, effects attributed to ozone might have been due to (unmeasured) PM_{10} levels. The possible role of sulphates (or nitrates) in the PM_{10} fraction probably cannot be evaluated by epidemiological studies and will have to await more detailed animal toxicology data.

There is evidence that aerosol acidity may also be important. As shown in fig 2, Lippmann and Ito[11] confirmed Ito and Thurston's earlier conclusion[31] that, in the London atmosphere, aerosol acidity (which was being measured only at one monitor) might be more predictive of mortality than either SO_2 or particles, although all three are strongly associated with mortality. Acid aerosol effects have been demonstrated in some field studies and Ostro *et al*[32] found that aerosol acidity was adversely affecting a panel of asthmatic subjects in Denver.

In terms of morbidity outcomes, recent data suggested that PM_{10} and tropospheric ozone are probably acting independently.[14 33 34]

Problem of biological plausibility

Reaching a causal inference from associative data is always complex and often divisive – even if those with vested interests are excluded.[35] Some scientists are unwilling to make a causal inference until the biological mechanism is understood,[36] others are prepared to do so if the criteria of consistency and coherence are met.[37]

The British report[2] concluded: "In terms of protecting public health it would be imprudent not to regard the demonstrated associations between daily concentrations of particles and acute effects on health as causal". This is an interesting use of the double negative.

The question of what kind of animal toxicological evidence one would require to state that the "biological plausibility of PM_{10} was established" is difficult to answer. It is not easy to replicate the actual city atmosphere subsumed under the general heading of "PM_{10}" as the process of collection or manufacture of aerosols might change the many complex organic compounds that are an important part of the fine fractions.

Seaton and his colleagues[23] proposed that the calculated fine particle loading of the alveoli might well be sufficient to trigger an alveolitis with the release of mediator substances; these, in turn, might affect blood coagulability and hence influence cardiovascular mortality and morbidity. This interesting hypothesis will undoubtedly lead to a more refined approach to animal experimentation on this question.

Conclusions

This review has attempted to provide a "defensive" knowledge of particulate air pollution for a chest physician who has not had to consider the detailed data and analyses that have been published. The topic has become very complex, and the reader should be warned that almost every statement made here could be qualified and elaborated.

The possible contribution of PM_{10} levels to increased mortality and morbidity is of prime importance from a public health standpoint. The estimated economic cost of the adverse health effects of air pollution is dominated by the effects of PM_{10} levels and any assumption about a threshold for PM_{10}s has a considerable effect on the economic estimates derived. What is now a considerable literature cannot be discussed in detail here, but two statistics may give an indication of the emerging field:

1. In the north east of North America, including Ontario and Quebec, using sulphate data only for computation, the mean health benefits (or reductions in the calculable costs incurred) from the modest reductions in SO_2 emissions projected in the 1990 US Clean Air Amendments have been calculated to amount to $40 billion per year by the year 2010.[38]
2. In Los Angeles the current adverse health costs would be met by imposing a 3 cent/mile tax on every automobile and a 52 cent/mile tax on every heavy diesel truck.[39]

There are differences in the interpretation of current air pollution/health data, well exemplified by the

LEARNING POINTS

* **Particles less than 10 μm in size (PM_{10}s) are associated with measurable increases in daily cardiovascular and respiratory mortality.**
* **PM_{10}s are also associated with hospital admissions for pneumonia, aggravation of asthma, and decrements of lung function in children.**
* **The biological mechanisms underlying these effects are not yet understood.**
* **The composition of fine particles in cities is very complex, but many are sulphates and most are derived from combustion, particularly of petroleum products (e.g. diesel) in vehicles.**
* **The economic costs attributable to particulate air pollution are likely to be considerable.**
* **The need for more stringent air pollution controls should be considered a high priority for the protection of public health.**

generally negative recent UK review of air pollution and asthma[40] and the much more positive recent US review of much of the same material.[41] It is to be hoped that the current controversy concerning the relevance of particulate pollution does not obscure the urgent need for more data, particularly on the possible biological phenomena underlying the epidemiological observations.

I am grateful to Dr D Dockery and Dr S Vedal for their criticisms of the first draft of this review. They are in no sense responsible for the final draft.

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