

DEPARTMENT OF HEALTH

**Committee on the Medical Effects
of Air Pollutants**

**Quantification of the
Effects of Air Pollution on
Health in the United Kingdom**

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Health in the United Kingdom: Professor JG Ayres

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1

Executive Summary

1.1 The Department of Health (DH) asked the Committee on the Medical Effects of Air Pollutants (COMEAP) to advise on the extent of effects of air pollutants on health in the United Kingdom (UK), including an estimate of the numbers of people affected. The Committee formed a sub-group which reviewed the available literature and drafted this report. The report has been endorsed by the Committee.

1.2 The terms of reference of the sub-group were to advise on:

“the number of people in the UK whose health was affected by exposure to air pollution”.

1.3 The sub-group has reviewed in detail the available information, has drawn heavily on the reports published by COMEAP and by the earlier Advisory Group on the Medical Aspects of Air Pollution Episodes (MAAPE), and has reviewed work published since the publication of these earlier reports.

Approach

1.4 A framework for estimating the impact of air pollution on health was defined. This involved identification of the most appropriate risk estimates linking concentrations of pollutants and effects on health, considering the extent of exposure of people in the UK to air pollutants and estimating the effects of this exposure on background rates of the relevant health effects.

1.5 It was decided that estimates of effects would only be provided when there were available:

exposure-response relationships (coefficients) which, in the view of the sub-group, could be applied in the UK with reasonable confidence;

and,

adequate data on the distribution of concentrations of air pollutants across the country which could be combined with data on population to provide estimates of population exposure.

These provisos led to the analysis being focused on the population of Great Britain (GB) (excluding Northern Ireland) and, in terms of health effects, on numbers of deaths and numbers of hospital admissions. Studies of the effects of sulphur dioxide, particles, nitrogen dioxide and carbon monoxide have tended to focus on urban areas. Satisfactory data on the concentrations of these pollutants were available for urban areas of GB and thus estimates of effects of these pollutants were limited to these areas. For ozone, data from rural areas were available and thus for this pollutant the analysis was widened to “all GB”.

1.6 The estimates of the exposure-response relationships are based on the results of time-series studies. These studies examine the relationship between daily levels of pollution and the risk of adverse health effects, on the same day or subsequent days, adjusting for climate and other factors. Risks have been expressed as percentage change in health effect per unit change in daily pollutant concentration. In subsequently estimating impacts

the country was divided into grid squares. For each grid square the effects of air pollutants on individual health outcomes were calculated by multiplying the exposure-response coefficient (derived from time-series studies) by the ambient concentration (using the appropriate averaging time), the background rate for the health outcome considered (eg, deaths per 100,000 population per year) and the population in the grid square.

1.7 It was agreed that sufficient data were available to allow estimates to be made of the effects of ozone, particulate matter and sulphur dioxide on both all causes of deaths and on admissions to hospital for respiratory disorders. For nitrogen dioxide we are much less sure about the reliability of estimates of effects. For this reason the results of the calculations relating to nitrogen dioxide are not included in this Executive Summary but are discussed in Chapter 8. For carbon monoxide there were insufficient data to allow estimates of effects in the UK to be made with acceptable accuracy.

1.8 For reasons explained in the Introduction (Chapter 2) the sub-group has chosen to present data derived from these calculations in terms of the number of deaths or hospital admissions affected by pollutants in the course of the given year. Deaths are affected by bringing forward the date of death; unfortunately it is not possible to estimate by how long. It is believed that for hospital admissions, which are not once-only events as are deaths, the available data can be extrapolated to say:

air pollution contributes to the causes for the admission to hospital of n people per year (this includes readmissions).

Some hospital admissions may be brought forward whilst others may be truly additional. The split between these groups, if any, is unknown.

1.9 With respect to deaths a number of other workers have stated the results of similar calculations in terms of *extra* events occurring in a given year. We think this form of presentation is misleading because it implies that the events would not have taken place during the given year had it not been for exposure to the air pollutants. There is no certainty that this is true. Both deaths and hospital admissions of the same individuals may well have occurred during the given year without the added effects of exposure to air pollution. It should be stressed that both the deaths and hospital admissions affected are likely to occur in patients with severe pre-existing disease.

1.10 An assumption of causality has been made in making the calculations reported here. This reflects the previous work of COMEAP in which most of the members of the sub-group had been involved. The sub-group's work included a new review of the methodological issues involved in assessing causality and how these might apply in the context of air pollution and health by a professional statistician (Professor M J Campbell). The purpose was to highlight to members the methodological issues in case anything important had previously been overlooked; it was not intended to fully review again the question of the causality of air pollution. This methodological review, included here as Appendix 1, did not lead the sub-group to revise its judgement: that the associations are causal is accepted as likely.

Results

1.11 The overall results are given in the following tables (see Tables 1.1 and 1.2). The estimates provided in these tables should be read in conjunction with the relevant chapters of the report. The effects of particles and sulphur dioxide are estimated assuming no threshold for the health effects of these pollutants. The main impacts are on the urban population and rural areas are not included in the calculations. For ozone, both urban and rural areas are considered but for the summer months only. The ozone estimates are strongly sensitive to assumptions regarding a threshold. In assuming no threshold of effect it has been accepted that extrapolation beyond the range of the reported data is allowable. This point is arguable and where it has been done our estimates should be interpreted as worst case estimates. A detailed discussion of the subject of thresholds is presented in Chapter 2.

1.12 It is stressed that the effects on mortality have not been fully quantified. Many of the deaths associated with days of higher air pollution are in the elderly and the sick. Episodes of cold weather and epidemics of the common cold hasten the deaths of such people and it seems likely that air pollutants could act in a similar manner, hastening death by a few days or weeks. If this is the major effect, the impact of air pollution episodes on mortality will be relatively small, but we have been unable to establish the extent by which the time of death has been altered.

Table 1.1 **Numbers of deaths and hospital admissions for respiratory diseases affected per year by PM₁₀* and sulphur dioxide in urban areas of Great Britain**

Pollutant	Health Outcomes	GB Urban
PM ₁₀	Deaths brought forward (all cause)	8100
	Hospital admissions (respiratory) brought forward and additional	10500
SO ₂	Deaths brought forward (all cause)	3500
	Hospital admissions (respiratory) brought forward and additional	3500

* PM₁₀: particulate matter generally less than 10 µm in diameter

Estimated total deaths occurring in urban areas of GB per year = c430,000

Estimated total admissions to hospital for respiratory diseases occurring in urban areas of GB per year = c530,000

Table 1.2 **Numbers of deaths and hospital admissions for respiratory diseases affected per year by ozone in both urban and rural areas of Great Britain during summer only**

Pollutant	Health outcomes	GB, threshold = 50 ppb	GB, threshold = 0 ppb
Ozone	Deaths brought forward: all causes	700	12500
	Hospital admissions (respiratory)	500	9900
	brought forward and additional		

1.13 Two important points should be emphasised in interpreting the results shown above:

- (a) co-variation of pollutants means that in some instances we do not know which individual pollutant or mixtures of pollutants has caused the recorded effects or whether some additive or synergistic effects have taken place;
- (b) it follows that a reduction in the concentration of a single pollutant may produce different benefits than predicted by exposure-response relationships based on observational studies.

Long-term effects

1.14 In the view of the sub-group and COMEAP, in addition to the effects recorded here, it is likely that long-term exposure to air pollutants also damages health. At present there are insufficient UK data to allow acceptably accurate quantification of these effects and the sub-group was not confident in applying to the UK estimates of exposure-response coefficients from long-term studies undertaken elsewhere. However, if estimates made elsewhere, especially in the USA, do apply in the UK, they suggest that the overall impacts may be substantially greater than those that we have as yet been able to quantify.

Future work

1.15 In the view of the sub-group and COMEAP, the results presented in this report provide a compelling case for more research. It is recognised that, to some extent, this recommendation is already being met by the current DH/DETR/MRC research initiative on air pollution and health. However, we feel that research on the following is needed to allow an improvement of the estimates provided in this report:

- the years of life lost as a result of day to day variations in levels of air pollutants;
- the impact on health of long-term exposure to current levels of air pollutants;
- research on groups at special risk, the elderly and especially the chronic sick; and
- studies of the effects of air pollutants on outcomes other than death and hospital admissions.

2

Introduction

Background

2.1 The Sub-Group on the Quantification of the Effects of Air Pollution on Health in the UK was asked to produce a report, the object of which was to quantify - as far as practicable - the health effects of current levels of air pollution in the UK and devise confidence limits for such quantification. This was against the background of the United Kingdom National Air Quality Strategy, published by the previous Government in March 1997, which requires that reductions in levels of air pollutants will be assessed in terms of their benefits, including their benefits to health. While it was not the purpose of this report to move onto costing such effects, the report could be used as the basis for any such analysis.

2.2 The current Government has since adopted the air quality standards published in the United Kingdom National Air Quality Strategy. This work and that of an expert group of economists covering the monetary valuation of the benefits of reducing levels of air pollution will be an integral part of the review of the Strategy which the Government has announced.

Procedure

2.3 In theory, estimating the effects of air pollutants on health is straightforward; in practice it is very much more difficult. The following steps may be defined:

Identify the important pollutants which exert an effect and at what levels they are currently found in ambient air.

2.4 This is easily done by identifying those pollutants which have been shown to be associated with effects on health from the literature. The main pollutants to consider for the purposes of this report are particles, sulphur dioxide, ozone, oxides of nitrogen and carbon monoxide.

Assessment of the likely exposure of the relevant population(s) to these levels

2.5 Again, this is relatively easily determined by use of the UK database of air pollution levels. This is based on outdoor fixed site monitors. From the point of view of health effects on an individual, however, it is not just the concentration of pollutants in air which is important, as duration of exposure, concomitant physical activity and co-exposure to other pollutants (to name but some) may all play a role. However, the epidemiological studies assess risks to health in relation to outdoor fixed-site monitors also; thus, the quantification of impacts in a population can by-pass the issue of variations in personal exposures.

Definition of the relationship between health effects and ambient concentrations of air pollutant in terms of change for a given change in air pollutant level (exposure-response relationship)

2.6 The available epidemiological literature needs to be assessed to find studies of suitable quality to see how consistent are their estimates of effects per unit change in pollutant levels and to derive exposure-response relationships applicable to the UK. A particular difficulty is in assessing if thresholds exist at the population level. This was highlighted by the World Health Organization (WHO) which, in the latest revision of the Air Quality Guidelines for Europe, decided not to recommend a guideline level for particles but,

instead, defined a series of exposure-response relationships for different health endpoints.¹ These relationships make no assumptions regarding thresholds and comprise the reported regression relationships between concentrations of pollutants and effects on health. The World Health Organization came to a similar conclusion about ozone. This area of health effect estimation is poorly developed and in this report we have had to make a number of simplifying assumptions which are explained.

Application of the coefficients to the population(s) under consideration to quantify an overall effect

2.7 Once a coefficient has been established for a particular pollutant-health effect relationship, then the overall effect can be calculated by taking into account the number of people who are exposed and the levels of pollution to which they are exposed.

2.8 These provisos led to the analysis being focused on the population of Great Britain (GB) (excluding Northern Ireland) and, in terms of health effects, on numbers of deaths and numbers of hospital admissions. Studies of the effects of sulphur dioxide, particles, nitrogen dioxide and carbon monoxide have tended to focus on urban areas. Satisfactory data on the concentrations of these pollutants were available for urban areas of GB and thus estimates of effects of these pollutants were limited to these areas. For ozone, data from rural areas were available and thus, for this pollutant, the analysis was widened to “all GB”.

Outcomes

2.9 We have also had to address the problem of which health outcomes to assess, ranging from day to day changes in mortality through to changes in symptoms. We have considered the severe outcomes of mortality and hospital admissions bearing in mind that following an increase in daily pollution levels these effects will only occur in those patients with pre-existing severe disease, and not in healthy individuals. In the case of mortality, an individual's death may be brought forward by an increase in pollutant exposure on a prior day or days. The same increase in pollutant levels may result in hospital admission for one individual but not the next depending, amongst other factors, on disease severity.

2.10 We have also considered studies at the individual level which do not involve routinely collected health outcome data, such as panel studies which concentrate on symptoms and changes in lung function in groups of individuals. We found that for some outcomes only one or in some cases a few, studies have been reported. This makes the determination of a possible range of effects and the demonstration of consistency of effects impossible. Also, most studies have been undertaken in environments with different pollution levels than found in the UK. In addition, it was noted that differences between study findings tended to be greater for these outcomes than for mortality and hospital admissions.

Causality

2.11 Once an association between a health effect and an air pollutant has been identified, it has to be decided whether such an association is likely to be causal. For some pollutants, good consistent evidence of health effects is available, while for others it is less strong and often inconsistent. It is worth stating now that in making our estimates of effects we have assumed that the reported associations between the pollutants and the health outcomes considered are causal. The detailed review of the methodological issues involved in assessing causality, reported in Appendix 1, has focused attention on problems, but did not persuade members of the sub-group to move from the position taken in earlier DH reports, ie, that it would be imprudent not to regard the reported associations as causal. Note, however, the overall estimates of the health effects of an air pollution mixture may be reliable even if there remains doubt about the attribution of effects to the individual pollutants which contribute to the mixture as a whole.

Transferability

2.12 Most of the relevant studies that have been undertaken in recent years come from outside the UK. This gives rise to the problem of how well the results of such studies can be extrapolated to the UK, either qualitatively or - more importantly for the purposes of this report - quantitatively, or both. This is compounded by the small number of studies which are available for some pollutant-health relationships. If there are only one or two data sets available for a particular case then, while it may be possible to produce an estimate of size of effect, it would be difficult to be sure of how reliable such an estimate would be for the general UK population.

Sources

2.13 The series of reports published by the Advisory Group on the Medical Aspects of Air Pollution Episodes (MAAPE)²⁻⁵ and the Committee on the Medical Effects of Air Pollutants (COMEAP)^{6,7} have provided a basis for establishing the relationships between responses, in health terms and exposure to pollutants. These reports have dealt with ozone, sulphur dioxide, nitrogen dioxide and particles. The final report from MAAPE addressed the effects of mixtures of pollutants. In addition, we made use of the published literature from both the UK and abroad which had appeared since the publication of these reports. Where suitable UK data have been available these have been used; in other cases data from Europe and North America have been used.

Types of study considered for use in the report

2.14 A number of different types of study were considered for use in our deliberations. These may be divided into:

- a animal and *in vitro* studies;
- b chamber studies involving exposure of volunteers to carefully controlled levels of pollutants;
- c epidemiological studies.

Excluded studies

2.15 We have not used animal or *in vitro* studies as these cannot give an estimate of the size of human health effects.

2.16 We have used chamber studies solely as a means of confirming that effects can occur during short-term exposures to air pollutants. We have not attempted to use such studies to quantify health effects as they usually involve short-term exposures to often high concentrations of pollutants and involve the measurement of limited endpoints such as changes in indices of lung function. These studies also involve adult volunteers, either normal subjects or patients with mild disease. We took the view that population-based studies into the health effects of air pollution suggest that the individuals most likely to be affected are those with more severe disease who tend not to be recruited into chamber studies. Consequently, to extrapolate from studies of small numbers of volunteers to effects on overall populations might be misleading.

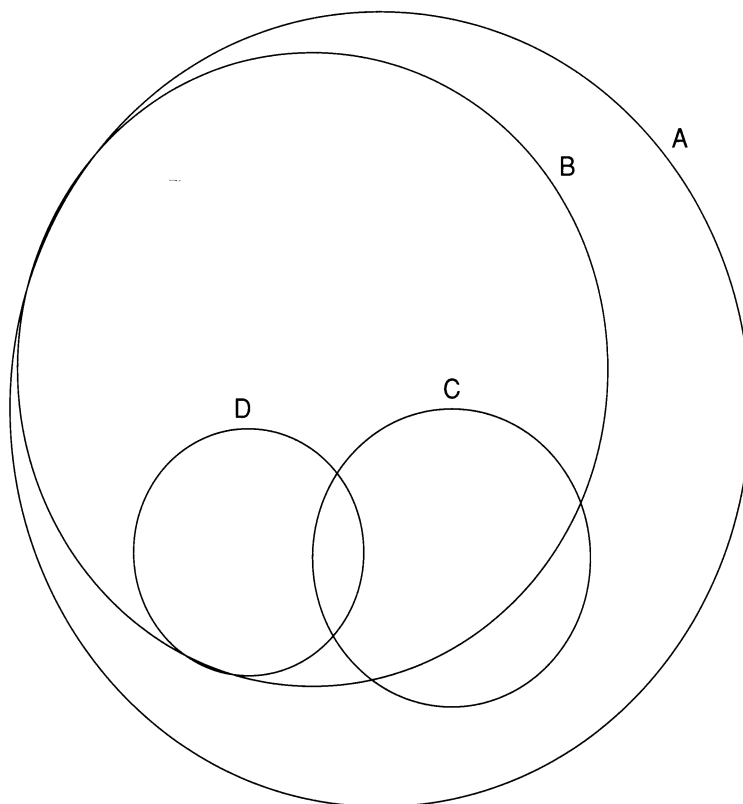
2.17 We have not examined studies of surrogates for ambient particles such as environmental tobacco smoke. Genotoxic carcinogens (eg, benzene, 1,3-butadiene) are excluded from this report as it is accepted that these are “non-threshold” compounds whose health effects are immeasurably small at levels currently prevalent in the ambient air of the UK.

Included studies

2.18 We have therefore concentrated on data derived from epidemiological studies which can be divided into two broad groups, a) time-series studies and b) cohort and cross-sectional studies. Time-series studies examine the more-or-less immediate effects of day-to-day changes in ambient pollution levels. The cohort studies and cross-sectional studies take into account the effects of longer-term exposure to ambient pollution. We also point out that the time-series data may shed light on a quite different population from that

considered in the cohort and cross-sectional studies. For instance, consider mortality and the effect of particles (see Figure 2.1).

Figure 2.1 **Relationship between deaths advanced by exposure to particles and deaths from illness induced by exposure to particles.**



The areas shown are illustrative only and should not be interpreted in any quantitative sense

- A Total deaths occurring in the UK
- B Deaths due to diseases that have been shown to be associated with day to day changes in concentrations of particles: eg, heart attacks and deaths from respiratory disorders
- C Deaths triggered or advanced by day to day variations in concentrations of particles
- D Deaths due to diseases caused by chronic exposure to particles

Deaths from only some causes, notably cardio-respiratory diseases, have been associated with day-to-day changes in levels of particles (Area B in the figure). Partly within this area, and overlapping each other to an extent, are those deaths which were triggered or advanced by day-to-day variations in levels of particles (Area C) and those whose deaths were due to diseases falling within Area B but which were induced by chronic exposure to particles (Area D). Those deaths in Area C will be covered by time-series studies whereas cohort studies will be embraced by Areas C & D. Consequently, some deaths may have been due

to a condition induced (at least in part) by air pollution but whose time of death was also determined by a change in particle levels on the day or so before or on the day of death. The figure is illustrative only as the exact areas of overlap and sizes of some of the areas are not known even approximately. Indeed the great majority of information on the health effects of air pollution concerns exacerbations of pre-existing disease (Area C), whereas the chronic effects of exposure to air pollution are less well understood and have been addressed by fewer studies. The actuarial method of assessing life lost on the basis of the cohort studies (eg, the Six Cities Study⁸) reported by the WHO¹ has been considered and we feel that this may provide an important estimate of the effect of long-term exposure to particles. However, we felt that there was insufficient information to quantify the induction of disease by air pollution in the UK.

2.19 The estimates of the exposure-response relationships that we have used are based on the results of time-series studies. These studies examine the relationship between daily levels of pollution and the risk of adverse health effects, on the same day or subsequent days, adjusting for climate and other factors. Risks have been expressed as percentage change in health effect per unit change in daily pollutant concentration. In subsequently estimating impacts the country was divided into grid squares. For each grid square the effects of air pollutants on individual health outcomes were calculated by multiplying the exposure-response coefficient (derived from time-series studies) by the ambient concentration (using the appropriate averaging time), the background rate for the health outcome considered (eg, deaths per 100,000 population per year) and the population in the grid square. For reasons explained below, the sub-group has chosen to present data derived from these calculations in terms of the number of deaths or hospital admissions, affected by pollutants in the course of the year. Deaths are affected by bringing forward the date of death; unfortunately it is not possible to estimate by how long. It is believed that for hospital admissions, which are not once-only events as are deaths, the available data can be extrapolated to say:

air pollution contributes to the causes for the admission to hospital of n people per year (this includes readmissions).

Some hospital admissions may be brought forward whilst others may be truly additional. The split between these groups, if any, is unknown. With respect to deaths a number of other workers have stated the results of similar calculations in terms of extra events occurring in a given year. We think this form of presentation is misleading because it implies that the events would not have taken place during the given year had it not been for exposure to the air pollutants. There is no certainty that this is true. Both deaths and hospital admissions of the same individuals may well have occurred during the given year without the added effects of exposure to air pollution. It should be stressed that both the deaths and hospital admissions affected are likely to occur in patients with severe pre-existing disease.

Exposure-response relationships

2.20 We came to the conclusion that when calculating the size of the effect of a pollutant on a health-outcome indicator, two factors needed to be considered.

- a Firstly, what the exposure-response relationship was thought to be for the range of concentrations studied.
- b Secondly, whether the exposure-response relationship applied at low concentrations, ie, the existence or otherwise of a threshold of effect for each pollutant had to be determined.

2.21 It is accepted by many that at an individual level thresholds of effect for common pollutants are likely although epidemiological studies are unlikely to be able to determine a population threshold. One of the main reasons for this is the distribution of personal exposure which inevitably exists across a population. This cannot be taken into account when relating population-level measures of health effects to single, fixed-site measurements of concentrations of pollutants. The health effects have been dealt with on a pollutant by

pollutant basis, particularly as the database on individual pollutants is better developed than that on mixtures of pollutants and as the UK National Air Quality Strategy deals with individual pollutants.

2.22 As there are so many factors which can cause or contribute to each medical condition, for example, exacerbations of respiratory disease, only those studies where adequate allowance was made for the effects of confounding factors were considered, particularly as, at an individual level, the effects of air pollution are small. In time-series studies of effects in a given population the main confounders concern seasonal and climatic effects.

2.23 In cohort or cross-sectional studies which contrast the experience of populations in different locations, factors such as cigarette smoking, occupational exposures and poverty are also important. Cross-sectional studies which did not take account of confounders at the level of the individual subject were not included. Additionally, the so called “Two Town” studies were not considered because of the low statistical power of this type of study.

2.24 More generally, the sub-group informally assessed the available studies which were divided into three categories:

- a suitable for use in UK quantification of effects;
- b limited value for UK quantification of effects;
- c inadequate for UK quantification of effects.

Consequently, while the original aim was to quantify as many health effects as possible, in many cases the data available were not considered adequate to the task.

2.25 In establishing the basis for quantification of effects, we first determined whether there was sufficient evidence available for an exposure-response relationship to be identified for each pollutant. A choice had to be made on the shape of any such relationship, eg, linear or curvilinear, and we took the view that, for the purposes of this exercise, the computational simplicity of using linear relationships justified the approximations involved. A clear biological mechanism of effect was not deemed necessary for an effect to be quantified although the biological plausibility for such an effect was important supporting information.

2.26 We then had to decide for each pollutant whether a threshold of effect existed or whether the evidence suggested a relationship which was maintained right down to very low levels of pollutant exposure. The next step was to decide how to partition the effects on health, ie, identifying all effects (whether due to anthropogenic emissions or not) or just limit our estimates to those thought to be due to man-made emissions. For example, in the case of particles it is generally accepted that there is no threshold for health effects at a population level and that the exposure-response relationship extends to zero. This is, of course, based on statistical extrapolation beyond the data and on theoretical considerations but not on any empirical evidence. However, there is a background level of exposure which is due to airborne dust from surface soil, sea salt, etc, which is responsible for about $5 \mu\text{g}/\text{m}^3$ of urban levels of PM_{10} . If one accepts that there is no threshold, then quantification can either deal with mortality attributable to all particle elevations above zero concentration or with those deaths associated with exceedances above background levels. If one accepts that daily mortality increases by 1% for each $10 \mu\text{g}/\text{m}^3$ increase in PM_{10} then on a day when the total PM_{10} concentration is $30 \mu\text{g}/\text{m}^3$ the percentage excess deaths due to particles will be 3% “if all particles are considered” or 2.5% “if only anthropogenic particles are considered” (assuming that $25 \mu\text{g}/\text{m}^3$ of the total $30 \mu\text{g}/\text{m}^3$ are of anthropogenic origin).

2.27 Though there is some evidence to support the idea that non-anthropogenic particles are less injurious to health than anthropogenic particles, it was decided that it would be unwise to try to apportion the effects on this basis. Detailed toxicological data are lacking and available epidemiological studies relate effects to total particle concentrations.

The problem of chronic effects

2.28 The long-term effects of continued exposure to pollutants may well be more important than acute effects of brief episodes, but they are more difficult to study. People who live in polluted areas are likely to differ in various ways from people who live in an unpolluted environment. It is not easy to allow for the confounding variables (eg, smoking, diet) particularly if they include subtle sociological and behavioural factors. This is not an issue with the acute studies, since the background factors are constant. Another problem is that information about exposure is usually available only for the present and the fairly recent past, while some of the effects may be attributable to exposure in childhood. It is difficult to estimate the relationship between exposure and chronic effects unless conditions have remained constant for many years. Because of this we decided not to try to estimate the effects on health of long-term exposure to air pollution. It was recognised that work in this area is developing rapidly and estimates of average life lost due to exposure to ambient concentrations have been made (see Chapter 3). It is accepted that if work underway in the UK confirms these estimates then our estimates of effects will require revision. Relating the impact on health of short-term variations in levels of pollution to the effects of long-term exposure will not be easy.

Summary

2.29 We decided that risk estimates could be produced for the urban population of Great Britain, and for both the urban and rural population in the case of ozone, but that it would be difficult to define confidence limits for such effects. Much thought was devoted to the problem of providing some indication of the likely accuracy of the estimates made. It was felt that the available data did not allow the calculation of formal confidence limits and that any informal estimate of upper and lower bounds was liable to misinterpretation. Thus, only our best estimates of likely effects have been reported.

Coda

2.30 This work had to be conducted within a short span and we took the view that predominant use of secondary sources of information was appropriate especially as a number of the Committee members were involved in the production of earlier reports produced by the Department of Health. We feel that our approach provides a reasonable estimate of the extent to which air pollution has been shown to be currently affecting the health of the population of the UK, though other effects currently assessed as unquantifiable, especially the effects of longer-term exposures, may also have a significant impact.

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3

Particulate Matter

Introduction

3.1 The epidemiological and other evidence linking ambient particulate air pollution with both acute and chronic health effects has been reviewed frequently and extensively in recent years.¹⁻⁴ We do not intend to review that evidence here.

3.2 We have taken as a working basis that ambient particles are causally related to both 'acute' and 'chronic' health effects. The task then becomes one of identifying what health endpoints should be included in the quantification; with what indices of particles they should be related; and what are the most appropriate exposure-response functions for representing that quantification.

Diverse ways of representing ambient particles in epidemiological studies

3.3 Ambient particles are a complex mixture, varying in size and in composition, and there is diversity in how particulate air pollution is characterised in various epidemiological studies. This diversity is described in more detail in the COMEAP Report on Non-Biological Particles and Health.²

Criteria for selecting indices of particles

3.4 In selecting which indices of particles are most relevant to this quantification, we have taken account of:

- a what is known about the relative toxicity of various kinds of inhalable particles;
- b the strength of international epidemiological evidence linking various indices of ambient particles to acute and chronic health effects, with special reference to studies in the UK and elsewhere in Europe;
- c the ability to link exposure-response functions to sufficiently reliable maps of background concentrations of air pollution in the UK; and
- d relevance to environmental policy.

Toxicity: what particles are biologically relevant?

3.5 Although several possible mechanisms of the acute or chronic effects of particulate air pollution on health are under consideration currently, none of these is as yet well-established and widely accepted as a biological explanation of the observed epidemiological relationships. Correspondingly, there is not a clear picture of the relative toxicity of various kinds of inhalable particles.

3.6 There is however evidence, and strong conjecture, that the reported effects on health are due principally to particles from combustion sources (both primary particles, emitted directly from combustion processes; and secondary particles, formed subsequently when gases emitted from combustion interact with other atmospheric components); and that, per unit concentration of PM_{10} , the generally coarser natural dusts are much less associated with health effects than the finer particles.²⁻⁴

3.7 It is probable that the toxicity of particles varies also according to their composition and surface properties, and, for example, is greater with higher acidity, and less in proportion to their solubility. Finally, there may be complex interactions between particles

and other constituents of airborne pollution though, in general, this has not been demonstrated in epidemiological studies.

Range of epidemiological studies, including indices from UK and European studies

3.8 There are now many studies internationally which use PM_{10} as the principal index of ambient particles.⁴ These are mostly but not exclusively from North America. In the UK, PM_{10} was used in a recent study of mortality and hospital admissions in Birmingham.⁵ The major European APHEA study, across 12 cities, does not include any with measures of PM_{10} but some cities report results using PM_7 or PM_{13} .⁶ PM_{10} has, however, been studied in relation to mortality in Amsterdam.⁷

3.9 There are several UK studies, including both earlier⁸ and recent analyses of air pollution and health in London,⁹⁻¹¹ where particulate matter is characterised in terms of Black Smoke (BS). Black Smoke was also the available measure of particles in many of the cities studied by the APHEA group.⁶ These studies have led to exposure-response relationships being reported in terms of levels of Black Smoke. The problem, from the viewpoint of quantification, is the lack of suitable maps of background concentrations of BS (see below).

3.10 There is as yet a limited amount of epidemiological evidence on the health effects of $PM_{2.5}$, sulphates and other fine fractions of ambient particulate matter.^{2,3} The available evidence comes almost entirely from North America.

Mapping of background concentrations

3.11 If we have or assume a linear exposure-response relationship, no threshold, and independence of daily effects of pollution, then it is sufficient in quantifying acute effects to characterise background pollution in terms of annual average concentrations. In addition, the annual average is the appropriate characterisation in studying chronic effects.

3.12 Background concentrations of annual average PM_{10} have been mapped in the UK, using measurements from urban PM_{10} monitors, from the more extensive network of NO_x monitoring, and suitable NO_x/PM_{10} conversion factors. Using available data from other studies, it is possible also to construct suitable maps in terms of background (annual average) concentrations of $PM_{2.5}$ and of sulphates. Despite widespread monitoring of BS, there are, however, no existing suitable maps of background concentrations.

Choice of index of particulate matter

3.13 A number of different indices of particulate matter might be chosen and it might be asked whether the choice made is of critical importance. Our conjecture is that it does not matter much. Briefly, any quantification of the effects of total background particles, as in this exercise, involves a stage of linking background concentrations with exposure-response functions expressing the effect of unit concentration of particles on health outcome. The *product* of background concentration, and (%) change in health effect per unit concentration, is more-or-less invariant to the choice of particle index. For example, if $PM_{2.5}$ rather than PM_{10} is used as the basis of quantification, then the background concentrations (in terms of $\mu g/m^3$) will be lower, and the % change per unit exposure will be higher, by approximately the same factor; and so the product of background concentration and percentage change will be similar under the two characterisations of ambient particles.

3.14 Against this background, the sub-group decided to base its quantification on particles expressed as PM_{10} only and, as far as practicable, only to use exposure-response functions from studies where PM_{10} was investigated directly.

Thresholds

3.15 For particles it is likely on toxicological grounds that for each individual there is a level of exposure below which no significant effects on health are likely. It also seems likely that there will be a distribution of individual thresholds in a population: that everybody should have exactly the same threshold of effect seems exceedingly unlikely.

There is, however, no good evidence of a threshold at the population level; ie, it appears that, for a large population even at low background concentrations measured at single, fixed-site monitors, some vulnerable people are exposed some of the time to concentrations which for them have an adverse effect. It is likely that in any population there will be a variation of personal exposure across the population. The combination of variations in individual sensitivity and individual exposure are likely to combine to make any attempt to define a 'population threshold' illusory.

3.16 Of all pollutants this understanding first grew in the context of ambient particles, where the 'no threshold' concept is now quite well established as a basis for understanding and for policy. Against this background, the quantification of particulate health effects has been carried out assuming no threshold. This involves extrapolation beyond the data reported in epidemiological studies since these are normally conducted in cities where daily levels of particles almost never reach zero.

General remarks on transferability

3.17 A major underlying issue in any assessment of this sort is the balance between specifically UK studies, and the wider international evidence. The international evidence remains very important in influencing judgements on the reliability of associations, and on causality. In terms of quantification, however, there is a trade-off between the much greater weight of evidence from studies internationally, compared with those in the UK; and the greater direct relevance of UK studies.

US/Europe comparisons/ transferability

3.18 Most existing quantifications of air pollution impacts have been highly dependent on results from epidemiological studies carried out in North America. Fortunately, now, for severe acute health effects (mortality and hospital usage), there are extensive European data, principally from APHEA.^{6,12}

3.19 Differences between the results reported by North American workers and those in the UK and Europe remain. For acute mortality, where the evidence is strongest, the estimated effect of particles is generally lower in Europe than in North America. The reasons for this are not well established; but they may relate to the higher exposure to acidic aerosols in the US or, perhaps less plausibly, be because of higher co-exposures to SO₂ in Europe.

3.20 For particles (PM₁₀), the estimated effects on respiratory hospital admissions (expressed as % change per unit concentration) are also substantially lower in Europe than in North America.

3.21 These results strongly suggest that exposure-response functions should not be transferred without qualification from North America to Europe. The issue is particularly important for health outcomes where there are no suitable European studies.

Within UK, UK relative to US/Europe

3.22 Once again, the main evidence refers to acute mortality and hospital admissions. The main studies are from London/SE England,⁹⁻¹¹ and from Birmingham,⁵ though the results differ. Briefly, the recent London results do not show a strong particle effect and are comparable to the general APHEA findings from Western European cities. However, the most recent Birmingham results, in terms of PM₁₀, show acute mortality effects much more like the US values than the (lower) European ones. In terms of percentage change in health outcome per unit change in PM₁₀, the Birmingham results on respiratory hospital admissions are higher even than the North American estimates.

3.23 These differences do not necessarily reflect or imply correspondingly large differences in particle effects from place to place within the UK. The Birmingham results show wide confidence intervals and some variation between studies is to be expected, even if the underlying effects are the same. However, they do caution against simple

extrapolation of results from any one UK city to another. Also, it is unclear whether, in quantification, the UK overall fits best into the West European pattern or into the wider international scene, as dominated still by North American studies.

Acute health effects

Acute mortality

3.24 There is more information available about acute mortality than about any other endpoint. From the extensive international literature, Table 3.1 gives some exposure-response relationships which might be used. Two of these are from major recent analyses, combining results from several cities:^{4,6} hence the narrow confidence intervals compared, for example, with the Birmingham single-city study.⁵

Table 3.1 **Acute Mortality (All Cause) and Particles (PM₁₀)**

Population	Source	% Change per $\mu\text{g}/\text{m}^3$	95% CI
Total	Europe, APHEA Meta-analysis, Katsouyanni <i>et al</i> ⁶	0.044	0.026, 0.061
Total	Birmingham, Wordley <i>et al</i> ⁵	0.110	0.010, 0.210
Total	International, WHO ⁴	0.074	0.062, 0.086

3.25 The APHEA meta-analysis uses results from six European cities (Barcelona, Bratislava, Cologne, Lyon, Milan and Paris).⁶ The WHO summary of findings is based on results from 17 studies internationally, including 12 in the USA, three in Europe and two in Latin America.⁴ The WHO estimate, reflecting largely the American experience, is higher than that of APHEA, based on European cities only.

3.26 The estimate for Birmingham is higher than either of these, but is well within the range of the individual city results on which the WHO summary of findings is based.

3.27 The London mortality study⁹ reported results in terms of BS, with an estimated percentage increase of 0.120% per $\mu\text{g}/\text{m}^3$ BS. It should be recalled that BS is a measure of particles of diameter less than $4.5\ \mu\text{m}$. Using a conversion factor $\text{BS} = 0.7\text{PM}_{10}$, which of course is an approximation, the London results are equivalent to an increase of 0.084% per $\mu\text{g}/\text{m}^3$ PM₁₀; ie, are very similar to the WHO summary of findings.

3.28 In the light of these considerations, we consider that the WHO summary of findings is a suitable figure for quantification of acute mortality effects in the UK, in relation to concentrations of PM₁₀.

Respiratory hospital admissions

3.29 We have considered what is the suitable level of disaggregation of the respiratory hospital admissions data.

3.30 Several of the APHEA cities report results by type of respiratory hospital admission, especially chronic obstructive pulmonary disease (COPD) and asthma.^{10,13-15} There are some differences in the relative importance of different pollutants, by specific hospital admission endpoint. However, it is difficult to identify really clear patterns by specific endpoint, partly because the numbers, eg, of daily admissions for asthma, are quite small. Also, at this stage, economic evaluation does not differentiate between specific type of hospital admission. So the exposure-response functions we provide are for all respiratory hospital admissions.

3.31 Table 3.2 gives exposure-response functions for particles in terms of PM_{10} . Relevant results were available from APHEA for Western European cities only. The exposure-response function from APHEA shown in Table 3.2, is a typical value from the city, (Paris), in which PM_{10} was analysed.¹³ (Like the APHEA authors, we have taken PM_{10} as equivalent to PM_{10} .) A meta-analysis from the APHEA study considering only admissions for COPD,¹² gave an estimated effect (% change) which was slightly higher than the function for respiratory hospital admissions from Paris.

Table 3.2 Respiratory Hospital Admissions and Particles (PM_{10})

Population	Source	% Change per $\mu g/m^3$	95% CI
Total	W Europe, Dab <i>et al</i> ¹³	0.044	0.005, 0.083
Total	Birmingham, Wordley <i>et al</i> ⁵	0.237	0.110, 0.364
Total	International, WHO ⁴	0.080	0.048, 0.112

3.32 The WHO summary of PM_{10} and respiratory hospital admissions is based on six cities, four in the USA, one in Canada, and Paris in Europe.⁴ The analysis average of 0.08% increase per $\mu g/m^3$ PM_{10} again reflects higher North American exposure-response relationships. Indeed, the Paris estimate was the lowest of the six cities considered.

3.33 The Birmingham results⁵ (0.237% per $\mu g/m^3$ PM_{10}) are very markedly higher than either of these. However, results from London¹⁰ showed no significant relationship between BS and admissions, with an estimated relative risk of approximately one, ie, zero percent increases per unit change in PM_{10} concentration.

3.34 Against this background, we have again used the WHO estimates as the best basis for quantification of effects in the UK.

Cardiovascular hospital admissions

3.35 The acute mortality deaths associated with air pollution are from (non-malignant) cardio-respiratory causes. It is logical therefore to expect pollution-related increases in cardiovascular as well as in respiratory hospital admissions. The WHO Working Group did not attempt to quantify the relationships between ambient particles and cardiovascular hospital admissions;⁴ and so the underlying studies are presented here in greater detail than those for other outcomes. Particles were not studied in the earliest paper reporting associations between daily concentrations of air pollutants, notably carbon monoxide, and congestive heart failure in people aged 65+ in seven US cities.¹⁶ A separate paper¹⁷ reported results from Detroit in greater detail. This study focused on daily hospital admissions among those aged 65 or more; but examined PM_{10} as well as ozone, SO_2 and CO and considered ischaemic heart disease (IHD) as well as congestive heart failure. Results from two-pollutant models, taking due account of longer-term trends and cycles and of climate, showed statistically significant associations between congestive heart failure and both PM_{10} and CO. Adjustment for either of these pollutants had little effect on the estimated impact of the other; ie, the estimated effects of particles and CO were relatively independent; and by implication were additive also. Both SO_2 and CO, as well as PM_{10} , individually showed statistically significant associations with IHD; but only PM_{10} remained clearly related to IHD in two-pollutant models.

3.36 Cardiac as well as respiratory hospital admissions were studied over six years (1983-88) at 168 acute care hospitals in Ontario, Canada.¹⁸ Pollutants considered were particles (sulphates) and ozone. Overall, ozone was not related to cardiac hospital admissions; particles (sulphates) were related, however. This study considered people of all ages; separate analyses of those under and over 65 years of age showed relatively small differences in estimated effects (3.5% increase per $13 \mu g/m^3$ sulphates in those

aged 65+; 2.5% in those aged under 65). After suitable scaling, including conversion to PM_{10} (sulphates = $0.25 PM_{10}$),¹⁹ these estimates imply a similar percent increase per $\mu g/m^3$ as Schwartz and Morris;¹⁷ but with the major difference that they apply to younger people also.

3.37 In the UK, daily levels of PM_{10} were examined in relation to a wide range of endpoints, including daily hospital admissions for IHD and for cerebrovascular disease, among people in Birmingham.⁵ Having adjusted for temporal patterns and for climate, there was no good evidence of a relationship between IHD admissions and daily PM_{10} . There was, however, a statistically significant relationship between acute cerebrovascular admissions and same-day (but not earlier) PM_{10} .

3.38 A more recent UK study examined relationships between emergency admissions to London hospitals 1987-94 for circulatory diseases and daily concentrations of various air pollutants, including particles measured as Black Smoke.¹¹ Results were examined for several different sub-groups of circulatory diseases. Adjusting for longer-term trends, for cyclical variations, for temperature and humidity, and allowing for autoregression, the relationships between various air pollutants and diagnostic groupings were examined using Poisson regression. Within this framework, there were associations of Black Smoke with acute myocardial infarction, angina and all circulatory diseases, but not with cerebrovascular diseases or heart failure.

3.39 Cumulatively, these studies support the view that daily concentrations of ambient particles are associated with cardiovascular hospital admissions. However, the number of studies involved is as yet relatively few, and there are important differences between studies both in exactly which diagnostic categories are associated with daily particles, and in what are the estimated effects.

3.40 For these reasons, we have not attempted to quantify cardiovascular hospital admissions and particles in the UK.

3.41 However, as an indication of the potential effect, Table 3.3 gives estimates of exposure-response functions linking daily particles with three specific diagnostic categories of circulatory hospital admissions: congestive heart failure, ischaemic heart disease and cerebrovascular diseases.

Table 3.3 Cardiovascular Hospital Admissions and Particles (PM_{10})

a)	Congestive heart failure		
b)	Ischaemic heart disease		
c)	Cerebrovascular		
Population	Source	% Change per $\mu g/m^3$	95% CI
a) 65+	Schwartz and Morris ¹⁷	0.099	0.038, 0.160
b) All	Poloniecki <i>et al</i> ¹¹ & Wordley <i>et al</i> ⁵	0.070	-0.042, 0.181*
c) All	Wordley <i>et al</i> ⁵ & Poloniecki <i>et al</i> ¹¹	0.043	-0.060, 0.151*

* These CIs are indicative only

The estimates from the London study¹¹ of risks of acute myocardial infarction (ICD 410) and angina pectoris (ICD 411) are assumed to apply to ischaemic heart disease as a whole (ICD 410-414); and we use the approximate conversion factor, that $1 \mu g/m^3$ BS is equivalent to $0.7 \mu g/m^3 PM_{10}$.

Respiratory emergency room visits (ERVs)

3.42 This is a difficult endpoint, in that ERVs reflect North American rather than European hospital usage. The nearest equivalent UK endpoint is that of Accident and Emergency attendances, for which results are not yet available. In view of this non-equivalence, it was decided not to include ERVs in the estimates.

Restricted activity days (RADs)

3.43 There are no UK studies of this health outcome and we are concerned that its definition may be imprecise and may vary from country to country and from study to study. In view of this it was decided not to include this in the estimates.

Acute effects in patients with asthma

3.44 Several studies show that particulate pollution can exacerbate asthma, in patients with asthma.²⁰ 'Asthma attack' is not a well-defined health-outcome, in the sense that criteria for what constitutes an asthma attack are not consistent across studies. Here, and in accordance with the approach adopted by WHO,⁴ we propose the following outcomes for characterising effects on patients with asthma:

- a. increased use of medication (bronchodilator usage);
- b. increase in respiratory symptoms.

Bronchodilator usage

3.45 The exposure-response functions shown in Table 3.4 are from two European studies. The results are given separately for children²¹ and for adults.²² Note that these studies are based on small numbers of subjects, in only one European country (The Netherlands); and so there may be important problems of representativeness.

Table 3.4 **Bronchodilator Usage in Asthmatic Subjects and Particles (PM₁₀)**

Population	Source	% Change per µg/m ³	95% CI
Children (up to 15)	Roemer <i>et al</i> ²¹	0.230	0.073, 0.387
Adults (15+)	Dusseldorp <i>et al</i> ²²	0.180	0.004, 0.357

There was a lower percentage increase in adults compared to children.

Cough

3.46 Table 3.5 shows, again separately for children and for adults, exposure-response functions for increased cough days in patients with asthma. The exposure-response function for adults comes from a small European study.²² That for children is from the US.²³

Table 3.5 **Cough in Asthmatic Subjects and Particles (PM₁₀)**

Population	Source	% Change per µg/m ³	95% CI
Children (up to 15)	Pope and Dockery ¹⁹	0.508	0.226, 0.790
Adults (15+)	Dusseldorp <i>et al</i> ²²	0.306	-0.115, 0.727

Lower respiratory symptoms, principally wheeze

3.47 Table 3.6 gives functions for PM_{10} , separately for young people²¹ and for adults,²² from European studies.

Table 3.6 Lower Respiratory Symptoms in Asthmatic Subjects and Particles (PM_{10})

Population	Source	% Change per $\mu g/m^3$	95% CI
Children (up to 15)	Roemer <i>et al</i> ²¹	0.330	0.134, 0.526
Adults (15+)	Dusseldorp <i>et al</i> ²²	0.220	-0.220, 0.650

3.48 The latter three health-outcomes have not been included in our impact estimates. The reasons for this include doubts about the transferability of data relating to the management of asthma from one country to another and the lack of UK studies.

Chronic health effects

3.49 Though evidence from the United States offers clear support for the adverse effects of chronic exposure to air pollutants, and especially fine particles,^{3,4,24-26} the absence of suitable UK and European cohort or longitudinal studies has led us not to make any deductions from these studies and not to provide any estimates of the effects of long-term exposure to particles in the UK. One key difficulty lies in the estimation of the number of years of life lost as a result of long-term exposure to particulate air pollution. There are many uncertainties in this process. As an illustration of the *potential* impact, using results from the American cohort studies, it has been estimated that lifelong exposure to $10 \mu g/m^3$ $PM_{2.5}$ may reduce life expectancy by a year or more among men in The Netherlands.⁴ Preliminary work-in-progress on UK impacts, under similar assumptions (several of which are untestable on current knowledge) suggests a similar effect, eg, one-year loss in life expectancy per lifelong exposure to $25 \mu g/m^3$ PM_{10} .

3.50 These are provisional, illustrative figures. It is difficult to assess them in comparison with the more reliable estimates of acute effects of air pollution presented elsewhere in this report. Indeed, the acute effects would contribute to the differences in life expectancy as estimated from cohort studies and provisionally indicated above. However, if these results are at all reliable, they suggest that the overall impacts from long-term exposures may be substantially greater than those that we have been able to quantify with sufficient confidence to include in the Executive Summary of this report.

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4

Sulphur Dioxide

Introduction

4.1 Sulphur dioxide (SO_2) is a colourless, soluble gas with a characteristic pungent smell. It is produced by the combustion of fossil fuels that contain sulphur and has been monitored for many years in ambient air in the UK because of the damage it causes to the environment as well as its health effects. During recent years the use of coal for domestic heating has declined in Britain and other West European countries, with a consequent reduction in atmospheric SO_2 concentrations. Coal-fired power stations are now the major source. Atmospheric SO_2 levels tend to fluctuate widely from day to day, particularly in large cities and also show a seasonal pattern of variation, levels tending to be higher in the winter, although this seasonal pattern is much less marked than was the case before the Clean Air Act of 1956.

4.2 It has long been recognised that SO_2 is a potent respiratory irritant when inhaled acutely in the laboratory at levels achieved during exceptional air pollution conditions. This is especially the case in patients with asthma. Of the pollutants dealt with in this report, SO_2 is the only one for which there is clear clinical evidence of increased sensitivity amongst asthma sufferers. Over the last decade or so, SO_2 had come to be regarded as less important as a pollutant from the health point of view than previously, though recent studies, largely from Europe, have clearly identified this gas as a continuing cause of effects on health.

4.3 This section attempts to quantify the effects of SO_2 on human health. It examines the evidence relating to both acute and chronic effects, drawing on the results of meta-analyses where possible.

Acute effects

4.4 A number of published studies have examined the relationships between concentrations of SO_2 and daily variations in various indices of health, such as number of deaths, hospital admissions and (in panels of patients or healthy volunteers) symptoms or indices of lung function. There are certain difficulties in interpreting these relationships. Like other atmospheric pollutants, SO_2 tends to accumulate in some weather conditions and disperse in others, so many of these studies have attempted to allow for potential confounding factors such as season and temperature. Circumstances that favour a rise in SO_2 are likely to cause a rise in other pollutants, and it is not always easy to be sure which pollutant is responsible for an observed effect on health, or whether an effect is attributable to a pollutant that was not measured. In some areas, particulates and SO_2 arise from the same sources and are therefore especially correlated, so that it is sometimes difficult to distinguish between their effects. Also, SO_2 contributes to air pollution by the secondary formation of sulphate particles. It is also uncertain as to whether acute effects might be greatest on the same day as a peak of SO_2 or on a subsequent day, so different studies have “lagged” the correlations with health indices by different numbers of days or not at all.

Mortality

4.5 A meta-analysis has been performed on the results of the APHEA project¹ which has the advantage that, within the limits of the APHEA project, it is free from the biases that often affect meta-analyses due to incomplete ascertainment or failure to include relevant studies (publication and selection biases); furthermore, the data were easily combined because of the common protocol. There were, however, some differences between the

statistical analyses conducted on the various centres' data: for example, each centre determined from its own data the lagging interval that gave the closest correlations between particle concentrations and effects on health. For all-cause mortality, a substantial degree of heterogeneity was found between the data from Western European cities on the one hand and Central and Eastern European cities on the other hand. The Western European data are probably more relevant to the UK, particularly as London was one of these centres, so only these data will be presented here. The distinction between Western and Central plus Eastern Europe was already defined in the protocol as a potential determinant of heterogeneity, so this restriction is not subject to the bias that might arise if it were arrived at *post hoc* from the data.

4.6 Table 4.1 shows the relative risks associated with a rise of $50 \mu\text{g}/\text{m}^3$ in the daily average SO_2 concentration. For all-cause mortality the estimate is based on seven Western European cities and corresponds to a 3% rise in total deaths. Although this is very unlikely to be a chance effect (the confidence limits show that the true effect is probably between 2.3% and 3.5%), there was a significant degree of residual heterogeneity in the model - ie, the relationship between SO_2 and mortality may not be the same in all these seven cities. In the Central and Eastern European cities the relationship was much weaker and not statistically significant. For cardiovascular and respiratory mortality the data relate to five cities and show increases (highly significant statistically) of 4% and 5% respectively for each $50 \mu\text{g}/\text{m}^3$ rise in SO_2 .²

Table 4.1 Changes consequent upon a rise in SO_2 of $50 \mu\text{g}/\text{m}^3$ (24 h average): Summary of APHEA estimates for SO_2 in Western European cities

Outcome	Age	No cities	RR	95% CL
All cause mortality		7	1.029*	1.035, 1.023
Cardiovascular mortality		5	1.04	1.01, 1.06
Respiratory mortality		5	1.05	1.03, 1.07
Respiratory admissions	15-64 yr	5	1.009	0.992, 1.025
	65+ yr	5	1.020	1.005, 1.046

* Fixed effect model

4.7 These findings are broadly consistent with reports from other studies. A recent review by Lebowitz³ identified seven studies of SO_2 and mortality in which daily SO_2 levels exceeded $80 \mu\text{g}/\text{m}^3$, and six of these showed a significant association. In East Berlin during the winters of 1981-1989, mortality increased by 2.3% for each $50 \mu\text{g}/\text{m}^3$ rise in SO_2 , after excluding days when concentrations exceeded $150 \mu\text{g}/\text{m}^3$.⁴

4.8 It is unclear what mechanism could be responsible for these substantial effects. One question that must be considered is whether episodes of pollution merely hasten deaths that would have occurred within a few days anyway or whether lives have been appreciably shortened. This issue will be addressed below.

Hospital admissions

4.9 Table 4.1 also shows the effects of SO_2 on admissions to hospital for respiratory diseases from the APHEA data. Under the age of 65 years there is no significant effect, but above this age an increase of $50 \mu\text{g}/\text{m}^3$ is associated with 2% more admissions.⁵ Other studies have shown associations of varying strengths. In Barcelona (another APHEA centre) an increase of $25 \mu\text{g}/\text{m}^3$ was associated with increased emergency room attendances amounting to 6% in winter and 9% in summer, after adjusting for other variables.⁶ Positive associations with respiratory admissions in the elderly have also been reported in two American cities,⁷ and with asthma admissions in Birmingham UK⁸ and in Oulu, Finland.⁹ In Birmingham, the effect appeared to vary with the season, the greatest being seen in winter.

Other acute effects

4.10 A number of workers have followed up groups of persons, usually with known respiratory disease, to see whether fluctuations in pollution levels are reflected in variations in daily symptoms or lung function indices. For example, in a panel of 73 Dutch children with chronic respiratory symptoms, SO₂ was associated positively with wheeze and bronchodilator use and negatively with peak expiratory flow rates.¹⁰ This was attributable to an episode in which 24-hour average SO₂ concentrations rose to 105 µg/m³ and PM₁₀ exceeded 105 µg/m³. A British study of 75 adults with chronic respiratory disease showed similar associations, although the SO₂ levels did not breach WHO guidelines during the course of the study.¹¹ Other examples are listed by Lebowitz.³ These findings confirm the impression that fairly small changes in SO₂ levels can have a range of effects upon health which are not confined to bringing forward the deaths of seriously ill individuals, although it is difficult to separate the effects of SO₂ and particulates in some of these studies.

Chronic effects

4.11 A number of studies have examined the effects on health of long-term exposure to differing average concentrations of SO₂. There are a number of problems associated with such studies of chronic effects of air pollutants: these have been discussed in Chapter 2, paragraph 2.28.

Mortality

4.12 Geographical studies relating death rates to exposure levels have suggested that an association exists which does not seem to be entirely explained by the obvious confounding variables.³ A study in different regions of the Czech Republic found a strong association between SO₂ exposure and the respiratory mortality of infants aged one month to one year; number of deaths between areas with the highest and lowest quintiles of exposure (annual geometric means > 57.9 and < 12.5 µg/m³, respectively) differed by a factor of 5.41 after adjusting for socio-economic variables, and by 3.91 when particulate and NO_x levels were allowed for.¹² There was also a relationship with particulate exposure, and it may prove to be impossible to separate the effects of these pollutants, since they tend to be associated with each other. Quantifying the effect is also very difficult; the Department of Health's Advisory Group on the Medical Aspects of Air Pollution Episodes¹³ was not able to address the question of exposure-response on the basis of existing data, although there was evidence of a qualitative relationship.

4.13 A Japanese study of two areas partly circumvented the problem of confounding because one area showed first a worsening and then an improvement in air pollution over a period of 21 years.¹⁴ As air pollution deteriorated, mortality due to asthma and chronic bronchitis increased; when air quality improved, asthma mortality decreased immediately and chronic bronchitis mortality declined gradually, reaching the level in the unpolluted area 4-5 years after SO₂ concentrations began to satisfy air quality standards.

Symptoms and lung function

4.14 In relation to symptoms, the Department of Health Advisory Group¹³ arrived at a "qualified judgement about exposure-response" on the basis of selected studies as follows. An annual mean concentration of 24-hour mean SO₂ of 60-140 µg/m³ is associated with increased respiratory symptoms in adults. At 140-200 µg/m³ associations have been reported with increased respiratory illnesses in children. There are no clear indications of a threshold level. Some of the relevant studies did not control for environmental tobacco smoke.

4.15 Lebowitz³ notes the association between SO₂ and the prevalence of chronic obstructive pulmonary disease (COPD); he estimates a relative risk for COPD of 1.5-2.5 as the annual SO₂ and TSP concentrations concurrently exceed 100 µg/m³.

4.16 A study in Arizona compared the respiratory health of children in four areas that had different degrees of air pollution.¹⁵ The children were followed up so that the incidence of symptoms and the changes in lung function could be recorded. The degree of SO₂ pollution was correlated with the prevalence but not the incidence of symptoms, while the development of lung function with age was roughly the same in the four areas. It was concluded that intermittent elevations in SO₂ concentrations, in the presence of moderate particulate sulphate levels, cause some bronchial irritation but no chronic effects.

4.17 Lebowitz⁸ summarises the evidence on lung function by stating that significant decrements of 3-8% in FEV₁ appear to be related to ambient annual SO₂ and sulphate concentrations above 100 µg/m³ in children. Decreases occur more frequently and are greater in those starting with low lung function, bronchial hyperresponsiveness and chronic respiratory disease.

Conclusions

4.18 There is little doubt that SO₂ both causes and aggravates symptoms particularly in patients with pre-existing asthma. In association with particles, it appears to increase mortality both in the short- and the longer-term, although it is uncertain which component of pollution is mostly responsible. The associations with raised mortality do not seem to be attributable simply to a more rapid demise of people who are dying in any case, since there is some evidence that death rates in chronically polluted areas remain substantially higher than those of cleaner areas. The best current estimates of the acute effects are that each 50 µg/m³ rise in the 24-hour average concentration raises the death rate by 3% for all causes, 4% for cardiovascular diseases, and 5% for respiratory diseases. It is much more difficult to quantify the chronic effects at present and we take the view that exposure-response relationships for chronic effects for the UK are not devisable.

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5

Nitrogen Dioxide

Introduction

5.1 Nitrogen dioxide is perhaps the most confusing of the common air pollutants. It is produced, with nitric oxide, in large quantities by motor vehicles and is a good marker of vehicle-generated air pollution. High levels are periodically recorded in urban areas and episodes of pollution have been studied and effects on health demonstrated.¹ Despite this, epidemiological studies which have looked at the effects of the mixture of air pollutants commonly found in ambient air have tended not to show that nitrogen dioxide contributes much to the overall effects. Other pollutants, including particles and sulphur dioxide, tend to figure more strongly in the analyses and control for the effects of particles has not always been adequate in studies which report an effect of nitrogen dioxide. Studies involving the exposure of volunteers, both healthy and suffering from respiratory diseases to nitrogen dioxide have not consistently revealed effects at ambient concentrations. There is some evidence that long-term exposure to raised concentrations of nitrogen dioxide has effects on health. The evidence is reviewed in detail in the 3rd report of the Advisory Group on the Medical Aspects of Air Pollution Episodes² and, more briefly, below.

Acute effects

5.2 The most extensive and consistent evidence on the acute effects of air pollution is currently being analysed in two major European collaborations, the APHEA study which relates time-series of routinely collected statistics (mortality and hospital activity) to daily air pollution records, and the PEACE study which relates daily symptoms and lung function to daily air pollution data. Draft manuscripts from the APHEA study were made available to the sub-group, some of them early drafts, but there is much less information available from the PEACE study.

Mortality

5.3 Early studies of the effects of air pollution on daily mortality were generally too small to draw any conclusions on the role of NO₂, even when this was measured and available for analysis.^{3,4} In meta-analyses from the APHEA study, Touloumi *et al* have concluded that all cause mortality is increased by 3.5% (95% CI 1.6-5.4%) for every increase of 100 µg/m³ in 24 hour average NO₂.⁵ This analysis is based on data from 6 European cities and the effect may be greater in cities where the Black Smoke levels are higher. On the other hand, using data from the same study, Zmirou looked at cause specific mortality in 4 of the same cities and found no consistent effect on cardiac deaths and no increase in respiratory deaths associated with 24 hour levels of NO₂.⁶

Hospital admissions and attendances

5.4 There are, so far, no results from the APHEA study on all cause (excluding external causes) admissions. Spix, however, has reported no consistent association between all respiratory admissions and NO₂ levels in an analysis of data from 5 of the cities while noting that the effect of Black Smoke levels on admission rates did seem to be greater on days with high NO₂ levels.⁷ Admissions for obstructive lung disease, on the other hand, do seem to be associated with days with high ambient levels of NO₂. Sunyer *et al*⁸ have estimated an increase of 2.6% in asthma admissions (95% CI: 0.6-4.9) for every 50 µg/m³ increase in 24 hour average NO₂ and Anderson *et al* have estimated an increase of 1.9% (95% CI: 0.2-4.7) in COPD admissions for every 50 µg/m³ increase in 24 hour average NO₂.⁹ It is possible that emergency room attendances are even more strongly affected by levels of NO₂,^{10,11} but there is less information on this, and none from the APHEA study.

Symptoms and lung function

5.5 The PEACE study may provide much more extensive information on the effects of air pollutants on acute changes in symptoms and lung function. However, these data are not yet available. Hoek and Brunekreef¹² have meanwhile reported a small negative effect of NO₂ on children's lung function during periods in which there was no major pollution episode, and experimental studies suggest that NO₂ exposure may lead to increases in inflammatory markers and changes in epithelial function.¹³⁻¹⁵ On the other hand Samet¹⁶ reports a large cohort study in New Mexico as showing no discernible effect of NO₂ exposure or gas cooking on lung health up to the age of 18 months, and Linn reports no effect of NO₂ 300 ppb (564 µg/m³) with O₃ or O₃ and sulphuric acid.¹⁷ The most prominent feature of these studies at the present time is their lack of consistency. A large proportion of all studies on the acute effects of NO₂ emphasise the heterogeneity of response between groups defined either by personal characteristics or by coexistent exposures. A number of authors have emphasised that patients with asthma are more likely to respond to NO₂.^{14,18} This coincides with evidence that NO₂ may enhance the response to allergen either alone,^{19,20} or in the presence of SO₂,²¹ though one of the few epidemiological studies of this hypothesis has failed to show an increase in the response to pollen on days with high NO₂ as measured by personal exposure.²² Helleday has suggested that smokers and non-smokers respond differently to NO₂.²³ Li *et al* have suggested that the effects of NO₂ on children as reported have varied by age, location and the precise effect studied.²⁴ Others have suggested that NO₂ may have synergistic effects with SO₂,^{21,25} ozone²⁶ and Black Smoke.⁵

Chronic effects

5.6 Several studies have reported cross-sectional associations between health effects and exposure to NO₂ either measured directly or implied from known sources of NO₂ such as traffic or gas stoves. Whether these are due to acute effects or chronic effects of exposure to NO₂ is generally unknown but they will be assumed here to be chronic effects.

5.7 Three ecologic studies have linked local NO₂ levels with use of medical services. Leuenberger²⁷ in a preliminary report from the Swiss SAPALDIA study has estimated that each 10 µg/m³ increase in annual mean NO₂ leads to an increase of 10% in rhinitis, 6% in dyspnoea on effort (grade 1), 6% in wheeze, 9% in chronic sputum production and 7% in chronic cough. Walters *et al*²⁸ have shown that admissions to hospital with respiratory conditions at all ages are related to local NO₂ levels, and Ozawa *et al*²⁹ have shown that consultation rates with hayfever are higher in districts with high NO₂ levels and do not seem to be associated with pollen counts.

5.8 Infante-Rivard³⁰ showed a dose-response relation between personal exposure of children to NO₂ and the diagnosis of asthma, though Samet¹⁶ was unable to show any effect of NO₂ exposure or gas cooking on respiratory health below the age of 18 months and Strachan³¹ was unable to show any effect of 'gas cooking' on the likelihood of 'severe' asthma in children. The lack of consistency in the results of studies maintains the uncertainty over whether there is an effect of NO₂ on respiratory symptoms and lung function in children, and does not yet permit estimates of any such effects.

5.9 However, other studies have demonstrated adverse effects of gas cooking on adults.³²⁻³⁶ These have shown heterogeneity, Comstock *et al*³² showing effects in men but not women, Jarvis *et al* showing effects in women but not men.³⁷ The results from the European Community Respiratory Health Survey overall confirmed the results of Jarvis' analysis of the English data, showing effects in women but not men and tending to show greater effects in non-smokers and atopic individuals.³⁷ However, the effects were heterogeneous between centres and this heterogeneity has not been explained. This increases the difficulty in providing an overall estimate of the effect size that will be relevant in all situations. Moreover, the possibility has to be borne in mind that the effects seen with gas cooking may not be due to the increased exposure to NO₂.

Summary

5.10 The effects of NO₂ are among the most difficult to assess at the moment as they appear to be dependent on a wide range of modifying influences. However, it is of some comfort that in the APHEA study, in spite of this, the effects seem to be relatively homogeneous between cities in Western Europe at least. In estimating effects for costing, the 'whole population-all cause' effects are probably the most relevant. These are not always available. All cause mortality is increased by approximately 3.5%/100 µg/m³ on days with elevated NO₂. The principal difficulty is in estimating whether this represents a substantial increase in the number of deaths over a year or not. There is little evidence that admissions to hospital are increased by increased levels of NO₂ when all respiratory causes are looked at together. There are, however, apparent increases in admissions for COPD and asthma. Short-term changes in disability and symptoms due to daily changes in exposure to NO₂ are far less well documented, though these may be better documented when the PEACE study reports its findings. Evidence so far suggests that these effects will be dependent on other modifying factors. Estimates of chronic effects, many of which use unquantified and indirect measures of exposure, suggest that the effects of NO₂ exposure could be substantial. They are however not yet based on a very firm footing.

Conclusion

5.11 In view of these difficulties and doubts about the relationships between exposure to nitrogen dioxide and effects on health it was decided not to include nitrogen dioxide in the estimates of the effects of pollutants on health. A relevant calculation has however been undertaken for the possible effect of nitrogen dioxide on respiratory hospital admissions. This is described in Chapter 8.

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6

Ozone

Introduction

6.1 The aim is to summarise what is known about the health effects of ambient ozone exposure that would assist in estimating possible short- and longer-term health effects in the population. Epidemiological evidence indicates that a wide variety of health outcomes are possible: short-term effects on mortality, indicators of health service use, symptoms and lung function. At an experimental level, human evidence relates to short-term physiological and pathological changes in the respiratory system. Although potentially more important, there is much less evidence about longer-term effects.

6.2 Ozone is a powerful oxidant created by the action of sunlight on nitrogen dioxide in the presence of volatile organic compounds. Ambient concentrations show marked year to year, seasonal and diurnal variation. Ozone and its precursors may be transported over long distances which makes population exposure assessment feasible in both rural and urban areas, although allowance needs to be made for lower levels in urban areas due to scavenging by nitric oxide from vehicle exhausts. Because of its reactive nature, indoor concentrations of ozone are lower than those outdoors by 20 to 80%.

Short-term effects of ambient ozone on lung function

6.3 Most evidence of this type comes from panel studies which, typically, measure lung function daily for some weeks or months, along with air pollution exposure and other relevant factors. Levels of exercise and therefore ozone intake and response, are generally not standardised between studies. The DH Advisory Group on the Medical Aspects of Air Pollution Episodes (MAAPE) report on ozone concluded, on the basis of the North American studies available at the time, that effects of ambient ozone on lung function were detectable at concentrations as low as 70 ppb ($140 \mu\text{g}/\text{m}^3$), and that these effects tended to be greater than might have been predicted by chamber studies.¹ There is considerable individual variability in the response to ozone.

6.4 Kinney and co-workers, in a meta-analysis of 5 panel studies estimated a mean coefficient of $-0.55 \text{ ml/ppb ozone for FVC}$.² There was little evidence of heterogeneity between the studies. Kinney estimated that this effect was equivalent to or even greater than the effects of ozone observed in chamber studies of adults under maximum exercise conditions. More recently, Kinney has reported a meta-analysis of six US studies.³ For this analysis the raw data were obtained and analysed using standardised statistical procedures. Five of the six studies showed a statistically significant result and the mean effect was $-0.50 \text{ ml/ppb ozone for FEV}_1$, equivalent to a 1.13% drop in FEV_1 for a 50 ppb ($100 \mu\text{g}/\text{m}^3$) increase in 1 h ozone. No indication of threshold or dose response curve is revealed by these analyses. The studies included were selected by availability of data and it should be noted that a number of other North American panel studies not included in the meta-analysis did not find significant effects of ozone on lung function. A systematic meta-analysis of all available panel studies has yet to be done.

6.5 The available data from European studies are less and somewhat conflicting. A large study among children in rural areas of Holland obtained significant coefficients for FEV_1 and FVC (-0.42 and $-0.40 \text{ ml/ppb 1 h average ozone concentration}$, respectively).⁴ This was equivalent to a reduction of 1% for an increase of 50 ppb ($100 \mu\text{g}/\text{m}^3$) 1 h average ozone concentration and only slightly less than the effects reported by Kinney from the US. However, another large study of primary school children in the UK (semi-rural Surrey) found no significant association between ventilatory capacity and ozone over a summer period during which there were a number of exceedances of the UK Air Quality Standard

for ozone recommended by the DETR/DH Expert Panel on Air Quality Standards (EPAQS) and WHO (1987) guidelines.⁵ The best estimate was 0.069 ml/ppb and +0.11 ml/ppb for FVC for 8 h and 1 h average ozone concentrations, respectively, and neither effect was statistically significant. For a 50 ppb (100 $\mu\text{g}/\text{m}^3$) increase in 1 h average ozone concentration this is equivalent to an increase of about 0.26% in FVC. In a panel study of adults in North West England with chronic obstructive pulmonary disease there was a significant reduction of PEF with increases in ozone concentration among subjects with increased levels of bronchial hyperreactivity.⁶ This study did not, however, involve measurement of or allowance for the effects of particles.

6.6 For children it is concluded that the epidemiological evidence, while pointing to acute effects of ambient levels of ozone on lung function in a number of studies, is not consistent either between studies in the same continent or between continents. Possibly this inconsistency reflects differences in factors such as the exercise level of the children, the nature of the mixtures and methodology. For health impact assessment purposes relevant to the UK, the choice is between North American and Dutch studies which show an effect and the only UK study which does not. For adults, there is less information and the only UK study is not useful for health impact purposes because the results cannot be extrapolated. In view of these uncertainties it was decided not to include effects on lung function in children or adults in our estimates of the effects of ozone on health.

Respiratory symptoms

6.7 No meta-analysis of the effects of ozone on symptoms is available. Panel studies of children have not observed associations between ozone and respiratory symptoms in healthy children, nor in most studies of asthmatic children.⁷ An indication of possible effects is shown by the panel study of children in the Six Cities study.⁸ An increase of 30 ppb (60 $\mu\text{g}/\text{m}^3$) in 24 h average ozone concentration was associated with an increase of 22% in "cough", without evidence of a threshold. These effects were virtually independent of those of PM_{10} . For another outcome measure, "lower respiratory symptoms", an increase of 30 ppb (60 $\mu\text{g}/\text{m}^3$) in 24 h average ozone concentration was associated with a 35% increase in symptoms but this was not statistically significant and was reduced in multi-pollutant models. The range of exposure to ozone was not unlike that in the UK. This study, in view of its size and quality would be the best one on which to base a quantitative estimate for children. Other studies such as those from Mexico city^{9,10} have involved much higher levels of 1 h average ozone concentration (frequent days above 120 ppb [240 $\mu\text{g}/\text{m}^3$]) and are less relevant to the UK.

6.8 A number of well conducted studies among adults have reported associations between photo-oxidant levels or ozone and symptoms.^{6,11-13} The Californian studies could not convincingly separate the different components of "photo-oxidant" pollution and a specific effect of ozone is, therefore, not available. It is notable that in the studies of nurses reported by Schwartz^{12,13} symptoms tended to occur at over 200 ppb (400 $\mu\text{g}/\text{m}^3$) 1 h average ozone concentration. A UK panel study of COPD patients in the community found significant odds ratios for symptoms of wheeze and dyspnoea;⁶ but, because of possible inadequacies in the analysis, these results require confirmation. Furthermore, they relate to a sub-group of COPD patients characterised by high bronchial hyperreactivity and there is no means of establishing the prevalence of this sub-group of the population for health impact assessment purposes.

6.9 It is concluded that the existing evidence does not enable the relationship between ozone and symptoms to be quantified for risk assessment purposes.

Short-term effects on hospital attendances and admissions

6.10 A number of time-series analyses have examined the association between ozone and daily emergency-room attendances or hospital admissions for respiratory, and to a lesser extent, cardiovascular diseases. An advantage of hospital admissions over mortality data is that the diagnosis is probably reasonably accurate (within broad categories), and that for some respiratory diseases, particularly asthma, a considerable proportion relate to children and young adults. The first studies were from North America but more recently evidence has become available from Europe, including the UK. Most studies have used Poisson autoregressive techniques of analysis which lead to an estimate of the relative risk

of daily events for a given increment of pollutant. This is useful for estimating attributable risk and is amenable to meta-analysis.

Admissions for all respiratory diseases

6.11 Analyses of the whole group of respiratory diseases included under ICD 460-519 (9th revision) have the advantage of greater statistical power and, for international comparisons, less of a potential problem with diagnostic transfer. Emergency rather than total admissions are generally used, where available. Schwartz¹⁴ has listed the effects of ozone on all respiratory admissions from six North American studies (Buffalo, Ontario, New Haven, New York, Spokane and Tacoma) (see Table 6.1).

Table 6.1 **Relative risk of respiratory admissions for a 50 $\mu\text{g}/\text{m}^3$ increase in ozone¹⁴**

Location and admissions	Relative Risk	95% CI
All respiratory admissions		
Buffalo	1.06	0.99-1.12
Ontario	1.02	1.01-1.03
New Haven	1.03	0.99-1.07
New York	1.03	1.02-1.04
Spokane	1.24	1.00-1.54
Tacoma	1.10	1.03-1.13

Most results are for the 65+ age group, because these are eligible for Medicare. All relative risks were positive and most were significant, ranging from 1.05 to 1.54 for a 100 $\mu\text{g}/\text{m}^3$ increase in maximum 1 h average ozone concentration. In another paper,¹⁵ Schwartz estimates the weighted average of these coefficients to be 1.06 (1.05, 1.08) for a 100 $\mu\text{g}/\text{m}^3$ increase in maximum 1 h average ozone concentration. The smaller risks tended to be from studies of greater statistical power.

6.12 As part of the APHEA collaboration, four European cities (Amsterdam, London, Paris and Rotterdam) provided data on all respiratory admissions and ozone.¹⁶⁻¹⁸ The effects of ozone have been summarised by Spix *et al*¹⁹ (see Table 6.2). There was no significant heterogeneity between the cities and the summary estimate of the exposure-response relationship was significant and also strongest with the 8 h average ozone concentration. The usual lag was with the same or previous day. For the 15-64 age group the relative risk for a 50 $\mu\text{g}/\text{m}^3$ increase in 8 h average ozone concentration was 1.03 and for the 65+ age group 1.04. There tended to be a greater effect in the warm season. Broadly, the coefficients for Europe are similar to those reported from North America and the weighted averages are also very similar (for the 65+ age group 1.04 and 1.03, respectively). In both continents, there was no significant heterogeneity between cities, which provides reassurance regarding the generalisation of these data.

Table 6.2 **Summary of APHEA estimates for ozone**

Outcome	Age	Cities	Change pollution	RR (50 µg/m³)	95% CI
All cause mortality		2,3,5,6,7		1.027	1.013, 1.039
Cardiovascular mortality		3,5,6,7		1.02	1.00, 1.03
Respiratory mortality		3,5,6,7		1.06	1.02, 1.1
Respiratory admissions	15-64	1,5,7,8		1.031	1.013, 1.049
COPD admissions	65+			1.038	1.018, 1.058
Asthma	15-64	3,4,5,7		1.035	0.937, 1.144

Numbering of Cities

1. Amsterdam
2. Athens
3. Barcelona
4. Helsinki
5. London
6. Lyon
7. Paris
8. Rotterdam

Summary estimates for Amsterdam, Basel, Geneva and Zurich (not APHEA cities)

Outcome	Cities	RR (50 µg/m³)	95% CI
All cause mortality		1.021	1.013, 1.030

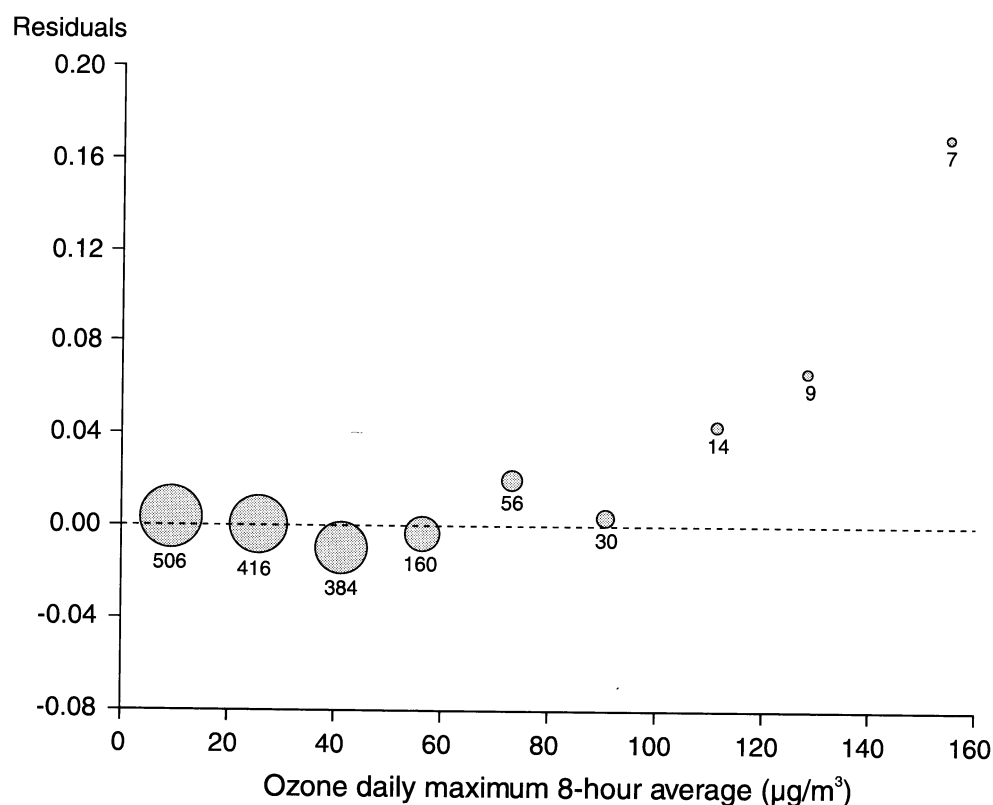
Touloumi *et al*⁴⁶

6.13 The analysis for London used admissions from 1987 to 1992 and provides coefficients for all ages, which might be more appropriate for health impact assessment.¹⁷ The London analysis also examined the exposure-response relationship and concluded that there was a threshold at between 40 and 60 ppb (80-120 µg/m³) (see Figure 6.1) but subsequent analyses of other parts of Southern England²⁰ indicate that out of London there is no evidence of a threshold, an observation which has been made by workers in North America. In view of this, and in view of the theoretical arguments against a threshold at the population level, we recommend that no threshold is assumed.

6.14 Some studies, including those of APHEA have analysed the effects of ozone by season. This seems relevant because ozone increases in the warm part of the year. Mostly, larger effects are seen in the summer than in the winter. Where appropriate seasonal coefficients are available it may be appropriate to use these for impact assessment.

6.15 The consistent associations between ozone and daily respiratory admissions provide a reasonable basis for health impact assessment. There may be systematic differences in pollution mixtures between North America and the UK (and the rest of Europe) which explain the tendency for European estimates of the exposure-response relationship to be lower. For quantification, the best options are either the APHEA estimate¹⁹ (see Table 6.2) or that for London.¹⁷ The results for 5 other regions of Southern Britain which are currently being prepared for publication are unlikely to be out of line with this estimate.²⁰

Figure 6.1 **Relationship between peak 8 hour average ozone concentrations and hospital admissions plotted as residuals¹**



¹ In this figure the area of the circles is proportional to the data available at the given concentrations. The number of 8 hour periods of given concentration is shown by the figures adjacent to the circles

Pneumonia admissions

6.16 There is evidence that ozone might interfere with antimicrobial defences and in this way promote chest infections. However, many pneumonia admissions in the elderly are likely to be complications of existing cardio-respiratory conditions and any ozone effect could operate through mechanisms which are directly toxic in nature. There is likely to be considerable diagnostic transfer between pneumonia and other respiratory causes. Pneumonia admissions were not specifically examined in APHEA but Schwartz has reported results from five North American cities (Birmingham, Minneapolis, Detroit, Philadelphia and Spokane).¹⁴ In a meta-analysis of the first four of these cities,¹⁵ a weighted average of 1.07 (1.04,1.10) for a 100 µg/m³ increase in maximum 1 h average ozone concentration was estimated, with no significant heterogeneity (see Table 6.3).

Table 6.3 **Ozone and pneumonia admissions (relative risk of death for a 100 µg/m³ increase in 1 hour average ozone concentration)¹⁵**

Pneumonia admissions	
Location	Relative Risk (95% CI)
Birmingham, Alabama	1.04 (0.97-1.13)
Minneapolis	1.06 (0.99-1.13)
Detroit	1.11 (1.05-1.17)
Philadelphia	1.04 (0.99-1.10)
Weighted average	1.07 (1.04-1.10)
Test for heterogeneity	$\chi^2 = 3.46$, df = 3, p = 0.33

This is almost identical to the figure for all respiratory admissions. There is, therefore, little justification for estimating the impact of ozone on pneumonia admissions separately from other respiratory disorders.

Chronic obstructive pulmonary disease admissions

6.17 Schwartz has estimated the weighted average effect of ozone on COPD admissions (mostly 65+ years) using data from Birmingham (Alabama), Detroit, Minneapolis and Philadelphia.²¹ The estimate of relative risk was 1.10 (1.06, 1.13) for a 100 $\mu\text{g}/\text{m}^3$ increase in 1 h ozone, with no significant heterogeneity. As part of the APHEA project, five cities (Amsterdam, Barcelona, London, Paris and Rotterdam) contributed COPD data and the summary estimate derived was 1.043 for a 50 $\mu\text{g}/\text{m}^3$ increase in 8 h average ozone concentration (see Table 6.2). There was no significant heterogeneity. The coefficients were only significant in the warm season but were also greater than 1.0 in the cool season. The equivalent figure for maximum 1 h average ozone concentration was 1.029, which was a little less than that for North America (~ 1.05). There was little difference between the sizes of the COPD and all-respiratory coefficients. It is recommended that no separate estimate for COPD admissions is attempted since it is included in “all-respiratory” admissions.

Asthma admissions

6.18 The evidence linking daily asthma admissions with ambient ozone concentrations is, in general, weak and contradictory. Where associations are observed it is difficult to disentangle ozone effects from those of associated pollutants. Early North American studies found no associations or negative associations.²²⁻²⁴ Later studies in western North American cities also found no associations.^{25,26} In the Eastern parts of North America a number of studies have found associations with the air pollution mixture of which ozone is a part.²⁷⁻³⁵ This “acid summer haze” contains, in addition to ozone, acid aerosols and sulphate particles and some studies have not been able to distinguish an effect of ozone from that of the mixture as a whole. It is likely that the ozone related mixtures in the UK and Europe are somewhat different, with lower levels of acid and, probably, sulphate.

6.19 The epidemiological evidence from Europe is also inconsistent. Associations have been reported in Helsinki, where concentrations are quite low^{36,37} but these workers have encountered problems in the statistical modelling of the data. The results from Barcelona are conflicting, with one study reporting significant associations³⁸ and another not.³⁹ In Paris, significantly negative effects were observed.¹⁸ Only in London was a significant positive association with asthma admissions observed.²⁰ Meta-analyses of APHEA data found significant heterogeneity and did not yield a significant summary coefficient.³⁸

6.20 Recent evidence does not, therefore, change the conclusion of the COMEAP report on asthma and outdoor air pollution⁷ which was that the association between ozone and asthma admissions is weak, inconsistent and in some cases even negative. It is recommended that possible effects of ozone on asthma are not included in any health impact assessment.

Cardiovascular admissions

6.21 Three North American studies have investigated air pollution and daily admissions for cardiovascular diseases and none have found an association. Morris and colleagues did not find significant associations between ozone and admissions for congestive cardiac failure in seven US cities.⁴⁰ In Detroit, Schwartz and Morris found no independent effect of ozone on admissions amongst the elderly for ischaemic heart disease or congestive cardiac failure, after taking particle concentrations into account.⁴¹ In Ontario, no association between ozone and cardiovascular admissions was observed.³³ Information on air pollution and daily cardiovascular admissions to London hospitals has been recently published.⁴² The most consistent finding was an effect on acute myocardial infarction, admissions for which were associated with Black Smoke, NO_2 , CO and SO_2 , though not with ozone. Scattered associations were also observed with angina and arrhythmias, but

none with cardiac failure. Though not corresponding in detail to the findings from North America, the London data indicate that cardiovascular admissions are likely to be affected by outdoor pollution. This has been commented on above.

Short-term effects on mortality

All cause daily mortality

6.22 A selection of studies of ozone and daily mortality have been reviewed by Schwartz (see Table 6.4).¹⁵

Table 6.4 **Ozone and all cause mortality (relative risk of death for a 100 $\mu\text{g}/\text{m}^3$ increase in 1 hour average ozone concentration)¹⁵**

Location	Relative Risk (95% CI)
Detroit	1.01 (0.99-1.02)
Eastern Tennessee	0.97 (0.81-1.15)
Los Angeles	1.00 (0.98-1.02)
São Paulo	1.01 (0.88-1.13)
St Louis	1.01 (0.94-1.09)
Overall	1.008 (0.999-1.017)
Test for heterogeneity	$\chi^2 = 3.47$, df = 3, p = 0.33

Data from Detroit, Eastern Tennessee, Los Angeles, St Louis and São Paulo were summarised and a nonsignificant weighted average of 1.008 (0.999, 1.017) was obtained for an increase of 100 $\mu\text{g}/\text{m}^3$ in maximum 1 h average ozone concentration. There was no significant heterogeneity.

6.23 A rather different impression is given by the results of studies of two large cities, Los Angeles and New York, in which significant associations between ozone and all cause mortality were found.^{43,44} For Los Angeles the effect was an increase of 2% in mortality for 100 ppb (200 $\mu\text{g}/\text{m}^3$) 1 h maximum average ozone concentration (lagged one day); the results for New York were similar. In a study by Loomis *et al* univariate analysis demonstrated that ozone had significant effects on mortality; however, these effects became nonsignificant in a multi-pollutant model including total suspended particulates (TSP) and sulphur dioxide.⁴⁵

6.24 Studies in APHEA cities as well as some other European cities also suggest that there is an effect of ozone on all cause mortality⁴⁶ (see Table 6.2). Data on ozone and daily mortality were obtained from Athens, Barcelona, London, Lyon and Paris. A significant relative risk of 1.027 (1.013, 1.039) per 50 $\mu\text{g}/\text{m}^3$ 8 h average ozone concentration was obtained and there was no significant heterogeneity. In addition, data are available from four other European cities which, while not part of APHEA, followed the general analytic approach. The summary estimate for these cities was 1.021 (1.013, 1.030) per 50 $\mu\text{g}/\text{m}^3$ 8 h average ozone concentration, very similar to that from the APHEA cities. Taking all the existing evidence into account, it is concluded that an association exists and is reasonably consistent across Europe and with large cities in the US. This justifies an estimate of risk and for UK purposes the APHEA summary estimate is an appropriate coefficient to use. This is similar to the estimate obtained for London, the only UK city for which such data exist.⁴⁷

Cardio-respiratory mortality

6.25 The Los Angeles study by Kinney *et al*⁴³ observed a significant effect of ozone on cardiovascular mortality (2.6% increase per 100 ppb [200 $\mu\text{g}/\text{m}^3$] 1 h average ozone

concentration). APHEA estimates are available for Barcelona, London, Lyon and Paris. The summary estimate is a relative risk of 1.02 (1.00, 1.03) per 50 $\mu\text{g}/\text{m}^3$ increase in 8 h average ozone concentration⁴⁸ (see Table 6.2).

Respiratory mortality

6.26 Respiratory mortality accounts for only about 15% of all mortality and sufficiently precise estimates can only be obtained from large cities such as London and Paris. The APHEA cities of Barcelona, London, Lyon and Paris provided data for meta-analysis. The summary estimate was 1.06 (1.02, 1.1) for a 50 $\mu\text{g}/\text{m}^3$ increase in 8 h average ozone concentration. This is larger than those obtained for cardiovascular and all causes of death.

Use of mortality-specific estimates

6.27 For both cardiovascular and respiratory mortality there are few estimates on which to base an estimate for health impact assessment. There is a case for confining mortality estimates to all causes (excluding accidents) and this approach was adopted.

Effects of chronic exposure

6.28 Epidemiological evidence for chronic effects of exposure to ozone is scanty. The only adequate cross-sectional study on adults is that reported by Schwartz who used data on adults of 18-65 years from the US National Health and Nutrition Examination Survey II.⁴⁹ Highly significant negative effects on lung function were observed for both ozone and NO_2 . However, because too few areas had data on both pollutants their independent effects could not be estimated. The effect of ozone (mean of day time levels over the previous year) became evident at about 40 ppb (80 $\mu\text{g}/\text{m}^3$). The regression coefficient was around -3 ml/ppb annual average ozone, in all models examined.

6.29 The other main source of evidence is the cohort study of Seventh Day Adventists in California.⁵⁰ Cumulative exposure to ozone was associated with the severity of asthma and incidence of diagnosed asthma in men only. The relative risk for asthma in all ages associated with asthma was 1.35 (0.93, 1.96) per 500 h/yr above 100 ppb (200 $\mu\text{g}/\text{m}^3$) 1 h average ozone concentration. This was not significant and the finding of a significant effect among men was not based on an a priori hypothesis.

6.30 It is not recommended that these estimates be used for quantitative risk assessment in the UK until there is replication, preferably in Europe. Also, there is the suggestion in both these studies that the effects observed were occurring at higher levels than are likely to occur in the UK.

Conclusions

6.31 For the purposes of health impact assessment it is concluded that only data for respiratory hospital admissions and all-cause mortality should be used. These are listed in Table 6.5.

Table 6.5 Summary of exposure-response coefficients for ozone

Pollutant	Health outcome	Dose-response relationship (All per 50 $\mu\text{g}/\text{m}^3$ 8 hr mean O_3 concentration)
Ozone	Deaths (all causes)	+3.0%*
	Respiratory hospital admissions	+3.5%*

* Rounded estimates based on APHEA studies

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7

Carbon Monoxide

Introduction

7.1 Carbon monoxide (CO) is a colourless, odourless, toxic gas produced by the incomplete combustion of organic compounds. For a cigarette smoker, by far the most important source of CO is cigarette smoke, which is also a source of exposure for people in the same room as a smoker ("passive smoking"). For a non-smoker, ambient CO may also have health effects, particularly in patients with pre-existing cardio-respiratory disease. The effects of acute poisoning with CO are well known and will not be dealt with here, the emphasis being on the effects of acute and chronic exposure to low concentrations of this pollutant.

Acute effects

Mortality

7.2 A study in Athens, forming part of the APHEA project, found an association between day-to-day fluctuations in CO concentrations and mortality.¹ The effect was greatest when same-day data were used in the comparison and was independent of variables such as temperature, humidity, season, and day of the week. For an increase in 8 hr average CO concentration of 10 mg/m³, the rise in deaths was 1.10 (95% confidence interval 1.05-1.15). Similarly, studies in Los Angeles have shown CO concentrations to be related to deaths from all causes² and cardiovascular diseases,^{2,3} allowing for other pollutants and temperature. In the latter study, the effect of CO on health, after adjustment for temperature and time trends, was given as follows:

"The estimated contribution to mortality for Los Angeles for an average carbon monoxide concentration [daily average concentration] of 20.2 ppm (23.13 mg/m³) (the highest concentration observed during the 4-month period), as compared with an average carbon monoxide concentration of 7.3 ppm (8.36 mg/m³) (the lowest concentration observed), is 11 deaths for that day, all other factors being equal."

The average number of deaths occurring per day was reported as 159. This study controlled for daily concentrations of oxidant pollutants but not for daily concentrations of particles.

Case fatality

7.3 An earlier study was conducted on data collected during 1958 in the 35 hospitals situated in the Los Angeles metropolitan area.⁴ The case fatality of myocardial infarction (ie, the proportion of cases of the disease that died) tended to be higher in hospitals that were in the more polluted areas, and the difference in case fatality between polluted and unpolluted areas became evident only when CO concentrations were relatively high. For the 13 weeks that had the highest mean daily CO levels for the whole area (8.5-14.5 ppm [9.73-16.6 mg/m³]), the more polluted area showed an excess case fatality averaging 12.4 deaths per 100 admissions compared with the less polluted area, whereas during the 13 weeks with the lowest mean daily CO levels (5.3-5.9 ppm [6.07-6.76 mg/m³]) the excess deaths in the polluted area averaged only 3.2 per 100 admissions (calculated from the data given in the paper). It was concluded that an association could exist between the case fatality of myocardial infarction and CO pollution.

Hospital admissions

7.4 A study in seven American cities showed that ambient CO levels were positively correlated with hospital admissions for congestive heart failure, independently of other pollutants, temperature, season, and weekly cycle.⁵ The rise in admissions associated with an increase of 10 ppm (11.45 mg/m³) in mean daily CO ranged from 10% to 37% in the seven cities. It is noteworthy that in this study no associations were discovered between congestive heart failure and concentrations of nitrogen dioxide, sulphur dioxide and ozone; no adjustment for possible effects of particles seems to have been made. A detailed analysis of data from one of these towns considered the day-to-day variations in particles, which were found to be related to daily admissions for ischaemic heart disease.⁶ PM₁₀ and CO concentrations were independently related to admissions for heart failure.

7.5 Another American study, in Tucson, Arizona, showed an association between atmospheric CO concentrations and hospital admissions for cardiovascular disease.⁷ Admissions increased by 1.0279 (95% CI 1.0051-1.0541) for an interquartile range increase (1.66 ppm [1.90 mg/m³]) of CO - ie, an increase of 10 ppm (11.45 mg/m³) would correspond to a rise of 16.8% in admissions. This association was similar to, but independent of, the effect of an interquartile range increase in PM₁₀ exposure.

7.6 A recent study in London found significant relationships between average daily CO concentrations and hospital admissions from 1987 to 1994.⁸ A rise of 10 ppm (11.45 mg/m³) in mean daily CO corresponded to 23% more admissions for acute myocardial infarction, 6.9% more heart failure admissions and 23% more admissions for all circulatory diseases.

7.7 A study of various pollutants in 10 Canadian cities showed an association between daily peak-hour CO concentration and daily admissions for congestive heart failure in the elderly.⁹ The relative risk for a change from 1 ppm to 3 ppm (1.145-3.44 mg/m³) (the 25th and 75th percentiles of the exposure distribution) was 1.065 (95% CI 1.028-1.104); by extrapolation, a rise of 10 ppm (11.45 mg/m³) would produce 21.7% more admissions. Although other pollutants showed some associations with admissions for heart failure, changes in CO alone accounted for 90% of the daily excess hospitalisations attributable to the entire pollution mix. The relationship with CO was least affected by adjustments for weather, and there was no suggestion of a concentration below which the association ceased to occur.

7.8 The pathological mechanisms responsible for these effects can only be surmised. It is known from experiments on patients that small changes in CO concentrations aggravate angina,¹⁰ so that less exercise is needed to provoke it.¹¹ Admittedly, these studies have used concentrations higher than those that would normally be encountered in the atmosphere, but there is a large population of people with heart disease, some of whom may be particularly susceptible at any one time. Presumably hearts that are already ischaemic or failing are particularly sensitive to any interference with their oxygen supply.

Chronic effects

7.9 There have been a number of reports, mainly from studies of occupational groups, suggesting that chronic exposure to CO increases the risk of ischaemic heart disease. For example, a study in Finnish foundry workers reported a dose-response relationship between CO exposure and the prevalence of angina.¹² The evidence is not clear, however, and reviewers differ as to whether CO is¹³ or is not¹⁴ likely to contribute to the cause of heart disease. It is not possible at present to estimate the size of any effect, if one exists.

Interactions with other pollutants

7.10 Pollution with CO seldom occurs alone. In so far as pollutants have common sources, fluctuations in their ambient concentrations tend to be correlated with each other, sometimes quite strongly.¹⁵ It can, therefore, be difficult to ascertain which pollutant is chiefly responsible for the adverse effects of pollution, or whether they are attributable to the mixture as such. Multiple regression techniques are usually employed to distinguish between the effects of associated variables, but the results have not been entirely consistent.

Thus, the effect of CO on mortality was independent of other pollutants in Los Angeles,^{2,3,16} whereas in São Paulo¹⁵ it became statistically non-significant when other pollutants were allowed for. The difficulty is increased by the imprecisions of estimating exposure. It has to be assumed that measurements at fixed points represent the concentrations in the air breathed by the population. So long as these concentrations fluctuate in parallel with each other, the variations over time at a fixed site may be taken to represent variations in the exposures of individuals within the area, even if the absolute levels are not the same. But the precision of fixed-site monitoring as a surrogate for individual exposure is not necessarily the same for all the pollutants, and this will affect the apparent importance of the pollutants entered into a multiple regression analysis: other things being equal, a factor that is more precisely measured will take precedence over other factors that are correlated with it. It has been suggested that fixed location monitors give a better indication of the average population exposure to other pollutants than to CO, and that CO exposure is liable to be underestimated.¹⁷ The combination of differential precision and underestimation of exposure may reduce the apparent importance of CO relative to other pollutants.

Conclusions

7.11 Recent evidence from several countries suggests that fluctuations in CO levels increase the risk of hospital admission or death due to cardiovascular disease (see Table 7.1).

Table 7.1. **Changes associated with a rise in CO concentration of 10 ppm**

Outcome	Area	Increase
All-cause mortality	Los Angeles ²	4%
	Los Angeles ³	5%
	Los Angeles ¹⁶	7%
	Athens ¹	11.5%
Cardiovascular admissions	London ⁸	23% ^{a,b}
	Tucson ⁷	17% ^b
	7 American cities ⁵ (over 65)	10%-37% ^c
	10 Canadian cities ⁹ (over 65)	22% ^c

^a acute myocardial infarction; ^b all cardiovascular diseases; ^c congestive heart failure

A rise of 10 mg/m³ CO is associated with increases of about 10% in all-cause mortality and 20% in hospital admissions for cardiovascular diseases. There is uncertainty about chronic effects.

7.12 The lack of UK studies and uncertainties regarding the effect of CO alone as compared with that of the urban pollution mixture led the sub-group to decide not to estimate the effects of exposure to ambient concentrations of CO on deaths and hospital admissions in the UK. It is recognised that information on the effects of CO is accumulating rapidly and that such an assessment may be possible comparatively soon. When this assessment is done it is likely that hospital admissions for cardiovascular disorders will need to be considered. It is also likely that a significant addition to deaths affected each year by exposure to air pollutants will be made.

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8

Quantification of the Effects of Air Pollution on Health in the United Kingdom

Method of calculation

8.1 The method adopted is as follows:

- a A map showing the distribution of concentrations, with relevant averaging times, of the chosen air pollutants in Great Britain (GB) has been constructed. Details of the type of mapping methods used for PM₁₀ and SO₂ (but not the exact maps used here) can be found in two papers by Stedman *et al.*^{1,2} Details of the method for mapping ozone concentrations are given in a third paper by Stedman *et al.*³
- b A map of the distribution of population density in Great Britain has been obtained. Population statistics are available on a 1 km grid basis for the 1981 census population. Data were not available on this basis, at the time of calculation, from later censuses. The country has been divided into rural and urban areas using land cover information derived from Fuller *et al* 1994.⁴ Urban areas have been defined as having at least 20% urban land cover in each 1 km grid square. The results of the 1981 census were compared with those made available from the Lung and Asthma Information Agency (LAIA) which related to the years for which health outcome data are available. The 1981 census totals are a little smaller than those shown in the LAIA data and in the calculations of health outcomes an adjustment was made so as to provide estimates consistent with the population statistics provided by LAIA.
- c The country has been divided into grid squares and for each day of the defined period and each grid square, the effects of air pollutants on individual health outcomes have been calculated by multiplying the relevant exposure-response coefficient by the ambient concentration (with the appropriate averaging time), the background rate for the health outcome considered (eg, γ deaths per 100,000 population per year) and the population in the grid square.
- d The results for the individual grid squares have been summed.
- e The sum for each day and thus for the whole period has been calculated.

8.2 For some pollutants, calculations have dealt only with the urban population. The reason for this is that in urban areas the mapping for primary pollutants is good; in rural areas it is less satisfactory. For ozone, both rural and urban populations have been considered. Ozone often occurs at higher concentrations in rural than in urban areas and it would be clearly unsatisfactory to concentrate only on the urban population. It is fortunate that for ozone, a secondary air pollutant, mapping in rural areas is very much more satisfactory than for the primary pollutants.

Background rates of health events

8.3 Annual statistics on health outcomes were required for the SO_2 , PM_{10} and NO_2 analyses. These were provided by LAIA. The crude annual death rate for GB (1995) per 100,000 population for all causes was 1106.4. This value was used for analysis and assumed to apply in both urban and rural areas.

8.4 The annual rate for respiratory hospital admissions for England in April 1994-March 1995 was 1342.3 per 100,000 population. This value was used for analyses of effects and assumed to apply to the whole of GB in both urban (population = 42,542,926) and rural areas (population = 14,413,874).

8.5 It was decided to undertake an analysis of the effects of ozone in the summer season (April-September) only. As already discussed, evidence for the effects of ozone in summer is stronger than that in winter and levels are higher. A rate of respiratory hospital admissions of 345 per 100,000 has been applied for the whole of GB. This value was provided by LAIA for earlier work and represents the admission rate for England for the summer of 1993. The summer (April to September inclusive) death rate statistics were provided by LAIA for the summer of 1995. The number of deaths per 100,000 were given as 506.8 (all causes excluding accidents) and 70.5 (all respiratory) for England and Wales. The values were used in the analysis for effects in GB.

Calculations for the pollutants

Particulate matter: PM_{10}

8.6 A map of estimated annual mean concentrations of PM_{10} was calculated for 1996. The estimated concentrations for each 1 km grid square included components from three sources:

primary vehicle derived particles: estimated from the National Atmospheric Emission Inventory (NAEI) estimate of vehicle emissions;

secondary particles: estimated from rural measurements of sulphate particles;

particles from other sources: assumed to be at a constant concentration across the country.

The relationships between these contributions and ambient particles concentrations have been calibrated using automatic monitoring data for 1996.

8.7 The exposure-response coefficients used were:

deaths, all causes: +0.75% per $10 \mu\text{g}/\text{m}^3$ PM_{10} (24 hour mean);

respiratory hospital admissions: +0.80% per $10 \mu\text{g}/\text{m}^3$ PM_{10} (24 hour mean)

Health outcomes attributable to PM_{10}

8.8 The results of the calculations are shown in Table 8.1. Figures have been rounded to the nearest 100.

Sulphur dioxide

8.9 A map of estimated annual mean SO_2 has been calculated for 1995. The estimated concentration in each 1 km grid square includes components from local sources (estimated from NAEI emission inventories) and more distant sources (estimated from a map interpolated from measurements at representative rural monitoring sites). The relationship between measured SO_2 concentrations and emissions inventories was calibrated using automatic monitoring data for 1995.

8.10 The exposure-response coefficients used were:

deaths, all causes: +0.6% per $10 \mu\text{g}/\text{m}^3$ SO_2 (24 hour mean);

respiratory hospital admissions: +0.5% per $10 \mu\text{g}/\text{m}^3$ SO_2 (24 hour mean).

Table 8.1 **Number of deaths and hospital admissions for respiratory diseases affected per year by PM₁₀^{*}, sulphur dioxide and nitrogen dioxide in urban areas of Great Britain**

Pollutant	Health outcomes	GB Urban
PM ₁₀	Deaths brought forward (all cause)	8100
	Hospital admissions (respiratory) brought forward and additional	10500
SO ₂	Deaths brought forward (all cause)	3500
	Hospital admissions (respiratory) brought forward and additional	3500
NO ₂	Hospital admissions (respiratory) brought forward and additional	8700

* PM₁₀: particulate matter generally less than 10 µm in diameter

Estimated total deaths occurring urban areas of GB er year = c430,000

Estimated total admissions to hospital for respiratory diseases occurring in urban areas of GB per year = c530,000

Health outcomes attributable to SO₂

8.11 The results of the calculations are shown in Table 8.1.

Some sensitivity analyses for PM₁₀ and SO₂

PM₁₀ map

8.12 PM₁₀ concentrations in 1996 were higher relative to earlier years at several monitoring sites in the UK by 1 or 2 µg/m³. This was due in part to a long-range transport episode of high particle concentrations during March 1996. Most of the DETR monitoring sites for PM₁₀ are in urban locations. Estimates of concentrations in rural areas in the map are, therefore, rather uncertain. Both of these factors combined to give rather higher estimated concentrations of PM₁₀ for 1996 compared with an earlier map prepared for 1994. Estimates for number of deaths based on the 1994 map is 7064 (GB urban).

SO₂ map

8.13 The map of estimated annual mean SO₂ concentration probably underestimates concentrations in small communities where coal is widely used for domestic heating. Measurements of SO₂ concentrations within UK Smoke and SO₂ Monitoring Networks by a bubbler method are available for about 130 sites for 1995/96. If these measured concentrations are assumed to apply to 1 km squares at the monitoring site locations, and then used instead of the mapped values for these locations, the increase in the number of estimated deaths is less than 1% of the total. If measured values are assumed to be representative of 5 km squares (probably larger than is realistic) then the increase is about 9%.

Mapping resolution

8.14 The analysis was repeated with pollutant concentrations averaged over 5 km squares rather than 1 km squares. This led to small decreases in the estimated number of deaths: less than 0.5% for PM₁₀ and less than 4% for SO₂, the difference between the pollutants being because SO₂ concentrations are more spatially variable than PM₁₀ concentrations.

Nitrogen dioxide

8.15 A map of estimated annual mean NO₂ has been calculated for 1996. The estimated concentration in each 1 km grid square includes components from local sources (estimated from NAEI emission inventories) and more distant sources (estimated from a map interpolated from measurements at representative rural monitoring sites). The relationship between measured NO₂ concentrations and emissions inventories was calibrated using automatic monitoring data for 1996.

8.16 For respiratory hospital admissions: +2.5% per 50 $\mu\text{g}/\text{m}^3$ NO_2 .

Health outcomes attributable to NO_2

8.17 The results of the calculations are shown in Table 8.1.

Ozone

8.18 Maps of estimated daily ozone concentrations for the summer of 1995 on a 5 km grid have been calculated according to the methods described by Stedman *et al.*³ The analysis has been completed for GB as a whole, rural and urban areas taken together. The number of health outcomes was calculated using two different approaches:

- a threshold of effect of 50 ppb (100 $\mu\text{g}/\text{m}^3$)
- no threshold.

8.19 The following dose response relationships (per 50 $\mu\text{g}/\text{m}^3$ 8 hour mean ozone concentration) have been used:

- Deaths (all causes) +3.0%
- Hospital admissions (respiratory) +3.5%

Health outcomes attributable to O_3 (summer only)

8.20 The health outcomes attributable to O_3 (summer only) are shown in Table 8.2. Ozone concentrations are higher in summer than winter and the study that yielded the exposure-response relationship dealt only with the summer period. Thus, the analysis was not extended to include the winter period.

Table 8.2 **Numbers of deaths and hospital admissions for respiratory diseases affected per year by ozone in both urban and rural areas of Great Britain during summer only**

Pollutant	Health outcomes	GB: threshold = 50 ppb	GB: threshold = 0 ppb
Ozone	Deaths brought forward: all causes	700	12500
	Hospital admissions (respiratory) brought forward and additional	500	9900

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9

Summary and Conclusions

The aim of this report

9.1 The aim of this report has been to attempt to quantify the effects of air pollution on the health of the population of the United Kingdom in terms of specific health impacts, such as admissions to hospital and advancement of death. We did not set out to cost these effects: this will be covered in a subsequent report.

Framework for assessment of the health impact of air pollution

9.2 In principle, quantification of the effects of air pollution is straightforward:

Firstly, establish what pollutants are involved and what levels currently occur in the air;

Secondly, assess the likely exposure of populations to these levels of pollution;

Thirdly, define the health effect in terms of change in health outcome for a unit level (or change in level) of pollutant;

Fourthly, produce a quantification of that effect if applied to the overall population.

9.3 As we have described in the preceding chapters, this relatively straightforward process is fraught with difficulties with many levels of uncertainty. This means that any estimate of effects can only be that: an estimate. It might be thought that the limits of our ability to estimate the effects of pollutants on health could be defined and that, perhaps, some guidance as to the likely range within which our estimate lies could be provided. Such a range might provide a best case and worst case estimate of risks.

9.4 Calculating such a range implies an understanding of the levels of uncertainty involved in the calculations. In the case of air pollutants we have only a very weak grasp of this and we have felt that to attempt to calculate what might loosely be regarded as confidence limits for our estimates would be misleading. It is likely in fact that such limits would be very wide, and so the estimates are presented without such limits. It is worth stressing again: the estimates provided in this report are our best estimates based on our judgement and on the inevitably incomplete data available.

Assessment of pollutants emitted

9.5 This has been relatively easy as the classical pollutants are well recognised and have been extensively studied. This is not to say that other, as yet unsuspected, pollutants may be playing a role but this seems unlikely to have a significant impact on our estimates.

9.6 We have therefore considered nitrogen dioxide, sulphur dioxide, ozone, particulate pollution and carbon monoxide for which adequate data sets exist from monitoring sites throughout the UK.

9.7 We have not considered organic substances such as benzene or 1,3-butadiene where long-term exposures may be associated with the development of cancer but where the health effects are deemed to be immeasurably small from levels to which the population are exposed in ambient air in the UK.

Assessment of likely exposure

Population base

9.8 We have based our calculations on the urban population of Great Britain (42,542,926) as the great majority of available information on the health effects of air pollutants other than ozone has been obtained from urban areas and, with the exception of ozone, our ability to estimate exposure to pollutants is greater in urban than in rural areas. For various reasons, there are potential difficulties in extrapolating these effects to rural populations resulting in uncertain estimates with very wide confidence intervals. We have thus taken the view that, for the purposes of this report, estimates should be confined to the urban population of Great Britain with the exception of ozone.

Exposure

9.9 Exposure to air pollution at a personal level depends on many different factors including the degree of activity that an individual undertakes, the time spent outdoors, and the presence of pre-existing disease and indoor sources. However, virtually all epidemiological work on the health effects of air pollution has used pollutant measures obtained from monitors. We have taken the view that as health effects have been demonstrated using such fixed-site, outdoor monitors, these data should be used while accepting that knowledge of personal exposures would markedly improve (ie, reduce the uncertainty of) the estimates of effects we have produced. We are also aware that policy on air pollution is likely to be implemented on the basis of measurements made at such fixed site monitors.

Size of acute effects

9.10 We approached the determination of size of effect by taking health outcomes (eg, hospital admissions and number of deaths) for mapped sub-populations within Great Britain having established an appropriate exposure-response relationship for each health outcome for each pollutant. Expert judgement was applied in choosing the coefficients of effect. Meta-analysis was considered as a means of arriving at overall coefficients but the lack of similarity of studies (only one group of studies, the APHEA group, has been designed specifically with meta-analysis in mind) made this impossible. Thus, final coefficients for use in the calculations were decided by the application of judgement to the available data. The coefficients used are summarised in Table 9.1.

Table 9.1 **Exposure-response coefficients**

Pollutant	Health Outcome	Dose-Response Relationship
PM ₁₀	Deaths (all causes)	+0.75% per 10 µg/m ³ (24 hour mean)
	Respiratory hospital admissions	+0.80% per 10 µg/m ³ (24 hour mean)
Sulphur dioxide	Deaths (all causes)	+0.6% per 10 µg/m ³ (24 hour mean)
	Respiratory hospital admissions	+0.5% per 10 µg/m ³ (24 hour mean)
Nitrogen dioxide	Respiratory hospital admissions	+2.5% per 50 µg/m ³
Ozone	Deaths (all causes)	+3.0% per 50 µg/m ³ 8 hr mean O ₃ concentration
	Respiratory hospital admissions	+3.5% per 50 µg/m ³ 8 hr mean O ₃ concentration

Selection of health outcome

9.11 By applying the respective coefficient to these population based health outcome rates and summing for the whole of Great Britain's urban population, we have produced estimates of health impact for each pollutant.

9.12 The air pollution literature has investigated health effects for a range of severity of health outcomes from the advancement of mortality through to estimates of worsening

symptoms in patients with asthma. However, a great deal of the information has been obtained in countries outside the UK. We have taken the view that we would consider only those endpoints for which there was adequate published quantitative work which could be applied to the UK population. The health outcomes we have used are:

- a mortality;
- b respiratory hospital admissions.

9.13 Where mortality or admission to hospital is identified as a health outcome related to changes in air pollution, it is very important to realise that these outcomes are likely to only apply to patients who already have severe, pre-existing disease (eg, COPD, ischaemic heart disease). In these circumstances, the increment in level of an air pollutant acts as the precipitating factor. This is not to deny that it is possible that the establishment of that pre-existing condition *ab initio* could have been contributed to by exposure to air pollution (ie, a chronic effect, see Chapter 2), a situation which is theoretically both plausible and probable. However, other factors are, on current evidence, far more important as a primary/main cause for initiation of those conditions with which we are concerned, eg, cigarette smoking is the main cause of COPD. An increase in, say, PM_{10} of $10 \mu g/m^3$, will not result in hospital admission for an individual with normal heart and lungs.

9.14 We did not use exposure-response relationships for less severe health outcomes (such as changes in symptoms in specific disease groups (eg, asthma), changes in medication usage, restricted activity days or casualty attendances) for a variety of reasons. In some cases, health care delivery in the UK differs from that in countries where a coefficient may have been produced, while in others, extrapolation of data obtained, for instance, in the USA, to the UK for quantitative purposes may be unreliable. Qualitatively such extrapolation is reasonable, but in some instances there are differences (where they can be compared) in sizes of effect for specific outcomes from studies from the UK and other countries, which suggested to us that it would be unwise to use such coefficients for the purposes of this report.

9.15 We accept that by omitting these morbidity indicators from our estimates we are likely to be understating the effects of air pollution on the effects of the population of Great Britain. We have taken the view that this report should only employ the most reliable available data and urge that the estimates we have derived should be revisited in the near future with the benefit of more UK based studies. We have recommended that such studies should be undertaken.

9.16 While we believe that it is likely that long-term exposure to air pollution at current levels does exert an effect on health, we have taken the view that there are insufficient data to quantify these effects. This should also be reassessed at a future date as soon as helpful data are available.

Particles

9.17 We have taken the view that there is no threshold of effect of particles (as PM_{10}) for either mortality or hospital admissions.

All cause mortality

9.18 We have taken as a coefficient of effect an increase of 0.75% per $10 \mu g/m^3$ PM_{10} as a 24 hour mean. On this basis, we estimate that PM_{10} contributes to the advancement of around 8,100 deaths in the urban population of Great Britain annually.

Hospital admissions for respiratory disease

9.19 We have taken as a coefficient of effect an increase of 0.8% per $10 \mu g/m^3$ PM_{10} as a 24 hour mean. On this basis we estimate that PM_{10} contributes to around 10,500 hospital admissions for respiratory disease in the urban population of Great Britain annually. As

explained in Chapter 2, this figure should not be taken as indicating the number of admissions per year that would be saved by removal of all air pollutants. Some are probably brought forward as a result of exposure to pollution.

Sulphur dioxide

9.20 We have taken the view that there is no threshold of effect of SO₂ for either mortality or hospital admissions.

All cause mortality

9.21 We took as a coefficient of effect an increase of 0.6% per 10 µg/m³ SO₂ as a 24 hour mean. On this basis, we estimate that SO₂ contributes to the advancement of around 3,500 deaths in the urban population of Great Britain annually.

Hospital admissions for respiratory disease

9.22 We took as a coefficient of effect an increase of 0.5% per 10 µg/m³ SO₂ as a 24 hour mean. On this basis we estimate that SO₂ contributes to around 3,500 hospital admissions for respiratory disease in the urban population of Great Britain annually.

Ozone

9.23 We have undertaken two different calculations to estimate the size of effect of ozone on deaths and respiratory hospital admissions: one assuming a threshold of effect at 50 ppb (100 µg/m³) (peak daily 8 hour average concentration), the other assuming no threshold of effect. The no threshold approach has been assumed by the WHO in their assessment of health effects of ozone and we believe that this is the correct approach to take. The effect has been limited to summer data because episodes of elevated ozone concentrations in the UK are confined to the summer months. It is accepted that had the whole year been studied then, using the “no threshold assumption” larger estimates of effects would have been produced.

Mortality - all cause

9.24 We took as a coefficient of effect an increase of 3% per 50 µg/m³ ozone as an 8 hour mean. On this basis, we estimate that ozone contributes to the advancement of death (from whatever cause) of around 12,500 deaths in the total population of Great Britain annually during the summer months.

Hospital admissions for respiratory disease

9.25 We took as a coefficient of effect an increase of 3.5% per 50 µg/m³ ozone as an 8 hour mean. On this basis, we estimate that ozone contributes to around 9,900 hospital admissions for respiratory disease in the total population of Great Britain annually during the summer months.

Nitrogen dioxide

9.26 We took the view that the available data referring to the effects of nitrogen dioxide on mortality and hospital admissions were less soundly based than that for the other pollutants, except carbon monoxide, considered in this report. Calculations of effects on respiratory hospital admissions are reported in Chapter 8 but these are not included here in view of our uncertainty regarding their reliability.

Carbon monoxide

9.27 We took the view that there was too little information for determining an effect of CO on either hospital admissions or mortality for the population of the UK.

Summation of effects

9.28 By only considering those studies for the purposes of this exercise which have adequately allowed for effects of co-pollutants in determining the coefficients, it would

be tempting simply to add these effects for an overall effect of air pollution. However, two factors need to be considered which would make this approach unwise. Firstly, the ozone effects are for summer only and for the total population whereas for the other pollutants the effects are for the urban population but for a full year. Including small ozone effects during the winter and the effects of the other pollutants on the rural population would increase the overall estimates of effect size. Secondly, there may be an additive effect due to the fact that a pollutant mix, rather than single pollutants, is inhaled by the populations under consideration, although this is likely to be small.

9.29 There will be effects at the level of lesser morbidity which would add to these overall assessments, but at present there are insufficient data from the UK to determine such an effect with any confidence.

9.30 Consequently, while we accept that we may have understated the overall effects of air pollution on health in the UK we can say with reasonable confidence that the effects are likely to be at least as large as stated in this report but will, in fact, be somewhat higher. The next stage of this study of health effects will incorporate an attempt to cost these impacts. We believe that this report provides a major contribution towards estimating the costs of air pollution on health in the UK by providing quanta for mortality and admissions to hospital.

Appendix 1

Causality and Air Pollution

Introduction

A1.1 The question of causality in environmental epidemiology has been discussed many times and it is the fact that all evidence is restricted solely to observational studies that makes interpretation difficult.

A1.2 Causality is often evaluated in terms of the extent to which studies meet what are often referred to as the Bradford Hill criteria¹ which are: temporality, consistency, coherence, strength of association, biological gradient, specificity, plausibility, freedom from or control of confounding and bias and analogous results found elsewhere. Hill¹ himself admitted:

“none of my nine viewpoints can bring indisputable evidence for or against the cause-and-effect hypothesis and none can be regarded as a *sine qua non*”.

Rothman² considers that the first criterion, namely the temporality of an association is a *sine qua non*; if the cause does not precede the effect, then that is indisputable evidence that the association is not causal. However, philosophically it is impossible to “prove” causality, and Hill’s criteria should not be regarded as a checklist, but rather as guidelines or an “aide-memoire”. Renton³ has also argued a pragmatic stance:

“The consistent association between a factor and a disease occurring in the correct time order in observational studies, where bias has been minimised, suggests a causal or confounded relationship. Hill’s criteria....shift attention towards the real material basis of disease causation”.

Indeed, it is not necessary for the full causal pathway to be elucidated before public health advice be given. The highly successful ‘Back to Sleep’ campaign to reduce Sudden Infant Death Syndrome (SIDS) was based on observational data, and the physiological reasons why babies lying prone are at higher risk are still being debated.

A1.3 Under Karl Popper’s philosophy, all scientific theories are merely provisional, accepted only until a better theory is devised; the sceptical scientist would prefer to reserve judgement, and Lanes⁴ has argued that causal inference is not part of science, but public policy. However, it is incumbent on all scientists advising public policy makers to come up with the best advice available at the time, although, of course this advice may vary over time as new evidence becomes available.

A1.4 Statisticians, particularly econometricians have often discussed causality, specifically when it is not clear which are the input and which are the outcome variables; in other words which variable is the cause and which is the result of this cause (“chicken-and-egg”). In environmental studies there is usually no such conflict because mortality and morbidity cannot cause air pollution, but there can be a problem deciding whether other factors have been adequately controlled for. Cox⁵ discusses causality from a statistical point of view, in particular causality via association: a variable x is regarded as a cause of y if it occurs in all regression equations for y whatever other variables z , usually called potential confounders, are included. A confounder is a variable that is related to the input x and to the output y but not as part of a causal pathway between x and y . Time-series analysis has produced a profusion of apparent correlations including the association of the number of stork’s nests in Holland with the birth rate, and the monthly death rate by deaths from drowning in the USA with sales of ice cream. These associations arise because of confounders; in the former example the confounder is the population of

Holland, and in the latter it is environmental temperature. In environmental epidemiology, multiple linear, logistic and other regression-based methods are commonly used to estimate and to assess the statistical significance of the relationship. Suitably used, these methods provide a reliable framework for assessing the relative contributions of various explanatory factors. It is difficult, however, to exclude the possibility that an unmeasured confounder, or one that is inadequately controlled for, remains as a potential source of biased estimates of relationships. An important point here is that in any particular application, the investigator is restricted to the variables actually observed. Association may be judged to have occurred through an unobserved variable, and so causality not necessarily inferred, even though a statistically significant correlation is found. On the other hand a real association may disappear if confounders are allowed to adjust for all variation in the outcome variable. A useful review of the problems in the design and analysis of studies to assess causality has been given by Morgenstern and Thomas⁶.

Types of Input

A1.5 Most time-series and panel studies measure levels of NO₂, SO₂, particulate matter (either PM₁₀, TSP “total suspended particles” or Black Smoke), ozone and CO, usually from a single meter in a town, either hourly or over 24 hours or a maximum value within a stated period, such as 8 hourly. Confounding factors include temperature, humidity, precipitation and wind. Confounders may vary depending on the local circumstances. Other factors to control for include outbreaks of influenza and other acute infective respiratory diseases.

Types of outcome

A1.6 Outcome is measured either at an individual level, or at a group level. Individual level measures would include spirometry, for example, FEV₁, FVC and PEFR, or symptom diaries. Group level outcomes include measures of morbidity, such as number of visits to emergency units for respiratory disease, and mortality, either total or cause specific.

Types of study

A1.7 There are three main types of study used to assess the effects of pollution on health: laboratory experiments, cross-sectional studies and longitudinal studies.

Laboratory experiments

A1.8 Laboratory experiments involve exposing healthy humans to the gases and particles that make up air pollution and monitoring the effects. They can measure individual direct effects of air pollution. There are a number of difficulties with this type of study:

- i) the subjects are usually healthy adult volunteers, and yet these are the least likely to react;
- ii) the concentrations of gases are usually much higher than is normally encountered in the environment, in order to produce an effect;
- iii) only short-term effects can be measured.

Cross-sectional studies

A1.9 Cross-sectional studies involve comparing different regions or countries and measuring their morbidity or mortality and levels of pollution over a fixed period of time, such as one year. They measure chronic effects, ie, the effect of being exposed to air pollution over a period of time. One disadvantage of these studies is that international comparisons of morbidity are fraught with problems. There is also the problem of disease definition, and access to facilities; in some countries it is easier to have access to a hospital than in others and so hospital admissions are likely to be higher. Another problem is that it is difficult to control for confounding variables, in particular the differing levels of smoking in different countries. For studies between countries, the outcomes are often better restricted to total mortality. One recent study overcame some of these objections by making individual lung function measurements in eight different areas of Switzerland,

with NO₂, SO₂ and PM₁₀ showing consistent effects on FVC, but no consistent effect of ozone.⁷ The limited number of study areas and high collinearity meant it was difficult to assess the effects of a single pollutant.

Longitudinal studies

A1.10 Longitudinal studies follow the same cohort over time, and measure outcomes over relatively short periods of time such as every day. They are often referred to as time-series studies. They overcome some of the problems of cross-sectional studies, since they use within group comparisons. Thus, disease definitions should be consistent, access to facilities remain constant, and smoking levels unlikely to change within one cohort. However, longitudinal studies of this type can only measure short-term acute effects of air pollution on health. In the case of mortality it is often unclear whether this temporal clustering has any long-term effect on number of deaths. It is possible that pollution has simply hastened the death of those already moribund by a few days. This has been termed the “harvesting” effect. A proper analysis of the public health impact would consider the “person years” lost, rather than simply the number of deaths. A major development, however, has been the publication in recent years of a small number of cohort/longitudinal studies of the effects of longer-term exposure to pollution on mortality and chronic respiratory disease in the USA. We have not used the results of these studies quantitatively, because of limitations in exposure assessment and/or other aspects of transferability. They do, however, suggest that adequate quantification of longer-term effects may be feasible in due course.

A1.11 One of the major concerns with time-series analysis is to allow for the confounding effects of seasonality and the weather. This can be a major problem if the effect of the confounder is itself seasonal. For example, without suitable adjustment for confounding by climate, pollution may appear to have a greater effect on very hot and very cold days, compared to more temperate days. On the other hand, failure to adjust suitably for climate effects may mask a pollution effect, for example, from ozone. The modelling strategy for most time-series analyses has been to include all possible confounders, before adding the pollution variables to the model. Whilst this strategy is necessary to demonstrate causality, if variables are included that are correlated with pollution variables, but are not true confounders, that is they are not intermediate in the causal pathway, then they may attenuate the true regression coefficient associated with pollution. In practice, the major time-series analyses, including those which underpin the quantifications of this report, pay careful attention to adjustment for season and the weather.

Ecological fallacy

A1.12 The ecological fallacy occurs when relationships found at a group level are assumed to exist also at an individual level (for example, countries with high wine consumption *per capita* have a low heart disease rate, but this does not necessarily mean that for an individual high wine consumption protects against disease). Time-series longitudinal studies usually have no personal measures of exposure and are often regarded as subject to the ecological fallacy, and so interpreted with caution. However, this is not inherently the case because for time-series studies there is only one group, and the levels of exposure vary within that group, not between groups. In individual studies, errors in exposure measurements tend to attenuate the risk estimates, but it is not clear whether this necessarily occurs in ecological studies with group exposure.

Causality in longitudinal studies: APHEA and HEI Phase 1

A1.13 There have been two major syntheses of time-series analyses of the acute effects of air pollution: the APHEA studies⁸⁻¹³ and the Health Effects Institute (HEI) Phase 1 study.^{14,15} The latter study was divided into Phase 1.A which was restricted to the association between particulate air pollution and daily mortality and Phase 1.B which looked at the relationship between 5 pollutants (NO₂, SO₂, CO, ozone and TSP) and mortality. The former set of studies looked at hospital admissions as well.

A1.14 Gamble and Lewis¹⁶ have examined the evidence for causality and particulate air pollution using the Bradford Hill criteria and concluded that, from the evidence available at the time, causality was not supported. We will use these criteria as headings to examine aspects of the causality hypothesis for other types of air pollution as well.

Temporality

A1.15 In view of the emphasis placed by Rothman² on temporality, it is perhaps surprising that the APHEA (Europe based) and HEI Phase 1 (US based) reports did not consider this more thoroughly. Each showed a lagged effect of a change in air pollution and a change in outcome, although sometimes the effect appeared instantaneous. What would be more convincing for causality would be to show that the change in morbidity or mortality did not occur *before* the change in air pollution level. As an example the results of a cross-correlation between the residuals from a model which removes seasonality, for environmental temperature and Sudden Infant Death Syndrome (SIDS)¹⁷ showed that the cross-correlation coefficients are consistently negative for positive lags, that is, when temperature change precedes the change in deaths there is a negative relationship between temperature and SIDS. However, the cross-correlations are small and inconsistent for negative lags, that is when temperature change comes after the change in deaths. This is reassuring that seasonal effects have been successfully removed. The data for mortality in Barcelona from 1986-1989 have been analysed. In this case models were fitted to the mortality and pollution series separately to allow for seasonality, epidemics, temperature and time-dependency. The residuals from the models were cross-correlated and shown in Figures A1.1 and A1.2. The results do not support the view that higher mortality *precedes* higher pollution, for any of the four pollutants considered. There is no real evidence of an ozone effect, ie, cross-correlations on Day 0 or subsequently are small. However, for each of SO₂, NO₂ and BS, there is clear evidence of a change at Day 0, with positive cross-correlations at Days 0-3. This implies that higher values of SO₂, NO₂ or BS are associated with higher mortality on the same day and on the three successive days. The SO₂ effect is clearest, and arguably is sustained through Days 4-6. The negative correlations for BS and NO₂ five to six days after the event are suggestive of "harvesting". In summary, there is strong evidence in these data that the temporal pattern of the associations is consistent with the causality of air pollution.

Consistency

A1.16 The major arguments favouring a causal association are consistency of the findings at different locations with different climatic and pollutant characteristics, and coherence of the findings, namely, increased morbidity (eg, hospital admissions) associated with daily concentrations of pollution. Confounding from weather and co-pollutants is said to be adequately controlled. Reanalyses by the HEI team¹⁴ of the Philadelphia data set on particulate air pollution and daily mortality has shown consistency with the original analyses, despite findings by others¹⁸ that different models produce different results. The APHEA project found consistent results over 6 cities for ozone related to total mortality,^{8,18} and for sulphur dioxide and PM₁₀ in twelve cities²⁰ but inconsistent results for NO₂.^{8,18}

Coherence

A1.17 Chamber studies of patients with asthma exposed to mixtures of polluted air containing particulate concentrations 30-100% higher than 150 µg/m³ PM₁₀ and 100-500 ppb SO₂ and NO₂ (286-1430 µg/m³ SO₂; 188-940 µg/m³ NO₂) showed no reduction in lung function.^{21,22} However, the type of person admitted to hospital during a high pollution day will not be the same kind of person to voluntarily submit themselves to chamber studies. However, a recent review showed strong evidence of both consistency and coherence of health effects across a range of related health outcomes and independent analytic studies.²³

Figure A1.1 The data consist of daily mortality, and daily levels of SO₂ and ozone in Barcelona, Spain from 1986 to 1989. For each series a model comprising terms for trend, seasonality, temperature and serial correlation was fitted, and then the fitted values subtracted from the observed values to leave the residuals. The mortality residuals were then cross-correlated with each of the pollution variables. The correlation coefficient obtained when the mortality series was lagged by -7, -6..., +7 days relative to the pollution was plotted on the figure, together with an estimate of ± 2 standard errors. Thus, a negative lag implies that mortality change preceded pollution change and a positive lag implies mortality change succeeds pollution change

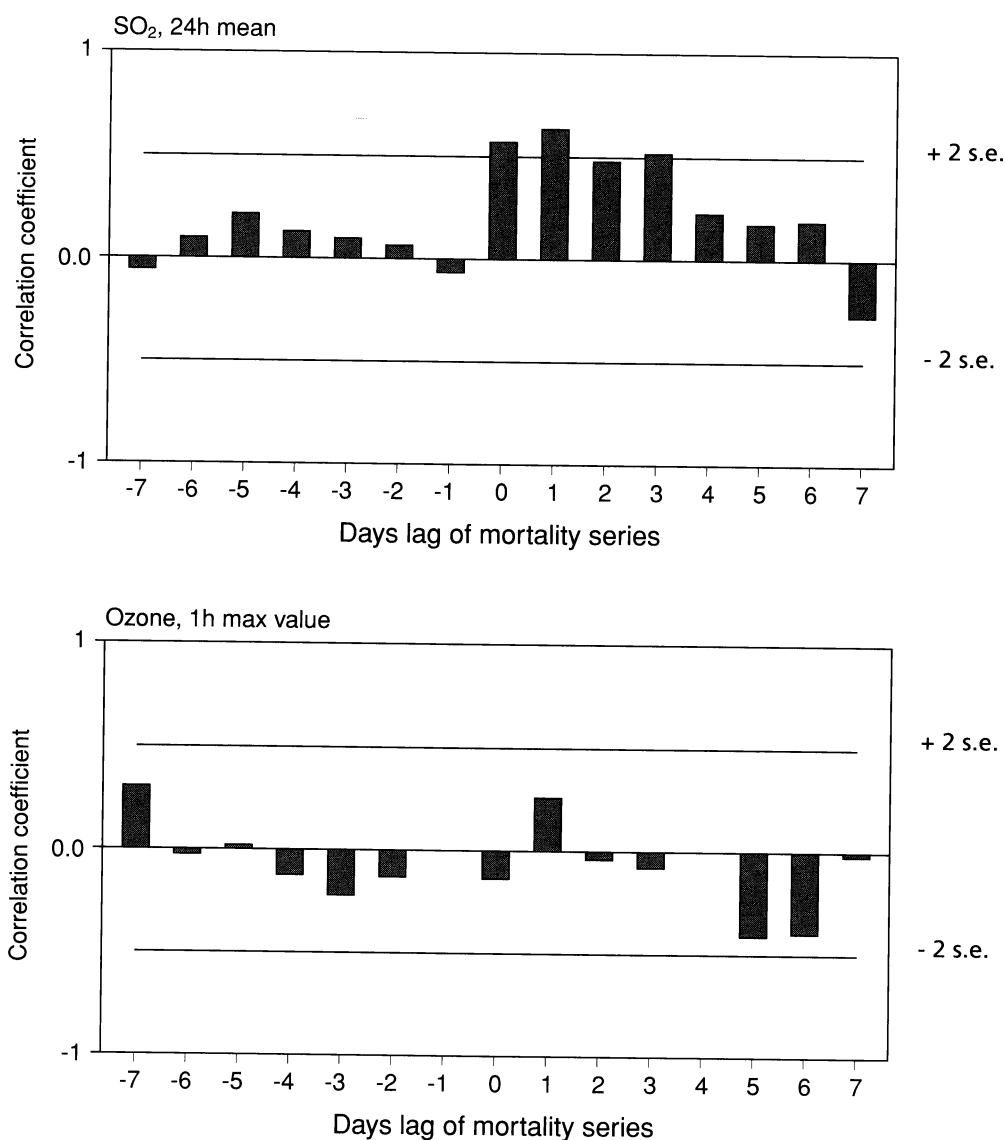
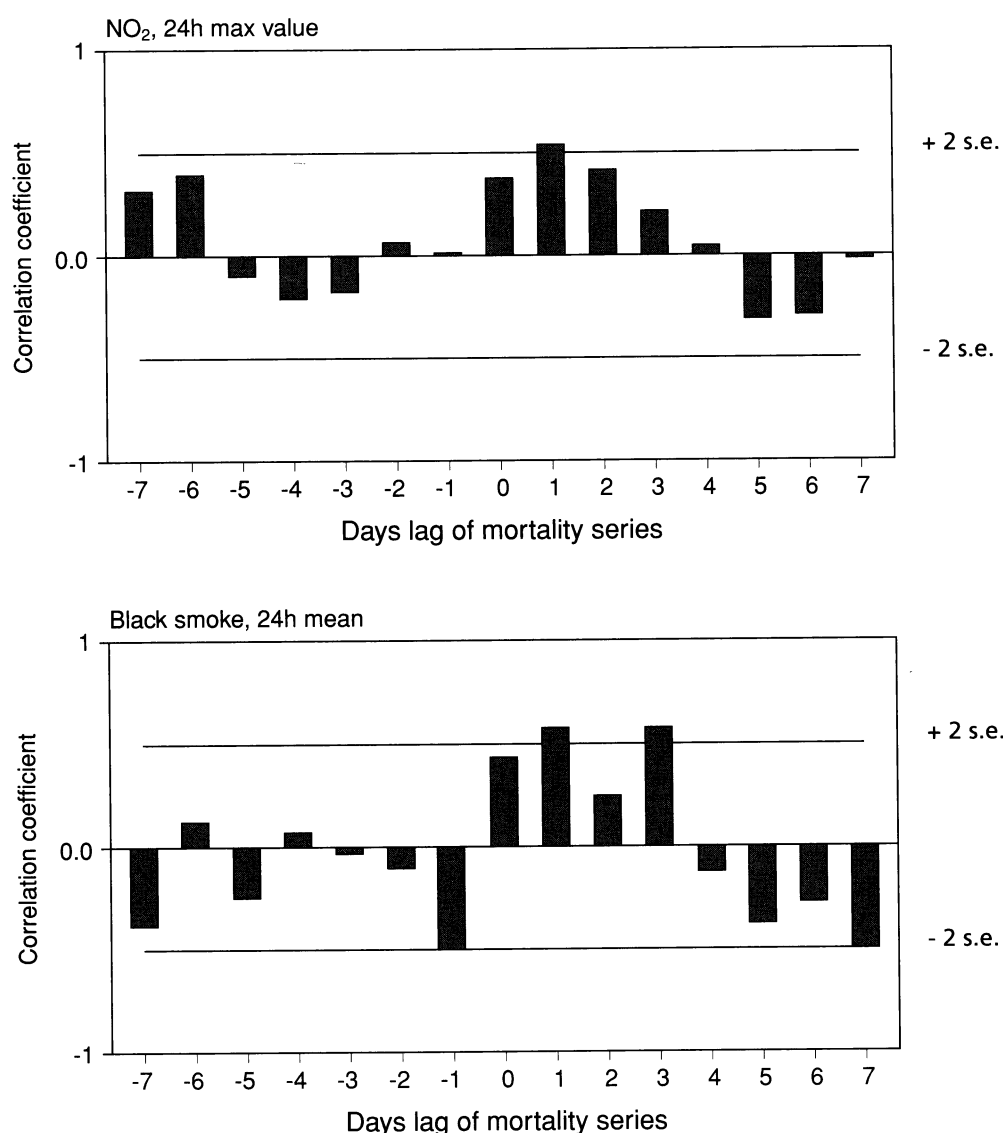


Figure A1.2 The data consist of daily mortality, and daily levels of NO₂ and Black Smoke in Barcelona, Spain from 1986 to 1989. For each series a model comprising terms for trend, seasonality, temperature and serial correlation was fitted, and then the fitted values subtracted from the observed values to leave the residuals. The mortality residuals were then cross-correlated with each of the pollution variables. The correlation coefficient obtained when the mortality series was lagged by -7, -6..., +7 days relative to the pollution was plotted on the figure, together with an estimate of ± 2 standard errors. Thus, a negative lag implies that mortality change preceded pollution change and a positive lag implies mortality change succeeds pollution change



Strength of association

A1.18 The association between air pollution and mortality or morbidity is weak, in the sense that ordinary daily variations in pollution are not a major influence on daily mortality, hospital admissions or other morbidity indices. For example, many studies estimate a Relative Risk (RR) < 1.50 for as much as a 100 $\mu\text{g}/\text{m}^3$ change in PM₁₀. The fact that the estimated effect is relatively small may have two disadvantages. First, the estimated effect may be sensitive to incomplete adjustment for confounders, notably climate, whose impact may be substantially greater than that of pollution itself. Confounding is considered in A1.21, below. Secondly, it may be difficult to identify a relatively small effect clearly, ie, with statistical significance, against a background of large unexplained variability. In practice, however, many studies individually show statistically significant results; and, when evidence is formally amalgamated across studies, the results can be very highly significant statistically. Briefly, air pollution epidemiology shows strong evidence of a weak effect.

Biological gradient

A1.19 There is evidence of a biological gradient when higher daily concentrations of pollution are associated with higher daily mortality, hospital admissions and other outcomes. The air pollution literature gives very strong evidence of exposure-response relationships; ie, of a biological gradient, despite the fact that confounders, and the effect of co-pollutants, complicate the estimation of these relationships. There are aspects of the shape of these relationships, notably that of threshold or not, which are not well established, and other difficulties such as measurement error make precise quantification difficult; but the overall evidence in favour of a biological gradient is compelling.

Plausibility

A1.20 The biological mechanisms to explain how low-level ambient pollution could cause the increased mortality and morbidity suggested by the time-series studies have yet to be determined in any detail. There are, however, other plausible hypotheses. One suggestion is that air pollution enhances airways responsiveness to ragweed and grass allergies.²⁴ Another is that of Seaton²⁵ regarding the possible role of ultrafine particles.

**Possible biases:
Confounding**

A1.21 Adjustment for weather has been incomplete, as indicated by the low R^2 of air pollution/mortality-morbidity studies relative to climate/mortality-morbidity studies. The issue has been investigated most thoroughly in a recent HEI report¹⁵ which showed that estimated pollution effects were relatively insensitive to different and complex ways of adjusting for weather. This, together with the relative consistency of estimated pollution effects in markedly different climate patterns gives strong reassurance that residual confounding by weather is not a major problem.²⁶

Measurement error

A1.22 The direction and magnitude of measurement error is problematic as the correlation between ambient and indoor air is poor, and between ambient and personal exposure is largely unknown.

Lag bias

A1.23 Lags for temperature vary by season. There is no consistent optimal lag time for pollutants among time-series studies, though lags identified as optimal are in the range 0-5 days. The lags used both for hot and for cold temperatures may also not be optimal, leaving the possibility of residual confounding. On this, see A1.21 above.

A1.24 Schwartz,²⁷ who is one of the major contributors in the field, concludes that the evidence seems to leave little room to doubt that particulate air pollution at commonly occurring levels is causally associated with a range of adverse outcomes, including early mortality. The limited results on temporality would support this, although many of the other traditional criteria are only weakly met.

A1.25 The results from the APHEA study also leave little room for doubt as to the roles of certain air pollutants. However, it is reported in Phase 1.B of the HEI study:

“Although individual air pollutants are associated with increased daily mortality in these data, the broader association of pollution with daily mortality in this city (Philadelphia) cannot be reliably attributed to any single criteria air pollutant....it is not possible to establish the extent to which particulate air pollution by itself is responsible for the widely observed association between mortality and air pollution in Philadelphia, but we can conclude that it appears to play a role”.

We conclude with a summary from the Health Effects Institute President:²⁸

“It is rare these days to see a study of the health effects of air pollution that does not observe that we cannot view each air pollutant in isolation, but must view air pollution as a complex mixture.....Understanding the whole mixture will not be a simple undertaking.”

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Appendix 2

Glossary of Terms and Abbreviations

Angina	Chest pain brought on by exercise and caused by inadequate blood supply to the heart
APHEA project	Short Term Effects of Air Pollution on Health: a European Approach using Epidemiological Time-Series Data. A project initiated and funded in the framework of the EC Environment 91-94 programme, the main objective being to provide quantitative estimates, using standardised methods, of the short-term effects of air pollution in Europe, with data from 15 large cities representing various social, cultural, environmental and air pollution situations
Asthma	A chronic respiratory disease in which the airways are unusually sensitive to a range of stimuli. This results in episodic airway obstruction
BS	Black Smoke. Non-reflective (dark) particulate matter, measured by the smoke stain method
CI	Confidence Interval. The 95% confidence interval is the range including the best estimate of a result for variability, where there is a 95% chance of the true result following
CO	Carbon monoxide
COMEAP	Committee on the Medical Effects of Air Pollutants
COPD	Chronic obstructive pulmonary disease
DETR	Department of the Environment, Transport and the Regions
DH	Department of Health
EPAQS	Expert Panel on Air Quality Standards
ERVs	Emergency room visits
FEV₁	The volume of air expired during the first second of a maximal or "forced" expiration
Fixed effect model	Assumes that the estimated effects (between cities) are estimates of the same underlying effect; ie, that the differences (in effects between cities) are not intrinsic, but are explicable by chance
FVC	Forced vital capacity. The volume of air expired in a forced expiration following maximum inspiration
GB	Great Britain
Genotoxic carcinogens	Substances causing cancer by attacking the genetic material (DNA) in cells
HEI	Health Effects Institute
ICD	International Classification of Diseases
IHD	Ischaemic heart disease
Inhalable particles	Particles which may be breathed in, ie, which enter the nose and mouth on inspiration. "Inhalability" is the orientation-averaged aspiration efficiency for the human head
LAIA	Lung and Asthma Information Agency

MAAPE	Advisory Group on the Medical Effects of Air Pollution Episodes
Meta-analysis	A statistical method used to combine the results of a number of individual studies
MRC	Medical Research Council
NAEI	National Atmospheric Emission Inventory
NO_x	Total oxides of nitrogen. Conventionally the mixture of NO and NO ₂ in the atmosphere
O₃	Ozone
PEACE study	Pollution Effects of Asthmatic Children in Europe. A multi-centre study of 14 institutes in 10 European countries, partly funded by the EU Environment Programme. The main objectives are to study short-term health effects of air pollution on the respiratory health of susceptible children and to compare results between urban and non-urban locations
PEFR	Peak expiratory flow rate
PM_{2.5}	Particle matter less than 2.5 µm aerodynamic diameter (or, more strictly, particles which pass through a size selective inlet with a 50% efficiency cut-off at 2.5 µm aerodynamic diameter)
PM₇	As with PM _{2.5} but with 7 µm as the cut-off point
PM₁₀	As with PM _{2.5} but with 10 µm as the cut-off point
PM₁₃	As with PM _{2.5} but with 13 µm as the cut-off point
ppb	Parts per billion
ppm	Parts per million
RADs	Restricted activity days
RR	Relative risk
Rural	Parts of the country outside towns and cities
SAPALDIA	Swiss Study on Air Pollution and Lung Diseases in Adults
SIDS	Sudden Infant Death Syndrome
Six Cities Study	A long-term cohort study underway in the United States of America
SO₂	Sulphur dioxide
TSP	Total suspended particulate. The gravimetrically determined mass loading of airborne particles. Most commonly associated with use of the US high volume air sampler in which particles are collected on a filter for weighing
UK	United Kingdom
Urban	That part of the country included by towns and cities
USA	United States of America
WHO	World Health Organization

Concentration Units and Conversion Factors

Concentrations of air pollutants are expressed in two ways, either as the mass of pollutant in a given volume of air (usually expressed as micrograms per cubic metre or $\mu\text{g}/\text{m}^3$) or as the ratio of the volume of the gaseous pollutant (expressed as if pure) to the volume of air in which the pollutant is contained (usually expressed as a volume mixing ratio or parts per million, ppm, or parts per billion, ppb).

The mass concentration as expressed above will be dependent on the ambient temperature and pressure and ideally these should be specified each time a concentration is measured as a mass/volume. The variation is discussed below and although not large may not be negligible where large variations in temperature and pressure occur.

The volume mixing ratio is independent of temperature and pressure, if ideal gas behaviour is assumed.

The relationship between the two sets of units can be expressed as follows:

$$\mu\text{g}/\text{m}^3 = \text{ppb} \times \frac{\text{molecular weight}}{\text{molecular volume}}$$

where:

$$\text{molecular volume} = 22.41 \times \frac{T}{273} \times \frac{1013}{P}$$

where T is the ambient temperature ($^{\circ}\text{K}$) and P is the atmospheric pressure (in millibars). Conversion factors for some common gaseous pollutants are given in the Table below for 20°C and 0°C and 1013 mb pressure. Pollutants which are present in particulate form in the atmosphere such as sulphates are normally only expressed in mass/volume units.

Pollutant	Molecular weight	To convert			
		ppb to $\mu\text{g}/\text{m}^3$		$\mu\text{g}/\text{m}^3$ to ppb	
		0°C	20°C	0°C	20°C
NO_2	46	2.05	1.91	0.49	0.52
NO	30	1.34	1.25	0.75	0.80
HNO_3	63	2.81	2.62	0.36	0.38
O_3	48	2.14	2.00	0.47	0.50
SO_2	64	2.86	2.66	0.35	0.38
CO†	28	1.25	1.16	0.80	0.86

* ie, to convert ppb of SO_2 at 0°C to $\mu\text{g}/\text{m}^3$ multiply by 2.86

† for CO the factors apply to the more commonly used conversions of ppm and mg/m^3

Appendix 3

Membership of the Committee on the Medical Effects of Air Pollutants

Chairman

Professor S T Holgate, BSc, MD, DSc, FRCP, FRCPE, FRSA

Members

Professor H R Anderson, MD, MSc, FFPHM

Professor J G Ayres, BSc, MD, FRCP, FRSA

Professor P G Blain, MB, BS, PhD, FRCP, FFOM

Professor P G J Burney, MA, MD, MRCP, FFPHM

Dr M L Burr, MD, FFPHM

Professor R L Carter, CBE, MA, DM, DSc, FRCPath, FFPM

Professor A Dayan, MD, FRCP, FRCPath, FFPM, CBiol, FIBiol

Dr A Gibbs, TD, MB, ChB, FRCPath

Professor R K Griffiths, BSc, MB, ChB, FFCM

Professor R M Harrison, PhD, DSc, CChem, FRSC, FRMetS, FRSH

Mr Fintan Hurley, MA

Dr D Purser, BSc, PhD

Professor R J Richards, BSc, PhD, DSc

Professor A Seaton, CBE, MD, FRCP, FFOM

Professor A Tattersfield, MD, FRCP

Mr R Waller, BSc

Dr S Walters, BSc, MRCP, MFPHM

Secretariat

Dr R L Maynard, BSc, MRCP, MRCPath, FFOM

Dr H Walton, BSc, DPhil (*Scientific*)

Mr J P Crook, BA(Econ), MA (*Administration*)

Miss J P Cumberlidge, BSc, MSc (*Minutes*)

Appendix 4

Membership of Sub-Group on Quantification of the Effects of Air Pollution on Health in the United Kingdom

Chairman

Professor J G Ayres, BSc, MD, FRCP, FRSA

Members

Professor H R Anderson, MD, MSc, FFPHM

Professor P G J Burney, MA, MD, MRCP, FFPHM

Dr M L Burr, MD, FFPHM

Professor M J Campbell, BSc, PhD

Professor R Harrison, PhD, DSc, CChem, FRSC, FRMetS, FRSH

Mr F Hurley, MA

