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Sub-priority 6.1.3.2.5: Socio-economic tools and concepts for energy strategy.

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“A Review of Literature on air pollution and health, with recommendations for quantification”

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1. Structure

1.1 Abstract

It has been recognized, in many studies of externalities, including ExternE, that the health effects of outdoor air pollution have, in many circumstances, a major influence on the final results. A comprehensive literature review of air pollution and health, with recommendations for concentration-response (C-R) and impact functions to be used in quantification, was therefore a priority for NEEDS, with the twin aims of (i) updating recommendations from ExternE and (ii) aligning these recommendations more fully with those of the World Health Organisation (WHO). Fortunately, the health impact assessment (HIA) for the cost-benefit analysis (CBA) of the Commission’s major Clean Air for Europe (CAFE) programme had similar requirements. This allowed joint effort on the two projects and a far more comprehensive analysis for each one that would have been possible with the funding for that project only.

Working within a framework determined in part, and in some respects determined crucially, by WHO’s evaluations for CAFE, the literature review considered a very wide range of health endpoints shown or believed to be associated with ambient particulate matter (PM) or ozone (O₃). Each of these was reviewed in turn to (i) check if there was sufficient evidence of a relationship to merit quantification and, if so, to (ii) estimate a suitable C-R function, (iii) estimate relevant background rates for quantifying effects in the EU-25, and (iv) link these into an impact function for use in quantification. Depending on the strength of evidence, some impact functions were included in core analyses, others in sensitivity analyses only.

1.2 Structure (organization of the work)

Detailed results from the CAFE-NEEDS literature review and evaluation have already been published (Hurley et al 2005a, b; also Holland et al 2005 a, b), and further summaries will be included as part of forthcoming WHO publications. The present report is also a summary. The Introduction (Chapter 2) gives background, leading to the need for a comprehensive review of the literature at
Chapter 3 describes the alignment of objectives between CAFE CBA and NEEDS. Chapter 4 describes how the work was organised between the two projects and Chapter 5 describes publications to date and others in preparation.

The main body of results is given in Chapters 6 and 7, which refer, respectively, to PM and to ozone. The focus, in this relatively short report, is on the impact functions themselves. The sources of the functions are given only briefly; further details are in Hurley et al (2005a). Similarly, the present report does not attempt a detailed or comprehensive assessment of uncertainties. For a qualitative assessment of some key end-points, see Hurley et al (2005b), while Holland et al (2005b) provide a quantitative assessment. Conclusions and strategic recommendations are presented in Chapter 8. Chapter 9 gives a full bibliography of references cited in Hurley et al (2005a), with the two purposes of (i) referencing all articles quoted in the present report and (ii) in addition, indicating the scope and scale of the underlying literature review.

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2. Introduction

2.1 The role of quantifying air pollution and health, within NEEDS

The team for Stream 1b of NEEDS, led by Dr. Rainer Friedrich at IER in Stuttgart, has extensive experience of studying the external costs of energy systems, notably but not only transport and electricity production. That experience has shown, again and again, that one key aspect of external costs is comprised of the health impacts, among the general public, of air pollution from transport or from forms of electricity production that involve burning of fossil fuels.

It was therefore recognised that a priority, within NEEDS, was to update and further develop the methodology for quantifying the public health effects of outdoor air pollution, especially particles in outdoor air.

2.2 Comprehensive ExternE reviews of air pollution and health

The NEEDS project, and especially Stream 2, draws heavily on work previously carried out for the Commission under the various projects on the ExternE programme, including some ongoing projects. This applies in particular to issues of air pollution and health, which are central to estimating quantitatively the effects of energy systems, including transport and electricity generation from fossil fuels, and where the ExternE methodology has been widely accepted and used, including by the Commission in its development of policies for air pollution control.

Within ExternE, the first comprehensive review of the literature on air pollution and health, with a view to quantifying health effects of pollution, was carried out in 1993-95. This review focussed on the ‘classical’ air pollutants – particles (expressed as PM$_{10}$) and the major combustion-related gases (ozone, SO$_2$, NO$_2$ and CO); i.e. it included those gases and particles emitted directly and those derived later, in the course of atmospheric reactions. It included:
i. An assessment of causality of various pollutants;

ii. An assessment of which health endpoints were associated with the pollutants that were considered to be causal – PM and ozone;

iii. Recommendations on key framework issues such as whether the evidence supported a population-level threshold for health effects;

iv. Recommendations for concentration-response (C-R) functions (i.e. % change in health effect per µg/m³ pollutant) for quantifying the many specific pathways to be included; with these estimates varying by as necessary by sub-population (e.g. children, elderly, people with asthma);

v. Recommendations for estimating background rates of morbidity for the various health endpoints; and

vi. Recommendations for aggregating across pollutants and health endpoints.

The review and recommendations were published in the first ExternE Methodology Report (1995) and were the basis for ExternE work for a number of years.

The second comprehensive review of the literature on air pollution and health, with a view to quantifying health effects of pollution, was carried out in 1997-98. This was necessary because (a) ongoing research on work and health had led to new information, including a much wider set of results in Europe, especially from the APHEA project; (b) understanding within the air pollution and health community continued to mature, and in particular, it was becoming more accepted that long-term exposure to ambient PM, as estimated from cohort studies, may have adverse effects on mortality that dominated those of short-term exposures (‘daily variations’). Furthermore, the ExternE team was uneasy about using ‘attributable deaths’ as the key outcome from the cohort studies, and had a major programme of development of methodology to express results in terms of life expectancy instead.
The review covered similar topics as before. Results and recommendations were published as part of the second ExternE Methodology Report (1999).

2.3 The need for a further comprehensive review within NEEDS

The pace of new research on air pollution and health has continued to grow, as has the understanding of air pollution and health, and reviews and meta-analyses by expert groups. To some extent these issues were identified in the various follow-on projects of ExternE (e.g. DIEM, NEWEXT) and, where practicable, *ad hoc* adjustments were made to the core ExternE quantification framework. It was clear, however, when the NEEDS proposal was being prepared, that a third comprehensive review was necessary to update the quantification framework for air pollution and health in the light of new evidence and understanding.

There were two other reasons for a comprehensive update. First, ExternE researchers, notably Ari Rabl in Paris, and Brian Miller and Fintan Hurley in Edinburgh, had continued to develop the methodology for estimating changes in life expectancy rather than ‘attributable deaths’ from long-term exposure to PM$_{2.5}$. Secondly, ExternE researchers had realised that, while their quantification model was good and in some respects leading edge, its use would become much readily accepted if it were seen to be consistent with evaluations from other sources, notably the World Health Organisation (WHO). On that basis, Leo de Nocker and Rudi Torfs from VITO in Flanders, and Fintan Hurley from the IOM, visited Dr. Michal Krzyzanowski of WHO, then based at Bilthoven. That meeting led to a WHO workshop on quantifying the health effects of outdoor air pollution, held in Bilthoven in November 2000 (WHO, 2001), and to much closer subsequent collaboration with WHO.
3. Organisation of the work

3.1 Links with the Cost-Benefit Analysis (CBA) of the Clean Air for Europe (CAFE) programme

Fortunately, this need coincided with the need also for a comprehensive review of the same issues, as part of the cost-benefit analysis (CBA) of the Clean Air for Europe (CAFE) programme. The CAFE programme was and is managed by DG Environment, under the overall direction of Dr. Matti Vainio, while Dr. André Zuber had a special responsibility for health effects estimation.

In addition, WHO under the leadership of Dr. Michal Krzyzanowski had carried out a series of reviews of the health effects of particles, ozone and NO₂, to assist CAFE in its work. These reviews were in the form of answers to questions from the CAFE Steering Group (WHO, 2003) and answers to CAFE Follow-up Questions (WHO, 2004a). Both of these reviews focused on hazard assessment, on issues such as threshold (or not) of effects, or what kinds of particles are responsible for the adverse health effects of PM. They did not provide specific information for quantification.

Two other WHO initiatives at about the same time did, however, provide quantitative recommendations. One of these was a series of annual meetings of the WHO-led Task Force on Health (TFH) of the UNECE Convention on the Long-Range Transport of Air Pollutants. The TFH provided specific quantitative guidance to the RAINS Integrated Cost-Effectiveness Model of IIASA in Austria. The guidance was focused on two areas:

- Effects on mortality (life expectancy) of long-term exposure to ambient PM₂․₅;
  and
- Effects on mortality (attributable lives shortened) of daily variations in ambient ozone.

As well as proposing specific functions for quantification, TFH of CLRTAP also set out a number of framework issues for quantification. These included that:
• Quantification of the classical air pollutant mixtures be restricted to the effects of PM and of ozone;

• Quantification of PM be based on anthropometric PM, without threshold;

• Components of the PM$_{2.5}$ ambient urban mixture be quantified (per µg/m$^3$) the same as the overall mixture itself; i.e. that the known or suspected differences in toxicity between different components of fine PM (i.e. PM$_{2.5}$) be ignored for quantification purposes.

• Quantification of ozone also be without threshold, but that ozone effects be estimated only above 35 µg/m$^3$ (8-hr daily max), on days when this level is exceeded.

In addition, Ross Anderson and colleagues in London carried out a WHO-sponsored meta-analysis of studies in Europe linking, variously, PM$_{10}$ or PM$_{2.5}$ or ozone with (i) all-cause and cause-specific mortality; (ii) respiratory hospital admissions or cardiovascular admissions; (iii) days of additional medication use in people with chronic lung disease; and (iv) cough days in people with chronic lung disease (WHO, 2004b).

It was decided that the quantification of health effects within CAFE CBA would be as consistent as practicable with all four of the above WHO initiatives (two qualitative and two quantitative). This was partly to maintain consistency within the CAFE process and partly because of the authority of WHO. It was recognised however that CAFE CBA would include a possibly wide range of morbidity endpoints, if suitable C-R functions could be found, and if background morbidity rates could also be estimated suitably.

Thus, the situation had arisen whereby there was a perfect alignment of goals between the planned literature review for NEEDS and the planned literature review for CAFE CBA.
This allowed joint effort on the two projects and a far more comprehensive analysis for each one that would have been possible with the funding for that project only.

3.2 Allocation of effort between CAFE CBA and NEEDS

The work on CAFE CBA started in December 2003 and that for NEEDS on 1 September 2004, somewhat later than had been anticipated, the administrative work having been more extensive than had been expected. Because of the relative timings, all the initial costs were charged to CAFE CBA. Costs were charged to CAFE CBA and to NEEDS as appropriate, once NEEDS had begun.
4. Scope, coverage and process of literature review

As noted above, the sharing of review work for the two projects enabled a substantially more thorough outcome than would otherwise have been possible. This was fortunate because overall, the review work itself was substantially more than had been anticipated. There were several reasons for this.

4.1 Reasons related to mortality and long-term exposure to PM

i. The focus of early work on CAFE CBA was on reconciling two life table approaches to estimating the life expectancy gains of reducing ambient PM$_{2.5}$. These were, respectively, the approach of the CAFE CBA team, based on experience within ExternE and the approach of RAINS, together with some of the framework assumptions of WHO. While there were many similarities in the two approaches, there were some important differences also, and work was needed to understand these differences and their implications. The differences included:

- Differences in choice of coefficient from Pope et al. (2002);
- The WHO framework decision to apply the same coefficient to all PM in the PM$_{2.5}$ (or PM$_{10}$) size range, regardless of source, composition or other characteristics that might be relevant to toxicity.

ii. In addition, whereas the ExternE team had for some year not estimated ‘attributable deaths’, on the grounds that the methods for doing so were suspect, a decision was taken (partly in the light of the comments of external reviewers) that ‘attributable deaths’ would be estimated. This led to unexpected methodological work in order to clarify the relationship between ‘attributable deaths’ and changes in life expectancy.

iii. The CAFE CBA/ NEEDS work has involved examining two other methodological questions relevant to life tables. These are:

- The relationship between results obtained from a sustained reduction in pollution, with associated sustained reductions in mortality hazards, and a set of consecutive one-year ‘pulse’ reductions, with
associated consecutive temporary reductions in mortality hazards. This is necessary because benefits and costs are compared on annual basis.

- The possible shape and importance what is known as the ‘cessation lag’, i.e. the time-period between reductions in pollution and consequent reductions in mortality.

4.2 Other reasons

iv. The existing C-R functions to be used were all fully reviewed. Some were dropped from consideration. Others were changed considerably in the light of new evidence in intervening years. Where C-R functions were taken from the same source studies as previously, those source studies were re-reviewed in detail, including in the light of their usage by other HIA teams, and where appropriate somewhat different C-R functions were proposed, or the rationale for the functions used was described in much greater detail. This applied in particular to two sets of studies whose results were known (from previous ExternE work) to have a substantial impact on final answers. These were:

- Estimates of the relationship between long-term exposure to PM and development of new cases of chronic bronchitis in adults, based on the US AHSMOG study; and
- Estimates of the relationship between PM and/or ozone and restricted activity days (RADs), or variants of the same.

v. Some new pathways were quantified, notably long-term exposure to PM and increased mortality in infants, and short-term exposure to PM and work days lost.

vi. Very substantial new work was carried out to produce better estimates than previously of background rates of morbidity across the EU 25.

vii. The entire process was subject to formal expert peer review, the reviewer for health effects estimation being Dr. Bart Ostro of the California EPA.
(Krupnick et al., 2004). This led to a number of revisions and improvements, and further under-pinned the reliability of the work.

viii. The entire process was also subject to close and detailed stakeholder involvement. This required resource and attention, including in due course a detailed response to the written comments of the industry body UNICE.
5. Outputs from the literature review

5.1 Web-published reports

Four detailed reports from the CAFE CBA/ NEEDS literature review have already been published on the World-Wide Web.

a. The single most important one is that by Hurley et al. (2005a). This report gives the detailed literature review, along with recommendations for C-R functions and for background rates, that underpins the quantification of health in CAFE CBA. The report also includes discussion of a wide range of relevant methodological issues.

b. Holland et al. (2005a) is an overview of the whole CAFE CBA Methodology, including a summary overview of health. Its description of health quantification is a good alternative for those who do not wish or need to know the full details.

c. Following detailed comments by UNICE as part of the consultation process, the CAFE CBA team prepared a detailed response (Hurley et al., 2005b). Although referring to an earlier draft of the overall Methodology than was published as Hurley et al. (2005a), the UNICE comments and the CBA team’s response are informative about uncertainties within the evaluation.

d. Holland et al. (2005b) is a complementary and quantitative analysis of uncertainties associated the quantification of health in CAFE CBA.

Of course these reports also benefited enormously from the involvement of other authors who are not part of this WP of NEEDS, especially Dr. Mike Holland (EMRC), Paul Watkiss (AEA Technology Environment) and Dr. Alastair Hunt (University of Bath/ Metroeconomica).

In addition, summaries of the CAFE-NEEDS methodology and results are being prepared for inclusion in two forthcoming WHO publications, one on particulate matter, the other on ozone. We have on occasions drawn on those summaries in preparing the details of the present report (Sections 6 and 7).
5.2 Papers on air pollution and health consulted and quoted in literature review

The Bibliography (Section 9.2) lists the many papers on air pollution and health (including background rates of morbidity) which not only were consulted as part of the literature review, but were quoted in the principal final report (Hurley et al, 2005a)
6. Quantifying the adverse effects on health of ambient particulate matter (PM)

6.1 Mortality in adults aged 30+ from long-term exposure to PM

It is widely recognised now that the Pope et al (2002) update of the American cancer society (ACS) cohort study is the key study for quantifying the effects on mortality of long-term exposure to PM. Following TFH of WHO-UNECE, CAFE CBA used as its principal C-R function for quantification an increase of

6% change in mortality hazards (95% CI 2-11%)\(^1\) per 10 µg/m\(^3\) PM\(_{2.5}\)

from Table 2 in Pope et al. (2002). These are estimates derived from using the average of annual average concentrations from two periods of measurement, one of them early (1979-83) and the other late (1999-2000) in the follow-up period of the ACS study. Given that in the USA ambient PM\(_{2.5}\) declined over the follow-up period, use of the ‘average’ pollution measures is consistent with a short cessation time-lag between changes in ambient PM and consequent reductions in the risk of mortality.

An alternative estimate, also from Table 2 of Pope et al (2002), is

4% change in mortality hazards (95% CI 1-8%) per 10 µg/m\(^3\) PM\(_{2.5}\),

derived from using annual average concentrations at the start of the follow-up period. This is consistent with a view of a longer cessation lag. WHO-UNECE recommended that this value be used in sensitivity analyses. Note that recent ExternE-based evaluations (e.g. DIEM, NewExt) used a coefficient of 5%, i.e. the average of the WHO-UNECE 1\(^{st}\) and 2\(^{nd}\) choice coefficients, above.

The changes in risk in any of these coefficients are applied at ages 30 or more, because the ACS study was based on adults in that age range. Primary implementation is via life table methods, using e.g. the RAINS implementation

\(^{1}\) 95% confidence intervals (CIs) are the smallest intervals which include the true risk coefficient 95% of the time, if the underlying model assumptions are true.
As noted earlier, CAFE CBA also included estimates of attributable deaths.

Also as noted earlier, these and all other C-R or impact functions for PM below, were applied to anthropometric PM (PM$_{2.5}$ or PM$_{10}$), without threshold, irrespective of the source or composition of the PM.

### 6.2 Mortality at all ages from short-term exposure to PM

An issue in quantification is whether deaths as estimated from time series studies of short-term exposures (daily variations in PM) should in some way be included also. The issue is to avoid double-counting while capturing the full effects of PM on mortality. The WHO meta-analysis of studies in Europe (Anderson et al, 2004) provides a suitable coefficient, with % change estimated as:

\[
0.6\% \text{ (95\% CI 0.4\%, 0.8\%) per 10 µg/m}^3 \text{ PM}_{10}
\]

all-cause mortality (excluding accidents), all ages

Note that some of the attributable deaths from time series studies are not already included in mortality as estimated from cohort studies, because the time series studies capture effects at ages less than 30 years, and also (by using the metric of PM$_{10}$) capture some direct effect of the coarse fraction of PM. These effects are small, however, compared with mortality in adults associated with longer-term exposure to PM$_{2.5}$. To avoid double-counting, Hurley et al (2005a) recommended not to add time series mortality effects attributable to PM to those from cohort studies.

### 6.3 Mortality in infants (aged less than 1 year) from long-term exposure to PM

Woodruff et al (1997), a US cohort study of 4 million infants, showed that post neonatal infant mortality, between the ages of one month and one year, was associated with mean outdoor concentrations of PM$_{10}$ in the 1st two months of life,
giving a concentration-response (C-R) function for change in (all-cause) infant mortality of

\[ 4\% \text{ per } 10 \mu g/m^3 \text{ PM}_{10} \text{ (95\% CI 2\% - 7\%)} \]

It is unclear to what extent these infant deaths associated with and presumably attributable to air pollution occur among young people who are already very frail, and so unlikely to survive into adulthood. This complicates assessment both of public health importance and of monetary valuation. Following Kaiser et al (2004), Hurley et al (2005a) estimated attributable deaths rather than life expectancy, though this transfers the problem to valuation rather than solving it.

6.4 Morbidity – general methodological remarks

The general approach to estimating the effects of PM (or ozone) on morbidity uses a concentration-response (C-R) function expressed as % change in endpoint per \((10)\mu g/m^3\) \text{PM}_{10}\ (or \text{PM}_{2.5})\ and links this with (i) the background rates of the health endpoint in the target population, expressed as new cases (or events) per year per unit population – say, per 100,000 people; (ii) the population size and (iii) the relevant pollution increment, expressed in \(\mu g/m^3\) PM. Results are then expressed as estimated new or ‘extra’ cases, events or days per year attributed to PM.

Note that the percentage change in probability can be combined with background rates to give a single impact function expressed as:

\[
\text{number of (new) cases, events or days per unit population (say, per 100,000 people)}
\]

\[
\text{per (10) } \mu g/m^3 \text{ annual average PM}_{10}\ (or \text{PM}_{2.5}) \text{ per annum}
\]

For many health endpoints, reliable data on background rates of morbidity in the EU-25 target population are not readily available. One strategy then is to use other general epidemiological studies of that health endpoint – not necessarily studies of air pollution and health – to provide estimates of background rates, for
example the International Study of Asthma and Allergies in Children (ISAAC) and, for adults, the European Community Respiratory Health Study (ECRHS). Another approach is to estimate an impact function from where the relevant epidemiological studies were carried out and then transfer and use that impact function for quantification in the wider European target population. The two approaches have been used (for different health endpoints) in the CAFE-NEEDS methodology. Otherwise, few if any morbidity endpoints would have been quantifiable.

6.5 **New cases of chronic bronchitis and long-term exposure to PM**

The US Seventh Day Adventist Study (AHSMOG: Adventist Health Smog) study examined people on two occasions, about ten years apart, in 1977, and again in 1987/88. Chronic bronchitis was defined as reporting chronic cough or sputum, on most days, for at least three months of the year, for at least two years. *New cases of chronic bronchitis* were defined as those who met the criteria in 1987/88, but not in 1977. Using a C-R function from Abbey et al. (1995a, Table 6), and a background incidence rate (adjusted for remission of chronic bronchitis symptoms) of 0.378% estimated from Abbey et al. (1993, 1995a), Hurley et al. (2005a) derived an estimated impact function of

\[
\text{New cases of chronic bronchitis per year per 100,000 adults aged 27+} = 26.5 (95\%\text{CI }-1.9, 54.1) \text{ per } 10 \mu g/m^3 \text{ PM}_{10}
\]

6.6 **New cases of chronic cardiovascular disease**

It is to be expected then that ambient PM also affects the development and/or the worsening of chronic cardiovascular disease. However, we have not found suitable studies of long-term exposure to quantify these impacts, other than those impacts which result in earlier mortality.

6.7 **Respiratory hospital admissions (RHAs: ICD 460-519)**
Hurley et al (2005a) used all-ages data, both for C-R function and for background rates, derived from APHEIS-3 (Medina et al, 2004), based on eight European cities. Together they imply an impact function:

Annual rate of attributable emergency RHAs

\[ = 7.03 \, (95\% \, CI \, 3.83, \, 10.30) \, \text{per} \, 10 \, \mu g/m^3 \, \text{PM}_{10} \, \text{per} \, 100,000 \, \text{people (all ages)} \]

**6.8 Cardiac hospital admissions (ICD 390-429)**

CAFE-NEEDS quantified an effect of PM$_{10}$ on cardiac admissions, using a C-R function based on APHEA-2 results from eight cities in Western and Northern Europe (Le Tetre et al, 2002) and a Europe-wide annual rate of emergency cardiac admissions estimated as the arithmetic mean of rates from eight European cities derived from the Appendices of the APHEIS-3 report (Medina et al, 2004). Together these imply an impact function:

Annual rate of attributable emergency cardiac hospital admissions

\[ = 4.34 \, (95\% \, CI \, 2.17, \, 6.51) \, \text{per} \, 10 \, \mu g/m^3 \, \text{PM}_{10} \, \text{per} \, 100,000 \, \text{people (all ages)} \]

**6.9 Emergency room visits**

Hurley et al (2005a) did not attempt to quantify a relationship between emergency room visits (ERVs) and PM. There are several studies from USA and Canada linking ERVs and air pollution, and so it is possible to find C-R functions that quantify relationships between daily variations in ERVs and in PM and ozone. However, ‘emergency rooms’ are a characteristic of the health care systems of North America, and so transferability to Europe is questionable. Their omission from quantification may imply some small under-estimation in total effects quantified.

**6.10 Consultations with primary care physicians (general practitioners)**

Studies in London have linked daily variations in ambient PM with consultations with primary care physicians for asthma (but not for lower respiratory diseases) (Hajat et al, 1999) and for upper respiratory diseases, excluding allergic rhinitis
(Hajat et al, 2002). These studies were based on numbers of people consulting (including home visits) in a 3-year period 1992-94, among about 282 000 registered patients from 45-47 general practices in the Greater London Area.

Because of differences in health care systems, it is difficult to know to what extent these relationships are transferable within Europe. Hurley et al (2005a) therefore proposed that they be used in sensitivity analyses only, to help assess if these endpoints are important.

### 6.10.1 Consultations for asthma

Separately by age-group, (i) C-R functions for warm season, adjusted for other factors (Hajat et al, 1999) (ii) mean daily numbers of consultations for asthma in the warm season and (iii) numbers of registered patients were linked and the results expressed as annual impact functions, to give

- 1.18 consultations (95% CI 0, 2.45) for asthma, per 1000 children aged 0-14
- 0.51 consultations (95% CI 0.2, 0.82) for asthma, per 1000 adults aged 15-64
- 0.95 consultations (95% CI 0.32, 1.69) for asthma, per 1000 adults aged 65+

per 10 µg/m³ PM$_{10}$, per year.

### 6.10.2 Consultations for upper respiratory diseases (URD), excluding allergic rhinitis (ICD 460-3; 465; 470-5 and 478)

Analyses by Hajat et al (2002), adjusted for season, day-of-the-week effects and climate, showed statistically significant associations between PM$_{10}$ and consultations by adults and by elderly people. Estimates for children, not statistically significant, but quite close to it, are included for completeness. These results, and background rates, were used to derive the following impact
functions, for attributable consultations for URD (excluding allergic rhinitis) per 10 µg/m³ PM₁₀, per year:

- 4.0 consultations (95% CI -0.6, 8.0) per 1000 children aged 0-14
- 3.2 consultations (95% CI 1.6, 5.0) per 1000 adults aged 15-64
- 4.7 consultations (95% CI 2.4, 7.1) per 1000 adults aged 65+

6.11 Restricted activity days and associated health endpoints

Ostro (1987) and Ostro and Rothschild (1989) used data on adults aged 18-64 from six consecutive years (1976-81) of the US Health Interview Study (HIS), a multi-stage probability sample of 50,000 households from metropolitan areas of all sizes and regions throughout the USA (Ostro and Rothschild, 1989). Within the HIS, RADs are classified according to severity as (i) bed disability days; (ii) work or school loss days and (iii) minor restricted activity days (MRADs), which do not involve work loss or bed disability, but do include some noticeable limitation on ‘normal’ activity.

6.11.1 Restricted activity days (RADs)

Ostro (1987) studied both RADs and work loss days (WLDs) among adults aged 18-64 in separate analyses for each of the six years 1976-81. A weighted mean coefficient for RADs was linked to estimated background rates of, on average, 19 RADs per person per year (ORNL/RFF, 1994) to give an estimated impact function of:

\[
\text{Change of 902 RADs (95% CI 792, 1013) per 10 µg/m}^3\text{ PM}_{2.5} \\
\text{per 1,000 adults at age 15-64:}
\]

In the main analyses of CAFE CBA, this impact function was applied to people at ages 15-64, as in the original study. In sensitivity analyses, the same impact function was used but applied to all ages, on the grounds that it is unlikely that health-related restrictions on activity do not cease at age 65.
6.11.2 Minor restricted activity days (MRADs) and work loss days (WLDs)

As an alternative, Hurley et al (2005) also derived impact functions for work loss days (WLDs) from Ostro (1987) and minor RADs from Ostro and Rothschild (1989), to give, respectively,

- Change of 207 WLDs (95% CI 176-238) per 10µg/m³ PM2.5 per year per 1000 people aged 15-64 in the general population
- Change of 577 MRADs (95% CI 468-686) per 10µg/m³ PM2.5 per year per 1000 adults aged 18-64

6.12 Medication (bronchodilator) usage by people with asthma

WHO (2004) concluded that there is sufficient evidence to assume a causal relationship between air pollution exposure and aggravation of asthma in children. On that basis, the CASFE-NEEDS quantification of Hurley et al (2005a) proposes impact functions for increased medication usage in people with asthma, although the specific evidence is weak. Separate results were given for children and for adults.

6.12.1 Effects in children aged 5-14 years

Hurley et al (2005) linked an estimated C-R functions from the WHO meta-analysis (Anderson et al, 2004), dominated by the PEACE study and not statistically significant, with estimates of the mean daily prevalence of bronchodilator usage among panels of school-children who meet the PEACE study criteria, to give an impact function of:

Annual change in days of bronchodilator usage

\[ = 180 \ (95\% \ CI \ -690, \ 1060) \ \text{per} \ 10 \ \mu g/m^3 \ PM_{10} \]

per 1000 children aged 5-14 years meeting the PEACE study criteria

European data from the International Study of Asthma and Allergies in Childhood (ISAAC Steering Committee, 1998) were used to estimate that
approximately 15% of children in Northern and Eastern Europe, 25% in Western Europe, met the PEACE study inclusion criteria.

6.12. Effects in adults aged 5-14 years aged 20+

A C-R functions from the WHO meta-analysis (Anderson et al, 2004) was linked with estimates of (i) the mean daily prevalence of bronchodilator use by people with asthma and (ii) the percentage of adults with asthma of a severity comparable to that of the Dutch panels on whom the C-R function was based, to give an estimated impact function for change in bronchodilator usage days:

\[ 912 \text{ (95\% CI -912, 2774) per year per 10 } \mu g/m^3 \text{ PM}_{10} \]

per 1000 adults aged 20+ with well-established asthma

(say, 4.5\% of the adult population)

6.13 Lower respiratory symptoms (LRS), including cough, in adults with chronic respiratory disease

A random effects meta-analysis of results from five panels was linked to both (i) estimates of the mean daily prevalences of LRS, including cough, in symptomatic panels, based on the studies underlying the C-R function, and (ii) estimates of the percentage of people qualifying for such panels, using data from ECRHS (1996) to give an estimated impact function:

Annual increase of 1.30 (95\% CI 0.15, 2.43) symptom days

(LRS, including cough) per 10 } \mu g/m^3 \text{ PM}_{10}

per adult with chronic respiratory symptoms (approx 30\% of the adult population)

6.14 Lower respiratory symptoms (LRS), including cough, in children in the general population

The recent systematic review by Ward and Ayres (2004) very strongly suggests that effects of PM on respiratory symptoms should be quantified for children generally, and not be confined to children with chronic symptoms. Hurley et al
(2005a) combined C-R functions from Ward and Ayres (2004) with an estimate of the mean daily prevalence of LRS, including cough, based on two general population Dutch studies of children (van der Zee et al, 1999; Hoek and Brunekreef, 1995), to give an estimated impact function:

Change of 1.86 (95% CI 0.92, 2.77) extra symptoms days per year per child aged 5-14, per 10 µg/m³ PM₁₀.

6.15 Acute respiratory symptoms in the population generally

Hurley et al (2005a) quantified acute respiratory symptoms in adults with chronic respiratory disease (Section 6.13) rather than in adults generally. However, for sensitivity analyses only, CAFE-NEEDS included also some estimates of the effect of PM on symptom days in the general population, based on Krupnick et al (1990), which had previously been used e.g. in ExternE (1995) to give

Annual change in symptom days per 1000 people at risk (all ages)

= 4650 (95% CI 210, 9090) per 10 µg/m³ PM₁₀

It is likely that this is a high estimate of the effects of PM on respiratory symptoms, especially for application in Europe. It was included in CAFE CBA with the intention that it be used only for sensitivity analyses, to indicate how big an effect might be.
7. Quantifying the adverse health effects of ozone

7.1 Effects on morbidity of long-term exposure to ambient ozone

There is no strong or quantifiable evidence that long-term exposure to ozone is associated with health effects additional to those which are the aggregate over time of the effects of short-term exposure, i.e. of daily variations in ozone. Consequently, no impact functions linking long-term exposure to ozone and health were proposed by Hurley et al (2005a).

7.2 Framework issue: ozone pollution metric used

The WHO evaluations (WHO 2003, 2004) concluded that there was no evidence for a threshold in the relationship between daily variations in ozone and mortality. However, these evaluations also recognised that, at lower concentrations of daily ozone, there was little evidence on which to base any judgement. Consequently, TFH of WHO-UNECE decided that, in the core analyses, the effects of daily ozone on mortality should be quantified only at ozone concentrations higher than 35 ppb (70 µg/m³), considered as a daily maximum 8-hour mean ozone concentration. In practice, this means that effects are quantified only on days when the daily ozone concentration (maximum 8-hour mean) exceeded 70 µg/m³, and then only the increment exceeding 70 µg/m³ is used for quantification. This increment, aggregated over all days of the year, was called SOMO35 and is the exposure metric used for quantification in CAFE-NEEDS.

WHO-UNECE emphasised that the use of a cut-off should not be interpreted as acceptance of a threshold, and recommended also that, as sensitivity analyses, effects be estimated with a cut-off of zero. In CAFE-NEEDS these recommendations regarding no threshold but yes a cut-off for daily ozone, originally developed in the context of daily mortality, were subsequently applied to all impact functions.
7.3 Mortality at all ages from short-term exposure to O₃

The WHO meta-analysis (Anderson et al., 2004) provided a concentration-response (C-R) function of an increase in all-cause mortality of

\[
0.3\% \ (95\% \ CI \ 0.1-0.43\%)
\]

per 10 µg/m³ increase in the daily maximum 8-hour mean O₃.

This C-R function, which applies to all ages, was used in CAFE CBA, in line with guidance from TFH of WHO-UNECE.

7.4 Respiratory hospital admissions (RHAs)

Anderson et al (2004) used results from five cities in Western Europe to estimate the change in all RHAs in various age groups in relation to daily variations in O₃ (8-hr daily average) with and effect – close to statistical significance – for elderly people only, giving a C-R function of 0.5% (95% CI -0.2%, 1.2%) per 10 µg/m³ O₃ (8-hr daily max) in people aged 65+. Background rates in people aged 65+ were taken from the APHEIS second year report (APHEIS, 2002), giving an impact function (see Section 6.4):

\[
\text{Annual rate of attributable emergency RHAs per 100,000 people at age 65+} = 12.5 \ (95\% \ CI \ -5.0, \ 30.0) \ per \ 10 \ \mu g/m^3 \ O_3 \ (8\text{-hr daily average})
\]

7.5 Cardiovascular hospital admissions

There is no strong or quantifiable evidence that daily variations in ozone are associated with cardiovascular hospital admissions or, indeed, with other cardiovascular morbidity endpoints.

7.6 Emergency room visits

Hurley et al (2005a) did not attempt to quantify a relationship between emergency room visits and ozone.
7.7 Consultations for allergic rhinitis (ICD9 477), with primary care physicians (general practitioners)

Hajat et al (2001) studied consultations for allergic rhinitis (ICD9 477) and found that relationships with ozone (8-hr daily max) were strongest using a cumulative index incorporating O₃ over four consecutive days, with lags 0-3 days, based on numbers of people consulting (including home visits) in a 3-year period 1992-94, among about 282 000 registered patients from 45-47 general practices in the Greater London Area. Hurley et al (2005) used these results, applying them as if to a single day’s pollution, and linked them to mean daily numbers of consultations and numbers of registered patients to give estimates of change in annual consultations for allergic rhinitis per 10 µg/m³ O₃ of:

- 3.03 consultations (95% CI 1.89, 4.29) per 1000 children aged 0-14
- 1.60 consultations (95% CI 1.22, 2.03) per 1000 adults aged 15-64

Because of differences in health care systems, it is difficult to know to what extent these relationships are transferable within Europe. We recommend that they be used in sensitivity analyses only, to help assess if these endpoints are important.

7.8 Minor restricted activity days (MRADs)

For current urban workers, aged 18-64, Ostro and Rothschild (1989) reported relationships between minor restricted activity days (MRADs) and ozone (two-week averages of the daily 1-hr max, in µg/m³). The weighted mean coefficient for ozone, adjusted for PM₂.₅, from separate analyses of each of the six years 1976-81 was linked with a mean background rate of 7.8 MRADs per year among people in employment aged 18-64 (Ostro and Rothschild, 1989) to give an estimated impact function:

Increase in MRADs = 115 (95% CI 44, 186) per 10 µg/m³ ozone (8-hr daily average) per 1000 adults aged 18-64 per year
Issues of uncertainty are addressed, as for other endpoints, in CAFE CBA Vol 3 (Holland et al, 2005a); in UNICE’s letter of concerns about the CAFE Methodology, and in the CAFE CBA team’s response (Hurley et al, 2005b).

7.9 Medication (bronchodilator) usage by people with asthma

As for PM (Section 6.12), the CAFE-NEEDS quantification of Hurley et al (2005a) proposes impact functions for increased medication usage in people with asthma, although the specific evidence is weak. Separate results were given for children and for adults.

7.9.1 Effects in children aged 5-14 years

A C-R function was derived from Just et al (2002), a small study of 82 children with medically diagnosed asthma in Paris in early summer 1996, and the only European study identified as a relationship between daily ozone (8-hr daily mean) and medication use in children with asthma. Background rates were derived from Gielen et al (1997) and from Just et al (2002), with different functions reflecting higher prevalences of childhood asthma in Western Europe than in Northern and Eastern Europe (ISAAC, 1998). These results were combined to give an estimated impact function of:

Annual change in days of bronchodilator usage
per 10 µg/m³ O₃ per 1000 children age 5-14 years (general population):

- 124 (95% CI 18, 227) in Northern and Eastern Europe;
- 310 (95% CI 44, 569) in Western Europe.

Two points should be noted. First, while the effects occur only in children with asthma, the impact function was derived to apply to the general population. Secondly, as noted, Just et al (2002) is a small study, in one location. Furthermore, the estimated odds ratio is very high, compared with other endpoints. The study may well be unrepresentative; it may be best to consider it as an upper limit, e.g. for sensitivity analysis only.
7.9.2 Effects in adults aged 20+ with asthma

Hiltermann et al (1998) gave results linking daily max 8-hr moving average O₃ with daily prevalence of bronchodilator usage was positive (OR 1.009 per 10 μg/m³ O₃; 95% CI 0.997, 1.020, i.e. not statistically significant) at the selected lag of 1 day, though when 7-day cumulative ozone was considered, the estimated effect was higher and statistically significant. Background rates were estimated using results from Hiltermann et al (1998) and from the European Community Respiratory Health Survey (ECRHS, 1996). These data were linked to give an estimated impact function:

\[
\text{Change in days of bronchodilator use of} \\
730 \ (95\% \ CI \ -255, \ 1570) \ \text{per} \ 10 \ \mu g/m³ \ O₃ \\
\text{per 1000 adults aged 20+ with well-established asthma} \\
\text{(approximately 4.5% of the adult population)}
\]

7.10 Acute respiratory symptoms in children in the general population

Work in progress by the Committee on the Medical Effects of Air Pollutants (COMEAP) in the UK suggests that there is convincing evidence that daily variations in ozone are associated with lower respiratory symptoms (LRS), including cough; and that these effects are not restricted to people with chronic respiratory symptoms such as asthma (Heather Walton, 2004, personal communication). The CAFE-NEEDS Methodology Report (Hurley et al, 2005a) used a small general population study of 91 children in Armentieres, Northern France (Declerq and Macquet, 2000), to quantify relationships linking (i) daily prevalence of cough and phlegm and (ii) lower respiratory symptoms (LRS), excluding cough with 8-hr daily max O₃. The relevant C-R functions were linked with background rates derived from Hoek and Brunekreef (1995) to give impact functions:
a change of 0.93 (95% CI -0.19, 2.22) cough days
and 0.16 (95% CI -0.43, 0.81) days of LRS (excluding cough)
per child aged 5-14 years (general population), per 10 µg/m³ O₃, per year
8. Conclusions and Recommendations

8.1 Conclusions
The joint activity of CAFE CBA and NEEDS has made possible

- A very detailed review of the relevant literature on air pollution and health
- Some underlying methodological work, especially on life table methods
- Proposals for quantification that are consistent with recent detailed work by the World Health Organisation and that have been peer reviewed independently (and favourably) by one of the world’s leading experts on air pollution HIA
- Two supplementary reports on uncertainty, one qualitative, one quantitative.

This has enabled us to meet the relevant objectives of NEEDS to a far higher standard than we would have thought possible when the NEEDS proposal was being prepared.

8.2 Recommendations
We recommend that, in the 1st instance, the current CAFE CBA/NEEDS reviews be used as the basis for quantification of health effects in NEEDS because:

- The review is detailed
- It is consistent with current WHO guidance
- It is consistent with current Commission practice in its flagship air pollution work (CAFE)
- It has been independently peer reviewed.

However, there is always scope for further improvement. In particular, the ExternE team has an established tradition of making judgements that not only reflect accepted current thinking, but in some respects are forerunners of what later becomes accepted. Examples include the inclusion, as early as 1995, of results from the ACS cohort study; and the judgement, also at that time, that the epidemiological evidence did not support a threshold for the health effects of daily variations in ozone (ExternE, 1995). We think it important and appropriate that,
in a research project such as NEEDS, this ExternE tradition be maintained. We therefore recommend that particular deviations from the CAFE CBA/NEEDS methodology should also be developed and implemented, at least as sensitivity analyses and as demonstrations of the possibilities.

Methodological work within NEEDS continues. This includes methodological work on life table methods, as part of an associated contract between the IOM and the UK Department of Health. Further reports will be prepared and published in the coming 12 months.
9. Bibliography

9.1 Publications from the CAFE-NEEDS literature review


9.2 References on air pollution and health from the main CAFE-NEEDS literature review of Hurley et al (2005a)


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