



Air pollution and the risks to human health – Epidemiology –

AIRNET Work Group 2 - Epidemiology -

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This report discusses the epidemiological evidence of the health effects of outdoor air pollution. It is written by members of the AIRNET Epidemiology workgroup. The report is the product of the group; the following list identifies the primary author of the various chapters.

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EXECUTIVE SUMMARY

The health effects of air pollution became evident during severe air pollution episodes in the first part of the 20th century. In response, air pollution abatement policies were initiated that reduced air pollution concentrations substantially during the 1960ies and 1970ies in many developed countries. Many felt that these lower pollution levels were no longer a public health problem. New studies conducted since the mid-1980s have however raised concerns about the safety of these lower air pollution concentrations. Epidemiology – which identifies the causes of a disease by studying its occurrence in a population – has mostly driven this change in assessment. The science employs statistical methods to assess whether exposure and disease are related to one another.

Over the last 15 years, European epidemiological research has highlighted how air once considered ‘safe’ may contain concentrations of pollutants that are hazardous to human health. Several studies demonstrated the public-health dangers of particulate air pollution, as well as of pollution by ozone, nitrogen dioxide and other gases. Other studies indicated that long-term exposure to air pollution probably affects people more adversely than short-term exposure.

Policymakers have paid attention to this research, revising air-quality guidelines and standards. Yet European research results from air-pollution epidemiology have not been fully exploited – often as a result of poor communication between researchers, the European Union (EU) and end-users.

AIRNET EPIDEMIOLOGY REPORT

Launched in 2002, the EU’s AIRNET initiative on air pollution and health fits neatly into the recent trend for more openness and multi-country research. AIRNET’s Epidemiology working group has identified key studies in its own field. The group’s findings are summarised by pollutant in this report. In addition to the main pollutants of outdoor air pollution, the report examines the effects of air pollution in general on cancer. It also highlights future epidemiology research priorities and the policy implications of findings so far.

The starting point for this report was research in air-pollution epidemiology funded under the EU’s Fourth and Fifth Framework Programmes. It puts this research into perspective, comparing them with other European and non-European research.

AIRNET’s ultimate objective is to create a platform for public-health policy to improve air quality. One of the thematic network project’s first tasks was to survey stakeholders – including policymakers, environmental organisations, healthcare professionals, patient-support groups and industry – to identify their information needs on air pollution and health. Some of the survey’s most frequently asked questions (FAQs), as well as answers to them, are listed in Annex 1 of this report.

PARTICULATE MATTER AIR POLLUTION

Many recent epidemiological studies have looked at particulate-matter air pollution – the small solid and liquid particles suspended in the air. These particles can be of natural origin or produced by vehicle emissions and processes such as industrial combustion or domestic heating and cooking.



Since the 1990s, numerous epidemiological studies have indicated that *short-term* increases in particulate-matter air pollution are linked with increased daily mortality and hospital admissions for respiratory and cardiovascular disease. The two EU-funded APHEA studies, for instance, have generated a database allowing researchers to evaluate health effects in numerous European cities. Much less evidence is available on effects of *long-term* average exposure to air pollution. But the existing evidence does suggest that such exposure may adversely affect human health considerably more than short-term exposure.

Particles from different sources

Many epidemiological studies have assessed the health effects of particulate matter characterized by the mass of the particles in the air. It is however very unlikely that all particles have the same health effect. Therefore researchers have tried to identify more specifically which particles matter. There is evidence that combustion particles are more important than particles of geological origin (wind blown dust). Emissions produced by motor vehicles appear to be most dangerous to humans.

Residential wood combustion is in some regions a major source of local air pollution, especially particles and hydrocarbons. The problem is made worse by the use of fires and stoves in poorly ventilated houses in developing countries. Epidemiological studies of ambient air from locations where residential wood combustion was a major source of air pollution all reported clear links between short-term variations in air-pollution levels and one or more adverse health outcomes.

Secondary particles form as a result of reactions of gases in the atmosphere and are a dominant component of fine particles. Epidemiological studies of secondary particles, especially sulphate particles, mostly conducted in Northeast America have documented short-term effects on mortality and hospital admissions in contrast to toxicological studies that have suggested that sulphate is harmless at ambient concentrations.

Polycyclic Aromatic Hydrocarbons (PAH) – which are found for example in soot, coal tar and cigarette smoke – have been suspected to be carcinogenic. Recent evidence suggests that carcinogenic PAH may have other effects than cancer, adversely affecting the health of foetuses and infants.

Particles of different size

Researchers have also attempted to study the effects of particles from different sizes. Particle size determines how far particles travel in the atmosphere, how easy particles penetrate into homes and where in the human airways the particle deposits. Studies distinguished coarse ($>2.5 \mu\text{m}$), fine ($<2.5 \mu\text{m}$) and ultrafine ($<0.1 \mu\text{m}$) particles. Various studies have documented that fine particles have a larger health effect than coarse particles. Nevertheless, there is also evidence that coarse particles may contribute at least to short-term effects.

Because of the lack of routine monitoring data for ultrafine particles, there are very few epidemiological studies. Several studies funded by the EU suggest that ultrafine particles may affect the heart. An important finding is that in many locations, the concentrations of fine and ultrafine particles correlate only weakly. Thus the original expectation that the large number of ultrafine particles in the air could explain the earlier findings of health effects related to particle mass, is unlikely. Instead, in risk assessment, ultrafine and fine particles should be considered as separate pollutants.

GASEOUS AIR POLLUTANTS

Because of the emphasis on particulate matter, less research has been performed on gaseous air pollutants in recent years. Epidemiological studies of three key gaseous pollutants can be summarised as follows:

- Ozone: short-term exposures are associated with mortality, hospital admissions and lung function, but there is little epidemiological evidence for long-term effects.
- Nitrogen dioxide (NO₂): Studies have found both short- and long-term effects in association with NO₂. It has been difficult to separate the health effects of NO₂ itself and other components that are simultaneously increased in the atmosphere because they are emitted by the same source (e.g. traffic) or are formed in the atmosphere from NO₂.
- Sulphur dioxide (SO₂): there are many studies suggesting that exposure to this pollutant is harmful to humans, affecting mortality, respiratory and cardiovascular health. However, because SO₂ levels are now so low, it is unlikely that SO₂ itself causes these effects. SO₂ is probably an indicator for a relevant mixture containing other pollutants that are responsible for health effects.

DOES AIR POLLUTION CAUSE CANCER?

Over the last 50 years, epidemiological studies have indicated that ambient air pollution causes cancer of the lung. This evidence comes from various types of studies, among them comparisons between urban and rural areas or between communities, as well as case-control, cohort and occupational research studies. It is difficult for epidemiological studies to disentangle the contribution of lung-cancer risk of single pollutants. But researchers conclude that particulate matter is probably responsible for an increased risk of lung cancer. They have not found convincing evidence that traffic-related air pollution causes childhood cancer.

POLICY IMPLICATIONS

Environmental policies are increasingly based on the use of scientific evidence either directly or via the use of risk or health impact assessment. Epidemiological studies have contributed in various ways to the information need: identification of the amount of risk associated with a certain exposure, identification of important pollutants, identification of a (lack of) threshold. The introduction of ever-tougher air-quality guidelines throughout Europe and elsewhere can be attributed directly to recent epidemiological research.

AIR-POLLUTION RESEARCH PRIORITIES

The AIRNET Epidemiology group is in little doubt that particulate air pollution has short-term effects on health. But many questions still need answering. For instance, which physical and chemical characteristics determine the toxicity of the particle mixture?

The group recommends that researchers concentrate on several areas: the long-term effects of particulate-matter exposure; characterization of source-specific mixtures instead of single pollutants; direct study of health effects related to policy interventions; effects on children. Pollutants requiring more attention are ultrafines and PM_{2.5}, secondary particles and carcinogenic PAH; To compensate for the lack of recent epidemiological studies into air pollutants other than particulates, the group also advocates further research into the role of ozone, nitrogen dioxide and sulphur dioxide.

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1 INTRODUCTION

1.1 KEY POINTS

- This Epidemiology report summarises evidence by pollutant. It is the product of meetings within AIRNET between scientists and various stakeholders in Europe over a three-year period.

1.2 PURPOSE OF REPORT

Over the last 15 years, epidemiological research has been the driving force behind the current interest in air-pollution health effects at concentrations of pollutants previously considered safe. This research has motivated revisions of air-quality guidelines and standards, reflected in new laws at the European level as well as in many countries, including the United States (US).

As a result of this process, epidemiologists now:

- see an increased interest in their work by persons and groups (policymakers, politicians, journalists, etc.) with whom they previously did not communicate, and are learning to interact more with them.
- Must take into account the needs of end-users and see their own work from the end-users' point of view, sometimes shaping their research to meet the needs of those end-users.

A substantial fraction of recent research in air-pollution epidemiology – the topic of this report – is taking place in Europe and a substantial proportion of it is funded by the European Union (EU) under the Fourth and Fifth Framework Programmes, as well as earlier programmes. The research has been identified and descriptions of the projects are posted on the AIRNET website.

Some of the projects are concluded or are in their final stage; others are ongoing or just starting. The purpose of this report is to assess these EU-funded projects, their objectives and results, in the context of other European and non-European research. This report is however not an exhaustive review of the literature.

It is clear that European research results have not yet been fully exploited. This is a result of sometimes poor communication among researchers on the one hand and between researchers and the EU or the end-users on the other. In recent years, improvements in communication have led to more homogenisation among European research groups and an increasingly open attitude. The EU's role, through the funding of multi-country proposals, has been crucial in this respect.

Many epidemiological studies over the last decade have focused on the short-term effects of air pollution. We have attempted to identify key studies in this report, in order to put the findings from EU-funded research into perspective. Obviously this is to some extent a subjective choice. In other cases, studies were included as examples to illustrate specific issues.

1.3 STRUCTURE OF REPORT

The epidemiological evidence is summarised by pollutant. We have selected the main pollutants of outdoor air pollution. Because of the importance and diversity of airborne particulate matter (PM), several PM fractions have been distinguished based on physical characteristics and sources. *Chapter 5* looks at air pollution in general and its effects on (lung) cancer. *Chapters 6 and 7* summarise the policy implications and research gaps. *Annex 1* provides a number of frequently asked questions and answers.

As one of the five reports produced by the AIRNET working groups, this report does not contain introductions on ambient concentration levels or factors affecting personal exposure (see the *Exposure report*). Nor does it discuss mechanisms of effects or results of controlled (animal or human) exposure studies (see the *Toxicology report*).

1.4 WHAT IS EPIDEMIOLOGY?

A working definition of epidemiology is the "identification" of the causes of a disease from a study of its occurrence. Epidemiological studies of air pollution are usually observational studies performed in the population.

1.5 WHAT IS AIRNET?

The AIRNET Thematic Network project on air pollution and health was launched in 2002, as the basis for a Europe-wide framework dedicated to the translation of air pollution and health research into evidence-based policy measures. AIRNET's overall objective is to help create a foundation for public-health policy to improve European air quality, one that would be widely accepted by policymakers, research institutions and stakeholders alike (<http://airnet.iras.uu.nl>).

Some 23 partners were brought into the project to this end. Nine contractors, representing the scientific community and various stakeholders, have led the project work. They have been supported by a further 14 organisations, all coordinators of ongoing or recently completed European Union studies on air pollution and health. Several additional institutions were introduced into the project because of their recent work in the field.

Team members have come from EU-funded projects in the field, the World Health Organisation (WHO) and related bodies involved in environmental health, EU institutions and selected national governments. Also from the automobile, oil and gas industries, patient support groups, health care professions and some key consumer organisations and environmental NGOs.

AIRNET is jointly coordinated by the Institute for Risk Assessment Sciences (IRAS) at Utrecht University and the Netherlands Environmental Assessment Agency (NEAA/RIVM).

1.6 THE AIRNET EPIDEMIOLOGY WORKGROUP

AIRNET consists of five working groups: Exposure, Toxicology, Epidemiology, Health Impact Assessment (HIA) and the Science/Policy Interface (SPI). The Epidemiology workgroup (WG3) was set up to:

- Identify the questions asked by end-users, including those arising from the EU's CAFE programme (questions asked to the scientific community through the World Health Organisation), and to explore end-users' needs through discussions and interaction with relevant organisations and their representatives.
- Identify all European research in the field and put it into context with research from outside Europe. A further goal was to provide non-specialist summaries of research findings, which are most relevant to end-users (AIRNET ALERT).
- Assess the potential policy implications of these findings and identify research needs and open questions.

2 ROLE OF EPIDEMIOLOGICAL STUDIES

2.1 KEY POINTS

- ❑ The first evidence of serious health effects related to air pollution was found in the first half of the 20th century.
- ❑ Air pollution has decreased substantially in response to abatement policies in many developed countries
- ❑ Studies conducted since the 1980's have documented that even relatively low pollutant concentrations can adversely affect human health.
- ❑ Epidemiology has provided most of the evidence on current air-pollution health effects, especially over the last decade.

2.2 AIR POLLUTION – A MAJOR HEALTH PROBLEM

The association between air pollution and health was established in the 20th century during the occurrence of major air-pollution episodes, which were followed by important increases in mortality and morbidity (Bell and Davis 2001). Legal measures and technical innovations have led to a decrease in air pollution in severe air-pollution episodes especially in the 1970ies and 1980ies. The last classical Europe-wide smog episode occurred in 1985. Concentrations of pollutants measured during these older episodes exceeded by far the concentrations measured today in Europe and North America.

Furthermore, experimental and chamber studies indicated that adverse effects of exposure to pollutants happened at concentrations exceeding ambient concentration in the 1980's. Therefore, until the late 1980s there was a line of thinking that considered that air pollution in Europe and North America was not a public health problem (Holland *et al.*, 1979). This was however not universally accepted.

In the early 1990s, the results of epidemiological studies, especially on short-term effects, started to accumulate. These results indicated that even those relatively low pollutant concentrations had adverse health effects, including an increase in daily mortality (Dockery and Pope 1994). It took a few years for these results to be accepted by the scientific community and policy-makers, but eventually particulate air pollution – as well as pollution by ozone, NO₂ and other gases – was back on the agenda as a potentially very important public health problem (Dockery and Pope, 1994). The two cohort studies published in 1993 (Dockery *et al.*) and 1995 (Pope *et al.*) showed that long-term exposure to air pollution probably had a greater impact on health than short-term peaks.

The main body of evidence on current air-pollution health effects was coming from epidemiology. However, several critics of these studies indicated that mechanisms were not clear, the understanding of the particles' specific characteristics which played a role were largely unknown, the results supported the existence of sensitive groups in the population which remained unidentified, and the extent of life-shortening in short-term studies had not been adequately investigated whilst long-term studies were few (Lipfert and Wyzga, 1995; Moolgavkar and Luebeck, 1996).

Over the last decade, epidemiological studies have responded to these challenges by realising several well-focused investigations, as described in this report. New results from experimental studies have also been published which broadly support the results from epidemiological studies (see *Toxicology report*). Lastly, a number of studies have investigated further the distribution and characteristics of individual and population exposure (see *Exposure report*).

Typical epidemiological studies observe exposure to air pollution and disease in normal living conditions in the population. The investigators usually have no influence on the exposure of the subjects, in contrast with experimental studies. Epidemiological design and statistical methods are used to assess whether exposure and disease are related to each other. The advantage of this approach is that relevant exposures are studied in the relevant (human) population. The disadvantage is that interrelated other risk factors may affect the disease being studied. This results in an incorrect estimate of the effect of air pollution if these other risk factors are not properly accounted for in either the design or the data analysis of the study.

3 END-USER INFORMATION NEEDS

3.1 KEY POINTS

- ❑ AIRNET surveyed stakeholders to discover information needs on air pollution and health
- ❑ Questions emerging from the survey guided the work of all five AIRNET workgroups.
- ❑ Stakeholders prefer information to be presented in short overviews and want practical information on links between research findings and policy implementation.

3.2 AIRNET STAKEHOLDER SURVEY

Under AIRNET, a survey of stakeholders (policy-makers, environmental organisations, healthcare professionals, patient-support groups and industry) was completed to systematically record information needs related to air pollution and health. The survey results are summarised in a report posted on the Internet (<http://airnet.iras.uu.nl/>), as well as in AIRNET products, AIRNET reports and newsletters.

The survey resulted in a list of questions that stakeholders consider important. These questions have guided the work of the five AIRNET workgroups, as underlined by the inclusion of frequently asked questions (FAQs) in all workgroup reports. In the current report, six FAQs that are partly from the stakeholder survey have been identified and answered (*Annex 1*).

From the responses received, it was noted that stakeholder questions were often more general than those scientists typically work with. Another observation was that stakeholders had problems in assimilating the wealth of information being produced. Two characteristic quotes from the survey illustrate this point. “It is not so much that sources are unavailable to us, it is more that time is in short supply” (a UK national government agency) and “There is a wealth of information and sources and it is a challenge to keep up with the new information” (a Belgian private-sector stakeholder).

3.3 AIRNET ALERT SERVICE

Stakeholders therefore preferred information presented in short overviews (one or two pages) using non-specialist language. They also preferred to receive information that provides practical links between research findings and policy implementation. This observation encouraged AIRNET to introduce the ALERT service. AIRNET ALERT contains short non-specialist summaries, written in newspaper style, of recently published papers in major journals (<http://airnet.iras.uu.nl/>). The Epidemiology workgroup has contributed summaries of recent (2002-2004) epidemiological papers.

4 HEALTH EFFECTS OF AIR POLLUTANTS

4.1 KEY POINTS

- ❑ Short-term increases in particulate-matter air pollution are associated with increased daily mortality and hospital admissions for respiratory and cardiovascular disease.
- ❑ The public-health effects of long-term exposure may considerably exceed the impact of short-term exposures.
- ❑ Increased mortality risks appear to be linked more to man-made (e.g. from motor-vehicle emissions) than naturally occurring fine particles.
- ❑ Wood smoke, a major source of local air pollution in some regions, is associated with respiratory problems.
- ❑ Coarse particles, such as those from road dust, may contribute at least to short-term effects
- ❑ Daily variation in the concentration of ultrafine particles is associated with several health effects. Ultrafines and PM_{2.5} must be monitored as separate pollutants.
- ❑ Exposure to Polycyclic Aromatic Hydrocarbons (PAH) may have other effects than cancer, adversely affecting fetuses and infants.
- ❑ In contrast to toxicological studies, short-term exposures to sulfates were associated with mortality and hospital admissions
- ❑ Short-term exposures to ozone are associated with mortality, hospital admissions and lung function, but there is little epidemiological evidence for long-term effects.
- ❑ Epidemiological studies have linked short- and long-term exposures to nitrogen dioxide with health effects, but it has been difficult to disentangle whether the effects are due to NO₂ itself or whether NO₂ is an indicator for other pollutants (e.g. soot particles) with which it is correlated because it is emitted by the same source
- ❑ Epidemiological studies document that sulphur dioxide exposures remain associated with health effects. It is unlikely that these effects are due to SO₂ itself

4.2 PARTICULATE MATTER

4.2.1 Particle mass

In most epidemiological studies, particulate-matter air pollution is represented by the mass concentration of a certain particle fraction. Earlier studies used variables such as Total Suspended Particulates (TSP) or Suspended Particles (SP). These variables tend to be poorly defined in terms of which particle sizes are included, but they typically contain particles considerably larger than 10 µm (one micrometer is one thousandth of a millimetre). In this section, only studies that used PM₁₀ (particulate matter with a diameter smaller than 10 µm) or PM_{2.5} (particulate matter with a diameter smaller than 2.5 µm) to characterise particulate air pollution are summarized.

Effects of short-term exposures

Many studies, especially those done since the early 1990s, have documented that short-term increases in particulate-matter air pollution are associated with increased daily mortality and hospital admissions for respiratory and cardiovascular disease.

The APHEA-1 and APHEA-2 studies have provided a database to evaluate health effects in a large number of cities in Europe (*Text box*). The APHEA-2 study found an average increase of 0.6% in daily total mortality when the PM₁₀ concentration increased by 10 µg/m³. It has become standard practice to express the effect of PM per 10 µg/m³, but this is a very modest change in concentration. An increase of the PM₁₀ concentration with 100 µg/m³ is approximately the difference between a low- and high-pollution day in moderately polluted European cities. The risk for a change of 100 µg/m³ is approximately 6%. The mortality increase for a 100 µg/m³ change in PM₁₀ concentration differed substantially between the different cities (Katsouyanni *et al.*, 2001). Higher risks were found in cities with a warmer climate and higher NO₂ concentrations. For example, in cities with low NO₂ concentrations, the percentage increase in mortality with an increase of PM₁₀ with 10 µg/m³ was 0.2%; it was 0.8% in cities with high NO₂ concentrations. One interpretation of this finding is that particles emitted by traffic are more toxic than other particles (section 4.1.2). The results of the APHEA-2 study are consistent with a large number of other European studies and studies conducted in the US and Canada. The largest study is the NMMAPS study conducted in 90 US cities. It demonstrated an average increase of 0.21% of total mortality when the PM₁₀ concentration increased by 10 µg/m³

(<http://www.healtheffects.org/Pubs/TimeSeries.pdf>). This is the estimate after taking into account the statistical problems identified with the software package Splus. For a discussion on this statistical issue, see the quoted website from the Health Effects Institute above. The NMMAPS study also observed differences in effects of PM₁₀ in different regions of the US.

Several studies have investigated whether the relationship between PM₁₀ or PM_{2.5} and mortality has a threshold below which no effect is found. Most studies have concluded that no such threshold is present. For example, a study in six US cities found a linear relationship between PM_{2.5} and daily mortality down to about 2 µg/m³, a very low concentration (Schwartz *et al.*, 2002). The lack of a threshold implies that there is no safe level at which a guideline can be set. A judgement has to be made which level of risk is considered acceptable, as is commonly done in assessment of cancer risks.

APHEA-2

- Multi-city study of association between daily fluctuations of air pollution and mortality/hospital admissions covering Europe
- Coordinated by University of Athens (Klea Katsouyanni)
- An increase of the PM10 concentration with 10 µg/m³ was on average associated with an increase of mortality of 0.6%
- An increase of the PM10 concentration with 10 µg/m³ was on average associated with an increase of asthma/COPD hospital admissions of 1-1.2%
- Significant differences in the risk of air pollution was found between cities
- Mortality was advanced by more than just a few days, indicating air pollution to be a relevant public health problem
- No threshold in air pollution – mortality relationship, indicating that there is no safe level of particulate air pollution

Key references: Katsouyanni *et al.*, 2001; Atkinson *et al.*, 2001; Le Tertre *et al.*, 2002



An important issue in the interpretation of the mortality time-series studies is how much death is brought forward by air pollution. If this were by only a few days, the public health relevance would clearly be limited. This question has been addressed by several studies in Europe and the US by checking the association between mortality and air pollution up to about two months before the day of death. These studies found that deaths are brought forward by more than a few days/weeks.

Indeed, the health impact of air pollution is seriously underestimated, if the mortality effect is only taken into account a few days after an air-pollution event. For example, in the APHEA-2 study an increase of PM₁₀ with 10 µg/m³ was associated with a 0.74% increase in respiratory deaths when only the same day and day before death were taken into account. If air pollution in the 40 days before deaths was taken into account, a 4.2% increase in respiratory deaths was found (Zanobetti *et al.*, 2003). The time-series design does not allow researchers to evaluate whether death is brought forward by even more than a few months, because a correction for season is made in the statistical analysis.

The APHEA-2 study also showed that hospital admissions for asthma increased with increasing PM₁₀ concentration. While effects on mortality are mostly observed in the elderly (>65 yr), effects associated with a 10 µg/m³ of PM₁₀ on asthma hospital admissions were very similar for the age groups 0-14 yr (1.2% increase), 15-64 yr (1.1% increase) and >65 yr (1.0% increase). Hospital admissions for cardiovascular disease also increased with increasing PM₁₀ concentrations. Many studies in the US, Canada and Europe have largely supported these associations.

In addition to time-series studies of routinely available data on health status and air pollution, researchers have performed studies in which they followed a panel of subjects for several months. Typical outcomes evaluated in these panel studies include acute respiratory symptoms, medication use for respiratory/cardiovascular disease and lung function. Most studies reported that at increased PM₁₀ concentrations, the occurrence of symptoms of the lower respiratory tract (e.g. wheeze, shortness of breath), the use of bronchodilators to relieve respiratory symptoms and a low lung function were increased.

This is important information, because more people will experience these endpoints than mortality/hospital admissions (see for example the health impact assessment by Kuenzli *et al.*, 2000). Kuenzli and co-workers estimated that a 10 µg/m³ PM₁₀ increase resulted in about a 5% increase in asthma attacks in children and adults. The frequency of occurrence of asthma attacks per one million inhabitants per year – averaged over the three countries in this study – was 59,000 for children and 172,000 for adults; this compared to 8,700 deaths from all causes.

Researchers have also evaluated more specific outcomes than death/hospital admissions, in order to understand better the mechanism of air-pollution effects. In the EU-funded Ultra study (*Text box section 4.2.5*), the panel design was used to study cardiac symptoms and physiologic variables (such as heart-rate variability, measured with a simple electrocardiogram). The authors found that increased PM_{2.5} concentrations were associated with increased “ST-segment depressions”, which is an indication for myocardial ischemia (‘heart attack’) (Pekkanen *et al.*, 2002). Other studies have found that blood coagulability was increased with increasing air pollution. Increased blood coagulability may result in clots blocking blood vessels, which may result in infarcts (localised area of dead tissue). Another study found that life-threatening arrhythmia (disturbance of the normal rhythm of the heart) in patients with an implanted defibrillator was increased with increasing PM_{2.5} concentrations (Peters *et al.*, 2000).

Effects of long-term exposure

Since the 1960s, some studies have compared mortality rates of large areas – especially in the US – with the long-term average air-pollution concentrations in these areas. Several of these studies found higher mortality rates in areas with higher particulate air pollution. The results of these ecological studies were rightly criticised, because no information on individual risk factors such as smoking and occupation were available.

More recently the results of two cohort studies in the US were published that did have data on important individual risk factors (Dockery *et al.*, 1993; Pope *et al.*, 1995). Both studies have documented that subjects living in cities with higher long-term average PM₁₀/ PM_{2.5} concentrations died earlier than subjects living in cities with low air pollution. Because of the importance of these studies in health impact assessment, an extensive reanalysis of these studies was conducted under the supervision of the US Health Effects Institute. The reanalysis supported the conclusions of the original papers (Brunekreef *et al.*, 2002). An update of the American Cancer Society study confirmed the earlier results (*Table*).

In Europe, there are no studies available to evaluate the relationship between increased long-term exposure to PM₁₀/ PM_{2.5} and mortality. Two cohort studies did suggest that mortality was associated with long-term average traffic-related air pollution in Europe (Hoek *et al.*, 2002; Nafstad *et al.*, 2004). PM₁₀ and probably PM_{2.5} concentrations, especially in Central/Eastern and Southern Europe, exceed the concentrations evaluated in the two US studies. Because of the small number of cohort studies and the uncertainty of extrapolating concentration response functions from the USA to Europe, estimates of the number of deaths related to long-term PM exposures in Europe is more uncertain than for short-term exposures.

The US cohort studies have raised much public concern, mostly because of their implications for public health. Researchers have concluded that the number of deaths attributable to air pollution calculated from the cohort studies is considerably larger than from the time-series studies. Compared to the estimated number of deaths related to PM₁₀ from the two US cohort studies, the number of deaths from short-term studies was estimated to be four to five times lower (Kuenzli *et al.*, 2000). Time-series studies can by design only detect deaths related to air pollution in the days or weeks after an air-pollution event. Therefore deaths related to air pollution-induced chronic (cardiorespiratory) disease are not counted (Kuenzli *et al.*, 2000). A detailed discussion of the topic can be found in Kuenzli *et al.*, 2001.

Mortality	Relative risk (RR)*
All causes	1.04
Cardiovascular and pulmonary	1.06
Lung cancer	1.08
Other than cardio-pulmonary and lung cancer	1.01

Table *Relative risk of death per 10 µg/m³ of the average PM_{2.5} concentration in the American Cancer Society study (Pope *et al.*, 2002).* * RR is the increase in the frequency of a given health effect associated with a given increase in exposure.

More information is available in Europe to assess the effect of long-term exposure to PM₁₀ on lung function and chronic respiratory symptoms mostly in children. A long study in three areas in the former East Germany found an association between the PM₁₀/TSP concentration in the city of residence, presence of chronic respiratory (especially bronchitic) symptoms and lung function growth. Two studies conducted in

Switzerland (SCARPOL and SAPALDIA) also found increased occurrence of respiratory symptoms with increased PM₁₀ concentrations in children and adults. Several studies from the US and Canada have also found increased bronchitic but not asthmatic symptoms in children and lower lung function at higher PM₁₀ concentrations. In a health impact assessment for three European countries, it was estimated that – averaged over several studies – a 10 µg/m³ increase of the long-term average PM₁₀ concentration resulted in about a 10% increase in bronchitis in adults and 31% in children (Kuenzli *et al.*, 2000). Recently, the EU-funded TRAPCA study suggested that respiratory symptoms were increased in one-two year-old children who lived in homes with higher traffic-related PM_{2.5} concentrations (Brauer *et al.*, 2002).

Conclusion

Debate continues about the details of the time-series studies, with respect to the methods used for correcting for other risk factors of mortality such as high temperatures. But it is now generally that particulate-matter air pollution has an acute effect on mortality and other cardio-respiratory endpoints. For a detailed discussion of modelling issues, (see <http://www.healtheffects.org/Pubs/TimeSeries.pdf>).

It is unlikely that all particles, irrespective of size/chemical composition/source, have the same health effect. Only limited information is available to judge which particle exposure produces the highest risk. Several studies conducted in the US have documented that especially the fine fraction (PM_{2.5}) of PM₁₀ is associated with health effects (mortality, lung function). Therefore the USEPA has decided to promulgate a PM_{2.5} standard, in addition to the already existing PM₁₀ standard. The lack of more specific data hampers the design of an effective air-pollution reduction strategy. In sections 4.2.2/4.2.7, more information is provided about particles from different sources/sizes.

Much less information is available on effects of long-term average exposure to air pollution. The available evidence suggests that the public-health impact of long-term exposure may considerably exceed the impact of short-term exposures.

4.2.2 Traffic and other combustion particles

Combustion particles, including those from traffic, significantly contribute to PM_{2.5} concentrations in urban environments. These particles are characterised by a carbonaceous core that can be measured by black smoke ('soot') or elemental carbon measurements (see *Exposure assessment report*). Combustion particles can contain organic carbohydrates condensed on their surfaces and can be measured as total organic carbon. In several studies dealing with air-pollution sources, a vehicular traffic-related factor has been identified. This factor appears to contain PM_{2.5}, ultrafine particles, CO, NO, NO₂, EC and OC, as well as specific elements Mn, Fe, Zn and Pb, that might be emitted or resuspended by traffic. CO, NO and NO₂ may serve as surrogates for the PM component of the vehicular traffic-related factor.

Short-term effects

Thanks to the tradition of measuring black smoke in Europe, measurements are available to study the association between combustion-related particles and health. An increase of 10 µg/m³ black smoke was associated with 0.6% increase in daily mortality in 12 European cities in 1997 as part of the APHEA study (Katsouyanni *et al.*, 1997). This result was confirmed in a follow-up study estimating a 0.6% increased risk for daily mortality in association with a 10 µg/m³ increase in black smoke or PM₁₀ based on data from 29 European cities (Katsouyanni *et al.*, 2001).

These studies could not distinguish between the results of PM₁₀ or black smoke, mainly because the concurrent measurements of both particle indexes were only rarely available. However, the studies used NO₂ concentrations as an indicator for the contribution of traffic to particle concentrations. In cities with high NO₂ concentrations, the associations between particles and daily mortality were stronger than in cities with low NO₂ concentration; this suggests that particles originating from traffic have a greater impact on health than particles from other sources.

A study in Dublin showed that black-smoke concentrations decreased by 36 µg/m³ after a coal ban in 1990 (Clancy *et al.*, 2002). In the following years, non-trauma deaths were reduced by 6% and deaths due to cardiovascular diseases decreased by 10%. This trend remained even after standardising on Irish death rates and thereby taking into account concurrent changes in mortality from other reasons. The Dublin study indicated that the benefit from reducing black-smoke concentrations exceeded the benefit one would have predicted on the basis of the APHEA studies' results.

Another study approached the subject by apportioning particle sources on the basis of their elemental composition, in six cities of the northeastern United States (Laden *et al.*, 2000). The study indicated that a 10 µg/m³ increase in PM_{2.5} originating from mobile sources was associated with a 3.4% increase in mortality, while a 10 µg/m³ PM_{2.5} originating from coal combustion was associated with a 1.1% increased risk of mortality. In the eastern United States, particles originating from coal combustion are regionally transported particles with high sulphate content (see chapter on secondary particles) and are therefore considered to be different from locally produced soot particles as studied in the Dublin study.

Long-term effects

Only a few studies have assessed the associations between particles and mortality. One study from the Netherlands assessed the association between long-term concentrations of black smoke and mortality: Hoek and colleagues followed a sample of 5,000 adults aged 55 to 69 years over an eight-year period (Hoek *et al.*, 2002). Living near a major road, i.e. within a distance of 50m to a major road or 100m to a highway was associated with a relative risk of 1.95. The estimated risk for the background black smoke concentrations assessed in the same statistical model seems to be nearly negligible (1.17 for a 10 µg/m³ increase in black smoke not being statistically significant). However, when taking into account earlier work by these authors and converting black smoke into PM_{2.5}, translates into a 6% increase in mortality for every 10 µg/m³ in 'background' PM_{2.5}. The results for the background levels from the Netherlands are consistent with the 16-year follow-up of 500,000 adults in the US (Pope, III *et al.*, 2002), indicating that the true risk is underestimated based on urban background concentrations only.

These studies taken together indicate that soot particles from combustion processes are associated with short-term effects and long-term effects on mortality. The combustion processes from which the soot particles originate might modify the particles' composition, and in particular the substances absorbed on their surfaces. The properties of the insoluble carbonaceous cores of the particles might, however, be quite similar and thus also the related health impact. The Netherlands study also indicated that the health impact of long-term exposures estimated on the basis of urban background concentrations might be vastly underestimated, as these estimates of the health impact do not take into account the exposures of persons living in the vicinity of major roads, which are far higher.

Studies assessing the respiratory health of children indicated that children attending schools situated close to major roads and living in their vicinity suffer health consequences. These consequences include reduced lung function and higher prevalence of respiratory symptoms including wheeze and higher asthma rates. Recent examples of these studies are the following publications: Janssen *et al.*, 2003; Nicolai *et al.*, 2003.

These studies have used surrogate measures of traffic-related particles such as NO₂ measurements, proximity of the residential address or school to major roads, or ratings on traffic density based on questionnaires. Studies of these associations – including the direct measurement of the physico-chemical properties of traffic-related particles – require well-planned large research projects, which have not been attempted by any funding agency so far. The outcomes evaluated in these studies are chronic respiratory symptoms, which impact the health and the well-being of the children. These symptoms might be without any long-term health consequences. However, the induction and promotion of allergic diseases will place a life-long burden on the affected children and will result in substantial health care costs. Also recent evidence of reduced lung function growth in children living in polluted areas of the Los Angeles basin adds additional concern (Gaudermann *et al.*, 2004). The exact damaging agents have not been identified and the pathophysiological mechanisms leading to disease are not fully understood. Yet the health impact seems to be enormous. An attempt to quantify this impact was made in the study by Kuenzli *et al.*, 2000, which analysed the public-health impact of traffic-related air pollution for Switzerland, France and Austria (with a total population of 74 million inhabitants). Exposure response relationships from cohort studies were used to quantify the influence of traffic exposure on total mortality, respiratory and cardiovascular hospital admissions, chronic bronchitis in adults, bronchitis in children, asthma attacks and reduced activity. The authors conclude that 3% of total mortality or 20,000 deaths per year are due to traffic emissions, based on measurements of PM₁₀ and the assumption that half of the ambient PM₁₀ concentration originates from vehicles. If one considers life expectancy rather than mortality, the conclusion is that the hypothetical complete omission of particles from automobile traffic would lead to a prolonged life expectancy of 0.35 years.

In summary, the short-term studies suggest that a number of source-types are associated with mortality and morbidity, including motor-vehicle emissions, coal combustion, oil burning, and vegetative burning. Some unresolved issues remain. Yet the evidence thus far seems to implicate fine particles of anthropogenic (produced or caused by man) origin – and especially motor-vehicle emissions – as being most important (versus crustal particles of geologic origin) in contributing to observed increased health risks.

4.2.3 Wood smoke

There is an increasing interest in sustainable, CO₂-neutral, energy production in Europe and globally. The potential for increased use of fuels made from biomass (plant materials and animal wastes) is significant.

Residential wood combustion is in some regions considered a major source of local air pollutants, especially for particles and hydrocarbons, and mainly during the cold season. Besides the major components CO₂ and H₂O, wood smoke mainly consists of a complex mixture of inorganic gases (e.g. CO, NO and SO₂), volatile organic hydrocarbons (e.g. butadiene, etene and benzene), heavier hydrocarbons (e.g. benzo[a]pyrene) and particles. The particulate mass can be divided into inorganic ash, soot and condensed organic material. If trace elements like cadmium, lead and zinc are present in the fuel, they can be volatilised (transformed from a liquid or solid form into a vapour during combustion in all kinds of appliances and be found as condensed species of emitted sub-micron particles.

Since the emissions from residential wood combustion include inhalable fine particles and a complex mixture of hydrocarbons, some of which are known to be toxic, it can be assumed that exposure to wood smoke is potentially harmful to human health. However, very few epidemiological studies deal with health effects of exposure to wood smoke as a complex mixture in ambient air. More studies focus on effects of the indoor air quality as a result of direct release from cooking/heating devices, leakage from boilers/stoves or infiltration of outdoor air pollution.

Indoor biomass pollution, especially in poorly ventilated houses in developing countries, is of major health concern. Based on epidemiological studies, it has been estimated that indoor air pollution in developing countries is responsible for nearly two million excess deaths annually. These deaths are caused, for example, by chronic obstructive pulmonary disease (COPD), tuberculosis, acute respiratory disease and cancer (Smith *et al.*, 2000).

Many animal toxicology studies with wood smoke have been performed. A recent review summarised the toxicology of wood smoke, mainly focusing on the animal studies and concluding that inhalation of combustion products from wood most probably can significantly exacerbate ongoing disease processes (Zelikoff *et al.*, 2002).

A later literature review focused on epidemiological studies of ambient air from locations where residential wood combustion was an important air-pollution source (Boman *et al.*, 2003). The nine included studies focused on effects of variations of short-term exposure, such as asthma admissions, respiratory symptoms, daily mortality and lung function. The most commonly used pollution indicator was particle mass expressed as PM₁₀ in eight studies. All the included studies reported clear links between short-term variations in air-pollution levels and one or more adverse health outcomes. PM was the parameter that showed the most frequent and most obvious associations with the addressed health effects. In all studies using particle concentration as pollution indicator, significant positive associations were found. Overall, the relative risks between an increase in ambient PM₁₀ with 10 µg/m³ and different health outcomes varied between 1.8 and 11.7%. CO showed significant positive associations with the addressed effects in three studies out of the four including CO in the analysis.

This review also compared the typical relative risks associated with particles with the results from five wood smoke studies dealing with asthma, together with one study with associations for cough. All 'wood-smoke studies' included showed significantly increased risks. In comparison with WHO's and other 'state-of-the-art' estimations concerning the effects of ambient PM on health in locations without significant wood-burning, the effects were even. Several of these asthma studies have reported that a very large proportion, 45-80%, of PM₁₀ during the heating season, comes from wood burning (Lipsett *et al.*, 1997; Norris *et al.*, 1999). One study, of winter seasons only, found no particle effect on asthma during warm conditions (Norris *et al.*, 1999). Another found no effect during the summer season (Sheppard *et al.*, 1999), while a third found a large part of the effect reflecting high particle levels from wood smoke during the winter months (Schwartz *et al.*, 1993). The strong 'wood-smoke effect' on asthma is coherent with, and may partly be explained by, results showing that use of a fireplace or wood stove on a given day strongly predicts exacerbation of respiratory symptoms in adult asthmatics (Ostro *et al.*, 1994).

4.2.4 Coarse particles and road dust

Introduction

Most coarse particles (often defined and measured as particles larger than 2.5 μm and smaller than 10 μm) are formed by mechanical processes such as material abrasion, corrosion and erosion. The coarse fraction may (in mass) be dominating over the finer fraction, especially in arid regions with much wind-blown dust. Road traffic does not generate only exhaust emissions, but also brake-wear and tyre-wear emissions as well as particles from the wear and tear of the road surface (Areskoug, 2000; Areskoug *et al.*, 2003). Most of these traffic particles are coarse particles. But the brake- and tyre-wear emissions affect also the mass of $\text{PM}_{2.5}$. Resuspension (the process of particles settled on the ground becoming airborne again) of 'road dust' depends on several factors, such as the road surface, the deposit of particles on the road, humidity, intensity of traffic and wind speed. Industrial activities, building and construction work and fires may locally and temporarily also contribute much to the coarse fraction.

Coarse particles have a higher settling velocity than fine particles, therefore the concentration of wind-blown dust falls off rather fast with the distance from a local source (such as a road or construction area). Since the coarse fraction often shows low site-to-site correlations within a city or region, a measure of coarse particles at one site may not be a good indicator of the average concentrations or population exposure in a larger neighbourhood (Wilson & Suh, 1997). In addition, coarse-mode particles do not infiltrate indoors as efficiently as fine-mode particles, and are also more rapidly removed by deposition. This makes it harder to detect any existing associations in epidemiological studies using data from one or a few fixed-site monitors.

Potential for health effects

Particle size affects the distribution and deposition in the lung. Coarse particles are more likely to deposit in the bronchial region, while fine particles are more likely to be deposited in the periphery of the lung, in particular in the respiratory bronchioles and alveoli. Physical properties of particles are also important for their uptake and clearance from the lung. Particles from stone material used in road pavement have been shown, in a varying degree, to induce inflammatory effects in animal. Bacterial endotoxin, known to exert inflammatory effects, are often found in the coarse fraction and may contribute to the health effects of the urban coarse particles. In some toxicological studies, the coarse fraction on a mass basis has produced a greater effect than the fine fraction. However, one should keep in mind that deposition of fine and coarse particles is different.

Studies of mortality

From the very few cohort studies done, there is no support for long-term effects of coarse particles on mortality. However, there are around 30 time-series studies investigating the short-term effect of both the coarse fraction and the more often studied fine fraction ($\text{PM}_{2.5}$) on mortality, hospitalisations, emergency visits and symptoms. Some of these studies have been analysed several times.

Most time-series studies of daily mortality did not find a significant association with coarse particles. The strongest support for an effect of the coarse fraction on the daily number of deaths comes from areas with relatively high concentrations of coarse particles, Phoenix (Mar *et al.*, 2000), Mexico City (Castillejos *et al.*, 2000) and Coachella Valley (Ostro *et al.*, 2000). Levels of coarse particles were high also in Santiago, and only in summer does the coarse fraction seem to have an independent effect (Cifuentes *et al.*, 2000). Most cities studied have low mean levels of coarse particles in the range of 10-12 $\mu\text{g}/\text{m}^3$, while some places have

averages as low as $6 \mu\text{g}/\text{m}^3$. When levels typically are low, local influences (i.e. from building and construction) may have a strong effect on the levels measured at one station. In arid regions, such as the western parts of the United States, geological dust makes up much of the coarse fraction; this may result in less spatial variability and less measurement error in the exposure estimates.

There are often relatively small differences between the risk estimates calculated for the fine and coarse-particle fraction, respectively. The percent excess in daily deaths usually is close to 0.8-2.5% per $10 \mu\text{g}/\text{m}^3$, while the highest effect-size estimates for the coarse fraction reach 3-4% per $10 \mu\text{g}/\text{m}^3$.

Studies of hospital admissions and emergency department visits

There are more than 10 studies of short-term effects on admissions and emergency visits analysing effects of both the coarse and fine fraction. Five of these studies are from Toronto, Canada, using different outcomes, study populations and particle-exposure metrics. The results indicate that the coarse fraction may be important especially for respiratory admissions, asthma and obstructive lung disease (Burnett *et al.*, 1999; Moolgavkar, 2000; Burnett *et al.*, 2001; Lin *et al.*, 2002). In general there was an increase in admissions of 2-6% per $10 \mu\text{g}/\text{m}^3$ for respiratory admissions. Some significant associations were found also for cardiovascular outcomes.

Road dust and dust storms

The composition of the coarse fraction may differ greatly from place to place and between seasons. Very few epidemiological studies have presented results for the coarse fraction stating that the major source is resuspension of road dust. One study from Finland found that the daily concentration of resuspended particles was associated with cough in symptomatic children, in the same way as were other particle measures (Tiittanen *et al.*, 1999).

One study of 17 dust storms in Spokane, US, reported that high levels of wind-blown dust were not associated with increased mortality (Schwartz *et al.*, 1999). On the other hand, in the Coachella Valley, California, daily levels of PM_{10} dominated by coarse particles of geologic origin were associated with daily mortality (Ostro *et al.*, 1999; Ostro *et al.*, 2000).

The daily number of emergency-room visits for bronchitis was associated with PM_{10} from dust storms in eastern Washington (Hefflin *et al.*, 1994), US. In Anchorage, Alaska, where much PM_{10} is coarse and composed primarily of earth crustal material and volcanic ash, outpatient visits for asthma and upper-respiratory diseases were associated with PM_{10} (Gordian *et al.*, 1996).

Conclusion

Given that the composition of coarse particles may vary greatly between the settings studied, it seems (with a precautionary approach) reasonable to assume that the coarse fraction, including road dust mainly in the coarse fraction, may contribute at least to short-term effects in the exposed populations.

4.2.5 Ultrafine particles

Ultrafine particles account for the preponderance of particles by number, but they rarely account for more than a few percent of the total mass of ambient air particles. Ultrafine particles are formed in local combustion processes and from the gas-to-particle conversion (nucleation and condensation) of atmospheric gases. The atmospheric lifetime of ultrafine particles in high concentrations is very short, but in

concentrations observed in urban air it can be a few hours. The short life time of ultrafine particles makes exposure assessment for them more demanding than it is for accumulation mode particles. At present it is not known, how well levels of ultrafine particles measured at a central site estimate personal exposure (Pekkanen, *et al.*, 2004).

Toxicological studies have shown that ultrafine particles or nanoparticles (diameter below 0.1 μm) are more toxic to animals than larger particles, when the mass doses are equal. One possible reason is the large surface area of ultrafine particles. In fact, the toxic effects of particles have a higher correlation with the particle number or surface area concentration than with the mass

concentration. Ultrafine particles also penetrate into the lung interstitium and may induce increased blood coagulability and thereby increase the risk of myocardial infarction.

There are currently very few published epidemiological studies on the health effects of ultrafine particles in urban air. A panel study of asthmatics from Erfurt (Peters *et al.*, 1997) suggested that ultrafine particles are more strongly associated with respiratory outcomes than fine-particle fractions. This was also seen in a panel study of adult asthmatics in Helsinki (Penttinen *et al.*, 2001a). Other panel studies of asthmatic children (Pekkanen *et al.*, 1997, Tiittanen *et al.*, 1999) in Finland or asthmatic adults in Helsinki (Penttinen *et al.*, 2001b) and Erfurt have shown similar associations of ultrafine and fine particles with respiratory health. In contrast, a panel study of COPD patients in the UK suggested that PM_{10} has stronger associations with respiratory health than ultrafine particles (Osunsanya *et al.*, 2001). In a 3.5-year time-series study of mortality in Erfurt, both ultrafine and fine particles were associated with mortality and the effects seemed to be largely independent of each other (Wichmann *et al.*, 2000).

The EU-funded ULTRA study (*Text box*) looked at the health effects of fine and ultrafine particles among coronary heart-disease patients. The mean 24-hour number concentrations of ultrafine particles were rather

ULTRA (1998-2000)

- Study of the association between fine and ultrafine particles and cardiorespiratory health among coronary heart disease patients
- Studied repeatedly 131 coronary heart disease patients aged 40-84
- Conducted in Amsterdam (NL), Erfurt (D), and Helsinki (FIN)
- Coordinated by KTL, Finland (Juha Pekkanen)
- Developed and made public detailed SOPs (<http://www.ktl.fi/ultra>)
- Documented similar levels of ultrafines in the three cities and low correlation between ultrafines and $\text{PM}_{2.5}$ in two cities
- Documented differences in the association of ultrafine and fine particles on different endpoints

Key references: <http://www.ktl.fi/ultra>

HEAPSS (2001-2003)

- Evaluates whether air pollution increases the risk of first and recurrent myocardial infarction.
- Conducted in Rome (I), Barcelona (E), Augsburg (D), Helsinki (FIN), and Stockholm (S).
- Coordinated by Rome E Health Authority, Italy (Francesco Forastiere).
- Levels of ultrafines modelled retrospectively using other pollutants and meteorology.
- Health effects from existing registries.

Key references: <http://www.epiroma.it/heapss>

RUPIOH (2002-2004)

- Investigates the relationship between indoor and outdoor particle counts and their association with respiratory health.
- Conducted in Amsterdam (NL), Birmingham (GB), Athens (GR), Helsinki (FIN).
- Coordinated by IRAS, the Netherlands (Gerard Hoek).
- 35 persons with chronic respiratory conditions followed intensely for one week.
- Respiratory health evaluated using daily diaries, lung-function measurements, exhaled-breath condensate, and urine sampling.

similar in the three cities, but the mass concentrations of particles, measured as $PM_{2.5}$, were lower in Helsinki than in Amsterdam and Erfurt (Ruuskanen *et al.*, 2001). The number concentration of ultrafine particles correlated poorly with $PM_{2.5}$ in Amsterdam and Helsinki. Ultrafine particles were only weakly associated with some symptoms (de Hartog *et al.*, 2003). In Helsinki, both ultrafines and $PM_{2.5}$ were independently associated with signs of myocardial ischemia, measured as risk of ST-segment depression during a light exercise test (Pekkanen *et al.*, 2002). Particulate air pollution, including ultrafines, was also associated with decrease in blood pressure (Ibald-Mulli *et al.*, 2004). The

study has thus started to provide an understanding of how (ultrafine) particles may affect cardiovascular health.

Several other ongoing EU-funded studies evaluate exposure to and health effects of ultrafines. The HEAPSS study (*Text box*) estimates the effects of daily variations in modelled levels of ultrafines on risk of first myocardial infarction, and subsequent risk of other cardiac events in patients hospitalised for first myocardial infarction.

The RUIPIOH study (*Text box*) evaluates how well variations in concentration of ultrafine particles measured outdoors at a central site predict variation in exposure indoors. This is the main uncertainty in the interpretation of time-series studies on ultrafines. Health effects are assessed in an asthma/COPD panel.

AIRGENE (2003-2005)

- Assesses effects of air pollution on levels of inflammatory markers and identifies susceptible subgroups through genotyping.
- Conducted in Rome (I), Barcelona (E), Augsburg (D), Helsinki (FIN), Athens (Gr) and Stockholm (S).
- Coordinated by GSF, Germany (Annette Peters).
- 1200 patients followed-up with 6 repeated measurements of inflammatory markers and with daily diaries.
- http://www.gsf.de/epi/en/ag_epi_luftsch_1.html#airgene

The AIRGENE study (*Text box*) compares repeated measurements of markers for inflammation with variations in daily levels of ultrafine particles and traditional air pollutants. The study also generates information on the mechanisms of action of ultrafines, by assessing which inflammatory genes modify the effects of air pollution.

Conclusion

The limited number of available epidemiological studies suggests that daily variation in the concentration of ultrafine particles is associated with several health effects. Much of the evidence is available from studies in a few locations in Finland and Germany. Results from ongoing European studies will significantly increase the knowledge base. It is unlikely that ultrafine particles explain all the health effects found in previous epidemiological studies associated with daily variations in PM_{10} or $PM_{2.5}$, due to the low correlation between the two particle fractions. Therefore, ultrafines and $PM_{2.5}$ may need to be monitored as separate pollutants.

4.2.6 Secondary particles

Particles produced by the intermediate reactions of gases in the atmosphere are called 'secondary particles'. Secondary sulphate and nitrate particles are formed by atmospheric reactions of sulphur oxides and nitrogen oxides initially released as gases and are usually a dominant component of fine particles. They can be transported over hundreds of kilometres and contribute to the regional background concentration of particles. In general, the particles are not pure sulphate or nitrate particles, but consist of a carbonaceous core and a variety of chemical substances ranging from transition metals to oxidised hydrocarbons.

Epidemiological studies on secondary particles such as sulphate particles cannot be differentiated from those on fine particles (commonly measured as $PM_{2.5}$) and the knowledge on health effects of $PM_{2.5}$ has been summarised in [section 4.2.1](#). However, much of the evidence for the health effects of sulphate particles originates from research in Canada, where sulphates were measured over extended periods of time. There, they represent the contribution of regionally transported particles originating from the northeast of the United States with peaks during the summer months.

In northeast America, studies associating daily mortality rates with different components of particulate matter found evidence in eight Canadian cities for sulphates playing a major role (Burnett, Brook *et al.*, 2000). This study emphasised that in addition to the sulphate concentrations, the presence of transition metals was important. Coherently, hospital admissions for respiratory as well as cardiovascular diseases were observed in association with sulphate concentrations (Burnett, Dales *et al.*, 1995). Not only short-term health effects of elevated concentrations of sulphate particles were observed but also an association with mortality was made evident in the American Cancer Society Study (Pope, Thun *et al.*, 1995). More recent studies have ceased to incorporate sulphates in the analyses (Burnett, Smith-Doiron *et al.*, 1999; Pope, III, Burnett *et al.*, 2002) as PM_{10} and $PM_{2.5}$ become the standard measure of particulate matter in air quality networks (see [chapter 4.2.1](#)).

Nevertheless, sulphates seem to contribute to the observed associations found with particulate matter whenever they were measured. There are generally no indoor sources for sulphate, so personal exposure to sulphates is highly correlated to ambient concentrations. Because in animal experiments it has generally not been possible to find harmful effects of sulphate aerosols – even at concentrations much higher than ambient (see chapter on toxicology)-, sulphate particles are considered as surrogate measures for other unmeasured particle properties.

Firstly, it had been argued, sulphate particles might be a useful surrogate measure for $PM_{2.5}$ and particle strong acidity (Lippmann and Thurston, 1996). However, an important difference between sulphate particles in northeast America and Europe is that the sulphate particles in northeast America are acidic whereas they are not in Europe. Because of the high ammonia concentrations in ambient air in Europe, acid sulphates are

completely neutralised. Secondly, it has been suggested that the health effects may be related to interactions between sulphate and iron in particles, inducing oxidative stress in the lung. Thirdly, sulphates might be a valuable measure to assess the contribution of soluble particles, which are regionally distributed; measurements of sulphate particles might provide a valuable surrogate measure in addition to PM₁₀, PM_{2.5} and carbon particles.

4.2.7 Polycyclic aromatic hydrocarbons (PAH)

Polycyclic aromatic hydrocarbons (PAH) are formed during incomplete combustion or pyrolysis (chemical decomposition by the action of heat) of organic materials such as oil, gas, coal and wood (WHO, 2000). Cigarette smoking is an important contributor to indoor air pollution. The most commonly studied PAH is benzo[a]pyrene (BaP). BaP is sometimes used as an indicator for the complex mixture of PAH. The ratio of BaP to other PAH is however not constant across different exposure conditions. Risk analysis has traditionally focused on the carcinogenic properties of PAH. In the 2000 evaluation by the World Health Organisation, the lung cancer risk for a lifetime exposure to 0.012 ng/m³ BaP is estimated to be 1.10⁻⁶. This risk magnitude is frequently used as an acceptable risk. Ambient concentrations of BaP in urban areas (especially in busy streets) significantly exceed this level, suggesting that PAH may contribute to the increased lung cancer associated with particulate matter (*section 4.2.1 and 5*).

Several recent studies have suggested that exposure to PAH may have other effects than cancer. Foetuses in particular are considered to be highly susceptible to a variety of toxicants because of their exposure pattern and physiologic immaturity (Šrám 1999). Their developing organ systems can be more vulnerable to environmental toxicants during critical periods, due to higher rates of cell proliferation or changing metabolic capabilities. Therefore, prenatal exposure to environmental pollution can result in some adverse reproductive outcomes.

Perera *et al.* (2003) evaluated the effects of prenatal exposure to airborne carcinogenic PAH monitored during pregnancy by personal air sampling in a sample of some 260 non-smoking African-American and Dominican women in New York. Total PAH exposure averaged 3.7 ng/m³ (range 0.4-36.5 ng/m³). Among African Americans, high prenatal exposure to PAH was associated with lower birth weight and smaller head circumference. No such effects were observed among Dominican women.

Intrauterine growth retardation (IUGR) is defined as infants below the 10th percentile of birth weight for gestational age and gender. Dejmek *et al.* (1999) examined the impact of PM₁₀ and PM_{2.5} on IUGR in a highly polluted area of Northern Bohemia (Teplice District), Czech Republic. A significantly increased risk of giving birth to a child with IUGR was established for mothers who were exposed to PM₁₀ levels >40 µg/m³ or PM_{2.5} > 27 µg/m³ during the first month of gestation. For each 10 µg/m³ increase in PM₁₀, the risk of IUGR was 1.25.

Analysing the same cohort, Dejmek *et al.* (2000) tested the association between carc-PAH (carcinogenic PAH) and IUGR in the districts of Teplice and Prachatice. The Teplice data showed a highly significant increase of IUGR risk for exposures to carcinogenic– again exclusively during the first gestational month. This relationship proved to be strongly dose-response related: per 10 ng/m³ elevation of carc-PAH level, the risk was 1.22. In contrast to the previous negative effects of PM₁₀ in Prachatice, the association between carc-PAH and IUGR was close to that found in Teplice (Dejmek *et al.*, 2000). Again, the only consistent carc-PAH/IUGR association in Prachatice was observed in the first gestational month. It seems that the primary role in elevation of IUGR risk is due to exposure to these carcinogenic PAH.

Vassilev *et al.* (2001) examined the association of polycyclic organic matter (POM) in outdoor air with the delivery of 'small for gestational age' (SGA) infants, which are defined in the same way as IUGR. They combined information from birth certificates in New Jersey from 1991-1992 with air-toxicity data from the USEPA Cumulative Exposure Project, using the predicted POM concentrations from annual exposure estimates. Risks for SGA outcomes for the highest exposure tertile (89% of the state's birth population, 0.611-2.830 $\mu\text{g}/\text{m}^3$) were 1.12. The results of this study suggest that residential exposure to airborne POM is associated with an increased prevalence of IUGR births among an urban population.

Biomarker studies from Poland and the Czech Republic indicated a relationship between ambient air pollution and an increase of DNA adducts in maternal and cord blood and/or in placentas, as well a relationship of these biomarkers to the development of newborns.

Data on the impact of carcinogenic PAH on pregnancy outcome have only been collected during the last decade. Such data significantly enhances the scientific knowledge base and must be incorporated into current risk-assessment procedures to improve children's health in polluted regions all over the world.

4.3 OZONE

Because of the recent attention paid to particulate-matter air pollution, the role of ozone has been much less studied in recent years. Ozone has been shown to be a toxic pollutant at near ambient levels in controlled exposure studies of humans and animals (Toxicology report). Furthermore, ozone is used in epidemiological studies as an indicator pollutant for photochemical air pollution in general. Under the conditions that are favourable for ozone formation, a range of other potentially harmful pollutants – such as aldehydes, nitric acid and sulphuric acid – are formed as well (*Exposure report*).

Effects of short-term exposures

Ozone presents at least two difficulties in the correct assessment of short-term health effects. First, ozone concentrations have a very strong seasonal pattern with high concentrations almost exclusively in the summer. Second, ozone concentrations tend to be highly correlated with temperature in the summer season. Therefore epidemiological studies need to adjust for season and temperature even more carefully than for other pollutants, in order to provide reliable effect estimates. In a recent review paper, Thurston and Ito (2001) showed that studies that modelled the impact of temperature on mortality more carefully showed a higher relative risk (RR = 1.056 per 200 $\mu\text{g}/\text{m}^3$ ozone increase), compared to all studies combined (RR = 1.03 per 200 $\mu\text{g}/\text{m}^3$).

There is a large body of literature that documents associations between short-term increases in ozone concentrations and lung function of children and adults. Both healthy and asthmatic subjects are affected. A series of studies conducted in children participating in summer camps in the US and Canada showed a decrement of FEV_{1.0} of about 40 ml associated with a 100 $\mu\text{g}/\text{m}^3$ increase of the ozone concentration. Assuming an average baseline FEV_{1.0} of 2,000 ml, this implies a decrement of about 2%. Transient pulmonary function decrements of this magnitude are generally not considered adverse. In a recent assessment of the public health benefits of reduced ozone concentrations, the acute lung function changes were not included (Levy *et al.*, 2001). One problem with this interpretation is that small changes in the population average may be accompanied with larger changes in the percentage of children experiencing a lung function decrement that is large enough to be of medical importance, as has been recently documented for studies relating PM₁₀ to Peak Flow (Hoek *et al.*, 1998). This is especially likely for ozone, since human

controlled exposure studies and a few epidemiological studies in US and Dutch school children have found that there was significant variability in the individual pulmonary function response to ozone. Several studies have documented pulmonary effects of high ozone concentrations during exercise of short duration (approximately one hour), e.g. Brunekreef *et al.*, 1994.

Recent studies, using sophisticated methods to correct for other important risk factors (“confounders”), in Europe, Canada and the US have found associations between ozone concentrations and mortality. In the APHEA-1 study (*Text box*), an increase of the one-hour maximum O₃ concentration with 100 µg/m³ was on average associated with an increase of total mortality of 6%. An increase of the O₃

concentration with 100 µg/m³ was on average associated with an increase of respiratory mortality of 12% and cardiovascular mortality of 4%. Averaged over 12 studies conducted between 1996 and 2001, an increase of the eight-hour ozone concentration with 100 µg/m³ was associated with an approximate 4% increase in all-cause mortality (WHO working group, 2003). A 2% increase of mortality was found when the one-hour maximum ozone concentration was evaluated. The higher effect estimate for eight-hour average ozone concentrations compared to one-hour maximum concentrations is consistent with human-controlled exposure studies that have documented an increase of the pulmonary function decrement with multi-hour exposure to ozone. This supports an air-quality guideline that is formulated in eight-hour averages rather than in the one-hour maximum.

An increase of the eight-hour ozone concentration with 100 µg/m³ was associated with an about 7% increase in respiratory hospital admissions, averaged over 11 studies conducted between 1996 and 2001 (WHO working group, 2003). The effect estimate was again smaller (5%) when the one-hour maximum ozone concentration was evaluated. Several studies in the US and Canada did not find consistent associations between increased ozone concentrations and hospital admissions for cardiovascular disease.

A threshold has not been consistently found in the limited number of studies that have evaluated the issue. There is thus less certainty about the lack of a threshold than in the case of particulate-matter air pollution.

Effects of long-term exposure to air pollution

Despite the convincing evidence about effects of short-term fluctuations in ozone concentrations on lung function, hospital admissions and mortality, the effects of increased long-term average ozone exposure are still somewhat unclear. This is partly due to the fact that ozone is a secondary pollutant and consequently average concentrations are rather similar over large areas. For example, in the Netherlands there is virtually no spatial contrast in annual-average ozone concentration.

APHEA-1

- Multi-city study of association between daily fluctuations of air pollution and mortality / hospital admissions covering Europe.
- Coordinated by University of Athens (Klea Katsouyanni).
- An increase of the O₃ concentration with 100 µg/m³ was on average associated with an increase of total mortality of 6%, respiratory mortality of 12% and cardiovascular mortality of 4%.
- An increase of the one-hour maximum ozone concentration with 100 µg/m³ was on average associated with an increase of COPD hospital admissions of 8%.

Key references: Touloumi *et al.*, 1997;
Zmirou *et al.*, 1998.

In the two key US cohort studies (Dockery *et al.*, 1993; Pope *et al.*, 2002), there was no association between the long-term average ozone concentration and mortality. At least in the American Cancer Society study (Pope *et al.*, 2002) there was sufficient contrast in ozone concentration.

The strongest evidence for health effects related to long-term exposure to ozone is for lung function. A series of studies in Austria has found decreased lung-function growth over the summer season in children living in communities with higher ozone concentrations. A difference in the annual-average ozone concentration of 20 $\mu\text{g}/\text{m}^3$ was associated with a 2% smaller FVC (Frischer *et al.*, 1999; Horak *et al.*, 2002). A large recent study in 12 communities in Southern California in two fourth-grade children's cohorts found that the percent growth of FVC was 0.3% less when comparing the highest versus the lowest polluted community (Gauderman *et al.*, 2002). Larger effect estimates were found on peak flow in particular. The difference in daytime ozone concentration was about 73 $\mu\text{g}/\text{m}^3$. In both cohorts, children who played more outdoors showed larger lung-function effects. Most cross-sectional studies found decreased pulmonary function in communities with higher ozone concentrations (WHO working group, 2003). These studies were conducted in the US and Canada. In the Swiss SAPALDIA study, no association between ozone and lung function was found. The range of long-term average ozone (31-51 $\mu\text{g}/\text{m}^3$) was small in that study compared to the US studies. No other European studies are available.

Associations between ozone and incidence or prevalence of asthma were not consistently found. Symptoms of bronchitis were not associated with ozone concentrations in the two studies that evaluated them (WHO working group, 2003).

Conclusion

Associations of short-term exposures to ozone with mortality, respiratory hospital admissions and lung function have been documented in a range of studies including European settings. These associations are consistent with the effects found in animal and human-controlled exposure studies. It is likely that a substantial fraction of the observed health effects is due to ozone itself with other photochemical pollutants possibly contributing to the observed effect.

In spite of the consistent associations found in short-term epidemiological studies and animal studies showing effects related to long-term ozone exposure, the epidemiological evidence of long-term effects is weak. The strongest evidence exists for impaired lung-function growth and lung function.

4.4 NITROGEN DIOXIDE

Epidemiological studies have been conducted to consider indoor and outdoor exposures. All the investigations, however, have to address an essential problem, namely that many studies conducted in the last decade all over the world have found that fine particulate matter is associated with mortality and morbidity. Nitrogen dioxide (NO_2) is strongly correlated with particles, because both come from the same combustion sources and NO_2 is converted in the atmosphere to particulate nitrates and thus contributes to fine particle mass. Therefore it is very difficult to differentiate the independent effects of NO_2 and other pollutants, especially particles.

Several epidemiological investigations have been conducted in indoor settings, and many studies indicate an increased incidence of lower respiratory symptoms among children in relation to indoor NO_2 . A meta-analysis of indoor studies concluded that long-term exposure to NO_2 of 30 $\mu\text{g}/\text{m}^3$ is associated with an approximately 20% increase in respiratory illnesses in children (Hasselblad *et al.*, 1992). More recent

investigations have suggested specific effects of NO₂. Chauhan *et al.* (2003) followed a cohort of asthmatic children in Great Britain, measuring personal NO₂ exposures weekly for up to 13 months, obtaining viral cultures for each illness episode, and assessing the severity of the illness. Personal exposure to NO₂ was associated with more severe illness and an increased risk of virus-related asthma morbidity in this study. In a birth cohort of new-borns having an asthmatic sibling, measured indoor NO₂ levels mainly from gas stoves were associated with increased risk for wheeze and cough in the first year of life (Belanger *et al.*, 2003). Even studies conducted indoors, however, are not free from the potential confounding effect of particulate air pollution: burning natural gas in gas stoves or in ice-resurfacing machines (used in ice rinks) produces ultrafine particles in addition to NO₂; cooking is also a source of particles.

Short-term effects

Many time-series studies have used maximum hourly concentrations and/or daily mean concentrations of NO₂ to evaluate a wide range of short-term adverse health effects.

The European APHEA study found a statistically significant effect of NO₂ on daily mortality: 1.3% increase in daily deaths per 50 µg/m³ NO₂ (one-hour maximum) (Touloumi *et al.*, 1997). The effect remained statistically significant (0.6%) after adjusting for black smoke. In multi-city studies in Italy, France and Spain, a positive and statistically significant effect of NO₂ on daily mortality was found. (Biggeri *et al.*, 2001; Le Tertre *et al.*, 2002; Saez *et al.*, 2002). A recent meta-analysis included 32 effect estimates for NO₂ from single-pollutant models and 15 from multi-pollutant models (Stieb *et al.*, 2002; Stieb *et al.*, 2003). The overall effect estimate from the single-pollutant model for all-cause mortality was 2.8% per 44 µg NO₂ m³, which fell to 0.9% in multi-pollutant models including particles.

The APHEA-2 study on daily mortality in 29 cities (Katsouyanni *et al.*, 2001) found that PM effects on daily mortality were stronger in areas with high NO₂. In cities with low average NO₂, the estimated increase in daily mortality for an increase of 10 µg/m³ in PM₁₀ was 0.19%, whereas in a city with high average NO₂ it was 0.80%. This positive interaction may be interpreted in two ways. First, that NO₂ per se enhances the effects of PM. Or second, that in areas with high NO₂, PM likely contains more noxious substances than in areas with low NO₂ (WHO, 2003).

There have been several time-series studies published on the effects of NO₂ on daily hospital admissions for respiratory disorders, including asthma in children and adults. In the APHEA-1 study, NO₂ was associated with COPD but not with total respiratory conditions. A black-smoke effect was detected only in the presence of high NO₂ levels, a finding in keeping with APHEA-2 results on daily mortality. The results for asthma were less consistent, since positive associations with NO₂ were found, but not in all age groups and not in all cities (Sunyer *et al.*, 1997; Anderson, 1997; Spix *et al.*, 1998).

Investigations completed after APHEA-1 have underlined the importance of NO₂ on hospital admissions for asthma, particularly in children. A study in Valencia, Spain, found an association of asthma admissions with NO₂ and ozone but not with black smoke and SO₂ (Tenias *et al.*, 1998). A parallel analysis of daily GP consultations for asthma and other lower respiratory conditions in London showed strong effects for NO₂ in children, particularly during summer, whereas no effect of NO₂ was found in adults (Hajat *et al.*, 1999). In Rome, Italy, NO₂ was strongly related to total respiratory admissions, and in particular to acute respiratory infections and asthma among children (Fusco *et al.*, 2001). All these findings suggest a difference between children and adults in susceptibility to the components of the ambient pollutant mix.



In comparison with the number of studies on respiratory diseases, fewer studies are available on hospital admissions for cardiovascular diseases. Some studies found positive associations with NO₂ (Burnett *et al.*, 1997; D'Ippoliti *et al.*, 2003), whereas other studies did not (Schwartz, 1997; Morris *et al.*, 1995). In some of the positive studies, the effect estimates are smaller and sometimes non-significant when the investigators corrected for particle concentrations.

Several panel studies have evaluated the role of air pollutants on the aggravation of symptoms among patients with respiratory conditions. Most studies concern asthmatic children, while far fewer observations relate to adult or elderly asthmatics or COPD patients. Braun-Fahrländer *et al.* (1992) used a diary to record symptoms among children as well as NO₂ passive samplers placed outside the home. Duration of symptom episodes was associated with outdoor NO₂ concentration. Children in the Netherlands were studied by Boezen *et al.* (1999), and categorised according to their bronchial responsiveness (BHR) and IgE levels. There was a strong association between occurrence of lower respiratory tract symptoms, including wheeze, and both PM₁₀ and NO₂ among subjects with increased BHR and high IgE level. Since episodes of airflow obstruction and aggravation of symptoms in asthmatic subjects are often precipitated by viral infections, the study of Linaker *et al.* (2000) is relevant. They investigated around 115 asthmatic children and followed them up for 13 months with respect to respiratory infection and development of asthmatic symptoms, and measured personal NO₂ exposure. The air pollutant was strongly associated with the risk of more asthmatic attacks following respiratory infections. Overall, an effect of NO₂ has been noted in most panel studies evaluating aggravation of asthma.

Finally, the role of air pollution on heart-rhythm disorders among patients with implanted defibrillators has been suggested by Peters *et al.* (2000). In this study, PM_{2.5}, black smoke, NO₂ and CO were associated with increased risk of defibrillator discharges and the concentration-response relationship for NO₂ was the steepest.

Long-term effects

There are fewer epidemiological studies on long-term respiratory effects of NO₂ than on particulate matter, but new evidence has been provided in recent years. Both cross-sectional and longitudinal studies indicate an association between NO₂ and lung function. The Southern California Children's Study showed that lung-function levels among 9-16 year-old children were lower in communities with higher NO₂ concentration (Peters *et al.*, 1999). Lung function growth, evaluated in a different longitudinal study, was also impaired among these children (Gauderman, 2002). The NO₂ effect was not affected by the inclusion of other pollutants (e.g. PM₁₀ and O₃) in the statistical model, but it was weakened when acid vapours (including NO₂-derived nitric acid) were simultaneously considered. The cross-sectional SAPALDIA study in Switzerland (Ackerman-Liebich, 1997; Schindler, 1998) gives support to the association of NO₂ exposure and lung-function decrement among adults.

Cross-sectional studies of children (Braun-Fahrländer *et al.*, 1997) provide some evidence of an association between NO₂ and acute bronchitis, while the Southern California Children's Study suggested that chronic respiratory symptoms (cough and phlegm) were more frequent among children with asthma in communities with higher NO₂ exposure (McConnell, 1999). Two cross-sectional studies found an association between NO₂ and cough and phlegm symptoms in adults (Forsberg, 1997; Zemp, 1999). The latest report of the California Children study (McConnell *et al.*, 2003) demonstrated an association between bronchitis symptoms among children with asthma and the yearly variability of NO₂ concentrations. In two-pollutant

models, adjusting for O₃, PM₁₀, PM_{2.5}, coarse particles, inorganic acid and elemental carbon, OC was the pollutant that retained most of its significance. PM_{2.5} and NO₂ also were clearly linked with symptoms.

Increased susceptibility and impairment of lung defences may be the mechanism by which NO₂ has an effect on lung function and increases the risk of chronic respiratory symptoms. Toxicological evidence suggests that NO₂ increases the susceptibility to infection by viruses and bacteria, while a recent epidemiological study in UK has indicated that personal exposure to NO₂ increases the risk of virus-related asthma morbidity in children (Chauhan *et al.*, 2003). This evidence may be interpreted as an indication that the inflammatory response to infections is altered by exposure to oxidants (and perhaps by exposure to fine particles, thus leading to aggravation of symptoms and increasing the number of infection-related hospital admissions.

Conclusions

Health risks from nitrogen oxides may potentially result from NO₂ itself or its reaction products including O₃ and secondary particles. Additionally, NO₂ concentrations closely follow vehicle emissions in many situations, so that NO₂ levels are generally a reasonable marker of exposure to traffic-related emissions. Finally, NO₂ may augment the effects of other pollutants. Epidemiological studies of NO₂ exposures from indoor and outdoor air are limited in their ability to separate these effects. In many studies when adjustment for particles was made, the risk estimates were greatly reduced and often became non-significant. This may support the view that the concentration response signal generated for NO₂ is largely the consequence of other pollutants, some of which are derived from NO₂. In some studies, however, especially in Europe, the strongest effect was found for NO₂ whereas particulate matter had a weaker effect. On the basis of these findings, one might speculate that NO₂ is a better marker of local traffic than particulate matter measured as PM₁₀ or PM_{2.5}.

4.5 SULPHUR DIOXIDE

Short-term effects

Virtually all studies of effects from short-term exposure to sulphur dioxide (SO₂) have utilised ambient air concentrations measured by stationary monitors in order to estimate exposure. Exposure time periods have included concentrations measured in minutes, 24-hour averages lagged by up to four days and mean exposure over a few days up to the day of the health event of interest.

Increases in mortality have been associated with increases in short-term exposure to SO₂ in Europe and Asia. A meta-analysis of daily mortality from 12 European cities (APHEA-2) found an approximately 3% increase in mortality associated with an increase of 50 µg/m³ in SO₂ concentrations (Katsouyanni *et al.*, 1997). Absence of associations between mortality and SO₂ has also been reported. A meta-analysis of Spanish cities found little evidence of an association (Schwartz *et al.*, 2001). Correlation between ambient concentrations of SO₂ and other pollutants may have led to difficulty in distinguishing effects that can be attributed in part or wholly to SO₂. A time-series analysis of mortality in London over a 15-year period found that all effects could be attributed to short-term exposure to particulates and not to SO₂ (Schwartz *et al.*, 1990). Other studies have, however, investigated and found independent effects from SO₂. Analyses that have specifically considered the concentration response relation between short-term exposure to SO₂ and health outcomes suggest that the relation, at least for mortality, is not linear (Schwartz *et al.*, 2001).

Sulphur dioxide exposure has also been associated with day-to-day hospital admissions for respiratory and cardiovascular diseases (Anderson *et al.*, 1997). Time-series analyses in London and Hong Kong, using identical methodology in both cities, found increases in respiratory and cardiac hospital admissions were associated with increases in SO₂ (Wong *et al.*, 2002). The association between cardiac admissions and SO₂ was more robust than for respiratory diseases in that it remained significant after adjustment for effects from another pollutant, whereas the association for respiratory diseases did not. The percent increase in cardiac admissions associated with a 10 µg/m³ increase in mean concentration of SO₂ ranged between 1.4 and 2.0%. In an another APHEA-2 analysis using data from seven European cities, the percentage increase in hospital admissions for cardiovascular diseases per 10 µg/m³ increase in SO₂ was 0.7 in subjects aged less than 65 years (Sunyer *et al.*, 2003a). Among respiratory admissions in the same study, only admissions for asthma in children were related with SO₂ (Sunyer *et al.*, 2003b).

Panel studies of peak flow and symptoms in children have not found associations between ambient SO₂ concentrations and respiratory health (Roemer *et al.*, 1998). In the European PEACE study of over 2,010 children, neither PM₁₀, black smoke, SO₂ or nitrogen dioxide were related to morning or evening peak expiratory flow or the daily prevalence of respiratory symptoms and bronchodilator use (Roemer *et al.*, 1998).

Although an extensive statistical methodology has been developed to control for other pollutants, meteorological and seasonal factors, the possibility remains that observed effects may be due to some other pollutant or environmental factor correlated with ambient SO₂ exposures. A comparison between short-term ambient pollution concentrations measured at fixed monitoring points and personal exposure has reported a poor correlation between ambient concentrations of SO₂ and personal exposure measured using personal air samplers. The association between ambient SO₂ and personal PM_{2.5} was also poor, thereby not supporting the hypothesis that SO₂ is actually representing for effects from fine particles.

An intervention study in Hong Kong documented that a reduction in SO₂ concentrations was followed by a significant drop in mortality (Hedley *et al.*, 2002), (*see Text box*).

Long-term effects

A re-analysis of the effects of the smog in greater London in 1952 found the effects from SO₂ and particulates persisted well beyond the month of the smog and that deaths as late as 1953 could be attributed to the smog's effects (Bell and Davis, 2001). The relative risk for a daily increase of 0.10 ppm (~ 260 µg/m³) on the previous day on mortality was 1.27 and for a mean increase of 0.10 ppm over the previous week was 1.28.

Hong Kong Intervention Study

- Mortality was compared before and after an intervention requiring reduction in the sulphur content of fuel oil.
- Mean ambient monthly SO₂ before the intervention ranged from 3 µg/m³ to 145 µg/m³ between the least and most polluted districts.
- Mean reduction of 50% in SO₂ over 2.5 years after the intervention. A significant drop in deaths from all causes, respiratory and cardiovascular causes in every age group in the first cool season after the intervention.
- Estimated an increase in life expectancy for men aged 25 years and older of 0.73 years per 10 µg/m³ reduction in SO₂

Similarly to short-term exposure estimates, routinely measured ambient air concentrations measured by stationary monitors are the most common source of information about long-term exposure to SO₂. A few studies have estimated individual exposures using information about subjects' residential history (Abbey *et al.*, 1999; Nyberg *et al.*, 2000). In the Californian AHSMOG cohort study, long-term exposure to SO₂ and other pollutants was modelled from monthly ambient concentrations between 1966 and 1992 to the level of subjects' residential zip code (Abbey *et al.*, 1999). No associations were found between SO₂ concentrations and mortality except mortality from lung cancer where the relative risk for an interquartile range difference SO₂ was 2.38 in men and 2.36 in women. The latest follow-up of 500,000 adults in the American Cancer Society cohort shows an association between SO₂ concentrations and lung cancer, as well as all cause and cardiopulmonary mortality between 1982 and 1998 (Pope *et al.*, 2002). By contrast a European study in which 1,000 subjects with lung cancer were compared to 2,300 controls found no relation between lung cancer and past SO₂ exposure. In this study a detailed assessment of subjects' individual past exposure was made due to home heating (Nyberg *et al.*, 2000).

In a study of 9,000 adults living in eight areas of Switzerland (SAPALDIA), mean lung function, measured by FVC and FEV₁, was 32.5 ml and 12.5 ml lower, respectively, per 10 µg/m³ increase in mean annual SO₂ concentrations (Ackermann *et al.*, 1997). No association was found in a six-week average exposure to SO₂ and respiratory symptoms in 625 Swiss pre-schoolchildren who participated in a daily diary study (Braun-Fahrlander *et al.*, 1997). However, reported symptoms of cough and bronchitis were related to ambient concentrations of SO₂ in the SCARPOL study of Swiss schoolchildren from 10 areas of Switzerland (Braun-Fahrlander *et al.*, 1997). Associations were also found between SO₂ concentrations and doctor-diagnosed asthma in a cross-sectional study of Czech and Polish schoolchildren (Pikhart *et al.*, 2001).

In summary, considerable epidemiological evidence has accumulated supporting a deleterious effect from SO₂ exposure on mortality, respiratory and cardiovascular health. However, these associations are unlikely to be causal, given the low levels currently attained. It is unknown if these associations are caused by other pollutants or whether SO₂ has a harmful effect at very low levels.

5 AMBIENT AIR POLLUTION AND CANCER

5.1 KEY POINTS

- ❑ Epidemiological studies show ambient air pollution causes lung cancer
- ❑ There is insufficient evidence for a link between air pollution and childhood cancer.
- ❑ Components of particulate matter may be responsible for an increased risk of lung cancer.

5.2 LUNG CANCER

In the epidemiological literature, the question of whether ambient air pollution is a human carcinogen has been addressed properly only for lung cancer and for childhood cancers. In summary, over the last 50 years there has been an accumulation of evidence that ambient air pollution has a lung-carcinogenic effect, evidence which stems from different types of studies. These studies indicate that ambient air pollution causes lung cancer and the increased risk may be of similar magnitude as that of passive smoking, i.e. 20-30%. Air pollution as a possible cause of childhood cancer has been studied to a lesser extent and the epidemiological literature is inconsistent.

Ecological urban-rural comparisons. Since Curwen and co-workers in 1954 observed an association between population density and lung-cancer rates in the UK (Curwen *et al.*, 1954) and suggested higher air-pollution concentrations in more densely populated areas as one possible explanation, a number of other ecological studies have demonstrated higher lung cancer rates in urban areas. These studies found lung-cancer rate ratios between 1.0 and 1.90, i.e. 0 to 90% higher lung cancer rates in urban areas. Although the higher rates in urban areas may, at least in part, reflect unaccounted-for differences in smoking habits and other factors than air pollution related to population density, the results coincide with urban-rural gradients in the mutagenicity of airborne particulate matter (Cohen *et al.*, 2000).

Ecological between-community studies. A number of studies found higher lung cancer rates in communities with higher levels of air pollution from industry or other sources. The rate ratios were similar to those found in the urban-rural studies. Again, lifestyle differences between communities and individuals may have contributed to the differences in lung-cancer rates.

Case-control studies. More than a dozen case-control studies on air pollution and lung cancer have been published during the last 50 years, with relatively simple methods used in the early studies (Stocks *et al.*, 1955) and more sophisticated methods for exposure assessment and correction for other risk factors (“confounders”) applied in later studies. For example, the study by Stocks and Campbell (1955) used current residence in urban or rural area for the exposure assessment and handled the potential influence of smoking by estimating effects of air pollution within different strata of smoking; relative risks were between 1.1 and 3.4. On the other hand, a recent study (Nyberg *et al.*, 2000) used advanced modelling of exposure at individual addresses decades back in time, and found a relative risk of 1.4 in association with a 16 µg/m³ increase in NO₂ concentrations – when allowing for a 20-year lag-time and adjusting for a number of smoking variables, occupation, radon, etc., at the individual level. In general, the case-control studies found increases in lung-cancer risks similar to those observed in the ecological studies.

Cohort studies. Over the years, the methods applied in the 10 or so cohort studies have progressed similarly to those of the case-control studies. Among the most recent studies, Dockery *et al.* (1993) reported a 37% insignificant increase in lung cancer mortality in association with a 19 $\mu\text{g}/\text{m}^3$ increase in $\text{PM}_{2.5}$. Pope *et al.* (2002) reported a significant 8% increase in lung-cancer mortality in association with a 10 $\mu\text{g}/\text{m}^3$ increase in $\text{PM}_{2.5}$. Significant increases were also observed for sulphate particles and SO_2 , but not for a number of other pollutants (Pope *et al.*, 2002). Abbey *et al.* (1999) reported significantly increased lung-cancer mortality for PM_{10} , SO_2 and NO_2 , but not for O_3 . Hoek *et al.* (2002) observed an insignificant 25% increase in lung-cancer mortality in association with a 28 $\mu\text{g}/\text{m}^3$ increase in NO_2 , but virtually no association for black smoke. A recent study by Nafstad *et al.* (2003) reported a significant 8% increase in lung-cancer incidence for a 10 $\mu\text{g}/\text{m}^3$ increase in NO_x , but no association for SO_2 .

Occupational studies. Numerous studies have shown increased risk for lung cancer among persons exposed to diesel-engine exhaust at work. A meta-analysis including 23 studies estimated the relative risk in association with exposure to be 1.33 (Bhatia *et al.*, 1998), which is similar to the risk estimates obtained in the other study categories. Moreover, the estimated relative risks were quite consistent between subgroups of studies. Both case-control and cohort studies showed pooled relative risks of 1.33, studies adjusting for smoking had a pooled relative risk of 1.35 and those not adjusting for smoking a relative risk of 1.33, and the pooled relative risk estimate was somewhat higher (1.43) for studies using an internal comparison group, which is usually considered more reliable than using external comparison groups.

Comparisons of various types of exposure to combustion-source pollutants. Combustion-source pollutants studied in relation to lung cancer include tobacco smoke showing relative risks of more than 20 for heavy smoking (Dreyer *et al.*, 1997), coal-burning in cook-ovens showing relative risks of 2.5-10.0 for exposed workers (Cohen *et al.*, 1995), diesel-engine exhaust showing a relative risk about 1.3 for exposed workers, and passive tobacco smoking showing a relative risk of 1.24 among non-smokers (IARC, 2002). It seems that lung-cancer risk in association with exposure to urban ambient air pollution is of similar magnitude as risk in association with passive smoking.

Which pollutants are responsible? Ambient air pollution is a complex mixture of substances, chiefly due to the incomplete combustion of fossil fuels. Several of the substances are carcinogenic or mutagenic and covariation between many of the single pollutants occurs, although the relative contribution to air pollution from different sources and the degree of co-variation between different pollutants differ with climate, location and calendar time. Moreover, usually in epidemiological studies, population density, traffic density or only a few measured or modelled pollutants are used as indicators of the air pollution mixture in general or indicators of pollution from specific sources. Therefore, it is difficult to disentangle the contribution to lung-cancer risk from single pollutants on the basis of epidemiological studies only. However, on the basis of the chemical composition and the toxicological properties, particulate matter is an obvious candidate among the air pollutants to be responsible for an increased risk for lung cancer (Cohen, 2000). In agreement with this, positive associations were found between $\text{PM}_{2.5}$ and lung cancer in two US cohort studies (Pope *et al.*, 2002; Dockery *et al.*, 1993). PM_{10} was significantly associated with lung cancer in one study (Abbey *et al.*, 1999), but no association was found in another study (Pope *et al.*, 2002).

5.3 TRAFFIC-RELATED AIR POLLUTION AND CHILDHOOD CANCER

The evidence for a carcinogenic effect of traffic exhaust derives mainly from studies of animals and occupationally exposed adults. In 1989, however, a study based on some 330 cases performed in Denver, US, showed significantly elevated risks for all cancers, leukaemia's and CNS (Central Nervous System) tumours but not lymphomas among children living near streets with a high traffic density (Savitz *et al.*, 1989). Although a crude method was used to assess exposure, the study was well performed and showed exposure-effect relationships. Since then, a few relatively small studies have similarly indicated increased risk for childhood cancer in association with traffic-related air pollution, but large studies lend no support for an association between traffic-related air pollution and leukaemia's, CNS tumours which are the most common cancer types in childhood, or all childhood cancers combined (Raaschou-Nielsen *et al.*, 2001; Reynolds *et al.*, 2004). In summary, the evidence is insufficient to infer a causal association between traffic-related air pollution and childhood cancer.

6 POLICY IMPLICATIONS OF EPIDEMIOLOGY FINDINGS

6.1 KEY POINTS

- ❑ Evidence-based policies are increasingly introduced at the European level
- ❑ Epidemiological studies play a vital role in guiding policy, because they concern people and real-life exposures. EU funded studies have played an important role in the development of EU policy towards air pollution
- ❑ Since there appears to be no safe level for PM and ozone effects, new standards and legislation should rely on the notion of “acceptable risk” and “acceptable concentration”

Environmental policies are increasingly based on the use of scientific evidence either directly or via the use of risk or health impact assessment. Thus the need for solid scientific evidence on the health effects of air pollution has increased. In recent years, it has been recognised that evidence from epidemiological studies is of central importance for policy, as epidemiology concerns above all else human populations and real-life exposures.

Epidemiological findings have been used in recent revisions of air-quality standards and guidelines (USEPA 1996; EC 1999; WHO 2000). This has been a consequence of the key role of epidemiology in the renewed interest of scientists, decision-makers and the public in air-pollution health effects.

However, epidemiological results should fulfil a number of criteria in order to be useful for policy-making (WHO Working Group 2000). When policy implications are central in the writing of a study report, there should be a clear account of the exposure levels and characteristics studied, the exposure-response function and the definition of effects. Science/policy interface is an important aspect for scientists to consider. AIRNET contributed to the communication of scientists and stakeholders as the first Europe-wide relevant network on air pollution and health issues. The needs of stakeholders can often form the basis of a study design. But the most important aspect for providing results useful in policy-making is the need for accumulated evidence on a specific issue, which will allow for a balanced assessment.

Epidemiological studies, partly funded by the EU FP4 and FP5, have documented that at the current concentrations occurring in Europe, adverse health effects still occur. The evidence also suggests that the impact reflects a substantial impact on public health. For example the impact of short-term changes in air pollution on mortality is not just bringing deaths forwards by a few days. Outdoor air pollution clearly belongs to the most important environmental problems. This suggests that further abatement of air pollution will result in gains in public health.

Several studies have suggested that there is no threshold in the relationship between (particulate matter) air pollution and mortality/disease. The implication is that air-quality guidelines cannot be set that provide absolute safety for the population. Instead an acceptable concentration needs to be defined, based on the concentration-response relationship and the accepted amount of risk.

It remains difficult to identify on the basis of epidemiological studies which particle characteristics / pollutants are associated with the largest health effects. Several studies have suggested the importance of motorised traffic emissions. Other studies have pointed towards combustion particles in general, including industrial and home heating as relevant sources. It is therefore unlikely that a PM10 standard is sufficient to regulate air pollution across Europe with the same level of certainty.

Although it is likely on the basis of epidemiological findings that health gains will be obtained by further reducing air pollution, the increasing costs of abatement measures call for more direct evidence that air pollution policies indeed bring the expected health gains. A few recent studies have shown decreased mortality after introduction of a regulation to abate air pollution. Inclusion of more of this type of research to evaluate the benefits of a regulation would be very useful.

Key issues for further epidemiological research in air pollution and health are identified in the next section. It is hoped that the activities of AIRNET and the recent EU SCALE initiative on Environment and Health will encourage the inclusion of air-pollution health effects in the current and future EU Framework Research Programmes.

7 FUTURE RESEARCH NEEDS

7.1 KEY POINTS

Priorities for future research include:

- ❑ The long-term effects of (particulate-matter) air pollution
- ❑ Assessment of particles from specific sources: especially but not exclusively motorised-traffic emissions.
- ❑ Health effects of interventions
- ❑ Ultrafine particles and PM_{2.5}, secondary particles and of carcinogenic PAH
- ❑ The role of gaseous pollutants, such as ozone, NO₂ and SO₂.

7.2 FUTURE RESEARCH PRIORITIES

While epidemiological studies have generated a wealth of information to better focus air pollution policies, questions remain that cannot be answered currently with the precision desired by policy makers. An illustration of this is the questions asked by policy-makers in the framework of the CAFE process (<http://www.euro.who.int/document/E82790.pdf>).

General issues

Whilst there is now little doubt that particulate air pollution has short-term effects on health, the effects of *long-term exposure* to (particulate matter) air pollution, has been very little researched in Europe. In health impact assessments, the long-term effect estimates dominate the estimated public health impact of particulate air pollution. Therefore, better understanding of these effects is greatly needed. Following research in the USA, the discussion focuses on mortality effects. Effects on morbidity from respiratory and cardio-vascular disease should be initiated as well, as these affect quality of life.

Most epidemiological studies have studied the effect of (multiple) single pollutants. In reality the atmosphere contains mixtures of pollutants that are often correlated in time and space. As it has not been possible to attribute observed health effects to a single pollutant, air pollution abatement policies struggle with the question which particles / pollutants should be reduced first. Pollution control mainly focuses on control of sources, another promising approach in epidemiology is to assess the health effects of exposure to (particulate) air pollution from a specific *source*. This allows assessing whether the health effect of the same mass of particles from e.g. coal burning, traffic emissions and wind blown dust. Specifically an important source for PM in Europe is motorised traffic emissions. Industrial emissions may be important as well.

As discussed in the previous chapter, studies that directly evaluate the benefits of a *regulation / intervention* would be very useful. This type of research provides a direct link between policy and health benefits.

Particulate matter

Whilst there is now little doubt that particulate air pollution has short-term effects on health, there is limited information on the physical and chemical characteristics, which determine the toxicity of the particle mixture. Specifically, in Europe more studies on ultrafines and PM_{2.5} should be conducted. Also the role of secondary particles and the role of carcinogenic PAH needs to be further investigated. Many of the current studies on particulate air pollution focus on adults and elderly. However, recent studies indicate important effects also among children, which need to be explored further.

The effect of PM appears to be heterogeneous across Europe. The reasons for this heterogeneity should be further explored and understood, as it may have consequences on which concentration response function to use in a certain area.

The issue of the threshold continues to raise discussion. The current evidence suggests that there is not threshold for PM effects. However, this may be because there are various thresholds specific to sensitive subgroups. This issue merits further investigation using more sophisticated designs.

Ozone, NO₂ and SO₂

In the 1990s many epidemiological studies addressed particulate air pollution effects and fewer studies investigated the role of other pollutants. There is more uncertainty about the effects of the gaseous pollutants *per se* and important aspects such as the presence of a threshold and the extent to which the observed association represents a significant decrease of life expectancy / quality of life.

For ozone, the existing evidence indicates mainly respiratory effects, but more research is needed because statistical modelling of ozone presents more difficulties compared to PM. There is very little information on long-term effects and further investigation is needed.

There is evidence on the health effects of NO₂ *per se* and also on synergy between NO₂ and other pollutants. NO₂ is also important as a precursor of ozone and a traffic pollution indicator. It is not yet clear how much of the effect identified may be attributed to NO₂ itself and of what NO₂ is exactly an indicator. This is a key issue, especially because traffic pollution is significant in urban areas of Europe and further research should be encouraged.

Sulphur dioxide (SO₂) concentrations have decreased in ambient air, as a result of a number of specific measures, to levels, which should not be harmful to health. However, SO₂ continues to appear as a statistically significant predictor of both short and long-term health effects. It is not well understood whether SO₂ represents another air-pollution mixture, which may be specifically health relevant, and more investigation of this issue is warranted.

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ANNEX 1 – FREQUENTLY ASKED QUESTIONS

Question 1: What is the public health relevance of air pollution in Europe?

Answer: In many epidemiological studies, current-day air-pollution concentrations have been associated with changes in various indicators of health in the population. With the advance of more sophisticated methods of exposure assessment, health assessment and statistical analysis, small effects can nowadays be detected that are not necessarily of great public health consequence. An example of this is transient, small changes of lung function associated with an air-pollution episode.

Several organisations, such as the American Thoracic Society, have attempted to classify health responses as being 'adverse' or not. If one compares this scheme with the health effects observed in epidemiological studies, it is clear that mortality, hospital admissions, asthma attacks and medication use would be assessed as 'adverse effects'.

Recent studies have documented that the mortality increases observed in time-series studies are not just deaths brought forward a few days, but at least in the order of months. It has also been estimated that long-term exposure to airborne particles results in a loss of life expectancy of about one to two years. The public health impact was recently quantified for Austria, France and Switzerland. The study concluded that more than 40,000 deaths, more than 290,000 bronchitis episodes and 500,000 asthma attacks were attributable to air pollution. Air pollution therefore has a considerable impact on public health.

Question 2: Can reductions of emissions and/or ambient concentrations of PM, NO₂, ozone, NO, SO₂, and PAH be shown to have positive impacts on public health?

Answer: Several lines of evidence suggest that reducing emissions and levels of ambient air pollution will lead to positive impacts on public health of considerable magnitude (see [FAQ 1](#)).

According to numerous observational studies, on days of low air pollution there are fewer deaths and admissions to hospitals, while especially susceptible subjects have fewer symptoms, use less medication and have less limitation in their daily activities. The strength of the evidence differs for the different pollutants, but most time-series studies have studied urban areas, in which most or all of the pollutants listed in the question appear in a mixture that is harmful to health. The results from observational studies are supported by experimental studies in humans and in animals.

Historical evidence from the past air-pollution episodes shows that at very high levels, air pollution can have devastating effects on public health. It could be argued that no further improvement in public health is likely, given that the levels of air pollution are already so low in Europe. However, the observational studies mentioned above show no evidence of a threshold for the harmful effects of air pollution even at the current low levels.

There is less, but accumulating, evidence on the more long-term effects on health. Cohort and cross-sectional studies show that living in areas with less pollution or away from traffic has several beneficial effects on health. Some US studies also show that people who move to

areas with less air pollution experience improvements in lung function and lung growth. Recently, there is also direct evidence of improvements in public health associated with a reduction in the emissions and levels of air pollution due to specific measures taken to reduce air pollution (e.g. banning of coal sales for residential heating in Dublin, Ireland).

Taken together, there is now convincing evidence that reducing emissions and levels of ambient air pollution will lead to positive impacts on public health, even at the low levels of air pollution currently observed in Europe.

Question 3: Is there a proper health indicator to facilitate communications with politicians and the public?

Answer: Not really. People tend to use health indicators as they want. The assumption that politicians and the public have only one use for a health indicator is no more warranted than the assumption that this is so for researchers.

What may lie behind this question is the confusion created by reports that relate to different outcomes. These outcomes may be selected according to what makes the most impressive news story, rather than what is most appropriate. As a result, it becomes difficult to assess the relative importance of different pollutants with respect to each other or to other hazards.

This difficulty is a common in economic evaluations and has led to 'standardised' evaluations of 'quality-adjusted life years' and similar measures, so as to provide a common metric that captures both excess mortality and effects on quality of life. These evaluations have been helpful, but have some limitations: they are not value free and may be insensitive to specific differences that are nevertheless perceived to be of importance.

Nevertheless, it might be useful to have greater standardisation of outcome measures in air-pollution research. This would be as much a task for politicians and the public as the researchers.

Question 4: How do effects of air pollution compare with those of other indoor risk factors such as smoking and fungi?

Answer: Since different risk factors are to some extent associated with different health effects, it is not easy to compare the risks of air pollution to those of other risk factors. An interesting approach to putting different outcomes on the same scale is the so-called DALY (Disability-Adjusted Life Years) concept. The DALY combines information on years of life lost and years lived with a disability, using weights for the severity of the disability. The concept has been applied widely in the World Health Organisation's Global Burden of Disease (GBD) project.

Recently, DALYs have been calculated by researchers of the National Institute for Public Health and the Environment (RIVM) in the Netherlands, for a variety of environmental exposures in that country. The long-term effects of particulate air pollution were ranked second in the evaluated risk factors, approximately equal to domestic accidents and traffic accidents. The effect of Environmental Tobacco Smoke (ETS) was an order of magnitude lower and the effect of damp homes almost two orders of magnitude lower. The short-term effects of particulate matter and ozone were assessed to have similar effects as damp homes.

The calculation of the DALY depends on the severity weights, which depend on the value attached to specific health effects. Nevertheless, the calculation suggests that (particulate) air pollution belongs to the more important environmental risk factors.

Question 5: Are there important substances for which no standards have been drawn up yet?

Answer: There are two principal types of standards that try to limit the harmful health effects of outdoor air pollution. First, the Air Quality Guidelines, most importantly those by the WHO. These guidelines have no legal status, but as generally accepted recommendations they have considerable impact. Such guidelines exist for a very large number of substances.

Second, there are legally binding standards, like the limit values set by the EU. Such standards exist for a much more limited number of substances. Currently in the EU there are limit values for the classical air pollutants, which occur in the atmosphere in relatively high concentrations, such as CO, SO₂, NO₂, ozone, and PM₁₀, particulate air pollution, and for selected toxic substances, such as lead and benzene. Currently, the EU is in the process of starting the regulation of PAH and some heavy metals (As, Cd, Ni).

Urban air pollution is a very complex mixture that contains hundreds or thousands of substances. It is not possible to have standards for all of these substances. However, the existing standards protect the public also from the harmful health effects of many other substances, as they also serve as indicators of a pollution mixture. Examples are NO₂ for photochemical pollutants and PM₁₀ for numerous inorganic and organic compounds.

In some situations these general indicators of air pollution exposure may not be enough. For example, close to a factory or other point source, the levels of some specific, more rare substances may be high without generally increased levels of other pollutants. When considering limit values for this kind of harmful substance, the extent of exposure in the population and in specific population groups needs to be considered.

It is likely that the current standards regulate the majority of the public health burden caused by air pollution. However, the evidence on the health effects of air pollution is accumulating rapidly and the legislation needs to be updated continuously. For example, it is questionable whether the existing standards sufficiently reduce the health effects associated with emissions from traffic. So there is a need for new information to allow a more targeted, cost-effective regulation of air pollution emissions in the future.

Question 6: Is black smoke a relevant indicator for health effects?

Answer: Black smoke provides important information on airborne particles – information that is missed when one relies only on PM₁₀ or PM_{2.5} as an indicator of airborne particles. Specifically, black smoke is a better marker for diesel soot than PM₁₀/PM_{2.5}, which in experimental and epidemiological studies has been related to adverse health effects.

Black-smoke measurements have been conducted in Europe for more than 50 years to characterise airborne particulate matter. The method is based on measuring 'black particles' through the reflectance of a filter on which particles have been sampled. The measurements

were started at a time when combustion of coal was a major source of outdoor air pollution and as a result a large fraction of airborne particles was 'black' or 'soot'. Airborne particles are actually a mixture of particles from different sources, including 'non-black' particles, which are not characterised by the traditional Black Smoke method. Examples of non-black particles are sulphates and nitrates.

Current air-quality guidelines for particulate matter are formulated typically as the mass of particles of a specific size, mostly PM_{10} (particles smaller than $10\ \mu\text{m}$). As a result, monitoring agencies have stopped doing BS measurements and replaced them with PM_{10} measurements. This is probably not a good strategy, because black smoke is currently a good indicator of diesel soot and in some areas also of smoke from wood burning.

Several studies have documented that the impact of motorised-traffic emissions on air quality is not well characterised by $PM_{10}/PM_{2.5}$. Black smoke turned out to be a much better indicator. There is now increasing evidence that motorised-traffic emissions are associated with adverse respiratory effects in especially children. Several studies have suggested that diesel-fuelled traffic in particular plays an important role. Experimental studies have also linked diesel-soot exposures with respiratory effects, including inflammation. To characterise these effects, black smoke is probably a better indicator than PM_{10} or $PM_{2.5}$. Black smoke thus provides additional information to mass-based particle indicators.

ANNEX 2 – ACRONYMS

The following is a brief explanation of acronyms and abbreviations used in this report:

AHSMOG	Adventist Health Study on Smog (US)
AIRGENE	Air Pollution and Inflammatory Response in Myocardial Infarction Survivors: Gene-Environment Interaction in a High Risk Group, http://www.gsf.de/epi/en/ag_epi_luftsch_1.html#airgene
AIRNET	Thematic Network on Air Pollution and Health, http://airnet.iras.uu.nl/
APHEA	Air Pollution and Health – A European Approach
AQG	Air Quality Guidelines
BHR	Bronchial Responsiveness
CAFE	Clean Air For Europe programme, http://www.europa.eu.int/comm/environment/air/café/
CO₂	Carbon dioxide
COPD	Chronic Obstructive Pulmonary Disease
DALY	Disability Adjusted Life Years
EC	Elemental Carbon
EU	European Union
FEV	Forced Expiratory Volume
FVC	Forced Vital Capacity
HEAPPS	Health Effects of Air Pollution on Susceptible Subpopulations
IARC	International Agency for Research on Cancer, http://www.iarc.fr/
IgE	Immunoglobulin E
IRAS	Institute of Risk Assessment Sciences, Utrecht University
ISAAC	International Study on Allergy and Asthma in Children
IUGR	Intrauterine Growth Retardation
KTL	National Public Health Institute, Finland
NGO	Non-Governmental Organisation
NH₃	Ammonia
NMMAPS	National Morbidity, Mortality and Air Pollution Study (US)
NO₂	Nitrogen dioxide
NO_x	Nitrogen oxides (NO ₂ + NO)
OC	Organic carbon
PAH	Polycyclic Aromatic Hydrocarbons
PEACE	Pollution Effects on Asthmatic Children in Europe,
PM_{2.5}	Particles with a size less than 2.5 micrometres
PM₁₀	Particles with a size less than 10 micrometres
POM	Particulate Organic Matter
RIVM	Rijksinstituut voor Volksgezondheid en Milieu (National Institute for Public Health and the Environment), http://www.rivm.nl/
RR	Relative Risk, the risk of disease in high versus low exposed subjects
RUPIOH	Relationship between Ultrafine and fine Particulate matter in Indoor and Outdoor air and respiratory Health, http://www.iras.uu.nl/research/projects_env_and_health/eh08.php
SAPALDIA	Swiss Study on Air Pollution and Lung Diseases in Adults, http://www.sapaldia.ch/

SCARPOL	Swiss Surveillance Program of Childhood Allergy and Respiratory Symptoms with respect to air pollution and climate, http://www.research-projects.unizh.ch/med/unit41000/area179/p3647.htm
SGA	Small for Gestational Age
SO2	Sulphur dioxide
SP	Suspended Particles
TRAPCA	Traffic-Related Air Pollution on Childhood Asthma
TSP	Total Suspended Particles
ULTRA	Exposure and risk assessment for fine and ultrafine particles in ambient air, http://www.ktl.fi/ultra/
USEPA	United States Environmental Protection Agency, http://www.epa.gov/ebtpages/air.html

