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Air Quality and Health.

2010 The Year of the LUNG
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AUTHORS

Nino Künzli, Laura Perez, Regula Rapp

Swiss Tropical and Public Health Institute, Basel, and

University of Basel, Basel, Switzerland

W www.Swisstph.ch

E Nino.Kuenzli@unibas.ch

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Avenue Ste-Luce 4, 1003 Lausanne, Switzerland

T +41 21 213 01 01

F +41 21 213 01 00

E info@ersnet.org

W www.ersnet.org

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1.
EDITORIAL

THE CONTINUING CHALLENGE OF AIR POLLUTION

Once a severe but local problem of highly industrialised and densely populated cities, air pollution has now morphed into a more insidious threat to the public health of entire nations. Smoke from domestic coal fires, power plants and heavy industries has largely vanished from our skies. This has been achieved through the use of clean fuels, filtration of flue gases, improvements in process technology – and export of the most polluting industries to countries with lower wages, and less pollution control. At the same time, motor vehicle transport has increased enormously, and other sources of air pollution such as intensive livestock farming have emerged. Pollution is transported over long distances, and secondary pollutants such as ozone are formed through photochemical reactions. The erstwhile distinctions between 'dirty' cities and the 'clean' countryside have become blurred as a result, and nowadays a much larger fraction of the population is exposed to some form or level of hazardous air pollution than 50 years ago. Because air pollution, in some ways, is now less visible and less immediately irritating than it used to be, understanding and communicating the health risks has become more of a challenge.

The members of the ERS Environment Committee have now produced a booklet on air pollution and health that is an elegant attempt to explain to a wide audience what air pollution is in the current day and age, and what damage it still does to our health. The authors have found a welcome mix of scientific authority and clarity that will appeal to clinicians, public health practitioners, patient organisations, stakeholder representatives and informed members of the lay public.

That does not mean that this material is suitable for casual reading on the train home from work. This is only logical; a vast topic such as the health effects of air pollution cannot be treated too lightly, and the reader will need to dig in more than just occasionally. I recommend reading one chapter at a time – so that the next one can be appreciated even more the next day.

Bert Brunekreef, PhD
Professor of Environmental Epidemiology
Institute for Risk Assessment Sciences, Utrecht University, the Netherlands

Breathing is the most basic human function required to sustain life. More air enters the body and the bloodstream than any other substance. Unfortunately, humans are exposed to a variety of polluting substances due to industrial, heating and traffic emissions. These substances, notably particulate matter and gases, remain in the atmosphere as a dirty umbrella over cities and large urbanised areas. Breathing air contaminated with toxic substances entails health risks for individuals and has public health consequences. The health effects of air pollution have been observed over several decades. Policy measures during the 1960s and 1970s were able to reduce drastically the air contamination of the past and a widespread illusion was disseminated that the war against air pollution had been won. Research since the early 1990s, however, has clearly indicated that health effects still exist even at lower air pollution levels. Strict air quality guidelines have thus been advocated by the World Health Organization (WHO Air Quality Guidelines, 2006).

The European Respiratory Society believes that free access to clean air is a fundamental need and right for all citizens in the European Union. European, national, and local governments have a responsibility to assure that this fundamental right of the individual is respected and to act so that the maximum pollutant levels indicated by the WHO are observed. Unequal distribution of health risks associated with differential exposure to poor air quality between countries and communities, and within population groups in the same community, is a violation of the basic principle of environmental equity.

When it comes to dealing with the health effects of air pollution, respiratory physicians are immediately called upon: incidence and aggravation of asthma; chronic obstructive pulmonary disease (COPD); and lung cancer within their own professional field; but also cardiovascular conditions (including ischaemic heart disease and heart failure), often in patients already affected by smoking-related pulmonary diseases.

Against this background, the Environment and Health Committee of the European Respiratory Society has launched an initiative to provide respiratory physicians with instruments and tools to better understand all the complicated issues related to exposure to air pollution and its health effects. Nino Künzli, a leading figure in air pollution research, together with his collaborators, has conducted an extraordinary effort to condense in a few pages what all physicians and educated people need to know: the present state of our air, and of the research into the effects of air pollution.

But the duty of physicians is not limited to expanding their scientific knowledge in a rapidly evolving area: we believe that they should act as advocates to help reduce the ambient contamination of the air. They should recognise that air pollution is the largest environmental challenge for European citizens, one that currently limits the fundamental right of all individuals to breathe clean air. This challenge is associated with large health effects – effects that will continue to menace public health in the future. A strong commitment, then, is requested: take a leadership and an advocacy role in order to educate patients, and ask for large-scale strategies to reduce the harmful effects of air pollution.

Nikolaos Siafakas
ERS President 2009–2010

Francesco Forastiere,
ERS Environment and Health Committee Chair

2. INTRODUCTION

What this booklet does and does not cover

Ambient air pollution is an established cause of morbidity and mortality – like tobacco smoke. Even more than passive smoking, air pollution is not a lifestyle choice but a ubiquitous involuntary environmental exposure, which can affect 100% of the population, from womb to death. Large parts of Europe's population continue to live in areas with unhealthy air quality. For some pollutants and in some regions, this situation is not improving and is even deteriorating. Moreover, changes in combustion and fuel technologies, industrial production, movement of goods and urban planning affect the constituents and thus possibly the toxicity of air pollution as well as people's exposure.

Understanding the public health implications of this important environmental hazard is challenging for both researchers and policy-makers in their efforts to protect public health in a sustainable manner. Just as medicine should be evidence based, public health action and policy must be grounded in science. Thus, current scientific knowledge must reach policy-makers in a comprehensible way. This is particularly urgent in the European Union, where air-quality standards are far less stringent than in many member states and other areas of the world – and are in conflict with research findings. As with tobacco smoke, the voice of physicians and other health professionals is instrumental in shaping the opinions of the public and policy-makers. The purpose of this booklet is to empower physicians and other health professionals to promote better air quality, to defend the health needs of citizens and to advise patients. This booklet provides an overview of the current knowledge about the nature and health consequences of this continuing environmental problem.

CONTENT

The content of this booklet is restricted to ambient (or "outdoor") air pollution, originating from anthropogenic sources and activities such as industry and traffic. These sources are common to all nations and require international policy frameworks: air pollution respects no national boundaries. In contrast to tobacco smoke – the single most important and preventable health hazard throughout Europe – people are left with very limited options to escape personal exposure to ambient air pollution. While people spend most of their time indoors, it is important to note that air pollution from outdoor sources remains a key determinant of indoor personal exposure to toxicants. Air pollution from indoor sources per se is not covered by this booklet: the most important indoor health hazard – environmental tobacco smoke – is the subject of another ERS publication – *Lifting the smokescreen: 10 reasons for a smoke free Europe* [1]. Likewise, while biomass combustion for cooking and heating poses an enormous health threat in many countries around the world, the issue is not addressed directly in this booklet. A review on biomass combustion effects has been published recently [2].

Each chapter of this booklet comprises main text, illustrative figures and tables, and standalone boxes to complement key issues addressed in the text. The booklet not only summarises the health effects of air pollution but gives some basic insights into methodological issues, sources and concentrations of air pollution and evaluation of the public health risks. The booklet ends with "The role of physicians and health professionals", a summary of the role that health professionals can play in combatting this issue. The health effects of ambient air pollution are caused by a complex mixture of hundreds of pollutants. Most of the processes by which the different pollutants of the mixture affect health are still not understood, but some pollutants have been studied extensively and are subject to regulations. The Annex of this booklet details the regulatory framework for some of individual pollutants and summarises their main health effects. Abbreviations and references follow at the end.

The booklet is not an exhaustive review of the literature but a synthesis of knowledge, with references to a selected set of studies with a particular focus on European findings or other key investigations. More recent studies and reviews are cited preferentially. We hope this booklet will empower the reader to be an informed citizen, who is able to contribute to a science-based discussion in support of stringent policies that protect public health from a preventable cause of health problems: ambient air pollution.

3.
POLLUTION, PATIENTS AND THE PUBLIC

A few concepts and issues fundamental to the link between air pollution, its health effects and its relevance for the public.

While ambient concentrations of a range of pollutants have decreased over the past 50 years, current levels continue to affect the health of people. The challenges in understanding pollution and its link to health range from comprehending the processes behind the emission of air pollution, including sources and the interaction between the pollutant mixture; grasping people's exposure or changes in exposure to air pollutants; disentangling the effects of air pollution from other causes; and understanding the interdependence of effects from other co-factors (Box 3a). These fundamental issues have to be taken into account not only when investigating the health effects of air pollution but also when interpreting research findings, and in the evaluation and communication of air pollution's relevance for patients and public health.

POLLUTANTS AS MARKERS OF A MIXTURE

Ambient air pollution is a ubiquitous and complex exposure (see Chapter 4), and the associated health effects are not easily studied. The mixture of air pollutants can be neither characterised fully nor replicated easily in experiments involving animal or volunteer exposure in the laboratory. These experimental studies tend to investigate the toxicological properties of single pollutants rather than the complex interactions of the mixture. Epidemiological studies use one or a few pollutants as markers of the mixture of pollutants (*e.g.* NO_2 or PM10) but associations between some markers of pollution and health effects may not necessarily reflect a simple causal relationship. The effects detected could be the consequence of one or several ambient pollutants whose presence correlates with the marker used in the studies. The target of policies may thus be a source-specific mixture of emissions rather than one single pollutant.

BROAD RANGE OF HEALTH EFFECTS

One consequence of the complexity of air pollution is that the health effects of air pollution are also complex, ranging across numerous and unspecific ailments. The nose and lungs are where pollution first comes into contact with the human body. Depending on the physical and chemical characteristics of the pollutants, the anatomical or physiological state of the person and their breathing pattern or level of activity, pollutants may impact at various depths within the respiratory system. Coarse particles affect the upper airways in particular, while fine particles reach the smaller airways and alveoli, although they are also deposited in the nose. Water-soluble gases (such as SO_2) react with the mucus layer of the upper airways while less soluble gases (such as NO_2) are more likely to reach the alveoli.

Pollutants can compromise the respiratory system's own defences. The mucus layer and ciliated cells are an important first line of defence against pollutants reaching the upper airways. Pollutants, however, may affect the composition or production of the mucus and/or degrade the function of the ciliary epithelia. Moreover, pollutants may affect sensory cells ending between the epithelia along the airways, affecting the smooth muscle and resulting in hyperreactive airways or increased mucus secretion leading to cough or phlegm.

In the lower airways, air pollutants may affect the secondary defence line, namely alveolar macrophages and the cellular layer responsible for the exchange of gases with the blood. Local inflammation affects gas exchange and chronic inflammation results in the thickening of the air–blood barrier. Inflammatory mediators and autonomic effects drive systemic responses to local pulmonary events, a phenomenon that explains the range of cardiovascular ailments associated with ambient air pollution. The observation of systemic effects has opened new research into reproductive as well as neurogenic effects. The range of health effects of air pollution are discussed in Chapter 6.

ACUTE AND CHRONIC EFFECTS

The acute effects of pollution may be felt within hours or days of exposure, but other health effects of air pollution result from long-term chronic exposures, leading to chronic pathologies. While the acute and chronic effects of air pollution are partly interrelated, the distinction is very important when planning and interpreting epidemiological studies, as discussed in Chapter 5.

INDIVIDUAL RISKS AND PUBLIC HEALTH

The risk that ambient air pollution poses to the health of a specific person can neither be quantified nor observed. There is no clinical test or diagnostic tool that can assess the role and effect of ambient air pollution on the health of an individual. Nevertheless, a large body of data provides quantitative measures of risks associated with ambient air pollution, typically expressed in relative terms, as a relative risk (RR), or – similarly – as an odds ratio (OR). These measures provide an estimate of the (theoretical) extra probability that an exposed subject will experience a health problem. Thus, while an RR or OR of 1.0 means that the exposed and unexposed have the same health risk, it tells us nothing about the absolute risk or probability of getting the disease. Obviously, this is not sufficient to quantify the public health relevance of air pollution and of clean air policies. The paradox of small relative risks and a large public health burden due to air pollution is discussed in Chapter 8.

Box 3a

Understanding air pollution and health: the challenges

The interaction between air pollution and health is a complex and difficult subject: interpreting the research, and communicating its meaning, is not easy. Some of the main current challenges in air pollution research are listed below.

AIR POLLUTION HAS MULTIPLE SOURCES

Numerous emitters contribute to pollution. Mobile and stationary combustion processes play a particularly dominant role.

AIR POLLUTION IS A MIXTURE OF MANY POLLUTANTS

Air pollution comprises hundreds of pollutants, only a few of which may be monitored, investigated and regulated.

AIR POLLUTION IS A DYNAMIC PROCESS

Once emitted, pollutants interact with each other and the environment in complex ways, which may depend on temperature, humidity and other environmental conditions. Thus, pollution changes in concentration, composition and possibly toxicity.

EXPOSURE VARIES

A range of factors determine whether and to what extent pollution leads to exposure – the contact between pollution and the human body. Proximity to the source, physical barriers between sources and people, time spent in polluted air and level of physical activity all influence the amount of exposure and, ultimately, the dose reaching the target organs.

LOW EXPOSURE LEVELS ARE STILL RELEVANT

In most European and Western countries, air quality is far better than it was in the 1950s. Thus, the health effects of air pollution are expected to be smaller and far less obvious than, for instance, the drastic increase in mortality and morbidity during smog episodes in the 1950s. A simple look at a few health statistics will never reveal the health effects of current air pollution.

CAUSE AND EFFECT ARE NOT ALWAYS CLEAR

While patients may present a range of symptoms and pathological signs resulting in a clinical diagnosis compatible with pollution-induced health problems, the latter are usually "unspecific" to pollution, so their presence does not disclose the underlying cause of the problem. For example, a myocardial infarction caused by air pollution cannot be distinguished from an infarction caused by any other trigger of a thrombosis. There is no "air pollution-specific disease", nor is the treatment of air pollution-related ailments cause specific (see Chapter 9).

POLLUTION DOES NOT ACT IN ISOLATION

Health is the result of a wide range of exogenous and endogenous factors, interacting in complex ways. Thus, the type and extent of air pollution-related health effects may ultimately depend on the combined set of co-factors.

4. POLLUTANTS, SOURCES AND LEVELS

The main constituents of air pollution, their sources and the current situation in Europe in terms of emissions and air quality.

INTRODUCTION

Air pollution refers "to the components of the atmosphere – such as particulate matter, chemical substances or biological material – that cause adverse health effects to humans or other living organisms, or damage the environment. Air pollution includes both substances not naturally found in the air and natural substances found at greater concentrations or in different locations than normal. Air pollution is produced both by natural processes such as volcanic activity or dust storms, and by human activity such as fossil fuel combustion or chemical production". Pollution produced by humans is the focus of policy-makers and of this booklet. This chapter summarises general information extracted from the United States Environmental Protection Agency, the World Health Organization, the European Environmental Agency and others in relation to air pollution components, sources, emissions and concentrations.

Air pollutants can be classified as either primary or secondary, depending on how they were formed. Primary pollutants are those emitted directly from a human-driven process, such as carbon monoxide emitted from motor vehicle exhaust, or sulphur dioxide released from factories. Secondary pollutants are those that form when primary pollutants react or interact in the atmosphere. One important secondary pollutant is ground-level ozone (O_3), which results from chemical reactions between primary pollutants and sunlight (see Box 4a). Some pollutants, such as particulates of various sizes, may be both primary and secondary.

Pollutants can also be classified by source. It is also useful and relevant to distinguish emissions from ambient concentrations ("imission") or air quality.

COMMON AND MINOR AIR POLLUTANTS

In developed countries, the major pollutants emitted into the atmosphere include sulphur dioxide (SO_2), nitrogen oxides (NOx) including nitrogen dioxide (NO_2), volatile organic compounds (VOCs), particulate matter (PM) and ammonia (NH_3). These pollutants form the main focus of this booklet.

Sulphur dioxide, or SO_2, belongs to the family of sulphur oxide gases (SOx). Sulphur is present in raw materials including crude oil, coal and the ores of common metals such as aluminium, copper, zinc, lead, and iron. SOx gases are formed when fuel containing sulphur is burned, when gasoline is extracted from oil and when metals are extracted from ore.

NOx is the generic term for a group of highly reactive gases, all of which contain nitrogen and oxygen in varying proportions. NOx are emitted primarily as a result of high-temperature combustion. Road traffic is a dominant source of NOx.

In addition to their health effects, sulphur and nitrogen compounds emitted into the air are potentially acidifying and can harm sensitive terrestrial or aquatic ecosystems. Nitrogen compounds are also potentially eutrophying, that is they can cause an oversupply of nutrients in soils and water.

VOCs are organic chemical compounds that have sufficiently high vapour pressures under normal conditions to vaporise significantly and enter the atmosphere. A wide range of carbon-based molecules, such as aldehydes, ketones and other light hydrocarbons are classed as VOCs. Depending on the context, the term may refer both to well-characterised organic compounds and to mixtures of variable composition.

PM pollution includes primary and secondary particulates, formed from PM precursor gases such as SO_2, NOx, NH_3 and VOCs. PM pollution is a complex mixture of extremely small particles and droplets. Particulate pollution is made up of a number of components, including acids (such as nitrates and sulphates), organic chemicals, metals, and soil or dust particles, and is typically categorised by its size. Box 4B describes this very important group of pollutants in more detail.

O_3 is another major pollutant gas in many regions. Although not emitted directly, O_3 is formed in the atmosphere by reactions between NOx and VOCs in the presence of heat and sunlight. Box 4a describes this highly relevant and toxic secondary pollutant in more detail.

NH_3 is a common byproduct of animal waste, owing to the inefficient conversion of feed nitrogen by the animal. Livestock and poultry are often fed high-protein feed, which contains surplus nitrogen, to ensure that their nutritional requirements are met. Nitrogen that is not metabolised into animal protein (milk, meat or eggs) is excreted in the urine and faeces. Further microbial action releases ammonia into the air during manure decomposition.

Other air pollutants are usually emitted in smaller quantities, but they can have important health effects at the local or regional scale and some of them are regulated together with more common air pollutants.

Lead emissions remain an important threat to health, despite their dramatic decline in recent years. Lead is found naturally in the environment as well as in manufactured products. The major source of lead emissions has historically been motor vehicles and industrial sources. Owing to the removal of lead from gasoline in the USA, emissions of lead from the US transportation sector fell by 95% between 1980 and 1999, and levels of lead in the air decreased by 94%. A full ban on the use of leaded gasoline in the European Union became effective in 2000. Leaded gasoline is still in use in some parts of South America, Asia, Eastern Europe and the Middle East, but a growing number of countries have drawn up plans to ban leaded gasoline in the near future. In countries where leaded gasoline is banned, the highest levels of lead in air are usually found near lead smelters. Other stationary lead sources

include waste incinerators and lead-acid battery manufacturers.

Another example of a minor group of pollutants emitted into the atmosphere that can nonetheless have serious health effects is the persistent organic pollutants (POPs). POPs are organic compounds that are resistant to environmental degradation through chemical, biological and photolytic processes. Because of this, they have been observed to persist in the environment, be capable of long-range transport, bioaccumulate in human and animal tissue, biomagnify in food chains and have potentially significant impacts on human health and the environment. The POPs include pesticides such as aldrin, chlordane, DDT, dieldrin or endrin. Others are substances used in industrial processes and in the production of a range of goods such as solvents, polyvinyl chloride and pharmaceuticals. Yet more are byproducts of industrial processes such as waste combustion.

Table 4.1 summarises the main primary and secondary pollutants produced by human activity.

Table 4.1. Major primary and secondary air pollutants produced by human activity

POLLUTANTS	ABBREVIATION	SOURCE AND FORMATION MECHANISM
PRIMARY POLLUTANTS		
Sulfur oxides/sulfur dioxide	**SOx/SO_2**	Emitted from burning of coal and oil
Nitrogen oxides/nitrogen dioxide	**NOx/NO_2**	Emitted from high-temperature combustion
Carbon monoxide	**CO**	A product of incomplete combustion of fuel such as natural gas, coal or wood. Vehicular exhaust is a major source of CO
Carbon dioxide	**CO_2**	Greenhouse gas emitted from combustion
Volatile organic compounds	**VOCs**	From hydrocarbon fuel vapours and solvents
Particulate matter	**PM**	Produced by erosion or combustion processes. PM10 is the fraction of suspended particles 10 μm in diameter and smaller that will enter the nasal cavity. PM2.5 have a maximum particle size of 2.5 μm and will enter the bronchia and lungs
Ammonia	**NH_3**	Emitted from agricultural processes
Lead	**Pb**	Naturally occurring, produced by lead smelters, contained in old paints and plumbing
Persistent organic pollutants	**POPs**	Produced through industrial processes or from their byproducts
SECONDARY POLLUTANTS		
Particulate matter	**PM**	Formed from gaseous primary pollutants and compounds in photochemical smog, such as NO_2
Ozone	**O_3**	Formed in the presence of sunlight by a chemical reaction between NOx and VOCs

AIR POLLUTION SOURCES

There are multiple sources of air pollution in cities and rural areas. There are many ways to characterise these sources. Below are some of the main sources and their associated pollutants.

Road transport

The major source of air pollution in many areas of the world is road transport. Road transport refers to all road traffic emissions, irrespective of the size or purpose of the vehicle. Road emissions contribute in different ways to air pollution. Although in many modern vehicles exhaust gas is passed through a catalytic converter before being emitted, combustion of gasoline or diesel fuel by motor vehicles leads to the production of exhaust gases containing several pollutants. These pollutants typically include CO, NOx, VOCs, suspended PM and a range of additives. Some countries still use lead additives in gasoline.

Exhaust emissions are not the only source of traffic-related pollutants. Evaporative fuel emissions can also be important, especially from gasoline-powered vehicles. Moreover, traffic spreads and resuspends substantial amounts of particles originating from the wear of tyres or brake components and abrasion of road surface material. In contrast to other sources of pollution, traffic emissions occur very close to the places where people live, work, walk and commute. It is for that reason that traffic-related pollutants required particular attention from researchers and policy-makers alike (see Box 4d and Annexe 1).

Stationary combustion sources

The burning of fossil fuels at industrial plants, refineries and power plants, and for domestic use such as heating and cooking, is also a major source of air pollution. High-temperature combustion can be a source of NOx, and also SO_2 if sulphur is present in the fuel. Fuel combustion also emits VOCs, especially from coal and oil. This pollution can also result from leakage from chemical plants. Heating and cooking with wood is associated with particulate imissions.

Intermittent sources

Forest fires and biomass burning represent a major source of combustion emissions, including NOx, CO, VOCs and PM. Dioxin emissions can result from the incineration of refuse but also from accidental fire and even planned events such as bonfires. Any industrial operations may also generate intermittent fugitive emissions: for example, PM can be emitted when wind blows raw materials from exposed stockpiles.

Natural sources

Many trace gases and particles found in the atmosphere are generated by natural processes. Trees and other vegetation can release biogenic VOCs. Ash is released from volcanic eruptions. Sea spray and wind-blown soil are also produced by natural processes. Dust storms can cause increases in PM concentrations not only in arid regions but where dust is transported by climatic conditions (see Box 4c).

AIR POLLUTANT EMISSIONS IN EUROPE

Human activities are the driving forces behind air pollution. Energy consumption, industrial activities, transport demand and agriculture are the specific forces most directly linked to emissions. The level of development of a country also directly influences the type and level of emissions.

WHERE DOES EMISSION DATA IN EUROPE COME FROM?

Emission levels and trends in Europe are summarised based on the annual European Community Long-range Transboundary Air Pollution (LRTAP) Convention emission inventory report [3], which presents the principal sources of air pollution emissions in Europe and related trends since 1990. The report is completed annually by the European Commission as an official submission to the secretariat for the Executive Body of the LRTAP Convention. Parties to the LRTAP Convention (including the European Community) report emissions data for a number of important air pollutants, including SOx, NOx, non-methane VOCs, NH_3, CO, primary PM (PM_{10} and $PM_{2.5}$), heavy metals and POPs. The report groups emissions into key source categories such as road transport, manufacturing industries and construction, public electricity, *etc.* Primary emissions from different sources are summed across

Box 4a

Ground-level ozone and the summer smog

Ozone is an odourless, colourless gas composed of three atoms of oxygen. Ozone occurs both in the Earth's upper atmosphere (stratosphere) and at ground level (troposphere). In the stratosphere, ozone protects the Earth's surface from ultraviolet light from solar radiation. Tropospheric ozone, however, is a major public health concern (see Box 6c). Ozone is the most abundant and reactive photochemical oxidant in the troposphere.

Ground-level ozone is created in the presence of sunlight by a complex chemical reaction between NOx and VOCs. The process consists of the oxidation of nitric oxide (NO) to nitrogen dioxide NO_2. The chemical breakdown of NO_2 molecules into smaller units through the absorption of light (photolysis) yields NO and a ground-state oxygen atom, which then reacts with molecular oxygen to form ozone. Because emission rates of ambient NOx and VOCs are directly related to the production rate of ozone, these gases, which are emitted by cars, power plants, industrial boilers, refineries, chemical plants and other sources, are called ozone precursors.

In an environment saturated with NOx, ozone concentration decreases with increasing NOx emissions. Thus in the vicinity of strong NOx emission sources, ozone tends to be "scavenged". These result in a paradox: ozone concentrations are often lower in urban centres, particularly along busy traffic arteries, and higher in suburban and rural areas. Moreover, ozone is subject to long-range atmospheric transport. Thus, even remote areas with low NOx or VOC emissions can be impacted by high ozone concentrations. Transport is determined by meteorological and chemical processes and can extend over several hundred kilometres.

Another consequence of the physico-chemical processes underlying ozone contamination is its strong seasonal and diurnal pattern. Ozone concentrations are higher in summer and in the afternoon as a result of its photochemical origin, with the highest daily peaks typically occurring during hot, dry periods in the summer.

Current ozone air-quality standards focus on minimising the number of days with high peak concentrations. The (typically few) days with very high concentrations usually receive great media attention, while the public is less aware of the (often long) periods of somewhat lower but still unhealthy ozone concentrations. Policies that result in sustained reductions in ozone concentrations lead to larger public health benefits than "emergency policies" aiming at the prevention of a few extreme peaks. For this reason, scientists and public health professionals call for regulations and policies that reduce ozone levels throughout the summer.

Box 4b

Particles in the air – PM10, PM2.5 and beyond

The mixture of solid and liquid particles suspended in the air is called "'particulate matter" (PM). The particles vary in number, size, shape, surface area, chemical composition, solubility, redox activity and origin. PM is generally categorised according to particle diameter. The following PM fractions are commonly defined, based on aerodynamic diameter:

- TSP: total suspended particles, including all particles up to 30 μm in diameter.
- PM10, with a diameter of ≤10 μm.
- Coarse particles, with a diameter of 2.5–10 μm.
- PM2.5 or "fine particles" with a diameter of ≤2.5 μm.
- Ultrafine (UF) particles or PM0.1 with a diameter of ≤0.1 μm (typically in the range of 1–100 nm).
- Nanoparticles cover the same size range as UF (1–100 nm), but the term is more commonly used for engineered material rather than ambient PM.

The level of PM pollution is commonly described in terms of its mass ($\mu g \cdot m^{-3}$) or its numbers (n per cm^3). The latter is particularly useful to describe the smallest fraction of ambient PM as the mass is very low, while the particle count number may be larger by several orders of magnitude. It has been proposed that PM characteristics that more specifically reflect toxicity rather than quantity should be used. For example, some studies have measured the redox activity of PM; this feature may serve as a proxy of the PM's potential to induce oxidative stress, one of the mechanisms through which ambient air pollution is thought to impact various health outcomes.

The above categories also attempt to reflect the source and formation processes of particles. While categories often overlap, the following can be used as a rule of thumb: coarse particles are derived primarily from suspension or resuspension of dust, soil, or other crustal materials from roads, farming, mining, windstorms or volcanoes. Coarse particles also include sea salts, pollen, mould, spores and other biological material. Fine particles are derived primarily from direct emissions from combustion processes, such as vehicle use of gasoline and diesel, wood burning, coal burning for power generation, and industrial processes, such as smelters, cement plants, paper mills and steel mills. Fine particles also consist of transformation products, including sulphate and nitrate particles, which are generated by conversion from primary sulphur and NOx emissions and secondary organic aerosol from VOC emissions. UF particles are typically fresh emissions from combustion-related sources, such as vehicle exhaust and atmospheric photochemical reactions. Primary UF particles have a very short life (minutes to hours) and grow rapidly through coagulation and/or condensation to form larger complex aggregates in the PM2.5 range. Along traffic arteries, UF particles are increasingly considered as markers of exposure to fresh vehicle exhaust.

Various toxicological and human studies suggest that fine particles may play a dominant role in affecting human health. Their toxicity may be due to sulphates, nitrates, acids, and metals. The various chemicals adsorbed onto the surfaces of PM may be relevant at all size fractions. Unlike larger particles, PM2.5 typically reach the small airways and alveoli. The fine fractions also remain suspended for longer periods of time, and are thus transported over much longer distances and penetrate more readily into indoor environments. New studies also suggest that UF particles may be more likely than larger particles to directly translocate from the lung to the blood and other parts of the body, giving them possible particular relevance for cardiovascular outcomes. The role and sources of coarse particles have been less investigated but more recent studies confirm that adverse health effects are associated with this size fraction too.

a geographical area to create emission inventories. It is a challenge to compile consistent and complete inventories because of the large amount of data and the complex modelling methods needed. While secondary pollutants are not measured directly, primary emissions may be used to estimate the formation of secondary byproducts. It should also be noted that in Europe, emission estimates are not always available for all pollutants in each year due to gaps in the data reported by countries. The time series of data for PM emissions (PM10 and PM2.5) are also limited.

In Europe, road transport is the most significant source of NOx, and the second-largest source of primary PM10 and PM2.5 emissions (fig. 4.1). Manufacturing industries and construction are also significant sources of NOx, PM10, PM2.5 and SOx. Public electricity and heat production is largest contributor to SOx emissions and is the second-most significant source of NOx emissions. Agricultural activities (manure management and direct soil emission) are responsible for the vast majority of NH_3 emissions, contributing more than 90% of the total.

When breaking data down by country, as is expected, the major emitters are countries with large populations. Per capita, however, Spain is a large emitter of NOx and SOx in Europe, while Poland, Bulgaria and Romania also produce large amounts of SOx (fig. 4.2).

A regulatory framework is in place to reduce emissions across Europe over various timescales (see Annexe 1). Although emissions of several pollutants are decreasing, reductions have yet to meet targets for most pollutants. Across Europe, the largest percentage reduction in emissions has been achieved for SOx: emissions in 2006 were almost 70% lower than in 1990 and are close to complying with targets (fig. 4.3). This reduction is the result of policies to force power plants producing heat and electricity to improve their equipment, switch to cleaner fuels and become more efficient. Emissions of

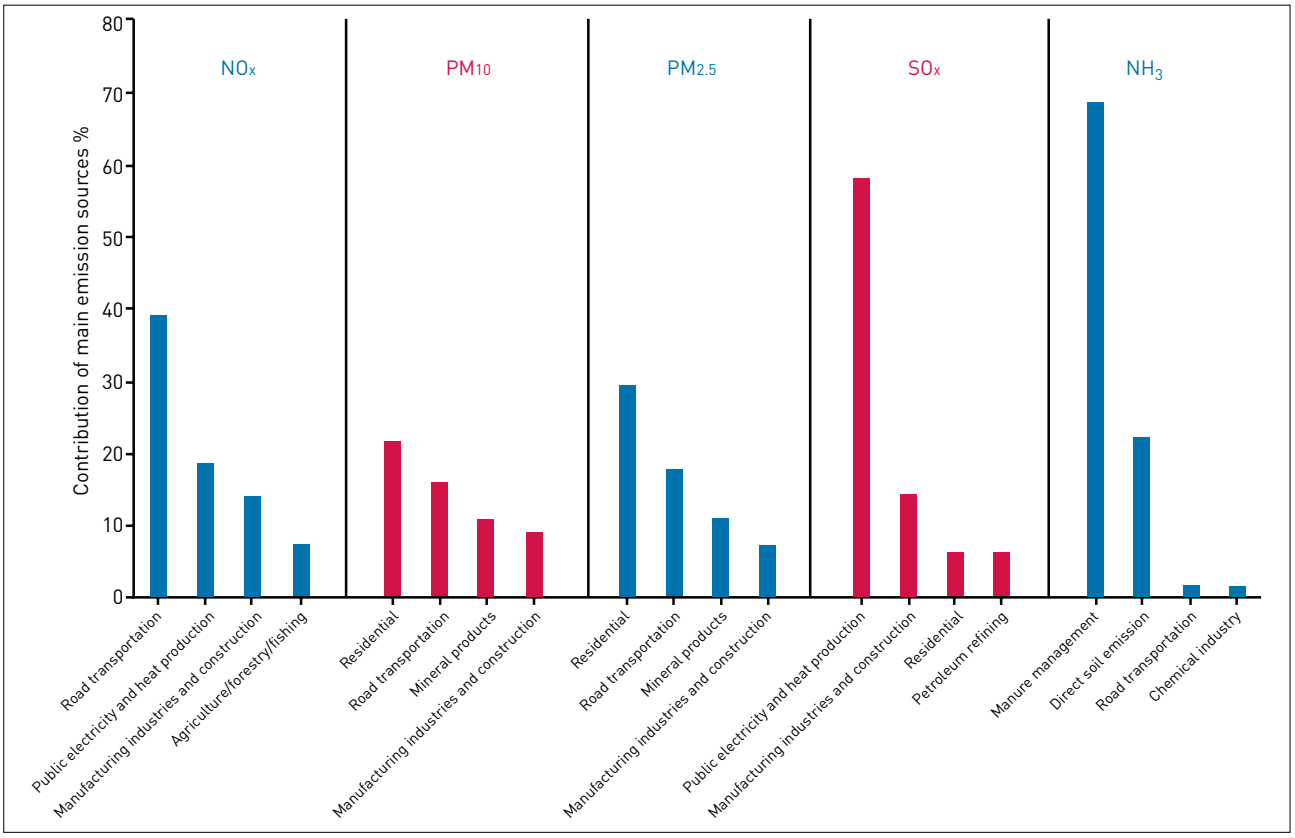

Figure 4.1. Contributions of various emission sources to total emissions of NOx, PM10, PM2.5, SOx, and NH_3 in Europe in 2006. Adapted from [3].

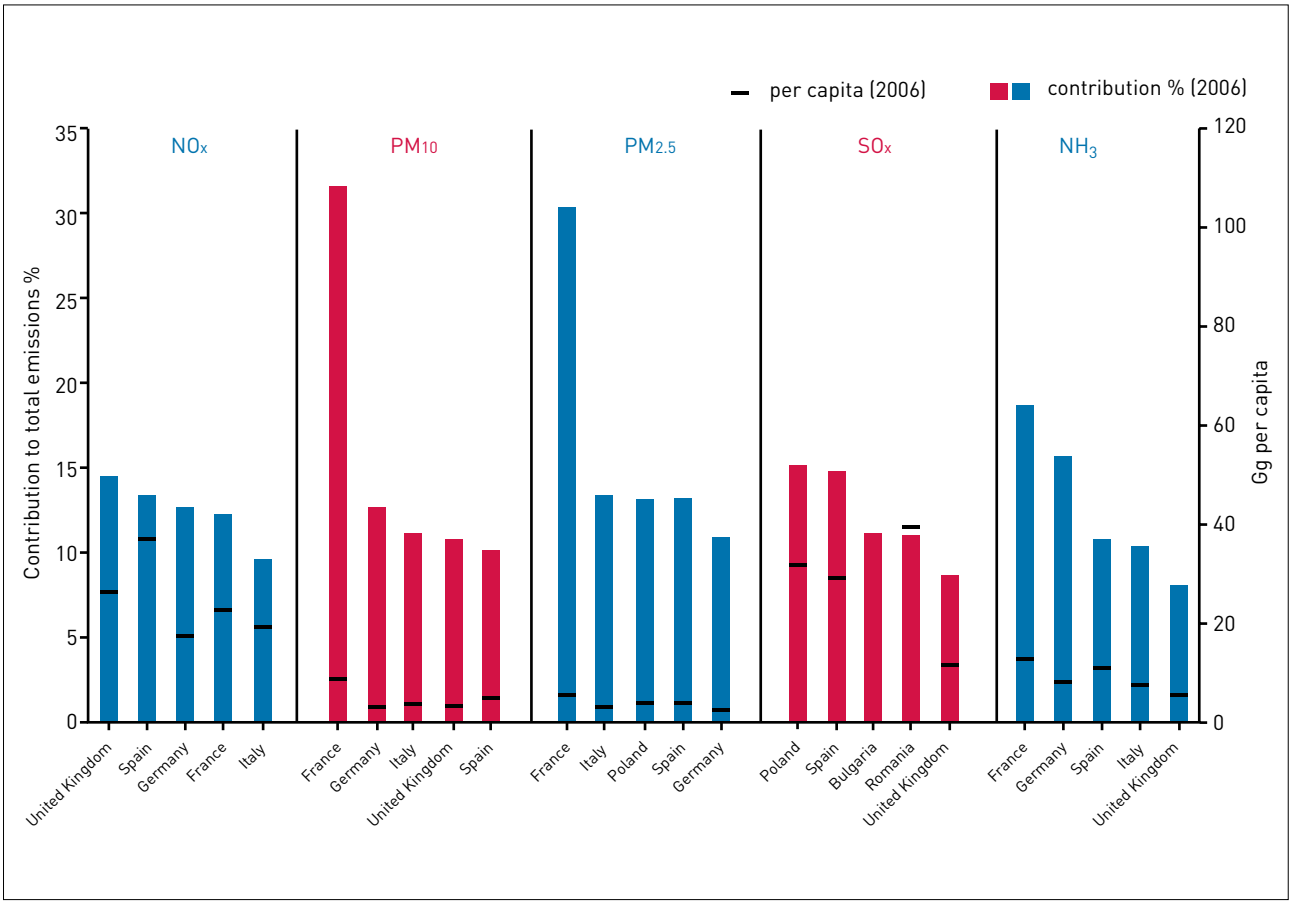

Figure 4.2. **National contributions to total emissions of NOx, PM10, PM2.5, SOx, and NH_3 across some European countries in 2006. Adapted from [3].**

other key air pollutants also fell during this period, but to a lesser degree. Over the same period, reductions in emissions of the three air pollutants primarily responsible for the formation of harmful ground-level ozone ranged from 35% for NOx, 44% for non-methane VOCs and 53% for CO. Figures for PM10 and PM2.5 emissions have been compiled for 2000–2006 only, during which emissions of both pollutants decreased by only approximately 10%. Road transport is an important source of PMs and NOx, and the slow reduction in these emissions reflects the fact that transport policies to limit emissions are not sufficient to compensate for the ever-growing use of personal cars and heavy-duty trucks in Europe.

AIR QUALITY IN EUROPE

Air quality – sometimes referred as "imissions" – depends both on emissions and on temporal and spatial patterns of dispersion, chemical reactions and the formation of secondary pollutants. Persistent emissions of air pollutants have resulted in very poor air quality in many parts of Europe. Concerns about poor air quality in Europe relate not only to the human health impact of exposure to particulate matter and ozone (and to a lesser extent NO_2, SO_2, CO, lead and benzene) but also to the acidification and eutrophication of ecosystems, damage to ecosystems and crops through exposure to ozone, damage to materials and cultural heritage due to exposure to acidification and ozone, and the impacts of heavy metals and POPs on human health and ecosystems.

Ambient concentrations across Europe still exceed the short- and long-term standards set by the European Union (fig. 4.4). Annexe 1 details the air-quality regulation framework in Europe and compares it to those of other regions or organisations. Of special concern are levels of ozone, PM10 and NO_2 that affect urban/suburban

Box 4c

Dust storms: not so inoffensive

Billions of tons of desert dust move through the atmosphere each year. The primary source regions include the Sahara and Sahel regions of North Africa and the Gobi and Takla Makan regions of Asia.

Wind-blown dust plays an important role in the global ecological cycle. For example, dust from the Sahara desert plays a crucial role in fertilising large areas of the Atlantic Ocean, because it is rich in nitrogen, iron and phosphorus.

However, winds also disperse significant quantities of desert dust to populated regions. Affected regions experience dramatically increased ambient air dust concentrations that may last several days. In areas such as southern Europe, Saharan dust events are a recurrent air-quality problem, with particulate levels on dust days exceeding regulatory or recommended levels. While the newly adopted European regulation for daily values of PM10 excludes days when excess levels result from natural atmospheric events such as dust storms, the potential threat to human health of this dust alone or in combination with anthropogenic particles is still debated. Dust particles have been shown to be loaded with fungi, virus and bacteria that may act as inflammatory of allergic agents and some population studies have related health effects to dust events.

Modelling studies show that the quantity of dust involved is sufficient to affect the climate as well. By partly absorbing and partly reflecting sunlight, the dust particles heat the air but cool the ocean surface. This encourages cloud formation, which reinforces the reflection of light back into space. Recent studies show, however, that these clouds inhibit precipitation. The reduction of precipitation from clouds affected by desert dust can cause drier soil, which in turn raises more dust, thus providing a possible feedback loop to further decrease precipitation and possibly accelerate climate change. The impact of dust storms on the environment and health may be greater than anticipated and deserves further attention.

Box 4d

Air pollution and climate change: a common battle

Historically, air pollution and climate change have been treated as separate problems by policy-makers. It is now recognised that air pollution affects the regional and global climate, both directly and indirectly, and that most greenhouse gas emissions are linked to air pollution emissions. The key sources of both problems widely overlap: fossil fuel combustion in energy and industrial production as well as in transport are responsible for most carbon dioxide emissions and much of the air pollution. Thus, many strategies that cut combustion come with attractive co-benefits (see table 4d.1 for examples of some specific pollutants).

Most developed countries have reduced (some) air pollution emissions by improving energy production efficiency and, more recently, by using cheap end-of-pipe emission control technologies. The main strategy for reducing carbon dioxide emissions is emission prevention. Prevention can be achieved by structural changes in the energy sector (improved efficiency and carbon-free renewable energies) and by behavioural changes (reduced energy use). Reducing fossil fuel use would address both climate change and air pollution. The problem is to develop policies to find a mixture of end-of-pipe, structural and behavioural measures that meet air pollution and climate change targets at acceptable cost. Cooperation in the policy-making process is particularly important, in order to promote synergistic rather than competing policies. An example of the latter is the promotion of diesel cars, based on their higher fuel efficiency, regardless of the adverse health effects of diesel exhaust on human health.

An additional important reason for integrating policies is to shorten the time taken for benefits to become apparent. Some greenhouse gases, such as carbon dioxide, stay in the atmosphere for a very long time. Therefore, measures to reduce their emissions will only start to show an effect after a few decades. In contrast, the co-benefits of reduced concentrations of air pollutants such as PM, ozone, or methane results in both immediate and long-term health benefits.

Table 4d.1. Pollutant links between climate change and air pollution

Particulate matter	Particulate matter plays an important role in global warming because of its contribution to cloud formation. Thus, measures to cut particle emissions, for instance from diesel combustion, will have double benefits, protecting both human health locally and also the climate regionally and worldwide.
Ozone	Ground-level ozone is a greenhouse gas itself because it inhibits the process by which plants contribute to carbon uptake from the atmosphere; carbon in the atmosphere contributes significantly to global warming.
Methane	Methane, a gas emitted from agriculture, energy and waste management activities, in addition to being one of the Kyoto Protocol greenhouse gases also contributes to the formation of ground-level ozone. Methane emissions have grown very rapidly since pre-industrial times. Cutting these emissions will reduce health- and ecosystem-damaging ozone levels and reduce the extent of climate change.

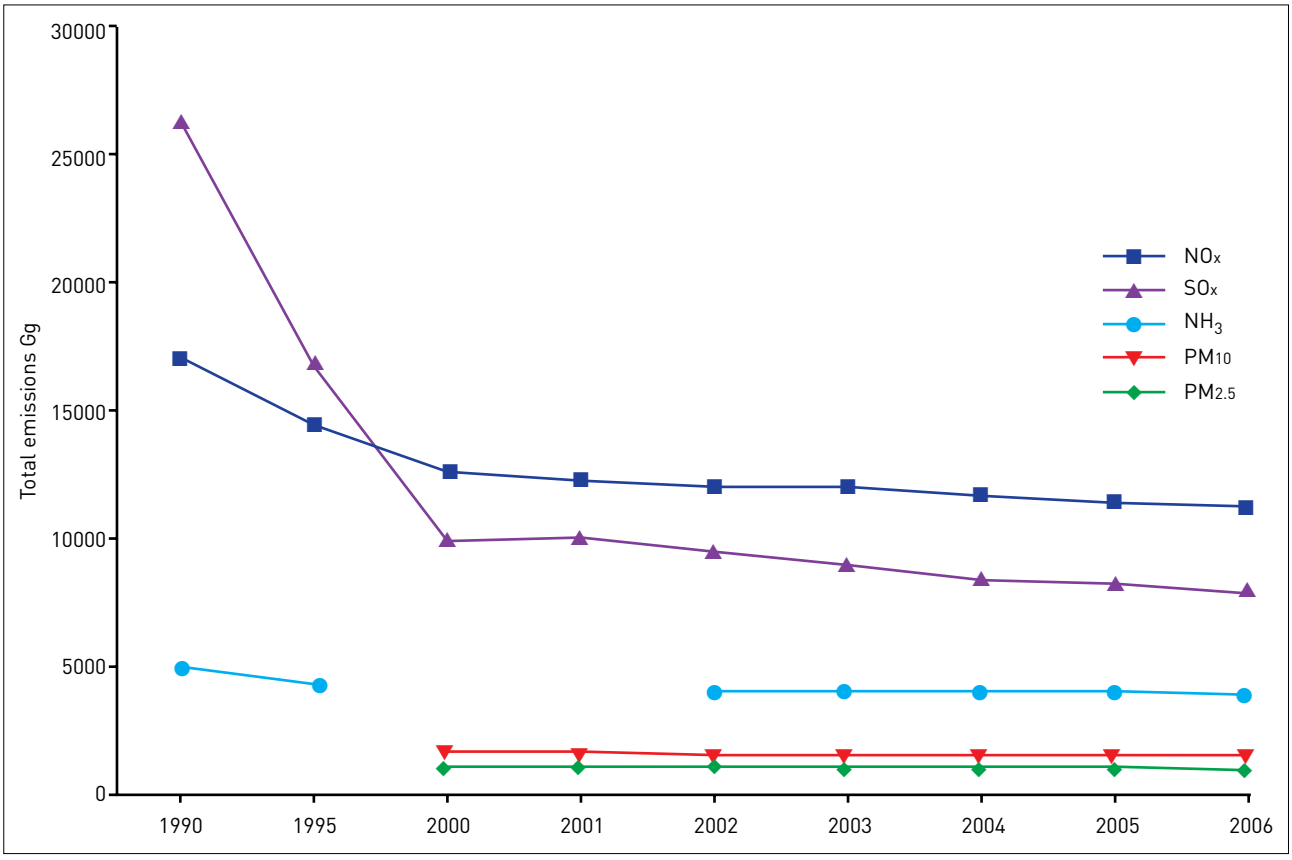

Figure 4.3. **Emission trends for NOx, SOx and NH_3 between 1990 and 2006 and for PM10 and PM2.5 in Europe between 2000 and 2006. Gg: gigagrammes. Adapted from [3].**

WHERE DOES AIR-QUALITY DATA IN EUROPE COME FROM?

Nowadays, assessment of air quality is conducted routinely by national or local authorities in many countries. This is a fundamental starting point for air-quality management. In most countries, however, only a limited number of air pollution indicators are measured to characterise air quality. In general, these include the most common air pollutants described previously. These parameters are the ones that have been used as indicators in epidemiological studies. Methods of measuring air quality vary substantially and range from intermittent campaigns conducted with passive samplers to automatic remote monitoring systems based on light absorption spectroscopy. In Europe, great efforts have been undertaken in the past decade to standardise and harmonise monitoring techniques and to set up platforms for data exchange.

The overview of the recent air-quality situation in Europe presented below is based on an assessment by the European Environmental Agency (EEA), using air pollutant concentration data reported by member countries in AirBase, an online database of European air-quality information [4]. It should be emphasised that the data in Airbase are heavily dependent upon monitoring station locations relative to sources. Monitoring stations are generally classified as rural, suburban or urban, and there are hot spot stations near concentrations of road traffic or industrial activity, but the definitions of these categories may vary between agencies and countries.

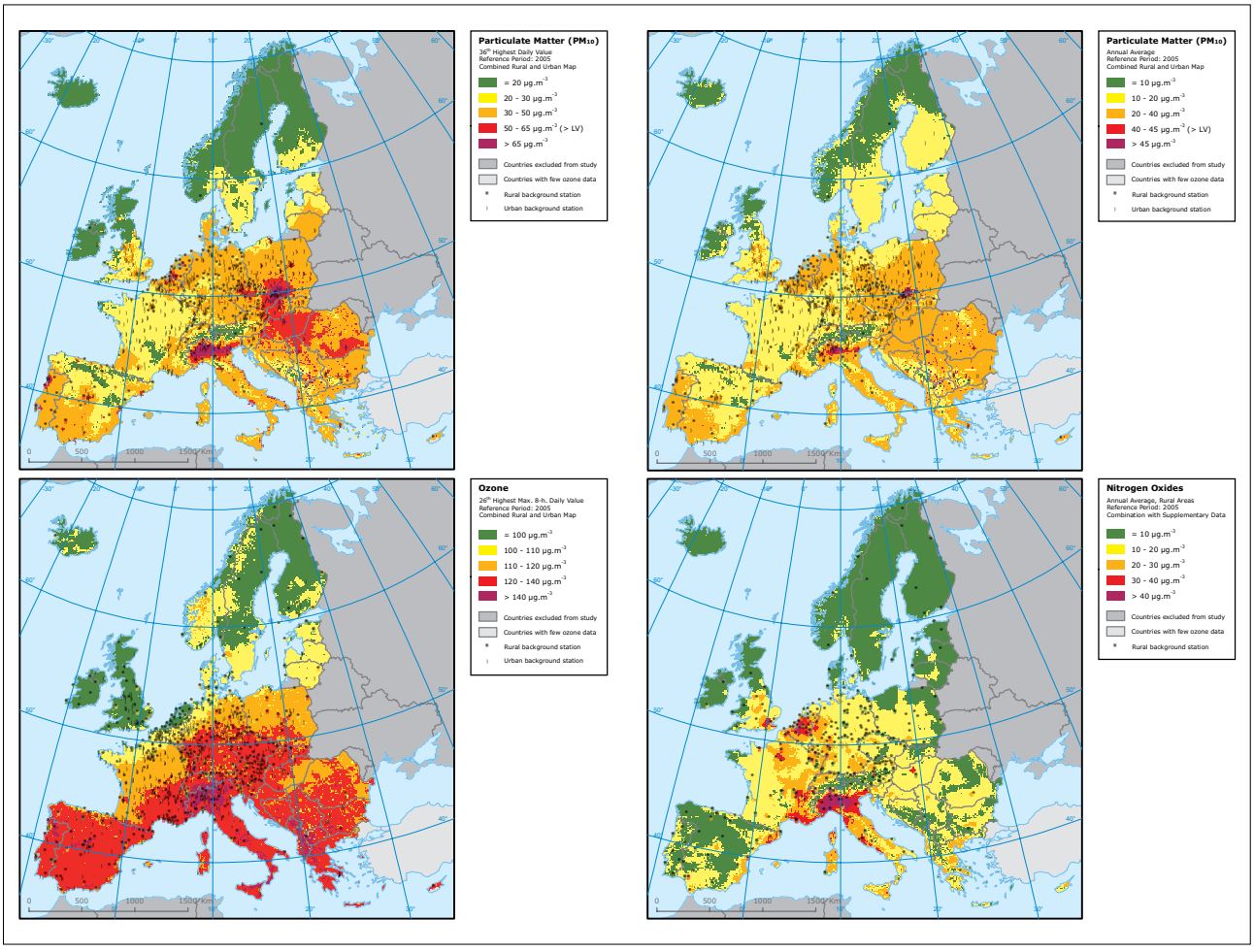

Figure 4.4. Interpolated maps showing air quality in Europe for ozone, PM10 and NO_2. The maps are provided by the EEA and are available at: http://dataservice.eea.europa.eu. They derive from measurement data in AirBase in combination with other emission models. These maps are assessment tools for use at the European scale and may differ from assessments made at national scale.

areas as well as rural areas. For example, although ozone concentrations across Europe are currently lower than the extraordinarily high values seen in 2003 when concentrations across most of Europe exceeded permitted levels due to long periods of high temperature, daily ozone concentrations in most of continental Europe still exceed the European Union target value. Peak concentrations during summer smog frequently exceed 140 µg·m^{-3}, reaching 200 µg·m^{-3} in some areas. The European Union limit value is 120 µg·m^{-3} (8-hourly mean).

Daily average PM10 concentrations in excess of the short-term European criteria (the daily limit value of 50 µg·m^{-3} to be exceeded on no more than 35 days) are observed in many rural areas. At traffic hot spot stations, the daily PM10 limit value is exceeded in many countries in southern Europe. Urban background locations also frequently exceed the daily PM10 limit value in several European regions. Annual averages of PM10 above the European target level (40 µg·m^{-3}) are also observed in the main industrial areas of Europe.

Exceedances of NO_2 target annual values are observed across Europe, overlapping with locations where PM10 targets are exceeded. In contrast, SO_2 concentrations are now relatively low across Europe and there are only limited exceedances of the EU standard.

In the absence of personal measurements, ambient concentrations can be considered the best proxy of

people's exposure to pollutants of outdoor origin. Despite air-quality management plans undertaken at local, regional, national and European level during the past decade, trends in population exposure for different air pollutants show mixed results.

Trends in exposure and breaching of limit values

The fraction of the urban population exposed to SO_2 concentrations above short-term limit values (125 µg·m^{-3} daily mean to be exceeded on a maximum of 3 days a year) decreased to less than 1% between 1997 and 2006, reflecting policies enacted over the past decade to "clean" industrial emissions (fig. 4.5). The situation for NO_2 has also improved, although approximately 25% of the urban population still lives in areas with daily or annual mean concentrations above the limit. Any improvement of the situation for ozone and PM is harder to find. In normal years, a maximum of 25% of the urban population is still exposed to concentrations above limit values; in 2003 – a year with extremely high ozone concentrations – this fraction increased to approximately 60%. For PM10, the urban population potentially exposed to ambient air concentrations in excess of the European Union limit value varied between 23% and 45% between 1997 and 2004 with no discernible downward trend over the period. Although PM2.5 exposure may be a better indicator of health effects than PM10, there is significantly less monitoring data available for it. Estimation of levels of PM2.5 based on a PM2.5/PM10 ratio of approximately 0.8 suggests that the target value of the new European Union Air Quality Directive was exceeded in many urban areas in 2004.

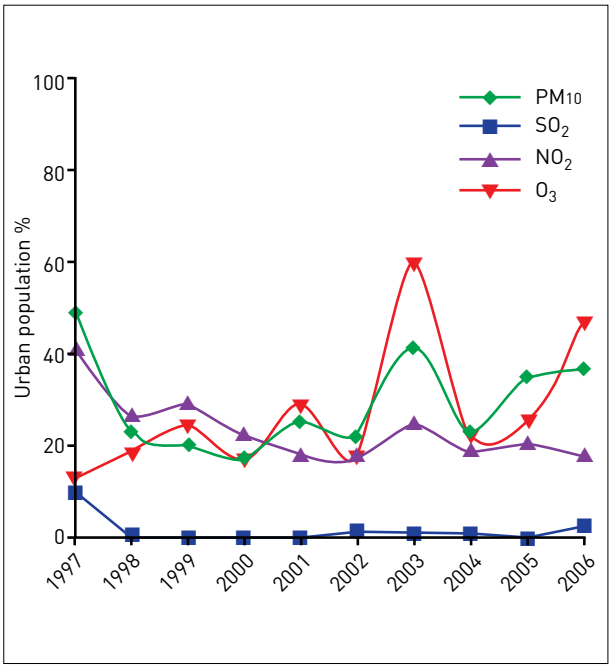

Figure 4.5. Percentage of the European urban population resident in areas where pollutant concentrations are higher than selected limit/target values, for years 1997 to 2006. Targets are as follows. PM10: a limit value of 50 µg·m^{-3} (24-hour average), not to be exceeded more than 35 times a calendar year. NO_2: an annual mean limit value for of 40 µg·m^{-3}. Ozone: a target value of 120 µg·m^{-3} as daily maximum of 8-hour mean, not to be exceeded more than 25 days per calendar year, averaged over 3 years. SO_2: a limit value of 125 µg·m^{-3} as an daily average, not to be exceeded more than three times a calendar year. Adapted from [5].

Long-term average exposure is particularly relevant in the development of chronic health problems; thus, low annual mean concentrations are an important policy objective. The annual European Unit limit value for PM10 (annual average of 40 µg·m^{-3}) appears not to have been exceeded by many countries in 2005, although with the exception of Scandinavia, most countries still exceed the target value proposed by the World Health Organization (WHO; 20 µg·m^{-3}), a science-based limit still ignored by European Union policy-makers. The same holds for ozone and PM2.5.

POLLUTION MIXTURES AND MARKERS

Both emission- and air quality-based policy approaches focus on single pollutants; however, health effects are likely to be the result of concurrent exposures to complex mixtures. In fact, the current epidemiological and toxicological literature provides no evidence that any single pollutant or source is responsible for the full range of observed health effects (see Chapter 6 and Annexe 2).

The toxicity of the complex mixture of air pollutants is not well understood. Once in the atmosphere, pollutants emitted by the different sources are further transformed and affected by environmental factors such as temperature and humidity. These processes modify the composition, and thus probably the toxicity or biological properties, of the mixture. For example, the associations between

daily mortality rates and both ozone and PM appear to be stronger when both pollutants are present.

In light of these physico-chemical processes and the simultaneous emission of multiple pollutants, emissions and ambient concentrations of single pollutants may serve as markers of more complex pollution phenomena. Some pollutants may serve as markers of emissions from specific sources. For instance, ultrafine particles or elemental carbon may be better markers than other PM sizes or characteristics of exposure to fresh combustion; and "traffic proximity" may better reflect exposure to the complex emissions from traffic than any single pollutant measured at a fixed-site monitor. New markers of air pollution, such as redox properties or species of PM, are being explored. However, the availability of such monitoring data is sparse and consequently of limited use as yet in research and policy-making.

5.
HOW DO WE KNOW WHAT WE KNOW ABOUT HEALTH?

An overview of the methods used to investigate the effects of air pollution on health, with their strengths and limitations. Epidemiological research methods are crucial in understanding the health effects of air pollution.

Ambient air pollution is one of the most prevalent public health problems of environmental origin. Clean-air policies are thus a very important tool to protect public health. The evidence that air-quality regulations protect public health is based on a broad range of interdisciplinary research methods. Experimental and epidemiological approaches provide the two most important tools to investigate the effects of ambient air pollution on health.

EXPERIMENTAL STUDIES

Experimental studies contribute crucial information to improve our understanding of the mechanisms that lead to health problems among those exposed to airborne pollutants. Experimental studies provide the opportunity to expose people, animals, cell cultures or other biological material to well-specified pollutants under controlled conditions. Methods, as well as exposure levels, can be standardised fully. Human studies are often conducted under different levels of physical activity to modify the dose, and at various concentrations of pollutants. Symptoms, physiological and functional parameters, and blood or urine markers can be used in these studies to evaluate health effects. Experiments can be designed to target specific aspects of the complex mechanisms linking air pollution with health. For example:

- A range of experiments focus on the ability of ambient particles to induce redox cycling, confirming the contribution of PM to oxidative stress as a relevant pathway for a broad range of health effects [7].
- The novel hypothesis of an atherogenic role of air pollution has initially been investigated in animals rather than humans. These studies have revealed that rabbits, mice or rats chronically exposed to concentrated ambient particles develop atherosclerosis [8].
- A human chamber study observed greater allergic inflammation among sensitised subjects exposed to both allergens and diesel particles compared with those exposed to allergen alone. The adjuvant effect of diesel particles was particularly strong among subjects with a deficiency in two genes relevant in the antioxidant defence in the airways, namely the gluthatione transferases GSTM and GSTP [9].

Despite the advantage of controlled exposures, experimental studies have limitations or disadvantages compared with epidemiological studies. These studies are restricted to examining the effects of single pollutants or, at best, combinations of two pollutants, while ambient air pollution comprises a far more complex mixture. The use of urban particles in animal studies is a major novel attempt to mimic real-world conditions in experimental settings. Experimental findings from animal studies cannot be generalised to humans, and studies conducted in young and healthy adult people – the typical participants in human chamber studies – can not be generalised to the potentially most susceptible groups such as the unborn, infants and adolescents or people with severe diseases. The most important limitation of experimental approaches is the inability to properly investigate the chronic health effects of long-term or lifetime exposure to ambient air pollutants. The only reliable approach for investigating such effects in humans is epidemiology. The same holds for investigations of very severe effects of air pollution, such as death or acute morbidities requiring hospitalisations or emergency room visits.

EPIDEMIOLOGICAL STUDIES

Observational studies can be conducted in the general population as well as in selected groups. In contrast to experimental studies, epidemiological investigations may address the effects of air pollution across a very broad range of outcomes and can be designed to address the acute, subacute and chronic effects of pollution alike. Moreover, epidemiological approaches are very versatile in identifying subgroups with increased or decreased susceptibility to the adverse effects of air pollution. For example, a controlled trial has shown that Mexican children with a high intake of antioxidants are protected against the adverse effects of ambient oxidant pollutants on lung function [10]. A recent study also shows that exposure to traffic-related air pollution has stronger effect on myocardial infarction survivors than among the general population [11].

None of the ailments that have been related to air pollution are specific to air pollution exposure: many other factors may cause or contribute to identical or similar health problems. The list of health effects attributed to air pollution has a lot in common with those described for smoking and passive smoking. Moreover, short-term variations in air pollution are not the only cause of daily fluctuations in health problems (symptoms, doctor visits, hospital admissions, death, *etc.*) as many other relevant factors change daily as well (*e.g.* temperature or other weather factors). As a consequence, epidemiological studies need to control rigorously for other important risk factors. Studies unable to control for confounders – such as purely ecological comparisons of disease frequencies between a few communities with different levels of pollution – should not be used to evaluate the health consequences of air pollution. Boxes 5a and 5b describe key study designs used in air pollution research.

The risk calculated from epidemiological studies is typically expressed in relative terms, *i.e.* as a relative risk

(RR) or as an odds ratio (OR). Air pollution exposure can be quantified on a continuous scale: in most cases, all study participants are exposed to some degree. Therefore, RRs are usually not expressed for "exposed" *versus* "unexposed" but instead for some (arbitrarily chosen) units of a pollutant. For example, the association between daily changes in ambient $PM_{2.5}$ levels and daily mortality is often reported for a 10 $\mu g \cdot m^{-3}$ change in $PM_{2.5}$, but other scales are frequently used. Knowing the scales used is essential when comparing study results and risks.

Due to the multifactorial causes of morbidities and mortality, RRs associated with single factors are expected to be rather small. This is true both for exogenous and endogenous causes of complex diseases. For example, the strongest association (*i.e.* largest RR) between a gene and asthma as observed in a genome-wide association study reached only 1.88: the relative risk due to any other gene appears to be much smaller [12]. Accordingly, associations between ambient air pollution and complex phenotypes are expected to be "small" as well: usually smaller than those observed in smokers, whose exposure to pollutants (some of them the same as those found in ambient air) is usually far higher than that of nonsmokers. A Dutch cohort study reported a 3.4-fold greater risk of cardiopulmonary death among smokers of 20 cigarettes a day for 25 years compared with never-smokers; in contrast, the risk of cardiopulmonary death in people living close to busy roads – where traffic-related pollutants reach far higher concentrations than further away – was below 2.0 [13]. Typically, the acute effects of ambient air pollution are particularly small. A large body of studies, for instance, indicates that a 10 $\mu g \cdot m^{-3}$ increase in daily ambient PM2.5 is associated with a 0.5–1.0 % increase in daily mortality, corresponding to an extremely small, but highly significant and relevant, RR of 1.005–1.01.

Under real-life conditions, temporal as well as spatial contrasts in exposure to air pollution are limited: the difference between the lowest and highest levels of air pollution is often less than three-fold and "unexposed" subjects do not exist. This is strongly different from the situation in tobacco research, where many people are never-smokers and heavy smokers may have 10–20 times higher exposure than occasional smokers. The risk ratios between groups of people exposed to different levels of air pollution may thus be much smaller than those seen between smokers and nonsmokers. To describe and appropriately quantify such "small" effects of ambient air pollution thus necessitates not only good control of confounding factors but in most cases very large populations. For instance, the largest cohort study to date in air pollution research – the American Cancer Society Study – involved 500,000 subjects, followed over 16 years, with air pollution data. The range of the lowest to highest long-term average $PM_{2.5}$ concentrations across communities was only up to three-fold and the risk of death during follow-up varied by 10–15% across this range (*i.e.* RRs were 1.10 to 1.15). As expected, heavy smokers – as compared with never-smokers – had a larger risk of death during follow-up, with RR exceeding 2.0. Due to the large sample size, the findings related to air pollution were precise and clearly statistically significant.

Intervention studies – the gold standard in evidence-based medicine – are uncommon in air pollution research, since it is difficult to assign exposure and to have 'nonexposed' subjects. However, based on cohort designs or cross-sectional designs, some studies have been able to investigate changes in health parameters following changes in air quality driven by regulation or caused by people changing their place of residence. These studies are of great relevance for policy makers and will be discussed further in Chapter 7.

Box 5a

Epidemiological studies to investigate the acute effects of air pollution

Air pollution concentrations change daily or even hourly, primarily due to the strong influence of weather conditions on dispersion and accumulation. This variability provides an opportunity to investigate the acute effects of air pollution on short-term changes in health (fig. 5a.1). Hundreds of studies have investigated the association between daily changes in air quality and the frequency of a range of events such as arrhythmias, myocardial infarction, stroke, respiratory symptoms, doctor visits, hospital admissions or death. Others have focused on changes in physiological or functional subclinical markers of health, such as lung function or inflammatory markers in the blood. If other varying factors, such as weather conditions and day of the week, are properly controlled for in the analyses, these studies are extremely powerful and efficient tools for investigating the acute effects of air pollution. Common to the acute effect study designs listed below is the fact that that other individual characteristics (smoking status, diseases, genetic factors, *etc.*) do not confound the association between air pollution and acute effects, as these co-factors do not change from day to day. Moreover, in both case–crossover and panel studies, subjects serve as their own control.

- *Time series* analyses are the most frequently used method to statistically explore short-term associations between daily air pollution data and frequencies of events (death, hospital admissions etc.). These studies can often rely on routinely available air pollution and health registry data. Studies involving data from many cities analysed using the same protocol are of particularly high value. The repetition of such time series analyses enables changes over time in associations between pollution and health to be monitored. For example, a Dutch investigation monitored the association between ambient black smoke concentrations and daily death across a 34-year period. The association remained significant and quite stable from 1972 to 2006, despite a decrease in absolute levels of black smoke and various other changes in air quality.
- *Case–crossover studies* are a useful variant of the time series approach. Pollution levels at or before a registered event (*e.g.* death or heart attack) are compared with levels on a selected "control day". Under the null hypothesis, air quality should not differ between event day and control day.
- *Panel studies* are particularly efficient in investigating acute effects among highly selected groups (or panels) of people (*e.g.* asthmatics or patients with a history of a heart attack). Participants in panel studies are asked to repeatedly provide health data (daily peak flow measurements, repeated analyses of blood markers, *etc.*). Under the null hypothesis, daily changes in air quality should not be associated with daily fluctuations in health outcomes.

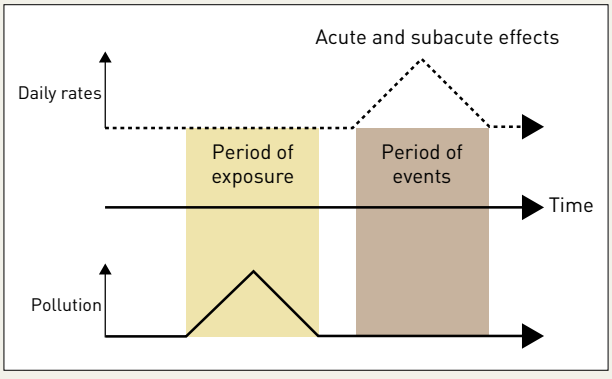

Figure 5a.1. Schematic representation of epidemiological short-term studies in air pollution. Short-term studies attempt to find associations between changes in concentrations during some time period and changes in outcome rates the same day or a few days after exposure. Modified from [14].

Box 5b

Epidemiological studies investigating long-term effects

Specific study designs are needed to investigating the long-term consequences of repeated or continuous and often lifetime exposure to ambient air pollution. Long-term exposure to air pollution differs between people owing to spatial rather than temporal contrasts in air quality. Thus, long-term studies need to involve people living in places with different mean levels of air pollution, resulting in multi-city or multi-community studies such as the 12-community Southern Californian Children's Health Study or the Swiss 8-City study SAPALDIA. In contrast to acute effect studies, the focus of the investigation of long-term effects is on pre-clinical or clinical pathological conditions (*e.g.* calcification of the arteries), functional states (*e.g.* lung function), prevalences of chronic diseases (*e.g.* chronic obstructive pulmonary disease (COPD)), or life expectancy rather than "events" such as hospitalisation, myocardial infarction, stroke or death.

The most widely used study designs in chronic effect research are cohort studies and cross-sectional surveys (fig. 5b.1). Cohort studies are the gold standard for investigating the new onset of chronic diseases or changes in health conditions over time in relation to air pollution. Cross-sectional studies are particularly informative when investigating the prevalence of chronic conditions or functional levels (*e.g.* lung function) measured at a point in time in relation to past exposure to air pollution.

A formidable challenge common to all these studies is the characterisation of long-term exposure to ambient air pollution. Often, exposure on a community level has been defined only with data from a few – or even a single – fixed-site monitors. This is valid only for small communities and for pollutants with small spatial variation (e.g. ozone). However, pollutants such as those originating from traffic may vary substantially within communities and depend on proximity to traffic arteries (see Box 6d). Thus, the current gold standard of exposure assessment requires characterisation of local – most often residential – pollutant levels. To accomplish this goal, studies combine local measurements with modelling techniques to map the spatial distribution of pollutants. Geocoding of residences or work locations enables individual assessment of exposure, resulting in very powerful investigations of chronic effects. An important initiative of the European Union's 7th Framework Programme for Research and Technological Development is the funding of the ESCAPE collaboration (www.escapeproject.eu). The project maps the spatial distribution of traffic-related pollutants all across Europe. Participants of more than 30 existing European cohort studies will be linked to these exposure data to investigate the long-term effects of traffic-related pollution on a broad range of chronic conditions and life expectancy.

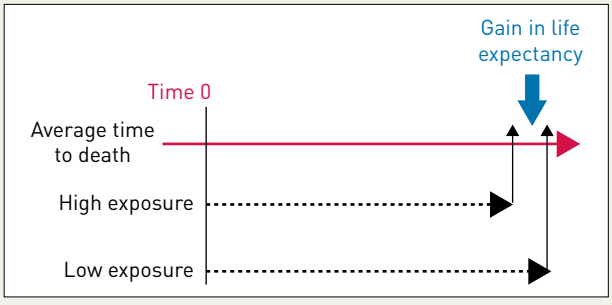

Figure 5b.1. **Schematic representation of epidemiological long-term studies in air pollution. Cohort studies follow a population through time and compare outcomes (e.g. time to death) among people with different levels of exposure (see Box 8A).**

6.
HEALTH AT STAKE

The main health effects associated with current levels of ambient air pollution.

In December 1952, several thousand people died in London, UK, as a consequence of an atmospheric inversion that lasted several days, trapping smoke from the burning of coal in open fireplaces. This event provided some of the earliest evidence that air pollution may be related to adverse health outcomes. Since then, numerous epidemiological studies have confirmed that short-term exposure to air pollution is associated with morbidity and mortality (see Box 6a). More recently, epidemiological studies of chronic exposure to air pollution have also reported associations with several health outcomes. Until the 1990s, population studies focused mainly on respiratory health, as the airways are the primary gateway for pollution to the human body. As further insight into the systemic effects of pollution became available, the designers of epidemiological and experimental studies began to recognise that pollution also affects the cardiovascular system. Although the evidence for a causal association between air pollution and some outcomes remains weak, improved research methodologies mean that the list of effects of air pollution is unfortunately growing continuously (table 6.1).

This chapter gives a review of what is known about the acute and chronic effects of urban air pollution, derived from epidemiological studies. (For a broader description of general mechanisms linking pollutants with health effects, and further details of the effects of some important single pollutants, see Annexe 1). It is worth emphasising once again that the health effects of pollution are likely to be caused by a range of pollutants rather than by single constituents of the mixture.

Table 6.1. Health outcomes for which there is at least some evidence of an association with air pollution

Acute effects
Daily mortality
Respiratory hospital admissions
Cardiovascular hospital admissions
Emergency room visits for respiratory and cardiac problems
Primary care visits for respiratory and cardiac conditions
Use of respiratory and cardiovascular medications
Days of restricted activity
Work absenteeism
School days missed
Self-medication
Avoidance behaviour
Acute symptoms
Physiological changes, *e.g.* in lung function
Chronic effects
Mortality from chronic cardiorespiratory disease
Chronic respiratory disease incidence and prevalence (asthma, COPD)
Chronic change in physiological function (*e.g.* lung function)
Lung cancer
Chronic cardiovascular disease
Other effects
Low birth weight
Pre-term delivery
Adversely affected cognitive development in infants

SHORT-TERM EFFECTS

A large number of epidemiological studies have shown that the daily mortality, mainly from cardiovascular and respiratory diseases, follows the daily fluctuation of air pollution. The seminal multi-city time series analysis APHEA, carried out in 29 (mostly European) study centres, found an increase of deaths from illness of 0.6% per 10 $\mu g \cdot m^{-3}$ increase in PM10 concentration (mean on the day of death *versus* the day before). Deaths from cardiovascular diseases increased by 0.7%. These results are similar to those of a previous meta-analysis conducted on behalf of WHO, which found the same effect size for total mortality and a slightly higher effect size for cardiovascular deaths (0.6% and 0.9%, respectively, per 10$\mu g \cdot m^{-3}$ increase in PM10 concentration). Although the RR is higher for respiratory mortality, more people die from cardiovascular diseases, suggesting that the impact on the cardiovascular system of air pollution is large.

The daily variation in disease burden due to urban pollution is also shown by increases in the numbers of emergency visits and hospital admissions due to cardiovascular diseases, stroke and respiratory diseases, including asthma. APHEA found an increase in cardiac admissions of 0.7% per 10 $\mu g \cdot m^{-3}$ increase in PM_{10} concentration. Increases were: 1.2% for asthma in children; 1.1% for asthma in adults aged up to 64 yrs; and 0.9% for all respiratory diseases (including COPD, asthma and other respiratory diseases) in the elderly.

As detailed in Box 6b, people are not affected equally by ambient air pollution. Patients with asthma, especially children without anti-inflammatory or bronchodilator therapy, suffer more on or after days with higher pollution levels. Because of the large individual day-to-day variation, with many concomitant influencing factors, effects in asthmatics are not easily demonstrated without strict control of adherence to the study protocol and individualised exposure assessment. However, panel studies on asthmatics employing such rigorous methods have found increased wheezing, cough and attacks of breathlessness, accompanied by a lower lung function and need of additional relief medication, associated with daily variations in levels of PM and NO_2.

The acute effects of ozone on individuals have been observed consistently in epidemiological studies. Box 6b provides specific details about the health effects of this particular pollutant.

LONG-TERM CONSEQUENCES OF AIR POLLUTION

As discussed in Chapter 5, long-term or lifetime exposure to ambient pollutants may not only trigger acute health problems but also contribute to pathologies that ultimately result in chronic ailments. The investigation of these effects usually requires large studies and lots of time; thus, the current evidence on the long-term effects of air pollution rests on fewer studies than that on the acute effects. However, in the past 10 years, many studies have confirmed the adverse effects of even moderate levels of air pollution.

AIR POLLUTION AND LIFE EXPECTANCY

While death is in itself an acute event, life expectancy or time to death are the result of both acute and chronic pathologies. Due to the known acute effects of air pollution on mortality and the interrelation between acute and chronic pathologies, it is impossible to distinguish and apportion clearly the acute and chronic effects of air pollution on mortality. However, cohort studies do – by default – measure time to death, thus contributing substantially to our understanding of the chronic effects of air pollution. Studies conducted in Europe, the USA and Canada confirm that the overall effects of pollution on mortality are far larger than the fraction attributed to acute exposures.

In epidemiological studies on mortality, respiratory diseases are less often the cause of death than cardiovascular diseases. Therefore, the two are often combined in the category of cardiopulmonary mortality. Cardiopulmonary mortality was associated with long-term differences in PM and sulphate concentrations between cities in the famous Harvard Six Cities Study and in the American Cancer Society (ACS) study. Comparison of community-level concentrations of fine PM with death rates among more than 500,000 participants in the ACS study showed a 6% increase in cardiopulmonary deaths 16 years later per 10 $\mu g \cdot m^{-3}$ of $PM_{2.5}$. The estimate for

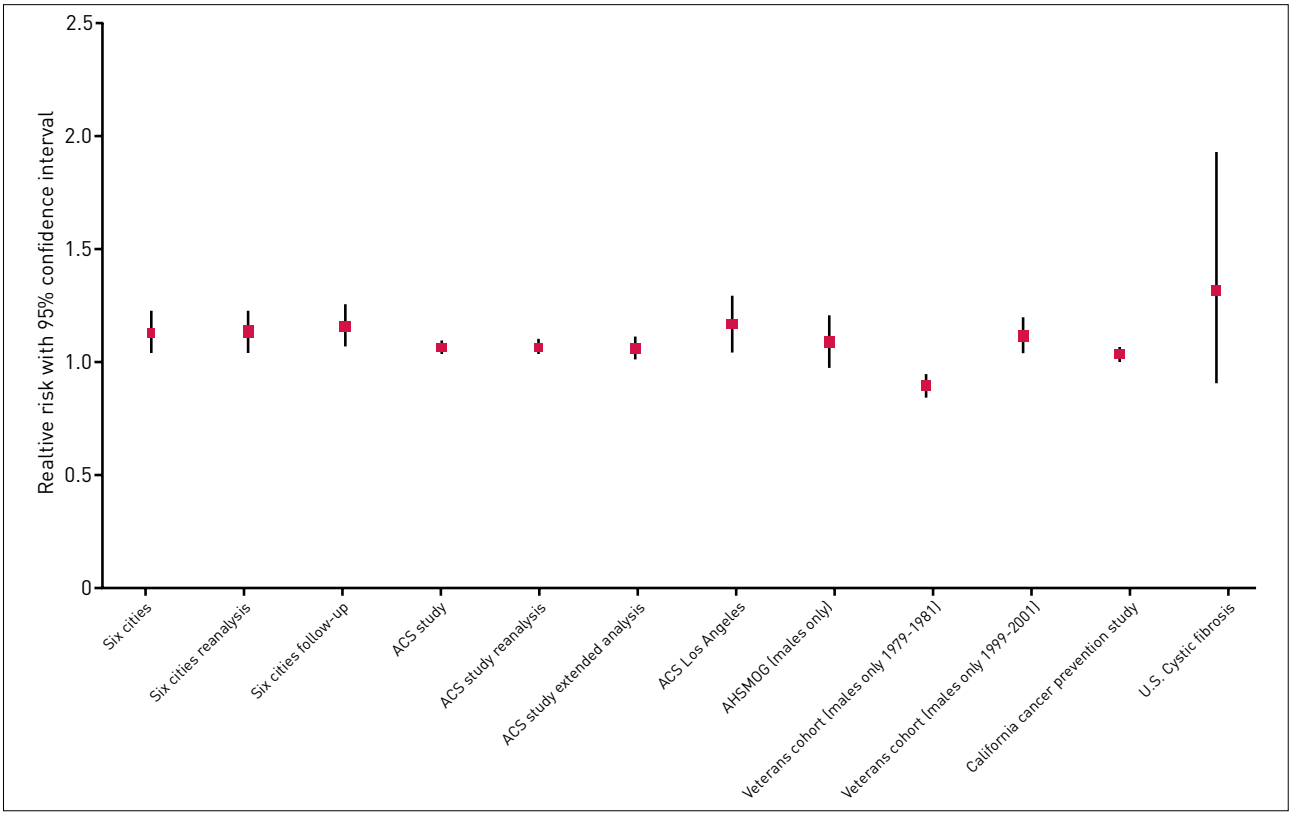

Figure 6.1. **Relative risk estimates (and 95% confidence intervals) for associations between long-term exposure to $PM_{2.5}$ (per 10 $\mu g \cdot m^{-3}$) and mortality for the main cohort studies conducted in North America. The figure presents only the common name of the study. Further information on studies can be found in [15, 16].**

Box 6a

The pyramid of acute health effects: evidence for a causal relationship

In any given population, susceptibility to adverse effects of air pollution (or any other health threat) is expected to differ widely between people, and – within the same subject – over time. For example, while the least susceptible "healthy people" may experience no symptoms at all or only clinically irrelevant changes, similar exposure may trigger serious exacerbations of health problems among the frail. Similarly, some asthmatics may suffer attacks once air pollution increases while other asthmatics remain stable.

Air pollution epidemiology has utilised this pattern of varying susceptibility and severity, investigating associations between pollution and the broad range of health outcomes, ranging from minor changes (*e.g.* some blood marker) to mortality. This paradigm is depicted in figure 6a.1. The pyramid also makes it clear that the number of people affected by the most extreme effects is much smaller than those affected by less severe outcomes. This has been confirmed in many air pollution health impact assessments. The coherence of results observed across this broad range of interrelated outcomes provides a very strong argument for a causal role of pollution on public health.

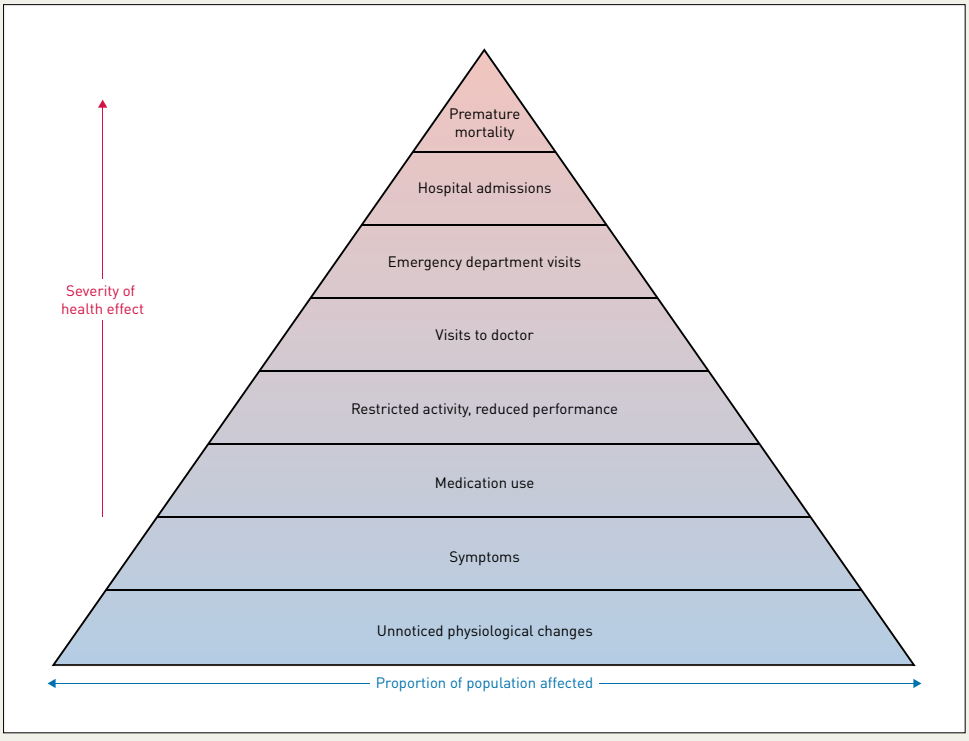

Figure 6a.1. **Pyramid of health effects associated with air pollution [21].**

Box 6b

We are not all equal – susceptibility matters

Not all smokers suffer from tobacco-related diseases – and not all people are affected by ambient air pollution. A more difficult task is to identify susceptibility factors. While some factors modify the level of exposure, other characteristics may determine how an individual will be affected by exposure to ambient air pollution. The increase in ventilation rate during physical activity results in higher exposure to pollutants. Depending on where people engage in physical activity, they may face a trade-off between the health benefits of the activity and higher exposure to toxicants.

A range of susceptibility factors is currently under investigation, and some preliminary patterns can be described:

- As a general rule, children are more affected due to their relatively higher ventilation and metabolic turnover during childhood and adolescence. However, not all children are equally affected and the following issues apply to children as well.
- Pre-existing diseases may determine susceptibility. This is particularly well established for the acute effects of ambient air pollution: air pollution can cause exacerbations among patients with asthma or COPD. Subjects with heart disease or atherosclerosis may suffer a heart attack or stroke after exposure to ambient air pollution. A few studies have shown diabetics to be more strongly affected by acute cardiovascular effects of ambient air pollution.
- Any factor involved in the mechanisms of air pollution-related morbidities and mortality is a potential determinant of susceptibility. Foremost among these are genetic factors, for instance those involved in oxidative stress and systemic inflammation. Some findings suggest that genetic defiencies in the detoxification of xenobiotics – *e.g.* the null variant of glutathione *S*-transferase Mu 1– amplify the adverse effects of ambient air pollution.
- Antioxidant intake has also been implicated as a susceptibility factor: children with a higher intake of antioxidants appear to be better protected against the oxidative effects of ozone and other ambient pollutants.
- Subclinical systemic inflammation: while the evidence is not yet established, subjects in a state of chronic subclinical inflammation could be considered to be more strongly affected by the inflammatory effects of air pollution. For instance, experimental studies indicate that obesity and diabetes are associated with stronger effects of ambient pollutants.
- Potential interactions between medical treatment and effects of air pollution should be taken into account. One study reported that associations between air pollution and heart-rate variability are not seen in patients who have been prescribed statins. Well-controlled asthmatics are likely to be less affected by the adverse respiratory effects of air pollutants (see Chapter 9).

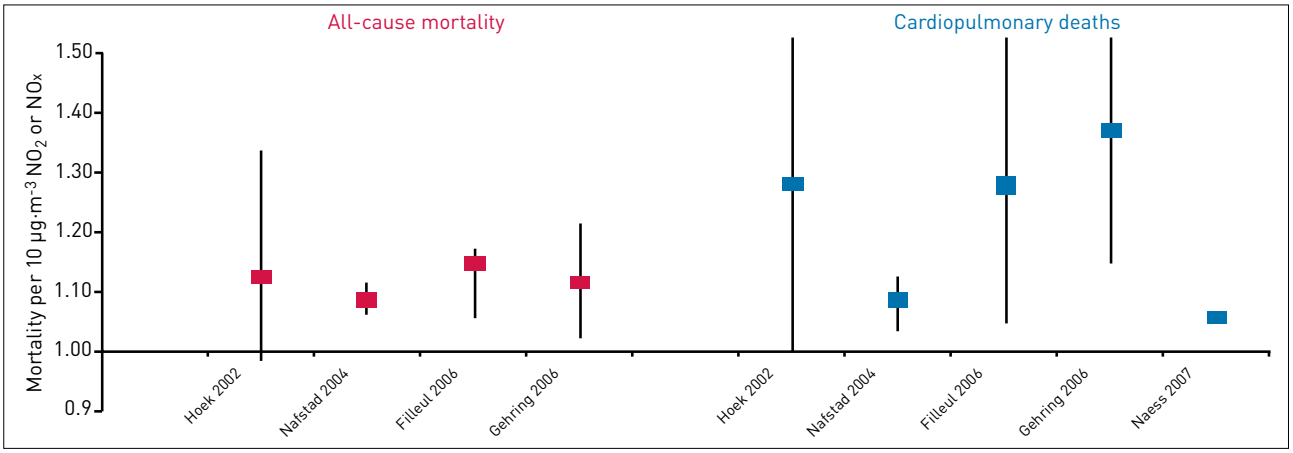

Figure 6.2. Relative risks with 95% confidence intervals from European cohort studies on air pollution and mortality, expressed per 10 µg·m^{-3} NO_2 or NOx [17].

total mortality was 4%. In a reanalysis of 18 years of ACS follow-up from the Los Angeles area, a modelled PM2.5 exposure was assigned to each residence. This improved exposure assignment resulted in larger estimates. Cardiopulmonary mortality increased by 20%, and death due to ischaemic heart diseases by 49% per 10 µg·m^{-3} increase in PM2.5. Many other cohort studies exist from the USA showing an association with mortality.

Cohort studies in Europe have been able to confirm the relationship between cardiopulmonary death risk and pollution. Three other European studies were able to analyse the data for respiratory and cardiovascular mortality separately. The results showed that urban air pollution, assessed individually for all participants by modelling traffic emissions of NOx, was associated with overall mortality, mortality from ischaemic heart diseases, respiratory mortality, lung cancer mortality and weakly also with cerebrovascular mortality. But not all cohort studies have found consistent effects on cardiovascular mortality. A Dutch cohort study on nutrition and cancer with exposure data over 20 years observed only nonsignificant relations between cardiovascular deaths and NO_2 or black smoke, and a weak association of cardiopulmonary death with traffic density on the nearest main road. In contrast, respiratory deaths were related to NO_2, black smoke, traffic density within a radius of 100 m and living near a main street.

RESPIRATORY HEALTH IN CHILDREN

Long-term effects on the respiratory system are often investigated in children, as they are more susceptible to the effects of air pollution than adults, for several reasons. Children are more active and have more outdoor activities. They breathe faster and their metabolic rate is higher than adults'. Children's immune systems are not fully developed, so the incidence of respiratory infections is high. The lung is still growing and any deficit in growth will be relevant for the whole of the child's life. Moreover, possible confounding or modifying factors, such as active smoking, occupational exposure to dust and smoke or medical treatments of diseases, are largely absent. Of particular interest and relevance are investigations of lung function development in children and the incidence

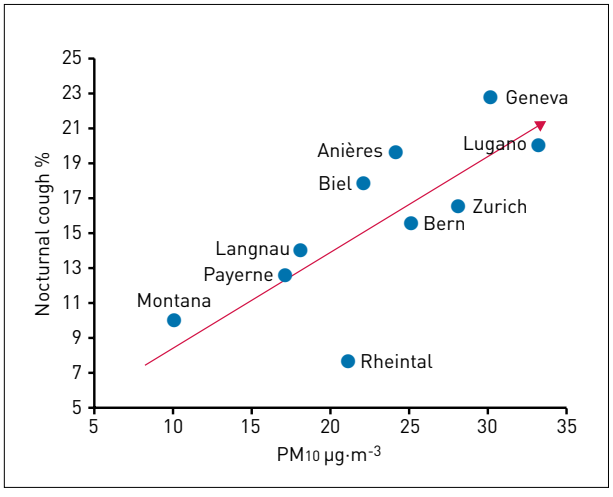

Figure 6.3. Prevalence of nocturnal cough and annual community mean PM10 levels in the SCARPOL study of Swiss schoolchildren [18]. The arrow indicates higher prevalences in communities with higher PM10 levels.

of asthma – the most important chronic disease in children.

Several cross-sectional studies from Germany, Switzerland, France and the USA found as early as the 1980s that school-age or pre-school children in communities exposed to higher levels of dust, SO_2 and NO_2 suffered more from cough and acute bronchitis compared with children in less polluted regions.

More recently, many cross-sectional studies have reported lower lung volumes in children living in more polluted areas. While exacerbations of asthma clearly correlate with air quality, geographical comparisons of the prevalence of asthma or allergies do not follow gradients in urban background levels of pollutants, *e.g.* PM2.5 or PM10. Novel approaches now integrate local measurements of traffic-related pollutants, geographic information systems, land-use data and spatial modelling techniques to characterise the intra-community distribution of traffic-related pollutants. The latter are poorly characterised by urban background monitors, and people living at busy roads might experience several-fold higher exposures to traffic-related pollutants than people living some 50–100 m further away (see Box 6d).

RESPIRATORY HEALTH IN ADULTS

The most important risk factor for chronic respiratory diseases in adults is smoking, and the health effects of smoking and ambient air pollution appear largely to overlap. Moreover, residential proximity to streets may not only be a proxy for exposure to pollution but may also indicate differences in socio-demographic factors, including smoking. Studies evaluating the impact of outdoor air pollution on diseases such as COPD and asthma in adults need to take into account the intercorrelation of these factors, in addition to individual traits such as age, sex and genetic factors. Results based on never-smokers are particularly valuable.

Chronic cough and phlegm as well as lung function decrement have been associated with long-term ambient inhalable PM exposure in several repeated cross-sectional studies in the USA and Europe.

Interestingly, some of these studies have shown that respiratory symptoms are more prevalent among participants living in proximity to main streets, independent of background pollutant concentrations

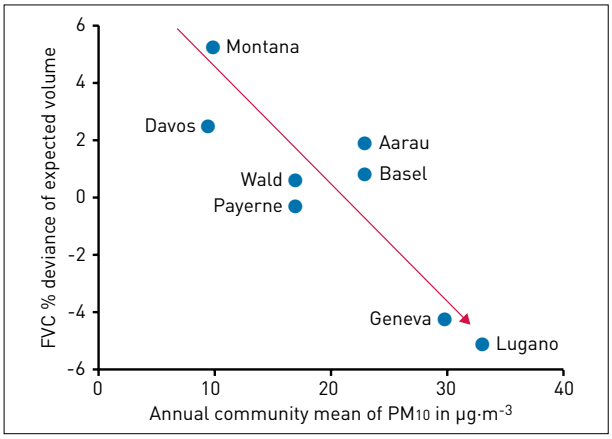

Figure 6.4. Adult lung function, represented by % deviance of expected forced vital capacity (FVC) and annual community mean PM10 levels in eight communities in Switzerland, from the SAPALDIA study [19]. The arrow indicates lower lung capacity in communities with higher PM10 levels.

(see Box 6d). Moreover, reduction in exposure attenuated age-related decline in lung function.

As in children, asthma in adults is not correlated with urban background levels of pollution. The few studies investigating the contribution of local traffic-related air pollution to asthma onset in adults have produced similar findings to those looking at childhood asthma incidence, but more research is needed to clarify these results and the interaction with atopy and other host factors. The contribution of air pollution to COPD also needs further investigation, and proper control for smoking is crucial, but a few studies have supported the notion that air pollution contributes to COPD.

CARDIOVASCULAR HEALTH

In recent years, the main focus of pollution research has shifted from respiratory to cardiovascular diseases because the associations between air pollution and cardiovascular health appear to be stronger than first thought. A cross-sectional study in Germany found an effect of traffic on the prevalence of coronary heart disease independent of PM2.5 (Heinz Nixdorf RECALL study), where myocardial infarction, stent and bypass interventions were more prevalent in people living close to high concentrations of road traffic. Coronary risk decreased with increasing distance to the main road. However, infarction – like death – is an event; thus, the

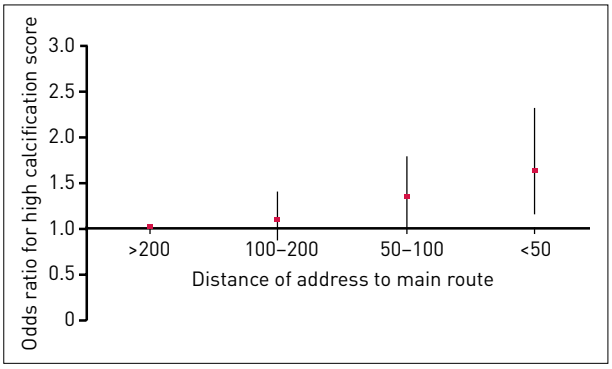

Figure 6.5. Risk of coronary artery calcification and distance from residence to the nearest route with heavy traffic [20].

study could not unambiguously distinguish the acute effects of pollution on heart attacks from its chronic effects on the underlying cardiovascular pathology.

The most important pathology in cardiovascular disease is atherosclerosis. Atherogenesis – the development of atherosclerosis – is the result of a long-term process. The first evidence of a link between pollution and atherogenesis came from studies conducted in animals that developed atherosclerosis after long-term exposure to concentrated urban PM. This evidence prompted human studies looking at the association between air pollution and calcification of the coronary arteries. After controlling for individual risk factors, a study in Germany found that a 50% reduction in the distance between the subject's residence and the nearest major road was associated with a 7% higher calcification score, independent of background PM2.5 levels (fig. 6.5) [20].

A small number of studies have confirmed these results, suggesting that urban pollution not only triggers cardiac events but may also add to the underlying cardiovascular pathologies. Efforts are under way to identify further steps in the pathophysiological path to heart disease, such as chronic imbalance of the autonomic control of the heart, which may enhance susceptibility to arrhythmia and heart attacks, or increased levels of inflammation and coagulation factors.

CANCER FROM TRAFFIC EXHAUST

Based mostly on experimental and occupational data, the international agency for research on cancer has evaluated: benzene, benzo(a)pyrene, 1,3-butadiene and polycyclic aromatic hydrocarbons (PAHs) containing soot as carcinogenic for humans (group 1); diesel engine exhaust and other hydrocarbons as probably carcinogenic to humans (group 2A); and gasoline engine exhaust as possibly carcinogenic to humans (group 2B). The California Environmental Protection Agency also considers diesel exhaust to be carcinogenic.

In childhood, leukaemia, lymphomas and brain cancer are the most frequent malignancies. Two early case–control studies in the USA found a link between traffic exposure and leukaemia risk in children. Benzene or other VOCs from traffic were suspected as possible causes. Since then, several case–control studies and some ecological registry studies have focused on this topic with mixed results. Overall, the results are still inconsistent.

In adults, death from lung cancer is of primary interest. Lung cancer is a relatively rare disease (in nonsmokers) with a long latency period. The time from diagnosis to death is often short, and treatment is of limited success. To look at lung cancer in population-based studies, the population sample has to be large and the follow-up time long. In the American Cancer Society cohort study, lung cancer incidence increased by 8% per 10 $\mu g \cdot m^{-3}$ increase in PM2.5 levels measured as between-city difference; in a Norwegian cohort study lung cancer incidence increased by 11% per 10 $\mu g \cdot m^{-3}$ increase in NOx from traffic. However, despite the coherence of experimental information, occupational studies and many results in population studies, not all long-term epidemiological studies have shown a link between ambient air pollution and lung cancer risk. In addition to the overwhelming effect of smoking, a weak effect may be masked by misclassification of exposure, changes of addresses, individual lifestyle factors and occupational risks in the follow-up period. Pollutants with a small within-city gradient, such as PM2.5, may not capture differences in traffic exhaust exposure. Even NO_2 and black smoke may not be sufficiently representative to be a measure of exposure to fresh traffic exhaust. Commuting patterns – a relevant determinant of exposure to diesel exhaust – have not been taken into account in any study.

REPRODUCTIVE OUTCOMES

A review of studies on low birthweight, intrauterine growth retardation and pre-term birth concluded that the evidence for an adverse effect of PM pollution was still inconsistent. Since then, several large registry studies in

Box 6c

Ozone and health effects

Due to its oxidative properties (see Box 3a), ozone is a major concern for public health. The acute effects on individuals have been observed consistently not only in clinical studies but also in panel and field studies on children and adults, both males and females, who engage in outdoor activity. These effects encompass reduced pulmonary function, lung inflammatory reactions and respiratory symptoms. The broad range of individual susceptibility to ozone is only partly explained by genetic predisposition. Generally, the response depends on three parameters: concentration (the higher the ozone level, the more people affected); duration (the longer the exposure, the stronger the reaction); and respiratory volume (the more intense the activity, the stronger the reaction).

Acute lung function and inflammatory reactions are reversible when the exposure ends. Many studies have observed an attenuated reaction after repeated ozone exposures, and reactions generally diminish over the course of the summer.

Despite this reversibility of and adaptation to the short-term clinical effects in individuals, many epidemiological studies of registry data have confirmed that ozone is associated with acute mortality and also morbidity. A meta-analysis of European registry studies on behalf of the WHO found an increase in all-cause mortality of 0.3% and an increase of cardiovascular death of 0.4% per 10 $\mu g \cdot m^{-3}$ increase in ozone levels (8-h mean). Although questions remain about the underlying mechanisms, an expert panel of the US National Academy of Sciences concluded that the association between daily changes in ozone concentrations and death during summer months is causal [22]. Part of the ozone-associated effects may be related to concomitant pollutants in summer smog, such as secondary aerosols. High temperatures may also amplify the effects of ozone.

People with asthma are especially affected by ozone through the enhancement of airway responsiveness and increases in inflammatory cells and mediator release in the lung. Daily ozone levels have been associated with cough and reduced lung function in panel studies on asthmatics – especially in children – and with school absences, emergency consultations, and hospital admissions for asthma exacerbations. Hospital admissions related to other respiratory diseases have not been as consistently linked with ozone.

People in areas with high oxidant pollution have been shown to have chronic inflammatory damage of the nasal mucosa. Prospective studies on lung function growth in children and young adults in California have not produced clear-cut results, in contrast to cross-sectional analyses of lung function in young people, which showed reductions in the small airway function of students with a higher lifetime ozone exposure. Medium-term ozone exposure over a summer season has been shown to be related to lung function reduction or diminished lung function growth in German and Austrian school children, conscripts and harvesters.

Individual ozone exposure is determined mainly by time spent outdoors and engaging in outdoor activities, and much less by mean ozone levels outdoors, even at the subject's home address. The difficulties of assessing lifelong exposure accurately may be one reason why most studies have failed to detect chronic effects of long-term ozone exposure.

Table 6c.1. **Reduction of lung function with increasing ozone levels in the population and in susceptible people (WHO Euro, health effects of smog episodes, 1992).**

MAXIMUM HOURLY CONCENTRATION, µG·m^{-3}	MEAN REDUCTION OF LUNG FUNCTION (FEV1) IN OUTDOOR- ACTIVE PEOPLE	
	POPULATION	MOST SUSCEPTIBLE 10%
< 100	none	none
100 – 200	5%	10%
200 – 300	15%	<30%
>300	25%	>50%

the USA, Canada and East Asia have found associations of fetal growth and duration of pregnancy with traffic-related pollutants, and less consistently with PM2.5. An Australian study, looking at rather low levels of pollution, did not find such associations. All the studies modelled the exposure in pregnancy with a spatial resolution at least for the postcode area of the address, some with extensive modelling over the whole time of pregnancy. Newer results following women during their pregnancies add to the evidence of an association between fetal health and traffic pollution, although several methodological problems remain to be overcome, such as taking into account individual susceptibility factors and improving exposure assessment.

NEURODEVELOPMENT, NEURODEGENERATION AND TRAFFIC POLLUTION

Organic lead is the best known traffic pollutant linked to neurodevelopmental deficits in children. Dose–response relationships between intelligence deficits and blood lead levels have been observed, without indications of a lower threshold, down to 10 µg·dL^{-1} blood. Cohort studies on lead-exposed adults suggest that long-term lead exposure as measured by lead stored in the bones is also related to premature cognitive decline. Banning organic lead from fuel has produced declines of >90% in population mean blood lead levels in industrialised nations. Actual concentrations of lead in the air are judged to be minimal even next to main routes with heavy traffic.

A newer area of concern, however, is ultrafine particles from combustion processes. These have been shown in animals to translocate from the nose through the olfactory nerve to the brain, resulting in inflammatory processes resembling degenerative diseases. A Mexican research team observed more brain inflammation and accumulation of amyloid in *post mortem* examination of individuals from areas with heavy air pollution compared with individuals from areas of better air quality. Intelligence score has also been shown to be lower in children with higher PAH exposure in pregnancy. However, in these studies, all exposure indicators were strongly correlated with social indicators as education and race of mothers, income and noise exposure, and the cohorts had high dropout rates. Therefore, it is not yet possible to conclude that these effects are truly the consequence of ultrafine particles.

Box 6d

Living close to traffic: a health concern

A large proportion of the European population lives in apartments or houses built alongside busy streets. Exhaust pollutants, such as ultrafine particles, carbon monoxide or other primary gases, reach very high concentrations along streets – with the most extreme conditions found in narrow streets lined with tall buildings. Due to dispersion and aggregation, concentrations of these pollutants rapidly decrease to urban background levels within only 50–100 m of main traffic arteries. Diesel cars, trucks and buses emit particularly high concentrations of soot and large numbers of very toxic substances are loaded on these fine particles; toxic substances are also found in the coarse particles formed from brake wear and road surface abrasion and these particles are re-suspended in the air by moving traffic. As a result, exposure to these pollutants can be very high during busy commuting periods, and among people walking, playing or living close to main streets.

Many newer epidemiological studies are investigating or have investigated health outcomes as a function of proximity to traffic. With potential confounding factors taken into account, these studies suggest strongly that living close to a busy road poses a risk to health due to pollution. However, these studies are also very heterogeneous in their methodology, and a recent critical review called for more targeted research, since the current evidence for a range of outcomes is suggestive but not conclusive (see table 6d.1). The development of asthma in children is an exception: large amounts of data are available. With a recent publication from the Californian Children's Health Study, the evidence has become strong that traffic-related pollutants contribute to the development of childhood asthma, at least among children who are genetically susceptible [23]. This evidence raises new challenges for policy-makers as urban planning decisions may have major public health implications. The findings may also initiate debates in school boards and communities about the location of schools and day care facilities in immediate vicinity of major traffic arteries.

Table 6d.1. **Current evidence for a causal detrimental role of local traffic-related air pollution. Modified from the Health Effects Institute Report on the health effects of traffic-related exposure [24]. The HEI review was restricted to the more recent literature investigating only the local effects of those pollutants that occur in very high concentrations in proximity to busy roads. Evidence for health effects of 'urban background pollution' (such as PM2.5 and other secondary pollutants which are also largely due to traffic) is for many health outcomes stronger.**

HEALTH OUTCOME CLASSIFICATION	CLASSIFICATION	MAIN REASON FOR
All-cause mortality	Suggestive but not sufficient	Too few studies
Cardiovascular mortality	Suggestive but not sufficient	Too few studies
Cardiovascular morbidity	Suggestive but not sufficient	Failure to include potentially important confounders
Asthma incidence and prevalence	Sufficient, or suggestive but not sufficient	Concerns about precision of estimates
Exacerbations of symptoms for children with asthma	Sufficient	
Exacerbations of symptoms for children without asthma	Inadequate and insufficient	Effects may be asthma driven
Healthcare utilisation for children measure	Inadequate and insufficient	Concerns about validity of outcome
Adult-onset asthma	Inadequate and insufficient	Only one study
Respiratory symptoms in adults	Suggestive but not sufficient	Inconsistent results between proximity and model-based estimates of association
Pulmonary function (all ages)	Suggestive but not sufficient	Heterogeneity of designs and function measures
Chronic obstructive pulmonary disease	Insufficient	Only two studies
Allergy	Inadequate and insufficient	Inconsistent methods
Birth outcomes	Insufficient	Only four studies
Cancer	Inadequate and insufficient	Too few studies

Definition of classifications. Sufficient: chance, bias and confounding could be ruled out with reasonable confidence to conclude for an association; Suggestive but not sufficient: chance, bias and confounding could not be ruled out with reasonable confidence to conclude for an association; Inadequate and insufficient: studies of insufficient quality, consistency or statistical power.

7. BEFORE AND AFTER: PUBLIC HEALTH BENEFITS OF IMPROVED AIR QUALITY

Examples of improvement of public health after policy interventions that resulted in a reduction of ambient air pollution.

The paradigm of evidence-based medicine is based on the assumption that decisions taken by physicians to treat patients ought to be based on scientific evidence (fig. 7.1). The gold standard of medical evidence comes from controlled clinical trials. The same paradigm also applies to the "treatment" of public health problems, such as air pollution. The important question is whether air pollution abatement policies would not only improve air quality but also have a positive impact on health. Controlled trials are obviously not feasible in this context. However, several "semi-experimental" studies have been conducted in recent years, reporting on the impact – or "accountability" – of air-quality improvements on health [26, 27]. While methodological challenges are usually inherent to such observational studies, the results of such "natural experiments" very much support the conclusions from epidemiological studies discussed in Chapter 6. The examples in this chapter illustrate the health benefits that result directly from air pollution exposure reduction.

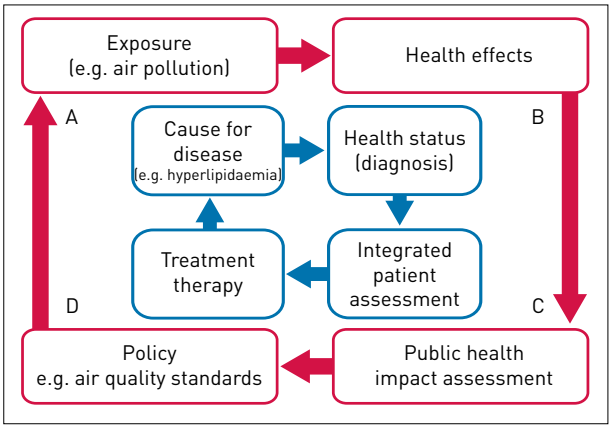

Figure 7.1. The paradigm of evidence-based medicine (inner cycle) and the related concept of evidence-based public health (outer cycle) [25].

In the mid-1980s a strike at a steelworks in the Utah Valley, USA – the most important source of air pollution in the area – created the conditions for an unintentional experiment into the effect of reducing air pollution. During the closedown, which lasted from August 1986 to September 1987, various markers of public health – including hospital visits, preterm birth, and death – improved. After the reopening of the steel mill, pollution promptly rose, as did a range of health problems (fig. 7.2). Experimental studies of particles collected before, during and after the strike confirmed that particles emitted during steel mill operation were substantially more toxic [28].

The restructuring of much European heavy industry since the political upheaval of the early 1990s has led to improvements in some health measures. For example, as shown in figure 7.3, the burden of particulates and sulphur dioxide in the New Laender of Germany and, concomitantly, of bronchitis symptoms in schoolchildren, has declined [31].

An intriguing "natural experiment" was reported from the Southern Californian Children's Health Study in the USA. During the annual follow-up period of the first cohorts, many children moved to other communities throughout the USA. Those living in the western states were visited and had their lung function measured again. The study revealed benefits in terms of lung development among those children moving to cleaner communities. In contrast, those moving to places with higher pollution experienced attenuated development of the lung [32].

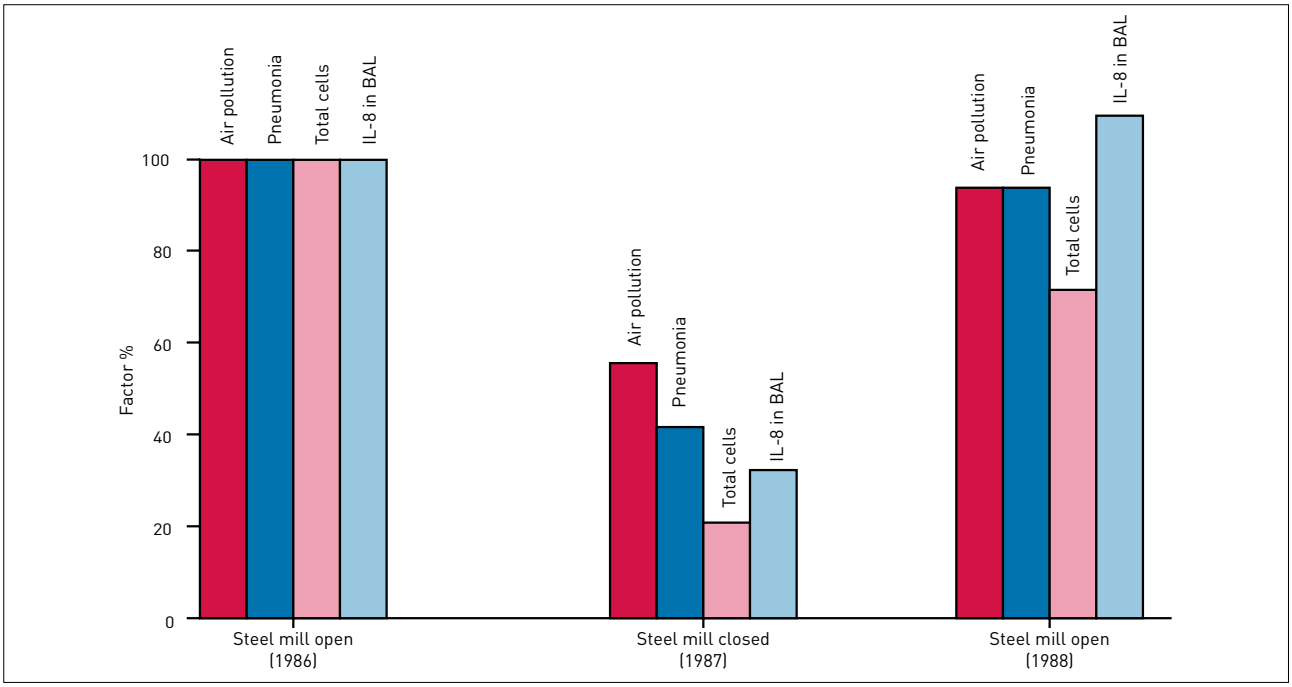

Figure 7. 2. Air pollution changes and hospital admission, cellular and bronchoalveolar effect changes during and after a 1-year closure of the steel mill in Utah valley. Effects observed from epidemiological, toxicological and experimental studies. [28–30].

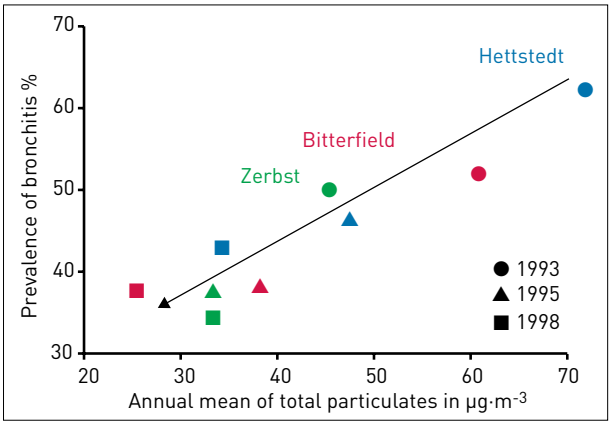

Figure 7.3. Particulate pollution and bronchitis in schoolchildren in Saxony, Germany [31]. The arrow indicates lower prevalence in communities with lower particle levels over the years.

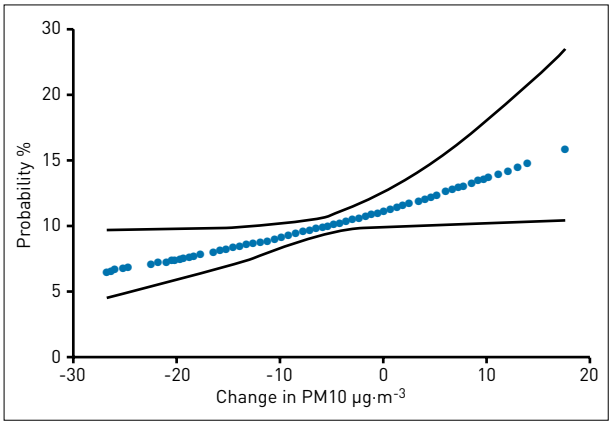

Figure 7.4. Probability with 95% confidence interval of reporting chronic cough or phlegm depending on change in PM10 pollution between 1991 and 2002 in the SAPALDIA study [34].

While most policies result in subtle long-term improvements, the coal ban implemented in Dublin, Ireland, in 1990 is an example of an environmental policy targeting one dominant source of pollution [33]. The policy resulted in immediate and sustained improvements in air quality. A 35% drop in black smoke levels comparing the 3 years prior to with the 3 years following the ban was paralleled by a significant (10–15%) decline in cardiovascular and respiratory mortality. This is one of the few "accountability studies" able to confirm the health benefit of a single (although drastic) policy. The observed reduction in death rates were close to those expected from extrapolations of the results of epidemiological investigations into the association between ambient air pollution and mortality.

Concerted policies implemented in Switzerland and neighbouring countries in the 1990s resulted in a decrease in air pollution and a range of health improvements [34–36]. Repeated cross-sectional investigations in school classes observed a decrease in irritative symptoms and respiratory disease in children. This change was correlated with a decline in PM levels. The Swiss cohort study SAPALDIA followed lung function decline among adults during the same time span. Age-related lung function decline was associated with air quality; in particular, the 11-year decrease in individually estimated home outdoor PM10 levels was associated with attenuated decline in lung function. Air-quality improvements also had a beneficial effect on respiratory symptoms: a mean decline of PM10 of 6 µg·m^{-3} coincided with 259 fewer subjects with regular cough, 179 fewer subjects with chronic cough or phlegm and 137 fewer subjects with wheezing with breathlessness per 10,000 adults. Moreover, a decline in new onset of asthma in adults, indicated by chronic cough, was associated with the change in pollution (fig. 7.4).

Studies conducted before and after the Olympic Games provide an opportunity to assess the public health benefits of air pollution reduction in a city [37, 38]. In 1996, Atlanta, USA, implemented several drastic measures to reduce pollution. During the 3 weeks of the Games, less pollution was measured (ozone peak-hour levels fell 28%, NO_2 peak-hour levels fell 7%, carbon monoxide 8-hour levels fell 19%, PM10 daily mean fell 16%) than in the 3-week periods before and after the games. Consultations in medical practices for asthma in children decreased during the games by over 40%, while asthma-related visits to emergency departments by 11–19%. Over the same period, children's medical visits for other reasons barely changed. For the summer Olympic Games in Beijing in 2008, mean PM2.5 and PM10 concentrations were lower by 31 and 35%, respectively, during the Olympic period compared with the non-Olympic period. Several ongoing panel studies are examining associations between air pollution and subclinical health outcomes before, during and after the 2008 games. These panel studies should provide a unique opportunity to assess the public health benefits of air pollution reduction in a city with very high air pollution levels.

8.
THE AIR POLLUTION PARADOX: SMALL RISKS, LARGE PUBLIC HEALTH BURDEN

While the relative risks associated with current levels of ambient air pollution are usually quite small, the overall impact of air pollution on public health is substantial, and thus the benefit of clean air policies can be very large.

Inter-individual differences in air pollution exposure are usually limited. Accordingly, the differences in health risks between "high" and "low" exposure individuals are expected to be small compared to the results of exposures such as smoking: heavy smokers have exposures that are orders of magnitude higher than those of occasional smokers or nonsmokers. However, to assess and compare the health relevance of different preventable risk factors, and thus to distinguish "large problems" from less important health issues, it is not sufficient to evaluate the relative risks (RR). Three quantities need to be taken into account jointly.

- The underlying frequency (in the population) of the disease to which air pollution may contribute.
- The distribution of the exposure, *i.e.* how many people are exposed to what levels of pollution.
- The RR, indicating the additional risk of disease due to air pollution.

In contrast to many other preventable risk factors of diseases, exposure to air pollution affects an extremely high proportion of the population. There are in essence no unexposed people, and everyone who lives in an urban area continues to be exposed to substantial amounts of ambient air pollution. This is the key reason for a paradox that is best revealed in assessments of the public health impact of ambient air pollution – also sometimes referred to as air pollution health impact assessments (HIAs). HIAs take into consideration the difference between risks faced by individuals *versus* those faced by populations (see Box 8A). HIAs translate research findings from the epidemiological or toxicological literature – *i.e.* RRs or ORs – into a rough quantification of the total health problem in a given region, country or city that may be attributable to air pollution. The use of HIAs is not restricted to air pollution: for instance, they have provided key evidence to show a need for smoking regulation in public places in Europe and elsewhere.

Air pollution HIAs have also been a very effective tool to inform policy-makers and the public about the approximate size of the air pollution problem. In Europe, for instance, they have been used to show that the overall health burden attributable to air pollution is considerable. HIAs have driven air-quality regulation by informing policy-makers of the likely public health benefits of policies to reduce air pollution.

HIAs are developed to provide crude estimates for health problems such as death (or life expectancy: see Box 8b), hospital admissions and respiratory problems attributable to air pollution, and for selected changes in air pollution levels that can represent future or past policy scenarios. Policy- and decision-makers need information that will help them take decisions on the suitability or prioritisation of public policy, given limited resources. Cost–benefit analyses based on the monetary valuation of health benefits are sometimes an integral part of HIAs. At the European level, many local HIAs exist for different cities or regions and for various objectives. Some are commissioned to estimate the degree of a health problem, while others evaluate the potential benefits of air pollution abatement strategies. We present below some of the most important HIA initiatives conducted in recent years in Europe.

In the mid 1990s, the Swiss government took a leading role in studying air pollution, and this resulted in one of the first HIAs conducted in Europe [39]. This study estimated the impact of outdoor and traffic-related air pollution on public health in Austria, France and Switzerland, and concluded that air pollution caused 6% of total mortality, or >40,000 attributable cases per year. About half of all mortality caused by air pollution was attributed to motor traffic, which was also responsible for more than 25,000 new cases of chronic bronchitis (adults), more than 290,000 episodes of bronchitis (children), more than 500,000 asthma attacks, and more than 16 million person-days of restricted activities. This study was in fact part of the Swiss governmental strategy to internalise the so-called "external" costs of heavy traffic – usually covered by the taxpayer – into the Swiss heavy traffic policy. The quantification of health-related costs was thus an important step in this HIA.

The Clean Air for Europe Cost–Benefit Analysis (CAFE–CBA) is an important HIA initiative in Europe [40]. The aim of CAFE–CBA was to develop long-term, strategic and integrated policy advice to protect against significant negative effects of air pollution on human health and the environment. CAFE–CBA estimated the health burden of outdoor air pollution based on emissions projections to 2020 for all of Europe and for 25 European Union member states with respect to various emissions-control policies. It provided a cost-–benefit analysis for emissions regulations in Europe. The analysis revealed that large benefits were predicted to occur over this time – with quantified air pollution impacts falling by €89bn–€183bn a year by 2020 – as a result of new emissions-control legislation. This excluded benefits not included in the monetary framework – notably reductions in damage to ecosystems and cultural heritage. However, despite these improvements, the evaluation showed that baseline damages in 2020 will remain significant – estimates ranged €191bn–€611bn a year. The CAFE initiative has led to a thematic strategy setting out the objectives and measures for the next phase of European air-quality policy.

Air Pollution and Health: a European Information System (APHEIS) [41, 42] was created in 1999 to provide policy- and decision-makers, environmental and health professionals, the general public and the

Table 8.1. **Examples of the health benefits attributed to air pollution reduction in selected areas of Europe**

POLLUTANT/SCENARIO[a]/ HEALTH BURDEN	26 EUROPEAN CITIES [41]	AUSTRIA, FRANCE, SWITZERLAND [39]	ITALY 13 CITIES [45]	SPAIN BARCELONA METROPOLITAN AREA [43]
Population exposed (millions)	~41.5	~80.0	~10.0	~3.9
PM10				
Current levels (annual mean)	54 $\mu g \cdot m^{-3}$ [b]	21 $\mu g \cdot m^{-3}$	45 $\mu g \cdot m^{-3}$	50 $\mu g \cdot m^{-3}$
Reduction scenario	Reduction annual level to 40 $\mu g \cdot m^{-3}$	Reduction annual level to 7.5 $\mu g \cdot m^{-3}$	Reduction annual level to 40 $\mu g \cdot m^{-3}$	Reduction annual level to 40 $\mu g \cdot m^{-3}$
Health benefits (outcome avoided)				
Deaths (long-term exposure)	8,550	40,600	2,270	1,200
Hospital admissions for respiratory causes	—	18,508	225	390
Hospital admissions for cardiovascular causes	—	29,500	176	210
Chronic bronchitis adult	—	47,100	1,114	1,900

[a]: Assumes a reduction of current levels to levels proposed in scenario; [b]: Only 8 cities with levels above 40 $\mu g \cdot m^{-3}$

media with resources on air pollution. The most recent evaluation of APHEIS, APHEIS-3, covered 23 cities with a total population of almost 39 million inhabitants. It estimated that 11,000 premature deaths could be prevented annually if long-term exposure to $PM_{2.5}$ were reduced to 20 $\mu g \cdot m^{-3}$. The evaluation estimated that the mean life expectancy of a 30-year-old person could be prolonged, depending on the geographic area, by 2–13 months if $PM_{2.5}$ concentrations were restricted to ≤15 $\mu g \cdot m^{-3}$. The project provided evidence that the current air-quality standards legislated by the European Union were insufficiently stringent to protect a large part of the European population.

APHEKOM (Health Impact Assessment of Urban Air Pollution in Europe) – an expansion of the APHEIS project – will also evaluate the impact of traffic proximity and the related pollution on health. European HIAs have yet to examine this particular impact, but a Californian assessment shows it may be substantial [43].

On a global level, the WHO has developed two important HIA initiatives. Since 1990, the Global Burden of Disease (GBD) project has been compiling a consistent and comparative description of the burden of diseases and injuries and the risk factors that cause them in all regions of the world [44]. The GBD results are a very important input to health decision-making and planning processes globally and nationally. According to the most recent WHO assessment of the GBD due to air pollution, >2 million premature deaths each year can be attributed to the effects of urban outdoor air pollution and indoor air pollution (from the burning of solid fuels). Specifically, the overall estimated GBD due to outdoor air pollution may account for ~1.4% of total mortality, 0.5% of all disability-adjusted life years (DALYs) lost and 2% of all cardiopulmonary diseases. More than half of this disease burden is borne by the populations

of developing countries. The GBD framework is key to assess the comparative importance of diseases, injuries and risk factors in causing premature death, loss of health and disability in different populations and through time.

The second initiative conducted by the WHO is the development of air-quality guideline levels. The most recent update, from 2005, proposes new guidelines for PM, ozone, NO_2 and SO_2 [20]. In this update, HIA results took a central role for defining the guidelines, synthesising the available scientific information about the threat posed by the pollutants, their impact on the population and on specific susceptibility groups, and the social cost of regulation. While the guidelines are neither standards nor legally binding criteria, they are designed to offer guidance in reducing the health impacts of air pollution based on expert evaluation of the current scientific evidence.

There are many local examples of HIAs: for instance, city- or country-specific projects have been conducted in France, Italy, Spain and the UK. Table 8.1 gives several examples of HIAs at regional, national and multi-city scales.

There are inherent uncertainties associated with the process of quantification in HIAs: evaluating population exposure, taking into account population susceptibilities, or attributing a monetary value to a life. As a result of these uncertainties and of variations in input data and assumptions, comparisons between HIAs may reveal inconsistencies. However, despite this, all HIAs conclude that pollution contributes substantially to public health problems. Estimates of the impacts of (changes in) pollution on health, and the cost implications of this, are an important tool for policy-makers and may enhance the implementation of better, science-based regulations.

Box 8a

Small changes in lung function: big impact on public health

Although the reported effects of air pollution on human health are accepted by the majority of scientists, the impact on the population is often underappreciated. The relevance of this impact can be exemplified in the context of respiratory health.

Epidemiological studies of air pollution and lung function reveal a difference of a few per cent in lung function for a difference in exposure of, for instance, 10 $\mu g \cdot m^{-3}$ in fine particle concentrations. From a clinical perspective, a difference in lung function of that size is irrelevant.

So why are the epidemiological findings of any significance? Because epidemiological studies do not report the percentage change in lung function of any individual person but rather the overall shift in the distribution of lung function occurring in populations with higher levels of exposure. This shift in the population mean is illustrated in figure 8a.1 using forced vital capacity (FVC) as a measure of lung function loss.

Such a shift in fact represents a "leftward" shift in the population lung function distribution: in other words, an increase in the number of people with clinically relevant decrements in lung function (for example, those with a FVC <80% predicted). This results in an increase in the number of patients with pathological degrees of lung function deficit, with the concomitant increase in morbidity, costs and premature mortality.

New epidemiological results suggest that air pollution may also affect the pulmonary development of children. It is likely that a child suffering a pollution-related lung function deficit will continue to have less healthy lungs throughout his or her life. And as for adults, small decrements in lung function early in life may lead to important public health consequences later on. The evaluation of this long-term public health impact remains incomplete, because we lack a complete understanding of the link between loss of lung function in early life and future morbidity and mortality.

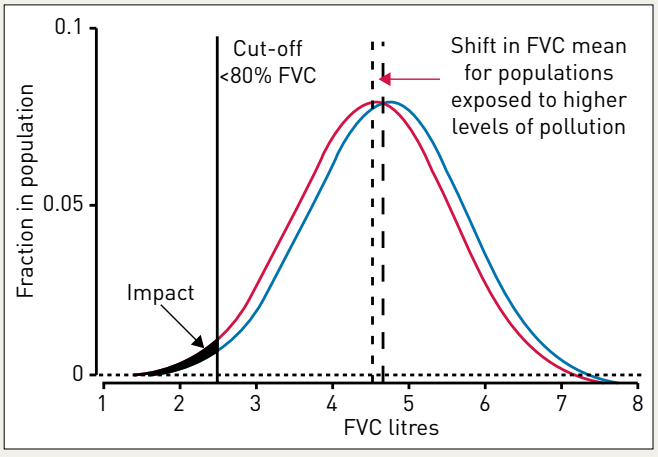

Figure 8a.1. The impact of a small shift of the population mean forced vital capacity (FVC) and its impact on the number of subjects with FVC <80% predicted (area under the curve approximately doubled by black area). Adapted from [46].

Box 8b

We all die: why care about air pollution?

Many risk assessments provide estimates of the number of deaths attributable every year to air pollution. These are based on widely used methods and this is a very common approach in communicating the extent of public health risks – it is used in particular to express the burden of smoking. However, the air pollution research community has advanced the discussion about the strength and limitations of using "attributable deaths" when referring to long-term effects.

Death is ultimately never preventable and if a birth cohort is followed for long enough, everybody dies – no matter how clean the air is or how many subjects smoke. Moreover, the derived rate of attributable deaths does not remain constant over time. Due to changes in the age distribution in a population in which age-specific mortality rates decrease due to removing a risk factor (such as air pollution), the population does, in essence, get older. Therefore, the total (absolute) number of deaths gradually *increases* as the population ages and, thus, the calculated attributable deaths will gradually decrease.

Translating attributable deaths into years of life lost resolves these inconsistencies. Assuming that life is in fact shortened by air pollution, the health benefits attributable to sustained improvement in air quality can be expressed in terms of the gain in the life expectancy of a population. In HIAs, gains in life expectancy for a specific air pollution scenario are the difference between the life expectancy calculated using observed age-specific mortality data for the population, and the revised life expectancy calculated using age-specific mortality data modified to take into account the envisaged change in air pollution levels.

Several cohort studies have estimated losses or gains in life expectancy related to changes in air quality. Estimates include reductions in life expectancy of 1.11 years in the Netherlands, 1.37 years in Finland and 0.80 years in Canada resulting from increases in ambient $PM_{2.5}$ concentrations of 10 $\mu g \cdot m^{-3}$. A recent ecological study investigated the association between life expectancy across the USA and changes in the community-level air quality. This study produced very similar results to cohort studies, attributing a 7-month gain in life expectancy to a 10 $\mu g \cdot m^{-3}$ improvement in ambient $PM_{2.5}$ concentration [47].

Expressing results in terms of changes in life expectancy has its own limitations and, like the concept of attributable death, requires some assumptions. Life expectancy is in fact a rather theoretical concept; thus, the communication of such estimates can pose a challenge, while attributable deaths are easily understood. However, the advantages of the life expectancy measure are likely to lead to a broader use of "years of life lost" to express the benefits of improvements in air quality.

9.
THE ROLE OF PHYSICIANS AND HEALTH PROFESSIONALS

How physicians and health professionals can influence the various levels of preventive action to reduce exposure and health effects.

The health effects of air pollution have a lot in common with those related to active or passive smoking (see Chapter 6). However, environmental problems pose a rather different set of challenges to physicians and other health professionals.

Four target levels of action may result in a reduction of the health impact of air pollution. The first two levels act on the environment rather than the individual: 1) abatement of ambient air pollution at the source to improve ambient air quality; and 2) reduction of pollution in the indoor environments where people spend most of their time. The other two downstream strategies depend entirely on the individual: 3) individual action to reduce personal exposure or dose; and 4) treatments taken to modify personal responses to air pollution, and/or to strengthen defence mechanisms.

ACTION TARGET 1: ABATEMENT OF AMBIENT AIR POLLUTION

Sustained improvement of air quality through the reduction of emissions is the most important strategy. Stringent air-quality regulations are needed to improve air quality (see Chapter 4). The role of health professionals is the same as that of any informed citizen: to call for and support air-quality regulations. The opinions of health professionals on health-related issues can be influential in the decision-making process. To publicly defend the scientific evidence, which calls unambiguously for better air quality in large areas of Europe and the world, is thus a very relevant role for physicians and other health authorities.

ACTION TARGET 2: REDUCING INDOOR POLLUTION OF OUTDOOR ORIGIN

People spend most of their time indoors. The most prevalent problem for indoor air quality is still environmental tobacco smoke, and other indoor sources – fireplaces, kerosene heaters and consumer products (or, in certain regions, radon from underground) – may influence air quality in the home more than outdoor air pollutants. In the absence of indoor pollution sources, however, indoor levels of "outdoor" pollutants are strongly dependent on outdoor air quality. People may have some – albeit limited – means to reduce the impact of outdoor pollution on indoor air quality. Concentrations of highly reactive gases such as ozone are far lower indoors with ultrafine particles from fresh exhaust tend to accumulate over time and with proximity to sources. So measures such as opening windows only outside rush hour times and hours with high ozone levels may help to minimise indoor air pollution.

Concentrations of several ambient air pollutants are lower in air-conditioned rooms such as modern offices and public indoor spaces. On the other hand, air conditioning uses a lot of energy, and thereby may add to outdoor pollution levels, depending on the type of power generation. A contentious question is whether patients – in particular those with respiratory diseases – should invest in indoor air filter systems. While air cleaners with HEPA filters do indeed reduce PM concentrations in experimental indoor settings, very few studies have confirmed that the use of such HEPA filters improves health under real-life conditions. While the possible benefits should not be dismissed, such solutions must be weighed against costs, energy consumption, nuisance caused by the device and the relative importance of exposure during time spent in all other places. People should be discouraged from buying "air cleaners" that produce ozone or other gases known to have adverse health effects.

ACTION TARGET 3: MODIFYING PERSONAL EXPOSURE OR DOSE

Air pollution will remain a reality for many years to come, so adverse health effects will be inevitable. In light of this fact, people might be interested in pursuing personal strategies to reduce their exposure or dose, in spite of poor air quality. Personal exposure and dose depend on location and time–activity patterns.

Location matters

People living within 50–100 m of a busy road face much higher exposure to traffic-related pollutants. Health risks ultimately depend on distance to the road, traffic density and type (*e.g.* stop-and-go, uphill/downhill, diesel trucks/buses), as well as urban structure and wind direction. Concentrations of primary traffic-related pollutants dilute to background levels within only a few dozen to hundreds of metres. They are also lower in the upper levels of multi-storey buildings than in the ground floor.

Patients as well as young families may have options to make healthier choices if they have access to appropriate advice. While individuals cannot influence ambient levels of pollutants directly, and moving may not be possible, they may have options about where to spend their time. Walking along roads where traffic flow is heavy results in far higher exposure than using an adjacent street with low or no traffic (*e.g.* a pedestrian zone). Given the known health effects (see Box 6D), jogging along highways and busy roads should be discouraged and alternative routes with lower levels of pollution should be chosen instead. Consequently, day care institutions, schools and sports grounds should not be placed next to busy roads.

Time and activity matters

Ambient concentrations of many air pollutants have typical diurnal patterns, *e.g.* with higher pollution during rush hours, or peaks in oxidants (summer smog) in the afternoon and early evening. The dose of pollutants reaching the target organs increases with physical

activity. Therefore, choices about time and activity levels ultimately affect exposure and dose. What constitutes a "high pollution period" in one area may be considered normal in other, more polluted, cities. Therefore, it is not possible to give recommendations for limiting activity at distinct pollutants concentrations. Generally, in periods of summer smog, outdoor activities requiring endurance (distance events, soccer, *etc.*) should be shifted to morning hours. At times of very high particulate pollution, schools may choose to organise their sporting events in indoor arenas rather than outdoors.

Under conditions of extreme air pollution, people may opt to wear masks. The health benefits of wearing masks against the adverse effects of ambient air pollution has not been investigated in the general population. Masks cannot provide full protection against exposure to ambient air pollutants. PM exposure – in particular the fine and coarse fractions as well as the dust – can be reduced to some extent. It is known from investigations of occupational exposure that the fit of a mask is much more important than the type of filter [48].

ACTION TARGET 4: CLINICAL ACTION AND PREVENTIVE TREATMENT – THE ROLES OF PHYSICIANS

Clinical role

The clinical problems caused by air pollutants are not specific, and therefore stringent diagnostic proof that a patient suffers from a problem related to ambient air pollution is most probably impossible. The treatment and counselling of patients suffering from health problems "possibly related to air pollution" is no different from dealing with these health issues when they have other causes. The risks of exacerbations of chronic diseases such as asthma or COPD as well as cardiovascular problems increase during periods of higher pollution. Patients may be advised to comply with preventive treatments during such periods. In some cities, monitoring data and/or short-term prognosis of air pollution concentrations are readily available and may guide susceptible patients.

Preventive role
Counselling

Patients may know about air pollution-related health effects and/or may confront physicians with their opinions, beliefs and fears about air pollution. Clinicians need to put air pollution into the rational and broader context of a patient's life and personal situation. The comparison of this environmental risk with other health-relevant factors the patient may be exposed to is relevant here. First and foremost, physicians should explain to smokers that the risk related to air pollution is incomparably smaller than the one due to the smoking habit – and it is far easier and more effective to change the latter. Parents who smoke must understand that passive exposure of children to smoke poses a health risk of similar magnitude to that posed by ambient air pollution.

Preventive interventions

Should doctors treat patients to protect them against the adverse effects of air pollution? The literature on the interaction of air pollutants with preventive treatments is limited.

Antioxidants and vitamins. Many ambient air pollutants are very strong oxidants. Moreover, endogenous oxidative stress is a consequence of effects mediated by the effects of ambient air pollution. It is therefore plausible to expect that antioxidants could have a role in defending against the effects of air pollution. There have been very few controlled studies in this area. Two have been conducted, in Mexico and the Netherlands, looking at the modifying role of antioxidant vitamin supplements on the respiratory effects of air pollution in children (fig. 9.1). It is uncertain whether the findings can be extrapolated to other areas of the world, other health outcomes and other age-groups. The role of a healthy diet – with fruit and vegetables rich in antioxidants – is acknowledged in the prevention of various diseases in general. As a "no-regret" strategy, it is therefore appropriate to inform patients about a possible protective role of antioxidants against at least some of the health effects related to air pollution.

Asthma treatments. The responses of asthmatics to air pollutants are not specific and therefore treatment against the effects of air pollution is the same as treatment for asthma in general. Clinical studies have shown that leukotriene receptor antagonists and salmeterol decrease pollutant-induced bronchoconstriction in asthmatics. Corticosteroids may attenuate inflammatory response to ozone, but they do not influence pollutant-induced lung function decrease. New research is focusing on the induction of enzymatic antioxidant defences, especially for individuals with increased-risk genetic variants of

key antioxidant enzymes [23]. The evidence from panel studies on asthmatics investigating symptoms or lung function effects related to pollutants is not consistent. Some studies observed fewer distinct pollutant effects in asthmatics on anti-inflammatory therapy, possibly due to a protective effect of this medication. Others found a stronger effect, possibly due to the fact that the group of asthmatics using anti-inflammatory therapy consists of the more severe cases.

Statins. Statins have anti-inflammatory properties. Interactions of these drugs with the inflammatory effects of air pollution are conceivable but have rarely been investigated. Therefore, to prescribe statins in an attempt to abate effects of air pollution would be an entirely inappropriate interpretation of the current evidence.

Genetic counselling. Genetic make-up is also a determinant of a subject's susceptibility to the effects of ambient air pollution. As shown in Annexe 1, a range of biological pathways underlies the mechanisms linked with the effects of ambient air pollution. Thus, functional variants of genes along these pathways might also affect the biological effects of air pollution. So far, the literature on this gene–environment interaction is very slim and potentially affected by a publication bias favouring positive findings. A stream of such studies is expected to be published in the future. While these results will be of high scientific interest, they cannot give guidance to physicians on how to advise patients. In addition, there are inherent limitations of gene-based counselling for preventive measures regarding environmental health effects.

Inherent limitations of preventive treatment. The contribution of drugs, vitamins or single genetic variants to the amplification or reduction of the effects of air pollution is uncertain but it is not expected to be large. In contrast to strategies that tackle the environmental problem and exposure *per se*, preventive action at the individual level will remain limited, costly and ultimately inefficient.

In summary, the focus of prevention must be on improving ambient air quality. All other actions are less efficient and unsustainable, and shift the burden of action from causes to individuals. Individual strategies are more likely to target acute effects only, so long-term effects may occur regardless. The individual approach raises problems of compliance and applicability. It further amplifies environmental injustice, in that the socially deprived have far less opportunity to adopt personal preventive strategies.

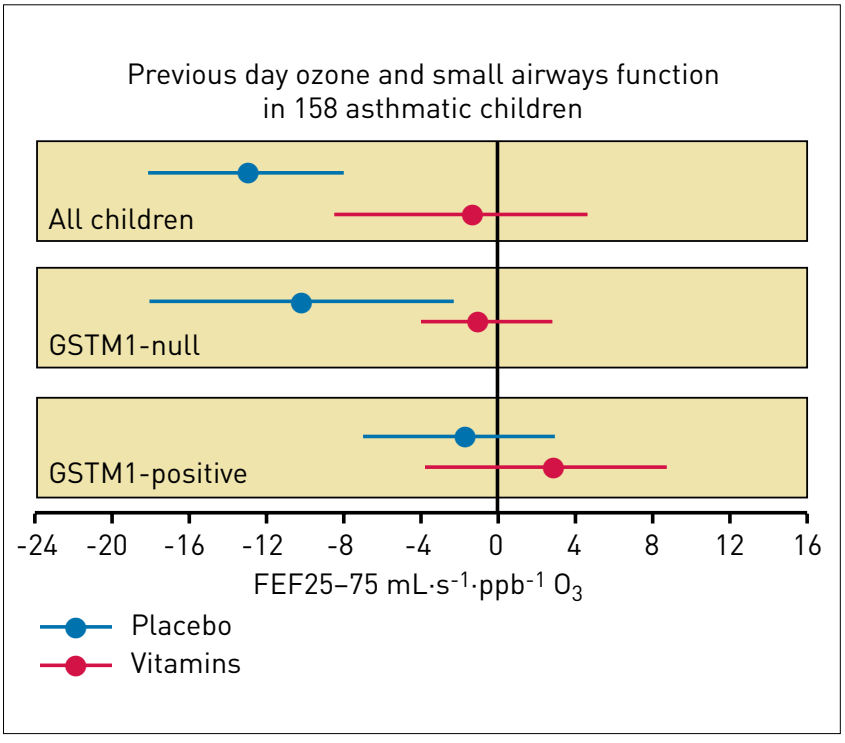

Figure 9.1. **The association between small airway function, indicated by FEF25–75, and ambient ozone concentrations (previous day) in 158 asthmatic children participating in an 18-month controlled intervention study. Associations were particularly strong among those not taking antioxidant supplementation. Moreover, the effects of ozone were much stronger too among those with a non-functional variant in the GSTM gene – relevant in oxidative defence mechanisms. Modified from [10, 49].**

10.
ANNEXE 1: EMISSION AND AIR-QUALITY REGULATION IN EUROPE

Emission regulation framework in Europe

In the European Union, at Member State level, the National Emission Ceilings Directive (NEC Directive 2001/81/EC) imposes emission ceilings for emissions of four key air pollutants (NOx, SOx, non-methane VOCs and NH_3) that harm human health and the environment. The proposal to amend the NECD is still under preparation and should set emission ceilings to be respected by 2020 for the four already regulated substances and for the primary emissions of PM2.5 as well. The revision will also take into account the European Union legislation for specific source categories, such as the Euro 5/6 emission standards for on-road heavy- and light-duty engines, the revision of the integrated pollution prevention and control (IPPC) directive (Directive 2008/1/EC) and the decision of the European Council of March 2007 to reduce greenhouse gas emissions by 20% and to have 20% renewable energy by 2020. To help reach NEC emission targets, current European Community legislation includes a directive on the reduction of emissions from large combustion plants and various recent directives on vehicle emissions, the quality of gasoline and diesel fuels and the sulphur content of certain liquid fuels. A directive on the storage and distribution of petrol and the Solvents Directive on the reduction of emissions from the industrial use of organic solvents both aim to limit emissions of VOCs. On December 21, 2007, the Commission adopted a Proposal for a Directive on industrial emissions (IED). The Proposal recasts seven existing Directives related to industrial emissions into a single clear and coherent legislative instrument. The recast includes in particular the IPPC Directive.

Table A1.1. Air emissions reduction targets for the European Union and its member states under the directives of the EU (NECD, 2001) and UNECE-CLRTAP

POLLUTANT	EMISSION REDUCTION REQUIRED	TIME PERIOD[1]
SO_2	63%	1990–2010
NOx (as NO_2)	41%	1990–2010
VOC (non-methane)	40%	1990–2010
NH_3	17%	1990–2010

NECD: National Emission Ceilings Directive; UNECE-CLRTAP: United Nations Economic Commission for Europe -Convention on Long-range Transboundary Air Pollution; EU: European Union; [1] The first year of the period constitutes the reference year. Source: EC, 2001c; UNECE, 1999.

At the international level, air pollution emission ceilings are also addressed by the United Nations Economic Commission for Europe Convention on Long-range Transboundary Air Pollution (the LRTAP Convention) and its protocols. The Gothenburg "multi-pollutant" protocol under the LRTAP Convention contains national emission ceilings that are equal to or less ambitious than those in the NEC Directive.

AIR-QUALITY REGULATION FRAMEWORK IN EUROPE

Air-quality regulation in Europe is currently legislated by the existing European Union (EU) air-quality policy framework. This legislation has established health-based standards and objectives for a number of air pollutants. Specifically, council Directive 1999/30/EC relates to limit values for SO_2, NO_2 and NOx, PM10 and lead (Pb) in ambient air. The directive is the so-called "First Daughter Directive". The directive describes the numerical limits and thresholds required to assess and manage air quality for the pollutants mentioned.

The EU recently adopted a new air-quality directive, the Directive on Ambient Air Quality and Cleaner Air for Europe (Directive 2008/50/EC). It is the first EU directive to include limits on ambient concentrations of PM2.5 (fine particulate matter). In addition, it requires reducing exposure to PM2.5 in urban areas by an average of 20% by 2020 based on 2010 levels. The directive also accounts for the possibility to discount natural sources of pollution when assessing compliance against limit values and for time extensions of three years (PM10) or up to five years (NO_2, benzene) for complying with limit values, based on conditions and the assessment by the European Commission. This new directive consolidates various existing pieces of air-quality legislation into a single directive. Governments have been given two years (from June 11, 2008) to bring their legislation in line with the provisions of the Directive.

Although the new air-quality directive is a step forward towards reducing air pollution in Europe, leading environmental health scientists emphasised that the current scientific evidence calls for much more stringent standards. The new EU PM2.5 limit value will not

adequately protect public health. Moreover, the exclusion of all 'natural' PM from compliance considerations is without scientific evidence and further jeopardises the protection of public health from PM_{10}. The new directive sets target values less stringent than those adopted by several EU member states, or the USA, for example. The new directive also does not follow the guidelines developed by the World Health Organization in 2005. These WHO guidelines are neither standards nor legally binding criteria, but were designed to offer guidance to policy-makers in reducing the health impacts of air pollution based on expert evaluation and current scientific evidence.

The table below presents a comparison of the current EU target with selected guidelines and standards in Europe, the USA and Japan.

Table A1.2. **Clean air policy targets set by different authorities**

Source	SO_2 µg·m^{-3}				NO_2 µg·m^{-3}			PM10 µg·m^{-3}		PM2.5 µg·m^{-3}		Ozone µg·m^{-3}	
	1 year	24 hr	1 hr	10 m	1 year	24 hr	1 hr	1 year	24 hr	1 year	24 hr	8 hr	1 hr
WHO [21]		20		500	40		200	20	50[a]	10	25[a]	100	
European Union (revised 2008) [50]		125[a]	350[f]		40		200[e]	40	50[b]	25		120[f]	
Switzerland [51]	30	100[d]			30	80[d]		20	50[d]				120[d]
France [52]	50	125[a]	350[f]		40		200[e]	40	50[b]				
Sweden [53]		100	200		40	60	90	40	50				
UK [54]		125[a]	350[f]	266[b]	40		200[e]	40	50[b]	25		100	
Japan [55]		105	262			113			100				118[c]
USA [56]	78	366			100			50	150	15	65	157	
California [57]		105[c]	655				470[c]	20	50	12	65	137	180[c]

[a]: Not to be exceeded more than 3 days per year; [b]: Not to be exceeded more than 35 days per year; [c]: Photochemical oxidants; [d]: Not to be exceeded more than one time per year; [e]: Not to be exceeded more than 18 times a year; [f]: Not to be exceeded more than 24 times a year. Modified from [21].

ANNEXE 2: SINGLE POLLUTANTS AND THEIR EFFECTS

This Annexe provides a pollutant-specific perspective on toxicity and health effects. It is restricted to ozone, nitrogen oxides, particulate matter, diesel exhaust and carbon monoxide. It summarises the main results from experimental studies collected in the WHO air-quality guideline report [21].

INTRODUCTION

The penetration of a pollutant in the respiratory tract is dependent on the type of pollutant and may ultimately drive specific health effects. The site of absorption on an inhaled gas is related to its solubility in water. The less water soluble the gas, the further down it will penetrate the respiratory tree. So sulphur dioxide is mainly absorbed in the conducting airways whereas ozone and nitrogen dioxide spread to the lower respiratory tract and penetrate to the alveoli. The penetration depth of particulate matter depends on the particle size. Particles larger than 10 μm are kept in the humid environment of the mouth and nose, smaller particles penetrate the respiratory tract, and particles smaller than 2–3 μm enter the alveolar region. Very small, so-called ultrafine particles (<0.1 μm) are less well cleared by the alveolar macrophages than larger particles and remain longer in the alveolar region. In addition, their surface area is much larger compared with the surface of an equivalent mass of larger particles. This large surface area facilitates the absorption and dissolution of gases and soluble material as salts, acids or transition metals.

Oxidative stress is suggested as the main mechanism leading to local and systemic inflammation following inhalation of pollutants. A first step may be through the generation of reactive oxygen species in the lung cells from the contact with carbon core of inhaled particles where toxic substances such as sulphates, nitrates and metals are adsorbed. Markers for local inflammation in the airways include inflammatory cells as neutrophils and macrophages in induced sputum or bronchoalveolar lavage, protein concentrations, cytokines as interleukines IL-6, IL-8, IL-10, cell adhesion molecules, and TNF-α. A noninvasive marker for increased inflammation, especially in asthmatics linked also with pollution levels, is exhaled nitric oxide in breath. Local inflammation may be the reason for enhanced airway responsiveness as shown in clinical studies for several pollutants. In asthmatic patients, worsening inflammation may increase airway responsiveness to allergens. This has been shown for ozone and also suggested for particles.

The propagation of the inflammation to the circulation may come about through the transport of mediators as cytokines and inflammatory cells through the alveolar epithelium to the blood. Results of animal studies showed that ultrafine particles enter the circulation and may also trigger inflammation in the endothelial tissue, changes in coagulation parameters and effects in other target organs directly. Translocation of particles in the circulation has not yet been demonstrated satisfactorily in humans. The extent to which particles can penetrate organs such as the liver, heart or brain, is currently under study.

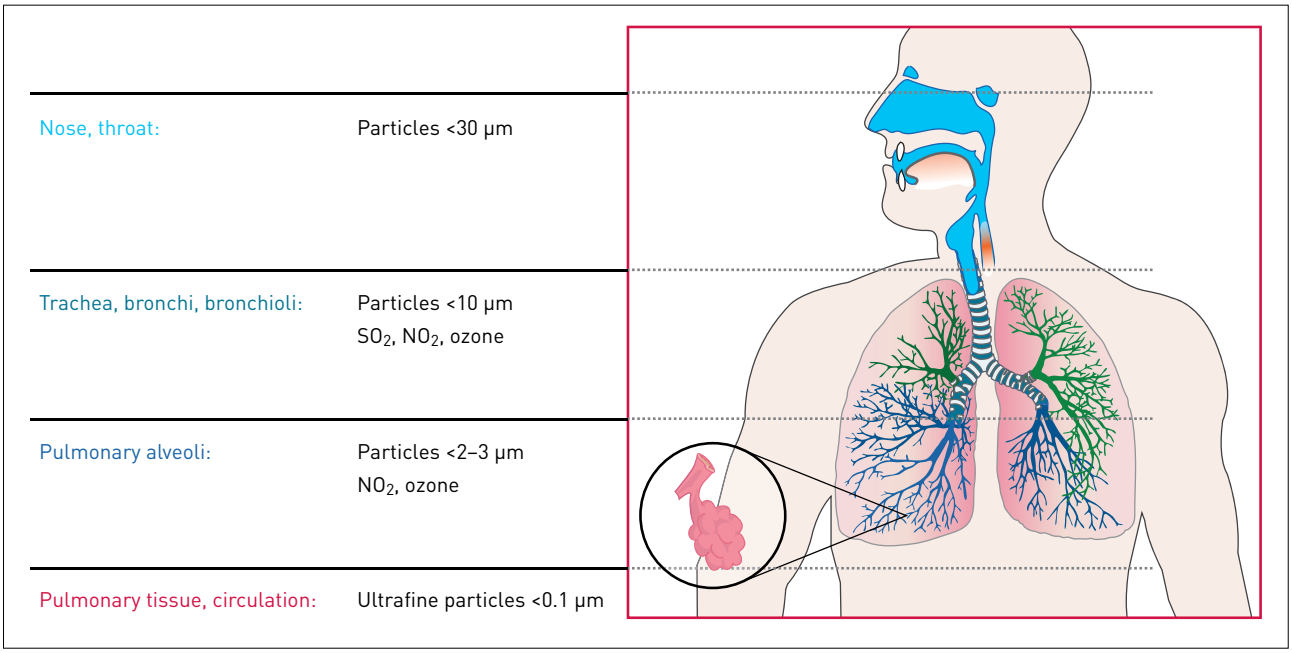

Figure A2.1. **Penetration depth of pollutants in the respiratory tract**

Table A2.1. **General pathophysiological effects of inhaled pollutants**

TRACHEA, BRONCHI	Irritation of mucous membranes, local inflammation, changes in mucous compounds, immigration of inflammatory and immune defence cells
	Impairment of ciliar activity, impairment of epithelial clearance, *e.g.* of upward transport of particles, bacteria, *etc.*
	Constriction of bronchia through muscular spasm and swelling of mucosa
PULMONARY ALVEOLI	Impairment of ability of immune cells to ingest and dissolve foreign material and debris
	Local inflammation, change in permeability of cell membranes
	Transfer of inflammatory proteins and of ultrafine particles in the pulmonary tissue and the circulation
CIRCULATION	Inflammation in endothelia of blood vessels, enhanced formation of plaques, coagulation, thrombosis
	Changes in regulation of autonomic nervous system, *e.g.* heart rate variability.

OZONE (O_3)

Ozone is a highly reactive gas and potent irritant with strong oxidative activity in the airways. It reacts with the antioxidants in the epithelial lining fluid (mainly glutathione, ascorbic acid, uric acid, albumin and tocopherol) and may lead to a depletion of antioxidants and imbalance between oxidants and antioxidants in the extracellular fluid and in the cells, so-called oxidative stress. This leads to oxidation and structural changes in molecules and to reactive products of protein and lipid origin. Free radical reactions induce the cascade of inflammation in the airways, such as an increase in polymorphonuclear leucocytes, albumin, total protein, cytokines (*e.g.* interleukin-6), LDH and MPO.

A wide range of controlled human studies have consistently shown a significant impairment of the lung function through short-term ozone exposure down to levels of 120 $\mu g \cdot m^{-3}$ over 6.6 hours of exposure. These effects are paralleled by respiratory symptoms and an enhanced bronchial reactivity. The severity of the response is dependent on the concentration of ozone, the duration of the exposure, and the ventilation rate, or physical activity, of the individuals. The changes are reversible but may last up to 24 hours after the end of the exposure.

There is a large individual variation in response to ozone, which is not yet fully understood. In the clinical setting, the responsiveness for symptoms and lung function changes was strongest in young adults. It was diminished in elderly people, in contrast to time-series studies on mortality, where short-term relationships to ozone were more consistent in older individuals. Polymorphisms in genes coding oxidant defence mechanisms (*e.g.* in glutathione-S-transferase genes or TNF-genes) may also convey a higher susceptibility. Other factors to heighten sensitivity to ozone may be pre-existing inflammatory airway disease as asthma, impaired immune mechanisms and concomitant exposure to other pollutants or allergens. People with chronic bronchitis and smokers are not generally more affected, and not all people with asthma show a stronger response. However, many or most people with extrinsic asthma show an enhancement of the response to inhaled allergen after a prior exposure to ozone.

Compared with ozone effects in panel studies, the effects in

controlled exposures are smaller. One reason is suggested to be the longer duration of the overall exposure in the environment: not limited to 8 hours, or even 1 hour with the maximum daily concentration. Another reason may be concomitant exposure to other oxidants in summer smog. After several repeated exposures the response of lung function to ozone is attenuated, but this so-called adaptation disappears after a few days without ozone exposure.

PARTICULATE MATTER (PM)

PM in urban and non-urban environments is a complex mixture with components having diverse chemical and physical characteristics. Experimental studies have shown that PM *per se* may be responsible for the range of health effects observed in population studies.

First, controlled exposure studies of humans have shown that ambient PM has direct effects on the respiratory tract. These effects mainly involve production of an inflammatory response, exacerbation of existing airway disease (*e.g.* hyperreactivity) or impairment of pulmonary defence mechanisms. Inhaled PM may thus increase the production of antigen-specific immunoglobulins, alter airway reactivity to antigens or affect the ability of the lungs to handle bacteria, suggesting that exposure may result in enhanced susceptibility to microbial infection. In recent years, studies using concentrated ambient air particulate matter (CAPs) have also focused on cardiovascular endpoints. The advantage of these studies is that they use exposure that is closer to real conditions than other experimental studies. Short-term exposures of human volunteers and laboratory animals at concentrations near the upper bound of current ambient PM levels have been associated with statistically significant changes in heart rate, heart rate variability, abnormal heartbeats, arrhythmias, and in flow changes in brachial arteries. Where compositional data were available, these effects were most closely associated with the inorganic components, *i.e.* EC and trace metals.

In studies on animals, subchronic exposures to particles from ambient air at concentrations approximating the current annual US $PM_{2.5}$ standard of $15 \mu g \cdot m^{-3}$ have produced persistent changes in heart rate, heart rate variability, enhancement of aortic plaque size, changes in brain cell distribution and function; fatty liver deposits; and progression of the metabolic syndrome. The results on cardiopulmonary outcomes provide biological plausibility for the association observed between cardiovascular outcomes, including building of atherosclerosis plaque, and air pollution, detected in several epidemiological studies.

DIESEL MOTOR EXHAUST

Diesel cars are an important contributor to particulate and gaseous exposure in urban areas. In clinical studies with volunteers who were exposed to diluted exhaust from diesel motor and to filtered air for 1 or 2 hours, lung function was generally not changed in healthy subjects, whereas in asthmatics bronchial reactivity was increased. Concomitantly, diesel exhaust induced neutrophilic inflammation with increased secretion of cytokines and number of neutrophils. In the lowest particle dose, these reactions were limited to the bronchi, whereas in the alveolar region, the same inhaled dose led to an increased production of antioxidant substances, suggesting that this represents a first line of defence. Two recent studies in young healthy volunteers showed that diesel exhaust and ozone have additive effects on airway inflammation.

Clinical studies have also shown that allergic people may be especially at risk from diesel exhaust exposures through different mechanisms. First, pollen allergens may bind on diesel particles facilitating the transport and deposition in the airways. Secondly, it is known from experiments on animals that the allergic inflammation is enhanced by the interaction between diesel exhaust particles and the immune system. The secretion of reactive oxygen species by diesel-activated macrophages could play an important role in this process. People with variants in glutathione-transferase genotype are less able to detoxify reactive oxygen species and may be most affected by diesel particle-induced exacerbation of allergic symptoms.

A few recent clinical studies have focused on the cardiovascular health effects of diesel exhaust, with some interesting results. Healthy young persons did not show changes in blood pressure, heart rate or heart rate variability after exposure to diluted diesel exhaust, but showed signs of vascular dysfunction and impaired fibrinolysis. Some changes persisted up to 24 hours after exposure. Similarly in coronary patients, blood pressure and heart rate were not different between diesel exhaust exposure and filtered air, but in the exercise periods during exposure to diesel exhaust significantly larger S-T segment depressions were observed. In contrast to

the healthy subjects, no changes were seen in vascular function, whereas some indicators of fibrinolysis were changed as well.

NITROGEN DIOXIDE (NO_2)

NO_2 is a gas that appears reddish and has a pungent smell when present at concentrations above several hundred $\mu g \cdot m^{-3}$. It reacts with organic compounds on the surface of the respiratory epithelium and enters the circulation mainly as nitrite (NO_2^-). In animals, acute exposures NO_2 in concentrations as they occur in ambient air have rarely been observed to cause effects. Subchronic and chronic exposures (weeks to months) to low levels caused a variety of effects, including alterations to lung metabolism, structure and function, as well as inflammation and increased susceptibility to pulmonary infections. Due to the inherent differences between mammalian species and the lack of information available on tissue response of different species to a given dose of NO_2, it is difficult to extrapolate quantitatively the effects that are caused by a specific inhaled dose or concentration to humans.

Controlled human exposure studies investigating the effects of NO_2 were used as the basis for establishing the current WHO 1-hour guideline value of 200 $\mu g \cdot m^{-3}$. These studies show health effects at lower levels more consistently in asthmatic patients than non-asthmatics. In asthmatic patients, nitrogen dioxide concentrations as low as 380–560 $\mu g/m^3$ for periods of one hour or longer may enhance bronchoconstriction, the reaction to allergens and a range of responses within the lung suggestive of airway inflammation and alteration in lung immune defences.

In healthy adults, concentrations of NO_2 in excess of 1,880 $\mu g \cdot m^{-3}$ (1.0 ppm) are necessary to induce changes in pulmonary function

CARBON MONOXIDE (CO)

CO is an odourless, colourless and tasteless gas that binds to haemoglobin with an affinity 250 times that of oxygen to build carboxyhaemoglobin (COHb). COHb is also an endogenous product of metabolism, with levels in healthy people up to 1.4%. Fever or certain medications may elevate this level up to 4%, smoking increases the COHb levels dose-dependently. Contrary to other gases, the adverse health effects associated with exposure to CO are not related to lung injury. COHb interferes with the blood's ability to carry oxygen, with adverse effects mainly to the brain and heart. Therefore, exposure to high levels of carbon monoxide (above 580 $mg \cdot m^{-3}$) can lead to respiratory failure and death. In clinical studies, low-level exposures to CO cause adverse health effects in people with coronary artery disease when they exercise. In these studies, COHb levels of 2–6% have been associated with cardiovascular endpoints such as shortening of time to onset of angina. This could limit the daily activities of susceptible individuals and affect their quality of life. Some other clinical studies have suggested that CO exposure may increase the risk of sudden death from arrhythmia. Continuous exposure to levels less than 10 $mg \cdot m^{-3}$ should not cause COHb levels >2% in healthy nonsmokers.

Experimental research in animals suggests that low exposure to CO may be related to the development of atherosclerosis.

11. ABBREVIATIONS

$\mu g \cdot m^{-3}$	micrograms per cubic metre
95% CI	95% confidence interval
ACS	American Cancer Society Study
APHEA	Air Pollution and Health: a European Approach
APHEIS	Air Pollution and Health: a European Information System
APHEKOM	Improving knowledge and Communication for Decision Making on Air Pollution and Health in Europe
BS	black smoke
CAFE	Clean Air For Europe
CO	carbon monoxide
CO_2	carbon dioxide
COPD	chronic obstructive pulmonary disease
CRF	concentration-response function
DALY	disability-adjusted life years
EC	Elemental carbon
EPA:	Environmental Protection Agency
EU	European Union
FEF_{25-75}	forced midexpiratory flow rate
FEV1	forced expiratory volume in 1 s
FVC	forced expiratory vital capacity
GBD	Global Burden of Disease
GSTM1	glutathione-*S*-transferase Mu 1 gene
HIA	health impact assessment
LRTAP	long-range transboundary air pollution
NEC Directive	National Emission Ceilings Directive
NH_3	ammonia
NO_2	nitrogen dioxide
O_3	ozone
OR	odds ratio
Pb	lead
PM	particulate matter
PM_{10}	particulate matter with aerodiameter <10 micrometers
$PM_{10-2.5}$	particulate matter with aerodiameter 10–2.5 µm
$PM_{2.5}$	particulate matter with aerodiameter <2.5 µm
POP	persistent organic pollutant
RR	relative risk
SO_2	sulphur dioxide
TSP	total suspended particles
UF	ultrafine particles
UNECE	United Nations Economic Commission for Europe
VOC	volatile organic compounds
WHO	World Health Organization

12.
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European Respiratory Society Avenue Ste-Luce 4 1003 Lausanne Switzerland
T + 41 21 213 01 01 F + 41 21 213 01 00 E info@ersnet.org W ersnet.org

Authors: Nino Künzli, Laura Perez, Regula Rapp.