The Health Impact of Air Pollution

An expert report of the International Society for Environmental Epidemiology (ISEE) and the European Respiratory Society (ERS)

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Abstract

The air pollutants particulate matter, ozone and nitrogen dioxide affect the health of populations in Germany, as well as in Europe. The effects start in the lung, but air pollution has impacts on the entire body. In 2005, the World Health Organization (WHO) revised the 2005 global Air Quality Guidelines for particulate matter, ozone and nitrogen dioxide [1], recommending values that are exceeded in many places in Germany [2]. Those pollutants have been proven to reduce life expectancy and induce respiratory and cardiovascular diseases [3]. Since 2005, scientific evidence showing health effects of all three pollutants has increased substantially. The carcinogenic effect of particulate matter is now considered to be proven [4]. Furthermore, adverse effects on foetal development during pregnancy [5, 6, 7], lung and brain development in children [8, 9], diabetes [10, 11] and dementia [12] have been shown. Importantly, recent studies have documented that adverse effects can be observed at concentrations below the current WHO guideline values [13-15]. In particular, the EU standard for particulate matter smaller than 2.5 µm (PM2.5) should be lowered considerably and brought into line with the recommendations of the World Health Organization.

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What are the air pollutants particulate matter, ozone and nitrogen oxides?

Particulate matter consists of particles less than 10 micrometres in size. It has many sources [16]: particulate matter is generated by motor vehicles, power plants, home furnaces and heaters as well as industrial facilities that directly release such particles. In addition, these sources emit the gaseous pollutants sulphur dioxide and nitrogen oxides that, along with ammonia emissions from agriculture, contribute to the formation of particulate matter in the atmosphere and thereby to pollution [17]. Particulate matter can also arise from natural sources, for example by soil erosion or particles that originate from plants and microorganisms.

Ozone is formed close to the ground from pollutant precursors, mainly nitrogen oxides and volatile organic compounds, through photochemical processes by intense solar radiation [18].

Nitrogen oxides (nitrogen monoxide and nitrogen dioxide) are released during combustion processes. The main sources of nitrogen oxides are internal combustion engines and coal, oil, gas, wood and waste incinerators. In urban areas, road traffic is the main source [19]. Nitrogen oxides are also major precursors of ozone and contribute to the formation of particulate matter.

How do the air pollutants particulate matter, ozone and nitrogen dioxide affect the lung?

Particulate matter is inhaled into the lung through the airways. In particular, particulate matter smaller than 2.5 µm (PM2.5) is able to get into the smallest airways and pulmonary alveoli. Ultrafine particles under 100 nanometres in size may also enter the blood circulation and thereby reach other organs. The adverse health effects of the particles are due to a wide variety of chemical and physical properties, which mainly cause oxidative stress and inflammatory reactions throughout the body [20]. The particles that we inhale are a mixture from many sources. Experimental studies have identified particles from combustion processes as especially hazardous to health [21].

Ozone and nitrogen dioxide are irritant gases and have oxidation capacity. They penetrate deeply into the lungs, cause oxidative stress [22], provoke inflammatory reactions and interact with pulmonary wall structures. Nitrogen monoxide on the other hand, a substance that is also produced by the body, is harmless to the human body [23].

How are the effects of air pollutants investigated in scientific studies?

Experiments on cells and animals, controlled exposure of volunteers to pollutants, and epidemiological studies contribute to the overall scientific evidence on the health effects of air pollutants. In total, more than 71,000 studies are currently available in the medical literature. The primary purpose of experimental studies is to examine the adverse effects of air pollutants on health due to their chemical and physical properties and to understand the mechanisms by which they interact with cells and organs. Human exposure studies investigate short-term effects. Large-scale epidemiological observation studies are the method of choice for assessing the long-term effects on public health. Large cohort studies are especially worth mentioning in this regard, as they are able to include children or patients with health problems.

What diseases are caused by air pollutants?

Particulate matter can cause respiratory diseases and cardiovascular disorders, resulting in lower life-expectancies [24, 25]. The effects range from short-term health effects such as hospital admissions, and ultimately to death. Such effects may occur acutely in response to high concentrations of particulate matter or as a consequence of long-term exposure [cf. 3]. The evidence for lung cancer and cardiovascular diseases is now recognised as “causal”, and the evidence for other respiratory diseases as “probably causal” [26]. In addition, it is probable that air pollution exposure has effects on the whole body [5], especially on foetal development during pregnancy [6, 7], lung and brain development in children [8, 9], diabetes [11] and dementia [12].

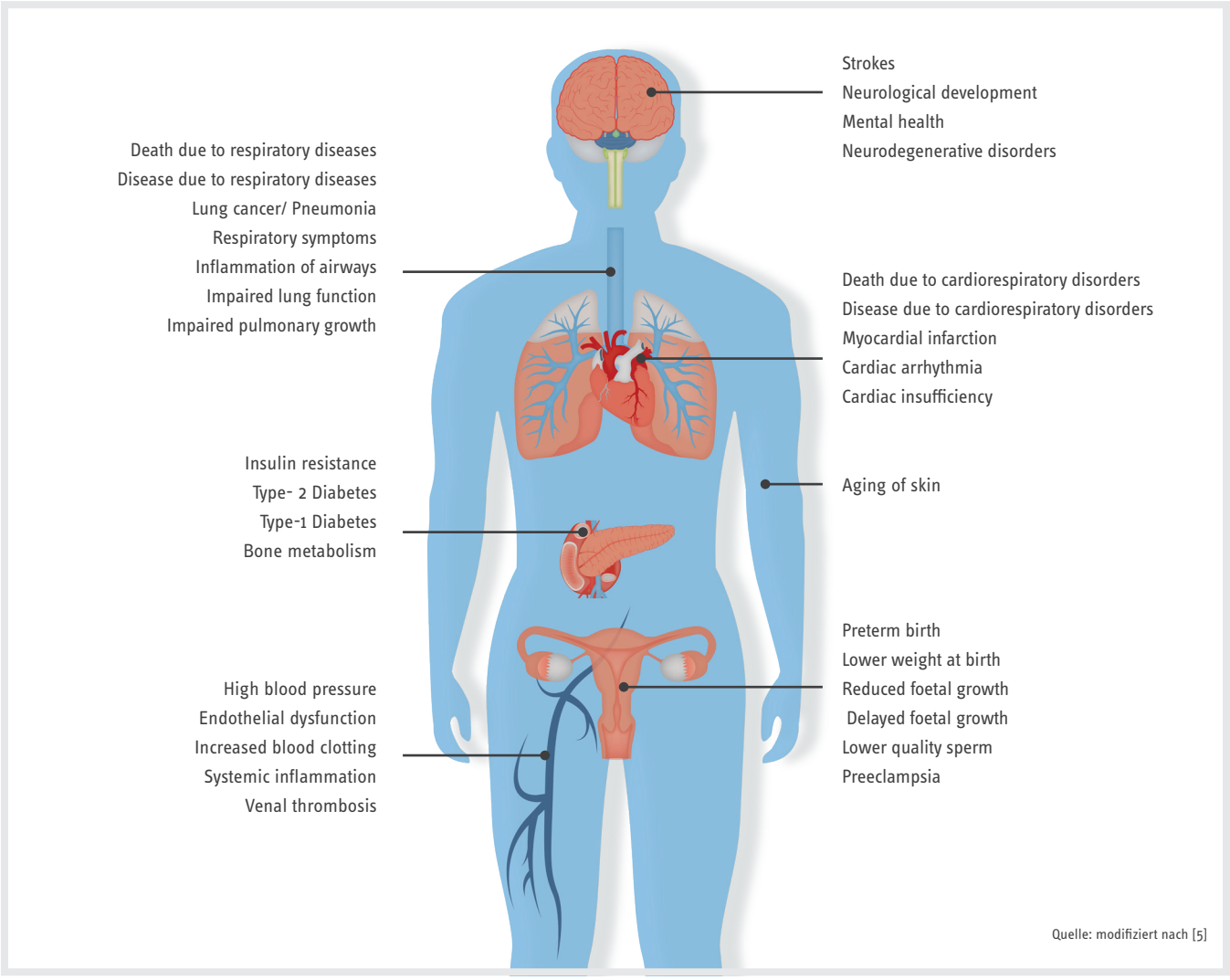
Ozone leads, in the short-term, to increased mortality due to respiratory diseases and to increases in respiratory-related emergency treatment and hospitalisation, effects which are classified as “causal” [27]. Short-term ozone exposure is classified as “probably causal” with respect to the increase in overall mortality and in cardiovascular mortality. Long-term exposure to ozone pollution is correlated with increased respiratory-related mortality, an increased numbers of asthma cases and exacerbated symptoms among asthma-patients, which is also classified as “probably causal” [27].

Nitrogen dioxide leads to exacerbation of health problems among asthmatics and is classified as “causal” [28, 29]. It is classified as “probably causal” for the occurrence of other respiratory diseases [29]. Recent studies [30-34] and a systematic review [35] also indicate an association with cardiovascular diseases [30-35] and diabetes [35].

The following table summarises these established relationships, which are based on published assessments up to 2016. Relationships are considered to have been proven to be causal if sufficient studies are available that 1) rule out the influence of random associations, biases and other confounding factors, and 2) are based on environmentally relevant concentrations of pollutants. In general, relationships can be substantiated by observational studies as well as experimental studies. “Probably causal” refers to correlations where there are clear indications of a causal link but the current data are insufficient to satisfy all criteria of causality.

Pollutant	Effects on health	Assessment	Source
Particulate Matter (<2.5µm)	Death	causal	[26]
	Cardiovascular diseases	causal	[26]
	Lung cancer	causal	[4]
	Respiratory diseases	probably causal	[26]
Ozone	Short-term effects on respiratory diseases	causal	[27]
	Short-term effects on cardiovascular diseases	probably causal	[27]
	Respiratory diseases	probably causal	[27]
Nitrogen dioxide	Short-term effects on respiratory diseases	causal	[29]
	Respiratory diseases	probably causal	[29]

It should be noted, however, that the established causal effects constitute only part of the effects on health. The figure below (adapted from [5]) gives an overview of the effects on the whole body observed in population-based studies.



Symptoms resulting from exposure to air pollution cannot be clinically distinguished from the same symptoms that may have resulted from other causes. In practice, a physician cannot usually identify the immediate cause of a heart attack or of an asthma attack because there are often many different contributing causal factors.

Are the effects of air pollutants independent from one another?

Particulate matter, ozone and nitrogen dioxide have common sources, and often occur at the same time and place, and this affects the human body in combination [36]. Further, there are additional air pollutants, such as soot, ultrafine particles (tiny particle of just a few nanometres) or organic carbohydrates that may be present together with the particulate matter and nitrogen dioxide [3]. Particularly in the case of nitrogen dioxide, it is controversial whether the long-term effects are attributable to nitrogen dioxide alone or rather to a mixture of pollutants for which nitrogen dioxide is an indicator [3]. There is an urgent need for research to disentangle the contribution of correlated air pollutants, especially for soot and ultrafine particles [3].

How are the recommendations for guideline values derived?

International expert committees regularly summarise the available scientific literature. The scientific evidence is discussed intensively and evaluated according to systematic, transparent and reproducible criteria. The summaries are reviewed by third parties. The 2005 recommendations of the WHO were based on studies available at the time. It was particularly challenging to derive a target value for particulate matter and nitrogen dioxide because the epidemiological studies gave no indications of threshold values, below which no adverse effects on health are expected [1]. The recommended target value of 40 µg/m3 for nitrogen dioxide was determined on the basis of long-term animal studies and population-based studies [1].

The emergence of new scientific findings led the European Union to commission two technical reports in 2013, in which an updated analysis of the evidence for the WHO recommendations was conducted. These reports indicated that statistically significant effects on health were observed at nitrogen dioxide concentrations as low as 20 µg/m3 [3, 37], based primarily on a meta-analysis of more than 15 long-term nitrogen dioxide studies [25]. A comprehensive review of the 2005 recommendations based on the 2013 assessment [3] and additional scientific findings since then is currently in progress under the direction of the WHO.

How do recommendations become standards?

The definition of standards is a political process that takes scientific recommendations into consideration, including those of the WHO. In the European Union, the standards are adopted by the EU Parliament and incorporated into national law by means of implementation provisions. The European Union relies partially on the WHO recommendations. For example, in 2008 the WHO standard for nitrogen dioxide. In the case of particulate matter, a significantly less protective value of 25 µg/m3 was implemented, instead of the WHO recommended value of 10 µg/m3 for PM2.5.

United States legislation is derived from periodically updated scientific assessments required by law [26, 27, 29]. Overall, these region-specific procedures result in differences in legislation worldwide [38]. Europe urgently needs to reduce the standards on particulate matter in accordance with the latest scientific findings. In Switzerland, a standard of 30 µg/m3 was adopted for nitrogen dioxide, which was even lower than the 2005 WHO recommendations [39, 40]. To date, seven countries have implemented the WHO recommendations for particulate matter into their national legislation (average of 10 µg/m3 of PM2.5) [38]

Calculating the burden of disease from air pollutants

> Calculating the burden of disease reveals how strongly health risk factors affect the entire population and enables comparisons to show which risk factor gives rise to a particularly large number of diseases, reduced years of life expectancy or death. This can be used as a basis for setting priorities in prevention.

> Typical risk factors used in these comparisons to calculate the burden of disease includes smoking status, malnutrition, air pollution, noise and lack of exercise.

> The calculations follow a recognised method that is used on a regular basis by the WHO and other institutions. Comparative calculations are performed for individual countries and the entire world as part of the Global Burden of Disease Project conducted by the US-based Institute for Health Metrics and Evaluation (IHME). According to their results, air pollution is the ninth largest risk factor in Germany and is by far the greatest environmental risk factor for diseases and reduced life expectancy [49].

> Each year, the European Environmental Agency calculates the burden of disease for certain air pollutants, namely particulate matter, nitrogen dioxide and ozone, in order to provide Europe and the individual Member States with information about the importance of the air pollutants and to study trends in the burden of disease over time [50].

> These calculations are also performed in Germany to examine certain issues. Last year, for example, a study commissioned by the Environmental Office was published that investigated the burden of disease due to nitrogen dioxide in recent years [35]. It was determined that nitrogen dioxide, as an air pollutant or indicator of a mixture of air pollutants, has been observed to have adverse effects on life expectancy.

Current points of debate concerning the impact of air pollutants on health

"Smoking is far more toxic and the dosage is much higher, which is why no damage can occur from comparatively low doses of air pollution"

> There are many biological contexts in which the relationship between dosage and effect is not linear. Instead, the additional effects diminish as the dosage increases, as is well illustrated by the case of smoking: a smoker of 20 cigarettes a day has around a 100 % higher risk of heart attack than a non-smoker [41]. Despite the far lower dosage, exposure to passive (second-hand) smoking on a regular basis or smoking one cigarette per day increases the risk of a heart attack by about 50 % compared to individuals not exposed to cigarette smoke [42-45]. Long-term exposure to an additional 5 µg/m3 of particulate matter increases the probability of a heart attack by about 10 % [46]. Thus, the dose-to-effect ratio is not linear but rather flattens out as the dosage increases [41, 47]. If that non-linear relationship is taken into account properly, the effect sizes of exposure to the various air pollutants, passive smoking and active smoking combine well.

> Smoking and air pollution also differ for other reasons:
- The pattern of exposure is different: smoking involves intense exposure followed by breaks between cigarettes. Air pollution, on the other hand, causes continual daily and yearly exposure without interruption.
- Active smoking primarily affects adults, whereas air pollution also affects foetuses, infants, asthmatic children and the elderly.
- In principle, even though it can be incredibly difficult, we can control our smoking and quit on our own initiative, whereas air pollution cannot, or only with great difficulty, be avoided.

"There is no typical pattern of toxicity"

> **Particulate matter, ozone and nitrogen oxides** show a typical pattern of effects, such as oxidative stress and inflammatory reactions [e.g., 20, 48], with consequences similar to those of tobacco smoke. The best known pollutant is particulate matter. We know from countless experiments and observational studies that particulate matter causes inflammatory reactions in the lungs and entire body, promotes blood clotting, causes cardiac arrhythmia, increases arteriosclerosis and alters lipid metabolism. In addition, particulate matter can penetrate the brain or affect the foetus. Those same biological changes can be seen in active and passive smokers. The same diseases are produced, including heart attacks, strokes, respiratory diseases and lung cancer.

"Nobody dies from particulate matter or nitrogen oxides"

> This may be true, but according to that logic, nobody dies from smoking either. Nevertheless, we know that smoking, just like air pollution, is harmful over the long-term and can lead to potentially fatal diseases such as respiratory and cardiovascular illnesses. Such associations are only observable in long-term studies, however, rather than in the case of an individual patient or fatality. In the case of a single patient or a single death, it is almost always impossible to determine how the risk factors causally interacted to cause the illness or death. On the population scale, such associations can be expressed in terms of a reduction of life expectancy or years of life lost due to various risk factors such as smoking or air pollutants.

"The studies fail to take other risk factors into account and therefore result in a far too high burden of disease"

> This statement is false. Other health-related risk factors are taken into account very precisely in high-quality epidemiological studies (for example, smoking, physical inactivity, nutrition, education, income, etc.). The recognised methods of a high-quality observational study (such as epidemiological studies) expressly require taking all further health risk factors into account.

> It is likewise false to say that the studies merely compare the rural population with the urban population. On the contrary: most contemporary studies compare urban populations exposed to different degrees of pollution using estimates of long-term air pollution concentrations at each home address.

"The nitrogen dioxide limits in the USA are over twice as high, so nitrogen dioxide can't be all that bad"

> This is not quite true. The nitrogen dioxide limit in the USA (100 µg/m3) is truly higher than in the EU (40 µg/m3), but Americans have much stricter regulations on emissions, for example, on the level of nitrogen oxides in vehicle exhausts. This means they directly regulate the source (i.e., the automobile) much more stringently, so that German cars in America require a special upgrade. In the EU, 270 mg/km of nitrogen oxides in a vehicle exhaust is currently allowed, whereas the maximum permissible emissions level in the USA is 100 mg/km (nitrogen oxides and organic methane gases), meaning that the overall average emissions level of a motor vehicle is less than 20 mg/km. On the other hand, the EU follows the WHO recommendations and has adopted the WHO's recommended target value for atmospheric nitrogen dioxide. This means that the EU tends to focus on the concentrations of pollution that we actually breathe.

> Moreover, when regulating air quality, different pollutants such as particulate matter and nitrogen dioxide must be analysed in combination. The US regulations impose a very strict limit on particulate matter (i.e., 12 µg/m3 for PM2.5). In contrast, the EU limit on particulate matter is more than twice as high (25 µg/m3).

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