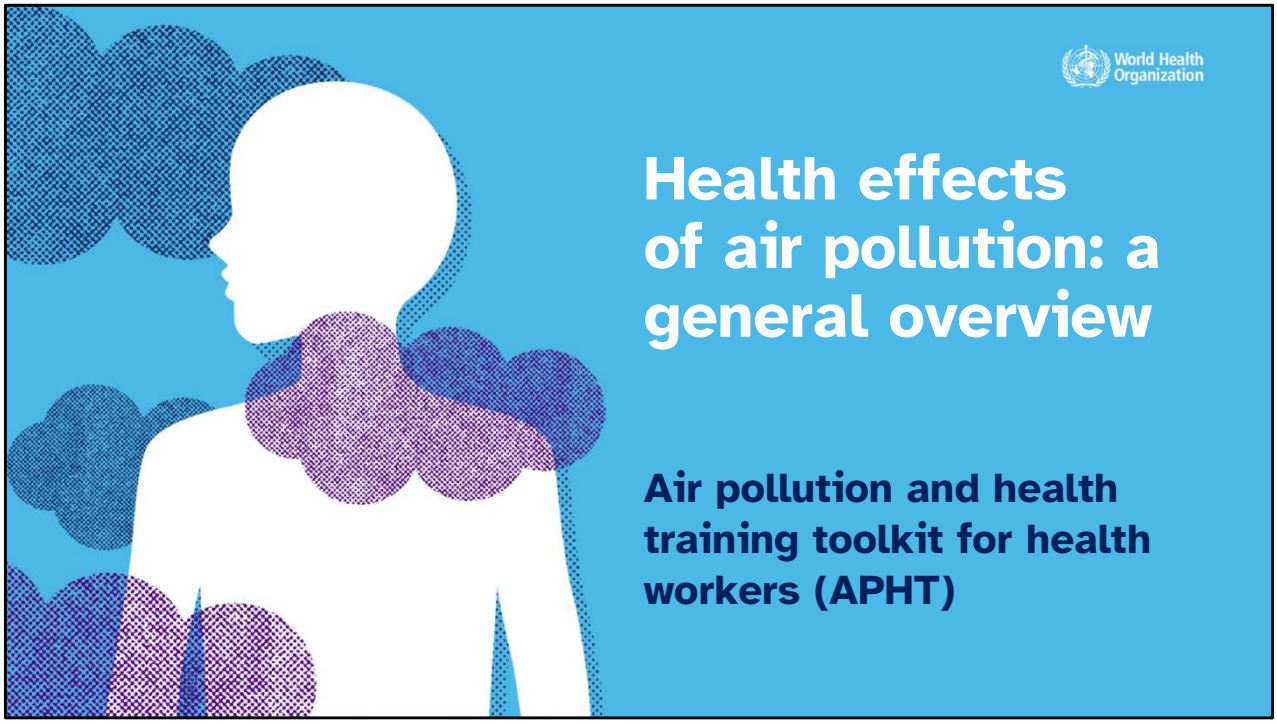


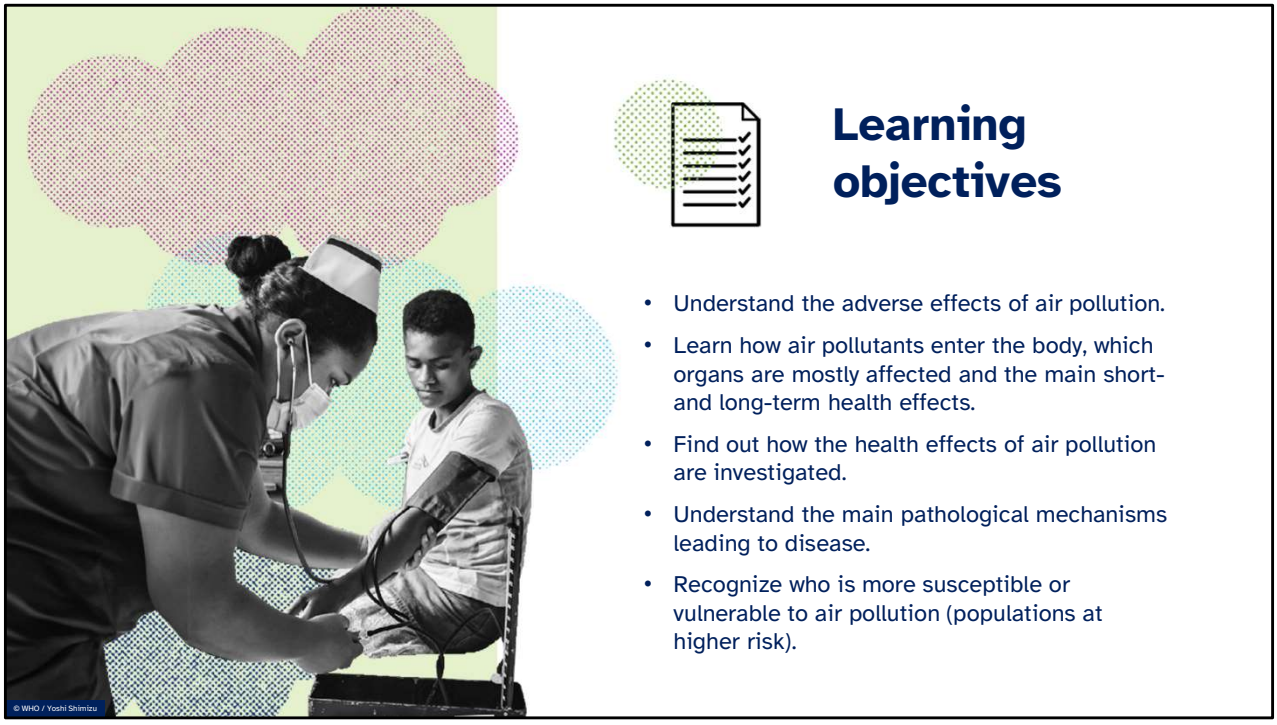
Notes

- The World Health Organization (WHO) reference number for the module ***Health effects of air pollution: a general overview*** is WHO/HEP/ECH/AQE/2024.5 © WHO 2024. Some rights reserved. This work is available under the CC BY-NC-SA 3.0 IGO licence.

- This module contains a large set of slides from which the presenter should select the most relevant ones to use in a specific presentation. These slides cover many facets of the problem. Present only those slides that apply most directly to the local or regional situation. Where relevant, you can adapt the information, statistics and photos within each slide to the particular context in which this module is being presented.

- This module belongs to the Air Pollution and Health Training toolkit targeting health workers (APHT). It has been developed in collaboration with more than 30 experts from government agencies, WHO collaborating centers, non-state actors, including medical and environmental health associations, as well as academic institutions. The methodology used for development included a mapping of existing air pollution and health training opportunities targeting health workers which informed gaps and needs for a global set of materials. Experts identified through existing collaborations with WHO contributed on the definition of outline and populating the training modules with contents. Peer review and pilot test coordinated by WHO ensured the collection of feedback and input for finalization of the products. WHO made all possible effort to ensure geographical and gender balance for the development of the training toolkit acknowledging limitations in terms of expertise, experience and overall feasibility. You can use and have access to other APHT modules where relevant. To see the full package visit: https://www.who.int/tools/air-pollution-and-health-training-toolkit-for-health-workers

- For more information on WHO's work on air quality, energy and health, please visit: https://www.who.int/teams/environment-climate-change-and-health/air-quality-and-health



Learning objectives for this module include:

1. Understand theadverse effects of air pollution.
2. Learn how air pollutants enter the body, which organs are mostly affected and the main short- and long-term health effects.
3. Find out how the health effects of air pollution are investigated.
4. Understand the main pathological mechanisms leading to disease.
5. Recognize who is more susceptible or vulnerable to air pollution (populations at higher risk).

Acronyms

ALRI	acute lower respiratory infection
ATS	American Thoracic Society
CNS	central nervous system
CO c	carbon monoxide
COHb	carboxyhaemoglobin
COPD	chronic obstructive pulmonary disease
CVD	cardiovascular disease
NOS	endothelial nitric oxide synthase
EPC	endothelial progenitor cells
ERS	European Respiratory Society
FEV_1	forced expiratory volume in 1 s
FVC	forced vital capacity
GSTM-1	glutathione S-transferase mu-1
HAP	household air pollution
HPA	hypothalamic-pituitary axis
IARC	International Agency for Research on Cancer
IHD	ischaemic heart disease
LMICs	low- and middle-income countries
MMP	matrix metalloproteinase
NADPH	nicotinamide adenine dinucleotide phosphate
NCD	noncommunicable disease
NF-kb	nuclear factor kappa
NO_2	nitrogen dioxide
O_3	ozone
PM	particulate matter
PM_{10}	particulate matter of diameter < 10 µm
$PM_{2.5}$	particulate matter of diameter < 2.5 µm
RNA	RiboNucleic Acid
RNS	reactive nitrogen species
ROS	reactive oxygen species
SDG	Sustainable Development Goal
SGA	small for gestational age
SO_2	sulfur dioxide
TLR	toll-like receptor
TNF	tumour necrosis factor
TRAP	traffic-related air pollution
VOC	volatile organic compound
WHO	WHO World Health Organization

Module outline

1. What are adverse health effects of air pollution?

- evolution in the definition over the years;
- pyramid of health effects of air pollution.

2. From exposure to illness:

- concentration, exposure, dose;
- routes of exposure.

3. Building the scientific evidence:

- epidemiological studies;
- toxicological studies.

4. General pathological mechanisms:

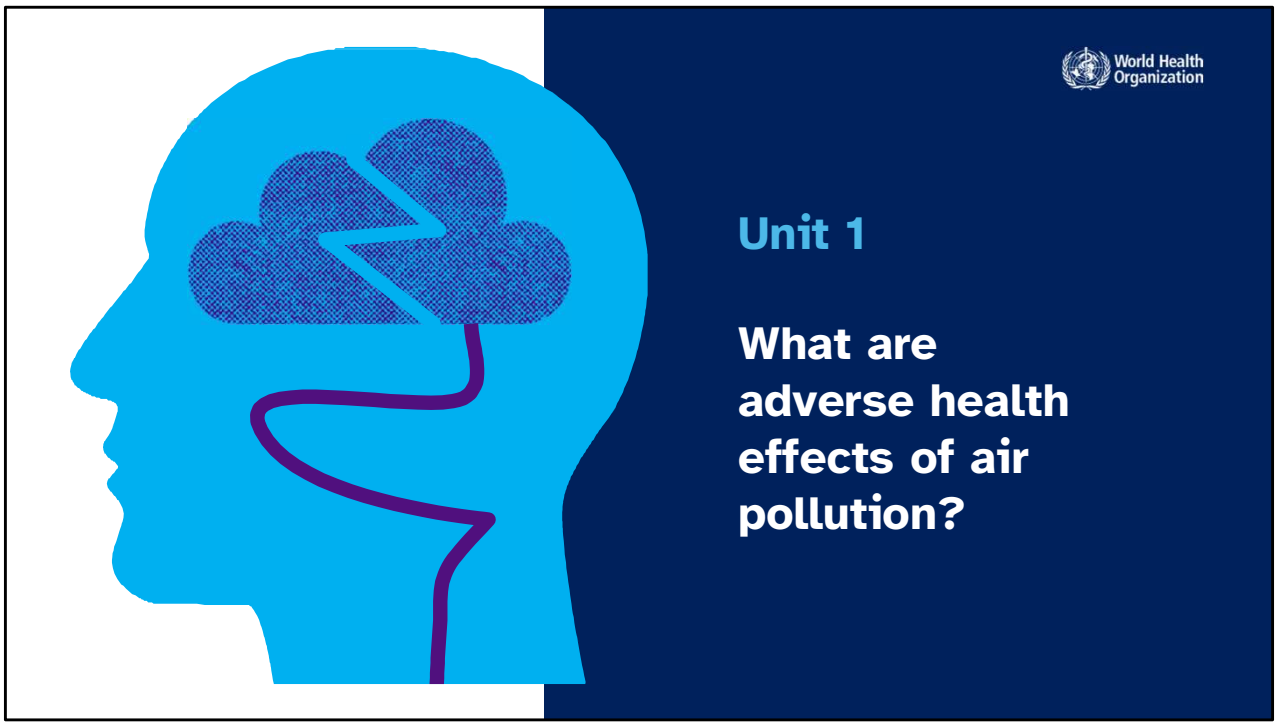
- main mechanisms leading to disease;
- a focus on $PM_{2.5.}$

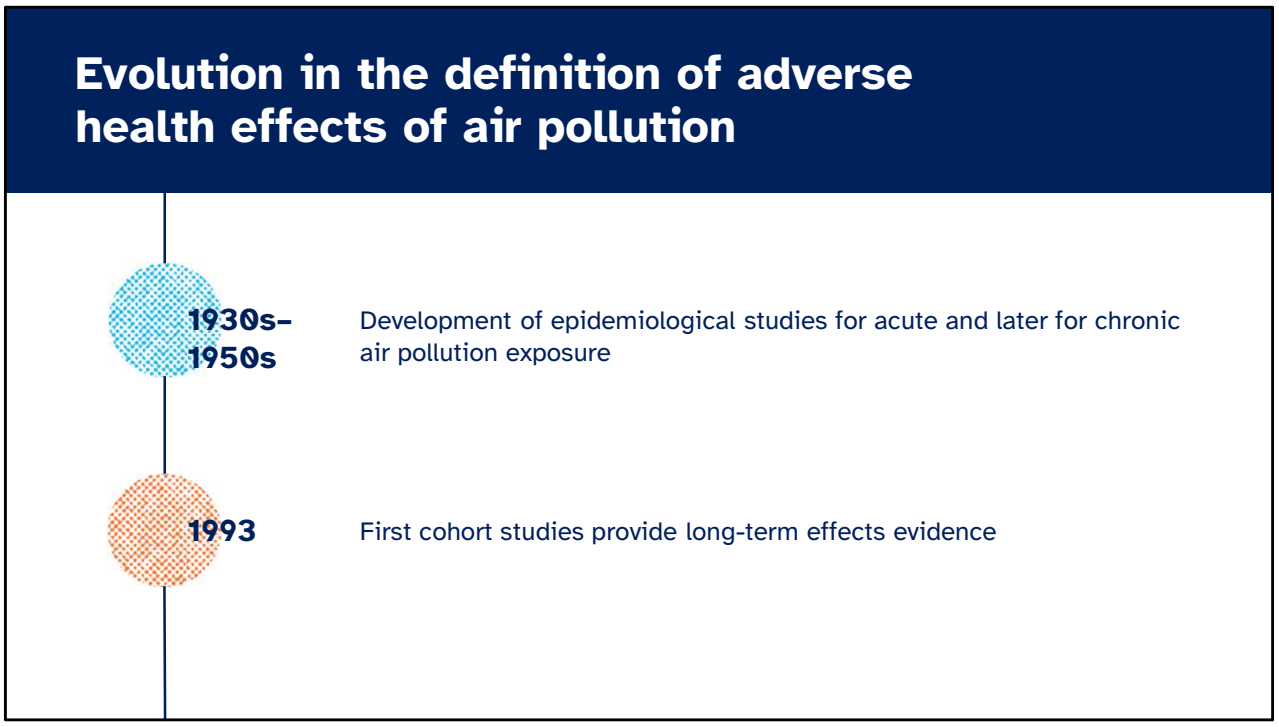
5. Effects of air pollution on health:

- global and regional data;
- short-term and long-term health effects;
- deeper dive of main health outcomes.

6. Population at higher risk:

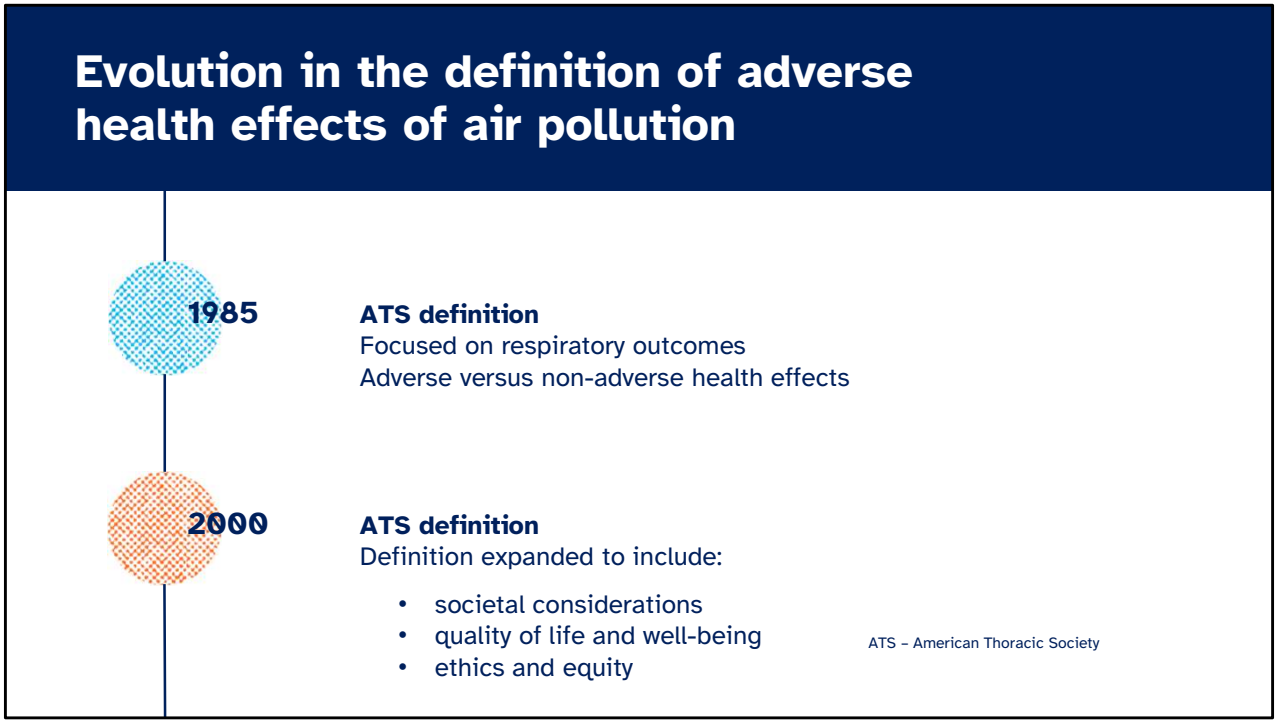
- susceptibility versus vulnerability;
- older people, women and children.


World Health Organization
Unit 1
What are adverse health effects of air pollution?



After episodes of acute exposure to air pollution in Europe (between the 1930s and 1950s) epidemiological research started collecting data that later offered evidence about the health effects of air pollution.

In 1993, the results of the first cohort studies in the United States of America were available linking air pollution and mortality exceedance for lung cancer and cardiopulmonary diseases.



In the last 30 years, important statements were made by medical societies.

The American Thoracic Society (ATS) provided its first definition of the adverse health effects of air pollution in 1985 including a distinction between reversible and irreversible effects. The definition was mainly focused on the respiratory outcomes. At the time, the distinction between adverse and non-adverse health effects was only based on medical and pathophysiological considerations.

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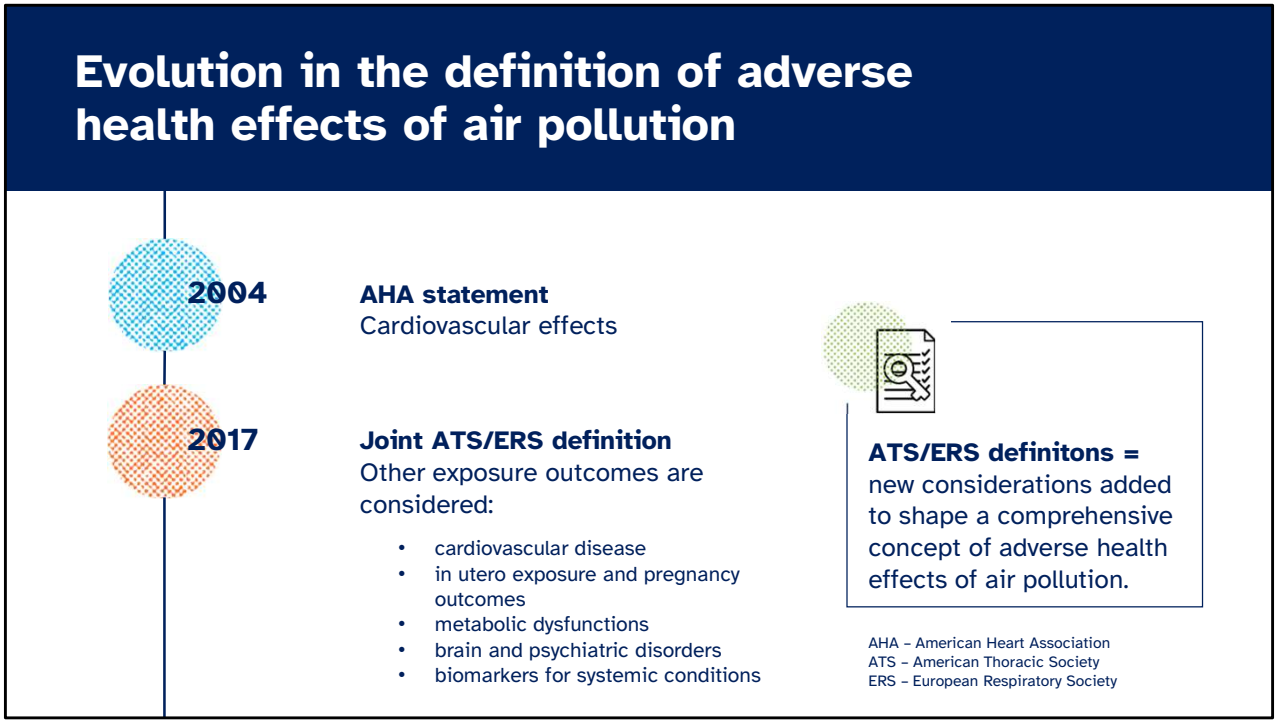

It was in the 2000s, that societal considerations, quality of life and well-being, as well as ethics and equity components, were included in the definition of adverse health effects.

In 2004, a statement from the American Heart Association (AHA) recognized the cardiovascular effects of air pollution exposure.

In 2017, an updated definition was jointly developed by the European Respiratory Society (ERS) and the America Thoracic Society. The scope was extended to other outcomes beyond respiratory to include cardiovascular diseases, in utero exposure and pregnancy outcomes, metabolic dysfunctions, neurological effects and psychiatric disorders.

The growing importance of the role of biomarkers for systemic conditions was also highlighted.

We should look at all these definitions as a progression of new considerations added to shape a comprehensive concept of adverse health effects of air pollution, rather than each statement replacing the previously released version.

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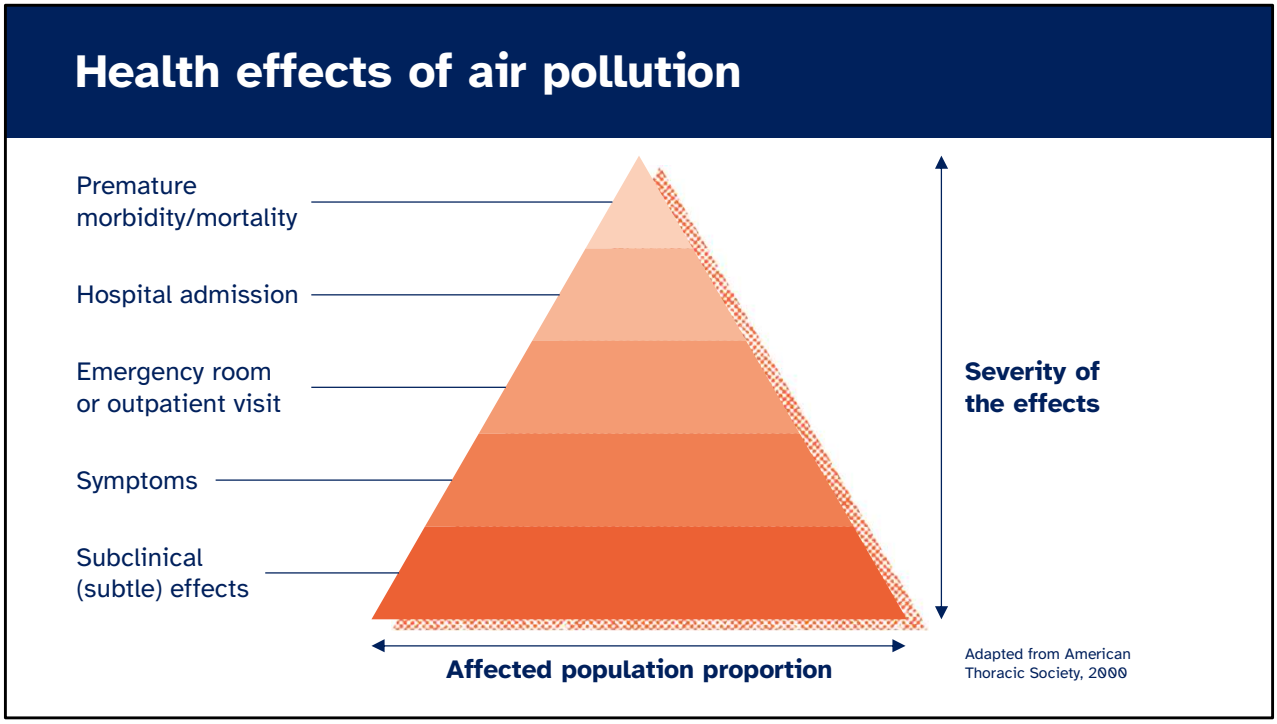

The symptoms and magnitude of the health effects of air pollution can be represented as a pyramid:

- the less frequent and most severe health outcomes are at the top of the pyramid; and
- the less severe effects, which are yet experienced by a larger proportion of the population, are displayed at the bottom.

At the top of the pyramid, we find **premature morbidity** and **mortality**.

By definition:

- premature means that the event occurs at any age lower than the life expectancy of a certain population;
- morbidity refers to the presence of diseases and implies a decrease in the quality of life.

Moving towards the base of the pyramid, we see increased hospital admissions, emergency room visits and/or outpatient visits which are due to the onset or exacerbation of symptoms that are the result of pathophysiological changes in the cardiovascular system, or for example impaired lung function due to air pollution exposure.

These initial changes in the body, at first undetectable at the clinical level, are called **subclinical**, or subtle, **effects**.

Subclinical effects are manifestations that don't always have recognizable signs or symptoms, but which lead to a reduction in quality of life as they represent the first stage of a variety of pathologies. Epidemiological and toxicological studies on air pollution are also based on these important subclinical health outcomes.

It is important to note that some diseases are attributable to a single pollutant and others are associated with multiple pollutants. In addition, some pollutants may cause a health effect after long-term exposure (months or years), whereas some may affect individual health within a few days. Pollutants can also interact with each other or may interact with other factors such as temperature.

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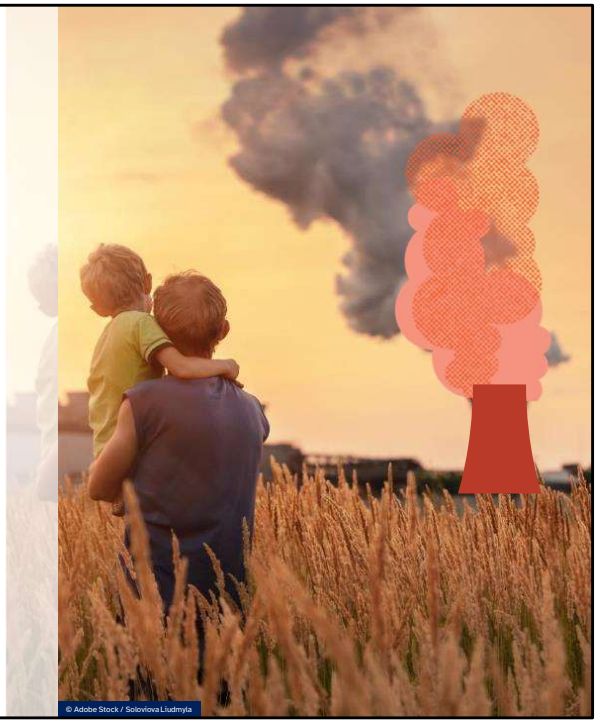
Subclinical effects don't always have recognizable signs or symptoms, yet could represent the first stage and increase the risk of more severe health effects.

Epidemiological and toxicological studies are also based on subclinical health outcomes.



Subclinical effects are manifestations that don't always have recognizable clinical signs or symptoms, but which could represent the first stage and increase the risk of more severe effects in otherwise healthy people.

Epidemiological and toxicological studies on air pollution are also based on these important subclinical health outcomes. Some examples are heart rate variability, hyperlipidaemia, or air inflammatory biomarkers.

Biomarkers are indicators of susceptibility, exposure, or effects. They can be measured for example in exhaled air, blood, or bronchoalveolar lavage fluid and other fluids like urine, breast milk and sputum.

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- American Thoracic Society. Guidelines as to what constitutes an adverse respiratory health effect, with special reference to epidemiologic studies of air pollution. Am Rev Respir Dis. 1985;131(4):666–9.
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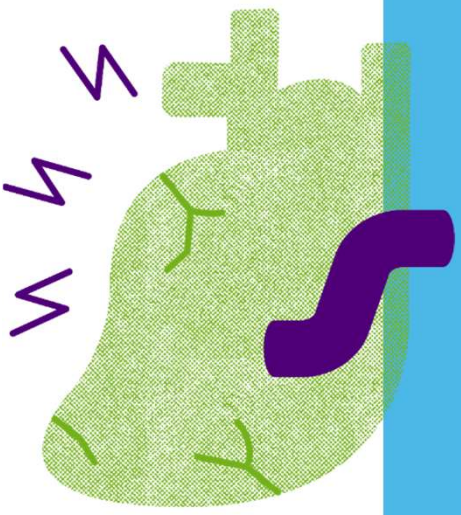
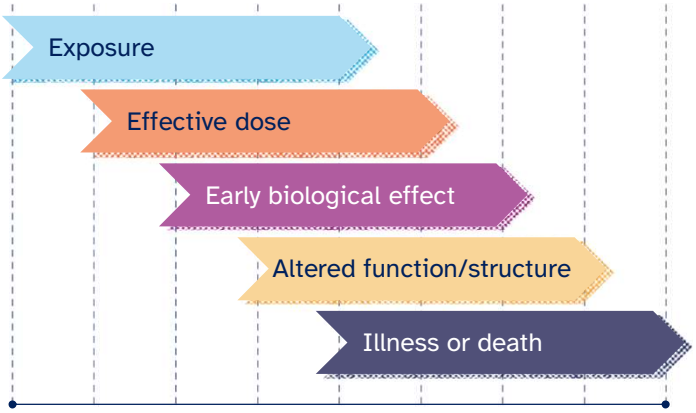


World Health Organization

Unit 2

From exposure to illness

Continuum between exposure and disease



There is no threshold of air pollution levels under which no negative effects are found.

When we determine how air pollution impacts human health, we usually assume a **continuum** or temporal sequence between the exposure and the health effects.

Once the individual has contact with a specific concentration of the pollutant in the environment – meaning this individual is exposed – the "**effective dose**" is the amount of the substance that interacts with a target site, such as the respiratory system or the eyes, over an interval of time to produce harm or illness.

Ideally, we should be able to observe a considerable gradient proceeding from left to right in the continuum between exposure and illness.

Even apparently healthy people are susceptible to the effects of long-term exposure to air pollutants, without initial detectable clinical signs.

Exposure can potentially accelerate the progression of a disease, or perhaps even initiate it or make it clinically diagnosable.

It is important to remember that science tells us that there is no threshold under which no negative effects are found.

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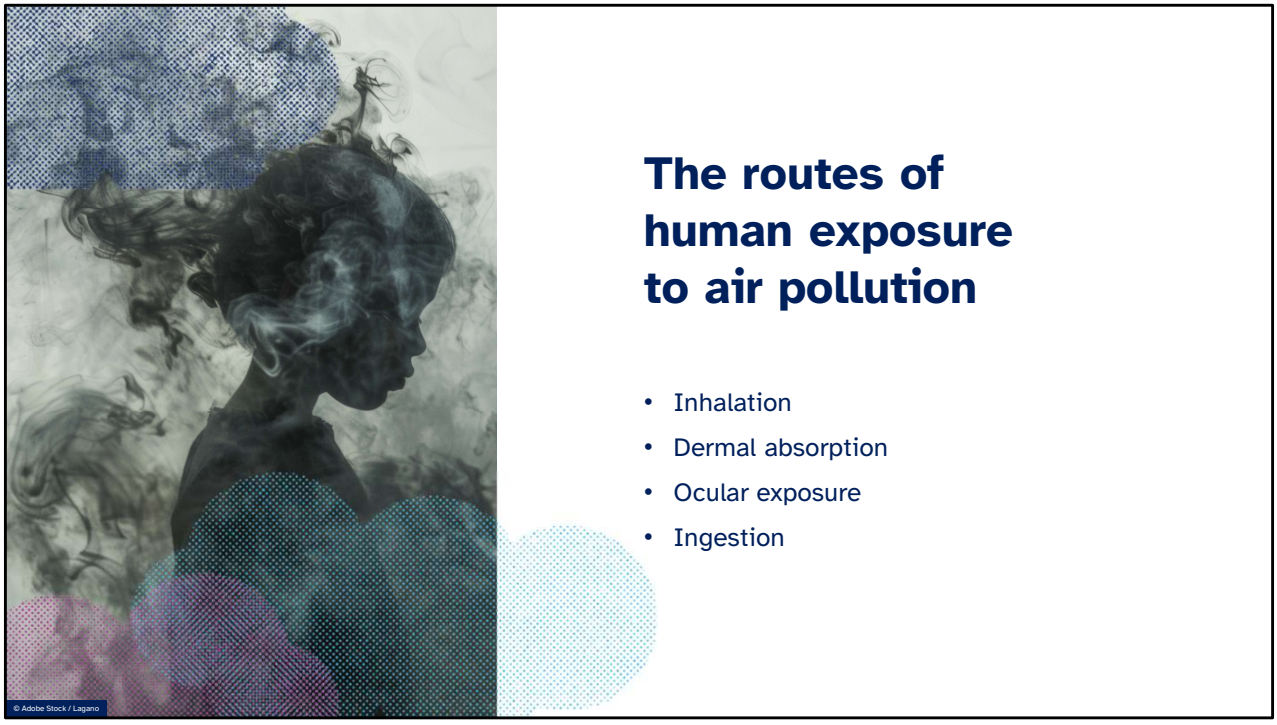

The routes of human **exposure** to air pollution include:

- inhalation
- dermal absorption
- ocular exposure
- ingestion.

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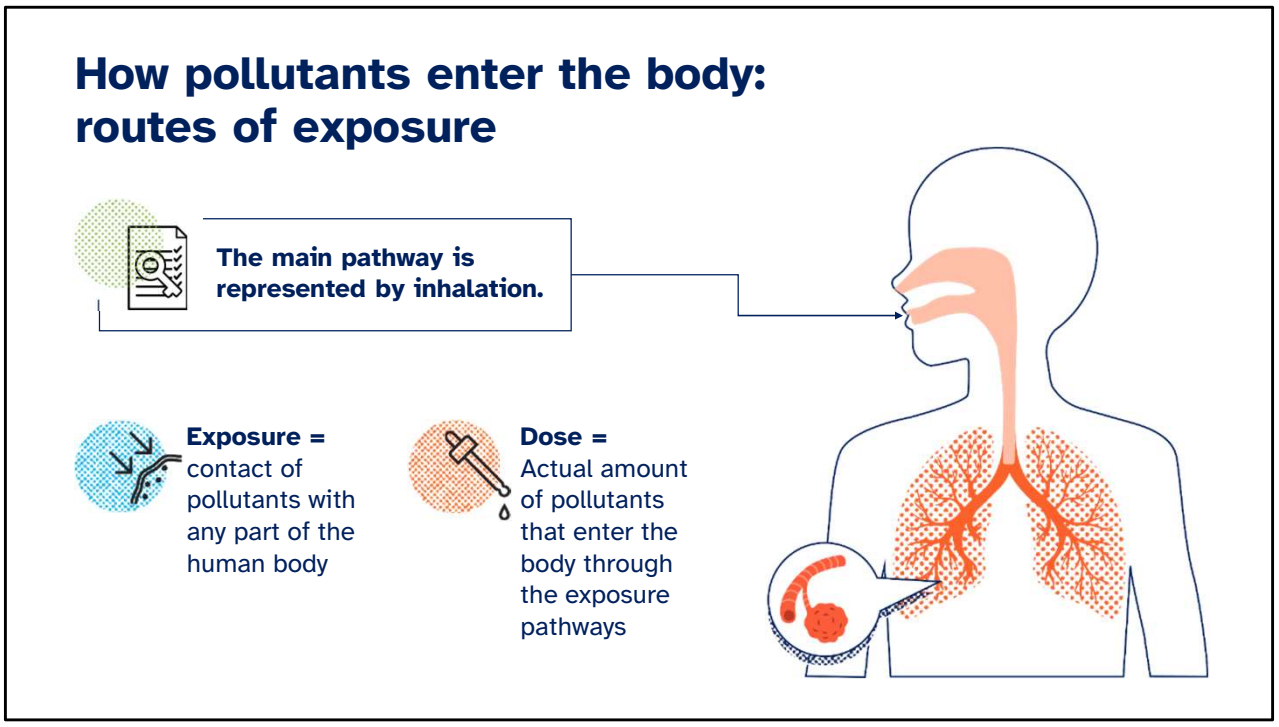

The main pathway is represented by **inhalation**.

Through inhalation, air contaminants reach different parts of the respiratory tract depending on several factors. This includes the:

- **exposure** – the contact of pollutants with any part of the human body; and
- **dose** – the actual number of pollutants that enter the body through the exposure pathways.

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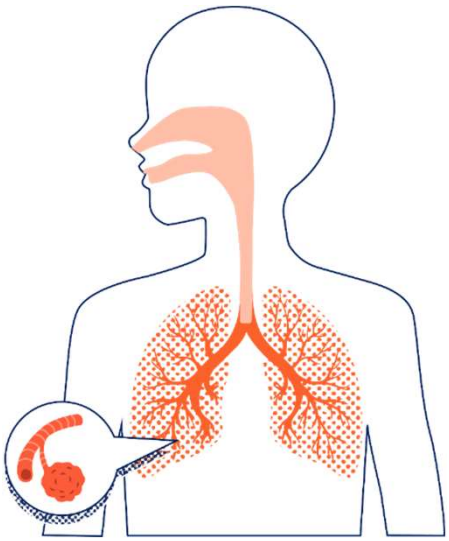
How pollutants enter the body: routes of exposure

Dose is influenced by:

- Characteristics of the exposure: e.g. concentration of pollutants and how long a person is exposed.
- Specific characteristics of the pollutants: e.g. size for particles, water solubility for gases.
- Physiological factors: e.g. personal susceptibility, level of physical activity.



Dose is influenced by:

- the **characteristics of the exposure** (for example, for how long a person is exposed);
- the **specific characteristics of the pollutants** (mainly size for particles and water solubility for gases); and
- **physiological factors**, including personal susceptibility, level of physical activity and any skin conditions.

Bibliography

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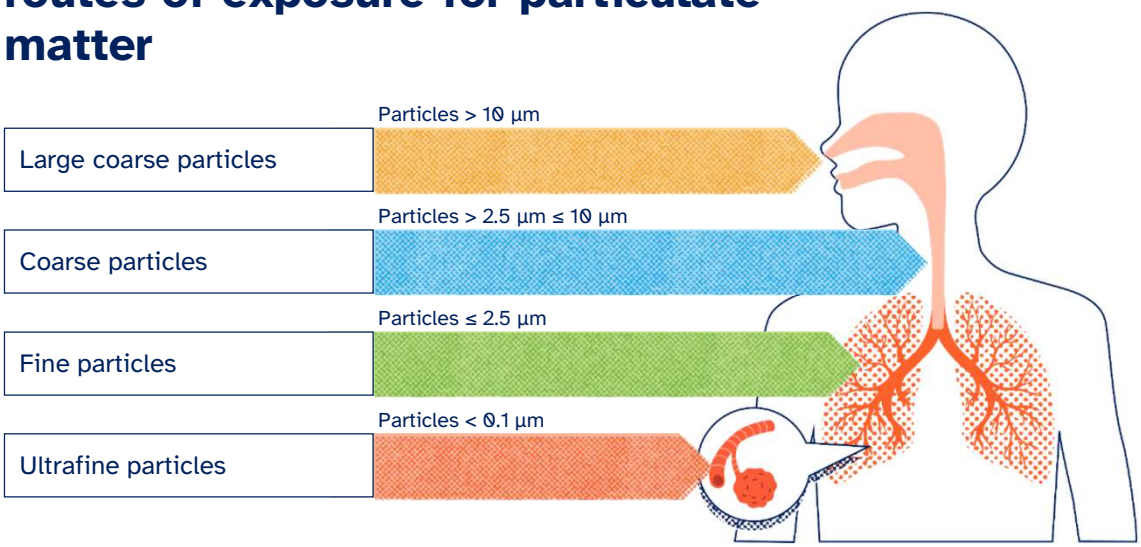
How pollutants enter the body: routes of exposure for particulate matter



Particles larger than 10 µm (also referred to as **large coarse particles**) persist in the humid oral and nasal cavities.

Particles larger than 2.5 µm and smaller than 10 µm (referred to as **coarse particles**) reach the upper airways and mucous membranes, causing coughing and tearing.

Particles smaller than 2.5 µm (referred to as **fine particles**) can reach the bronchioles and alveoli.

Finally, ultrafine particles, which are a subset $PM_{2.5}$ particles and which have a diameter smaller than 0.1 µm, are able to pass the alveolar–capillary membrane.

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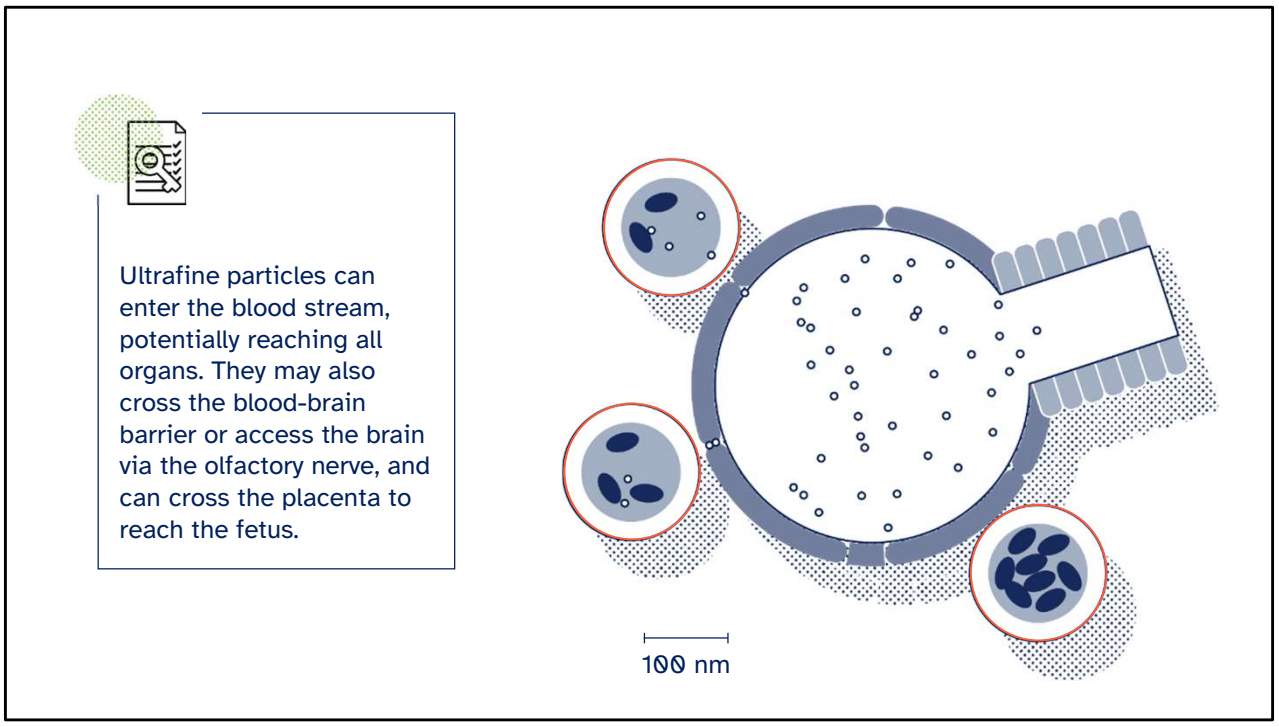

Alveoli are air sacs surrounded by capillaries that oxygenate blood. Here we can see a cross-section of the alveoli; the light blue dots represent the particles that are able to cross the alveoli–capillary barrier to enter the blood stream, represented by the round red circles.

Once in the blood stream, they then can reach all organs of the body, and potentially accumulate at sites of disease. There is also evidence that ultrafine particles can access the brain through the blood brain barrier or translocation via the olfactory nerve. Blood-borne particles can also cross the placenta to reach the fetus.

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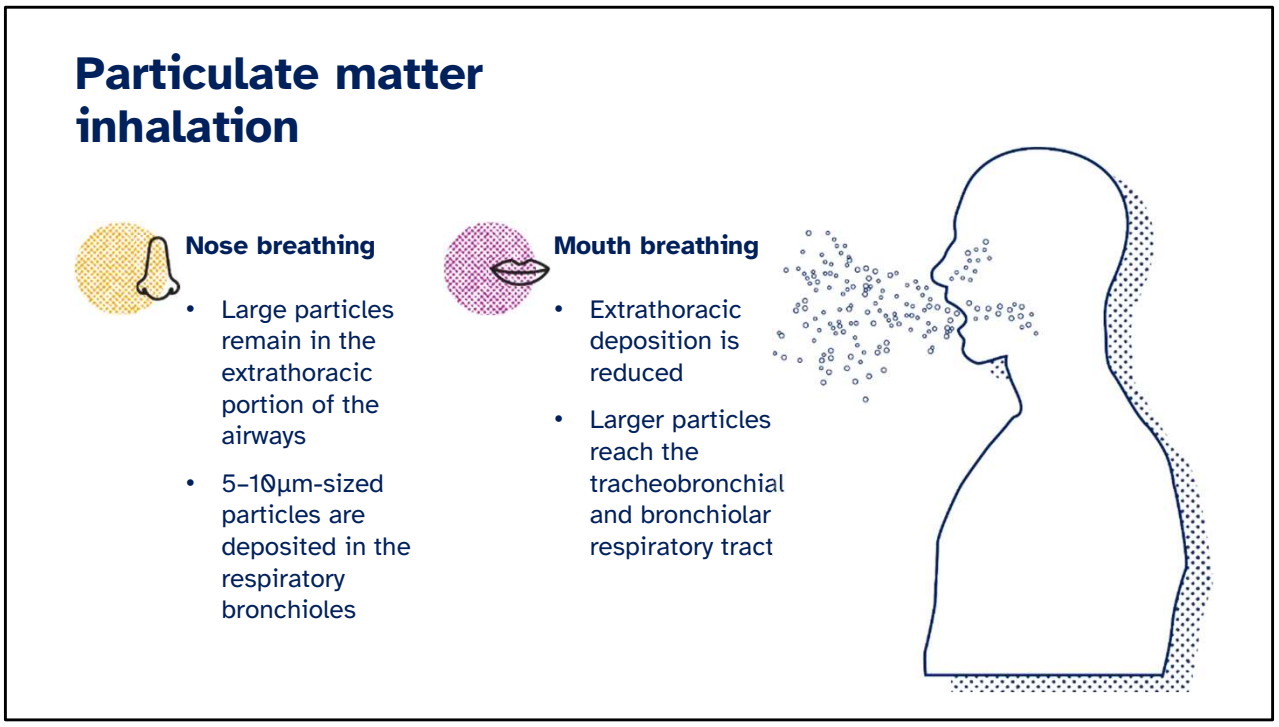

As we have discussed, the **deposition of inhaled particles** is influenced by their **size**.

Breathing patterns play a significant role in **how far** a particle can travel into the respiratory tract.

The two breathing patterns are:
- **nose breathing**, in which larger particles remain in the extrathoracic portion of the airways, while 5- to 10-µm-sized particles are deposited in the respiratory bronchioles; and
- **mouth breathing**, in which the extrathoracic deposition is reduced, allowing larger particles to reach the tracheobronchial and bronchiolar respiratory tract.

Breathing patterns are influenced for example by:
- resting or exercising;
- standing or sitting;
- sleeping or even;
- talking.

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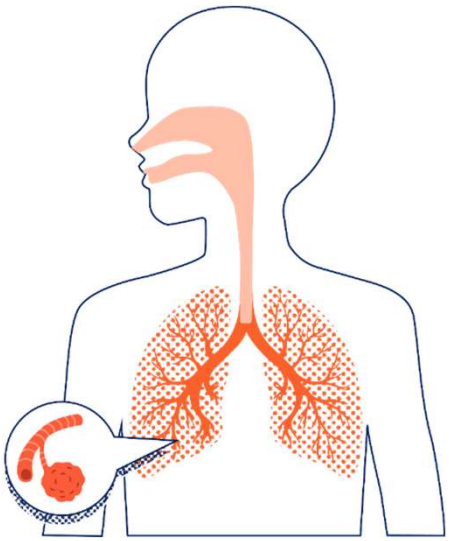
How pollutants enter the body: routes of exposure

Factors influencing gas penetration in the respiratory tree:

- water solubility
- concentration
- oxidizing power



With regards to gases there are different factors influencing their penetration in the respiratory tree, such as:

- water solubility
- concentration
- oxidizing power.

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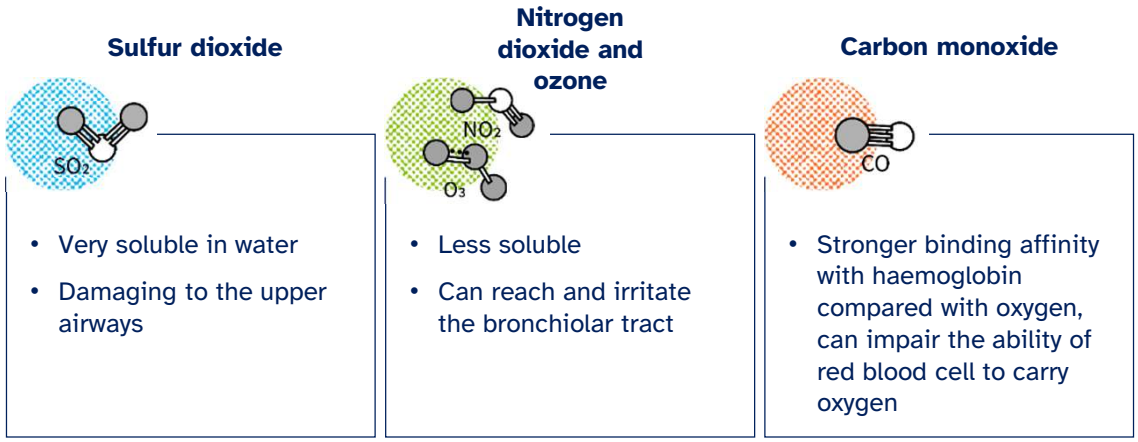
Pollutant solubility and its penetration into the lung



Considering **water solubility**, the less soluble the gas, the deeper it penetrates into the lung.

- **sulfur dioxide** is very soluble in water, and therefore damaging to the upper airways;
- **nitrogen dioxide** and **ozone** are less soluble, and can therefore reach and irritate the bronchiolar tract of the respiratory tree;
- **carbon monoxide** is peculiar as its adverse health effects are not related to lung injury; rather, its stronger binding affinity with haemoglobin compared with oxygen can impair the ability of the red blood cell to carry oxygen to the body tissues and organs.

Mixtures of air pollutants are also very important, as people are exposed to a complex cocktail of contaminants.

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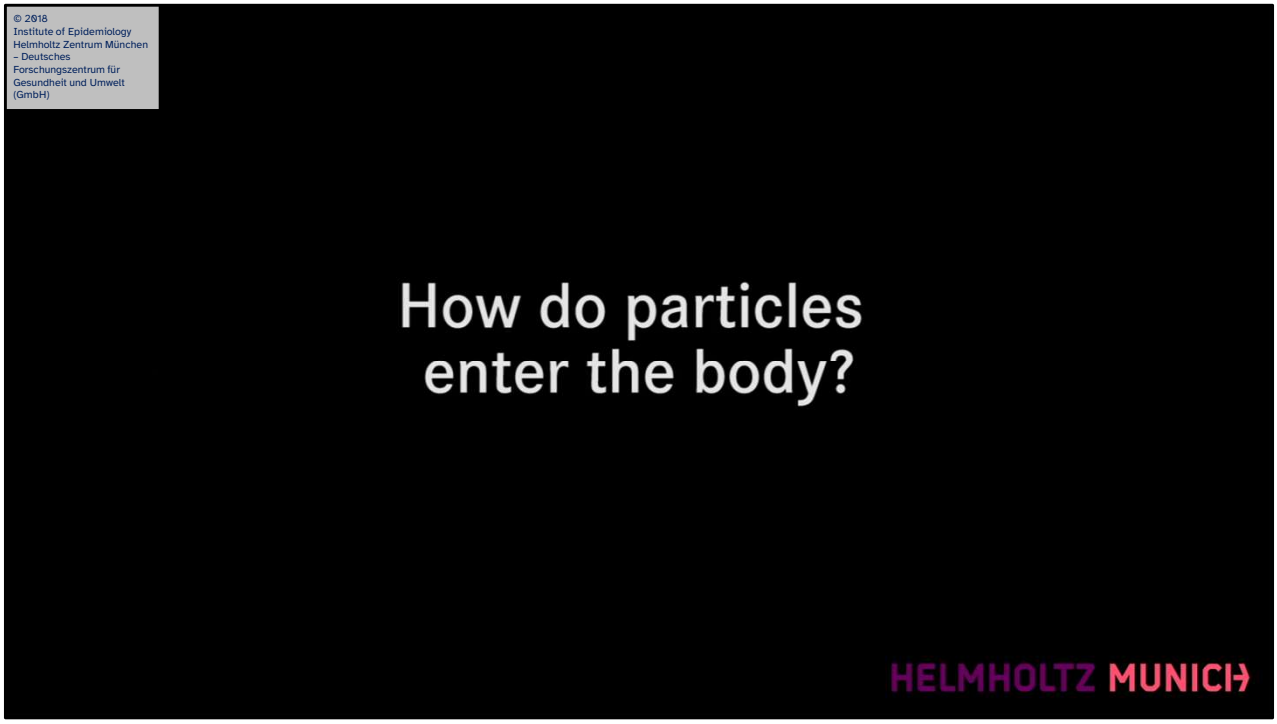


<this is a video to recap, the video has sound but you can also use the text below to provide explanations>

This video from 2018 demonstrates how particles being breathed can reach different parts of the respiratory tree according to their size. Coarse particles reach the upper airways and mucous membranes, causing coughing and tearing. Fine particles can reach bronchioles and alveoli, while UFPs are able to pass the alveolar–capillary membrane and enter the blood stream. Alveoli are air sacs surrounded by capillaries that oxygenate blood. You can see in the video a cross-section of the alveoli; the light blue dots represent the particles that are able to cross the alveoli–capillary barrier to enter the blood stream, here represented by the round red circles.

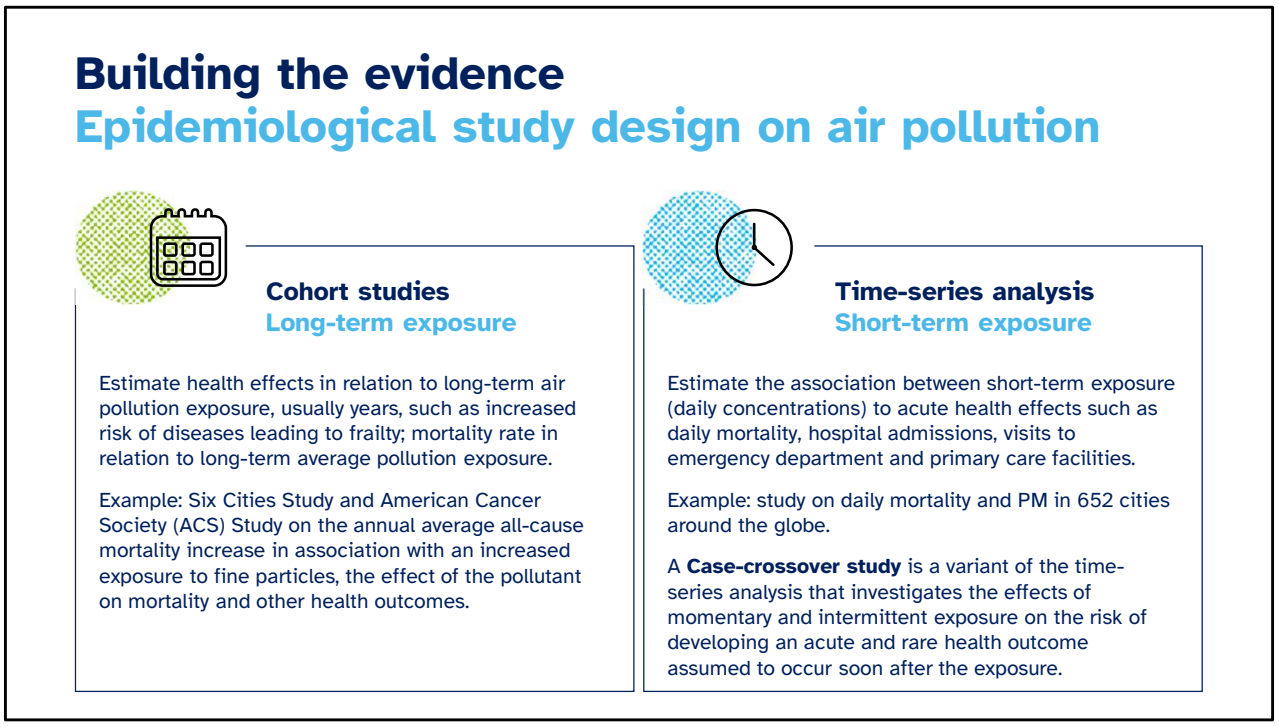
When particles enter the blood stream, negative health effects can occur elsewhere in the body.

New evidence shows that UFPs can also enter the brain directly by translocation from the nasal epithelium via the olfactory nerve.

World Health Organization

Unit 3

Building the scientific evidence



The effect of ambient air pollution on morbidity and mortality has been the subject of considerable investigations over the past decades.

There are two broad types of observational epidemiological study design that have been used in air pollution and health research:

- **individual-level studies**, such as cohort studies that can investigate long-term exposure; and
- **aggregate-level studies**, such as time-series that instead capture short-term exposure.

In cohort studies, subjects are followed over time and their health status is observed during the study. The data used to construct the exposure can be collected prospectively or retrospectively. This study design has been mainly used to evaluate the effects of long-term pollution exposure. Two examples of cohort studies are the Harvard Six Cities Study, a longitudinal study that was designed to test the adequacy of the federal standards for SO_2 and PM in the USA, and the American Cancer Society (ACS) study that linked air pollution to mortality.

In contrast, time-series studies explore the day-to-day changes in pollutant concentrations associated with a disease in population groups, rather than individuals. This study design usually combines data from central sites at different locations with grouped data from hospital discharge, disease or mortality registries. Ecological studies (which include time-series studies) fail to control for individual confounding factors and may suffer the “ecologic fallacy”, which refers to drawing inferences incorrectly from data on groups or about individuals in the groups. One example of a time-series study is the evaluation of the association between PM and daily mortality across 652 cities from multiple countries around the world.

A case-crossover study is a variant of a time-series analysis, in which each case serves as his/her own control. It is used to investigate the effects of intermittent exposure on the onset of acute outcomes.
It is important to note that short-term studies are based on a temporal comparison, whereas long-term studies are based on a spatial comparison.

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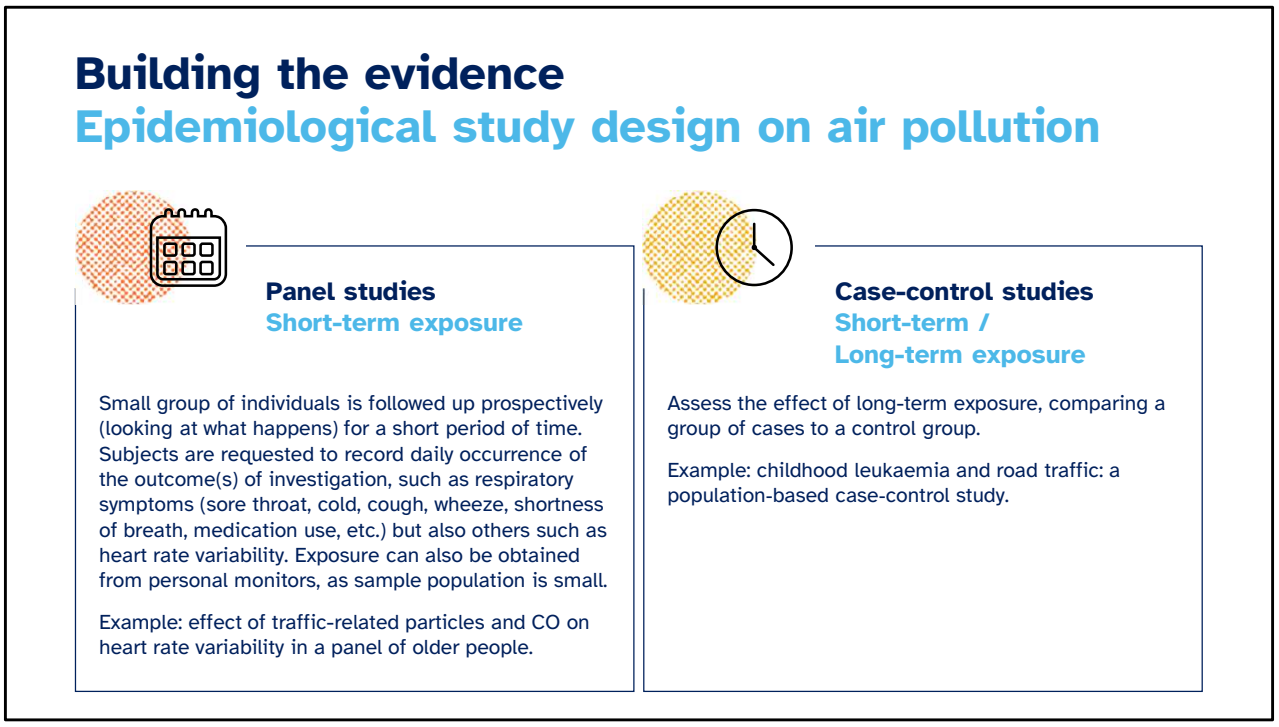

Two other study designs that are worth mentioning are **panel studies** and **case–control studies**.

Panel studies are a particular design of longitudinal study in which the unit of analysis is followed at specified intervals over a long period. This study design is commonly used to evaluate the short-term health effects of air pollution, for example: a study to evaluate the effects of traffic-related particles and CO on the heart rate variability of older people, where subjects were seen once a week for up to 12 weeks.

In case–control studies subjects are identified according to a specific outcome of interest (e.g. the cases are subjects with the disease, and controls are free from the disease but could potentially fall ill). Reconstructed exposure of both cases and controls is used to estimate the odds ratio of exposure in diseased subjects relative to the odds of exposure in the non-diseased. An example is a study of the association between childhood leukaemia and road traffic air pollution.

A case-crossover study is a variant of a case–control design in which each case serves as his/her own control. It is used to investigate the effects of an intermittent exposure on the onset of acute outcomes.

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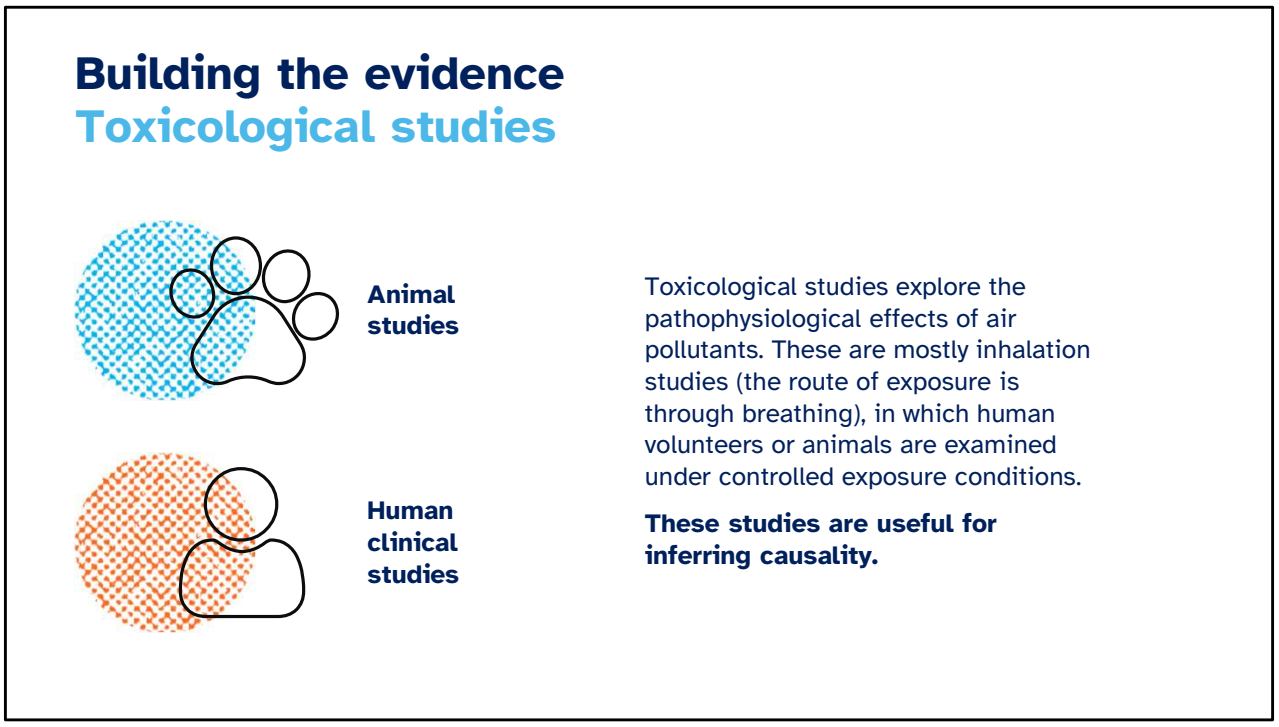

Different from epidemiological studies, toxicological studies explore the pathophysiological effects of air pollutants. These are mostly inhalation studies (the route of exposure is through breathing), during which human volunteers or animals are examined under controlled exposure conditions.

Toxicological studies conducted in humans are described as “human clinical studies”. In this type of study, it is possible to assess subclinical respiratory and cardiovascular effects such as changes in the lung function, blood pressure and heart rate. Using this approach the action of specific pollutants can be explored in isolation, removing many of the confounders of real-world settings. Also repeated visits allow for volunteers act as their own controls.

These studies are useful to infer causality. The effects of both single air pollutants as well as combinations of pollutants can also be assessed. This is particularly important for the identification of individual mechanisms of action for each pollutant. Further, combinations of pollutants can provide a better representation of real-life conditions of exposure. Indeed, we all breathe a mixture of air contaminants.

All three approaches (epidemiology, human controlled exposures and animal/cell studies) are needed as these allow to overcome the limitations of each other, address specific hypotheses and ultimately build up a bigger picture of how air pollution affects health.

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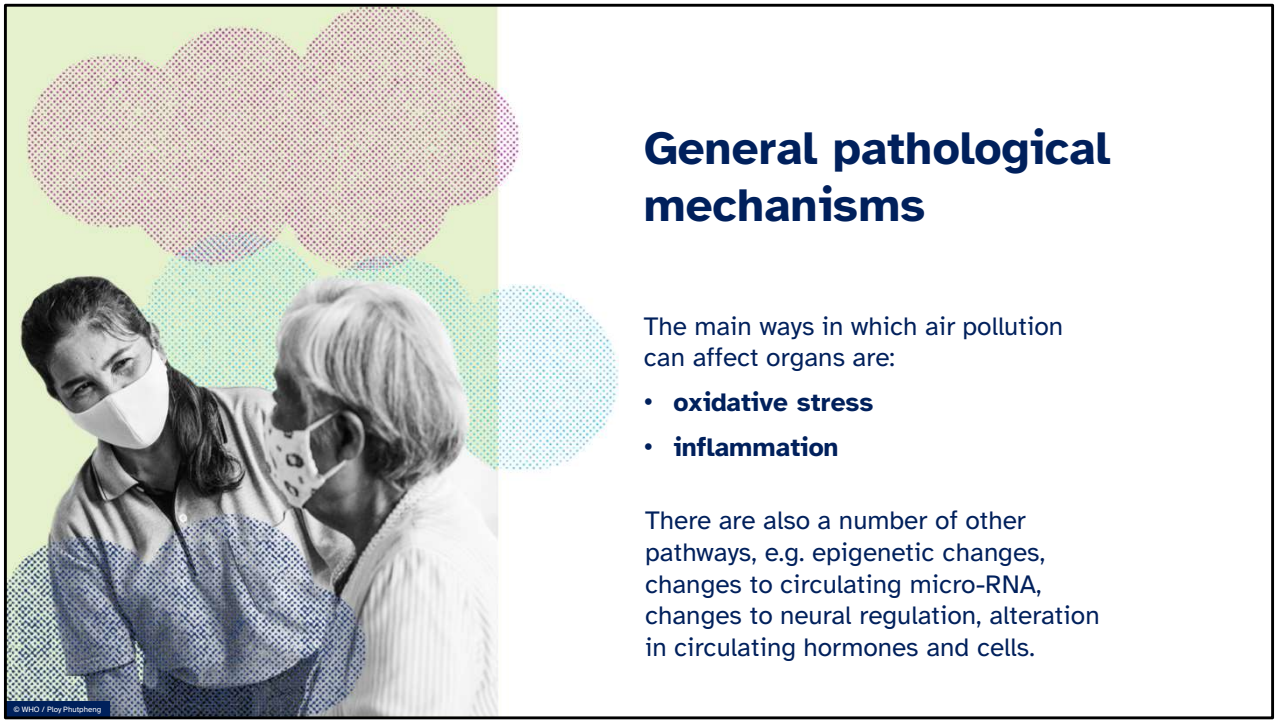
World Health Organization

Unit 4

General pathological mechanisms



The main ways in which air pollution can affect organs are:
- **oxidative stress**
- **inflammation**

There are also a number of other pathways that are specific to certain cells and organs or lead to interaction between them such as epigenetic changes, changes to circulating micro-RNA, changes to neural regulation, alteration in circulating hormones and cells.

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General pathological mechanisms of $PM_{2.5}$

$PM_{2.5}$ is able to interact with and activate local cells:

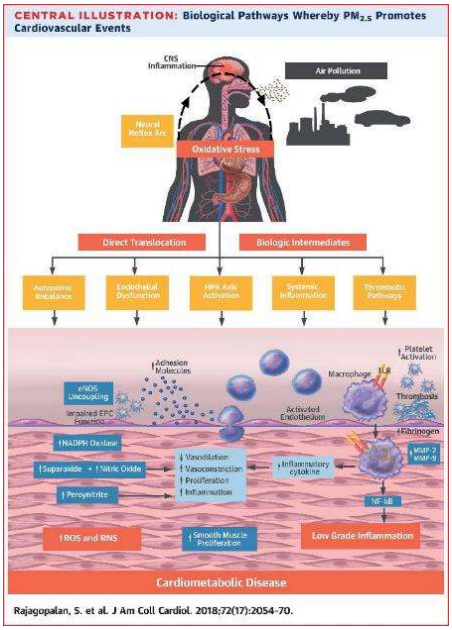
- resident macrophages
- dendritic cells
- alveolar/ endothelial cells

Modifies endogenous structures:

- cell membranes
- surfactant lipids
- antioxidants

Inflammatory response

- also via TNF-α, IL-6, C-RP, TLR-4



Once inhaled, $PM_{2.5}$ penetrates deep into the pulmonary tract, reaching the alveoli.

$PM_{2.5}$ is able to interact with and activate local cells such as resident macrophages, dendritic cells and alveolar/endothelial cells, while modifying structures such as cell membranes, surfactant lipids and antioxidants. An inflammatory response can be instigated by mediators of oxidative stress such as free radicals, in response to the activation by $PM_{2.5}$. Ultrafine particles are able to pass the alveolar–capillary membrane and therefore directly interact with other organs beyond the lungs, to induce oxidative stress or inflammation in those organs.

As per the graph represented here, for practical reasons and educational purposes, pathological pathways are divided into primary and secondary. The red boxes show the main pathological pathways, while the yellow boxes include secondary pathways.

Cytokines such as tumor necrosis factor alpha (TNF-α) and interleukin-6 (IL-6) are involved in the systemic inflammatory response induced by exposure to particulate matter air pollution.
In addition, acute phase response proteins (e.g. C-reactive protein) and proteins such as toll-like receptor 4 (TLR-4) lead to cytokine production, which further potentiate the inflammatory response.

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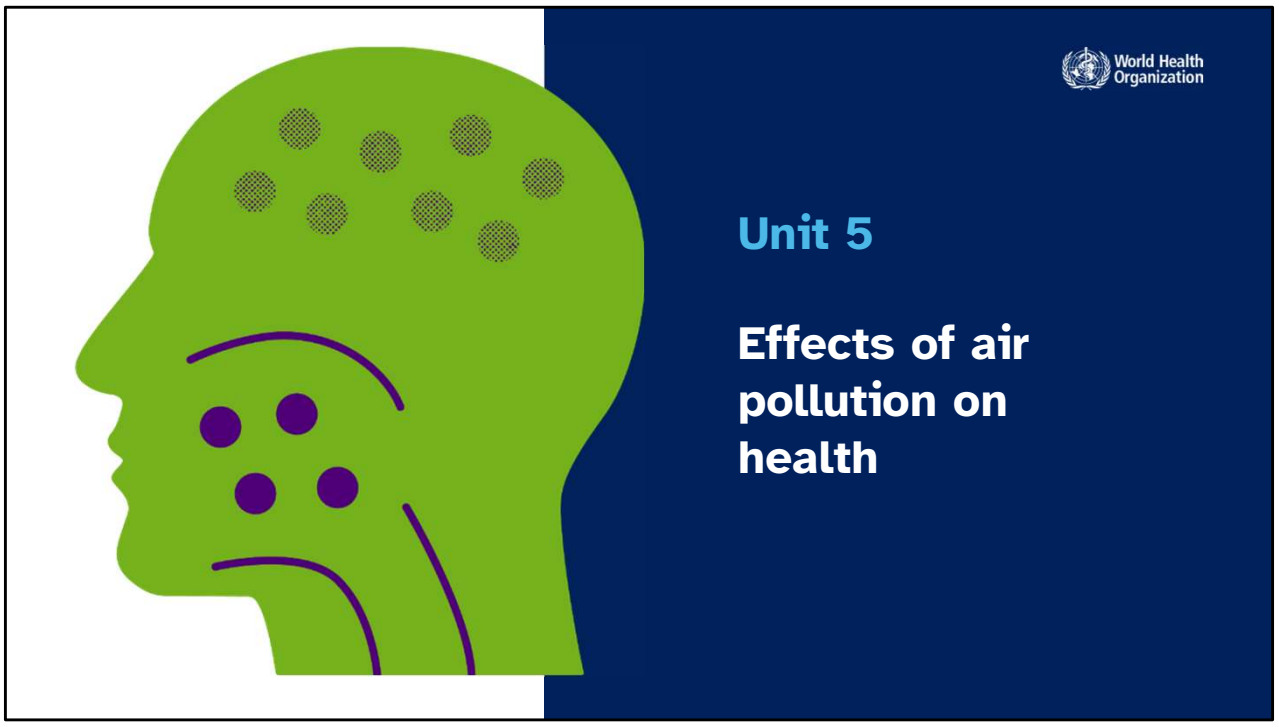
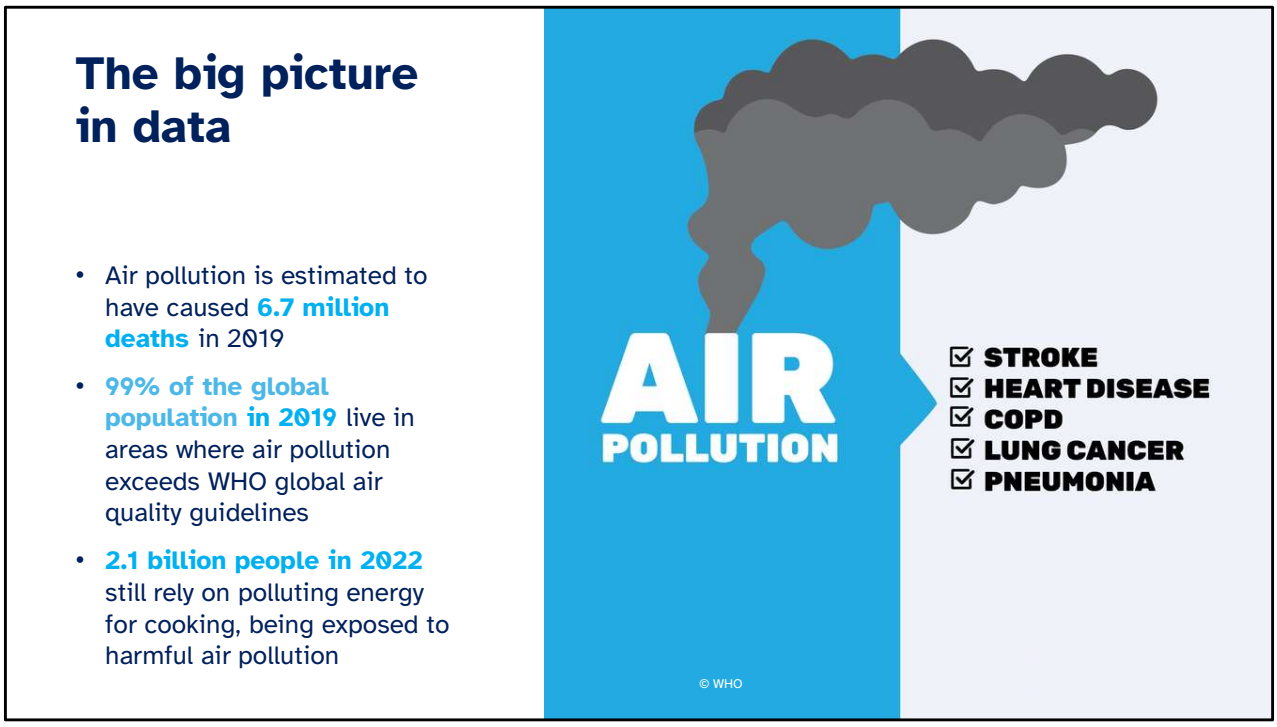
Note to the figure: CNS = central nervous system; eNOS = endothelial nitric oxide synthase; EPC endothelial progenitor cells; HPA = hypothalamic-pituitary axis; MMP = matrix metalloproteinase; NADPH = nicotinamide adenine dinucleotide phosphate; NF-kB = nuclear factor kappa; RNS = reactive nitrogen species; ROS = reactive oxygen species; TLR = Toll-like receptor.


World Health Organization
Unit 5
Effects of air pollution on health



Globally, air pollution is estimated to have caused 6.7 million deaths in 2019.

WHO data show that 99% of the global population in 2019 breathe air containing high levels of pollutants.

In addition, 2.1 billion people in 2022 still rely on polluting energy for cooking, being exposed to harmful air pollution.

These data are based on $PM_{2.5}$ as this is considered the best indicator for estimating the health impacts of air pollution.

Mortality wise, air-pollution-related diseases for which there is strong evidence of the causal role of air pollution as an environmental risk factor, are:

- **cardiovascular diseases**, such as ischaemic heart disease and ischaemic stroke;
- **respiratory diseases**, such as chronic obstructive pulmonary diseases and acute lower respiratory infections; and
- **lung cancer**.

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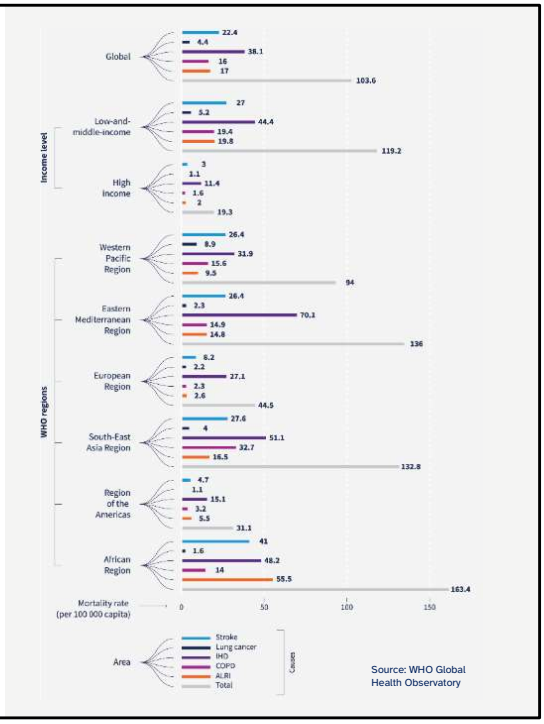
Age-standardized mortality rates (per 100 000 capita) attributed to joint effects of household and ambient air pollution in 2019, by region, income level and cause

- **104 per 100 000 population died globally in 2019 due to** the exposure to air pollution.
- **Cardiovascular diseases** represent the greatest burden.
- **The most affected countries are low- and middle-income countries**, with a mortality rate six times higher than that observed in high-income countries.



In this figure, the mortality rate attributable to the joint effects of household and ambient air pollution is shown. It refers to the Sustainable Development Goal (SDG) indicator 3.9.1 for which WHO is custodial agency, to monitor the environmental health target of the SDG 3 on health. As shown, 104 per 100 000 capita died globally in 2019 due to the exposure to air pollution; being cardiovascular diseases (i.e. ischaemic heart disease and stroke) the ones with the greatest burden. Due to higher levels of pollution, the most affected countries are low- and middle-income countries, with a mortality rate six times higher than that observed in high-income countries. On the other hand, the highest mortality rates in the African and Eastern Mediterranean WHO Regions stand out.

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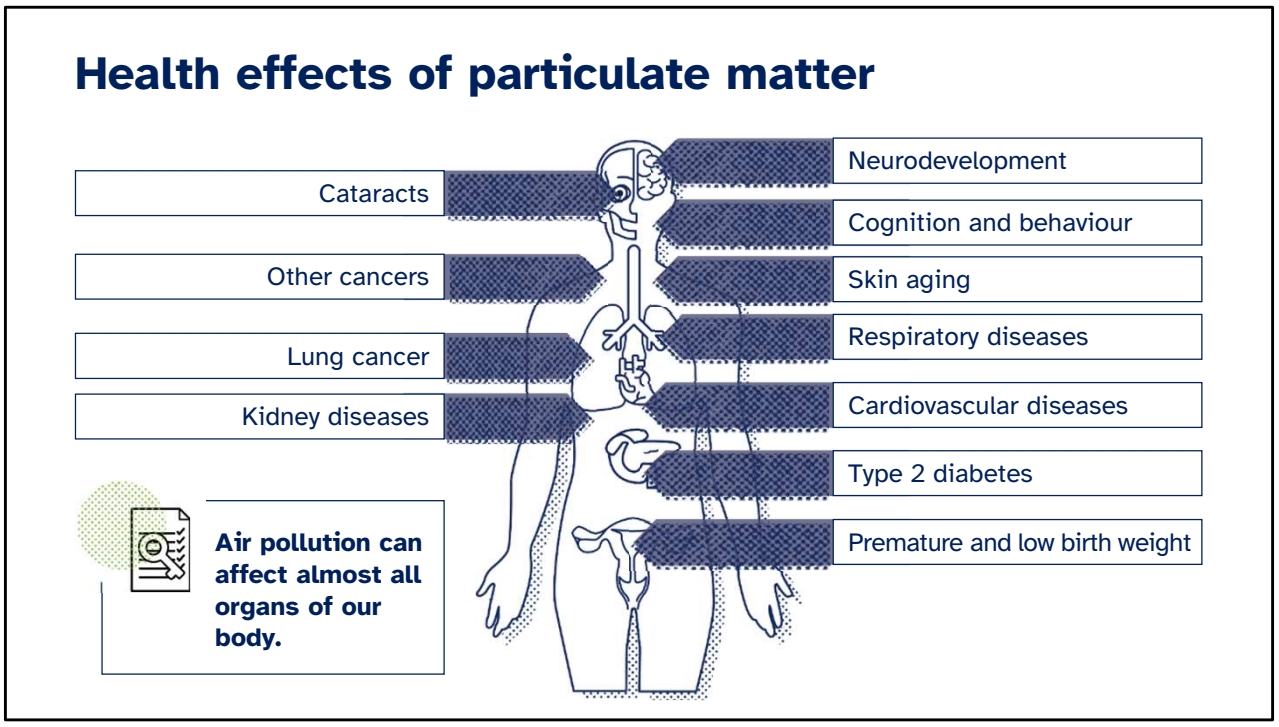

Bodies of evidence have shown that air pollution has the potential to harm almost all organs of our body. The main health effects can include:

- respiratory diseases: asthma, chronic obstructive pulmonary disease and pneumonia;
- cardiovascular diseases including stroke, ischaemic heart disease and high blood pressure;
- lung cancer and other cancers;
- type 2 diabetes;
- cataracts;
- premature birth and low birth weight;
- neurodevelopment;
- cognition and behaviours; and
- skin ageing.

Remember that routes of exposure to air pollution beyond inhalation include ocular exposure, ingestion and dermal absorption.

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Main short-term effects by pollutant

Short-term exposure (hours, days or weeks)

Pollutant	Health effects
PM	• **All-cause, cardiovascular, stroke and respiratory mortality;** • **Emergency due to CVD, respiratory, COPD;** • **Hypertension, arrythmia;** • **Exacerbation of disease, increase in symptoms or medication in patients with asthma;** • **Worsening of the disease or symptoms in patients with COPD;** and • Urgent acute conditions such as hypoglycaemia, heart failure and asthma exacerbations.
NO_2	• **Asthma symptoms and respiratory medical visits;** • **Emergency access and mortality for respiratory conditions;** • **Non-accidental mortality;** and • Outpatient visits for schizophrenia and dry eye disease.
CO	• COHb up 20%, reducing O2-carrying power of the blood; • Respiratory hospitalizations including asthma and pneumonia; and • **Cardiovascular events and hospitalizations.**
O_3	• Inflammatory markers into the bronchoalveolar lavage fluid; • Risk of developing asthma in children; • **Asthma, allergic and rhinitis symptoms;** • **Emergency due to respiratory diseases, asthma;** • **COPD exacerbations;** and • Sugar and metabolic disorders/diseases (e.g. diabetes).

Strongest evidence in **bold**

COHb: carboxyhaemoglobin; COPD: chronic obstructive pulmonary disease; CVD: cardiovascular disease; O_2: oxygen; O_3: ozone.

Short-term exposure (hours, days, weeks) to ambient air pollutants has been associated with chronic obstructive pulmonary disease (COPD), respiratory illnesses, higher rates of hospital admission or medical visits, and all-cause and specific-cause mortality.

The effect of short-term exposure to PM also includes conditions such as hypoglycaemia, arrhythmia and heart failure, while short-term exposure to NO2 has been linked to schizophrenia risk and increased visits to ophthalmological emergency departments.

Studies have revealed that short-term exposure to peak levels of O3 may increase susceptibility to inhaled allergens, increase the risk of developing asthma in children, decrease lung function and temporarily affect the lungs and respiratory tract.

Note: This table is not intended to be exhaustive, and the weight of evidence for many conditions is ever changing. Many different air pollutants have many different effects throughout the body, to exacerbate diseases which have a huge burden in terms of morbidity and mortality.

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Main long-term effects by pollutant

Long-term exposure (months or years)

Pollutant	Health effects
PM	• **Respiratory, cardiovascular and lung cancer incidence and mortality;** • **Atherosclerosis, hypertension, arrhythmia, blood coagulation;** • Decreased lung function (FVC, FEV_1) and COPD development; • Diabetes • Risk of depression, dementia (e.g. Alzheimer's disease) and a marginally increased risk of suicide; and • Prenatal DNA methylation, low birthweight and poor neuro development.
NO_2	• Asthma; • Impaired lung function/growth; • Chronic bronchitis; and • Risk of Parkinson's disease and decrease child mental development.
CO	• Increased risk of chronic diseases and low birth weight.
O_3	• Asthma onset; • Increased allergy symptoms; and • Exacerbation of disease or increased symptoms or medication in patients with asthma.

Strongest evidence in **bold**

COPD: chronic obstructive pulmonary disease; DNA: deoxyribonucleic acid; FEV_1: forced expiratory volume; FVC: forced vital capacity.

Long-term exposure (months, years) to PM has been associated with the onset of lung and heart disease, poor mental health and cancer, as well as cardiovascular and cardiopulmonary mortality. These causes of death and disease have also been associated with other pollutants such as NO2, CO and O3. Long-term exposure to air pollution includes a wide range of physical and mental health effects, including respiratory symptoms (cough and sneeze), decreased lung function and the development of diseases such as asthma, bronchitis, emphysema, COPD and cancer.

Exposure to fine PM, NO2 and CO during pregnancy has been associated with adverse pregnancy outcomes, with health consequences for individuals throughout their life cycle.

The fact that the burden of morbidity and mortality from air pollution estimated in epidemiological studies is higher at the population level for long-term exposure than for short-term exposure demonstrates that long-term effects are not merely the sum of short-term effects.

Note: This table is not intended to be exhaustive, and the weight of evidence for many conditions is ever changing. Many different air pollutants have many different effects throughout the body, to exacerbate diseases which have a huge burden in terms of morbidity and mortality.

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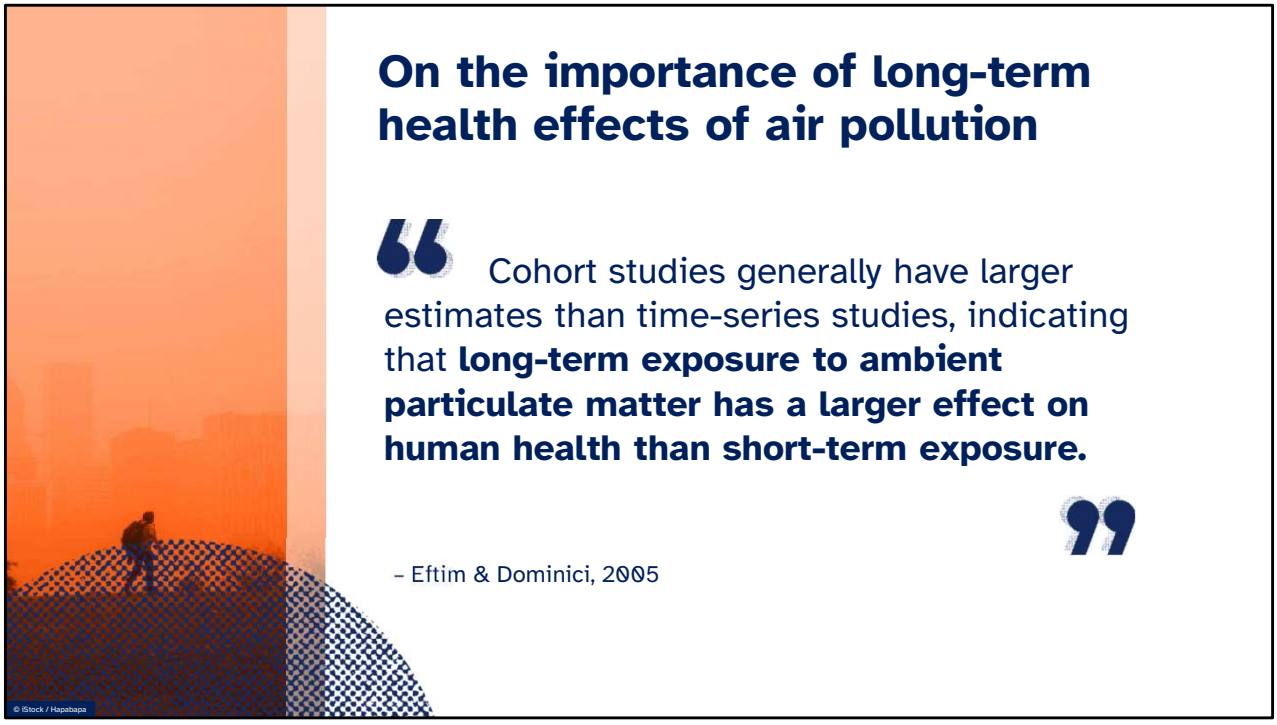

While in the past researchers were focusing their attention on the short-term effects of air pollution, this changed considerably when it became clear that long-term exposure to PM has a much greater effect on human health than short-term exposure.

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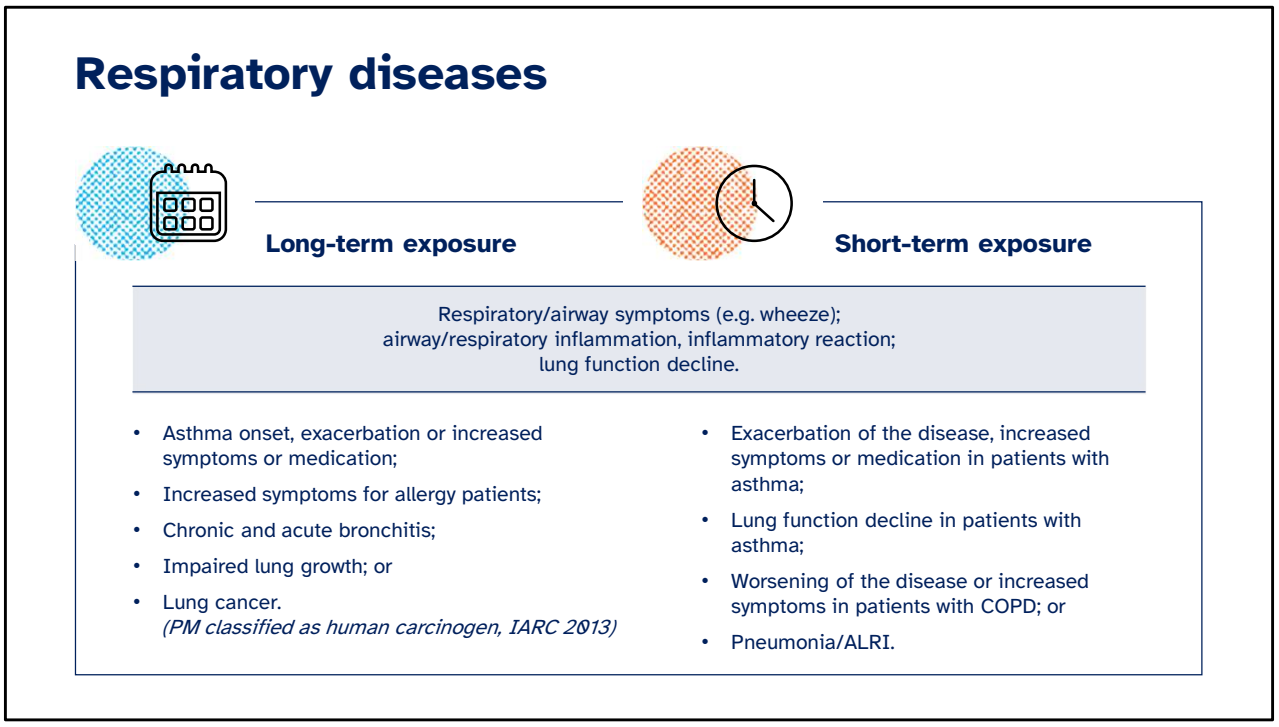

Respiratory/airway symptoms such as wheeze, airway/respiratory inflammation and inflammatory reaction, as well as lung function decline are associated with both short- and long-term exposure to air pollution.

Long-term exposure to air pollution can cause asthma onset and the development of COPD. There is also strong evidence that air pollution causes lung cancer. The International Agency for Research in Cancer (IARC), which conducts extensive reviews of the evidence, classified PM as a carcinogen in 2013.

Short-term exposure to air pollution leads to the exacerbation of both asthma and COPD. Long-term exposure leads to the development of new onset asthma in young children and has also been shown to be associated with the development of COPD. In addition, children exposed to higher levels of air pollution show reduced lung function, which raises concerns about early life exposures leading to COPD in later life. Short-term exposure to air pollution also causes pneumonia or acute lower respiratory infections (ALRI), this is particularly relevant in the context exposure to household air pollution for women and children.

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Air pollution and lung cancer

The International Agency for Research on Cancer (IARC) classified the following as **Group 1** (**carcinogenic** to humans):

- Ambient air pollution (2013)
- Ambient particulate matter (2013)
- Household combustion of coal (2010)
- Diesel engine exhaust (2013)

IARC classification of carcinogenicity	
Group 1	Carcinogenic to humans
Group 2A	Probably carconogenic to humans
Group 2B	Possibly carcinogenic to humans
Group 3	Not classifiable as to its carcinogenicity to humans

In 2013, the International Agency for Research on Cancer (IARC) classified ambient air pollution, and especially PM, as carcinogenic to humans. Both epidemiological and clinical evidence supported that decision. By conducting a thorough review of all available scientific literature, the IARC Monographs Working Group evaluated whether the air pollution mixture as a whole causes cancer. The IARC Monographs Programme had previously confirmed that components of air pollution (e.g. benzene) and air pollution mixtures (e.g. diesel exhaust and coal smoke) are carcinogenic. The latest review identified that air pollution as a whole, as well as the small particles that make up part of air pollution (measures of $PM_{2.5}$ and PM_{10}, PM monitored in air pollution and epidemiological studies), are carcinogenic.

The Working Group looked at more than 1000 studies from five continents, covering the scientific fields of atmospheric science, epidemiology and toxicology. Evidence from all of these different types of research involving humans, animals and experimental systems leads to the conclusion that air pollution causes cancer.

Scientific studies showed a consistent association between outdoor air pollution and lung cancer as well as other diseases (such as respiratory and heart diseases). There is also a positive association with an increased risk of bladder cancer. Household combustion of coal was also classified as Group 1 (carcinogenic to humans) by IARC in 2010. Diesel exhaust is a cause of lung cancer (sufficient evidence) and also noted a positive association (limited evidence) with an increased risk of bladder cancer (Group 1).

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Cardiovascular diseases

Both **short-** and **long-term** exposures have been shown to increase cardiovascular mortality.

Short-term exposure

Exacerbation of pre-existing ischaemic heart disease, heart failure, arrhythmia or ischaemic stroke.

Long-term exposure

Development of atherosclerosis, hypertension, pulmonary hypertension and cardiometabolic disease (e.g. diabetes).

Global deaths and DALYs attributed to joint effects of household and ambient air pollution in 2019, by cause

Source: WHO

Cardiovascular diseases (CVDs) are disorders of the heart and blood vessels, including diseases of the coronary blood vessels supplying the heart (coronary heart disease) and of the blood vessels supplying the brain (cerebrovascular disease). It is usually more intuitive to consider that air pollution affects the lungs. However, the effects on the cardiovascular system are important to recognize. This requires an understanding of the underlying scientific pathophysiological mechanisms described before, as well as routes of exposure.

According to the latest estimates, the biggest burden of disease due to joint ambient and household air pollution is due cardiovascular diseases, which bear 62% of the total attributed burden. First, ischemic heart diseases accounts for over 2.5 million deaths deaths, while stroke accounted for 1.5 million deaths.

There is an extensive body of evidence linking the effects of short-term exposure to air pollution and exacerbation of pre-existing CVD, including ischaemic heart disease (IHD), heart failure, arrhythmia and ischaemic stroke. There is also an association between out-of-hospital cardiac arrests, and hospitalization and mortality from CVD.

Long-term exposure to air pollution (i.e. over months and years) is associated with the development of atherosclerosis, hypertension, pulmonary hypertension and cardiometabolic disease (e.g. diabetes). Research has shown that ambient concentrations of $PM_{2.5}$ and nitrogen oxides (NOx) are strongly associated with accelerated atherosclerosis, as shown by computed tomography assessment of coronary artery calcium over a 10-year period.

Both short- and long-term exposures have been shown to increase cardiovascular mortality.

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Pregnancy and birth control outcomes

- Chronic exposure to PM and other pollutants is linked with birth outcomes such as preterm birth, low birth weight, small for gestational age (SGA), and stillbirth.
- Prenatal exposure to PM leads to greater likelihood of chronic wheezing and asthma in childhood.
- Prenatal exposure to air pollution is associated with a range of adverse effects on health of the child later in life.
- Evidence has suggested a possible relationship between exposure to PM and preeclampsia and gestational diabetes.

There is suggestive evidence that exposure to air pollutants may affect maternal and fetal health during pregnancy, possibly through systemic inflammation and oxidative stress as a biological mechanism. The strength of the evidence varies across different pollutants and outcomes. For birth outcomes, the overall evidence is suggestive of adverse effects from exposure to PM, O_3, and NOx . Evidence also suggests that particulate matter and ozone exposure are associated with pregnancy outcomes. A recent assessment of global burden of adverse perinatal outcomes due to the exposure to ambient and household $PM_{2.5}$ pollution suggest that about 2.8 million cases of low birthweight and 5.9 million preterm births globally, could have been averted in 2019. South Asia and sub-Saharan Africa combined could have decreased the 2019 low birth weight and preterm birth incidence by about 78% (see Ghosh et al. 2021).

Main take home messages are summarized as follow:

- Chronic exposure to PM and other pollutants is linked with birth outcomes such as preterm birth, low birth weight, small for gestational age, and stillbirth.
- Prenatal exposure to PM leads to greater likelihood of chronic wheezing and asthma in childhood.
- Pre-natal exposure to air pollution is associated with a range of adverse effects on health of the child later in life
- Evidence has suggested a possible relationship between exposure to PM and preeclampsia and gestational diabetes.

Current evidence warrants further research on air pollution, pregnancy and birth outcomes.

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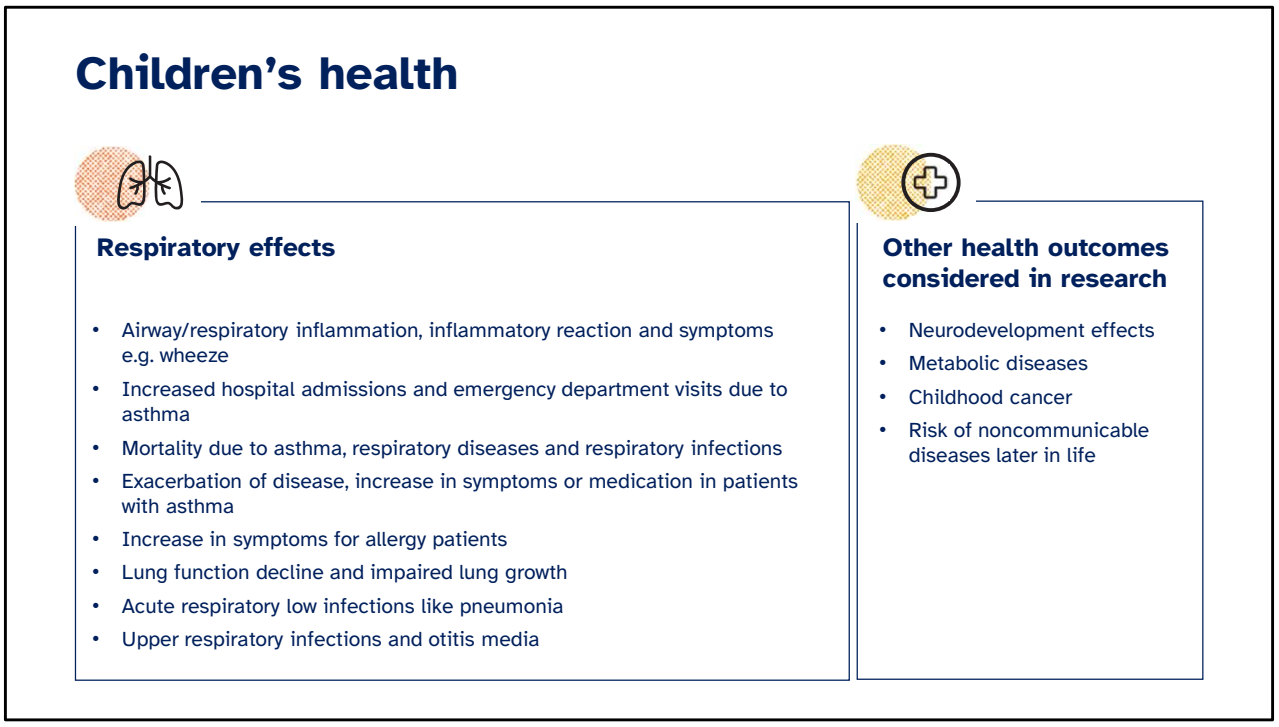

There is robust evidence linking some ambient air pollutants to childhood respiratory effects including, including acute lower respiratory infections such as pneumonia, changes to lung function and development, and exacerbation of asthma as well as increased hospital admissions and mortality due to respiratory diseases.
Other emerging health outcomes in children that are being studied, but for which there is currently limited, mixed or inconclusive research include:

- neurodevelopmental effects such as autism spectrum disorders, cognitive and behavioural effects;
- metabolic diseases like obesity and diabetes;
- childhood cancer;
- risk of noncommunicable diseases later in life such as childhood overweight and obesity, lung cancer and cardiovascular disease.

It is important to note that assessing whether a particular pollutant is linked to a certain child health outcome is difficult. Air pollution is always a mixture of chemicals and particles and therefore children are likely to be exposed to multiple pollutants at one time. Continued research on the effects of exposure to air pollutant mixtures, as well as modifying influences such as genetics and nutritional status, is still needed.

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Cataract

- The **leading cause of blindness** in low-income countries.
- **Strong evidence** of association between exposure to household air pollution and cataract formation.
- In the African region, around 25% of cataract in women is due to household air pollution exposure.

Estimated PAFs for household air pollution

Region	Population Attributable Fraction
Global	12.3%
Afr	25.5%
Amr	3.4%
Sear	14.0%
Eur	2.6%
Emr	12.1%
Wpr	8.8%

Cataract's PAF (applies only to women ≥ 25 years)

Source: WHO Global Health Obeservatory

Cataract is clouding of the lens of the eye preventing clear vision, representing an important cause of poor vision in both developed and developing countries.

The treatment of cataract is surgical and very successful in restoring sight. The opaque lens is removed and replaced with an artificial intraocular lens. However, in many remote parts of the developing world, people remain blind from cataract because of a lack of access to eye care. Globally, at least 2.2 billion people have a near or distance vision impairment. In at least 1 billion of these, vision impairment could have been prevented or is yet to be addressed.

As people in the world live longer, the number of people with a cataract is anticipated to grow.

Burning fuels such as dung, wood and coal in inefficient stoves or open hearths produces a variety of health-damaging pollutants, including PM, CO and other contaminants. Burning kerosene in simple wick lamps also produces significant emissions of fine particles and other pollutants.

The burden is greater in women compared with men, probably because of the greater and longer exposure of women to HAP. In the African region, around 25% of cataract in women is due to household air pollution exposure

Evidence has been provided from studies in both India and China, and through supporting toxicological evidence in animal studies.

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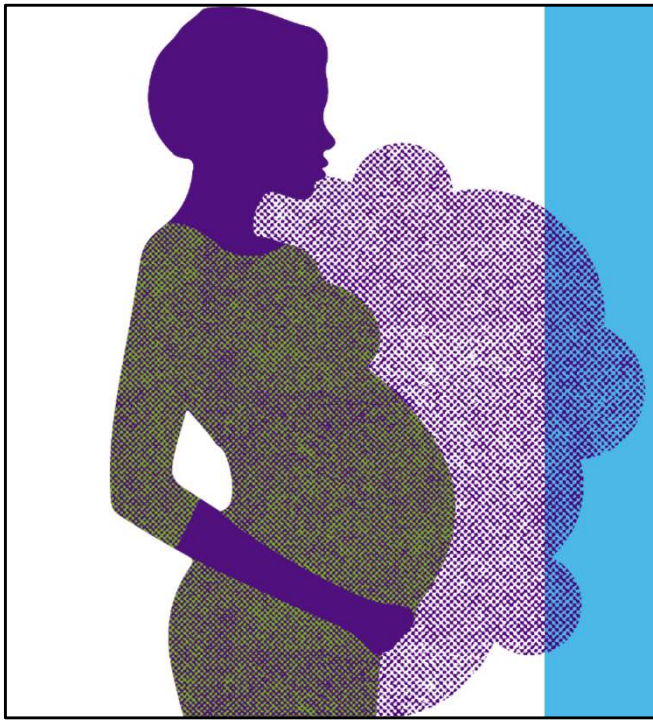
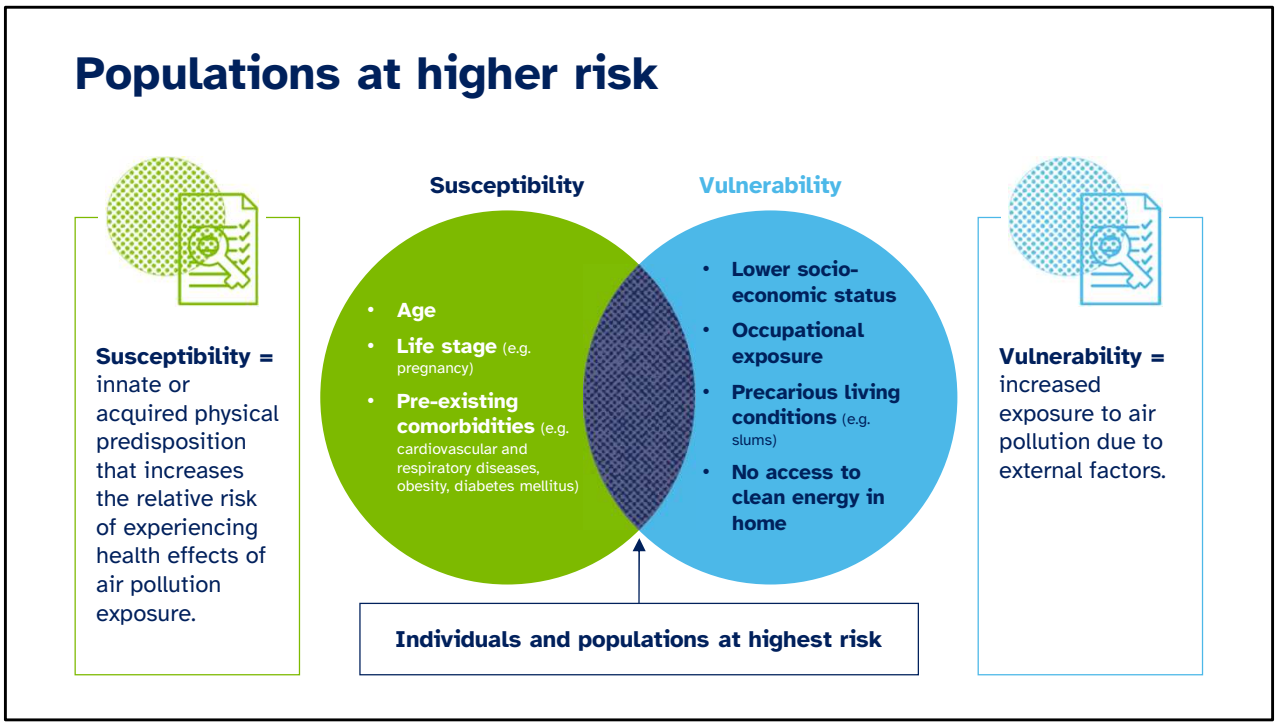


World Health Organization

Unit 6

Populations at higher risk



To understand who is at higher risk from the adverse effects of air pollution, it is important to clarify the concepts of susceptibility and vulnerability.

Susceptibility is an innate or acquired physical predisposition that increases the relative risk of experiencing health effects as a result of air pollution exposure – such as pre-existing conditions or diseases.

Factors that influence risk and **susceptibility** include:

- **life course factors**, for example, being an older person, a child or a pregnant woman;
- **genetic factors** including certain polymorphisms as well as genetic disorders; and
- **pre-existing conditions or comorbidities**, such as chronic diseases, respiratory diseases, and other noncommunicable diseases like diabetes.

Vulnerability means that people have increased exposure to air pollution due to external factors, such as:

- place of residence (work or home, especially if close to traffic or to other sources of emissions);
- precarious living conditions (for example living in slums);
- type of occupation (for example street vendors or other outdoor workers);
- low socioeconomic status.

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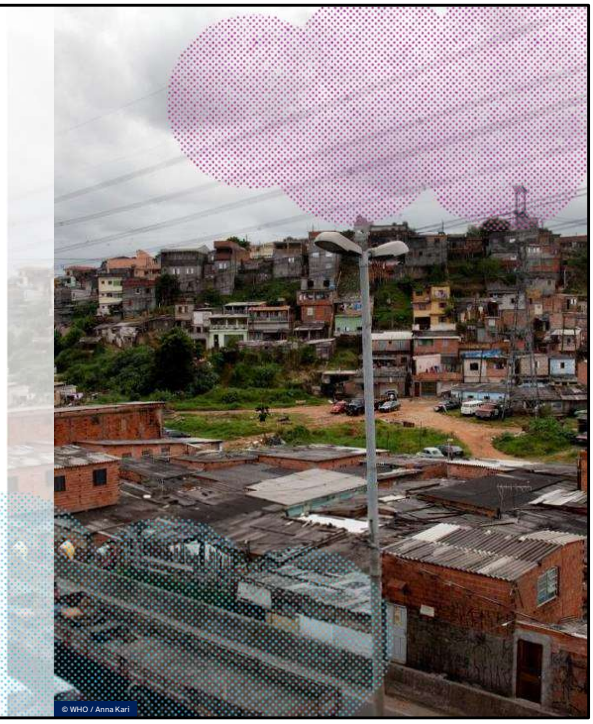
Other vulnerability factors

Socioeconomic factors that increase the risk include:

- poor diet
- lack of exercise
- lack of access to green space
- lack of access to health care
- living next to a busy road
- having to commute in busy traffic
- residence in close proximity to industry
- exposure to improper disposal of waste e.g. burning
- lack of access to clean energy at the household level



Factors associated with **lower socioeconomic status** can make a person more vulnerable to exposure to air pollution, include:

- poor diet;
- lack of exercise;
- lack of access to green space;
- lack of access to health care;
- living next to a busy road;
- having to commute in busy traffic;
- residence in close proximity to industry;
- exposure to improper disposal of waste e.g. burning;
- lack of access to clean energy at the household level.

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We are not all equal
Susceptibility & vulnerability

Life stages
- older people
- children
- pregnant women

Genetic factors
- polymorphisms (GSTM-1, TNF-alpha)
- genetic diseases (cystic fibrosis, alpha-1 antitrypsin deficiency)

Comorbidities
- respiratory diseases (asthma, COPD, etc.)
- heart diseases and atherosclerosis
- diabetes and obesity

Demographic
- pace of living (highways, busy roads, slums)
- socioeconomic factors
- race/ethnicity
- sex
- occupation (outdoor workers)

Nutrition
- antioxidant intake
- omega-3 fatty acids

Given the complexity of this issue and the obvious overlap between personal and external factors, “susceptibility” is more generally used than “vulnerability” to broadly indicate the condition of “being at increased risk” of experiencing the adverse health effects of air pollution exposure.

Life stage factors: for example, being an older person, child or woman (especially a pregnant women).

Genetic factors: including certain polymorphisms such as glutathione S-transferase mu-1 (GSTM-1) or TNF-α, as well as genetic disorders such as cystic fibrosis and α-1 antitrypsin deficiency. Many factors, including genetics, affect our ability to defend against the oxidative stress, inflammatory and immune effects from exposure to PM and other pollutants. For example, GSTM-1 is an important enzyme in the pathway for protection against oxidant injury; one of the polymorphisms of this enzyme has a null allele with no protein expression, which confers reduction in antioxidant protection. This allele is present in 40% of the population of the USA. Children with the GSTM-1 null allele have reduced lung function growth and appear to be more susceptible to the effects of ambient O_3 exposure. GSTM-1 and other polymorphisms may also play a role in enhancing nasal immunoglobulin E response to exposure to diesel exhaust particles.

Comorbidities: such as chronic diseases, respiratory diseases, CVDs and diabetes all make people more susceptible to the negative effects of air pollution.

Demographic factors: such as place of home of work, especially if close to traffic, or in slums or closer to other sources of emissions. Socioeconomic status is also an important factor that can influence the exposure of a person to air pollution. Poorer people more often live in highly polluted areas or closer to traffic, and have less access to health care, than wealthier people.

Nutrition: there are studies showing that antioxidant intake and omega-3 fatty acids may play a role in protecting our body from the effects of air pollution, yet further research is needed therefore it is currently premature to considering additional supplements to be added to specifically protect against air pollution.

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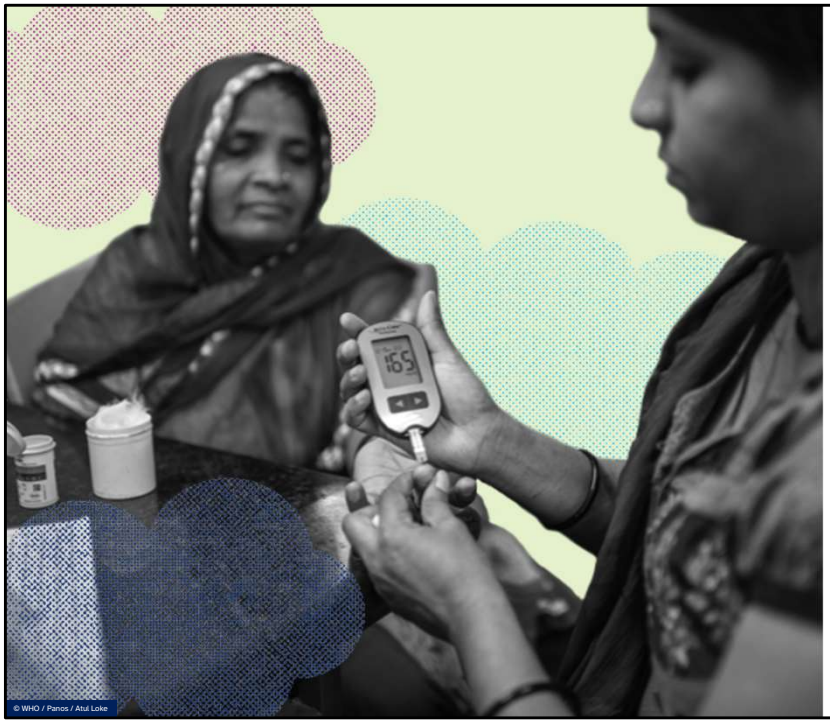


Exposure can potentially accelerate progression of a disease, or perhaps even initiate it, until it is clinically diagnosed.

The most susceptible to the effects are those with an unstable and/or chronic condition.

Susceptible population groups differ between short-term or long-term exposures.

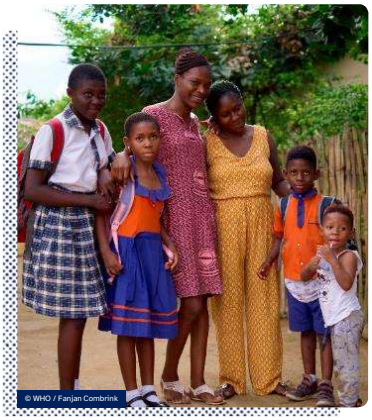
Even apparently healthy people are susceptible to the effects of **long-term exposure** to particulate matter. Exposure can potentially accelerate progression of a disease, or perhaps even initiate it, until it is clinically diagnosed.

However, the most susceptible to the effects of **short-term exposures** are those with an unstable and/or chronic condition or comorbidities.

Main population at higher risk by life stage factors

Older people

Children



Pregnant women

As noted, different life course factors can bring increased susceptibility to air pollution - in particular for:

- older people
- children
- pregnant women.

The number of people aged over 60 is expected to double by 2050, a new demographic reality that must be taken into account when we consider diseases related to air pollution at the population level.

The reason for the increased susceptibility is that, at a biological level, ageing is associated with the gradual accumulation of molecular and cellular damage.

Over time, this damage leads to a gradual decrease in physiological reserves, with increased risk of many diseases and general decline which make older people more fragile.

Increased exposure to pollution has been associated with increased mortality, hospital admissions and emergency-room visits for older people, mainly the result of exacerbations of chronic diseases or respiratory tract infections.

As we said, comorbidities can affect susceptibility, and older people are the population group most likely to suffer from such conditions.

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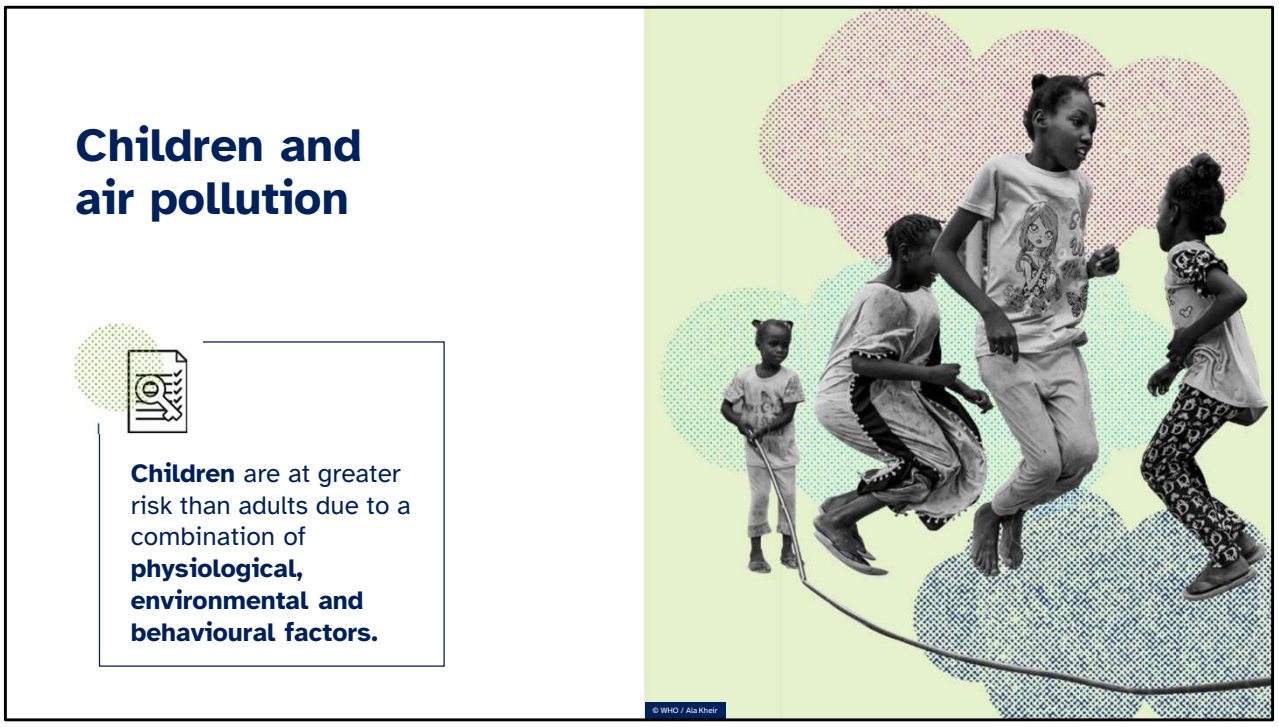
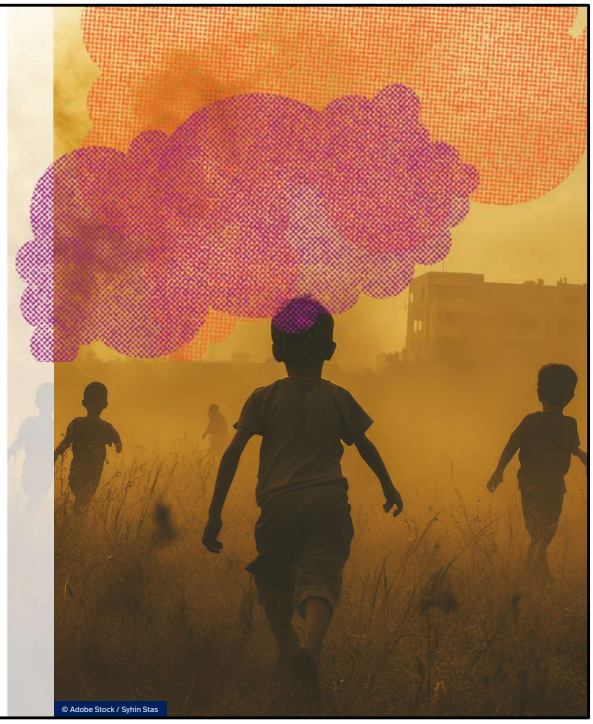


Children are also at greater risk than adults from the many adverse health effects of air pollution because of a combination of physiological, environmental and behavioural factors.

Children and air pollution

Some factors which increase children's risk:

- developing immune, respiratory and central nervous systems
- susceptible during fetal development
- higher breathing rates and more likely to breathe through their mouths
- lower height (closer to peak pollutant concentrations on the ground)
- more likely to engage in outdoor physical activity



Physiologically, children are human beings that are still developing, meaning that their immune, respiratory and central nervous systems are immature and highly sensitive to environmental stimuli, including air pollution.
Children are especially susceptible during fetal development and in their earliest years, while their lungs, organs and brains are still maturing.

Their bodies are rapidly developing and therefore more vulnerable to inflammation and other damage caused by pollutants. The inside lining of the respiratory tract is permeable in young children, making them especially vulnerable to irritants in the airways.

An infant also breathes at a rate about five times that of an adult, while children aged 3–5 years breathe at a rate 60% higher than that of adults. Environmental toxicants in the air are therefore delivered to children at higher internal doses relative to adults. Children also have high rates of mouth-breathing, bypassing nasal filtration, which can also expose them to higher levels of air pollution.

Being of a lower height than adults, children live closer to the ground where some pollutants reach peak concentrations.

They may also spend more time outdoors, playing and engaging in physical activity in potentially polluted air. In the womb, they are vulnerable to their mothers' exposure to pollutants. Children have a longer life expectancy than adults, so latent disease mechanisms have more time to emerge and affect their health.

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Children are exposed starting from the womb, as they are vulnerable to their mothers' exposure to pollutants.

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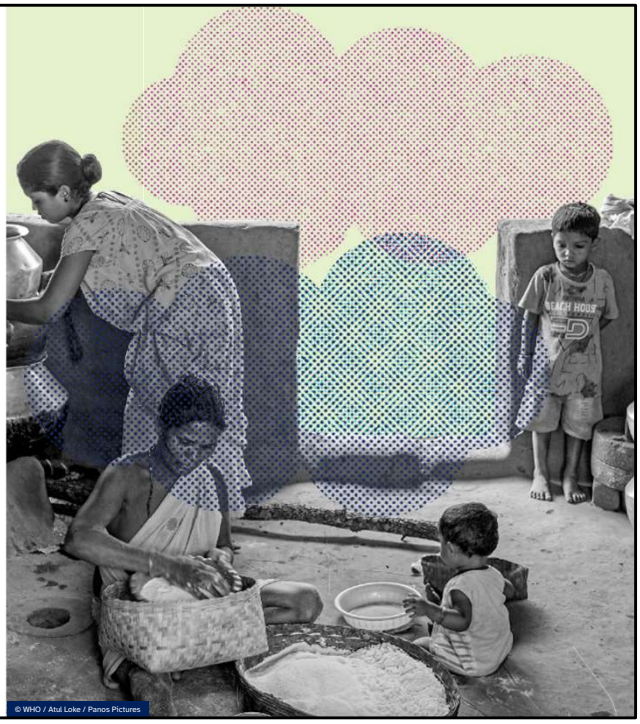
Children and air pollution

Young children spending time in the home are exposed to household air pollution from unclean fuels and technologies for cooking, heating and lighting.



Particularly in low- and middle- income countries, young children spending time with their mothers in the home are exposed household air pollution from the use of unclean fuels and technologies for cooking heating and lighting.

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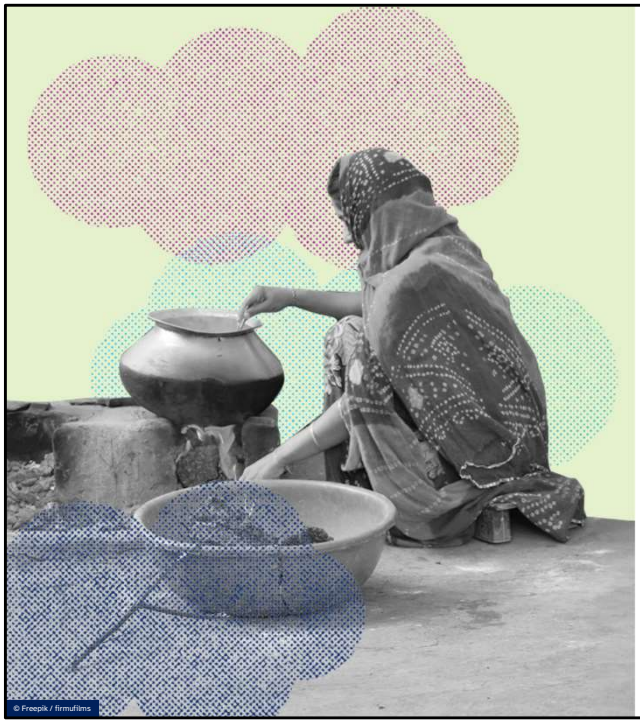

Children, women and air pollution

Especially in low- and middle-income countries, women are generally more exposed to air pollution deriving from the use of unclean fuel and technologies for cooking, heating and lighting in and around the home.

Women are considered a population group at higher risk of experiencing the negative health effects of air pollution particularly in the context of household air pollution.

The reason for these gender inequities is that, in low- and middle-income countries, women are generally more exposed to air pollution deriving from the use of unclean fuel and technologies for cooking, heating and lighting in and around the home.

Together with children, especially girls, they are the main procurers of fuels which is linked to both health and safety risks as we learned in Module 2.

Women and children accounted for more than 60% of all deaths from household air pollution in 2016.

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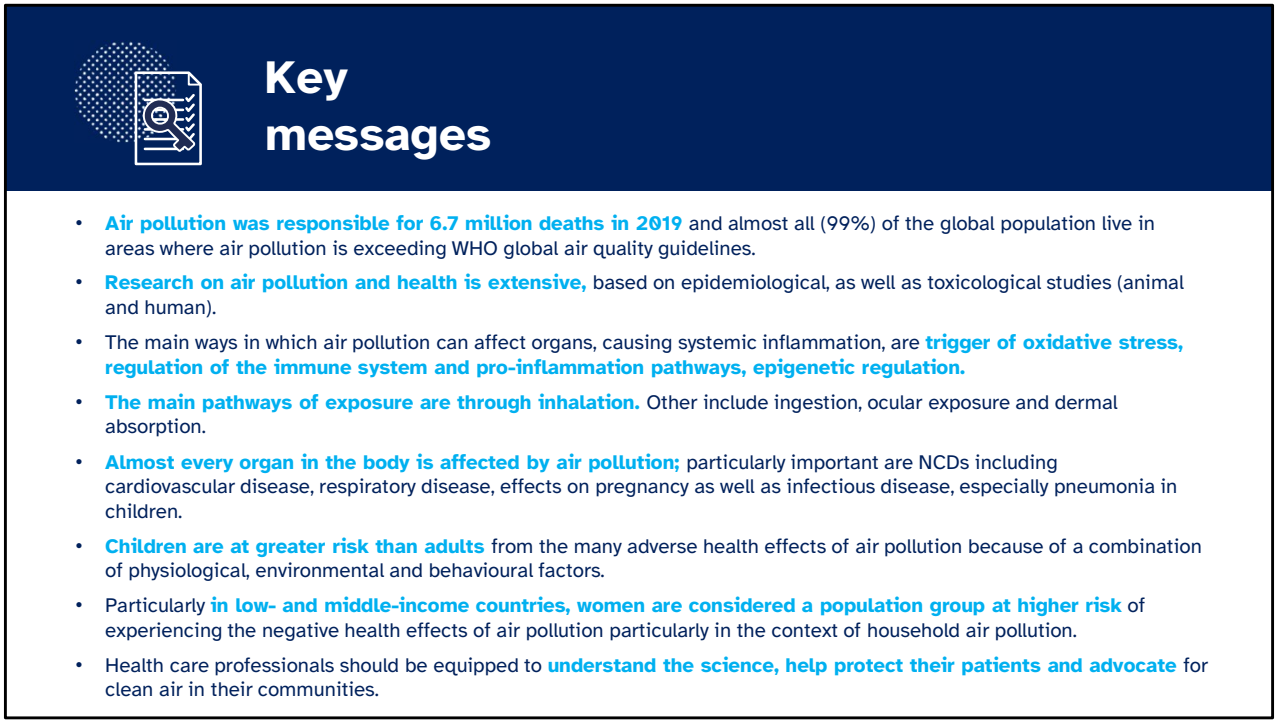

The key messages from this module are as follows.

- Air pollution was responsible for 6.7 million deaths in 2019 and almost all (99%) of the global population live in areas where air pollution is exceeding WHO global air quality guidelines.
- Research on air pollution and health is extensive, based on epidemiological, as well as toxicological studies (animal and human).
- The main ways in which air pollution can affect organs, causing systemic inflammation, are trigger of oxidative stress, regulation of the immune system and pro-inflammation pathways, epigenetic regulation.
- The main pathways of exposure are through inhalation. Other include ingestion, ocular exposure and dermal absorption.
- Almost every organ in the body is affected by air pollution; particularly important are NCDs including cardiovascular disease, respiratory disease, effects on pregnancy as well as infectious disease, especially pneumonia in children.
- Children are at greater risk than adults from the many adverse health effects of air pollution because of a combination of physiological, environmental and behavioural factors.
- Particularly in low- and middle-income countries, women are considered a population group at higher risk of experiencing the negative health effects of air pollution particularly in the context of household air pollution.
- Health care professionals should be equipped to understand the science, help protect their patients and advocate for clean air in their communities.

Glossary

All-cause mortality: A term used by epidemiologists and scientists to refer to death from any cause.

Concentration: Amount of a substance in a medium, usually expressed in terms of mass per unit volume (e.g. $\mu g/m^3$).

Dose: The amount of a substance available for interactions with metabolic processes or biologically significant receptors after crossing the outer boundary of an organism.

Exposure: Contact made between a chemical, physical or biological agent, and the outer boundary of an organism (e.g. skin, lungs or gut).

Forced vital capacity (FVC): Refers to the volume of air that can be forcibly exhaled after having taken the deepest breath possible.

Pre-eclampsia: High blood pressure in pregnant women after 20 weeks of pregnancy. It can be asymptomatic or manifest with signs of damage to other organ systems, most often the liver and kidneys. If pre-eclampsia is accompanied by seizures (convulsions), it is then called eclampsia.

Premature death: Death that occurs before the average age of death in a certain population.

Small for gestational age (SGA): Fetus or newborn's weight below the 10th percentile for the gestational age.

Susceptibility: An innate or acquired physical predisposition that increases the relative risk of experiencing health effects as a result of air pollution exposure – such as pre-existing conditions or diseases.

Vulnerability: Means that people have increased exposure to air pollution due to external factors.

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Contributors and acknowledgements

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Disclaimer

This module contains a large set of slides from which the presenter should select the most relevant ones to use in a specific presentation. These slides cover many facets of the problem. Present only those slides that apply most directly to the local or regional situation. Where relevant, you can adapt the information, statistics and photos within each slide to the particular context in which this module is being presented.

This module belongs to the Air Pollution and Health Training toolkit targeting health workers (APHT). It has been developed in collaboration with more than 30 experts from government agencies, WHO collaborating centers, non-state actors, including medical and environmental health associations, as well as academic institutions. The methodology used for development included a mapping of existing air pollution and health training opportunities targeting health workers which informed gaps and needs for a global set of materials. Experts identified through existing collaborations with WHO contributed on the definition of outline and populating the training modules with contents. Peer review and pilot test coordinated by WHO ensured the collection of feedback and input for finalization of the products.

WHO made all possible effort to ensure geographical and gender balance for the development of the training toolkit acknowledging limitations in terms of expertise, experience and overall feasibility. You can use and have access to other APHT modules where relevant.
To see the full package visit: https://www.who.int/tools/air-pollution-and-health-training-toolkit-for-health-workers

For more information on WHO's work on air quality, energy and health, please visit: https://www.who.int/teams/environment-climate-change-and-health/air-quality-and-health

HEALTH EFFECTS OF AIR POLLUTION: A GENERAL OVERVIEW

Air pollution and health training toolkit for health workers (APHT)

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QR code
to toolkit