How Do Scientists Determine The Health Risks From Air Pollution?

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Air pollution is a major global health issue. It is not limited to urban areas, but is pervasive in nearly all cities, with the negative effects spilling over to ecological and economic systems. Pollutants like particulate matter (PM), specifically $PM_{2.5}$ and PM_{10}, NO_2 and ozone are linked to higher rates of chronic diseases. Short-term effects include coughing, headaches, and asthma, while long-term exposure can damage vital organs and contribute to non-communicable diseases such as heart disease, cancer, pulmonary disease, diabetes, and even mental health conditions. Although air pollution levels have declined over the past decades in Europe, only a handful of regions meet the safe concentration levels recommended by the World Health Organization (WHO) in 2021.

Box 1. Did you know that polluted air may increase the risk of depression?

Depression is one of the leading causes of disability globally, affecting approximately 280 million people around the world. In the European Union (EU), recent data estimates that 7.2% of the population suffers from chronic depression. This percentage has increased over the years.

Several studies have found that exposure to air pollution may increase the risk of developing depression, as well as worsen existing cases. The mechanisms through which air pollution contributes to depression are complex and not fully understood, but various pathways have been proposed based on existing studies. For example, air pollution may influence the levels and activity of **neurotransmitters** in the brain and affect the regulation of **stress hormones**, both of which play crucial roles in mood regulation. Moreover, pollutants such as PM can induce **chronic inflammation**, a recognized factor in various mental health disorders, including depression, as well as **oxidative stress** in the brain, which can lead to neuroinflammation and neuron damage. It is also possible that direct transport of particles to the brain plays a role. While these associations have been observed, establishing causal links is challenging due to the complex nature of depression. It is also possible that exposure to traffic noise, which is often related to air pollution and shares a common source, may play a role, and that a pathway might be through **decreased sleep quality**.

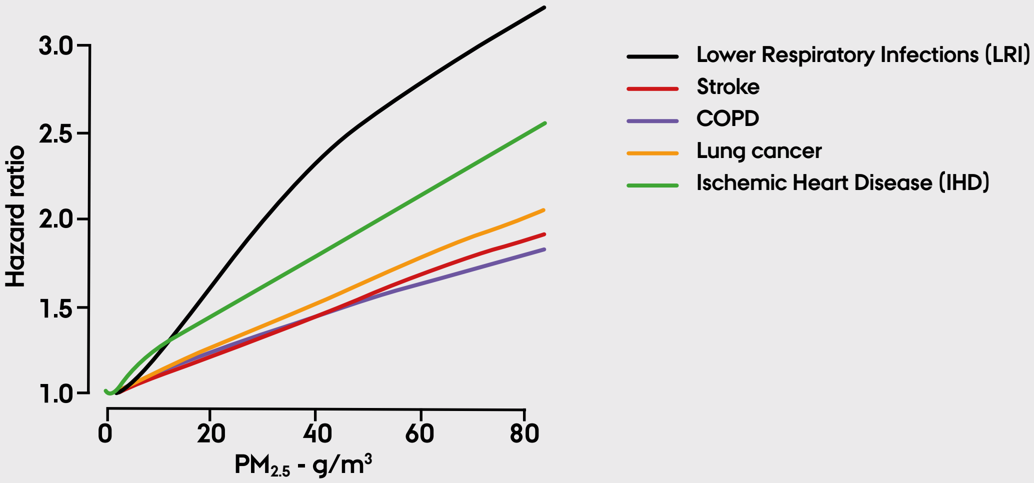
How Do Scientists Establish Associations between Exposure to Air Pollution and Health Risks?

Typically in environmental and socio-economic analyses, **exposure-response functions** are used to estimate how much the risk of disease or premature death can statistically be expected to increase for a given increase in air pollution.

An exposure-response function is a mathematical relationship that describes how the risk or severity of a health outcome changes with a change in exposure to an environmental factor, such as air pollution. This function is a **key tool** in environmental health studies as it quantifies the link between the level of exposure (e.g., to air pollutants like $PM_{2.5}$) and the probability of a health effect (e.g., depression, respiratory disease, heart attack, premature death).

These exposure-response functions are represented in function graphs in which the x-axes show exposure levels, represented by the concentration or dose of an environmental factor (in this case air pollution), and the y-axes indicate the response (health outcomes), measured as incidence rates or **relative risk**. The latter refers to the risk of a given health outcome in a group exposed to an environmental factor compared to the risk of the same health outcome in a (control) group that is not exposed or exposed to the lowest levels of that factor.

Figure 1. The concentration of $PM_{2.5}$ in the air and the incidence of different diseases. Exposure-response function



Source: Burnett R, Chen H, Szyszkowicz M. Global estimates of mortality associated with long-term exposure to outdoor fine particulate matter. PNAS (2018). https://doi.org/10.1073/pnas.1803222115

If the exposure-response function is increasing and linear, it indicates that for each increment in PM2.5 concentration, there will be a constant corresponding increase in the risk of developing disease.

The shape of the exposure-response function provides crucial information. It can take various forms (linear, logarithmic, exponential, etc.) depending on the relationship between exposure and response. A **straight-line** (linear relationship) indicates that health risks increase at a constant rate with exposure. However, risks may be non-linear, increasing at varying rates with changes in exposure levels, such as increasing risk at higher exposures. For example, while a small increase in exposure may double the probability of a health outcome at lower levels of exposure, it may triple the probability at higher levels of exposure. In some cases, no effect on risk is observed until a **threshold** exposure level is reached, after which the risk increases.

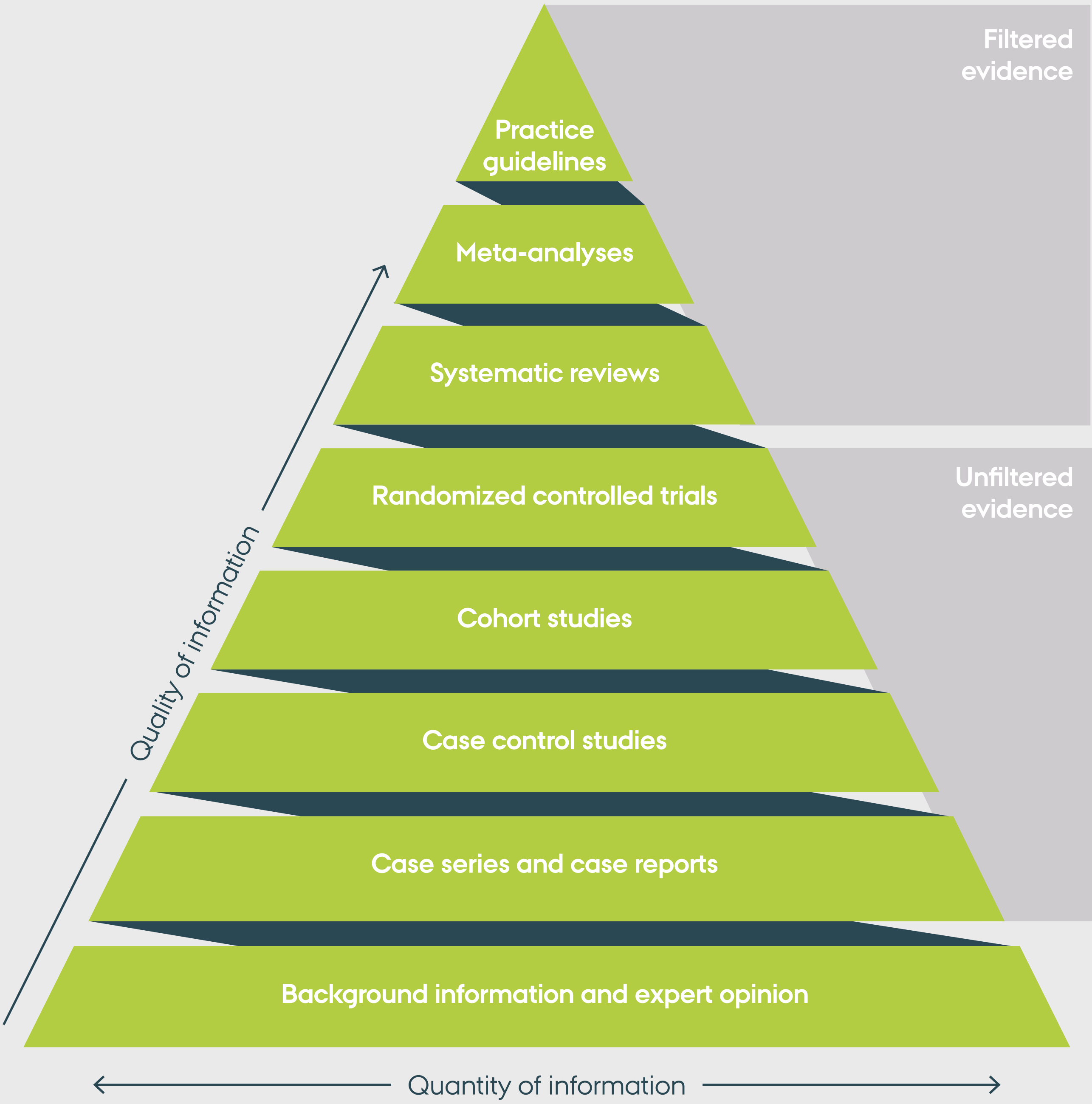
Exposure-response functions have a wide range of **applications**. If the links between environmental exposures and health outcomes are determined, they can help inform policy, standards, and guidelines to protect public health. Moreover, they can be used to determine the expected health benefits of measures to reduce air pollution, by allowing the estimation of the impact of reduced exposures. Such estimations can be further translated into economic benefits and applied in socio-economic analyses.

In order to identify exposure-response functions, scientists often have to rely on **epidemiological studies** (e.g., cohort and case-control studies). Epidemiological studies are observational and may be subject to residual confounding - when the outcome is explained by unknown or unobservable confounding factors. To overcome this limitation, scientists use **systematic reviews** that consider all the available evidence to reduce potential bias in the original studies. Systematic reviews and meta-analyses are indispensable in synthesizing and evaluating an expansive body of environmental health studies.

Once the effect of exposure to air pollution on health outcomes is reliably quantified, it can be transformed into the **economic value** associated with the changes in health outcomes. This allows the estimation of the effect of air pollution in monetary terms, which is useful to justify public investment in air quality improvement measures. For instance, an argument in favor of a given measure can be made by illustrating that the implementation of the policy would result in net benefits to society. That is, the cost involved in implementing the measure (in monetary terms) would be lower than the **saved costs from improved health outcomes** (in monetary terms).

Box 2. Are you familiar with the pyramid of evidence?

Research studies can be classified by **the strength of their evidence and methods**. This figure visualizes this classification in the form of a pyramid. The top layer corresponds to the strongest evidence, while the bottom to the weakest. Notably, the bottom layer is where often most information is available. Sometimes, the amount of the highest quality evidence is insufficient to reach conclusive results. When that happens, we look for the next best quality evidence.



Source: UNE Library Services. https://library.une.edu/research-help/help-with/evidence-based-practice/the-evidence-pyramid/#:~:text=The%20levels%20of%20evidence%20can,pyramid%2C%20but%20decreases%20in%20quality

What Are Systematic Reviews and Meta-Analyses?

Systematic reviews are a rigorous process of gathering and assessing all available studies related to a particular exposure-outcome pair. This process allows us to:

- **Synthesize the evidence** by comprehensively screening the literature. This reduces the risk of bias inherent in relying on individual studies and ensures a thorough examination of the existing evidence as a whole.
- **Harmonize disparate findings**. Studies often use different methods which can lead to conflicting or unclear results. Systematic reviews combine various findings to find common trends and patterns. This makes it easier to understand and interpret the overall evidence.
- **Identify research gaps** by pinpointing gaps in evidence or highlighting areas warranting further investigation, and **contributing** to the iterative process of science to guide future research efforts.

A meta-analysis is a statistical technique used to combine the results of multiple studies identified through a systematic review. Meta-analyses provide a more precise estimate of the effect size by increasing the sample size and power of the study. They combine and analyze data from multiple studies on the same topic to find overall trends and conclusions. Through statistical methods, meta-analyses provide an estimation of the overall effect size of an exposure-outcome relation, i.e, the exposure-response function. However, the results of a meta-analysis can change as they are based on the existing evidence at the time they are conducted.

The MARCHES Project Contribution to Exposure-Response Functions for Air Pollution

The MARCHES (Methodologies for Assessing the Real Cost to Health of Environmental Stressors) project will improve our understanding on how air pollution affects mental health and other chronic conditions. Focusing on pollutants $PM_{2.5}$, NO_2, and ozone, it will systematically review the scientific evidence for potential links between air pollution and two understudied outcomes: depression and inflammatory bowel disease (IBD). When enough literature is available, exposure-response functions will be calculated through meta-analyses.

The MARCHES project

The Horizon Europe MARCHES project aims to advance methodological rigor and consistency in accounting for the welfare economic health costs of pollution, based on systematic reviews of health effects. MARCHES will calculate the impacts of air pollution and nitrates in drinking water on public health and to quantify the economic benefits of reducing emissions and exposures. Establishing updated exposure-response functions is essential for accurately estimating the societal costs of pollution and highlighting the societal value of implementing mitigation measures. This will be demonstrated in case studies where MARCHES partners will collaborate with public authorities in six countries (Czechia, Denmark, Estonia, Kosovo, Spain and Sweden). Learn more about the research and activities of the MARCHES project here: https://projects.au.dk/MARCHES

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