



Isabella Annesi-Maesano

Research Director, Professor of Environmental Epidemiology, Department of Environmental and Prevention Sciences, University of Ferrara, Italy

“The most exciting frontier in allergy and respiratory epidemiology lies in moving beyond the ‘one-size-fits-all’ model toward precision prevention”

Citation:

EMJ Allergy Immunol. 2026;11[1]:54-56.
<https://doi.org/10.33590/emjallergyimmunol/QN5DK645>

Q1 What initially drew you to respiratory epidemiology and environmental health, and how did your journey from medicine, physics, and epidemiology shape the way you approach allergy and immunology research today?

Since my first readings (among the most important, Albert Schweitzer on leprosy in Lambaréné, Gabon), my idea was to protect human health. To reach it, my ‘journey’ was shaped by interdisciplinarity. Medicine (which for me is the human anchor needed to start) has provided the foundational understanding of the biological toll that health status (allergies and respiratory diseases in my research activity) takes on patients. It ensures that my research remains patient-centred as an entity of the general population, focusing not just on data, but on ‘pathological consequences’ and the real-world efficacy of prevention, primary when possible. Physics (which, for me, represents the structural lens) introduced the rigor of assessments, complex systems modelling, and validation of the methods. This background allows me to critically evaluate the limitations of current environmental models. It has encouraged looking at the ‘mechanics’ of exposure, for example, in the case of air pollution from particle emission to atmospheric behaviour and then penetration in the human body. Finally, epidemiology (for me, the population perspective) has served as the bridge, translating individual biological mechanisms, clinical outcomes, and external

exposures into public health imperatives. It provides the methods and statistical toolkit to quantify without risk of bias, and the framework to advocate for large-scale interventions, such as environmental surveillance and the promotion of peace as a prerequisite for health.

Q2 The exposome concept has gained traction as a framework for understanding disease causation. In your view, what are the biggest methodological challenges in measuring the exposome, and how are advances in data science helping to overcome them?

For a researcher with a background in physics and epidemiology like me, the exposome (the totality to which every individual is exposed in his/her life and that shapes his/her health) is essentially a signal-to-noise problem. Data science provides the ‘filter’ needed to extract meaningful biological signals and clinical outcomes from the noisy environmental data of modern, conflict-affected landscapes. Advances in assessments and computation are transforming the exposome from a theoretical concept into a quantifiable metric. I’m directly involved in individual assessment of air pollution exposure with personal sensors. Major methodological challenges include:

- The spatio-temporal resolution gap. Exposure is dynamic, but our measurement tools are often static. While we can measure pollutants at a specific station, ascribing that level to a person moving

through a city is difficult.

- High-dimensionality and 'the cocktail effect'. Traditional epidemiology struggles with the sheer volume of variables. Individuals are not exposed to single risk factors, but to mixtures (heavy metals, particulate matter, biocontaminants, noise, heat, and psychosocial stress, among others for instance). Statistical models often suffer from multi-collinearity (where exposures are correlated) and the 'curse of dimensionality', making it hard to isolate the specific driver of a health outcome.
- Latency and life-course tracking. The most critical exposure for an adult-onset respiratory disease may have occurred *in utero* or during early childhood (the developmental origins of health and disease concept).

Q3 Air pollution, climate change, and biodiversity loss are increasingly implicated in allergic and respiratory diseases. Which of these environmental drivers do you believe has the most immediate impact on patient outcomes, and what evidence still needs to be strengthened?

All these factors are all very important as they constitute the triple planetary crisis impacting allergic and respiratory health through different mechanisms and timeframes. In my view, and supported by current clinical and epidemiologic data, air pollution remains the most immediate threat to patient outcomes, while biodiversity loss represents the most significant 'blind spot' in our long-term preventative strategy. Air pollution acts not only as an immediate trigger, but also as a contributing factor for several

respiratory diseases' development, the so-called incidence. Robust data exist for asthma, COPD, idiopathic pulmonary fibrosis, and lung cancer.

Moving beyond simple correlation toward causation, strengthening the evidence for both the development (incidence) and exacerbation of respiratory diseases as a consequence of the exposome requires:

- Closing the resolution gap: integrating hyper-local data to capture acute, point-source exposures.
- Understanding 'the cocktail effect': investigating how multi-pollutant mixtures synergise with heat and allergens.
- Life-course tracking: solidifying the links between early-life (*in utero*) environmental insults and adult-onset chronic disease through epigenetic and 'multi-omic' research.

This requires substantial data and resources, typically supported through dedicated projects and associated funding. Unfortunately, research funding is becoming increasingly limited.

Q4 Your work often focuses on early-life exposure and critical windows of vulnerability. What have we learned about interventions in pregnancy and early childhood that could meaningfully reduce lifelong allergy or respiratory disease risk?

Research into the developmental origins of health and disease hypothesis has confirmed that the prenatal period and the first 1,000 days of life are the most critical windows for immune

'programming' and later health. With other colleagues in the frame of the international Pregnancy and Childhood Epigenetics (PACE) consortium, we have published that environmental risk factors already act on newborns' epigenome. More importantly, interventions during these stages are not just about preventing paediatric symptoms; they are about altering the structural and epigenetic trajectory of the immune system and the lungs for a lifetime. Interventions include nutritional and supplementation strategies (vitamin D, omega-3 fatty acids, early allergen introduction), and implementing the need for early biodiversity exposure or reducing air pollution exposure.

Q5 Twin cohorts and multi-omics approaches are powerful tools in disentangling genetic and environmental influences. What unique insights have twin studies provided in your research, and where do you see their limitations?

Twin studies act as a 'natural experiment' that allows us to bypass the noise of genetic variability, providing the unique insight that, while genetic predisposition sets the 'ceiling' for lung function, environmental hits, especially in early life, determine whether that ceiling is reached. By comparing monozygotic twins, my research in the EU Health and Environment-Wide Associations Based on Large Population Surveys (HEALS) project has highlighted how discordant environmental exposures, such as growing up in a high-pollution urban centre versus a rural area, lead to distinct epigenetic signatures and 'multi-omic' profiles despite identical DNA. However, a primary limitation of twins studies lies in representativeness; twins often have different prenatal

growth patterns (e.g., lower birth weight) than singletons, which can confound respiratory outcomes. Furthermore, even monozygotic twins are not truly 'identical' at the molecular level due to somatic mutations and stochastic epigenetic drift, meaning that while they help disentangle the 'nature versus nurture' debate, they cannot fully account for the sheer complexity of the individual exposome.

Q5 During the COVID-19 pandemic you studied interactions between air pollution and viral infections. What surprised you most about these relationships, and how might this knowledge inform preparedness for future respiratory pandemics?

The shift in understanding SARS-CoV-2 as a primarily airborne pathogen, to which I contributed by signing the first published paper on the topic, has fundamentally redefined the landscape of respiratory protection, moving the focus from surface hygiene to the 'atmospheric commons'. This realisation underscored the urgent need for structural prevention, particularly through the implementation of pharmaceutical-grade ventilation and high-efficiency particulate air filtration in public spaces to mitigate the concentration of infectious aerosols. Furthermore, since air pollution can upregulate entry receptors like angiotensin-converting enzyme 2 (ACE2), the 'clean air mandate' must be viewed as a critical form of environmental

prophylaxis; by reducing the baseline of particulate matter and gaseous pollutants, we can effectively lower population-wide susceptibility to viral penetration. Ultimately, integrated environmental and clinical surveillance is essential to transform our indoor and outdoor air from a vector of transmission into a primary barrier against future respiratory pandemics.

Q6 Machine learning and big data are increasingly used in epidemiology. How do you balance the promise of these methods with concerns about interpretability and bias, especially when translating findings into public health policy?

I'm presently working on AI application to air pollution (for instance, on the 'cocktail effect' of complex mixtures) and pollen assessment and interpretation of molecular allergy (the so-called 'chips'). In the former case, to translate these findings safely into policy, we must prioritise interpretability, ensuring that the identified 'risk clusters' align with biological plausibility and clinical reality, while implementing strict algorithmic auditing to detect and correct for socioeconomic and geographic biases. Ultimately, machine learning should be viewed as a sophisticated tool for hypothesis generation, which must then be validated through traditional causal inference and clinical expertise before being codified into public health mandates.

Q7 Looking ahead, what do you consider the most exciting unanswered questions in allergy and respiratory epidemiology, and where should the next generation of researchers focus their efforts to drive meaningful prevention strategies?

The most exciting frontier in allergy and respiratory epidemiology lies in moving beyond the 'one-size-fits-all' model toward precision prevention that accounts for the dynamic plasticity of human beings. The next generation of researchers must focus on closing the 'resolution gap' by integrating hyper-local, real-time exposomics with multi-omic data to identify not just who is at risk, but during which critical windows environmental scarring, such as epigenetic changes from air pollution or biodiversity loss, can be reversed. By leveraging explainable AI to decode the 'cocktail effect' of complex mixtures and advocating for the peace-health nexus, young scientists can transform our understanding of the atmosphere from a passive backdrop into a manageable biological shield. The ultimate goal is to design urban environments and public health policies that proactively 'programme' immune tolerance rather than merely reacting to chronic inflammation.

