

# Understanding environmental exposures in early life for lifelong health

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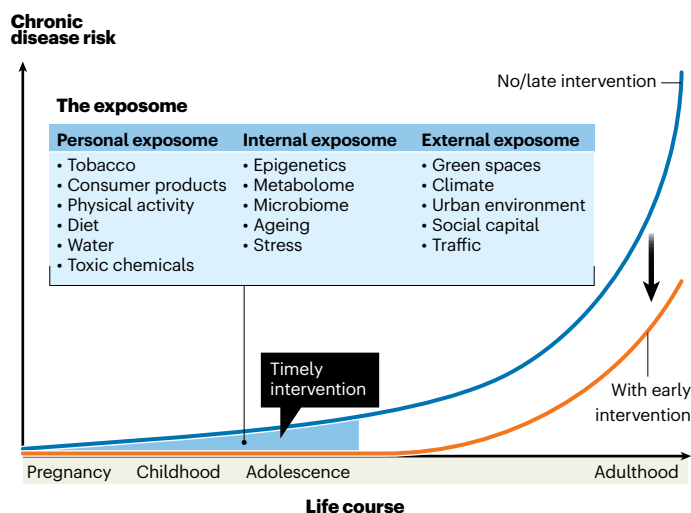
Understanding early-life environmental exposures is crucial for protecting lifelong health and should be prioritized in developing exposomics studies and infrastructures worldwide.

Early-life environmental exposures – from chemical pollutants to psychosocial stressors – shape lifelong health, yet their complexities remain poorly understood. Exposomics approaches can capture this real-world complexity by integrating comprehensive exposure data with molecular insights and advanced data analytics. To protect health from the earliest, most-vulnerable life stages, we must now scale early-life exposomics and ensure translation to actionable policy.

## Why early-life environmental exposures matter

Children are exposed to many different environments that have a profound influence on their growth and development. Indeed, early life, from conception through childhood and adolescence, has long been recognized as being especially vulnerable to the effects of environmental exposures that disrupt developmental processes, with lifelong consequences – as captured by the developmental origins of health and disease paradigm<sup>1</sup>. Before conception, environmental contaminants may damage the reproductive cells of both the father and mother with mutations and epigenetic changes that can be passed on to the next generation. The pregnancy period involves unique physiological changes and epigenetic, metabolic and immune adaptations, and even small disruptions can have detrimental consequences for the mother and fetus<sup>2</sup>. The placenta, a largely understudied organ that acts as both a pathway for chemical transfer to the fetus and as a mediator of health effects, is central to this period. For example, the placenta is vulnerable to chemicals that can disrupt the endocrine system, including pesticides and perfluoroalkyl and polyfluoroalkyl substances, which may cause oxidative stress and alter epigenetic programming, gene expression and placental function. Following birth, children remain highly susceptible to environmental exposures owing to their rapidly developing organ systems, smaller body size and unique exposure profiles. Proportionately higher rates of intake through food, water and air, coupled with behaviours such as hand-to-mouth contacts, increase their chemical burden. Furthermore, non-chemical stressors such as noise, temperature extremes, built and natural environment characteristics, socioeconomic disadvantage and psychosocial factors are increasingly recognized for their role in ‘biological embedding’, shaping immune, metabolic and neuroendocrine pathways. Finally, puberty is a period of rapid physiological and developmental transformation, which makes it highly sensitive to environmental influences – yet these effects remain under-researched.

Many noncommunicable diseases, including type 2 diabetes, cardiovascular disease, lung disease and mental disorders, trace at



**Fig. 1 | Exposome research can underpin early-life interventions to improve lifelong disease trajectories.** Chronic disease risk increases throughout the life course and the trajectory is determined in the first decades of life (blue area)<sup>1</sup>. Exposome research can underpin the identification of complex and combined environmental risk factors and biomarkers during early life, opening the possibility of early interventions. Timely interventions in early life (blue area) can have a large effect on later disease risk, shifting the trajectory from high risk (blue line) to low risk (orange line).

least part of their origins to these early decades. For instance, half of all cases of chronic obstructive pulmonary disease originate from early-life exposures that impair lung development<sup>3</sup>; preventing childhood lung damage could thus be as vital as mitigating adult smoking or occupational hazards. Similarly, adolescent body mass index – even within the normal range (50th–74th percentile) – correlates strongly with cardiovascular and all-cause mortality over 40 years of follow-up<sup>4</sup>. Targeting these vulnerable periods for preventative measures can offer a more effective strategy for improving lifelong disease and ageing trajectories than treatments administered after the disease manifests<sup>1</sup> (Fig. 1).

## The challenge of complexity

Many early-life risk factors are now well established; maternal obesity, smoking during pregnancy and poor childhood diets are known to contribute to chronic diseases later in life<sup>1</sup>. Similarly, air pollution, lead contamination and some other well-documented environmental pollutants have been clearly linked to adverse child health and development. However, many other environmental risks remain poorly understood and insufficiently regulated, including many chemical contaminants, microplastics and nanoplastics, unhealthy living environments,

climate-related stressors, psychosocial stress and adverse childhood experiences. Most research has focused on single exposures in isolation, and rarely addressed how they cluster and interact, or how social and neighbourhood contexts shape them. This complexity is further compounded by the fact that environmental exposures are highly variable over time and thus across the vulnerable time windows, and require repeated measurements to accurately characterize exposure profiles. Moreover, of the more than 100,000 chemicals registered on the global market, thousands cause widespread population exposure, but only a small proportion has undergone comprehensive assessment of potential hazards to health, creating the “silent threat of chemical pollution”<sup>5</sup>. Finally, early-life exposures may trigger biological responses at the molecular and preclinical level, which may remain clinically undetected until adulthood. Traditional research approaches have struggled to fully capture the complexities of early-life environmental exposures and relate these to long-term health trajectories.

## The opportunities of exposomics

Exposomics – the systematic and comprehensive study of environmental influences on health – offers a promising approach to disentangling these complexities, by moving beyond isolated stressors to prioritize the integrated compilation of the physical, chemical, biological, social and psychosocial exposures of the real world<sup>6</sup>. Over the past two decades, exposomics has evolved from a conceptual framework into a data-driven scientific field, enabled by advances in analytical chemistry, geospatial modelling, wearable and digital technologies, multiomics integration, and big data analytics and artificial intelligence (AI). For example, high-resolution mass spectrometry platforms can now detect tens of thousands of molecular features in a single blood or urine sample, which means they now enable the non-targeted identification of previously unknown chemical substances and their interactions with endogenous molecules. Geospatial exposure modelling (including satellite-based remote sensing of air pollutants) and mapping of natural, built and social environments are capable of characterizing many external environment exposures at a fine spatial resolution across very large populations. Further, a range of sensor and wearable-based techniques are available for real-time personal monitoring. These include passive sensors (such as silicone wristbands and diffusion tubes to measure airborne chemical exposures) and digital sensing technologies, such as smartphone applications and wearables to measure mobility, activity and exercise patterns, physical exposures (light, noise and temperature) and social-media-related behaviours. Integrating comprehensive exposure data from these methods with large-scale omics platforms (such as genomics, proteomics and metabolomics) allows us to elucidate mechanisms and develop predictive biomarkers for future disease risk related to our environment.

## Early-life exposome cohorts as a crucial resource

Longitudinal early-life cohorts are particularly powerful for studying repeated exposures, windows of susceptibility, and long-term health outcomes, from conception onwards. Some of these cohorts already offer proof of concept that systematic and comprehensive early-life exposome research is feasible. For example, the Human Early Life Exposome (HELIX) cohort has successfully integrated multiple early-life environmental exposures and studied their influence on a range of child health end points (Table 1). Results from this cohort show, for example, that urban exposure clusters – which combine air pollution, noise and lack of green space – can contribute to elevated blood pressure in childhood, an important marker of later cardiovascular

disease risk<sup>7</sup>. Further, HELIX identified mixtures of endocrine disruptors, including perfluoroalkyl and polyfluoroalkyl substances and heavy metals, that jointly drive paediatric liver injury and metabolic syndrome<sup>8</sup>. Children from low socioeconomic backgrounds appeared to be more vulnerable to the effects of chemical mixtures, which underscores the importance of integrating social determinants<sup>9</sup>. Multiomics integration resulted in an early-life exposome–omics catalogue, which maps how environmental exposures interact with molecular pathways to influence child health outcomes<sup>10</sup>, and in child-health risk scores that can help to identify high-risk children and inform targeted prevention strategies<sup>11</sup>.

However, a critical bottleneck remains: early-life exposome studies currently rely on modest sample sizes of a few thousand participants at most. The integration of increasingly high-dimensional exposome and multiomics data requires much larger sample sizes. Although there are many birth cohorts worldwide (including some large ones such as the Japan Environment and Children’s Study (JECS) study; Table 1)), these cohorts have mostly focused on traditional single-exposure approaches. The harmonization and joint analysis of existing cohorts offers an important opportunity for achieving the larger sample sizes needed for exposomics studies. For example, the EU Child Cohort Network has harmonized and standardized many early-life stressors and health outcomes across European birth cohorts, and made data available through a FAIR (findable, accessible, interoperable and reusable) data infrastructure that can be accessed through a federated non-disclosive data analysis interface<sup>12</sup>; similar efforts are underway in other parts of the world (Table 1). However, even after harmonization, the scattered availability of data across cohorts still hinders the full implementation of integrated, exposome-wide analyses, and the harmonization and integration of omics data in these infrastructures is extremely challenging.

## Future vision

To move beyond proof of concept and realize the full potential of early-life exposomics, there are several key priorities.

**Scaling cohorts and infrastructure.** Large-scale adult cohorts with extensive exposure, multiomics and health data (such as the UK Biobank) are available in many countries. By contrast, early-life cohorts of comparable size and depth remain scarce. We must expand early-life cohorts and integrate these fully into large FAIR exposome data infrastructures that span the entire life course. New cohorts are also needed to address emerging environmental challenges that older cohorts could not anticipate, such as emerging pollutants, microplastics and nanoplastics, climate change stressors, and technological shifts.

**Mapping the unknown chemical space.** Current protections for the developing fetus and child against chemical hazards are insufficient. Scaling biomonitoring to the level of large biobanks (50,000–100,000 participants) is essential to capture the complexity of the vast, dynamic and largely unmeasured chemical exposome during early life. By leveraging infrastructures such as EIRENE (Research Infrastructure for Environmental Exposure Assessment in Europe), high-resolution mass spectrometry platforms can be used to capture the ‘silent threat’ of unmeasured chemical mixtures. Chemical biomonitoring in large-scale early-life cohorts should be integrated with mechanistic investigations in model systems and AI-driven toxicological tools to move risk assessment from single-pollutant models to real-world complexity.

**Table 1 | Examples of cohort data resources relevant for early-life exposome research**

Description	Exposome data	Link for data access
<b>HELIX cohort (n = 1,663 participants)</b>		
Collaborative study across six established and ongoing longitudinal population-based birth cohort studies in six European countries (EDEN (France), RHEA (Greece), KANC (Lithuania), MoBa (Norway), INMA (Spain) and BiB (UK)). Fully harmonized data collections measured exposures during pregnancy, childhood and adolescent periods, and omics signatures and health outcomes (cognition, behaviour and mental health, cardiometabolic health, respiratory health and allergies) during childhood and adolescence.	Central database including chemical, urban, lifestyle and social exposures, as well as genomics and multiomics (metabolomics, proteomics, transcriptomics, DNA methylation and metagenomics). Has been used for exposome-wide health association studies, exposure mixture studies and exposome-omics studies.	Full <a href="#">cohort data</a> from the central data warehouse, including exposures, biomarkers and health outcomes, are available to external researchers upon request
<b>EU Child Cohort Network (n &gt; 250,000 participants)</b>		
European network with FAIR data infrastructure that covers over 40 pregnancy and childhood cohorts across Europe with over 250,000 mother-child pairs, constructed as part of the <a href="#">LifeCycle project</a> and further expanded by the <a href="#">ATHLETE</a> and <a href="#">LongiTools</a> European exposome projects. Urban exposome variables generated using standardized protocols. Harmonized datasets available for federated analysis.	Harmonized data for several exposome domains, including chemical, urban, lifestyle and social factors. Metadata catalogue summarizes the harmonized variables. Has been used for single-exposure meta-analyses, and urban exposome studies.	Metadata <a href="#">catalogue</a> Harmonized variables available on request from the individual cohorts for federated, non-disclosive analysis through <a href="#">DataSHIELD</a>
<b>Environmental Influences on Child Health Outcomes (ECHO) cohort (n &gt; 50,000 participants)</b>		
The ECHO cohort, part of the NIH ECHO programme, integrates over 60 existing pregnancy and child cohorts across the USA. The cohort covers five child health outcomes, including obesity, prenatal, perinatal and postnatal outcomes, upper and lower respiratory disease, wellness, and neurodevelopment.	Harmonized data for several exposome domains, including chemical, urban, lifestyle, social and psychosocial factors. Has been used mainly for studies of single exposures and single-exposure families.	Harmonized deidentified data available through the Data and Specimen Hub ( <a href="#">DASH</a> )
<b>Birth Cohort Consortium of Asia (BiCCA) (n = 80,000–100,000 participants)</b>		
Collaborative platform to coordinate birth cohort research across Asia, focused on environmental exposures. The consortium includes over 30 birth cohorts across many Asian countries and regions, including Japan, South Korea, China, Taiwan and Singapore.	Individual cohorts with rich data on several exposome domains, including chemical and urban exposures. Currently no harmonized datasets available.	Development of BiCCA and harmonization protocols is <a href="#">ongoing</a>
<b>JECS (n &gt; 100,000 participants)</b>		
JECS is a government-funded birth cohort study that measures environmental exposures during pregnancy and childhood, and examines children's health periodically until 13 years of age. The study covers 15 regions throughout Japan. A substudy and regional adjunct studies collect more detailed data.	Data for several exposome domains, including chemical, urban, lifestyle and social factors. Has been used mainly for studies of single exposures and single-exposure families.	Limited full access owing to data protection regulation; inquiries about data access should be <a href="#">directed</a> to the cohort

ATHLETE, Advancing Tools for Human Early Lifecourse Exposome Research and Translation; BiB, Born in Bradford; EDEN, Étude des Déterminants pré et postnatals du développement et de la santé de l'Enfant; INMA, Infancia y Medio Ambiente project; KANC, Kanuas cohort; MoBA, Norwegian Mother and Child Cohort Study; NIH, National Institutes of Health.

**Integrating the social and contextual exposome.** Environmental contaminants do not act in isolation. Socioeconomic factors, neighbourhood conditions, psychosocial stress and lifestyle behaviours interact with chemical and physical exposures to shape health outcomes from early life onwards<sup>13</sup>. To achieve a deeper understanding of the complex, multilayered processes that drive disease development, these factors should not be treated merely as confounders but as overarching exposure drivers with both direct and mediated effects, which act at individual and collective levels.

**Ensuring that exposome findings inform actionable interventions and policy.** Early-life exposomics should not only generate knowledge but also inform actionable interventions and policies to protect child health. Potential causal links identified by exposome cohorts must be validated through intervention studies and mechanistic investigations. Interventions aimed at improving the early-life exposome are few and generally limited in the number of exposures that are tackled. Examples include school-based interventions to improve certain built and natural environment exposures for children<sup>14</sup> or interventions to reduce specific chemical exposures that result from dietary intake

and personal care products during pregnancy<sup>15</sup>. New exposome-scale biological and personal monitoring technologies should be leveraged to develop personalized intervention and prevention strategies directly targeted at early-life exposures. Advanced AI and statistical methods will be crucial for moving to causal inference models that can directly inform policy interventions; agent-based models and digital twins are examples of promising frameworks that allow researchers to simulate complex exposome-scale interventions. Partnerships among academia, communities and policymakers are essential to ensure that exposomics insights translate into transparent frameworks for preventing environmental exposure hazards in early life.

**Strengthening global cooperation.** Most early-life exposome efforts remain concentrated in high-income countries, which leaves vast infrastructure and knowledge gaps in low- and middle-income settings where environmental burdens (such as air pollution, climate stressors and hazardous wastes) are most severe and occur together with infectious diseases, poor nutrition and poverty. Global collaborative networks built through initiatives such as the International Human Exposome Network (IHEN) and the [Global Exposome Forum](#) are vital for local capacity building.

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## Competing interests

The author declares no competing interests.