



# Newborns health in the Danube Region: Environment, biomonitoring, interventions and economic benefits in a large prospective birth cohort study



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## ABSTRACT

**Background:** The EU strategy for the Danube Region addresses numerous challenges including environment, health and socioeconomic disparities. Many old environmental burdens and heavily polluted areas in Europe are located in the Danube Region, consisting of 14 countries, with over 100 million people. Estimating the burden of environmental exposures on early-life health is a growing research area in Europe which has major public health implications, but the data from the Danube Region are largely missing.

**Aim:** This review presents an inventory of current environmental challenges, related early-life health risks, and knowledge gaps in the Danube Region, based on publicly available databases, registers, and literature, as a rationale and incentive for a new integrated project. The review also proposes the concept for the project aiming to characterize *in utero* exposures to multiple environmental factors and estimate their effect on early-life health, evaluate economic impact, as well as identify interventions with a potential to harness social norms to reduce emissions, exposures and health risks in the Danube Region.

**Methods:** Experts in environmental epidemiology, human biomonitoring and social science in collaboration with clinicians propose to establish a new large multi-center birth cohort of mother-child pairs from Danube countries, measure biomarkers of exposure and health in biological samples at birth, collect centrally measured climate, air and water pollution data, conduct pre- and postnatal surveys on lifestyle, indoor exposures, noise, occupation, socio-economic status, risk-averting behavior, and preferences; and undertake clinical examinations of children at and after birth. Birth cohort will include at least 2000 newborns per site, and a subset of at least 200 mother-child pairs per site for biomonitoring. Novel biomarkers of exposure, susceptibility, and effect will be applied, to gain better mechanistic insight. Effects of multiple environmental exposures on fetal and child growth, respiratory, allergic, immunologic, and neurodevelopmental health outcomes will be estimated. Parent's willingness to pay for reducing health risks in children will be elicited by survey, while values of cost-of-illness will be gathered from literature and national statistics. Effects of risk reducing interventions will be examined.

**Abbreviations:** ADHD, attention-deficit/hyperactivity disorder; As, inorganic arsenic; B[a]P, benzo[a]pyrene; CHICOS, Developing a Child Cohort Research Strategy for Europe; CO, carbon monoxide; CR, Czech Republic; DPSEEA, Drivers, Pressures, State, Exposure, Effect, Actions; ENRIECO, Environmental Health Risks in European Birth Cohorts; EPIC, The European Prospective Investigation into Cancer and Nutrition; ESCAPE, European Study of Cohorts for Air Pollution Effects; HEALS, Health and Environment-wide Associations based on Large population Surveys; HELIX, The Human Early-Life Exposome; Hg, mercury; INTERGROWTH-21st, The International Fetal and Newborn Growth Consortium; IQ, intelligence coefficient; MeHg, methyl mercury; NO<sub>x</sub>, nitrogen oxides; NO<sub>2</sub>, nitrogen dioxide; O<sub>3</sub>, ozone; PAH, polycyclic aromatic hydrocarbons; PCB, polychlorinated biphenyl; PM, particulate matter; PM<sub>2.5</sub>, particulate matter with diameter < 2.5 μm; PM<sub>10</sub>, particulate matter with diameter < 10 μm; SINPHONIE, Schools Indoor Pollution and Health: Observatory Network in Europe; T, temperature; QALY, Quality-Adjusted Life Years; VSL, Value of Statistical Life; WTP, willingness to pay.

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**Conclusions:** The proposed project would provide novel estimates of the burden of early childhood diseases attributable to environmental exposures and assess health impacts of different intervention scenarios in the Danube Region, in an integrated approach combining human biomonitoring, epidemiological and social science research.

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## 1. Background

Danube Region, which consists of 14 countries (9 EU member states) and is home to over 100 million inhabitants, faces numerous challenges: big socio-economic disparities, underdeveloped potential of the Danube waterway, and a unique environment threatened by pollution. This is why the European Council in 2009 formally asked the European Commission to prepare an EU Strategy for the Region, which in 2011 resulted in the Danube Region Strategy, which identifies 11 thematic Priority Areas, one on environmental risks. Many old environmental burdens and heavily polluted areas in Europe are located in the Danube Region. Most of the countries with highest air pollution in Europe are situated within the Danube Region, including Bulgaria, Serbia, Hungary, Romania, Slovakia, and Czech Republic (Air Quality in Europe, 2014). Still, the extent of the environmental burden combined with specific socioeconomic conditions in the Region and risks to human health are poorly understood, due to lack of data.

The effect of *in utero* environmental exposures on early-life health is a growing area of research with major public health implications (Gluckman et al., 2008). Prenatal exposure to certain environmental chemicals, tobacco smoke, and air pollution during critical windows of development can lead to birth defects, low birth weight, impaired growth, immunological disturbances, respiratory symptoms and impaired lung, cognitive and psychomotor development (Gluckman

et al., 2008; Nieuwenhuijsen et al., 2013). Children, who are under development, are more susceptible to adverse effects of environmental exposures than adults, which can lead to lifetime chronic effects (Gluckman et al., 2008). A number of European studies have recently combined multiple European birth cohorts to study environmental exposures during pregnancy and early life health, including ENRIECO (Environmental Health Risks in European Birth Cohorts) (Vrijheid et al., 2012), CHICOS (Developing a Child Cohort Research Strategy for Europe, <http://www.chicosproject.eu/the-project/>), NewGeneris (a European study on maternal diet during pregnancy and child health) (Merlo et al., 2009), ESCAPE (European Study of Cohorts for Air Pollution Effects) (Pedersen et al., 2013; MacIntyre et al., 2014; Mölter et al., 2015), HEALS (Health and Environment-wide Associations based on Large population Surveys, <http://www.heals-eu.eu/>), and HELIX (The Human Early-Life Exposome) (Vrijheid et al., 2014). All these collaborative projects are based on existing birth cohorts from Northern (Sweden, Denmark, Netherlands), Western (Germany, UK, France) or Mediterranean regions (Spain, Italy, Greece) of Europe, while there are virtually no cohorts in the Danube Region (Vrijheid et al., 2012; Merlo et al., 2009; Pedersen et al., 2013; MacIntyre et al., 2014; Mölter et al., 2015; Vrijheid et al., 2014), except for two small mother–child cohorts from Czech Republic (CR) (Dejmek et al., 2000) and Slovakia (Sonneborn et al., 2008) included in ENRIECO (Vrijheid et al., 2012). Two Czech studies showed adverse effects of exposure to

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