# **Environmental Risk Factors**

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# 1. Introduction

In 2012, the World Health Organization (WHO) estimated that 12.6 million global deaths, representing 23% (95% CI: 13–34%) of all deaths, were attributable to the environment <sup>[1]</sup>. Air pollution and second-hand smoke are responsible for 52 million lower-respiratory diseases each year, representing 35% of the global cases <sup>[1]</sup>. Non-communicable diseases are also related to air pollution, chemicals, and second-hand smoke, which are responsible for 119 million cardiovascular diseases each year, 49 million cancers, and 32 million chronic respiratory diseases <sup>[1]</sup>. Environmental risks to health include pollution, radiation, noise, land use patterns, or climate change <sup>[2]</sup>.

Environmental health is a growing area of knowledge, continually increasing and updating the body of evidence linking the environment to human health. The Global Burden of Disease project considers 26 environmental and occupational risk factors in their estimations <sup>[3]</sup>. Such risk factors are those that have enough evidence to be translated with available global exposure data to quantify their impact across the globe. However, these are far from representing the totality of evidence related to environmental exposures and human health.

Global populations are also facing population growth and aging, increasing groups vulnerable to environmental risk factors. Around 10% of the global gross domestic product is spent on healthcare <sup>[2]</sup>, but little is allocated to primary prevention and public health. Being able to identify environmental risk factors is crucial in the decision-making process aiming to protect public health. The investment in measures and policies aiming to reduce environmental risks could help alleviate the health burden that healthcare systems around the globe are facing.

# 2. Air Pollution

We identified 14 air pollutants related to 34 diseases and mortality diagnoses. The air pollutant with the most extensive list of health impacts (29 diagnoses) was the particulate matter with less than 2.5 micrometers of diameter (PM2.5), followed by particulate matter with less than 10 micrometers of diameter (PM10) (17), nitrogen dioxide (NO2) (17), ozone (O3) (7), household air pollution (5), sulfur dioxide (SO2) (4), carbon monoxide (CO) (4),

solid fuel use (4), nitrogen oxides (2), desert dust (2), biomass burning (2), black carbon (1), and indoor air pollution from solid fuel (1). Air pollution was reported to affect all age groups and both sexes.

Long-term impacts of particulate matter (PM2.5 and PM10) were reported for 35 diagnoses and causes of death (Tables 1, 2, and 3). Adults exposed to PM2.5 or PM10 reported an increased risk of chronic kidney disease <sup>[4]</sup>, type 2 diabetes <sup>[5]</sup>, lung cancer mortality <sup>[6]</sup>, and cancer mortality <sup>[6]</sup>. Adults exposed to PM2.5 also reported an increased risk of Alzheimer's disease <sup>[8]</sup>, all-cause mortality <sup>[9]</sup>, cardiovascular mortality <sup>[10]</sup>, chronic obstructive pulmonary disease (COPD) <sup>[7]</sup>, colorectal cancer mortality <sup>[6]</sup>, dementia <sup>[11]</sup>, depression <sup>[12]</sup>, ischemic heart disease (IHD) mortality <sup>[1]</sup>, liver cancer mortality <sup>[6]</sup>, natural mortality <sup>[13]</sup>, respiratory mortality <sup>[13]</sup> stroke <sup>[14]</sup>, stroke mortality <sup>[16]</sup> and Parkinson's disease <sup>[15]</sup>. Adults exposed to PM10 reported an increased incidence of coronary events <sup>[16]</sup> and chronic bronchitis <sup>[17]</sup>. Pregnant women exposed to PM2.5 reported an association with offspring diagnosis of autistic syndrome disorder <sup>[18]</sup>, small for gestational age <sup>[19]</sup>, and those exposed to PM10 reported an associated with asthma <sup>[20]</sup>, acute respiratory infections <sup>[7]</sup>, and autistic spectrum disorder <sup>[21]</sup>. Moreover, children's exposure to PM10 was also associated with an increased risk of asthma <sup>[22]</sup> and autistic spectrum disorder <sup>[23]</sup>.

Particulate matter that includes PM2.5 and PM10 reported six diagnoses and causes of death related to short-term exposures (Table 2). In adults, short-term exposure to PM2.5 and PM10 were associated with out-of-hospital cardiac arrest <sup>[24]</sup>, cardiac arrhythmia <sup>[25]</sup>, daily cardiovascular, respiratory, and natural mortality <sup>[26]</sup>. In addition, for PM10, suicide was also reported as a short-term impact <sup>[12]</sup>. In children, short-term exposure to PM2.5 or PM10 was associated with pneumonia <sup>[27]</sup>.

Desert dust, an important natural source of particulate matter, was also associated with health impacts. This review identified one meta-analysis of adult exposure to desert dust, reporting an increased risk of cardiovascular mortality and natural mortality <sup>[28]</sup>. Another component of particulate matter is black carbon, which originates from fossil fuel and biomass combustion. We identified one meta-analysis on black carbon in children reporting an increased risk of asthma<sup>[22]</sup>.

Nitrogen oxides (NOx and NO2) were associated with 18 different diagnoses and causes of death. Pregnant women's exposure to NOx was associated with low birth weight <sup>[19]</sup> and preterm birth <sup>[19]</sup>. For the same group, exposure to NO2 reported an increased risk of low birth weight <sup>[19]</sup> and small for gestational age <sup>[19]</sup>. For adults, long-term exposure to NO2 was associated with an increased risk of all-cause mortality <sup>[10]</sup>, autistic syndrome disorder <sup>[18]</sup> cancer mortality <sup>[29]</sup>, cardiovascular mortality <sup>[10]</sup>, chronic kidney disease <sup>[4]</sup>, cancer mortality <sup>[29]</sup>, respiratory mortality <sup>[10]</sup>, and type 2 diabetes <sup>[30]</sup>. Furthermore, for adults, short-term exposure to NO2 was associated with an increased risk of out-of-hospital cardiac arrest <sup>[24]</sup>, cardiac arrhythmia <sup>[25]</sup>, conjunctivitis <sup>[31]</sup>, depression <sup>[32]</sup>, and natural mortality <sup>[17]</sup>. Lastly, children's long-term exposure to NO2 was associated with an increased risk of pneumonia <sup>[27]</sup>.

Ozone (O3) was found as a risk factor for seven diagnoses and causes of death. Long-term exposure to O3 was reported to increase IHD mortality <sup>[33]</sup> and Parkinson's disease<sup>[34]</sup> in adults and for pregnant women with preterm

birth <sup>[19]</sup>. Short-term exposure to ozone was associated as a risk factor for pneumonia in children <sup>[35]</sup> and in adults with out-of-hospital cardiac arrest <sup>[24]</sup>, all-cause mortality <sup>[36]</sup>, and cardiovascular and respiratory mortality <sup>[36]</sup>.

Sulfur dioxide (SO2) is a prevalent pollutant and was found as a risk factor for four diagnoses. SO2 is a gas primarily emitted from fossil fuel combustion at power plants and other industrial facilities as well as from fuel combustion in mobile sources like locomotives or ships. In their first trimester, pregnant women exposed to SO2 reported an increased risk of gestational diabetes mellitus <sup>[37]</sup>. Pregnant women exposed during any trimester also reported an increased risk of low birth weight <sup>[19]</sup>. Short-term exposures to SO2 were associated with pneumonia in children [24] and cardiac arrhythmia in adults <sup>[25]</sup>.

Carbon monoxide (CO) is a gas produced by fuel combustion in motorizing vehicles, small engines, stoves, and fireplaces, among others. We identified four health impacts associate with CO exposure. In short term exposures, CO was reported as a risk factor for pneumonia in children <sup>[27]</sup>, and cardiac arrhythmia <sup>[25]</sup>, and out-of-hospital cardiac arrest in adults <sup>[24]</sup>. CO exposure during pregnancy was also reported as a risk factor for preterm birth <sup>[19]</sup>.

Household air pollution represents indoor air pollution from multiple sources (e.g., cooking and heating) (Table 6). Under this review, we identified five types of cancers related to household air pollution exposure. Specifically, one meta-analysis reported an increased risk for cervical, laryngeal, nasopharyngeal, oral, and pharyngeal cancers <sup>[38]</sup>. Indoor air pollution from solid fuels was also found as a risk factor for hypertension [32]. Solid fuel use by pregnant women was associated with low birth weight, stillbirth, preterm birth, and intrauterine growth retardation in another meta-analysis <sup>[39]</sup>. Finally, biomass burning was associated with an increased risk of esophageal squamous cell carcinoma <sup>[40]</sup> and COPD <sup>[41]</sup>.

#### 3. Environmental Tobacco Smoke

Environmental tobacco smoke is an involuntary exposure to tobacco smoke, also known as passive smoke or secondhand smoke. Environmental tobacco smoke is generated by tobacco products' combustion and is a complex mixture of over 4000 compounds. These include more than 40 known or suspected human carcinogens, such as 4-aminobiphenyl, 2-naphthylamine, benzene, nickel, and various polycyclic aromatic hydrocarbons (PAHs) and N-nitrosamines. Furthermore present are several irritants, such as ammonia, nitrogen oxides, sulfur dioxide, and aldehydes, and cardiovascular toxicants, such as carbon monoxide, nicotine, and some PAHs <sup>[42][43]</sup>.

#### 4. Chemicals, Pesticides, and Heavy Metals

This review identified two health outcomes associated with childhood exposure to 1,3-butadiene. 1,3-Butadiene is a synthetic gas used primarily as a monomer to manufacture many different polymers and copolymers and as a chemical intermediate in industrial chemical production. Motor vehicle exhaust is also a source of 1,3-butadiene. One meta-analysis found that long-term exposure to 1,3-Butadiene during childhood increased the risk of acute lymphoblastic leukemia and all leukemias <sup>[44]</sup>. Another group of chemicals found to be associated with health impacts were the hydrocarbons. Hydrocarbons are present in a broad range of products, including petroleum and

other fuels, solvents, paints, glues, and cleaning products <sup>[45]</sup>. A meta-analysis of 14 studies showed that long-term exposure to hydrocarbons was associated with Parkinson's disease <sup>[46]</sup>. Organic solvents and other solvents were also found to be associated with neurological and rheumatological diseases. Specifically, long-term exposure to organic solvents was associated with multiple sclerosis <sup>[47]</sup> and Parkinson's disease <sup>[46]</sup>. Long-term exposure to solvents was also found to be associated with an increased risk of systemic sclerosis <sup>[48]</sup>. Organic solvents are used in many industries. They are used in paints, varnishes, lacquers, adhesives, glues, and degreasing and cleaning agents, and the production of dyes, polymers, plastics, textiles, printing inks, agricultural products, and pharmaceuticals.

In adults, long-term exposure to polychlorinated biphenyls (PCBs) were found to be associated with non-Hodgkin lymphoma <sup>[49]</sup>, in women with endometriosis <sup>[50]</sup>, and in children (<18 months of age), PCB 153 was found to be associated win increase risk of bronchitis <sup>[51]</sup>. Polychlorinated biphenyls are a large group of human-made organic chemicals that, due to their properties like non-flammability, chemical stability, high boiling point, and electrical insulating capacity, are widely used industrial and commercial applications. Bisphenol A (BPA), a chemical used primarily in the production of polycarbonate plastics and epoxy resins, for example, in food and drink packaging, was found to be a risk factor for diabetes <sup>[52]</sup> and obesity in adults <sup>[52]</sup>. Women's exposure to mono-(2-ethyl-5-hydroxyhexyl) phthalate (MEHHP) has been found as a risk factor for endometriosis<sup>[53]</sup>. MEHHP is a metabolite of phthalate acid esters (PAEs). MEHHP is often found in the blood and tissues of the general population. Studies have shown that women are more likely to be exposed to PAEs through products such as perfume, cosmetics, and personal care products. The review found evidence of dioxins as a risk factor for endometriosis <sup>[54]</sup>. Dioxins are a group of chemically-related compounds that are persistent environmental pollutants (POPs). Dioxins are unwanted by-products of a wide range of manufacturing processes, including smelting, chlorine bleaching of paper pulp, manufacturing some herbicides and pesticides, and incinerators.

Pesticide exposure also was found by multiple meta-analyses as a risk factor for several diseases in adults and children (Tables 9 and 10). In adults, pesticides, in general, were found to be associated with Alzheimer's disease [55], amyotrophic lateral sclerosis [56], brain tumors [57], myelodysplastic syndromes [69], and Parkinson's disease [58]. Organochlorine pesticides were associated with endometriosis [50]. Paraquat, a dichloride pesticide, was also found to be related to Parkinson's disease [59]. Non-Hodgkin lymphoma was also associated with multiple types of pesticides, like organophosphate [60], organochlorine [61], chlordane [62], diazinon [60], hexachlorobenzene [62], hexachlorocyclohexane [62], and dichlorodiphenyldichloroethylene(DDE) pesticides [62]. Finally, children (<18 months of age) reported a higher risk of bronchitis when exposed to DDE [63], and children's residential exposure to pesticides was reported as a risk factor for acute lymphoblastic leukemia, acute myeloid leukemia, and childhood leukemia [64].

In terms of mineral and heavy metals, aluminum, asbestos, cadmium, chromium, arsenic, lead, and silica, were also associated with multiples health outcomes. Aluminum was associated with dementia in adults <sup>[65]</sup>. Non-occupational asbestos was associated with mesothelioma <sup>[66]</sup>. Cadmium exposure was associated with cancer, especially lung cancer <sup>[67]</sup>. Chromium exposure was associated with schizophrenia <sup>[68]</sup>. Inorganic arsenic was

associated with type 2 diabetes <sup>[69]</sup>. Lead exposure to amyotrophic lateral sclerosis <sup>[70]</sup> and mild mental retardation <sup>[71]</sup>. Silica exposure with systemic sclerosis <sup>[72]</sup>.

### 5. Physical Exposures

Physical exposures refer to environmental factors such as temperature, noise, or radiation. Our review identified 21 meta-analyses covering 14 physical environmental exposures and 27 different diseases or causes of death among children, women, adults, and elderly populations. Ambient temperature and extreme weather were the most common physical environmental risk factor studied among the meta-analysis found in this review. Changes in ambient temperature (increases or decreases) were related to short-term health impacts. Particularly in adults, increases in the ambient temperature above the 93rd percentile were found to be a risk factor of suicide [73], those expose to temperatures above 90th percentile or below 10th percentile to diabetes mortality [74], and those under orthopedic procedure during warmer weather periods of the year had an increased risk of postoperative infection [75]. Comparing high versus low temperatures, high temperature increases the risk of low birth weight and stillbirth among pregnant women [76]. Furthermore, changes in diurnal temperature by increases of 10 degrees Celsius were <sup>77</sup>related to increased mortality <sup>78</sup>. Furthermore, heatwaves, defined as a high temperature lasting for several days, were associated with cardiovascular and respiratory mortality in adults <sup>[79]</sup> and preterm birth <sup>[76]</sup>. For the elderly populations, heat changes by 1 Celsius degree increment above a threshold were related to acute renal failure, cardiovascular disease mortality, cerebrovascular mortality, diabetes, ischemic heart disease mortality, respiratory disease, and respiratory mortality [80]. In terms of cold temperatures, reductions of 1 Celsius degree during winter times were related to an increased risk of cardiovascular mortality, cerebrovascular mortality, intracerebral hemorrhage, pneumonia, and respiratory mortality [80]. Cold waves were also associated with cardiovascular mortality [81]. For children, reductions of 1 degree Celsius during cold weather were related to an increased risk of asthma(<12 years old) [77].

Natural and artificial light exposure was also associated with positive and negative health impacts. Outdoor light exposure was found as a protective factor for myopia in children <sup>[82]</sup>. The main explanation for this effect is the impact of sunlight on eyeball size, neurotransmitters released in the retina, and vitamin D synthesis. In contrast, artificial light exposure at night was associated as a risk factor for women's breast cancer <sup>[83]</sup>. The main explanation for the increased risk of breast cancer is the impact of artificial light on reducing sleep duration and melatonin release. Melatonin is suggested as a carcinogenesis inhibitor; thus, low melatonin concentrations could contribute to breast cancer development. Ultraviolet radiation was found to be a protective factor for positive Epstein–Barr Virus Hodgkin lymphoma in adults <sup>[84]</sup>, and recreational sun exposure was associated with non-Hodgkin lymphoma <sup>[85]</sup>.

The noise was another environmental risk factor that was found to be associated with non-communicable diseases. In particular, noise exposure from any source was found to be a risk factor for diabetes <sup>[86]</sup>, and each increment of 5 decibels of ambient noise was associated with an increased risk of hypertension <sup>[87]</sup>. In addition, road traffic noise increments were associated with diabetes <sup>[86]</sup>, hypertension in men <sup>[87]</sup>, and ischemic heart disease <sup>[88]</sup>.

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### 6. Residential Surroundings

In this category, we summarized the environmental exposures related to residential surroundings, such as greenness, proximity to roadways and petrochemical complexes, or the degree of urbanization. We also located other residential exposures, such as the presence of pets that are suggested as a protective factor for non-communicable diseases. We identified two meta-analyses associating residential greenness as a protective factor for adults and newborns health. Specifically, we found evidence that greenness in a 300 m buffer around homes was associated with a reduced risk for mortality in adults <sup>[89]</sup> and a reduced risk of low birth weight <sup>[90]</sup>. In addition, residential greenness in a 500 m buffer from homes was also associated with a reduced risk of newborns being small for their gestational age <sup>[90]</sup>. Living near major roadways or being exposed to traffic around homes was found as a risk factor for type 2 diabetes in adults <sup>[91]</sup> and leukemia in children <sup>[92]</sup>. Living near petrochemical industrial complexes was also found to produce multiple types of leukemias. Specifically, living in an 8km radius from a petrochemical complex was found to be a risk factor for acute myeloid leukemia, chronic lymphocytic leukemia, and all leukemias <sup>[93]</sup>.

The degree of urbanization was also related to several health impacts. Specifically, living in a highly urbanized area was found to be associated with schizophrenia <sup>[94]</sup>. Urban exposure during childhood has been associated with an increased risk of Crohn's disease and inflammatory bowel disease <sup>[95]</sup>. Live in a modern house was (compared to traditional house) was found to be a protective factor for clinical malaria [109]. In contrast, living in rural areas has been suggested as a risk factor from Parkinson's disease <sup>[46]</sup>. Finally, having pets at home has been suggested to be a protective factor for non-communicable diseases in children and adults. Specifically, being exposed to pets in the first year of life was found to reduce the risk of acute lymphoblastic leukemia <sup>[96]</sup>. For adults, being exposed to a pet was suggested to reduce Crohn's disease and ulcerative colitis <sup>[95]</sup>.

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