Environmental Risk Factors

Subjects: Environmental Sciences
Contributor: David Rojas-Rueda, Shaker Qaidi

Environmental health is a growing area of knowledge, continually increasing and updating the body of evidence linking the environment to human health.

Keywords: environmental risk factors

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 [1]. Air pollution and second-hand smoke are responsible for 52 million lower-respiratory diseases each year, representing 35% of the global cases [1]. 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 [1]. Environmental risks to health include pollution, radiation, noise, land use patterns, or climate change [2].

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

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 [24], cardiac arrhythmia [25], daily cardiovascular, respiratory, and natural mortality [26]. In addition, for PM10, suicide was also reported as a short-term impact [12]. In children, short-term exposure to PM2.5 or PM10 was associated with pneumonia [27].

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 [28]. 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[22].

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 [19] and preterm birth [19]. For the same group, exposure to NO2 reported an increased risk of low birth weight [19] and small for gestational age [19]. For adults, long-term exposure to NO2 was associated with an increased risk of all-cause mortality [10], autistic syndrome disorder [18] cancer mortality [29], cardiovascular mortality [10], chronic kidney disease [4], cancer mortality [29], respiratory mortality [10], and type 2 diabetes [30]. Furthermore, for adults, short-term exposure to NO2 was associated with an increased risk of out-of-hospital cardiac arrest [24], cardiac arrhythmia [25], conjunctivitis [31], depression [32], and natural mortality [17]. Lastly, children's long-term exposure to NO2 was associated with an increased risk of asthma [20], and short-term exposure with an increased risk of pneumonia [27].

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 [33] and Parkinson's disease[34] in adults and for pregnant women with preterm birth [19]. Short-term exposure to ozone was associated as a risk factor for pneumonia in children [35] and in adults with out-of-hospital cardiac arrest [24], all-cause mortality [36], and cardiovascular and respiratory mortality [36].

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 [37]. Pregnant women exposed during any trimester also reported an increased risk of low birth weight [19]. Short-term exposures to SO2 were associated with pneumonia in children [24] and cardiac arrhythmia in adults [25].

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 [27], and cardiac arrhythmia [25], and out-of-hospital cardiac arrest in adults [24]. CO exposure during pregnancy was also reported as a risk factor for preterm birth [19].

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 [38]. 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 [39]. Finally, biomass burning was associated with an increased risk of esophageal squamous cell carcinoma [40] and COPD [41].

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 [42][43].

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 [44]. 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 [45]. A meta-analysis of 14 studies showed that long-term exposure to hydrocarbons was associated with Parkinson's disease [46]. 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 [47] and Parkinson's disease [46]. Long-term exposure to solvents was also found to be associated with an increased risk of systemic sclerosis [48]. 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 [49], in women with endometriosis [50], and in children (<18 months of age), PCB 153 was found to be associated win increase risk of bronchitis [51]. 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 [52] and obesity in adults [52]. Women's exposure to mono-(2-ethyl-5-hydroxyhexyl) phthalate (MEHHP) has been found as a risk factor for endometriosis[53]. 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 [54] . 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 [65]. Non-occupational asbestos was associated with mesothelioma [66]. Cadmium exposure was associated with cancer, especially lung cancer [67]. Chromium exposure was associated with schizophrenia [68]. Inorganic arsenic was associated with type 2 diabetes [69]. Lead exposure to amyotrophic lateral sclerosis [70] and mild mental retardation [71]. Silica exposure with systemic sclerosis [72].

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 [77]related to increased mortality [78]. Furthermore, heatwaves, defined as a high temperature lasting for several days, were associated with cardiovascular and respiratory mortality in adults [79] and preterm birth [76]. 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 [82]. 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 [83]. 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 [84], and recreational sun exposure was associated with non-Hodgkin lymphoma [85].

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 [86], and each increment of 5 decibels of ambient noise was associated with an increased risk of hypertension [87]. In addition, road traffic noise increments were associated with diabetes [86], hypertension in men [87], and ischemic heart disease [88].

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 [89] and a reduced risk of low birth weight [90]. 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 [90]. Living near major roadways or being exposed to traffic around homes was found as a risk factor for type 2 diabetes in adults [91] and leukemia in children [92]. 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 [93].

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 [94]. Urban exposure during childhood has been associated with an increased risk of Crohn's disease and inflammatory bowel disease [95]. 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 [46]. 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 [96]. For adults, being exposed to a pet was suggested to reduce Crohn's disease and ulcerative colitis [95].

References

1. Prüss-Ustün, A.; Neira, M. Preventing Disease through Healthy Environments: A Global Assessment of the Environmen tal Burden of Disease; World Health Organization: Geneva, Switzerland, 2016; Volume 259.
2. Prüss-Ustün, A. Environmental risks and non-communicable diseases. BMJ 2019, 365, 17–19.

3. Stanaway, J.D.; Afshin, A.; Gakidou, E.; Lim, S.S.; Abate, D.; Abate, K.H.; Abbafati, C.; Abbasi, N.; Abbastabar, H.; Abd-Allah, F.; et al. Global, regional, and national comparative risk assessment of 84 behavioural, environmental and occupational, and metabolic risks or clusters of risks for 195 countries and territories, 1990-2017: A systematic analysis for the Global Burden of Disease Study 2017. Lancet 2018, 392, 1923–1994.
4. Wu, M.Y.; Lo, W.C.; Chao, C.-T.; Wu, M.S.; Chiang, C.K. Association between air pollutants and development of chronic kidney disease: A systematic review and meta-analysis. Sci. Total Environ. 2020, 706.
5. Yang, M.; Cheng, H.; Shen, C.; Liu, J.; Zhang, H.; Cao, J.; Ding, R. Effects of long-term exposure to air pollution on the incidence of type 2 diabetes mellitus: A meta-analysis of cohort studies. Environ. Sci. Pollut. Researc 2020, 27, 798–811.
6. Kim, H.-B.B.; Shim, J.-Y.Y.; Park, B.; Lee, Y.-J.J. Long-Term Exposure to Air Pollutants and Cancer Mortality: A Meta-Analysis of Cohort Studies. Int. J. Environ. Res. Public Health 2018, 15, 2608.
7. Burnett, R.T.; Arden Pope, C.; Ezzati, M.; Olives, C.; Lim, S.S.; Mehta, S.; Shin, H.H.; Singh, G.; Hubbell, B.; Brauer, M.; et al. An integrated risk function for estimating the global burden of disease attributable to ambient fine particulate matter exposure. Environ. Health Perspect. 2014, 122, 397–403.
8. Tsai, T.L.; Lin, Y.T.; Hwang, B.F.; Nakayama, S.F.; Tsai, C.H.; Sun, X.L.; Ma, C.; Jung, C.R. Fine particulate matter is a potential determinant of Alzheimer’s disease: A systemic review and meta-analysis. Environ. Res. 2019, 177, 108638.
9. Hoek, G.; Krishnan, R.M.; Beelen, R.; Peters, A.; Ostro, B.; Brunekreef, B.; Kaufman, J.D. Long-term air pollution exposure and cardio- respiratory mortality: A review. Environ. Health 2013, 12, 43.
10. Faustini, A.; Rapp, R.; Forastiere, F. Nitrogen dioxide and mortality: Review and meta-analysis of long-term studies. Eur. Respir. J. 2014, 44, 744–753.
11. Tsai, T.L.; Lin, Y.T.; Hwang, B.F.; Nakayama, S.F.; Tsai, C.H.; Sun, X.L.; Ma, C.; Jung, C.R. Fine particulate matter is a potential determinant of Alzheimer’s disease: A systemic review and meta-analysis. Environ. Res. 2019, 177, 108638.
12. Braithwaite, I.; Zhang, S.; Kirkbride, J.B.; Osborn, D.P.J.; Hayes, J.F. Air pollution (Particulate matter) exposure and associations with depression, anxiety, bipolar, psychosis and suicide risk: A systematic review and meta-analysis. Environ. Health Perspect. 2019, 127, 126002.
13. Faustini, A.; Rapp, R.; Forastiere, F. Nitrogen dioxide and mortality: Review and meta-analysis of long-term studies. Eur. Respir. J. 2014, 44, 744–753.
14. Yuan, S.; Wang, J.; Jiang, Q.; He, Z.; Huang, Y.; Li, Z.; Cai, L.; Cao, S. Long-term exposure to PM2.5 and stroke: A systematic review and meta-analysis of cohort studies. Environ. Res. 2019, 177, 108587.
15. Kasdagli, M.I.; Katsouyanni, K.; Dimakopoulou, K.; Samoli, E. Air pollution and Parkinson’s disease: A systematic review and meta-analysis up to 2018. Int. J. Hyg. Environ. Health 2019, 222, 402–409.
16. Cesaroni, G.; Stafoggia, M.; Galassi, C.; Hilding, A.; Hoffmann, B.; Houthuijs, D.; Ostenson, C.; Overvad, K.; Pedersen, N.L. Long term exposure to ambient air pollution and incidence of acute coronary events: Prospective cohort study and meta-analysis in 11 European cohorts from the ESCAPE Project. BMJ 2014, 7412, 1–16.
17. Héroux, M.; Anderson, H.; Atkinson, R.; Brunekreef, B.; Cohen, A.; Forastiere, F.; Hurley, F.; Katsouyanni, K.; Krewski, D.; Krzyzanowski, M.; et al. Quantifying the health impacts of ambient air pollutants: Recommendations of a WHO/Europe project. Int. J. Public Health 2015, 60, 619–627.
18. Chun, H.K.; Leung, C.; Wen, S.W.; McDonald, J.; Shin, H.H. Maternal exposure to air pollution and risk of autism in children: A systematic review and meta-analysis. Environ. Pollut. 2020, 256.
19. Guo, L.-Q.; Chen, Y.; Mi, B.-B.; Dang, S.-N.; Zhao, D.-D.; Liu, R.; Wang, H.-L.; Yan, H. Ambient air pollution and adverse birth outcomes: A systematic review and meta-analysis. J. Zhejiang Univ. Sci. B (Biomed. Biotechnol.) 2019, 20, 238–252.
20. Khreis, H.; Ramani, T.; De Hoogh, K.; Mueller, N. Traffic-related air pollution and the local burden of childhood asthma in Bradford, UK. Int. J. Transp. Sci. Technol. 2018, 8, 116–128.
21. Lam, J.; Sutton, P.; Kalkbrenner, A.; Windham, G.; Halladay, A.; Koustas, E.; Lawler, C.; Davidson, L.; Daniels, N.; Newschaffer, C.; et al. A systematic review and meta-analysis of multiple airborne pollutants and autism spectrum disorder. PLoS ONE 2016, 11, e0161851.
22. Khreis, H.; Ramani, T.; De Hoogh, K.; Mueller, N. Traffic-related air pollution and the local burden of childhood asthma in Bradford, UK. Int. J. Transp. Sci. Technol. 2018, 8, 116–128.
23. Lam, J.; Sutton, P.; Kalkbrenner, A.; Windham, G.; Halladay, A.; Koustas, E.; Lawler, C.; Davidson, L.; Daniels, N.; Newschaffer, C.; et al. A systematic review and meta-analysis of multiple airborne pollutants and autism spectrum disorder. PLoS ONE 2016, 11, e0161851.

24. Zhao, R.; Chen, S.; Wang, W.; Huang, J.; Wang, K.; Liu, L.; Wei, S. The impact of short-term exposure to air pollutants on the onset of out-of-hospital cardiac arrest: A systematic review and meta-analysis. Int. J. Cardiol. 2017, 226, 110–11 7.

25. Song, X.; Liu, Y.; Hu, Y.; Zhao, X.; Tian, J.; Ding, G.; Wang, S. Short-Term Exposure to Air Pollution and Cardiac Arrhyth mia: A Meta-Analysis and Systematic Review. Int. J. Environ. Res. Public Health 2016, 13, 642.

26. Liu, C.; Chen, R.; Sera, F.; Vicedo-Cabrera, A.M.; Guo, Y.; Tong, S.; Coelho, M.S.Z.S.; Saldiva, P.H.N.; Lavigne, E.; Mat us, P.; et al. Ambient Particulate Air Pollution and Daily Mortality in 652 Cities. N. Engl. J. Med. 2019, 381, 705–715

27. Nhung, N.T.T.; Amini, H.; Schindler, C.; Kutlar Joss, M.; Dien, T.M.; Probst-Hensch, N.; Perez, L.; Künzli, N. Short-term association between ambient air pollution and pneumonia in children: A systematic review and meta-analysis of time-se ries and case-crossover studies. Environ. Pollut. 2017, 230, 1000–1008.

28. Stafoggia, M.; Zauli-Sajani, S.; Pey, J.; Samoli, E.; Alessandrini, E.; Basagaña, X.; Cernigliaro, A.; Chiusolo, M.; Demari a, M.; Díaz, J.; et al. Desert Dust Outbreaks in Southern Europe: Contribution to Daily PM 10 Concentrations and Short -Term Associations with Mortality and Hospital Admissions. Environ. Health Perspect. 2016, 124, 413–419.

29. Kim, H.-B.B.; Shim, J.-Y.Y.; Park, B.; Lee, Y.-J.J. Long-Term Exposure to Air Pollutants and Cancer Mortality: A Meta-An alysis of Cohort Studies. Int. J. Environ. Res. Public Health 2018, 15, 2608.

30. Bellou, V.; Belbasis, L.; Tzoulaki, I.; Evangelou, E. Risk factors for type 2 diabetes mellitus: An exposure-wide umbrella review of meta-analyses. PLoS ONE 2018.

31. Chen, R.; Yang, J.; Zhang, C.; Li, B.; Bergmann, S.; Zeng, F.; Wang, H.; Wang, B. Global Associations of Air Pollution a nd Conjunctivitis Diseases: A Systematic Review and Meta-Analysis. Int. J. Environ. Res. Public Health 2019, 16, 3652.

32. Fan, S.J.; Heinrich, J.; Bloom, M.S.; Zhao, T.Y.; Shi, T.X.; Feng, W.R.; Sun, Y.; Shen, J.C.; Yang, Z.C.; Yang, B.Y.; et al. Ambient air pollution and depression: A systematic review with meta-analysis up to 2019. Sci. Total Environ. 2020, 701, 134721.

33. Atkinson, R.W.; Butland, B.K.; Dimitroulopoulou, C.; Heal, M.R.; Stedman, J.R.; Carslaw, N.; Jarvis, D.; Heaviside, C.; Vardoulakis, S.; Walton, H.; et al. Long-term exposure to ambient ozone and mortality: A quantitative systematic review and meta-analysis of evidence from cohort studies. BMJ Open 2016, 6, e009493.

34. Kasdagli, M.I.; Katsouyanni, K.; Dimakopoulou, K.; Samoli, E. Air pollution and Parkinson's disease: A systematic revie w and meta-analysis up to 2018. Int. J. Hyg. Environ. Health 2019, 222, 402–409.

35. Nhung, N.T.T.; Amini, H.; Schindler, C.; Kutlar Joss, M.; Dien, T.M.; Probst-Hensch, N.; Perez, L.; Künzli, N. Short-term association between ambient air pollution and pneumonia in children: A systematic review and meta-analysis of time-se ries and case-crossover studies. Environ. Pollut. 2017, 230, 1000–1008.

36. Héroux, M.; Anderson, H.; Atkinson, R.; Brunekreef, B.; Cohen, A.; Forastiere, F.; Hurley, F.; Katsouyanni, K.; Krewski, D.; Krzyzanowski, M.; et al. Quantifying the health impacts of ambient air pollutants: Recommendations of a WHO/Euro pe project. Int. J. Public Health 2015, 60, 619–627.

37. Zhang, H.; Wang, Q.; He, S.; Wu, K.; Ren, M.; Dong, H.; Di, J.; Yu, Z.; Huang, C. Ambient air pollution and gestational diabetes mellitus: A review of evidence from biological mechanisms to population epidemiology. Sci. Total Environ. 202 0, 719, 137349.

38. Josyula, S.; Lin, J.; Xue, X.; Rothman, N.; Lan, Q.; Rohan, T.E.; Dean, H.; Iii, H. Household air pollution and cancers ot her than lung: A meta-analysis. Env. Health 2015.

39. Amegah, A.K.; Quansah, R.; Jaakkola, J.J.K. Household air pollution from solid fuel use and risk of adverse pregnancy outcomes: A systematic review and meta-analysis of the empirical evidence. PLoS ONE 2014, 9, e113920.

40. Okello, S.; Akello, S.J.; Dwomoh, E.; Byaruhanga, E.; Opio, C.K.; Zhang, R.; Corey, K.E.; Muyindike, W.R.; Ocama, P.; Christiani, D.D. Biomass fuel as a risk factor for esophageal squamous cell carcinoma: A systematic review and meta-a nalysis. Environ. Health 2019, 18.

41. Yang, Y.; Mao, J.; Ye, Z.; Li, J.; Zhao, H.; Liu, Y. Risk factors of chronic obstructive pulmonary disease among adults in Chinese mainland: A systematic review and meta-analysis. Respir. Med. 2017, 131, 158–165.

42. Leonardi-Bee, J.; Smyth, A.; Britton, J.; Coleman, T. Environmental tobacco smoke and fetal health: Systematic review and meta-analysis. Arch. Dis. Child. Fetal Neonatal Ed. 2008, 93, F351–F361.

43. Chen, Y.; Liu, Q.; Li, W.; Deng, X.; Yang, B.; Huang, X. Association of prenatal and childhood environment smoking exp osure with puberty timing: A systematic review and meta-analysis. Environ. Health Prev. Med. 2018, 23.

44. Filippini, T.; Hatch, E.E.; Rothman, K.J.; Heck, J.E.; Park, A.S.; Crippa, A.; Orsini, N.; Vinceti, M. Association between O utdoor Air Pollution and Childhood Leukemia: A Systematic Review and Dose–Response Meta-Analysis. Environ. Healt h Perspect. 2019, 127, 046002.

45. Palin, O.; Herd, C.; Morrison, K.E.; Jagielski, A.C.; Wheatley, K.; Thomas, G.N.; Clarke, C.E. Systematic review and meta-analysis of hydrocarbon exposure and the risk of Parkinson's disease. Park. Relat. Disord. 2015, 21, 243–248.

46. Bellou, V.; Belbasis, L.; Tzoulaki, I.; Evangelou, E.; Ioannidis, J.P.A. Environmental risk factors and Parkinson's disease: An umbrella review of meta-analyses. Park. Relat. Disord. 2016, 23, 1–9.

47. Belbasis, L.; Bellou, V.; Evangelou, E.; Ioannidis, J.P.A.A.; Tzoulaki, I. Environmental risk factors and multiple sclerosis: An umbrella review of systematic reviews and meta-analyses. Lancet Neurol. 2015, 14, 263–273.

48. Belbasis, L.; Dosis, V.; Evangelou, E. Elucidating the environmental risk factors for rheumatic diseases: An umbrella review of meta-analyses. Int. J. Rheum. Dis. 2018, 21, 1514–1524.

49. Freeman, M.D.; Kohles, S.S. Plasma levels of polychlorinated biphenyls, non-hodgkin lymphoma, and causation. J. Environ. Public Health 2012, 2012.

50. Cano-Sancho, G.; Ploteau, S.; Matta, K.; Adoamnei, E.; Louis, G.B.; Mendiola, J.; Darai, E.; Squifflet, J.; Le Bizec, B.; Antignac, J.P. Human epidemiological evidence about the associations between exposure to organochlorine chemicals and endometriosis: Systematic review and meta-analysis. Environ. Int. 2019, 123, 209–223.

51. Gascon, M.; Sunyer, J.; Casas, M.; Martínez, D.; Ballester, F.; Basterrechea, M.; Bonde, J.P.; Chatzi, L.; Chevrier, C.; Eggesbø, M.; et al. Prenatal exposure to DDE and PCB 153 and respiratory health in early childhood: A meta-analysis. Epidemiology 2014, 25, 544–553.

52. Rancière, F.; Lyons, J.G.; Loh, V.H.; Botton, J.; Galloway, T.; Wang, T.; Shaw, J.E.; Magliano, D.J.; Loh, V.H.Y.; Botton, J.; et al. Bisphenol A and the risk of cardiometabolic disorders: A systematic review with meta-analysis of the epidemiological evidence. Environ. Health 2015, 14, 46.

53. Cai, W.; Yang, J.; Liu, Y.; Bi, Y.; Wang, H. Association between Phthalate Metabolites and Risk of Endometriosis: A Meta-Analysis. Int. J. Environ. Res. Public Health 2019, 16, 3678.

54. Cano-Sancho, G.; Ploteau, S.; Matta, K.; Adoamnei, E.; Louis, G.B.; Mendiola, J.; Darai, E.; Squifflet, J.; Le Bizec, B.; Antignac, J.P. Human epidemiological evidence about the associations between exposure to organochlorine chemicals and endometriosis: Systematic review and meta-analysis. Environ. Int. 2019, 123, 209–223.

55. Yan, D.; Zhang, Y.; Liu, L.; Yan, H. Pesticide exposure and risk of Alzheimer's disease: A systematic review and meta-analysis. Sci. Rep. 2016, 6, 1–9.

56. Belbasis, L.; Bellou, V.; Evangelou, E. Environmental Risk Factors and Amyotrophic Lateral Sclerosis: An Umbrella Review and Critical Assessment of Current Evidence from Systematic Reviews and Meta-Analyses of Observational Studies. Neuroepidemiology 2016, 46, 96–105.

57. Van Maele-Fabry, G.; Gamet-Payrastre, L.; Lison, D. Residential exposure to pesticides as risk factor for childhood and young adult brain tumors: A systematic review and meta-analysis. Environ. Int. 2017, 106, 69–90.

58. Yan, D.; Zhang, Y.; Liu, L.; Shi, N.; Yan, H. Pesticide exposure and risk of Parkinson's disease: Dose-response meta-analysis of observational studies. Regul. Toxicol. Pharmacol. 2018, 96, 57–63.

59. Tangamornsuksan, W.; Lohitnavy, O.; Sruamsiri, R.; Chaiyakunapruk, N.; Norman Scholfield, C.; Reisfeld, B.; Lohitnavy, M. Paraquat exposure and Parkinson's disease: A systematic review and meta-analysis. Arch. Environ. Occup. Health 2019, 74, 225–238.

60. Hu, L.; Luo, D.; Zhou, T.; Tao, Y.; Feng, J.; Mei, S. The association between non-Hodgkin lymphoma and organophosphate pesticides exposure: A meta-analysis. Environ. Pollut. 2017, 231, 319–328.

61. Luo, D.; Zhou, T.; Tao, Y.; Feng, Y.; Shen, X.; Mei, S. Exposure to organochlorine pesticides and non-Hodgkin lymphoma: A meta-analysis of observational studies. Sci. Rep. 2016, 6.

62. Luo, D.; Zhou, T.; Tao, Y.; Feng, Y.; Shen, X.; Mei, S. Exposure to organochlorine pesticides and non-Hodgkin lymphoma: A meta-analysis of observational studies. Sci. Rep. 2016, 6.

63. Gascon, M.; Sunyer, J.; Casas, M.; Martínez, D.; Ballester, F.; Basterrechea, M.; Bonde, J.P.; Chatzi, L.; Chevrier, C.; Eggesbø, M.; et al. Prenatal exposure to DDE and PCB 153 and respiratory health in early childhood: A meta-analysis. Epidemiology 2014, 25, 544–553.

64. Van Maele-Fabry, G.; Gamet-Payrastre, L.; Lison, D. Household exposure to pesticides and risk of leukemia in children and adolescents: Updated systematic review and meta-analysis. Int. J. Hyg. Environ. Health 2019, 222, 49–67.

65. Bellou, V.; Belbasis, L.; Tzoulaki, I.; Middleton, L.T.; Ioannidis, J.P.A.; Evangelou, E. Systematic evaluation of the associations between environmental risk factors and dementia: An umbrella review of systematic reviews and meta-analyses. Alzheimer's Dement. 2017, 13, 406–418.

66. Xu, R.; Barg, F.K.; Emmett, E.A.; Wiebe, D.J.; Hwang, W.-T. Association between mesothelioma and non-occupational asbestos exposure: Systematic review and meta-analysis. Environ. Health 2018, 17.

67. Nawrot, T.S.; Martens, D.S.; Hara, A.; Plusquin, M.; Vangronsveld, J.; Roels, H.A.; Staessen, J.A. Association of total cancer and lung cancer with environmental exposure to cadmium: The meta-analytical evidence. Cancer Causes Control 2015, 26, 1281–1288.

68. Ma, J.; Yan, L.; Guo, T.; Yang, S.; Guo, C.; Liu, Y.; Xie, Q.; Wang, J. Association of typical toxic heavy metals with schizophrenia. Int. J. Environ. Res. Public Health 2019, 16, 4200.

69. Wang, W.; Xie, Z.; Lin, Y.; Zhang, D. Association of inorganic arsenic exposure with type 2 diabetes mellitus: A meta-analysis. J. Epidemiol. Community Health 2014, 68, 176–184.

70. Meng, E.; Mao, Y.; Yao, Q.; Han, X.; Li, X.; Zhang, K.; Jin, W. Population-based study of environmental/occupational lead exposure and amyotrophic lateral sclerosis: A systematic review and meta-analysis. Neurol. Sci. 2020, 41, 35–41.

71. Lanphear, B.P.; Hornung, R.; Khoury, J.; Yolton, K.; Baghurst, P.; Bellinger, D.C.; Canfield, R.L.; Dietrich, K.N.; Bornschein, R.; Greene, T.; et al. Low-Level Environmental Lead Exposure and Children's Intellectual Function: An International Pooled Analysis. Environ. Health Perspect. 2005, 113, 894–899.

72. Belbasis, L.; Dosis, V.; Evangelou, E. Elucidating the environmental risk factors for rheumatic diseases: An umbrella review of meta-analyses. Int. J. Rheum. Dis. 2018, 21, 1514–1524.

73. Kim, Y.; Kim, H.; Gasparrini, A.; Armstrong, B.; Honda, Y.; Chung, Y.; Ng, C.F.S.; Tobias, A.; Íñiguez, C.; Lavigne, E.; et al. Suicide and Ambient Temperature: A Multi-Country Multi-City Study. Environ. Health Perspect. 2019, 127, 117007.

74. Yang, J.; Yin, P.; Zhou, M.; Ou, C.Q.; Li, M.; Liu, Y.; Gao, J.; Chen, B.; Liu, J.; Bai, L.; et al. The effect of ambient temperature on diabetes mortality in China: A multi-city time series study. Sci. Total Environ. 2016, 543, 75–82.

75. Vickers, M.L.; Pelecanos, A.; Tran, M.; Eriksson, L.; Assoum, M.; Harris, P.N.; Jaiprakash, A.; Parkinson, B.; Dulhunty, J.; Crawford, R.W. Association between higher ambient temperature and orthopaedic infection rates: A systematic review and meta-analysis. ANZ J. Surg. 2019, 89, 1028–1034.

76. Chersich, M.F.; Pham, M.D.; Areal, A.; Haghighi, M.M.; Manyuchi, A.; Swift, C.P.; Wernecke, B.; Robinson, M.; Hetem, R.; Boeckmann, M.; et al. Associations between high temperatures in pregnancy and risk of preterm birth, low birth weight, and stillbirths: Systematic review and meta-analysis. BMJ 2020, 371, 1–13.

77. Cong, X.; Xu, X.; Zhang, Y.; Wang, Q.; Xu, L.; Huo, X. Temperature drop and the risk of asthma: A systematic review and meta-analysis. Environ. Sci. Pollut. Res. 2017, 24, 22535–22546.

78. Lee, W.; Bell, M.L.; Gasparrini, A.; Armstrong, B.G.; Sera, F.; Hwang, S.; Lavigne, E.; Zanobetti, A.; Coelho, M.d.S.Z.S.; Saldiva, P.H.N.; et al. Mortality burden of diurnal temperature range and its temporal changes: A multi-country study. Environ. Int. 2018, 110, 123–130.

79. Cheng, J.; Xu, Z.; Bambrick, H.; Prescott, V.; Wang, N.; Zhang, Y.; Su, H.; Tong, S.; Hu, W. Cardiorespiratory effects of heatwaves: A systematic review and meta-analysis of global epidemiological evidence. Environ. Res. 2019, 177, 108610.

80. Bunker, A.; Wildenhain, J.; Vandenbergh, A.; Henschke, N.; Rocklöv, J.; Hajat, S.; Sauerborn, R. Effects of Air Temperature on Climate-Sensitive Mortality and Morbidity Outcomes in the Elderly; a Systematic Review and Meta-analysis of Epidemiological Evidence. EBioMedicine 2016, 6, 258–268.

81. Chen, J.; Zhou, M.; Yang, J.; Yin, P.; Wang, B.; Ou, C.Q.; Liu, Q. The modifying effects of heat and cold wave characteristics on cardiovascular mortality in 31 major Chinese cities. Environ. Res. Lett. 2020, 15.

82. Ho, C.-L.; Wu, W.-F.; Liou, Y.M. Dose-Response Relationship of Outdoor Exposure and Myopia Indicators: A Systematic Review and Meta-Analysis of Various Research Methods. Int. J. Environ. Res. Public Health 2019, 16, 2595.

83. Yang, W.S.; Deng, Q.; Fan, W.Y.; Wang, W.Y.; Wang, X. Light exposure at night, sleep duration, melatonin, and breast cancer: A dose-response analysis of observational studies. Eur. J. Cancer Prev. 2014, 23, 269–276.

84. Monnereau, A.; Glaser, S.L.; Schupp, C.W.; Smedby, K.E.; De Sanjosé, S.; Kane, E.; Melbye, M.; Forétova, L.; Maynadié, M.; Staines, A.; et al. Exposure to UV radiation and risk of Hodgkin lymphoma: A pooled analysis. Blood 2013, 122, 3492–3499.

85. Kricker, A.; Armstrong, B.K.; Hughes, A.M.; Goumas, C.; Smedby, K.E.; Zheng, T.; Spinelli, J.J.; De Sanjose, S.; Hartge, P.; Melbye, M.; et al. Personal sun exposure and risk of non Hodgkin lymphoma: A pooled analysis from the Interlymph Consortium. Int. J. Cancer 2008, 122, 144–154.

86. Zare Sakhvidi, M.J.; Zare Sakhvidi, F.; Mehrparvar, A.H.; Foraster, M.; Dadvand, P. Association between noise exposure and diabetes: A systematic review and meta-analysis. Environ. Res. 2018, 166, 647–657.

87. Fu, W.; Wang, C.; Zou, L.; Liu, Q.; Gan, Y.; Yan, S.; Song, F.; Wang, Z.; Lu, Z.; Cao, S. Association between exposure to noise and risk of hypertension: A meta-analysis of observational epidemiological studies. J. Hypertens. 2017, 35, 2358–2366.

88. Van Kempen, E.; Casas, M.; Pershagen, G.; Foraster, M. WHO Environmental Noise Guidelines for the European Region: A Systematic Review on Environmental Noise and Cardiovascular and Metabolic Effects: A Summary. Int. J. Environ. Res. Public Health 2018, 15, 379.
89. Rojas-Rueda, D.; Nieuwenhuijsen, M.J.; Gascon, M.; Perez-Leon, D.; Mudu, P.; Rojas-Rueda, D.; Nieuwenhuijsen, M.J.; Gascon, M.; Perez-Leon, D.; Mudu, P. Green spaces and mortality: A systematic review and meta-analysis of cohort studies. Lancet Planet. Health 2019, 3, e469–e477.
90. Zhan, Y.; Liu, J.; Lu, Z.; Yue, H.; Zhang, J.; Jiang, Y. Influence of residential greenness on adverse pregnancy outcomes: A systematic review and dose-response meta-analysis. Sci. Total Environ. 2020, 718, 37420.
91. Zhao, Z.; Lin, F.; Wang, B.; Cao, Y.; Hou, X.; Wang, Y. Residential Proximity to Major Roadways and Risk of Type 2 Diabetes Mellitus: A Meta-Analysis. Int. J. Environ. Res. Public Health 2017, 14, 3.
92. Boothe, V.L.; Boehmer, T.K.; Wendel, A.M.; Yip, F.Y. Residential traffic exposure and childhood leukemia: A systematic review and meta-analysis. Am. J. Prev. Med. 2014, 46, 413–422.
93. Lin, C.K.; Hsu, Y.T.; Brown, K.D.; Pokharel, B.; Wei, Y.; Chen, S.T. Residential exposure to petrochemical industrial complexes and the risk of leukemia: A systematic review and exposure-response meta-analysis. Environ. Pollut. 2020, 258.
94. Belbasis, L.; Köhler, C.A.; Stefanis, N.; Stubbs, B.; van Os, J.; Vieta, E.; Seeman, M.V.; Arango, C.; Carvalho, A.F.; Evangelou, E. Risk factors and peripheral biomarkers for schizophrenia spectrum disorders: An umbrella review of meta-analyses. Acta Psychiatr. Scand. 2018, 137, 88–97.
95. Piovani, D.; Danese, S.; Peyrin-biroulet, L.; Nikolopoulos, G.K.; Lytras, T.; Bonovas, S. Environmental Risk Factors for Inflammatory Bowel Diseases: An Umbrella Review of Meta-analyses. Gastroenterology 2019, 157, 647–659.
96. Orsi, L.; Magnani, C.; Petridou, E.T.; Dockerty, J.D.; Metayer, C.; Milne, E.; Bailey, H.D.; Dessypris, N.; Kang, A.Y.; Wesseling, C.; et al. Living on a farm, contact with farm animals and pets, and childhood acute lymphoblastic leukemia: Pooled and meta-analyses from the Childhood Leukemia International Consortium. Cancer Med. 2018, 7, 2665–2681.