Preface

Despite noteworthy developments and technological advances in the health and biomedical sciences in the last decades, with obvious improvements in the prevalence of some communicable diseases and in disease treatment in general, contemporary societies continue facing very significant health challenges. The average human life span has increased but individual wellbeing is challenged by an array of "contemporary" diseases. Differences in the health challenges industrialized nations and less developed countries face persist. Life expectancy at birth continues being higher in North America, Oceania and Europe, while mortality continues to be significantly higher in poor countries (European Environment Agency, 2013; United Nations, 2017), while the health issues that constitute priorities in these two broad categories of countries are also different (Prüss-Üstün, Wolf, Corvalán, Bos & Neira, 2016; European Environment Agency, 2013). Communicable diseases are a major concern in developing countries, while non-communicable diseases like cancers, diabetes, asthma, Autism Spectrum Disorders (ASDs) or heart attacks are on the rise in the industrialized world.

Albeit these disparities, there is a common trend relating to health issues worldwide. Environmental exposures or pressures constitute a major cause of contemporary diseases (Prüss-Üstün et al., 2016; European Environment Agency, 2013). WHO highlights the significance of environmental factors – which it defines as "factors external to a person, and all related behaviours, but excluding those natural environments that cannot be reasonably modified" (Prüss-Üstün et al., 2016) – for the state of human health.

In this context, environmental health arose as a science that studies the relation of different environmental factors with health impacts or correlates diseases with environmental exposures. It is a field of rising interest and particular relevance in our times, with important insights for environmental and health policy making. Given our increasing understanding of the intricate network of interrelated factors that contribute to environmental concerns as well as of the multiple impacts on human health, environmental health is a body of knowledge that draws from a variety of disciplines: medicine and public health, environmental sciences, sociology and communications, technology, policy-making, and legislation. As a consequence, it is a multidisciplinary field with noteworthy challenges and significant, much-promising developments.

Exposures to a great variety of environmental toxins and stressors pose serious risks to individual and public health. Environmental hazards include biological, chemical, physical and cultural ones, as well as some lifestyle choices (Prüss-Üstün et al., 2016). Biological hazards refer to disease-causing organisms such as bacteria, fungi and parasites including diseases caused by viruses. Chemical hazards include all harmful chemicals to which people get exposed in their environment via air, water, soil, food or human made products. Physical hazards can be natural phenomena such as fires, floods, earthquakes, hurricanes and volcanic eruptions, but also physical agents such as electromagnetic radiation (ultraviolet, radio

waves), noise, nanoparticles and climate change effects. Cultural hazards are associated with the social environment of an individual; e.g. conditions such as an unhealthy workplace, poverty and criminality. Lifestyle choices refer to those hazards that are a matter of individual choice, or at least are influenced by choice, like smoking, over-eating, alcohol or drug abuse. In contemporary societies, malaria and respiratory infections such as tuberculosis, diarrhea and various parasitic intestinal diseases constitute significant biological hazards. Humans get exposed to a wide and increasing range of chemical hazards; carcinogenic and mutagenic chemicals, heavy metals, persistent organic pollutants and endocrine disruptors are among the groups of chemicals that are of particular concern. Climate change, nanoparticles, noise and exposure to electromagnetic radiation (from radiofrequencies and infrared to UV and X-rays), constitute significant and disconcerting new physical hazards. Workplace exposures and stresses continue being an issue of concern, although technological approaches have contributed to the control of such hazards; however, new challenges arising from socio-political changes such as migration and ageing societies need to be addressed.

Due to the massive amount of health-related issues, scientific literature related to environmental health issues has increased significantly. Recent developments in the human genome, in epigenetics (Bollati & Baccarelli, 2010; Herceg, 2016; Lin, Liu, Hu, Cottrell, & Kass, 2018) and different omics (e.g. transcriptomics, metabolomics) and in environmental sciences, along with increased and more systematic environmental and biological monitoring have made invaluable contributions to our understanding of environmental challenges and human diseases. However, additional research investigating the interrelations of environment and health is required to improve the wellbeing of citizens worldwide. A primary challenge in the environmental health field is the effective combination of environmental monitoring data and bio-monitoring information (Dennis et al., 2017) taking into account many and diverse parameters such as genetic predisposition, environmental exposures, the processes that constitute these exposures and various threats throughout one's life time starting from conception. Thus, recent developments such as the exposome (Wild, 2005; Rappaport, 2011; Lioy & Rappaport, 2011; Wild, Scalbert & Herceg, 2013; Vrijheid, 2014; Buck Louis, Smarr & Patel, 2017; Johnson et al., 2017; Stingone, Buck Louis, Nakayama, Vermeulen, Kwok et. al., 2017; Sarigiannis, 2017; Sarigiannis, Karakitsios et al., 2018; Sarigiannis, Gotti, Handakas & Karakitsios, 2018) and the use of data analytics are promising future directions in the field (Lytras, & Papadopoulou, 2018). Now, massive amounts of medical and public health data related to numerous human health issues are available and there is an urgent need to apply big data analytics in healthcare (Papadopoulou, Lytras & Marouli 2018). Hot issues in the relevant sciences include single gene polymorphisms, genome sequences, gene expression data, exposure to carcinogens, endocrine disruptors, heavy metals (Ellis, et al., 2012) and other toxins, their metabolism and health impacts, exposome analysis (Larkin & Hystad 2017), risk analysis, (Turner et al., 2017) bioinformatics and data storage and handling (Papadopoulou, Lytras, & Marouli, 2018).

However, understanding only the science of the intricate relation between the environment and human health, a daunting task by itself, is limited. The uneven distribution of environmental health hazards and the marriage of informatics with health science and management make a discussion of social inequalities and injustices particularly relevant. Environmental health is a political and cultural issue, and these dimensions need to be understood and effectively addressed if we are to transition to sustainable and healthy societies (Papadopoulou, Lytras, & Marouli, 2018; Spruit & Lammertink, 2018). Environmental justice literature relating to a great variety of environmental issues, from waste management, air pollution, water pollution, to food, Genetically Modified Organisms (GMOs) or climate change, emphasize the different level of environmental risks various social groups are exposed to, the differential impact

of environmental exposures to human health in relation to social inequalities, as well as the differential access of marginalized peoples to the benefits healthy environments offer (Masuda, Poland & Baxter, 2010; indicatively, see also: Walker, 2012; Carmin & Agyeman, 2011; Gaffron, 2012; Wolch, Byrne & Newell, 2014; Cutts, Darby, Boone & Brewis, 2009; Bardsley & Wiseman, 2012). Social and power inequalities are important parameters that influence health. These beg for close consideration in the exploration of environmental health issues, and especially for the drafting of policies that promote healthy communities for all. Discourses from the environmental health sciences and the environmental justice field underline the need for contemporary societies to focus on interrelations, adopting a systemic view that incorporates knowledge from the environmental, bio-medical and socio-political sciences, and to develop integrative policies and other mechanisms – like education and public accountability. Given the increasing use of data analytics, policy, ethical and justice issues related with bio-data management and use are also important parameters that should be considered (Papadopoulou, Lytras, & Marouli, 2018).

This publication contributes to this challenging scene and presents some major contemporary environmental health hazards and their impacts. It approaches the contemporary exciting developments in the environmental health fields in an interdisciplinary manner covering from cutting-edge scientific developments to environmental justice and policy issues.

THE CHALLENGES

Human health hazards are intricate, their causes multi-faceted and health impacts are influenced by both individual characteristics and practices – like genetics or lifestyle choices – and social structures and inequalities. The challenges environmental health science faces are:

- **Research:** Establishing research efforts that are multi-disciplinary in terms of design, goals and methods is a persisting challenge, as well as the effective dissemination of the results to all stakeholders via good academic and management practices in a geographically dispersed environment.
- **Policies:** Establishing policies, legislation and procedures that aim for both a clean environment and health and wellness for all, while adequately reflecting the local and global organizational context and processes, is a prerequisite for the transition towards healthy societies.
- **Privacy and Security of Personal Health Data:** Establishing appropriate information technology precaution measures and socially appropriate policies for the handling and storage of health-related big data is a major challenge of our times. Securing personal privacy in the age of connected health data is a big challenge.
- **Social Inequalities:** Addressing social inequalities in exposure to environmental hazards and in access to proper health care with appropriate socio-political processes, policies, strategies, structures and institutions, as well as education for a wellness- and social solidarity-oriented culture and ethos.
- **Points of Intervention:** Identifying the most effective points of intervention in the spectrum society-politics-environment-health for sustainable and healthy communities, which requires further multidisciplinary and integrative research and inclusive governance processes. Establishing appropriate information technology precaution plans and disaster recovery plans is also a big challenge.

Numerous studies have been carried out toward meeting those challenges and continue onto providing good and sustainable solutions. Back in 2009 the International Life Sciences Institute (ILSI) Health and Environmental Sciences Institute (HESI) scientific portfolio, groups of experts of key government, academic, and industry scientists from around the world were assembled with the main goal to map the human and environmental health challenges for the decade (2010–2020) and offer suggestions and develop tools on the current and future landscape of scientific and regulatory challenges. This scientific mapping could serve as a valuable tool indeed which "HESI, individual companies, research institutions, government agencies, and regulatory authorities could use to anticipate key challenges, place them into context, and thus strategically refine and expand scientific project portfolios into the future" (Bonnefoi et al., 2010). As we are heading to the end of the decade it would be interesting to examine if such goals were met. The challenges of high or medium priority as defined at the January 2009 HESI Scientific Mapping Meeting in Japan are outlined and their present status is considered in comparison to what has been planned and what seems to have been achieved. Overall, it appears that whereas the goals and objectives were set in a clear way by the International Life Sciences Institute (ILSI) Health and Environmental Sciences Institute (HESI) scientific portfolio, groups of experts, the implementation for most of the plans is far from being materialized in most parts of the world despite some additional serious efforts to achieve such goals. Furthermore, many policies have been adopted for the protection of the environment, sustainable development and better health, but their implementation has still not brought about the desired results.

SEARCHING FOR SOLUTIONS: RECOMMENDATIONS

The book "Environmental Exposures and Human Health Challenges" aims to provide interdisciplinary insights into concepts and theories related to environmental health, and environmental exposures via chemical, biological or physical factors in the air, water, soil or food (Prüss-Üstün et al., 2016). It covers a diversity of environmental health topics of concern today. The exposome approach is one of the latest and very promising developments in the field, as it aims to connect both environmental and biological monitoring for a more holistic understanding of the way different exposures affect health. Autism spectrum disorders (ASDs) (Theoharides, Tsilioni, Patel & Doyle, 2016) and various autoimmune and inflammatory disorders have increased in the recent years, and it has been shown that environmental exposures, such as neurotoxins in commonly used synthetic fragrances, endocrine disruptors, (Braun et al., 2014) various molds and viruses among a number of other harmful exposures at critical stages of a human's life are main parameters contributing to their prevalence. Heavy metals constitute an important category of environmental health hazards in contemporary societies. Arsenic is one of these health risks and due to its serious health impacts, it has been investigated in several situations. Genetically modified food is another major challenge of our times, with health consequences that require further research and exploration. This need is further enhanced by recent research on the effects of Glyphosate on human health, a major constituent of the widely used pesticide Roundup, including research on toxicity of formulants and heavy metals in glyphosate-based herbicides and other pesticides. (Mesnage, Defarge, Spiroux de Vendomois & Seralini, 2015; Myers et al., 2016; Townsend, Peck, Meng, Heaton, Robison & O'Neill, 2017; Séralini et al., 2014; Defarge, Spirouxde Vendômois & Séralini, 2018). Food is generally a main issue of concern for human health, both in terms of food security – availability of adequate and good quality food - and of food quality. Cotton is a frequently used material in the world and its production

with conventional agricultural practices, including the use of pesticides, constitute a significant threat to human health. Appropriate methods for investigating environmental health issues are also discussed. The book also addresses environmental health policies as well as inequalities and injustices in relation to environmental exposures and health impacts.

This book examines in a cross-cutting way, how various environmental exposures affect individuals, workers, professions and populations from different regions of the world. It offers suggestions and recommendations so as to help increase awareness on issues of sustainability and to help improve human health and healthcare. Grounded on scientific evidence and up-to-date socio-political discourses on environmental health issues, this book aspires to contribute to the improvement of health, wellbeing and healthcare of citizens worldwide. This publication is designed for public health professionals, preventive medicine specialists, clinicians, data scientists, environmentalists, academicians, practitioners, researchers, and students. The book can also stimulate sharing opinions and ideas, so as to facilitate a better fusion of health-related issues and challenges including health informatics and other big data emerging technologies, including exposome analytics, to the academic and industry research, which combined, can lead to improvements in the quality of people's daily life.

ORGANIZATION OF THE BOOK

The book is organized into two sections. The first section focuses on the science of environmental exposures and their health impacts, while the second one delves into a discussion of policy and environmental justice aspects of selected environmental health issues.

The book includes 15 chapters. A brief description of each of the chapters follows:

Chapter 1 identifies how connectivity introduces a new exposome based paradigm in environmental health. This denotes an approach that builds on the exploration of the interconnections between the coexistence of multiple exogenous and endogenous stressors and the different scales of biological organization. Coupling the two results in the final adverse health effect. This differs from the conventional paradigm, which seeks to shed light on the identification of singular cause-effect relationships between stressors and health outcomes. It creates a new way of combining health-relevant information coming from different disciplines, treating all factors affecting internal and external exposome as covariates. Their functional integration results in understanding the complex interaction between genome and exposome. The connectivity approach is applied on toxicity assessment of nanomaterials; here multiple assays, human multi-omics and *in vitro* data are used to elucidate toxicity mechanisms.

Chapter 2 presents Autism Spectrum Disorder (ASD) as a developmental condition characterized by impaired social interactions and communication, as well as by stereotypic movements, that affects 1 in 59 children. The authors state that ASD is expected to reach 1 in about 40 children by 2020, yet it remains without distinct pathogenesis and effective treatment. Children with ASD respond with high anxiety to almost any unknown stimulus and appear to misread danger/threat signals, and may not experience anxiety in situations where normotypic children do. The authors propose that environmental stimuli stimulate the unique immune cells, known as mast cells (MC), which then trigger microglia, leading to dysfunctional neuronal connectivity in the amygdala. This process lowers or disrupts the "fear response" and leads to an exaggerated "fight-or-flight" reaction. Corticotropin-releasing hormone (CRH) could have a synergistic effect with environmental stimuli, especially mycotoxins. The authors

propose that recognizing this association and preventing stimulation of mast cells/microglia could lead to effective treatment of ASD.

Chapter 3 explores how the human brain develops and what the critical stages are in which a fetal brain may acquire genetic and developmental abnormalities through environmental agents. The authors summarize the prevailing theories regarding the etiologies of autism and present scientific data supporting the thesis that some of the most commonly used environmental agents that we have so easily accepted into our social fabric of life may be major contributors in the development of autism spectrum disorders (ASD). They provide a large body of scientific data carried out in their laboratory, utilizing developing human neurons exposed to femtomolar concentrations of chemicals found in fragrances. Their studies, the authors argue, demonstrate that synthetic fragrances can impart profound neuromodifications at the morphologic, immunologic and molecular levels. They hypothesize that high exposure to teratogenic neurotoxins in our environment during critical periods of development best explains the rapid rise of autism spectrum disorder diagnosis over the past three decades.

Chapter 4 focuses on the possible sources of arsenic (As), leading to environmental contamination, followed by its hazardous effects which pave the way to various human health manifestations. The authors explore how arsenic can cause various health disorders through acute and chronic exposures such as gastrointestinal, hepatic, respiratory, cardiovascular, integumentary, renal, neurological and reproductive disorders including stillbirth and infant mortality.

Chapter 5 is a specific case study of Arsenic exposure via contaminated water in Bihar, India of about 50 million people. In addition to health-related problems in the population like skin diseases, anemia, bronchitis, gastrointestinal problems, hormonal imbalance, according to the author's recent study, cancer risk is associated with daily consumption of 2 litres of water with inorganic arsenic 50 µg/L which has been estimated to be 1/100 denoting that elevated blood arsenic levels in a population can lead to various diseases including cancer. Skin and several types of internal cancers, including bladder, kidney, liver, gall bladder, lung, uterus and prostate cancers have been found associated with arsenic ingestion. Their hospital- based study also correlates the cause of cancer with arsenic contamination.

Chapter 6 reviews chemsensors and their role in various aspects of biomedical science, analytical and environmental chemistry. The toxic metal ions like Zn, Cd, Cu, Pb and Hg have increased gradually but now have reached an alarming situation, crossing the threshold value. Due to high toxicity of these heavy metals, there is an obvious need for a sensor system to detect their presence. The authors argue that chemsensors including surface acoustic wave sensors, enzymes, carbon nanotubes, nanoparticles and chromophore-based sensors have attracted increasing attention during the last few years. Chemsensors prove very promising as the system is rapid, selective, sensible, low cost, easy to use and has the ability to furnish real time signals. However, during recent times, considerable efforts have been devoted to the synthesis of sterically encumbered selenium containing species reported to display strong affinities with Hg^{2+} or Ag^{+}. This chapter overall, reviews the basic principles involved in the design of chemsensors, their variety and applications in various established and emerging fields.

Chapter 7 examines occupational epidemiology studies in terms of the distribution of health events and health-related determinants and its relation to the working environment. Environmental epidemiology focuses on the involuntary exposure to physical and chemical factors in the indoor or outdoor environment that may affect health patterns. Occupational and environmental epidemiology use similar methodology although the conditions differ. The environmental epidemiology studies, beyond the health effect of exposure to specific environmental factors, must consider the long-term impact of the environment on the populations. Molecular technologies allow to detect effects at the molecular level originated by

very low levels of exposure. The concept of the exposome is also briefly discussed as a kind of database with information concerning environmental exposure measurements in a life time and corresponding biomarkers concentrations in different biospecimen, considering internal individual genetic characteristics.

Chapter 8 seeks to highlight general concerns and potential lifelong effects of consuming GM plant-based food. The author argues that consumption of GM plant-based food is as risky as consuming conventional plant-based food. However, the alien genes in these products may be unstable leading to antinutritional and unintended short-term consequences. The author believes that due to the paucity of research, no long-term effects have been attributed to the lifelong consumption of these products. Nonetheless, possible lifelong health and socioeconomic effects may result from outcrossing of genes, increasing antibiotic resistance, development of new diseases, as well as potential effects on the environment and biodiversity. The author advises biotechnology companies to invest more in interdisciplinary research addressing the potential lifelong effects of these products. Although GM foods are safe for consumption, the author believes that clarification of current risks and lifelong effects is required.

Chapter 9 addresses the issue of the world dairy consumption. The author examines the impact the use of dairy products has on sustainability and health. This chapter provides an overview of milk consumption around the world, sustainability, health concerns, and dairy milk alternatives. In addition, advantages and disadvantages are discussed, as individuals are often faced with choosing the option that best meets their individual needs.

Chapter 10 informs the reader about cotton uses for the production of cotton textiles and apparel and the three different possibilities for cotton growth in the world: production of conventional, organic or genetically modified cotton. Their influence on human health, due to the application of pesticides, is discussed by the author. The influence of the pesticides on the environment, which, in turn, affects the human health through the water, soil, and food chain, is also discussed. The preferable cotton sector is presented, giving a chance to the customers of cotton textiles and apparel, to assess the positive influence of the existing initiatives in the cotton field on the human health and the environment.

Chapter 11 explores climate change and how it threatens human life and health by causing severe storms, floods, temperature fluctuations and droughts. The authors hold the belief, as predicted for the coming decades, that most of the global population will be impacted and the lives of millions will be at risk. In this context, the chapter investigates the existence of a symmetric and asymmetric causality between climate change and health between 1990 and 2015 for European countries, including EU, EFTA member and EU candidate states. In the first stage of the analysis, health scores are estimated by cluster and discriminant analyses; in the second stage, the relationships among these scores and climate variables are examined. The country-specific findings are obtained for the health effects of climate change variables according to factors such as geographical structure and seasonal characteristics. According to the results, while the health effects of changes in temperature and greenhouse gas emissions differ from country to country, the reduction in precipitation for nearly half of the countries is found to have a negative effect on health.

Chapter 12 examines how supporters of agricultural biotechnology have maintained a high enthusiasm for its role in improved agricultural yields and enhanced sustainability, for instance, in Africa. However, according to the author, critics are deeply skeptical. This chapter sketches some of the main arguments on both sides to provide a summary analysis. The discussion includes multiple climatic, socioeconomic, and public policy drivers that have collided with the ability of the average person to achieve food security. If food security is to be understood as a matter of human health, then the author argues, definitions and designs must recognize food's many roles in creating positive public health outcomes. Hence, the

discussion expands to include an integrative model of food security linking sociocultural, public policy, and ecological aspects to public health. The chapter concludes that extensive work must be done to steer policy initiatives toward common sense sustainability paths to achieve food security and/or sovereignty.

Chapter 13 explores how pharmaceuticals and personal care products (PPCPs) constitute an integral part of modern healthcare system which enter environment through various routes. Because of their inherent biological activity, their presence in soil and aquatic environment poses several eco-toxicological problems. Antibiotic contamination of soil and water bodies is leading to development of microbial resistance to antibiotics and this has been recognized by several global bodies like WHO and EPA. Effective steps need to be taken in this regard including increased awareness, reduced pharmaceutical discharges in environment, green and sustainable pharmaceutical practice by pharmaceutical industry and healthcare professionals and improved remediation/bioremediation methods. This chapter outlines the various anticipated routes of exposure of pharmaceuticals to the environment along with their detrimental effects, fate and degradation in aquatic and terrestrial environments. The chapter also dwells upon the role of various regulatory bodies and plausible measures that may be adopted to alleviate the problem.

Chapter 14 addresses the main issues that pertain to the health burden from waste management and energy resource use by highlighting the aspects that determine actual exposures and the socio-economic conditions that underlie them. Case studies covering biomass burning, acute and chronic exposure to urban and industrial waste are described by the authors. They refer to different areas in Europe and socio-economic strata focusing on susceptible population groups, which may be affected by enhanced exposure to environmental toxicants stemming from municipal and industrial waste management and domestic heating or cooking using biomass. These features, the authors argue, make socio-economic status and the consequent social (in)justice a key determinant of overall exposure early in life. The latter results in a high probability of onset or exacerbation of adverse health outcomes both in the medium term and later in life. Additional factors that affect the health impacts of environmental exposures comprise choice of diet, education level of parents, access to green or blue space and housing condition.

Chapter 15 explores the glaring scientific differences in the human health assessment of the popular herbicide glyphosate between European and American institutions. The International Agency for Research on Cancer (IARC) classified glyphosate as a probable human carcinogen, while the U.S. Environmental Protection Agency (EPA) concluded that glyphosate is not likely to be carcinogenic to humans. Both IARC's and the EPA's carcinogenic risk assessment processes are discussed by the author. With this work the author argues that uncertainties are reviled in the sciences of toxicology and epidemiology, as well as assumptions made in their applications for evaluating glyphosate. These uncertainties, along with the political context of chemical risk assessment, the author believes, are at the root of the divergent findings on the carcinogenic risks of glyphosate.

Paraskevi Papadopoulou
Deree – The American College of Greece, Greece

Christina Marouli
Deree – The American College of Greece, Greece

Anastasia Misseyanni
Deree – The American College of Greece, Greece

REFERENCES

Bardsley, D. K., & Wiseman, N. D. (2012). Climate change vulnerability and social development for remote indigenous communities of South Australia. *Global Environmental Change*, *22*(3), 713–723. doi:10.1016/j.gloenvcha.2012.04.003

Bollati, V., & Baccarelli, A. (2010). Environmental epigenetics. *Heredity*, *105*(1), 105–112. doi:10.1038/hdy.2010.2 PMID:20179736

Bonnefoi, M. S., Belanger, S. E., Devlin, D. J., Doerrer, N. G., Embry, M. R., Fukushima, S., ... van der Laan, J. W. (2010). Human and environmental health challenges for the next decade (2010–2020). *Critical Reviews in Toxicology*, *40*(10), 893–911. doi:10.3109/10408444.2010.506640 PMID:20854192

Braun, J. M., Kalkbrenner, A. E., Just, A. C., Yolton, K., Calafat, A. M., Sjödin, A., ... Lanphear, B. P. (2014). Gestational exposure to endocrine-disrupting chemicals and reciprocal social, repetitive, and stereotypic behaviors in 4- and 5-year-old children: The HOME study. *Environmental Health Perspectives*, *122*(5), 513–520. doi:10.1289/ehp.1307261 PMID:24622245

Buck Louis, G. M., Smarr, M. M., & Patel, C. J. (2017). The Exposome Research Paradigm: An Opportunity to Understand the Environmental Basis for Human Health and Disease. *Current Environmental Health Reports*, *4*(1), 89–98. doi:10.100740572-017-0126-3 PMID:28194614

Carmin, J., & Agyeman, J. (Eds.). (2011). *Environmental Inequalities Beyond Borders: Local Perspectives on Global Injustices*. Boston, MA: MIT Press. doi:10.7551/mitpress/8759.001.0001

Cutts, B. B., Darby, K. J., Boone, C. G., & Brewis, A. (2009). City structure, obesity, and environmental justice: An integrated analysis of physical and social barriers to walkable streets and park access. *Social Science & Medicine*, *69*(9), 1314–1322. doi:10.1016/j.socscimed.2009.08.020 PMID:19751959

Defarge, N., Spirouxde Vendômois, J., & Séralini, G. E. (2018). Toxicity of formulants and heavy metals in glyphosate-based herbicides and other pesticides. *Toxicology Reports*, *5*, 156–163. doi:10.1016/j.toxrep.2017.12.025 PMID:29321978

Dennis, K. K., Marder, E., Balshaw, D. M., Cui, Y., Lynes, M. A., Patti, G. J., ... Barr, D. B. (2017). Biomonitoring in the Era of the Exposome. *Environmental Health Perspectives*, *125*(4), 502–510. Epub-2016Jul6. doi:10.1289/EHP474 PMID:27385067

Ellis, J., Athersuch, T., Thomas, L., Teichert, F., Perez-Trujillo, M., Svendsen, C., ... Keun, H. C. (2012). Metabolic profiling detects early effects of environmental and lifestyle exposure to cadmium in a human population. *BMC Medicine*, *10*(1), 61. doi:10.1186/1741-7015-10-61 PMID:22713677

European Environment Agency. (2013). *Environment and human health*. EEA Report No 5/2013. doi:10.2800/9092

Gaffron, P. (2012). Urban transport, environmental justice and human daily activity patterns. *Transport Policy*, *20*, 114–127. doi:10.1016/j.tranpol.2012.01.011

Herceg, Z. (2016). Epigenetic Mechanisms as an Interface Between the Environment and Genome. *Advances in Experimental Medicine and Biology*, *903*, 3–15. doi:10.1007/978-1-4899-7678-9_1 PMID:27343085

Johnson, C. H., Athersuch, T. J., Collman, G. W., Dhungana, S., Grant, D. F., Jones, D. P., ... Vasiliou, V. (2017). Yale school of public health symposium on lifetime exposures and human health: The exposome; summary and future reflections. *Human Genomics*, *11*(1), 32. doi:10.118640246-017-0128-0 PMID:29221465

Larkin, A., & Hystad, P. (2017). Towards Personal Exposures: How Technology Is Changing Air Pollution and Health Research. *Current Environmental Health Reports*, *4*(4), 463–471. doi:10.100740572-017-0163-y PMID:28983874

Lin, D., Liu, J., Hu, Z., Cottrell, J. E., & Kass, I. S. (2018). Neonatal anesthesia exposure impacts brain microRNAs and their associated neurodevelopmental processes. *Scientific Reports*, *8*(1), 10656. doi:10.103841598-018-28874-0 PMID:30006558

Lioy, P. J., & Rappaport, S. M. (2011). Exposure science and the exposome: An opportunity for coherence in the environmental health sciences [Editorial]. *Environmental Health Perspectives*, *119*(11), A466–A467. doi:10.1289/ehp.1104387 PMID:22171373

Lytras, M. D., & Papadopoulou, P. (2018). *Applying Big Data Analytics in Bioinformatics and Medicine*. Hershey, PA: IGI Global. doi:10.4018/978-1-5225-2607-0

Masuda, J. R., Poland, B., & Baxter, J. (2010). Reaching for environmental health justice: Canadian experiences for a comprehensive research, policy and advocacy agenda in health promotion. *Health Promotion International*, *25*(4), 453–463. doi:10.1093/heapro/daq041 PMID:20615911

Mesnage, R., Defarge, N., Spiroux de Vendomois, J., & Seralini, G.-E. (2015). Potential toxic effects of glyphosate and its commercial formulations below regulatory limits. *Food and Chemical Toxicology*, *84*, 133–153. doi:10.1016/j.fct.2015.08.012 PMID:26282372

Myers, P. J., Antoniou, M. N., Blumberg, B., Carroll, L., Colborn, T., Everett, L. G., … Benbrook, C. M. (2016). Concerns over use of glyphosate-based herbicides and risks associated with exposures: a consensus statement, *Environmental Health, 15*. doi:10.118612940-016-0117-0

Papadopoulou, P., Lytras, M., & Marouli, C. (2018). Bioinformatics as Applied to Medicine: Challenges Faced Moving from Big Data to Smart Data to Wise Data. In M. Lytras & P. Papadopoulou (Eds.), *Applying Big Data Analytics in Bioinformatics and Medicine* (pp. 1–25). Hershey, PA: IGI Global. doi:10.4018/978-1-5225-2607-0.ch001

Prüss-Üstün, A., Wolf, J., Corvalán, C. F., Bos, R., & Neira, M. P. (2016). *Preventing disease through healthy environments: a global assessment of the burden of disease from environmental risks*. World Health Organization. Retrieved from http://www.who.int/iris/handle/10665/204585

Rappaport, S. M. (2011). Implications of the exposome for exposure science. *Journal of Exposure Science & Environmental Epidemiology*, *21*(1), 5–9. doi:10.1038/jes.2010.50 PMID:21081972

Sarigiannis, D. A. (2017). Assessing the impact of hazardous waste on children's health: The exposome paradigm. *Environmental Research*, *158*, 531–541. doi:10.1016/j.envres.2017.06.031 PMID:28711809

Sarigiannis, D. A., Gotti, A., Handakas, E., & Karakitsios, S. P. (2018). Informatics and Data Analytics to Support Exposome-Based Discovery: Part 2 - Computational Exposure Biology. In M. Lytras & P. Papadopoulou (Eds.), *Applying Big Data Analytics in Bioinformatics and Medicine* (pp. 145–187). Hershey, PA: IGI Global. doi:10.4018/978-1-5225-2607-0.ch007

Sarigiannis, D. A., Karakitsios, S. P., Handakas, E., Papadaki, K., Chapizanis, D., & Gotti, A. (2018). Informatics and Data Analytics to Support Exposome-Based Discovery: Part 1 - Assessment of External and Internal Exposure. In M. Lytras & P. Papadopoulou (Eds.), *Applying Big Data Analytics in Bioinformatics and Medicine* (pp. 115–144). Hershey, PA: IGI Global. doi:10.4018/978-1-5225-2607-0.ch006

Séralini, G.-E., Clair, E., Mesnage, R., Gress, S., Defarge, N., Malatesta, M., ... Spiroux de Vendômois, J. (2014). Republished study: Long-term toxicity of a Roundup herbicide and a Roundup-tolerant genetically modified maize. *Environmental Sciences Europe*, *26*(1), 14. doi:10.118612302-014-0014-5 PMID:27752412

Spruit, M., & Lammertink, M. (2018). Effective and Efficient Business Intelligence Dashboard Design: Gestalt Theory in Dutch Long-Term and Chronic Healthcare. In M. Lytras & P. Papadopoulou (Eds.), *Applying Big Data Analytics in Bioinformatics and Medicine* (pp. 243–271). Hershey, PA: IGI Global. doi:10.4018/978-1-5225-2607-0.ch010

Stingone, J. A., Buck Louis, G. M., Nakayama, S. F., Vermeulen, R. C., Kwok, R. K., Cui, Y., ... Teitelbaum, S. L. (2017). Toward Greater Implementation of the Exposome Research Paradigm within Environmental Epidemiology. *Annual Review of Public Health*, *20*(38), 315–327. Epub2017Jan6. doi:10.1146/annurev-publhealth-082516-012750 PMID:28125387

Theoharides, T. C., Tsilioni, I., Patel, A. B., & Doyle, R. (2016). Atopic diseases and inflammation of the brain in the pathogenesis of autism spectrum disorders. *Translational Psychiatry*, *6*(6), e844. doi:10.1038/tp.2016.77 PMID:27351598

Townsend, M., Peck, C., Meng, W., Heaton, M., Robison, R., & O'Neill, K. (2017). Evaluation of various glyphosate concentrations on DNA damage in human Raji cells and its impact on cytotoxicity. *Regulatory Toxicology and Pharmacology*, *85*, 79–85. doi:10.1016/j.yrtph.2017.02.002 PMID:28185844

Turner, M. C., Nieuwenhuijsen, M., Anderson, K., Balshaw, D., Cui, Y., Dunton, G., ... Turner, M. C. (2017). Assessing the Exposome with External Measures: Commentary on the State of the Science and Research Recommendations. *Annual Review of Public Health*, *20*(38), 215–239. doi:10.1146/annurev-publhealth-082516-012802 PMID:28384083

United Nations. (2017). *World Mortality 2017: Data Booklet*. Retrieved from http://www.un.org/en/development/desa/population/publications/pdf/mortality/World-Mortality-2017-Data-Booklet.pdf

Vrijheid, M. (2014). The exposome: A new paradigm to study the impact of environment on health. *Thorax*, *69*(9), 876–878. doi:10.1136/thoraxjnl-2013-204949 PMID:24906490

Walker, G. (2012). *Environmental Justice: Concepts, Evidence and Politics*. Routledge. doi:10.4324/9780203610671

Wild, C. P. (2005). Complementing the genome with an "exposome": The outstanding challenge of environmental exposure measurement in molecular epidemiology. *Cancer Epidemiology, Biomarkers & Prevention*, *14*(8), 1847–1850. doi:10.1158/1055-9965.EPI-05-0456 PMID:16103423

Wild, C. P., Scalbert, A., & Herceg, Z. (2013). Measuring the exposome: A powerful basis for evaluating environmental exposures and cancer risk. *Environmental and Molecular Mutagenesis*, *54*(7), 480–499. doi:10.1002/em.21777 PMID:23681765

Wolch, J., Byrne, J., & Newell, J. P. (2014). Urban green space, public health, and environmental justice: The challenge of making cities 'just green enough.' *Landscape and Urban Planning*, *125*, 234–244. doi:10.1016/j.landurbplan.2014.01.017