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## Supporting and implementing the beneficial parts of the exposome: The environment can be the problem, but it can also be the solution

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## ABSTRACT

In 2005, Christopher P. Wild introduced the exposome concept, encompassing the biochemical changes in the organism in response to the totality of all environmental exposures throughout the entire lifespan and their association with health outcomes. The exposome concept also aimed at to completing the genome, that describes the genetic predisposition as a determinant of disease and death as well as potential targets of intervention. The exposome can be subdivided into multiple pollutants related to specific chemical and physical pollutants (or other forms of environmental risks), periods of life (infancy, childhood, adolescence, adulthood, and old age) or geographical locations. While exposome research and, in general, health research of the last decades has predominantly focused on what factors contribute to and initiate morbidity and mortality, little is done on factors that will help to develop, maintain, or even increase human health. We want to contribute to this reorientation by supporting and implementing the beneficial exposome, comprising all environmental exposures with the potential to promote health.

## 1. Living in the anthropocene

During the last 125 years, humankind left a strong footprint on Earth and significantly interfered with planetary health and perturbed environmental integrity (Kress and Stine, 2017). This received an extra impetus from industrial and urban development during the “great acceleration” after world war II, intimately connected with the rapidly increasing use of fossil fuels and exponential growth of the world population, which more than doubled since 1900 and may even reach nine billion in 2050 (Steffen et al., 2011; Lelieveld, 2017). Scientists have coined the term “Anthropocene” to define the most recent geological epoch during which mankind has caused a major loss of biodiversity, and polluted the oceans, freshwater, soils and the air we breathe, among other unsustainable developments that are not easily reversible (Kress and Stine, 2017). The deterioration of air quality represents a dire hallmark of the Anthropocene (Munzel et al., 2022; Lelieveld and Pöschl, 2017; Pöschl and Shiraiwa, 2015), recognized by the World Health Organization (WHO) and United Nations, demanding that clean

air should be considered a human right, to be pursued by all necessary means including climate action, sustainable cities and clean energy (Lelieveld, 2017). According to reports by the Lancet Commission on Pollution and Health and the WHO (Landrigan et al., 2018; WHO report, 2016), all forms of chemical pollution together are responsible for an estimated 9 to 12.6 million deaths per year, reflecting 16–20% of the total annual global deaths, a number that exceeds that due to tobacco smoking, for example. Also, climate change, responsible for increasing heat waves, storms and floods, as well as extended periods of drought, is an anthropogenic hazard with a considerable impact on the global burden of disease, reflected by ranking “not-optimal temperature” as a leading health risk factor by the Global Burden of Disease (GBD) report (GBD Collaborators, 2020). Finally, urbanization increases the exposure of citizens to traffic noise and air pollution, also associated with a lack of green space, social isolation, work strain and economic inequity (Munzel et al., 2021a). Currently, well over 50% of the world population lives in urban areas and projections indicate that this number will rise to 70 % by the year 2050 (European Commission, 2020). It has been postulated

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that environmental risk factors may then contribute up to two-thirds to chronic, non-communicable diseases, which rationalizes the expression that “genetics load the gun but environment pulls the trigger” (Olden and Wilson, 2000). Therefore, efficient mitigation strategies against environmental stressors are urgently needed (Munzel et al., 2020).

## 2. Complementation of the Genome by the Exposome

To tackle the knowledge gaps relating to health effects of environmental exposures, in 2005 Christopher P. Wild postulated the exposome concept, which comprises the biochemical changes and alterations in the organism in response to the totality of all environmental factors (both positive and negative ones) over the whole lifespan and their health outcome association (Wild, 2005). This is also reflected by highlighting the importance of analytics for the exposome concept (Rappaport et al., 2014). In a certain sense, the exposome can be regarded as an environmental upgrade of the genome/proteome/metabolome. The exposome risk factors are not only based on physicochemical threats, such as air pollution, transportation noise, ultraviolet (UV) radiance and altered temperature, but also socioeconomic and mental health determinants such as poverty, low social status, loneliness, work strain or mourning (Vrijheid, 2014; Sainani, 2016; Wild, 2012; Munzel et al., 2023). These stressors represent the negative part of the general external environment, which can hardly be changed at the individual level. The other negative part of the exposome relates to lifestyle or behavioral risks such as natural stimulants (e.g., tobacco products, alcohol), overeating, sedentary lifestyle, and use of unhealthy consumer materials. These exposures determine the specific external environment, which can be changed in a simple way by each and everyone. In contrast, the air quality, environmental sound pressure level, socioeconomic status, or weather extremes, cannot be modified facilely by the individual. The exposome can be graduated into various pollutomes, which can be characterized by certain physicochemical exposures but also different stages in one’s life (e.g., fetal or seniority) or place of living (Landrigan et al., 2018). Accordingly, pollutomes represent timed and endemic exposures and their associated changes of human (patho-)physiology. However, we should keep in mind that the exposome is more than the sum of all pollutomes.

Importantly, the exposome concept was also introduced to complement the genome, that comprises genetic predisposition as a determinant of disease and death as well as identification of novel therapeutic targets, with an environmental equivalent associating exposure to biochemical pathomechanisms and health risks (Wild, 2005; Munzel et al., 2023). Notably, the exposome approach rather focuses on multi-exposure/multi-health-effect scenarios and interacting risk profiles, e.g. as recently shown for additive increase of diabetic risk by traffic noise, air pollution and lack of green space co-exposure (Sorensen et al., 2022), instead of classical one-exposure/one-health-outcome studies, e.g. road noise impact on hypertension (Jarup et al., 2008), impairment of endothelial function by aircraft noise (Schmidt et al., 2013) or air pollution effect on coronary events (Cesaroni et al., 2014). Consideration of multi-exposure scenarios is of great importance due to the frequent co-occurring of different exposures in urban/industrial areas (Munzel et al., 2021a, 2021b). Unfortunately, we only understand a limited fraction of the effects of different pollutomes on health because only few multi-pollutant studies have been conducted so far, but also because a large unknown and uncharacterized part of the pollutome is not included in the GBD study nor in other extensive, environmental health association studies. Therefore, the current estimate of 9–12.6 million premature deaths per year attributable to all forms of chemical pollution might be just the tip of the iceberg, particularly when considering the most encompassing estimates of about 8 million or more excess deaths per year attributable to air pollution alone (Lelieveld et al., 2019; Burnett et al., 2018). As a long-term output of exposome research, leading experts are calling for an “Environment-Wide Association Study (EWAS)” (Patel et al., 2010; Zheng et al., 2020) in analogy to

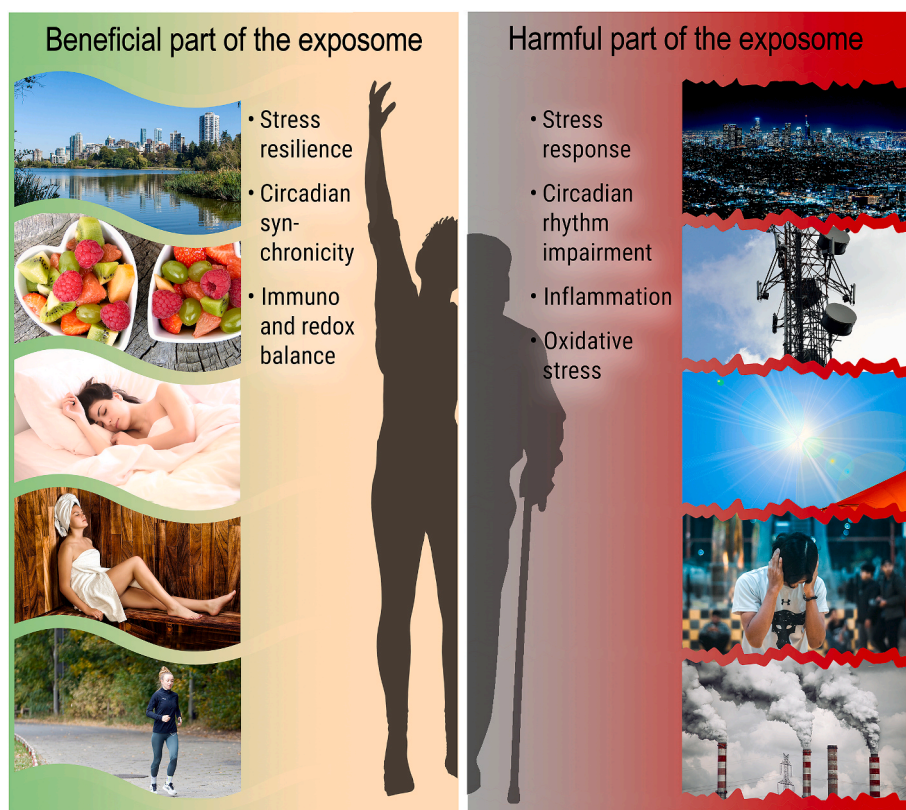
Genome-Wide Association Studies (GWAS) (Sainani, 2016).

## 3. The beneficial parts of the exposome

While exposome research and, in general, health research of the last decades has predominantly focused on what factors contribute to and initiate morbidity and mortality, little is done on a broad and all-encompassing concept that realigns from the question what makes sick towards what makes healthy, and what factors will help to develop, maintain, or even increase health. We want to contribute to this reorientation by supporting and implementing the beneficial/positive parts of the exposome. We recommend that more effort should be done to identify and implement the positive factors of the exposome that have the potential to benefit human physical and mental health. Reorienting from an environmental stress- and risk-oriented view to a framework that focuses more on exposures and factors from which human health can benefit at increasing amounts and doses is clearly needed. In other words, which types of exposure at increasing dose and amount have health benefits? It is important to note that exposome research has in general an agnostic view, meaning that the search for environmental drivers of health include both positive and negative effects. Indeed, many of the findings of exposome-based studies reveal positive relationships with human health and well-being (Vermeulen et al., 2020). However, there is no doubt that the work to this point has been weighted toward the adverse effects of exposures and introducing ways to better study the positive aspects of exposures would be useful. This is in line with a salutogenetic perspective, in contrast to a pathogenetic perspective, and also have an overlap with the concept of psychological resilience. In general, salutogenesis, a term that was coined by Aaron Antonovsky, refers to factors that increase well-being and human health, complementary to factors that were associated with disease (pathogenesis) (Antonovsky, 1996). Incorporating methods and findings of this concept along with the idea of resilience and combining them with the general framework of the exposome is promising.

Resilience is defined by the American Psychological Association (APA) as “the process and outcome of successfully adapting to difficult or challenging life experiences, especially through mental, emotional, and behavioral flexibility and adjustment to external and internal demands. A number of factors contributes to how well people adapt to adversities, predominantly the ways in which individuals view and engage with the world, the availability and quality of social resources, and specific coping strategies” (American Psychological Association). In other words, what factors contribute to the hardiness of individuals to cope with and withstand stress exposure and maintain good mental health? These questions are crucial especially in terms of healthy and resilient aging of the population – which should be addressed in the context of the beneficial parts of the exposome. It takes the question about what exposures and factors lead to disease, and whether reduction or the absence or avoidance of these factors lead to reduced risk of disease, a step further by focusing on what exposures in the environment at increasing doses will improve health throughout the human lifespan? This is related to healthy aging and increasing the healthspan.

It is important to acknowledge, that health is not defined as the mere absence of factors that are implicated in the pollutome, in the same way as human health cannot be described as the simple absence of disease. Actively targeting factors that are associated with increased human health, well-being, and quality of life should be encouraged. Consistent with the pollutome, the beneficial parts of the exposome is not limited to physical or chemical exposures, but also mental exposures such as social support, friendship, love, and personal success. In accordance with the basis of healthy aging and also of nature-based solutions, evidence that emerges from the beneficial exposome of the exposome should not only be seen in a descriptive but also prescriptive manner. This reorientation effort is directed in answering fundamental questions of our time such as which exposures positively influence health over the lifespan, what determines healthy and resilient aging, what favors human longevity,



**Fig. 1.** The beneficial parts of the exposome ("benignome") in contrast to the harmful parts of the exposome ("pollutome"). Included images were taken from open source image databases Pixabay (<https://pixabay.com/>).

are there different life phases where individuals benefit differently from certain factors, is there an interaction/synergy between factors to increase health (as a counterpart to the concept of syndemics (Mendenhall et al., 2022)). This perspective enables also to consider people with pre-existing conditions and to identify factors that will help to effectively cope with consequences and progression of their conditions in a beneficial way. These views have important public health and policy making implications, especially because we need a transition process that restructures our landscape and urban areas towards a more sustainable and environmentally friendly society, especially in view of climate change.

Within the exposome framework, numerous factors emerge as integral components of the beneficial parts of the exposome. These factors intersect and intertwine to create an environment conducive to human health and well-being. Factors that likely play a role in the beneficial parts of the exposome include (Fig. 1).

- Natural surroundings (Maller et al., 2006; Hartig et al., 2014) and greenspaces (Yang et al., 2021): Access to parks, gardens, and greenery not only provides recreational opportunities but also contributes to mental and physical health. These spaces offer respite from urban stressors, improve air quality, and enhance overall quality of life.
- Psychological resilience and associated factors (Kalisch et al., 2017): Developing psychological resilience involves equipping individuals with the tools to navigate life's challenges effectively, including those posed by a rapidly changing environment.
- Positive attitude towards nature (Rosa and Collado, 2019): This mindset encourages people to appreciate the intrinsic value of the environment and motivates sustainable behaviors. It also strengthens the emotional connection between individuals and the nature.
- Biodiversity (Sandifer et al., 2015; Methorst et al., 2021): Biodiversity plays a multifaceted role in the beneficial exposome. It enhances

ecosystem resilience, supports pollinators vital for agriculture, and contributes to human health and well-being by providing food, medicine, and ecosystem services.

- Daylight (Beute and de Kort, 2014): Adequate exposure to daylight regulates circadian rhythms, supports mental health, and can even reduce energy consumption by decreasing the need for artificial lighting.
- Physical activity (Warburton et al., 2006): Encouraging physical activity in urban settings is essential for combatting sedentary lifestyles and related health issues. Well-designed urban spaces can promote active transportation, such as walking and cycling, making physical activity an integral part of daily life.
- Nutrition (Block et al., 2011): Healthy nutrition promotes overall health and well-being by providing essential nutrients and supporting the body's vital functions.
- Social and emotional support (Reblin and Uchino, 2008): Robust social and emotional support networks within communities support people to cope with health challenges and contribute to overall resilience.

#### 4. Integrating existing concepts and future perspectives

There exist other concepts of health that have overlap with our suggestions that should be briefly mentioned. In addition to the above-described concepts of psychological resilience and salutogenesis, healthy aging is a related concept that is defined by the WHO as "a continuous process of optimizing opportunities to maintain and improve physical and mental health, independence, and quality of life throughout the life course" (WHO). In accordance with the WHO, healthy aging is targeted at establishing opportunities and environments that allow people to do what they enjoy throughout their lifespan. It is important to note that the absence of disease or injury is not a prerequisite for healthy aging, as many older people live with one or more

health conditions that, when properly managed, will have a small impact on their health and quality of life (WHO, 2020). The fundamental distinction between these established concepts and our suggestions lies in the integration within the exposome framework. While psychological resilience, salutogenesis, and healthy aging all emphasize the importance of holistic well-being, the exposome framework uniquely incorporates a comprehensive approach that considers the totality of environmental exposures, both positive and negative, and their impact on health. This integrated perspective allows for a more nuanced understanding of how various factors in our environment contribute to our overall health and well-being throughout our lives (Fig. 1). Specific future initiatives that will help to support and implement the beneficial parts of the exposome include education and awareness, data collection and analysis, urban planning and environmental design, personalized exposome health plans, community-based exposome interventions, and policy and healthcare integration. These initiatives, whether implemented individually or in combination, can contribute to a more profound understanding of the beneficial part of the exposome's impact on health and offer practical strategies to implement the beneficial exposome for individuals and communities.

Finally, we emphasize that despite the vast amount of data on the health benefits of factors such as physical activity (Warburton et al., 2006) from numerous national and international studies, major initiatives and global approaches on physical activity and health benefits in terms of large clinical, controlled trials in the general population are lacking. The same applies to other beneficial factors such as healthy nutrition and psychological resilience. How could this be approached in the future? We should strengthen efforts towards a global perspective on these factors. A crucial task for future developments will be to learn from and integrate existing models, methods, and findings into the beneficial parts of the exposome, which could also be termed the "benignome".

#### Availability of data and materials

Not applicable.

#### Author contribution

O.H., S.A.-K., J.L., T. M., and A.D. contributed to the conception of the research, acquisition of data, drafting, and revision of the manuscript.

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#### Ethics approval

Not applicable. This research does not involve the use of any animal or human data or tissue.

#### Consent to participate

Not applicable.

#### Consent for publication

Not applicable.

#### Declaration of competing interest

The authors declare no competing interests.

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