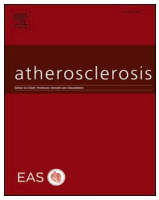
Atherosclerosis 403 (2025) 119160

Contents lists available at ScienceDirect

Atherosclerosis

journal homepage: www.elsevier.com/locate/atherosclerosis



The links between soil and water pollution and cardiovascular disease

Thomas Münzel [a,b,1,*], Marin Kuntic [a,1], Jos Lelieveld [c], Michael Aschner [d], Mark J. Nieuwenhuijsen [e,f,g], Philip J. Landrigan [h,i], Andreas Daiber [a,b]

[a] University Medical Center Mainz, Department of Cardiology at the Johannes Gutenberg University, Germany
[b] German Cardiovascular Research Center (DZHK), Partner Site Rhine Main, Mainz, Germany
[c] Atmospheric Chemistry Department, Max Planck Institute for Chemistry, Mainz, Germany
[d] Molecular Pharmacology, Albert Einstein College of Medicine, United States
[e] Institute for Global Health (ISGlobal), Barcelona, Spain
[f] Department of Experimental and Health Sciences, Universitat Pompeu Fabra (UPF), Barcelona, Spain
[g] CIBER Epidemiología y Salud Pública (CIBERESP), Madrid, Spain
[h] Global Observatory on Planetary Health, Boston College, USA
[i] Centre Scientifique de Monaco, MC, Monaco

ARTICLE INFO

Keywords:
Soil and water pollution
Pesticides
Heavy metals and nano- and microplastics
Inflammation and oxidative stress
Atherosclerotic processes
Cardio- and cerebrovascular disease

ABSTRACT

Soil and water pollution represent significant threats to global health, ecosystems, and biodiversity. Healthy soils underpin terrestrial ecosystems, supporting food production, biodiversity, water retention, and carbon sequestration. However, soil degradation jeopardizes the health of 3.2 billion people, while over 2 billion live in water-stressed regions. Pollution of soil, air, and water is a leading environmental cause of disease, contributing to over 9 million premature deaths annually. Soil contamination stems from heavy metals, synthetic chemicals, pesticides, and plastics, driven by industrial activity, agriculture, and waste mismanagement. These pollutants induce oxidative stress, inflammation, and hormonal disruption, significantly increasing risks for non-communicable diseases (NCDs) such as cardiovascular disease (CVD).

Emerging contaminants like micro- and nanoplastics amplify health risks through cellular damage, oxidative stress, and cardiovascular dysfunction. Urbanization and climate change exacerbate soil degradation through deforestation, overfertilization, and pollution, further threatening ecosystem sustainability and human health. Mitigation efforts, such as reducing chemical exposure, adopting sustainable land-use practices, and advancing urban planning, have shown promise in lowering pollution-related health impacts. Public health initiatives, stricter pollution controls, and lifestyle interventions, including antioxidant-rich diets, can also mitigate risks.

Pollution remains preventable, as demonstrated by high-income nations implementing cost-effective solutions. Policies like the European Commission's Zero-Pollution Vision aim to reduce pollution to safe levels by 2050, promoting sustainable ecosystems and public health. Addressing soil pollution is critical to combating the global burden of NCDs, particularly CVDs, and fostering a healthier environment for future generations.

1. Introduction

Healthy soil and clean water are fundamental to the environment and human health and well-being, yet they remain underappreciated in medical practice. Soil forms the foundation of terrestrial ecosystems, supporting food production, taking care for beneficial uptake of essential elements, biodiversity, and vital services like pollination [1]. Additionally, the soil aids in water retention, protects waterways from flooding and decreases the risk of waterborne diseases, and serves as a significant carbon sink, mitigating climate change. It is estimated that soil degradation nowadays jeopardizes the health of 3.2 billion people, or 40 % of the global population [1]. Furthermore, over 2 billion individuals lived in water-stressed regions as of 2021, a figure set to rise with continued climate change and population growth pollution of soil, water, and air constitutes a severe and escalating global health crisis [2]. The Lancet Commission on Pollution and Health identified pollution as the leading environmental cause of disease and premature mortality. In 2019, pollution-related illnesses caused 9 million premature

* Corresponding author. University Medical Center Mainz, Department of Cardiology, Langenbeckstrasse 1, 55131, Mainz, Germany.
E-mail address: tmuenzel@uni-mainz.de (T. Münzel).
[1] Both authors contributed equally.

https://doi.org/10.1016/j.atherosclerosis.2025.119160
Received 22 December 2024; Received in revised form 24 February 2025; Accepted 26 February 2025
Available online 2 March 2025

deaths—16 % of global mortality, surpassing deaths from AIDS, malaria, and tuberculosis combined [3]. Pollution also accounted for 268 million disability-adjusted life years (DALYs), mainly driven by air and water contamination [4,5]. Air pollution remains the leading pollution-related risk factor, contributing up to 8.3 million deaths annually [6], especially among older populations [7]. Water pollution, by contrast, drives high rates of infant mortality [3]. Soil and air pollution impact DALYs across all life stages, though soil pollution significantly affects older adults [3]. Alarmingly, 70 % of diseases caused by pollution are non-communicable diseases (NCDs), with cardiovascular diseases making up over 60 % of this burden (Fig. 1) [5].

Yet, pollution mitigation continues to be missing from the Global Action Plan to Prevent and Control NCDs [8]. This plan also overlooks non-chemical stressors such as noise, mental stress, nocturnal light pollution, and climate change, which may surpass genetic predisposition as contributors to NCDs. Environmental risk factors significantly exacerbate metabolic and mental disorders, including hypertension, diabetes, stroke, neurodegeneration, and cancers [9–11]. The underlying mechanisms of pollution-induced NCDs include oxidative stress, inflammation, hormonal disruptions, and circadian rhythm disturbances [12–14]. While less visible than air pollution, soil and water contamination remains critical [5]. Soil pollution arises from harmful substances such as heavy metals, synthetic chemicals, pathogens, plastics, and pesticides, primarily from industries, mining, fossil fuel combustion, agriculture, and urban waste mismanagement. Pollution-related diseases disproportionately affect developing and newly industrialised nations, where over 90 % of pollution-related deaths occur. These regions face acute soil and water contamination due to extensive pesticide use, industrial emissions, and inadequate waste management [15]. This review highlights the significant interplay between soil and water pollution and human health, with a particular focus on cardiovascular diseases.

2. Chemical pollution

Contaminated soil and water significantly threaten human health through exposure to toxic chemicals. According to the World Health Organization (WHO) estimates, 2 million deaths and 53 million disability-adjusted life years (DALYs) were lost in 2019 due to selected chemical exposures (Fig. 2), a sharp rise from 2016 figures [16]. Hazardous substances include heavy metals, polycyclic aromatic hydrocarbons (PAHs), per- and polyfluorinated substances (PFAS), pesticides, and organic solvents. Beyond cancer and respiratory diseases, these chemicals are increasingly associated with cardiovascular disease (CVD) [16]. Biomonitoring studies have detected concentrations of numerous chemicals in both European and U.S. populations [17,18].

2.1. Cellular side effects of chemicals

Pesticides and endocrine-disrupting chemicals activate the aryl hydrocarbon receptor (AhR), leading to inflammatory responses and oxidative stress [19] (Fig. 3). Pesticides impair glucose metabolism, alter mitochondrial function, and induce DNA damage, further promoting inflammation and metabolic disease [20]. Heavy metals, including cadmium, lead, and mercury, to name a few, interfere with redox status and antioxidant defenses, depleting glutathione (GSH), in turn, increasing oxidative stress [21,22]. Lead disrupts calcium homeostasis, promoting mitochondrial reactive oxygen species (ROS) formation, while mercury binds thiol groups in enzymes, causing functional impairment [23]. Arsenic activates G-protein-coupled receptors (GPCR), triggering vascular remodeling and inflammation [24]. Oxidative stress further impairs vascular function by depleting nitric oxide (NO) and uncoupling endothelial nitric oxide synthase (eNOS), leading to peroxynitrite formation [25]. Redox-sensitive inflammatory pathways are also activated, including the NFκB pathway, neutrophil extracellular traps (NETosis), and the NLRP3 inflammasome [26].

2.2. General diseases caused by chemicals

Heavy metals such as arsenic, cadmium, lead, and mercury cause cardiovascular diseases, cancer, and neurodevelopmental disorders [3]. Arsenic, classified as a Group 1 carcinogen, is a significant cause of water-mediated mortality worldwide, while cadmium and lead are linked to hypertension and ischemic heart disease [27,28]. Even low-level exposure to metals can significantly elevate cardiovascular risk [29]. Persistent organic pollutants (POPs), including dioxins, polychlorinated biphenyls (PCBs), and pesticides, bioaccumulate in tissues and disrupt endocrine pathways. Dioxin-like PCBs are associated with insulin resistance, hypertension, and diabetes [4]. Perfluoroalkyl and polyfluoroalkyl substances (PFAS) and bisphenol A (BPA) are known endocrine disruptors that elevate risks for obesity, dyslipidemia, and cardiovascular diseases [30,31] (Fig. 4). Another endocrine disruptor

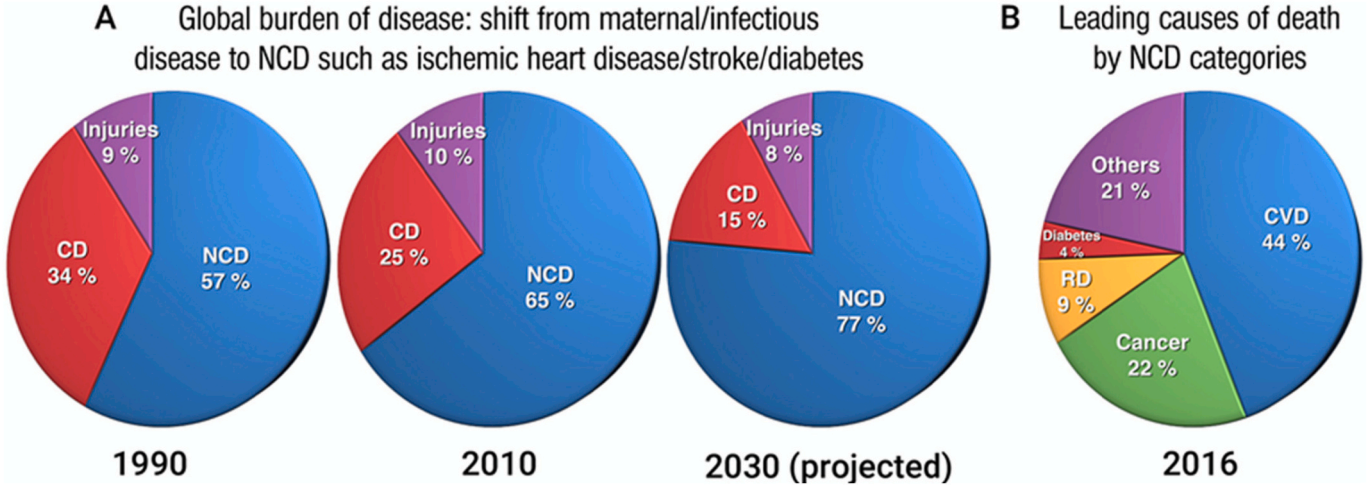


Fig. 1. Global burden of disease and non-communicable disease. (A) The proportional distribution of global deaths attributable to communicable diseases, non-communicable diseases, and injuries for 1990, 2010 and projected for 2030. Graphs generated from previous data [146,147] (B) Global World Health Organization status report on non-communicable diseases 2016 estimate the leading causes of death by different categories. The category 'Others' comprises neurodegenerative and other neurological diseases, musculoskeletal diseases, congenital anomalies, digestive disorders, endocrine/blood/immune disorders, genitourinary diseases, and other orphan disease categories. CD, communicable disease; NCD, non-communicable disease; CVD, cardiovascular disease; RD, respiratory disease. Graphs generated from previous data [148]. Presented graph was reused from Ref. [132] with permission.

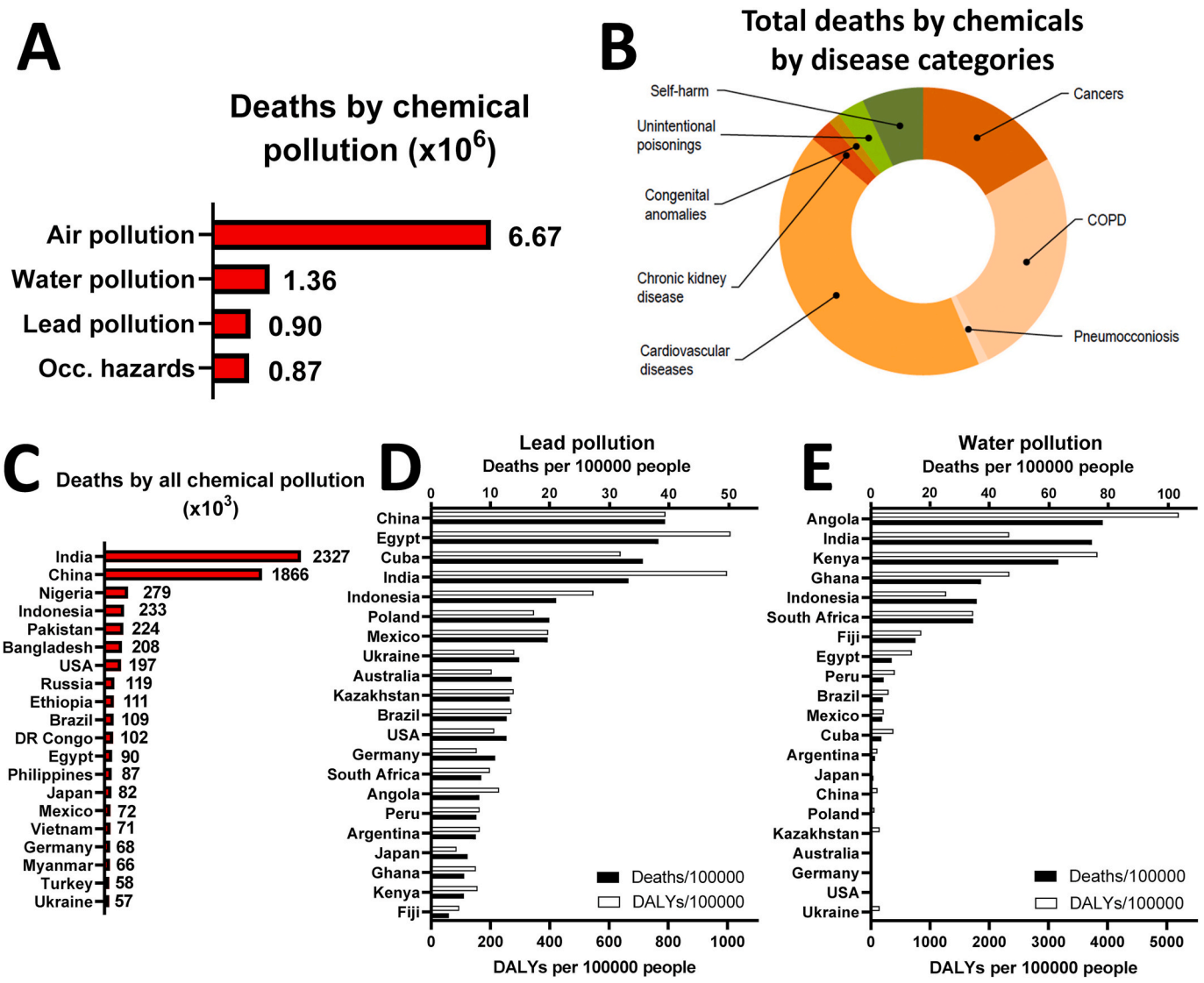


Fig. 2. Impact of chemical pollution from various sources on the global burden of premature deaths. Estimated global annual deaths by all sources of chemical pollution (A) [3] and the disease entities being associated with these deaths (B) [149]. (C) Deaths by all chemical pollution – ranking by top 20 countries [15]. Population-related rates of death and disability-adjusted life years (DALYs) for lead pollution as a typical soil pollutant (D) and water pollution (unsafe water source including chemical hazards) (E), listed for 20 representative countries of different WHO regions [150]. Presented graph was redrawn from Ref. [5] with permission.

family present in water are estrogen and its derivatives, most notably estrone, which have been associate with breast cancer [32] and disruption in energy balance, leading to obesity [33].

2.3. *Cardiovascular side effects of chemicals*

An extensive body of evidence links soil and water pollutants to cardiovascular outcomes. Lead exposure, even at low concentrations, is a well-established cause of hypertension and elevated cardiovascular mortality [34,35]. Cadmium exposure is associated with coronary artery disease, atherosclerosis, and heart failure [36,37]. Cadmium is even considered a risk factor of early atherosclerotic processes, based on pathophysiological processes such as damage of vascular cells, impaired endothelial function, and oxidative stress [38]. Methylmercury contributes to carotid atherosclerosis and increased risk of myocardial infarction [39], whereas copper promotes atherosclerotic processes by cuproptosis [40] or accumulation of copper in leukocytes [41]. Also an association between lead levels in blood and atherosclerosis in the carotid arteries was reported for a Swedish population-based cohort [42]. This was also confirmed by a US population-based study reporting an association of higher blood lead and cadmium levels with an increased risk of atherosclerotic cardiovascular disease among white adults [43]. Arsenic exposure was associated with adverse changes of the carotid intima-media thickness in humans, another accepted surrogate of early atherosclerosis and predictor of future ischemic heart disease [44,45]. Preclinical data support these human findings. Apolipoprotein E knockout mice develop more pronounced plaques in the aortic intima when exposed to arsenic [46,47] as well as cadmium [48]. Similarly, mercury exposure exacerbated markers of atherosclerosis in low-density lipoprotein receptor knockout mice [49]. This is due to higher levels of pro-inflammatory chemokines, cytokines, and markers of oxidative stress, all representing known drivers of atherogenesis [10].

Endocrine disruptors such as BPA and PFAS further exacerbate cardiovascular risks. Urinary BPA concentrations are consistently associated with higher CVD prevalence, hypertension, and congestive heart failure [50,51]. Acute organophosphate poisoning can trigger severe cardiac complications, including arrhythmias and QT prolongation [52]. There are also indications that BPA is associated with subclinical

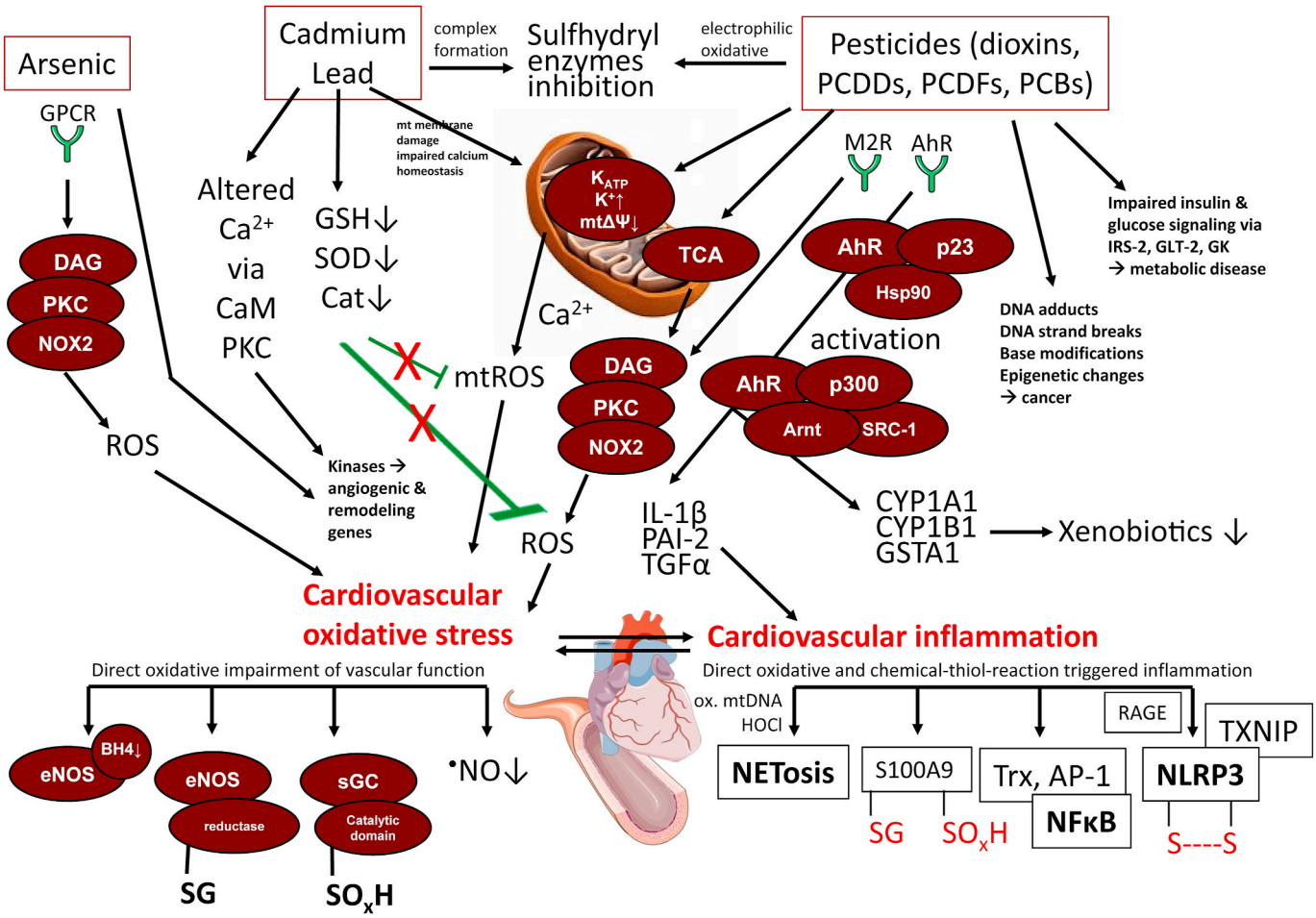


Fig. 3. Cellular pathophysiology of metals/metalloids and pesticides. Provides details and an explanation of the abbreviations in the text. Pathomechanisms summarized from Ref. [24] for arsenic, for lead [21], for cadmium [20,22] for pesticides. Oxidative mechanisms of endothelial/vascular dysfunction summarized from Ref. [25]. Activating redox mechanisms for inflammation summarized from Ref. [26]. Other pathomechanisms summarized from Ref. [10] for heavy metals and [19] pesticides or other endocrine-disrupting chemicals. GPCR, G-protein-coupled receptor; DAG, diacylglycerol; PKC, protein kinase C; ROS, reactive oxygen species; NOX2, phagocytic NADPH oxidase isoform 2; CaM, calmodulin; GSH, reduced glutathione; SOD, superoxide dismutase; Cat, catalase; mtROS, mitochondrial ROS; eNOS, endothelial nitric oxide synthase; BH4, tetrahydrobiopterin; sGC, soluble guanylate cyclase; NO, nitric oxide; K_{ATP}, ATP-sensitive potassium channel; mtΔΨ, mitochondrial membrane potential gradient; TCA, tricarboxylic acid cycle; PCDDs, polychlorinated dibenzodioxins; PCDFs, polychlorinated dibenzofurans; PCBs, polychlorinated biphenyls; M2R, muscarinic receptor type 2; AhR, aryl hydrocarbon receptor; p23, co-chaperone of AhR; HSP90, heat shock protein 90; p300, regulator of AhR; ARNT, aryl hydrocarbon receptor nuclear translocator protein; SRC1, nuclear receptor coactivator of AhR; IL-1β, interleukin 1β; PAI2, plasminogen activator inhibitor 2; TGF, transforming growth factor; CYP, cytochrome P450; GSTA1, glutathione S-transferase α1; IRS2, insulin receptor substrate 2; GK, glucokinase; GLT2, glucose transporter 2; HOCl, hypochlorite; ox. mtDNA, free oxidized mitochondrial DNA; NETosis, neutrophil extracellular trap activation and release; S100A9, S100 calcium binding protein A9; TRX, thioredoxin; AP1, activator protein 1; NFkB, nuclear factor k light chain enhancer of activated B cells; RAGE, receptor of advanced glycation end products; TXNIP, thioredoxin-interacting protein; NLRP3, NOD-like receptor family pyrin domain-containing 3 (component of the inflammasome); -SG, S-glutathionylation; -SO_xH, sulfoxidation; -S-S-, disulfide bridge. Presented graph was redrawn from Ref. [5] with permission.

atherosclerosis via apoptotic microparticles [53]. Also PFAS were reported to cause dysregulation of lipid metabolism and accordingly may contribute to atherogenesis [54]. In general, endocrine-disrupting persistent chemicals such as pesticides, dioxins and plastic-associated compounds seem to have the potential to promote atherosclerotic processes by their common pathophysiological mechanisms [55,56]. This evidence is also supported by studies in apolipoprotein knockout mice showing enhanced atherosclerosis in response to dioxins [57], pesticide [58], BPA [59].

3. Micro- and nanoplastics (MNPs)

Global plastic production has surged from 2 million tons in 1950 to over 460 million tons 2019, with plastic waste projected to triple from 2019 to 1231 Mt in 2060 [60]. While macroplastics dominate visible pollution, microplastics (≤5 mm) and nanoplastics (≤1000 nm) result from the environmental breakdown of plastic waste, contaminating soil, water, and marine ecosystems [60]. While macroplastics dominate visible pollution, microplastics (≤5 mm) and nanoplastics (≤1000 nm) result from the environmental breakdown of plastic waste, contaminating soil, water, and marine ecosystems [61]. Microplastics are particular concern due to human exposure seafood consumption and inhalation. Additives such as phthalates, bisphenols, flame retardants, and heavy metals leach into tissues, acting as carcinogens, endocrine disruptors, and neurotoxicants [62].

3.1. Toxicity: cellular effects

High concentrations of micro- and nanoplastics (MNPs) exhibit cytotoxic effects, inducing cell death through necrosis or programmed pathways (Fig. 5) [63]. Surfactants present in MNP preparations compromise the integrity of the plasma membrane and surface structures, disrupting cellular signaling and overall physiology. Small nanoparticles (NPs) are internalized via endocytosis [64,65], which can pose

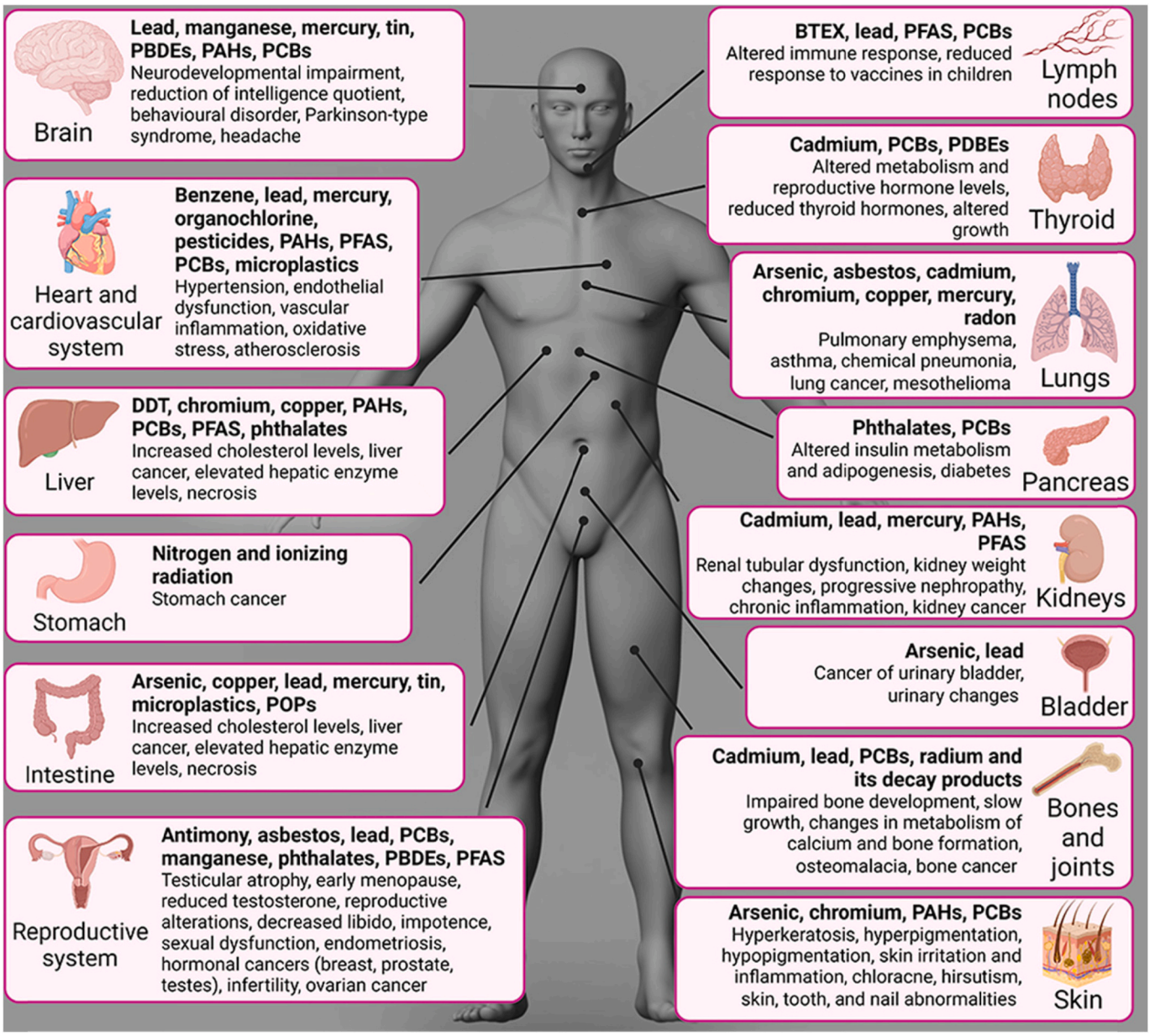
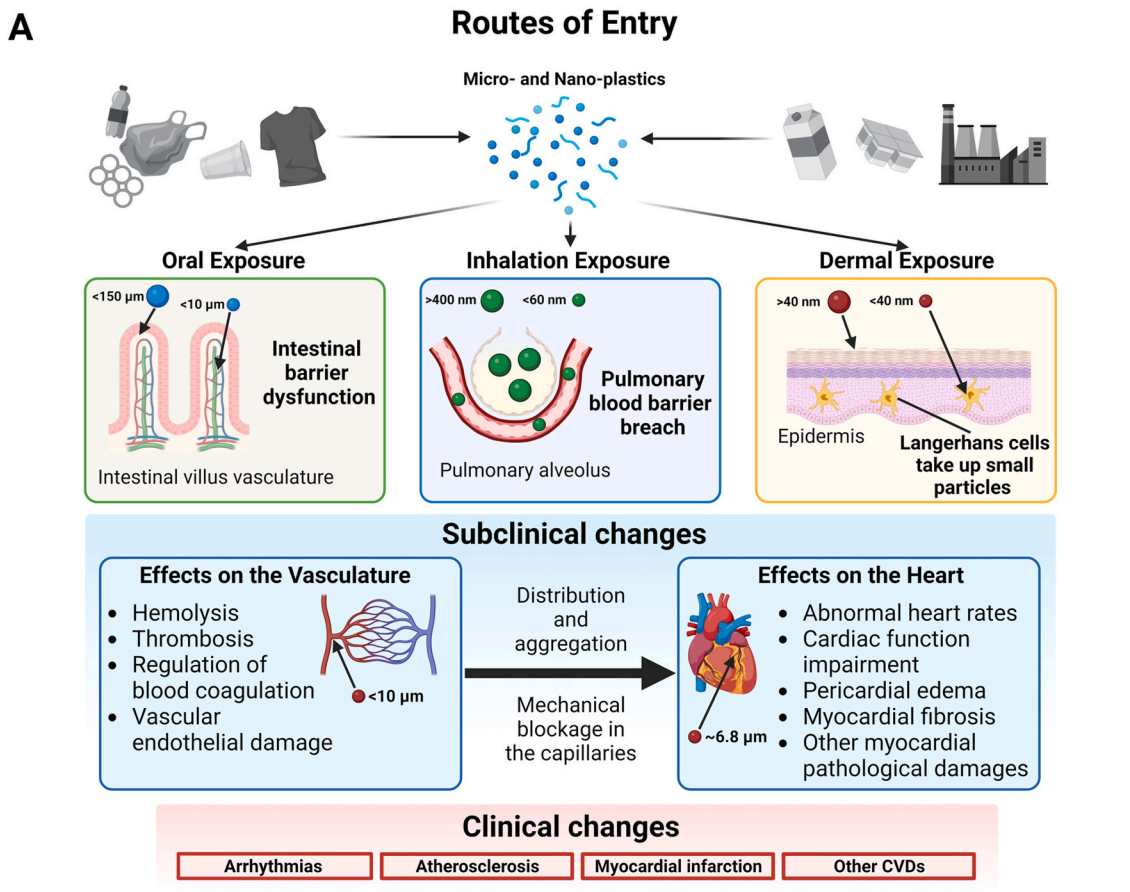


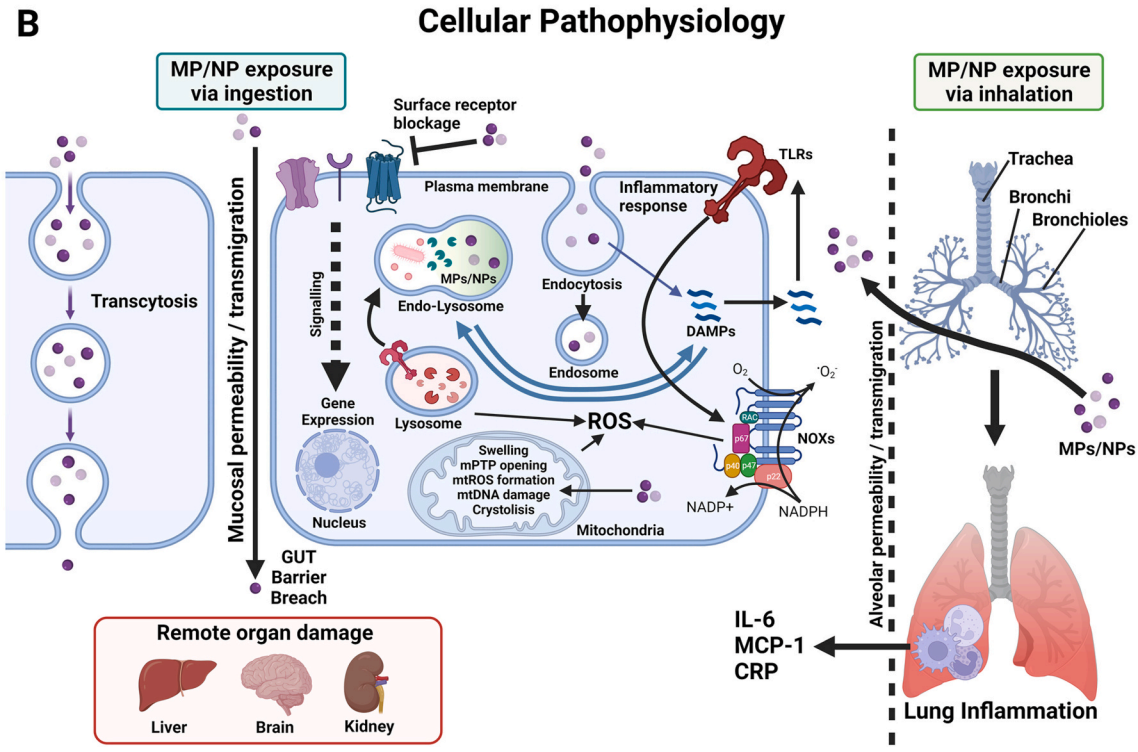
Fig. 4. Main effects of soil contaminants on human health, indicating the organs or systems affected and the contaminants causing them. PCBs, polychlorinated biphenyls; PBDEs, polybrominated diphenyl ethers; PFAS, per- and polyfluoroalkyl substances; POPs, persistent organic pollutants; BTEX, refers to the chemicals benzene, toluene, ethylbenzene, and xylene. Adapted from the report of the Food and Agriculture Organization of the United Nations (created from data in the Agency for Toxic Substances and Disease Registry [151] and Campanale et al. [152]), https://www. fao.org/3/cb4894en/online/src/html/chapter-04-3.html. Presented graph was redrawn from Ref. [5] with permission.

significant risks. At elevated concentrations, NPs may permeabilize endosomal membranes, inflicting damage on organelles such as mitochondria and interfering with cell division processes. Furthermore, MNPs impair cellular transport mechanisms [66,67], affecting protein turnover and key signaling pathways. Their accumulation within endosomes or lysosomes hinders macroautophagy [68], potentially leading to autophagic cell death, although in some contexts, they may stimulate autophagy [69].

As observed in Daphnia species, cellular stress induced by MNPs is a common outcome that triggers adaptive responses such as activating AMP-activated protein kinase (AMPK) [70,71]. A central component of this stress response is the overproduction of reactive oxygen species (ROS) [72], which often stems from mitochondrial dysfunction or the activity of NADPH oxidases [73]. These enzymes play a critical role in pathological conditions such as diabetes, hypertension, hypercholesterolemia, and heart failure.

A recent study has also focused on the effects of ultraviolet light on aged plastic bowls and the impact of exposure to them on the behavior and neurotoxicity of *Caenorhabditis elegans* (*C. elgans*) [74]. Changes in the composition and structure of aged plastic bowls and increased free radicals and reactive oxygen species were observed. Exposure to aged plastic bowls led to more significant neurotoxicity in worms than exposure to new plastic bowls, resulting in changes in their behavior and neuronal damage. The study also found a decrease in neurotransmitter levels and the expression of related genes, with a strong correlation between gene expression and behavior. Mutant worms lacking specific genes showed a lack of movement, highlighting the importance of these genes in mediating neurotoxicity. Overall, this research highlights the aging process and increased toxicity of aged plastic bowls, revealing the mechanisms behind their neurotoxic effects.





(caption on next page)

Fig. 5. Major routes of entry, adverse cardiovascular health effects and cellular mechanisms of pathophysiology of nano- and microplastic particles. A: The exposure routes, toxicological, subclinical, and clinical effects of MNPs on the cardiovascular system. B: Scheme of pathomechanisms of micro- and nanoplastics (MP/NP) toxicity (combination of experimentally confirmed pathomechanisms of MP/NP and anticipated processes established for airborne ultrafine and fine particulate matter particles). MPs/NPs uptake is mainly based on ingestion and inhalation. MPs/NPs can, on the one hand, increase mucosal and alveolar permeability, allowing transmigration of the particles (e.g. via gut barrier breach or transcytosis). On the other hand, severe lung inflammation caused by MP/NP interaction with phagocytic cells will cause the release of inflammatory cytokines such as IL-6, MCP-1, and CRP into the circulation. Once reaching the circulation and end organs, MPs/NPs can impair signaling via cell surface receptors and thereby cause changes in nuclear gene expression. Endocytosis of MPs/NPs will lead to the formation of endolysosomes, the release of damage-associated molecular patterns (DAMPs) and activation of Toll-like receptor (TLR)-mediated inflammatory signalling and oxidative stress. NPs can also directly penetrate mitochondria and cause multiple functional damages via swelling, cristolysis, opening of the mitochondrial permeability transition pore (mPTP), mitochondrial DNA (mtDNA) damage, and mitochondrial reactive oxygen species formation. Oxidative stress may arise from the NADPH oxidases (NOXs) and damaged mitochondria. Redrawn and modified from Yong et al. [63] with permission. Presented graph was redrawn from Ref. [5] with permission using biorender.com.

Microplastics are considered emerging contaminants commonly found to be charged in the environment, potentially causing harm to various organisms. However, the effects of polystyrene (PS), specifically carboxyl-modified PS (PS-COOH) and amino-modified PS (PS-NH2), on transgenerational reproductive toxicity and the mechanisms involved are not well understood.

In another study, *C. elegans* were exposed to environmentally relevant concentrations (0.1–100 μg/L) of PS, PS-COOH, and PS-NH2 in the parental generation (P0), with subsequent generations (F1-F4) raised under standard conditions [75]. Exposure to PS-NH2 at 10–100 μg/L resulted in more significant reproductive toxicity than PS or PS-COOH, reducing brood size, egg ejection rate, number of fertilized eggs, and cell corpses per gonad. Maternal exposure to 100 μg/L of PS-NH2 also caused more severe transgenerational reproductive effects in C. elegans. Increased levels of H3 on lysine 4 dimethylation (H3K4me2) and H3 on lysine 9 trimethylation (H3K9me3) were observed in the subsequent generation, along with the upregulation of set-30 and met-2 following exposure to PS, PS-COOH, and PS-NH2. Molecular docking studies suggested that PS-NH2 had a higher affinity for SET-30 and MET-2. Further analysis showed that transgenerational effects on reproduction were absent in set-30(gk315) and met-2(n4256) mutants, highlighting the importance of these genes in mediating the transgenerational impact [75].

The innate immune system is also highly responsive to MNP exposure. Toll-like receptors (TLRs), which detect endogenous molecules known as alarmins or damage-associated molecular patterns (DAMPs) [76], are activated by MNP-induced stress. This activation can result in *sterile inflammation*—an inflammatory response without microbial infection [77]. The resulting pro-inflammatory cytokines recruit circulating immune cells to the affected sites, intensifying localized inflammation and promoting tissue damage or cell death. Polystyrene nanoplastics interfere with lipid metabolism of murine and human macrophages increasing their pro-atherogenic potential [78]. In line with this, nano- and microplastics were also shown to activate vascular smooth muscle cells supporting their role in increased proliferation and formation of atherosclerotic lesions [79,80]. Administration of polystyrene particles to apolipoprotein knockout mice exacerbated the formation of atherosclerotic lesions [81,82].

Evidence from aquatic models, such as fish, indicates that NPs significantly stress the innate immune system [83]. Similar responses likely occur in mammalian cells, including those of humans, further underscoring the systemic risks associated with MNP exposure.

3.2. Ingestion and cardiovascular effects

Plastic waste undergoes mechanical and photochemical degradation in water and soil, breaking down into smaller, biologically active micro- and nanoparticles (MNPs). Approximately 50 % of the weight of manufactured plastics consists of chemical additives, including phthalates, bisphenols, flame retardants, PFAS, PCBs, and heavy metals (see paragraph on Chemical Pollution). These compounds impart desirable properties such as flexibility, flame resistance, and water repellency but include substances known to be carcinogenic, neurotoxic, and endocrine disrupting. Due to their loose integration within the plastic matrix, these additives can leach from plastic microparticles into the environment and human tissues with the highest concentrations found in the lungs, small and large intestine [84]. While research on MNPs is still in its early stage, high-quality studies have demonstrated their uptake, distribution, and toxic effects in marine organisms such as plankton, mussels, and fish [85,86]. Evidence suggests that humans may be exposed to contaminated seafood, dermal absorption, or inhalation, which has concerning health implications [62,87]. Experimental studies have shown that MNPs induce premature endothelial cell senescence by upregulating key regulators of senescence, such as p53, p21, and p16 [88]. Incubation of isolated pig coronary arteries with MNPs leads to endothelial dysfunction, oxidative stress, and impaired nitric oxide signaling mediated by NADPH oxidase and SIRT pathways (Fig. 5) [88]. In preclinical models, ingesting polystyrene beads promotes fat accumulation and cardiometabolic disease in mice [89]. Furthermore, Wistar rats exhibit oxidative stress-driven heart cell death, pyroptosis mediated via NLRP3/caspase-1 pathways, and cardiac fibrosis through Wnt/β-catenin signaling [90,91]. Further evidence links polystyrene nanoplastics to vascular injury, endothelial cell damage, inflammatory responses, and coagulation dysfunction by activating the JAK1/STAT3/TF pathways [92]. MNPs have been shown to alter heart rate, impair cardiac function, and cause conditions such as myocardial fibrosis and pericardial effusion [5].

A recent study in patients who were undergoing carotid endarterectomy for asymptomatic carotid artery disease has shown that microplastics and nanoplastics accumulate in atheromas and increase the risk of cardiovascular events such as myocardial infarction, stroke, or death from any cause at 34 months of follow-up [93]. Those individuals having higher plastic particle numbers in their plaque material also showed higher levels of inflammatory markers such as interleukin-6, tumor necrosis factor α and CD68. There is emerging evidence for deposits of different plastic particles in various vessel beds [94] and that these microplastics increase the risk of atherosclerotic sequelae in patients with acute coronary syndrome [95].

Additionally, MNPs exert prothrombotic effects and hemolysis [96,97]. Thus, MNPs can infiltrate the circulatory system, compromising cardiac and vascular health through mechanisms that include oxidative stress, inflammation, pyroptosis, and cellular injury. Beyond their intrinsic toxicity, MNPs act as carriers for hazardous chemical additives, amplifying the effects of environmental pollutants. While these findings raise serious concerns, significant gaps remain in understanding the precise cardiovascular risks posed by MNPs in humans, underscoring the need for further research.

4. Soil and water pollution: ecodisruptive causes

4.1. Climate change

The Food and Agriculture Organization (FAO) underscores the soil's critical role as a carbon sink, storing twice the carbon found in the

atmosphere and playing a key role in climate mitigation [98]. Climate change, however, is altering soil conditions globally, with significant impacts in Europe. The European Environment Agency (EEA) highlights declining soil moisture, increasing desertification risks, erosion, and altering coastal soils due to rising sea levels [99]. Ecosystem disruptions also increase the spread of infectious diseases, particularly vector-borne and zoonotic illnesses like Ebola. Rising temperatures pose serious risks to agricultural productivity, with some regions becoming unproductive while others gain new opportunities. A significant concern has been the thawing of permafrost, which releases greenhouse gases, intensifying global warming [100]. Restoration of forests, peatlands, and soil health is crucial for carbon sequestration. Practices such as converting arable land to grasslands or introducing cover crops offer practical, low-cost solutions to enhance soil carbon capture. Climate change also compromises water quality. Warmer temperatures, floods, and droughts exacerbate pollution from sediments, pathogens, and pesticides, while drought conditions contribute to the spread of toxins via wind-borne dust.

Additionally, prolonged droughts and extreme temperatures increase the frequency of wildfires, worsening air quality and cardiovascular risks [101]. Weather extremes accelerate the formation of particulate matter (PM) and ozone (O_3), particularly in urban areas [102]. Wildfires release previously deposited toxic pollutants (e.g., Hg, As, Pb) over vast distances, while non-optimal temperatures account for over 7.6 % of European cardiovascular deaths [103]. Europe, warming faster than the global average, experiences rising heat stress, which worsens cardiovascular and respiratory conditions by increasing heart rate, blood viscosity, and inflammatory responses [104]. Urban heat islands, promoted by urbanization, amplify health risks due to heat absorption by infrastructure and insufficient green spaces. Exposure to heat and air pollutants, such as PM2.5 and ozone, produces synergistic effects, exacerbating mortality in vulnerable populations [104].

According to forecasts, temperature changes during the next century will result in a clear increase of cardiovascular deaths on the US mainland [105]. High ambient temperature is associated with increased risk of stroke at the global level [106]. In summary, non-optimal temperatures are among the leading risk factors mentioned in the Global Burden of Disease report [107] with obviously extreme cold temperatures playing a more important role, which may however change in the future due to global warming [108,109].

4.2. Deforestation

Deforestation, primarily driven by agricultural expansion, logging, mining, and urbanization, profoundly disrupts ecosystems, exacerbates climate change, and endangers wildlife and human communities, particularly indigenous populations in regions like the Amazon and Central Africa. Forests serve as vital carbon sinks, storing substantial amounts of carbon dioxide, and their clearance not only releases greenhouse gases but also reduces the planet's capacity to absorb them [110]. Deforestation further disrupts the hydrological cycle, leading to altered rainfall patterns, droughts, and floods, and accelerates biodiversity loss by destroying habitats essential for countless species and ecosystem services, such as pollination and pest control.

Communities that rely on forests for sustenance, traditional medicine, and cultural practices face significant challenges, including displacement, food insecurity, and loss of livelihoods. While deforestation may offer short-term economic benefits through timber extraction and land for agriculture, these gains are outweighed by long-term environmental and financial costs, including reduced soil fertility, compromised water purification, and diminished tourism potential [111].

In the Amazon, wildfires—exacerbated by deforestation—accelerate biodiversity loss and greenhouse gas emissions, further destabilizing the region's hydrological system. At a critical tipping point of 20–25 % deforestation, the Amazon risks transforming into a savanna-like ecosystem, with profound consequences for agriculture and regional water availability [110].

The health consequences of deforestation are significant. Forest burning releases pollutants that impair air quality, increasing respiratory and cardiovascular diseases. Additionally, deforestation heightens human-wildlife interaction, facilitating the emergence of zoonotic diseases such as Ebola and Lyme disease and altering the distribution of vector-borne illnesses like malaria and dengue fever [112].

4.3. Overfertilization

Human activity has profoundly disrupted the global nitrogen cycle due to fossil fuel combustion, industrial food production, and fertilizer use to support a growing population [113,114]. While molecular nitrogen (N_2) is abundant in the atmosphere and essentially inert, it becomes reactive as nitrogen oxides (NO and NO_2) through natural processes such as lightning or microbial nitrogen fixation in soils. However, the excessive use of fertilizers (via the Haber-Bosch process), intensive livestock farming, and combustion processes have overwhelmed natural nitrogen cycles.

Excess nitrogen contributes to acidification, water contamination, and air quality degradation while releasing nitrous oxide (N_2O), a potent greenhouse gas, exacerbating climate change and depleting stratospheric ozone [115]. Overfertilization also increases atmospheric ammonia (NH_3), which reacts with sulfur and nitrogen oxides—particularly from fossil fuel combustion—to form PM2.5. In highly polluted areas, such as East Asia, parts of Europe, and the USA, ammonia-driven PM2.5 formation is a significant health concern, contributing to 20–40 % of pollution-attributable mortality [116,117]. Approximately 50 % of deaths from air pollution are linked to strokes and ischemic heart disease, underscoring overfertilization's role in CVD outcomes [118].

Studies have demonstrated the cardiovascular impact of exposure to nitrogen oxides. Elevated serum nitrite and nitrate (NOx) levels are associated with increased CVD mortality. For instance, Gumanova et al. linked NOx exposure to higher mortality rates [119], while Bahadoran et al. reported a hazard ratio (HR) of 1.98 for CVD mortality when serum NOx levels exceeded 30.5–32.5 μmol/L [120]. These findings emphasize the significant health risks posed by overfertilization and nitrogen pollution.

4.4. Airborne dust

Airborne dust, often overlooked as a health hazard, arises from soil disturbance through agriculture, unpaved roads, construction, and natural wind erosion from deserts (aeolian dust). The "dust belt" stretching from North Africa to South and Central Asia is the largest global source, accounting for 30–50 % of atmospheric aerosols [121]. Although abundant dust settles near its origin, extended plumes can travel thousands of kilometers, carrying pollutants that enhance their harmfulness [122].

While aeolian dust is considered "natural," it has a significant anthropogenic component, as atmospheric pollutants interact with dust particles during transport, increasing their oxidative potential. This process mobilizes metals and other toxic compounds, worsening the health risks [123]. Toxicological studies demonstrate that inhaled dust induces oxidative stress, inflammation, and respiratory and cardiovascular system damage [124]. Smaller dust particles can enter the bloodstream, exacerbating cardiovascular diseases and immune responses [125,126].

Epidemiological studies link desert dust exposure to increased respiratory and cardiovascular mortality risks. For instance, Asian dust events have been associated with acute myocardial infarction [127]. A meta-analysis showed a 2 % rise in cardiovascular mortality per 10 $\mu g/m^3$ of PM10-dust exposure, with lingering effects up to two days post-exposure [126]. As climate change accelerates As climate change accelerates drought conditions, desertification and extreme weather,

airborne dust is projected to become a growing component of air quality degradation, warranting further investigation and mitigation.

4.5. Unhealthy city design

Urbanization, especially in low- and middle-income countries (LMICs), is pivotal in tackling pollution and preventing global CVD. By 2050, urban areas will accommodate 68 % of the worldwide population, with 83 % of this growth concentrated in LMICs [128]. While urban living provides benefits such as improved access to healthcare and services [129], it also intensifies exposure to environmental pollutants in soil, water, and air due to industrial activity, traffic emissions, and inadequate waste management [10,130]. Poorly designed cities with high motorized traffic, particularly those lacking green spaces, exacerbate air and soil pollution. Dense urban areas with high traffic volumes release high amounts of nitrogen dioxide, sulfur dioxide, and particulate matter, which are linked to respiratory diseases, cancer, and CVD [2,3]. Limited vegetation intensifies these effects as trees and plants are absent to filter pollutants, absorb CO_2, and improve air quality [131,132]. Additionally, industrial zones can contaminate soil with heavy metals and hazardous chemicals, which, in turn, may leach into groundwater and/or enter the food chain [133].

Urban landscapes dominated by concrete and asphalt enhance the urban heat island effect, where elevated temperatures exacerbate heat-related illnesses and mortality, particularly among vulnerable populations such as the elderly or those with pre-existing health conditions [132].

Sedentary lifestyles, encouraged by car-centric city designs, further amplify risks of obesity, diabetes, and cardiovascular disease [134]. Urban runoff, carrying pollutants from roads and buildings, contaminates water systems. Persistent chemicals like PFAS and microplastics from tire wear present emerging health challenges [4]. Noise, overcrowding, and limited access to natural spaces heighten stress, adversely affecting mental health [135].

To address these issues, policymakers and urban planners increasingly prioritise sustainable and health-conscious city designs. Strategies include expanding green spaces [131], improving public transport, promoting pedestrian and cycling infrastructure, reducing space for motorized traffic, and enforcing stricter pollution controls [136].

5. Mitigation measures

Reducing soil and water pollution is strongly linked with substantial cardiovascular health benefits. Primary strategies include limiting chemical exposure through water filtration, air purification, avoiding contaminated foods and products, and smoking cessation, aligning with the European Commission's zero-pollution vision and EU Action Plan for 2050 [137]. Public health measures to reduce lead and cadmium exposure have demonstrated success. In the United States, reductions in blood lead and cadmium levels accounted for 22.5 % (52 deaths per 100,000 person-years) and 8.4 % (19.4 deaths per 100,000 person-years) of the decline in cardiovascular mortality from 1988 to 2004 [138]. Similar efforts for arsenic exposure remain limited. Fine particulate matter (PM2.5), containing metals like lead, cadmium, and arsenic, significantly contributes to soil and water pollution and cardiovascular risk. PM2.5 derived from fossil fuel combustion increases CVD incidence, while eliminating fossil fuels could prevent up to 5.1 million deaths annually [6]. Stricter pollution controls, air filtration systems, and the Clean Air Act have successfully reduced cardiovascular morbidity in the United States [139]. Chelating agents like EDTA and succimer effectively remove heavy metals from the body. The NIH-funded TACT trial found a 39 % reduction in cardiovascular events among diabetic participants receiving EDTA-based therapy [140]. Further studies, including TACT2, aim to validate these findings and measure metal biomarkers.

Dietary and lifestyle interventions, such as the Mediterranean diet, omega-3 fatty acids, and flavonoids (e.g., cacao), offer protective cardiovascular effects against chemical pollution [141]. Antioxidants like N-acetylcysteine can counter oxidative stress-induced damage, while blood donation and cholestyramine can reduce circulating chemical contaminants [142,143]. Although evidence linking reduced pesticide exposure to cardiovascular outcomes remains limited, these mitigation strategies underscore the need for further research to combat pollution-driven health impacts effectively.

6. Summary and outlook

Soil and water pollution from deforestation, overfertilization, plastics, pesticides, and the release of toxic chemicals significantly reduce biodiversity, threaten ecosystem sustainability, and endanger human health [5,13]. Soil pollution diminishes the quantity of beneficial microorganisms through toxic chemicals and contaminates groundwater, undermining food production and ecosystem balance. These environmental challenges—climate change, air and water pollution, and species extinction—pose severe risks to societal sustainability, driven by short-sighted economic practices and disregard for natural systems. Contaminated soil contributes to non-communicable diseases, particularly cardiovascular disease. Exposure to plastics, heavy metals, pesticides, and toxic agents induces oxidative stress, inflammation, disruption of circadian rhythms, and endothelial dysfunction, central mechanisms in disease development (see Graphical Abstract for summary). Nano/microplastic and chemical pollutants can synergize with other health-risk factors, exacerbating the burden of non-communicable diseases. Urban environments, with their high concentrations of air pollution, noise, light, and psychosocial stress, compound these risks, creating an underestimated disease burden. Urgent action is required, and health professionals, including physicians, must assume a leading role.

Pollution drives cardiovascular diseases, cancer, stroke, chronic obstructive pulmonary disease, and neurological disorders (e.g. dementia as a high cost case), yet it remains preventable. Pollution is not an inevitable byproduct of economic development. High-income countries have demonstrated that cost-effective, replicable solutions can control major pollution problems.

Nevertheless, pollution caused at least nine million premature deaths globally in 2015 [3]. In the EU, pollution accounts for one in eight deaths, primarily due to cardiovascular disease, including coronary syndromes, stroke, hypertension, and diabetes [144]. The European Commission's Zero-Pollution Vision and Action Plan for 2050 [137] aims to reduce pollution to levels safe for health and ecosystems, ensuring a cleaner, healthier environment for future generations. Concerning specifically polluted soil, the "EU Mission: A Soil Deal for Europe" includes specific aims such as reducing desertification, conserving soil organic carbon stocks, stopping soil sealing and increasing re-use of urban soils. The Mission also aims to reduce soil pollution and enhance restoration, prevent erosion, improve soil structure to enhance soil biodiversity, reduce the EU global footprint on soils and to improve soil literacy in society [145].

Author contributions

All authors were involved in writing the original manuscript and also critically revised it before submission.

Financial support

T.M. is PI of the German Cardiovascular Research Center (DZHK), Partner Site Rhine-Main, Mainz. The collaboration of the authors was funded by the environmental network EXPOHEALTH, funded by the Science Initiative of the state of Rhineland-Palatinate, Germany.

M.K. is supported by the Foundation Heart of Mainz, Germany.

The work on this article is funded by the European Union (Grant

Agreement # 101156161) and the Swiss State Secretariat for Education, Research and Innovation (SERI). Views and opinions expressed are, however, those of the author(s) only and do not necessarily reflect those of the European Union, the European Health and Digital Executive Agency (HADEA) or the SERI. Neither the European Union nor the granting authorities can be held responsible for them.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

[1] UN, Soil pollution a risk to our health and food security. https://www.unep.org/news-and-stories/story/soil-pollution-risk-our-health-and-food-security, 2020.
[2] R. Fuller, et al., Pollution and health: a progress update, Lancet Planet. Health 6 (6) (2022) e535–e547, https://doi.org/10.1016/S2542-5196(22)00090-0.
[3] P.J. Landrigan, et al., The Lancet Commission on pollution and health, Lancet 391 (10119) (2018) 462–512, https://doi.org/10.1016/S0140-6736(17)32345-0.
[4] T. Munzel, O. Hahad, A. Daiber, P.J. Landrigan, Soil and water pollution and human health: what should cardiologists worry about? Cardiovasc. Res. 119 (2) (2023) 440–449, https://doi.org/10.1093/cvr/cvac082.
[5] T. Munzel, et al., Soil and water pollution and cardiovascular disease, Nat. Rev. Cardiol. 22 (2) (2025) 71–89, https://doi.org/10.1038/s41569-024-01068-0.
[6] J. Lelieveld, et al., Air pollution deaths attributable to fossil fuels: observational and modelling study, Br. Med. J. 383 (2023) e077784, https://doi.org/10.1136/bmj-2023-077784.
[7] J. Lelieveld, et al., Cardiovascular disease burden from ambient air pollution in Europe reassessed using novel hazard ratio functions, Eur. Heart J. 40 (20) (2019) 1590–1596, https://doi.org/10.1093/eurheartj/ehz135.
[8] WHO, Global Action Plan for the Prevention and Control of Non- Communicable Diseases 2013–2020. Rep, WHO, Geneva, 2013. https://iris.who.int/bitstream/handle/10665/94384/9789241506236_eng.pdf;jsessionid=71BCEA94B3F85737AB42F3C84216E54A?sequence=1.
[9] H. Frumkin, A. Haines, Global environmental change and Noncommunicable disease risks, Annu. Rev. Publ. Health 40 (2019) 261–282, https://doi.org/10.1146/annurev-publhealth-040218-043706.
[10] K.E. Cosselman, A. Navas-Acien, J.D. Kaufman, Environmental factors in cardiovascular disease, Nat. Rev. Cardiol. 12 (11) (2015) 627–642, https://doi.org/10.1038/nrcardio.2015.152.
[11] T. Munzel, M. Sorensen, O. Hahad, M. Nieuwenhuijsen, A. Daiber, The contribution of the exposome to the burden of cardiovascular disease, Nat. Rev. Cardiol. (2023), https://doi.org/10.1038/s41569-023-00873-3.
[12] T. Munzel, et al., Environmental risk factors and cardiovascular diseases: a comprehensive review, Cardiovasc. Res. (2021), https://doi.org/10.1093/cvr/cvab316.
[13] U. Sagheer, et al., Environmental pollution and cardiovascular disease: Part 2 of 2: soil, water, and other forms of pollution, JACC Adv 3 (2) (2024) 100815, https://doi.org/10.1016/j.jacadv.2023.100815.
[14] M. Scimeca, et al., Impact of the environmental pollution on cardiovascular diseases: from epidemiological to molecular evidence, Heliyon 10 (18) (2024) e38047, https://doi.org/10.1016/j.heliyon.2024.e38047.
[15] GAHP, Report by the Global Alliance on Health and Pollution, Pollution and health metrics. https://gahp.net/wp-content/uploads/2019/12/PollutionandHealthMetrics-final-12_18_2019.pdf, 2019. (Accessed 19 December 2023).
[16] WHO. https://www.who.int/publications/i/item/WHO-HEP-ECH-EHD-21.01, 2021.
[17] HBM4EU, The European human biomonitoring initiative. https://www.hbm4eu.eu/, 2016.
[18] CDC, Centers for Disease Control and Prevention (US), National Biomonitoring Survey (2018). https://www.cdc.gov/biomonitoring/index.html. (Accessed 28 December 2023).
[19] Z. Liu, Y. Lu, K. Zhong, C. Wang, X. Xu, The associations between endocrine disrupting chemicals and markers of inflammation and immune responses: a systematic review and meta-analysis, Ecotoxicol. Environ. Saf. 234 (2022) 113382, https://doi.org/10.1016/j.ecoenv.2022.113382.
[20] R.O. Sule, L. Condon, A.V. Gomes, A common feature of pesticides: oxidative stress-the role of oxidative stress in pesticide-induced toxicity, Oxid. Med. Cell. Longev. 2022 (2022) 5563759, https://doi.org/10.1155/2022/5563759.
[21] N. Singh, A. Kumar, V.K. Gupta, B. Sharma, Biochemical and molecular bases of lead-induced toxicity in mammalian systems and possible mitigations, Chem. Res. Toxicol. 31 (10) (2018) 1009–1021, https://doi.org/10.1021/acs.chemrestox.8b00193.
[22] P. Rasin, A. Sreekanth, Cadmium exposure and cardiovascular diseases, Chem. Res. Toxicol. 36 (9) (2023) 1441–1443, https://doi.org/10.1021/acs.chemrestox.3c00184.
[23] M. Farina, M. Aschner, J.B. Rocha, Oxidative stress in MeHg-induced neurotoxicity, Toxicol. Appl. Pharmacol. 256 (3) (2011) 405–417, https://doi.org/10.1016/j.taap.2011.05.001.
[24] D.C. Ellinsworth, Arsenic, reactive oxygen, and endothelial dysfunction, J. Pharmacol. Exp. Therapeut. 353 (3) (2015) 458–464, https://doi.org/10.1124/jpet.115.223289.
[25] A. Daiber, et al., Targeting vascular (endothelial) dysfunction, Br. J. Pharmacol. 174 (12) (2017) 1591–1619, https://doi.org/10.1111/bph.13517.
[26] P. Wenzel, S. Kossmann, T. Munzel, A. Daiber, Redox regulation of cardiovascular inflammation - immunomodulatory function of mitochondrial and Nox-derived reactive oxygen and nitrogen species, Free Radic. Biol. Med. 109 (2017) 48–60, https://doi.org/10.1016/j.freeradbiomed.2017.01.027.
[27] J. Fawell, M.J. Nieuwenhuijsen, Contaminants in drinking water, Br. Med. Bull. 68 (2003) 199–208, https://doi.org/10.1093/bmb/ldg027.
[28] WHO, Mercury and Health, World Health Organization, 2017 [online], https://www.who.int/news-room/fact-sheets/detail/mercury-and-health. (Accessed 22 September 2020).
[29] K. Jomova, et al., Arsenic: toxicity, oxidative stress and human disease, J. Appl. Toxicol. 31 (2) (2011) 95–107, https://doi.org/10.1002/jat.1649.
[30] A.C. Gore, et al., Executive summary to EDC-2: the endocrine society's second scientific statement on endocrine-disrupting chemicals, Endocr. Rev. 36 (6) (2015) 593–602, https://doi.org/10.1210/er.2015-1093.
[31] L.G. Kahn, C. Philippat, S.F. Nakayama, R. Slama, L. Trasande, Endocrine-disrupting chemicals: implications for human health, Lancet Diabetes Endocrinol. 8 (8) (2020) 703–718, https://doi.org/10.1016/S2213-8587(20)30129-7.
[32] M. Cislak, I. Kruszelnicka, J. Zembrzuska, D. Ginter-Kramarczyk, Estrogen pollution of the European aquatic environment: a critical review, Water Res. 229 (2023) 119413, https://doi.org/10.1016/j.watres.2022.119413.
[33] K. Saito, X. Cao, Y. He, Y. Xu, Progress in the molecular understanding of central regulation of body weight by estrogens, Obesity 23 (5) (2015) 919–926, https://doi.org/10.1002/oby.21099.
[34] J. Schwartz, Lead, blood pressure, and cardiovascular disease in men, Arch. Environ. Health 50 (1) (1995) 31–37, https://doi.org/10.1080/00039896.1995.9955010.
[35] B.P. Lanphear, S. Rauch, P. Auinger, R.W. Allen, R.W. Hornung, Low-level lead exposure and mortality in US adults: a population-based cohort study, Lancet Public Health 3 (4) (2018) e177–e184, https://doi.org/10.1016/S2468-2667(18)30025-2.
[36] M. Tellez-Plaza, M.R. Jones, A. Dominguez-Lucas, E. Guallar, A. Navas-Acien, Cadmium exposure and clinical cardiovascular disease: a systematic review, Curr. Atheroscler Rep. 15 (10) (2013) 356, https://doi.org/10.1007/s11883-013-0356-2.
[37] R. Chowdhury, et al., Environmental toxic metal contaminants and risk of cardiovascular disease: systematic review and meta-analysis, Br. Med. J. 362 (2018) k3310, https://doi.org/10.1136/bmj.k3310.
[38] B. Messner, et al., Cadmium is a novel and independent risk factor for early atherosclerosis mechanisms and in vivo relevance, Arterioscler. Thromb. Vasc. Biol. 29 (9) (2009) 1392–1398, https://doi.org/10.1161/ATVBAHA.109.190082.
[39] K.M. Lim, et al., Low-level mercury can enhance procoagulant activity of erythrocytes: a new contributing factor for mercury-related thrombotic disease, Environ. Health Perspect. 118 (7) (2010) 928–935, https://doi.org/10.1289/ehp.0901473.
[40] S. Yang, Y. Li, L. Zhou, X. Wang, L. Liu, M. Wu, Copper homeostasis and cuproptosis in atherosclerosis: metabolism, mechanisms and potential therapeutic strategies, Cell Death Dis. 10 (1) (2024) 25, https://doi.org/10.1038/s41420-023-01796-1.
[41] G.D. Kinsman, A.N. Howard, D.L. Stone, P.A. Mullins, Studies in copper status and atherosclerosis, Biochem. Soc. Trans. 18 (6) (1990) 1186–1188, https://doi.org/10.1042/bst0181186.
[42] C. Guldbrand, et al., Low-level exposure to lead and atherosclerosis in the carotid arteries: results from the Swedish population-based cohort SCAPIS, Environ. Res. 244 (2024) 117900, https://doi.org/10.1016/j.envres.2023.117900.
[43] K. Wang, et al., Association of blood heavy metal exposure with atherosclerotic cardiovascular disease (ASCVD) among white adults: evidence from NHANES 1999-2018, Biol. Trace Elem. Res. 201 (9) (2023) 4321–4333, https://doi.org/10.1007/s12011-022-03537-4.
[44] Y. Chen, et al., Arsenic exposure from drinking water, arsenic methylation capacity, and carotid intima-media thickness in Bangladesh, Am. J. Epidemiol. 178 (3) (2013) 372–381, https://doi.org/10.1093/aje/kwt001.
[45] Y.H. Wang, et al., Effects of arsenic exposure and genetic polymorphisms of p53, glutathione S-transferase M1, T1, and P1 on the risk of carotid atherosclerosis in Taiwan, Atherosclerosis 192 (2) (2007) 305–312, https://doi.org/10.1016/j.atherosclerosis.2006.07.029.
[46] M. Bunderson, D.M. Brooks, D.L. Walker, M.E. Rosenfeld, J.D. Coffin, H.D. Beall, Arsenic exposure exacerbates atherosclerotic plaque formation and increases nitrotyrosine and leukotriene biosynthesis, Toxicol. Appl. Pharmacol. 201 (1) (2004) 32–39, https://doi.org/10.1016/j.taap.2004.04.008.
[47] S. Srivastava, E.N. Vladykovskaya, P. Haberzettl, S.D. Sithu, S.E. D'Souza, J. C. States, Arsenic exacerbates atherosclerotic lesion formation and inflammation in ApoE-/- mice, Toxicol. Appl. Pharmacol. 241 (1) (2009) 90–100, https://doi.org/10.1016/j.taap.2009.08.004.
[48] T.F. Oliveira, et al., Chronic cadmium exposure accelerates the development of atherosclerosis and induces vascular dysfunction in the aorta of ApoE(-/-) mice, Biol. Trace Elem. Res. 187 (1) (2019) 163–171, https://doi.org/10.1007/s12011-018-1359-1.
[49] M.I.C. Queiroz, et al., In vivo chronic exposure to inorganic mercury worsens hypercholesterolemia, oxidative stress and atherosclerosis in the LDL receptor knockout mice, Ecotoxicol. Environ. Saf. 275 (2024) 116254, https://doi.org/10.1016/j.ecoenv.2024.116254.

[50] I.A. Lang, et al., Association of urinary bisphenol A concentration with medical disorders and laboratory abnormalities in adults, JAMA 300 (11) (2008) 1303–1310, https://doi.org/10.1001/jama.300.11.1303.
[51] R. Moreno-Gomez-Toledano, Relationship between emergent BPA-substitutes and renal and cardiovascular diseases in adult population, Environ. Pollut. 313 (2022) 120106, https://doi.org/10.1016/j.envpol.2022.120106.
[52] E. Bar-Meir, et al., Guidelines for treating cardiac manifestations of organophosphates poisoning with special emphasis on long QT and Torsades De Pointes, Crit. Rev. Toxicol. 37 (3) (2007) 279–285, https://doi.org/10.1080/10408440601177855.
[53] P.L. Chu, C.Y. Lin, F.C. Sung, T.C. Su, Apoptotic microparticles mediate the association between bisphenol A and subclinical atherosclerosis in a young population: a population-based study, Ecotoxicol. Environ. Saf. 224 (2021) 112663, https://doi.org/10.1016/j.ecoenv.2021.112663.
[54] C.Y. Lin, S. Huey-Jen Hsu, H.L. Lee, C. Wang, F.C. Sung, T.C. Su, Examining a decade-long trend in exposure to per- and polyfluoroalkyl substances and their correlation with lipid profiles: insights from a prospective cohort study on the young Taiwanese population, Chemosphere 364 (2024) 143072, https://doi.org/10.1016/j.chemosphere.2024.143072.
[55] P.M. Lind, L. Lind, Are persistent organic pollutants linked to lipid abnormalities, atherosclerosis and cardiovascular disease? A review, J Lipid Atheroscler 9 (3) (2020) 334–348, https://doi.org/10.12997/jla.2020.9.3.334.
[56] A.M. Zago, N.M.X. Faria, J.L. Favero, R.D. Meucci, S. Woskie, A.G. Fassa, Pesticide exposure and risk of cardiovascular disease: a systematic review, Glob. Public Health (2020) 1–23, https://doi.org/10.1080/17441692.2020.1808693.
[57] D. Wu, et al., Activation of aryl hydrocarbon receptor induces vascular inflammation and promotes atherosclerosis in apolipoprotein E-/- mice, Arterioscler. Thromb. Vasc. Biol. 31 (6) (2011) 1260–1267, https://doi.org/10.1161/ATVBAHA.110.220202.
[58] C. Jin, et al., Propamocarb exposure has the potential to accelerate the formation of atherosclerosis in both WT and ApoE(-/-) mice accompanied by gut microbiota dysbiosis, Sci. Total Environ. 800 (2021) 149602, https://doi.org/10.1016/j.scitotenv.2021.149602.
[59] Y. Sui, et al., Bisphenol A increases atherosclerosis in pregnane X receptor-humanized ApoE deficient mice, J. Am. Heart Assoc. 3 (2) (2014) e000492, https://doi.org/10.1161/JAHA.113.000492.
[60] OECD, Global plastics outlook. https://www.oecd-ilibrary.org/environment/global-plastics-outlook_aa1edf33-en, 2022.
[61] S.L. Wright, R.C. Thompson, T.S. Galloway, The physical impacts of microplastics on marine organisms: a review, Environ. Pollut. 178 (2013) 483–492, https://doi.org/10.1016/j.envpol.2013.02.031.
[62] Y.L. Wang, Y.H. Lee, I.J. Chiu, Y.F. Lin, H.W. Chiu, Potent impact of plastic nanomaterials and micromaterials on the food chain and human health, Int. J. Mol. Sci. 21 (5) (2020), https://doi.org/10.3390/ijms21051727.
[63] C.Q.Y. Yong, S. Valiyaveettil, B.L. Tang, Toxicity of microplastics and nanoplastics in mammalian systems, Int. J. Environ. Res. Publ. Health 17 (5) (2020), https://doi.org/10.3390/ijerph17051509.
[64] N. Oh, J.H. Park, Endocytosis and exocytosis of nanoparticles in mammalian cells, Int. J. Nanomed. 9 (Suppl 1) (2014) 51–63, https://doi.org/10.2147/IJN.S26592. Suppl 1.
[65] S. Zhang, H. Gao, G. Bao, Physical principles of nanoparticle cellular endocytosis, ACS Nano 9 (9) (2015) 8655–8671, https://doi.org/10.1021/acsnano.5b03184.
[66] H. Horstmann, C.P. Ng, B.L. Tang, W. Hong, Ultrastructural characterization of endoplasmic reticulum–Golgi transport containers (EGTC), J. Cell Sci. 115 (Pt 22) (2002) 4263–4273, https://doi.org/10.1242/jcs.00115.
[67] A. Treyer, M. Pujato, X. Pechuan, A. Musch, Iterative sorting of apical and basolateral cargo in Madin-Darby canine kidney cells, Mol. Biol. Cell 27 (14) (2016) 2259–2271, https://doi.org/10.1091/mbc.E16-02-0096.
[68] S.L. Lim, et al., Targeted metabolomics reveals differential biological effects of nanoplastics and nanoZnO in human lung cells, Nanotoxicology 13 (8) (2019) 1117–1132, https://doi.org/10.1080/17435390.2019.1640913.
[69] M. Cordani, A. Somoza, Targeting autophagy using metallic nanoparticles: a promising strategy for cancer treatment, Cell. Mol. Life Sci. : CM 76 (7) (2019) 1215–1242, https://doi.org/10.1007/s00018-018-2973-y.
[70] E. Besseling, B. Wang, M. Lurling, A.A. Koelmans, Nanoplastic affects growth of S. obliquus and reproduction of D. magna, Environ. Sci. Technol. 48 (20) (2014) 12336–12343, https://doi.org/10.1021/es503001d.
[71] Z. Liu, et al., Age-dependent survival, stress defense, and AMPK in Daphnia pulex after short-term exposure to a polystyrene nanoplastic, Aquat. Toxicol. 204 (2018) 1–8, https://doi.org/10.1016/j.aquatox.2018.08.017.
[72] J. Jeong, J. Choi, Adverse outcome pathways potentially related to hazard identification of microplastics based on toxicity mechanisms, Chemosphere 231 (2019) 249–255, https://doi.org/10.1016/j.chemosphere.2019.05.003.
[73] K. Bedard, K.H. Krause, The NOX family of ROS-generating NADPH oxidases: physiology and pathophysiology, Physiol. Rev. 87 (1) (2007) 245–313, https://doi.org/10.1152/physrev.00044.2005.
[74] L. Li, et al., Neurotoxicity induced by aged microplastics from plastic bowls: abnormal neurotransmission in Caenorhabditis elegans, Sci. Total Environ. 952 (2024) 175939, https://doi.org/10.1016/j.scitotenv.2024.175939.
[75] H. Chen, et al., Transgenerational reproductive toxicity induced by carboxyl and amino charged microplastics at environmental concentrations in Caenorhabditis elegans: involvement of histone methylation, Sci. Total Environ. 949 (2024) 175132, https://doi.org/10.1016/j.scitotenv.2024.175132.
[76] T. Gong, L. Liu, W. Jiang, R. Zhou, DAMP-sensing receptors in sterile inflammation and inflammatory diseases, Nat. Rev. Immunol. 20 (2) (2020) 95–112, https://doi.org/10.1038/s41577-019-0215-7.
[77] H. Shen, D. Kreisel, D.R. Goldstein, Processes of sterile inflammation, J. Immunol. 191 (6) (2013) 2857–2863, https://doi.org/10.4049/jimmunol.1301539.
[78] I. Florance, N. Chandrasekaran, P.M. Gopinath, A. Mukherjee, Exposure to polystyrene nanoplastics impairs lipid metabolism in human and murine macrophages in vitro, Ecotoxicol. Environ. Saf. 238 (2022) 113612, https://doi.org/10.1016/j.ecoenv.2022.113612.
[79] Y. Zhong, et al., Polystyrene nanoplastics accelerate atherosclerosis: unraveling the impact on smooth muscle cells through KIF15-mediated migration, Ecotoxicol. Environ. Saf. 284 (2024) 116983, https://doi.org/10.1016/j.ecoenv.2024.116983.
[80] E. Persiani, et al., Virgin and photo-degraded microplastics induce the activation of human vascular smooth muscle cells, Sci. Rep. 15 (1) (2025) 4263, https://doi.org/10.1038/s41598-025-89006-z.
[81] J. Wen, H. Sun, B. Yang, E. Song, Y. Song, Long-term polystyrene nanoplastic exposure disrupt hepatic lipid metabolism and cause atherosclerosis in ApoE(-/-) mice, J. Hazard Mater. 466 (2024) 133583, https://doi.org/10.1016/j.jhazmat.2024.133583.
[82] J. Zhao, D. Gomes, F. Yuan, J. Feng, X. Zhang, T.E. O'Toole, Oral polystyrene consumption potentiates atherosclerotic lesion formation in ApoE(-/-) mice, Circ. Res. 134 (9) (2024) 1228–1230, https://doi.org/10.1161/CIRCRESAHA.124.324419.
[83] A.C. Greven, et al., Polycarbonate and polystyrene nanoplastic particles act as stressors to the innate immune system of fathead minnow (Pimephales promelas), Environ. Toxicol. Chem. 35 (12) (2016) 3093–3100, https://doi.org/10.1002/etc.3501.
[84] L. Zhu, et al., Tissue accumulation of microplastics and potential health risks in human, Sci. Total Environ. 915 (2024) 170004, https://doi.org/10.1016/j.scitotenv.2024.170004.
[85] C.J. Foley, Z.S. Feiner, T.D. Malinich, T.O. Hook, A meta-analysis of the effects of exposure to microplastics on fish and aquatic invertebrates, Sci. Total Environ. 631–632 (2018) 550–559, https://doi.org/10.1016/j.scitotenv.2018.03.046.
[86] K. Bucci, M. Tulio, C.M. Rochman, What is known and unknown about the effects of plastic pollution: a meta-analysis and systematic review, Ecol. Appl. (2019), https://doi.org/10.1002/eap.2044.
[87] G.E. De-la-Torre, Microplastics: an emerging threat to food security and human health, J. Food Sci. Technol. 57 (5) (2020) 1601–1608, https://doi.org/10.1007/s13197-019-04138-1.
[88] S. Shiwakoti, et al., Effects of polystyrene nanoplastics on endothelium senescence and its underlying mechanism, Environ. Int. 164 (2022) 107248, https://doi.org/10.1016/j.envint.2022.107248.
[89] J. Zhao, et al., Polystyrene bead ingestion promotes adiposity and cardiometabolic disease in mice, Ecotoxicol. Environ. Saf. 232 (2022) 113239, https://doi.org/10.1016/j.ecoenv.2022.113239.
[90] J. Wei, et al., The impact of polystyrene microplastics on cardiomyocytes pyroptosis through NLRP3/Caspase-1 signaling pathway and oxidative stress in Wistar rats, Environ. Toxicol. 36 (5) (2021) 935–944, https://doi.org/10.1002/tox.23095.
[91] Z. Li, et al., Polystyrene microplastics cause cardiac fibrosis by activating Wnt/beta-catenin signaling pathway and promoting cardiomyocyte apoptosis in rats, Environ. Pollut. 265 (Pt A) (2020) 115025, https://doi.org/10.1016/j.envpol.2020.115025.
[92] X. Wang, et al., Nanoplastic-induced vascular endothelial injury and coagulation dysfunction in mice, Sci. Total Environ. 865 (2023) 161271, https://doi.org/10.1016/j.scitotenv.2022.161271.
[93] R. Marfella, et al., Microplastics and nanoplastics in atheromas and cardiovascular events, N. Engl. J. Med. 390 (10) (2024) 900–910, https://doi.org/10.1056/NEJMoa2309822.
[94] S. Liu, et al., Microplastics in three types of human arteries detected by pyrolysis-gas chromatography/mass spectrometry (Py-GC/MS), J. Hazard Mater. 469 (2024) 133855, https://doi.org/10.1016/j.jhazmat.2024.133855.
[95] Y. Yang, et al., Microplastics are associated with elevated atherosclerotic risk and increased vascular complexity in acute coronary syndrome patients, Part. Fibre Toxicol. 21 (1) (2024) 34, https://doi.org/10.1186/s12989-024-00596-4.
[96] X. Zhu, C. Wang, X. Duan, B. Liang, E. Genbo Xu, Z. Huang, Micro- and nanoplastics: a new cardiovascular risk factor? Environ. Int. 171 (2023) 107662 https://doi.org/10.1016/j.envint.2022.107662.
[97] N. Ali, J. Katsouli, E.L. Marczylo, T.W. Gant, S. Wright, J. Bernardino de la Serna, The potential impacts of micro-and-nano plastics on various organ systems in humans, EBioMedicine 99 (2023) 104901, https://doi.org/10.1016/j.ebiom.2023.104901.
[98] FAO, Soil organic carbon, the hidden potential. https://www.fao.org/3/i6937e/i6937e.pdf, 2017.
[99] EEA, Soil moisture deficit. https://www.eea.europa.eu/en/analysis/indicators/soil-moisture-deficit, 2021.
[100] EPA, Climate Change Indicators: the Permafrost, 2021. www.epa.gov/climate-indicators/climate-change-indicators-permafrost#:~:text=Additionally%2C%20organic%20matter%20(like%20the,to%20further%20global%20climate%20change.
[101] IPCC, Intergovernmental Panel on Climate Change, 2019. https://www.ipcc.ch/site/assets/uploads/sites/3/2019/12/SROCC_FullReport_FINAL.pdf.
[102] R.M. Doherty, M.R. Heal, F.M. O'Connor, Climate change impacts on human health over Europe through its effect on air quality, Environ. Health : a global access science source 16 (Suppl 1) (2017) 118, https://doi.org/10.1186/s12940-017-0325-2.

[103] B. Alahmad, et al., Associations between extreme temperatures and cardiovascular cause-specific mortality: results from 27 countries, Circulation 147 (1) (2023) 35–46, https://doi.org/10.1161/CIRCULATIONAHA.122.061832.
[104] WHO, Heat and Health in the WHO European Region: Updated Evidence for Effective Prevention, World Health Organization, Regional Office for Europe, Copenhagen, Denmark, 2021. https://www.eea.europa.eu/publications/beating-cardiovascular-disease/non-optimal-temperatures-climate-change/#fn1.
[105] M. Mazidi, J.R. Speakman, Predicted impact of increasing average ambient temperature over the coming century on mortality from cardiovascular disease and stroke in the USA, Atherosclerosis 313 (2020) 1–7, https://doi.org/10.1016/j.atherosclerosis.2020.08.035.
[106] V.L. Feigin, M.D. Abate, Y.H. Abate, S. Abd ElHafeez, F. Abd-Allah, A. Abdelalim, G.B.D.S.R.F. Collaborators, et al., Global, regional, and national burden of stroke and its risk factors, 1990-2021: a systematic analysis for the Global Burden of Disease Study 2021, Lancet Neurol. 23 (10) (2024) 973–1003, https://doi.org/10.1016/S1474-4422(24)00369-7.
[107] G.B.D.R.F. Collaborators, Global burden of 87 risk factors in 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019, Lancet 396 (10258) (2020) 1223–1249, https://doi.org/10.1016/S0140-6736(20)30752-2.
[108] T. Munzel, M. Sorensen, O. Hahad, M. Nieuwenhuijsen, A. Daiber, The contribution of the exposome to the burden of cardiovascular disease, Nat. Rev. Cardiol. 20 (10) (2023) 651–669, https://doi.org/10.1038/s41569-023-00873-3.
[109] T. Munzel, H. Khraishah, A. Schneider, J. Lelieveld, A. Daiber, S. Rajagopalan, Challenges posed by climate hazards to cardiovascular health and cardiac intensive care: implications for mitigation and adaptation, Eur Heart J Acute Cardiovasc Care 13 (10) (2024) 731–744, https://doi.org/10.1093/ehjacc/zuae113.
[110] UNDRR, Wildfires in Latin America: a preliminary analysis, messages and resources, https://www.undrr.org/publication/wildfires-latin-america-preliminary-analysis-messages-and-resources, 2022.
[111] UN, The global forest goals report. https://www.un.org/esa/forests/wp-content/uploads/2021/08/Global-Forest-Goals-Report-2021.pdf, 2021.
[112] S. Morand, C. Lajaunie, Outbreaks of vector-borne and zoonotic diseases are associated with changes in forest cover and oil palm expansion at global scale, Front. Vet. Sci. 8 (2021) 661063, https://doi.org/10.3389/fvets.2021.661063.
[113] J.N. Galloway, et al., Transformation of the nitrogen cycle: recent trends, questions, and potential solutions, Science 320 (5878) (2008) 889–892, https://doi.org/10.1126/science.1136674.
[114] D. Fowler, et al., The global nitrogen cycle in the twenty-first century, Philos. Trans. R. Soc. Lond. B Biol. Sci. 368 (1621) (2013) 20130164, https://doi.org/10.1098/rstb.2013.0164.
[115] X. Zhang, B.B. Ward, D.M. Sigman, Global nitrogen cycle: critical enzymes, organisms, and processes for nitrogen budgets and dynamics, Chem. Rev. 120 (12) (2020) 5308–5351, https://doi.org/10.1021/acs.chemrev.9b00613.
[116] E.E. McDuffie, et al., Source sector and fuel contributions to ambient PM(2.5) and attributable mortality across multiple spatial scales, Nat. Commun. 12 (1) (2021) 3594, https://doi.org/10.1038/s41467-021-23853-y.
[117] J. Lelieveld, J.S. Evans, M. Fnais, D. Giannadaki, A. Pozzer, The contribution of outdoor air pollution sources to premature mortality on a global scale, Nature 525 (7569) (2015) 367–371, https://doi.org/10.1038/nature15371.
[118] J. Lelieveld, K. Klingmuller, A. Pozzer, R.T. Burnett, A. Haines, V. Ramanathan, Effects of fossil fuel and total anthropogenic emission removal on public health and climate, Proc. Natl. Acad. Sci. U. S. A. 116 (15) (2019) 7192–7197, https://doi.org/10.1073/pnas.1819989116.
[119] N.G. Gumanova, A.D. Deev, W. Zhang, A.Y. Kots, S.A. Shalnova, Serum nitrite and nitrate levels, NOx, can predict cardiovascular mortality in the elderly in a 3-year follow-up study, Biofactors 43 (1) (2017) 82–89, https://doi.org/10.1002/biof.1321.
[120] Z. Bahadoran, P. Mirmiran, Z. Tahmasebinejad, F. Azizi, A. Ghasemi, Serum nitric oxide metabolites and hard clinical endpoints: a population-based prospective study, Scand. Cardiovasc. J. 53 (4) (2019) 176–182, https://doi.org/10.1080/14017431.2019.1618493.
[121] G.P. Prospero Jm, O. Torres, S.E. Nicholson, T.E. Gill, Environmental characterization of global sources of atmospheric soil dust identified with the nimbus 7 total ozone mapping spectrometer (toms) absorbing aerosol product, Rev. Geophys. 40 (1) (2002) 2-1 - 2-31, doi:10.1029/2000RG000095.
[122] K.F. Ho, et al., Contributions of local pollution emissions to particle bioreactivity in downwind cities in China during Asian dust periods, Environ. Pollut. 245 (2019) 675–683, https://doi.org/10.1016/j.envpol.2018.11.035.
[123] Z. Yu, M. Jang, S. Kim, C. Bae, B. Koo, R. Beardsley, J. Park, L.S. Chang, H.C. Lee, Y.-K. Lim, J.H. Cho, Simulating the impact of long-range-transported asian mineral dust on the formation of sulfate and nitrate during the KORUS-AQ campaign, ACS Earth Space Chem 4 (7) (2020) 1039–1049, https://doi.org/10.1021/acsearthspacechem.0c00074.
[124] J.C. Fussell, F.J. Kelly, Mechanisms underlying the health effects of desert sand dust, Environ. Int. 157 (2021) 106790, https://doi.org/10.1016/j.envint.2021.106790.
[125] M.R. Miller, Oxidative stress and the cardiovascular effects of air pollution, Free Radic. Biol. Med. 151 (2020) 69–87, https://doi.org/10.1016/j.freeradbiomed.2020.01.004.
[126] K.S. Lwin, et al., Effects of desert dust and sandstorms on human health: a scoping review, Geohealth 7 (3) (2023) e2022GH000728, https://doi.org/10.1029/2022GH000728.
[127] S. Kojima, et al., Asian dust exposure triggers acute myocardial infarction, Eur. Heart J. 38 (43) (2017) 3202–3208, https://doi.org/10.1093/eurheartj/ehx509.
[128] UN, World population prospects 2019: highlights. https://population.un.org/wpp/Publications/Files/wpp2019_10KeyFindings.pdf, 2019.
[129] C. Dye, Health and urban living, Science 319 (5864) (2008) 766–769, https://doi.org/10.1126/science.1150198.
[130] M. Ezzati, C.J. Webster, Y.G. Doyle, S. Rashid, G. Owusu, G.M. Leung, Cities for global health, Br. Med. J. 363 (2018) k3794, https://doi.org/10.1136/bmj.k3794.
[131] R.F. Hunter, et al., Advancing urban green and blue space contributions to public health, Lancet Public Health 8 (9) (2023) e735–e742, https://doi.org/10.1016/S2468-2667(23)00156-1.
[132] T. Munzel, et al., Heart healthy cities: genetics loads the gun but the environment pulls the trigger, Eur. Heart J. 42 (25) (2021) 2422–2438, https://doi.org/10.1093/eurheartj/ehab235.
[133] J. Baumgartner, M. Brauer, M. Ezzati, The role of cities in reducing the cardiovascular impacts of environmental pollution in low- and middle-income countries, BMC Med. 18 (1) (2020) 39, https://doi.org/10.1186/s12916-020-1499-y.
[134] R. Guthold, G.A. Stevens, L.M. Riley, F.C. Bull, Worldwide trends in insufficient physical activity from 2001 to 2016: a pooled analysis of 358 population-based surveys with 1.9 million participants, Lancet Global Health 6 (10) (2018) e1077–e1086, https://doi.org/10.1016/S2214-109X(18)30357-7.
[135] T. Munzel, M. Sorensen, A. Daiber, Transportation noise pollution and cardiovascular disease, Nat. Rev. Cardiol. 18 (9) (2021) 619–636, https://doi.org/10.1038/s41569-021-00532-5.
[136] M.J. Nieuwenhuijsen, New urban models for more sustainable, liveable and healthier cities post covid19; reducing air pollution, noise and heat island effects and increasing green space and physical activity, Environ. Int. (2021) 106850, https://doi.org/10.1016/j.envint.2021.106850.
[137] EU, Zero pollution action plan towards zero pollution for air, water and soil. https://environment.ec.europa.eu/strategy/zero-pollution-action-plan_en, 2021.
[138] A. Ruiz-Hernandez, et al., Declining exposures to lead and cadmium contribute to explaining the reduction of cardiovascular mortality in the US population, 1988-2004, Int. J. Epidemiol. 46 (6) (2017) 1903–1912, https://doi.org/10.1093/ije/dyx176.
[139] EPA, US Environmental Protection Agency, Office of air and radiation. The benefits and costs of the clean air act from 1990 to 2020. https://www.epa.gov/clean-air-act-overview, 2020. (Accessed 4 January 2024).
[140] G.A. Lamas, et al., Effect of disodium EDTA chelation regimen on cardiovascular events in patients with previous myocardial infarction: the TACT randomized trial, JAMA 309 (12) (2013) 1241–1250, https://doi.org/10.1001/jama.2013.2107.
[141] H. Tong, Dietary and pharmacological intervention to mitigate the cardiopulmonary effects of air pollution toxicity, Biochim. Biophys. Acta 1860 (12) (2016) 2891–2898, https://doi.org/10.1016/j.bbagen.2016.05.014.
[142] S.J. Genuis, Y. Liu, Q.I. Genuis, J.W. Martin, Phlebotomy treatment for elimination of perfluoroalkyl acids in a highly exposed family: a retrospective case-series, PLoS One 9 (12) (2014) e114295, https://doi.org/10.1371/journal.pone.0114295.
[143] S. Kasperczyk, et al., Effect of N-acetylcysteine administration on homocysteine level, oxidative damage to proteins, and levels of iron (Fe) and Fe-related proteins in lead-exposed workers, Toxicol. Ind. Health 32 (9) (2016) 1607–1618, https://doi.org/10.1177/0748233715571152.
[144] EEA, European Environment Agency Report 21/2019, Healthy environment, healthy lives: how the environment influences health and well-being in Europe. https://www.eea.europa.eu/en/analysis/publications/healthy-environment-healthy-lives, 2019.
[145] EU mission: a soil deal for Europe. https://research-and-innovation.ec.europa.eu/funding/funding-opportunities/funding-programmes-and-open-calls/horizon-europe/eu-missions-horizon-europe/soil-deal-europe_en, 2020.
[146] R. Lozano, et al., Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010, Lancet 380 (9859) (2012) 2095–2128, https://doi.org/10.1016/S0140-6736(12)61728-0.
[147] WHO. https://colinmathers.com/wp-content/uploads/2022/05/global-projection-methods-2016-2060-1.pdf, 2022.
[148] WHO, https://www.who.int/data/gho/data/themes/topics/topic-details/GHO/ncd-mortality, In.
[149] WHO, Report by the World health organzation "the public health impact of chemicals: KNOWNS and unKNOWNS", Data addendum for (2019). https://www.who.int/publications/i/item/WHO-HEP-ECH-EHD-21.01. (Accessed 19 December 2023), 2021.
[150] GBD, Tool for access to GBD data, IHME global health data exchange tool. http://ghdx.healthdata.org/gbd-results-tool, 2023. (Accessed 19 December 2023).
[151] Agency for Toxic Substances and Disease Registry, Annual report. https://www.atsdr.cdc.gov/2018atsdrannualreport/index.html, 2018.
[152] C. Campanale, G. Dierkes, C. Massarelli, G. Bagnuolo, V.F. Uricchio, A relevant screening of organic contaminants present on freshwater and pre-production microplastics, Toxics 8 (4) (2020), https://doi.org/10.3390/toxics8040100.