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STATE-OF-THE-ART REVIEW

Environmental Pollution and Cardiovascular Disease

Part 2 of 2: Soil, Water, and Other Forms of Pollution

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ABSTRACT

With a growing body of evidence that now links environmental pollution to adverse cardiovascular disease (CVD) outcomes, pollution has emerged as an important risk factor for CVD. There is thus an urgent need to better understand the role of pollution in CVD, key pathophysiological mechanisms, and to raise awareness among health care providers, the scientific community, the general population, and regulatory authorities about the CV impact of pollution and strategies to reduce it. This article is part 2 of a 2-part state-of-the-art review on the topic of pollution and CVD—herein we discuss major environmental pollutants and their effects on CVD, highlighting pathophysiological mechanisms, and strategies to reduce CVD risk. (JACC Adv 2024;3:100815) © 2024 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

A global expansion of industrialization, rapid urban growth, and continued reliance on fossil fuels have led to a 65% rise in environmental pollution levels over the past 20 years, making it a leading risk factor for early mortality, responsible for 1 in every 6 global deaths.[1] Though the adverse effects of air pollution on cardiovascular diseases (CVDs) have recently been well appreciated, the impact of other environmental pollutants, such as contaminated water and soil, is often overlooked. The relationship between various pollutants and CVD is complex, often additive, and demonstrates regional variations that are influenced by industrial activity, community dynamics, and governance structures. Pollution is a global and widespread health challenge and its mitigation requires a multifaceted approach encompassing social, economic, legislative, and engineering solutions, in addition to lifestyle practices. Major worldwide guidelines for preventing CVD have focused on modifiable behavioral and metabolic risk factors, but environmental pollution has not been adequately highlighted up until recently. Recognizing and rectifying this gap by incorporating pollution-reduction measures in CVD

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ABBREVIATIONS AND ACRONYMS

BPA = bisphenol A

CAD = coronary artery disease

CIMT = carotid intima-media thickness

CVD = cardiovascular disease

DM = diabetes mellitus

HF = heart failure

HTN = hypertension

MetS = metabolic syndrome

MI = myocardial infarction

PCB = polychlorinated biphenyl

POP = persistent organic pollutant

RR = risk ratio

TCDD = 2,3,7,8-tetrachlorodibenzo-p-dioxin

prevention could notably enhance global CV outcomes.

In this second part of our 2-part review series, we discuss the epidemiological evidence regarding key critical environmental pollutants and CVD, such as water, soil, light, noise, pesticide, and metallic pollutants, among others. We also highlight strategies to mitigate CV risks stemming from these pollutants to improve health outcomes.

SOIL AND WATER POLLUTION. Soil and water pollution refers to harmful substances in the ground and water that can adversely affect living organisms. The main sources of pollutants are agriculture practices, industrial activities, and waste disposal. It can harm aquatic life, reduce crop yields, and impact human health. The Global Burden of Disease 2019 study estimated that 1.23 million deaths were attributable to water pollution due to unsafe water sources.[1] Common pollutants include heavy metals, pesticides, plastic waste, and persistent organic pollutants (POPs) (Table 1).

Plastics. Plastics are organic or synthetic polymers with desirable properties such as durability, flexibility, and low production costs that have led to high global demand. Unfortunately, roughly 7 billion of the 9.2 billion tons of plastic produced between 1950 and 2017 ended up as waste.[2] Plastic additives such as phthalates, bisphenols, and heavy metals also contribute to environmental pollution. Plastics have long degradation times, and their mechanical and photochemical degradation causes the release of highly toxic compounds such as POPs and leaching out of chemical additives such as plasticizers.[3] Microplastics and nanoplastics are emerging contaminants. Although there is limited information on their potential impact on human health, there is substantial evidence for the adverse CV effects of phthalates and synthetic chemicals such as bisphenol A (BPA). Microplastics, on the other hand, can stay in the body for extended periods, even decades, and with the production of plastics expected to double by 2040, there is an urgent need to determine their potentially harmful effects.

Phthalates are widely used in food packaging, medical devices, and household and personal care products. An emerging body of evidence suggests a potential link between phthalates and CVD, particularly coronary artery disease (CAD).[4] Elevated phthalate levels are associated with an increased carotid intima-media thickness (CIMT), atherosclerotic plaques, and higher levels of inflammatory and coagulation markers.[5] Higher phthalate levels are also linked to an increased risk of hypertension (HTN) and a greater likelihood of developing metabolic syndrome (MetS), oxidative stress, and insulin resistance. Supplemental Table 1 summarizes the major studies on the association between phthalates and CVD.

BPA is extensively used in the manufacturing of polycarbonate plastics and epoxy resins.[6] Several epidemiological studies, mostly from the National Health and Nutrition Examination Survey data set, have shown a significant association between BPA exposure and increased CVD risk, especially CAD and heart failure (HF).[7] A meta-analysis of 22,878 participants from 2013 to 2016 found an increased incidence of CVD associated with BPA exposure, with an OR of 1.13 (95% CI: 1.03-1.23).[7] Growing evidence also suggests a potential association of BPA exposure with diabetes mellitus (DM) and HTN. A meta-analysis of 16 epidemiological studies found a positive association between BPA levels and DM risk, with a pooled OR of 1.28 (95% CI: 1.14-1.44).[8] A randomized crossover clinical trial from the same group observed a ~5 mm Hg increase in systolic blood pressure where BPA exposure from drinking canned beverages (a 16-fold increase within 2 hours after drinking 2 canned beverages was seen compared to after consuming glass-bottled beverages).[9] Supplemental Table 2 summarizes the major studies on the association between BPA and CVD.

Pesticides. Pesticides are pollutants that are used to control pests that harm plants or animals, but human

HIGHLIGHTS

- Pollution is emerging as an important but underestimated, modifiable risk factor for CVD.
- Various pollutants, despite different physicochemical and biological characteristics, lead to CVD through common pathophysiological pathways, primarily by promoting oxidative stress, systemic inflammation, atherothrombosis, and autonomic dysfunction.
- Current global efforts are insufficient to mitigate pollution-induced adverse health outcomes, including CVD, necessitating better implementation strategies, funding for research, and novel solutions.

TABLE 1 Persistent Organic Pollutants and Cardiovascular Disease

Persistent Organic Pollutant	Uses	Exposure	Putative Mechanism of Cardiovascular Effects	Cardiovascular Associations
Phthalates	Food packaging, medical devices, and personal care products	Released into the environment during manufacture, use, or disposal since they are not covalently bound to the plastics	Oxidative stress Lipid peroxidation Endothelial dysfunction Activation of procoagulant pathways	HTN Atherosclerosis CAD Metabolic syndrome
Bisphenol A	To manufacture polycarbonate plastics and epoxy resins	Leaching out due to incomplete polymerization and degradation	Modification of cardiac Ca^{2+} handling Changes in protein expression Oxidative stress Alterations in the genome/transcriptome	HTN DM CAD MI HF
2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD)	Not produced or used for any commercial or beneficial purposes due to its highly toxic characteristics	Unintentional by-product in industrial manufacturing and waste incineration	Aryl hydrocarbon receptor activation Oxidative stress Systemic inflammation Endocrine disruption	HTN DM CAD
Dichlorodiphenyl trichloroethane (DDT)	Pesticide, but use has been banned in most of the developed countries Still in use in developing countries for controlling vector-borne diseases	Pesticide production and waste incineration	Oxidative stress Systemic inflammation Endocrine disruption Disruption of calcium homeostasis	HTN DM Metabolic syndrome HF
Hexachlorobenzene (HCB) and β-hexachlorocyclohexane (HCH)	Fungicide and manufacturing of rubber, aluminum, and dyes, but use has been banned in most of the developed countries	By products of other chemicals and burning waste	Oxidative stress Systemic inflammation Endocrine disruption	HTN Metabolic syndrome HF
Perfluoroalkyl substances (PFAS)	Commercial and industrial applications such as stain-resistant fabric, paper packaging for food, and heat-resistant/nonstick cookware	Bioaccumulation in the food chain	Oxidative stress Systemic inflammation Endocrine disruption	Atherosclerosis CAD PAD
Polychlorinated biphenyls (PCBs)	Dielectric fluids in transformers and capacitors, paint additives, and lubricants Production has been prohibited in most countries since 1979	Accumulate in the food chain due to a strong affinity for fats. Exposure is through consumption of high-fat animal products such as red meat, eggs, and dairy	Disruption of lipid metabolism Oxidative stress Systemic inflammation Endocrine disruption Endothelial dysfunction	HTN DM Atherosclerosis CAD MI HF

Common applications of widespread water and soil contaminants, their exposure routes, mechanisms leading to cardiovascular implications, and subsequent cardiovascular associations.
CAD = coronary artery disease; DM = diabetes mellitus; HF = heart failure; HTN = hypertension; MI = myocardial infarction; PAD = peripheral arterial disease.

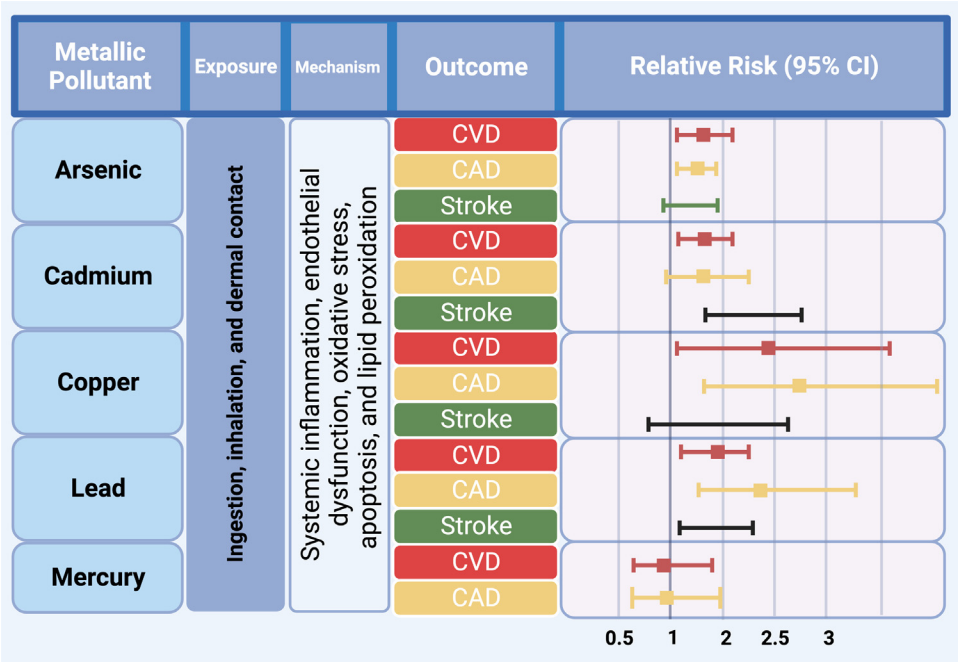
exposure may lead to adverse health effects. Evidence suggests that pesticide exposure can increase the risk of various types of cancer and has negative CV effects. These effects are likely caused by enhanced oxidative stress, inflammatory response, and atherosclerotic changes in the vascular wall. Many pesticides have been banned or restricted in developed countries due to their harmful health effects and environmental persistence.

2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) was first recognized in the 1960s when it was identified as a major contaminant in Agent Orange, a herbicide and defoliant abundantly used in the Vietnam War. Studies have shown that exposure to TCDD increased the risk of DM, HTN, and CVD among Vietnam veterans compared to non-Vietnam veterans.[10] A large international study among herbicide workers reported that exposure to TCDD or other chlorinated dioxins was associated with an increased risk of CAD with an RR of 1.6 (95% CI: 1.23-2.26).[11]

Dichlorodiphenyltrichloroethane and its major and very persistent metabolite, p,p'-dichlorodiphenyldichloroethylene, have been linked to an increased risk of CVD and CVD risk factors in several human cohort studies. A recent meta-analysis of 23 prospective studies reported that exposure to p,p'-dichlorodiphenyldichloroethylene was associated with an increased risk of DM with a pooled OR of 1.44 (95% CI: 1.00-2.07) and HTN with a pooled OR of 1.21 (95% CI: 1.07-1.38).[12]

Hexachlorobenzene and beta-hexachlorocyclohexane are organochlorides and have been linked to an increased risk of CVD, HTN, and MetS.[13] Additionally, studies from the Prospective Investigation of the

FIGURE 1 Metallic Pollutants and Cardiovascular Risk



Common metallic pollutants, paths of exposure, mechanisms underlying cardiovascular abnormalities, resulting cardiovascular outcomes, and their corresponding relative risk ratios. Random effects meta-analyses were used to calculate pooled risk estimates. The relative risk was determined by comparing the risk of each outcome between individuals with high exposure to metallic pollutants (highest tertile) and those with low exposure (lowest tertile). Data sourced from Chowdhury et al.[22] CAD = coronary artery disease; CVD = cardiovascular disease.

Vasculature in Uppsala Seniors cohort found positive associations between hexachlorobenzene exposure and increased left ventricle thickness and decreased left ventricular ejection fraction.[14,15]

Persistent organic pollutants. The expansion of industrialization and technological globalization has led to the creation of a vast number of chemicals, including POPs, that can accumulate in living organisms and the environment over time, leading to a range of environmental and health problems (Table 1).[13] Although many POPs have been banned or restricted, their widespread use in the past and their ability to bioaccumulate have led to their persistence in the environment and human bodies.[13]

Perfluoroalkyl substances are synthetic chemicals commonly used in various commercial and industrial applications. Studies have shown a positive association between perfluoroalkyl substances exposure and CVD incidence and mortality including an increase in CIMT and increased risk of CAD and peripheral arterial disease.[16,17]

Polychlorinated biphenyls (PCBs) are synthetic chemicals that accumulate in fatty tissues and can be found in high-fat animal products. A recent meta-analysis found that dietary exposure to PCBs was associated with an increased risk of CVD mortality, with a summary RR of 1.38 (95% CI: 1.14-1.66) for the highest vs the lowest background exposure levels.[18] A recent Danish study found that residential exposure to ≥3,300 ng/m^3 indoor air PCB per year had a higher risk of myocardial infarction (MI) with an HR of 1.17 (95% CI: 1.00-1.35) compared to the reference group.[19] Furthermore, PCB exposure has been associated with the development of DM, HTN, and HF.[14,20,21]

Metallic pollutants. Environmental degradation and exposure to metallic pollutants can contribute to the development of CVD, emerging as a significant global challenge for both individual and population health. Arsenic, cadmium, lead, copper, and mercury are among the most extensively studied environmental toxic metals that have been linked to CVD (Figure 1). Numerous studies have demonstrated that exposure to these metals, even at low levels, can increase the risk of CVD and related mortality (Table 2). However, the association between mercury exposure and CV outcomes has not been as consistent.

TABLE 2 Metallic Pollutants and Cardiovascular Disease

Metallic Pollutants	Arsenic	Cadmium	Copper	Lead	Mercury
Sources	Contaminated groundwater and soil. Fish, meat, poultry, and dairy products. Food products grown in arsenic-contaminated soil. Tobacco smoke. Industrial processes such as mining and processing of glass, pigments, textiles, and pesticides.	Contaminated groundwater and soil. Occupational exposures in mining, smelting, and battery manufacturing. Contaminated grains and leafy vegetables. Tobacco smoking and air pollution through industrial processes and waste incineration.	Contaminated water from copper pipes, brass fixtures, and fittings. Occupational exposures in mining, smelting, and electroplating. Copper cookware, plumbing fixtures, and electronics. Copper-rich foods, such as shellfish, nuts, and chocolate.	Contaminated water from lead-containing pipes and plumbing fixtures. Lead-based paint from homes and buildings built before 1978. Contaminated soil and dust from lead-based paint, industrial activities, and leaded gasoline. Occupational exposure in mining, smelting, battery manufacturing, and construction.	Occupational exposures in mining, smelting, and chlor-alkali production. Freshwater and marine fish and shellfish Dental amalgams Air pollution through industrial processes and waste incineration.
Putative mechanisms of CVD	Endothelial and smooth muscle cell dysfunction Systemic inflammation Oxidative stress Apoptosis Disruption of ion channels	Endothelial dysfunction Systemic inflammation Oxidative stress Alterations in lipid metabolism Disruption of ion channels	Endothelial dysfunction Systemic inflammation Oxidative stress Lipid peroxidation Catecholamine oxidation Mitochondrial damage	Endothelial dysfunction Systemic inflammation Oxidative stress Disruption of calcium signaling Interference with heme synthesis	Endothelial dysfunction Systemic inflammation Oxidative stress. Alterations in lipid metabolism Nitric oxide synthase dysregulation
CVD associations	Atherosclerosis Arrhythmias CAD HTN PAD Stroke DM	Atherosclerosis CAD HF HTN MI Stroke	Arrhythmias HF HTN	CAD HTN Stroke	CAD HTN Stroke
Acceptable exposure levels	Blood: <1 μg/L Urine: <50 μg in a 24-h collection of urine Nails and hair: ≤1 ppm in nails and hair	Blood: nonsmoker <1.2 μg/L; smoker <3.9 μg/L Urine: <2.0 μg/g creatinine; <3.0 μg in a 24-h collection of urine	Blood: Free serum copper <15 μg/dL Total copper <140 μg/dL Serum ceruloplasmin: <35 μg/dL Urine: 24-h urine copper <50 μg Liver copper <50 μg/g of tissue	Blood: <5 μg/dl	Blood: <10 μg/L Urine: <20 μg/L in a 24-h collection of urine

The rows depict the typical sources of prevalent metallic contaminants, mechanisms leading to cardiovascular effects, downstream cardiovascular consequences, and acceptable levels of exposure (to avoid cardiovascular injury).

CAD = coronary artery disease; CVD = cardiovascular disease; DM = diabetes mellitus; HF = heart failure; HTN = hypertension; MI = myocardial infarction; PAD = peripheral arterial disease.

Arsenic. Chronic exposure to high levels of water arsenic is associated with CVD, even at low to moderate levels. A meta-analysis of 11 studies reported a 7% increase in CVD and a 16% increase in CAD mortality with 20 μg/L arsenic in water compared to 10 μg/L.[23] Several studies have provided evidence supporting the association between high levels of arsenic in drinking water and DM and HTN. Supplemental Table 3 summarizes the major studies on the association between arsenic and CVD.

Cadmium. Both short-term and chronic exposures are linked to CV effects. A systematic review of 31 studies found that cadmium exposure was associated with an increased risk of CVD and CAD with RRs of 1.36 (95% CI: 1.11-1.66) and 1.30 (95% CI: 1.12-1.52), respectively.[24] Several studies have found a positive association between cadmium exposure and the prevalence of atherosclerotic plaques and coronary artery calcium, as well as an increased risk of MI. A decrease in cadmium exposure due to large-scale public health policies in Western countries may have contributed to some of the decline in CVD mortality in this region.[25] There is also evidence of a positive correlation between cadmium exposure and heart failure. Supplemental Table 4 summarizes the major studies on the association between cadmium and CVD.

Copper. Copper is an essential micronutrient in the human body that plays a vital role in regulating crucial biological processes. However, higher copper

intake and increased serum copper concentrations are associated with a higher risk of CVD, mainly due to its potential role in atherogenesis. Studies in middle-aged Finnish men showed a higher risk of CAD and CVD mortality for those in the highest quartile of serum copper concentration compared to the lowest quartile, during a follow-up of more than 25 years.[26,27] Cuproptosis, copper-induced cell death, is believed to promote the development of CVD. Elevated serum copper levels have been linked to the development of MetS, with higher levels found in obese individuals.[28] Higher serum ceruloplasmin levels, a protein that carries copper in the blood, have been associated with an increased incidence of HF in studies from the United States and Sweden.[29,30]

Proposed biological mechanisms. While the exact mechanisms remain unknown, most metallic pollutants appear to cause CVD through common potential pathophysiological pathways. These primarily involve the induction of oxidative stress and systemic inflammation.[10] The systemic inflammation subsequently fosters intravascular inflammation, which in turn results in endothelial injury and the activation of procoagulant pathways, predisposing to atherosclerosis.[10] Numerous toxic metals are known to augment lipid peroxidation, a recognized precursor to atherosclerosis.[10] Often, these toxic metals compete with vital metals in multiple physiological processes, thus amplifying the risk of CVD. The cardiotoxicity of lead, for instance, is partly attributed to its ability to mimic essential metals such as calcium and iron.[31] Similarly, cadmium and lead, owing to their structural similarities to zinc, can substitute for zinc in certain biological roles.[31] Furthermore, heavy metals might contribute to CVD by modulating other risk factors, notably by elevating the risk of HTN and obesity.[28]

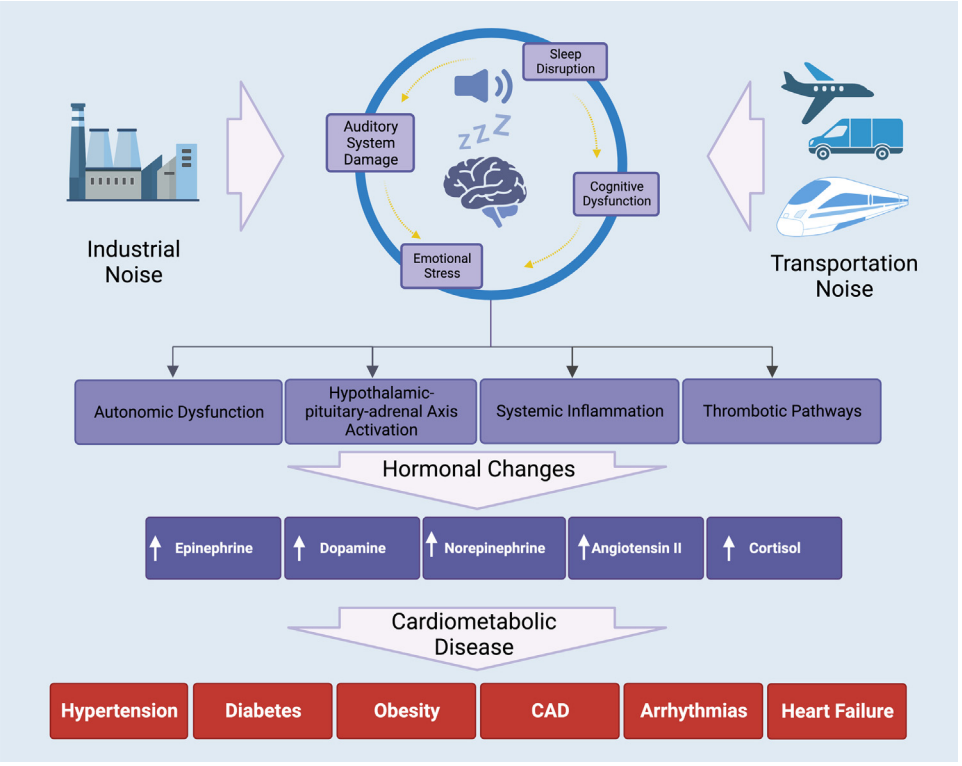
LIGHT POLLUTION. Light pollution has emerged as a novel environmental risk factor impacting health. Over 99% of the US and European populations experience light-polluted skies.[32] The disruption of circadian rhythm, melatonin suppression, and increased sympathetic activity by light pollution can activate metabolic and inflammatory pathways, potentially leading to CVD, depending on the intensity, and timing of light exposure.[32]

There is a strong correlation between light pollution and a heightened risk of CV morbidity and mortality, including CVD risk factors. Recent evidence links light at night exposure to the progression of CIMT as well as an increased risk of CAD. Night shift workers who are exposed to higher levels of light at night are at an increased risk of CAD, and the risk increases with the duration of night shift work.[33] A meta-analysis reported RRs of 1.23 (95% CI: 1.15-1.31) for MI and 1.24 (95% CI: 1.10-1.39) for CAD, in association with night shift work.[33] Research has shown a correlation between light pollution and an increased risk of HTN and DM. It is important to note that most of the research investigating the relationship between light pollution and CVD has been conducted on elderly populations in East Asia. Further research is necessary to broaden the scope of these findings, including the investigation of different geographical locations and all age groups. Supplemental Table 5 summarizes the major studies on the association between light pollution and CVD.

NOISE POLLUTION. Noise pollution is a significant risk factor for CVD and ranks second to air pollution in terms of the environmental factors most harmful to public health. The World Health Organization estimates that traffic noise in Western Europe alone results in the loss of at least 1 million disability-adjusted life years due to noise-related diseases.[34] The CV system's response to noise involves a combination of physiological and psychological stress reactions, mainly activation of the sympathetic nervous system and hypothalamus-pituitary-adrenal axis[34] (**Figure 2**). There is high-quality evidence linking noise exposure to CAD, including acute MI.[34] A recent pooled analysis of 9 Scandinavian cohorts found an increased risk of CAD and MI with exposure to transportation noise with HRs for CAD of 1.06 (95% CI: 1.03-1.08) and 1.05 (95% CI: 1.01-1.08) per 10 dB L_{den} (day-evening-night noise level) for road and railway noise, respectively, and the HRs for MI were 1.02 (95% CI: 0.99-1.05) and 1.04 (95% CI: 0.99-1.08), respectively.[35]

Studies have also noted a significant association between exposure to noise pollution and an increased risk of HF, atrial fibrillation, and CVD risk factors including HTN and DM. A large Canadian population-based retrospective cohort study measured noise levels as 24- and 8-hour nighttime average A-weighted decibels (LAeq24 and LAeqNight) finding that each interquartile range increase in LAeq24 and LAeqNight was associated with a 7% increase in the incidence of acute MI and a 6% increase in HF incidence.[36] Another study using the same cohort showed that every 10-dBA increase in long-term exposure to road traffic noise was associated with an 8% increase in incident DM and a 2% increase in HTN. A recent large German population-based study found a 25% and 22% increased risk of incidence of atrial fibrillation in response to industrial noise annoyance in men and women, respectively.[37] Noise annoyance

FIGURE 2 Mechanisms of Noise-Induced Cardiovascular Disease



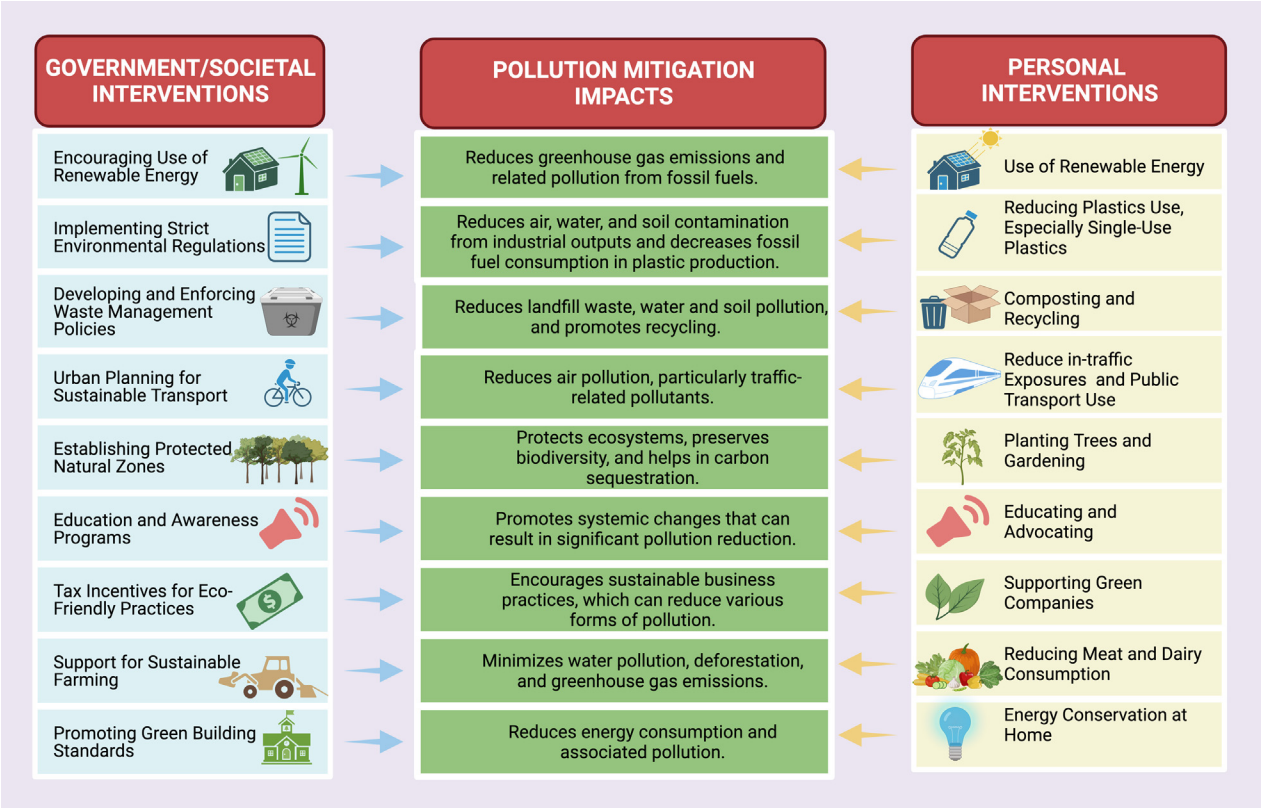
Noise exposure contributes to cardiovascular disease through multiple mechanisms, initiated by sleep disruption, and cognitive and emotional stress. This triggers the activation of the hypothalamic-pituitary-adrenal (HPA) axis, thrombotic pathways, systemic inflammation, and autonomic dysfunction. Consequently, levels of stress hormones rise, elevating the risk of cardiovascular events. CAD = coronary artery disease.

is a heterogeneous psychological construct representing the totality of negative emotions and cognition in connection with the noise source. Supplemental Table 6 summarizes the major studies on the association between noise pollution and CVD.

APPROACH TO POLLUTION MITIGATION. Mitigating pollution is a responsibility shared by individuals, governments, and society. On a personal level, individuals can make significant strides in reducing pollution by adopting eco-friendly practices like minimizing single-use plastics, opting for public transportation, efficient energy use, and supporting eco-friendly businesses. However, the fight against pollution requires actions beyond the individual level. Governmental bodies can institute strict environmental regulations, promote renewable energy, establish effective waste management strategies, and incentivize sustainable urban planning and tax benefits for green practices. Furthermore, societal entities, like educational institutions, corporations, and nonprofit organizations, can reinforce these efforts through sustainability education, corporate green initiatives, and community-led actions. Collectively, these interventions can substantially contribute to the reduction of pollution and pave the way toward a more sustainable planet (**Figure 3**). Individual strategies to lessen exposure to air pollution include remaining indoors during times of high seasonal pollutant levels or smoke from wildfires, utilizing in-house air purifiers, proper stove ventilation, wearing face masks, and commuting to work by foot or bicycle, or public transportation by using routes that avoid exposure to ambient air pollutants.

Our dietary choices not only affect personal health but also have a significant impact on the environment. A significant portion of environmental pollution, including deforestation, water pollution, and greenhouse gas emissions, can be traced back to the production of animal-based foods, particularly livestock farming. Animal agriculture is responsible for

FIGURE 3 Pollution Mitigation Strategies

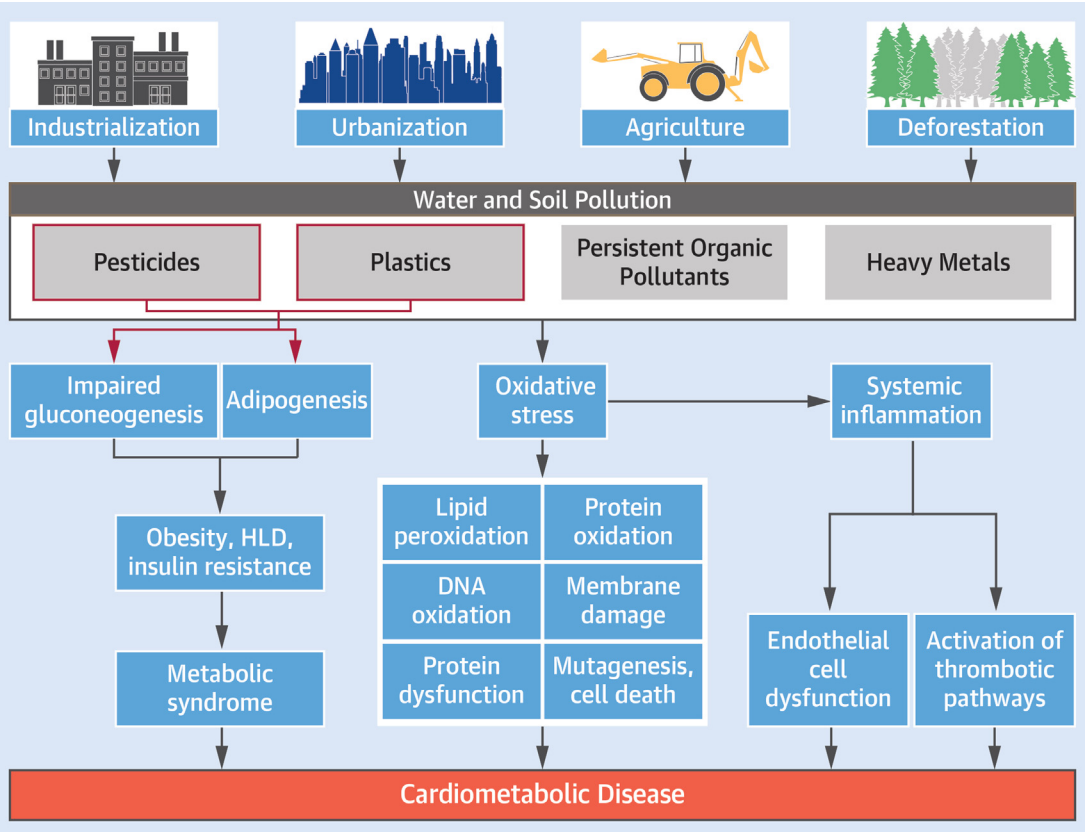


Multilevel interventions are needed to effectively mitigate pollution, encompassing individual, government, and societal approaches. The first column enumerates various approaches that can be applied at the governmental and societal level, while the third column lists various mitigation strategies that can be applied at the individual level. The central column lists the collective benefits of both approaches when used in concert.

about 15% of global greenhouse gas emissions for 20% of water consumption.[38] Current levels of intensive fish and livestock farming are unsustainable and lead to deforestation, ocean dead zones, and species extinction. Cattle farming has a carbon footprint that is about 45 times worse than that of farming protein-rich plants such as beans or soy and contributes to 70% of Amazonian deforestation.[39] Transitioning to a plant-based diet can mitigate many of these environmental challenges including the loss of biodiversity.[40] At the 26th UN Climate Change Conference, a target was set to reduce methane emissions by 30% and reverse deforestation by 2030. Major global professional cardiovascular societies, including the American Heart Association (AHA), American College of Cardiology, and European Society of Cardiology, have also advocated adopting more plant-based diets that achieve the multiple benefits of reducing air pollution and climate change, and improving CV health.[41,42]

Numerous epidemiological and experimental studies consistently demonstrate that a decrease in pollution exposure results in a lower risk of CVD. The AHA has issued a policy statement promoting efforts that counteract the detrimental health impacts of air pollution, while simultaneously fostering sustainable practices and infrastructure growth.[43] It emphasizes the crucial contributions of the health care sector and private industries in improving air quality.[43] Another recent AHA statement underlines the urgency to reinforce public health measures against metallic pollutants and develop advanced monitoring and treatment methods.[44] The Minderoo-Monaco Commission on Plastics and human health warns against the current levels of unsustainable production and disposal which leads to significant health, environmental, and economic issues.[45] It advocates for

CENTRAL ILLUSTRATION **Environmental Pollutants and Cardiovascular Disease**



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Rapid industrialization, urban expansion, intensified agricultural practices, and deforestation are primary contributors to water and soil contamination, predominantly from sources such as pesticides, plastics, POPs, and metallic contaminants. These environmental pollutants are implicated in the pathogenesis of CVD, primarily through shared mechanisms such as oxidative stress and systemic inflammation. These lead to endothelial cell injury and a prothrombotic state. Additionally, these environmental contaminants potentiate metabolic syndrome and atherothrombosis, with a resultant increase in cardiometabolic disorders. CVD = cardiovascular disease; DNA = deoxyribonucleic acid; HLD = hyperlipidemia; POPs = persistent organic pollutants.

urgent, large-scale actions to reduce plastic production and mitigation of their harmful effects.[45]

Several worldwide initiatives and approaches have achieved success in controlling pollution—we mention a few examples here: The Clean Air Act, aimed at protecting public health from the adverse effects of air pollution, has resulted in a decrease of ~50% in air pollutant emissions since 1990.[46] The overall benefits of this and similar approaches have exceeded the associated costs by a factor of over 30 to 1, indicating that they are financially viable.[46] On Earth Day 2022, the Health Sector Climate Pledge went into effect—it targets a 50% reduction in greenhouse gas emissions by the U.S. healthcare sector by 2030.[47] This and other similar initiatives such as the Million Hearts Climate Change & Cardiovascular Disease Collaborative aim to transition to renewable energy, reduce emissions, and build climate resilience. The Green Mortgage Insurance Premium incentivizes energy and water efficiency in long-term care facilities.[47] Thus, collective and sustained actions can get nations to achieve the goal of having carbon neutrality and net-zero emissions by 2050.

CONCLUSIONS

Pollution is a significant modifiable risk factor for CVD, with a large but underappreciated impact on overall global health. Both short-term and long-term

exposure to pollutants contributes to increased CVD-related morbidity and mortality. Different pollutants can act synergistically with other traditional CVD risk factors, increasing the incidence of CVD and its morbidity and mortality. Despite differing in their chemical composition and molecular pathways, these diverse pollutants trigger CVD through shared pathophysiological mechanisms that revolve around increasing oxidative stress, systemic inflammation, atherothrombosis, and autonomic dysfunction (**Central Illustration**). The final CV effects involve dysregulation and worsening of blood pressure, insulin resistance, atheroma formation, arrhythmias, atherosclerotic cardiovascular disease, and heart failure.

Despite significant evidence from around the globe that links pollution to adverse health and CV outcomes, prevention of pollution and combatting it are not receiving enough attention and action by governments. There is an urgent need for concerted, international public health strategies to curb pollution—this will require major policy changes, increased public awareness and involvement, and innovation. Governments, international health agencies, and cardiology providers should prioritize further research aimed at better understanding the CV effects of pollution, best practices to reduce pollution, and implementation strategies for universal adoption. To arrest the rapid pace of pollution-related CVD, there needs to be a rapid, substantial reduction in pollution to curb significant harm to our planet's ecosystems and human health. Clinicians must continue to be strong advocates for pollution control, raise awareness in their communities, and educate their patients on ways to avoid exposure to common pollutants.

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KEY WORDS global burden of disease, light at night, metallic pollutants, persistent organic pollutants

APPENDIX For supplemental methodology and tables, please see the online version of this paper.