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REVIEW

Air Pollution Within the Public Health Exposome Framework: Impacts on Cardiovascular Health

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Abstract

Purpose of Review Ambient air pollution drives cardiovascular disease (CVD), yet single-pollutant models overlook how risk emerges within broader environmental and structural contexts. This review applies the Public Health Exposome (PHE) framework, which integrates natural, built, social, and policy environments, to show how multilevel systems shape CVD vulnerability.

Recent Findings Extreme heat, humidity, and climate variability modify pollutant toxicity, while structural inequities, discriminatory policies, and inadequate planning intensify exposures in marginalized communities. Cumulative psychosocial stress further amplifies inflammatory responses, activating the endo-exposome. Multi-omics studies reveal that pollution alters epigenomic, transcriptomic, and metabolomic pathways linked to inflammation, oxidative stress, and endothelial dysfunction. Emerging tools like machine learning, high-resolution exposure modeling, graph-based analytics, and wearable sensing, enable integration of environmental data and support systems-level approaches.

Summary The PHE framework illustrates how layered environmental and structural stressors accumulate to elevate CVD risk. Reducing this burden requires coupling PHE science with equitable public policy.

Keywords Air pollution · Cardiovascular disease · Exposome · Lifecourse epidemiology · Environmental health · Social determinants

Introduction

A recent Global Burden of Disease study [1] shows that cardiovascular disease (CVD) remains the leading global cause of death, accounting for nearly half of all non-communicable disease mortality. Growing evidence demonstrates that environmental exposures, particularly long-term exposure to ambient air pollution, play a significant role in this burden [2]. Recent global estimates attribute nine million deaths annually to poor air quality, underscoring air pollution as a leading environmental determinant of premature mortality [2] with profound socio-economic impacts [3]. Air pollution has become increasingly studied as an environmental risk factor for CVD, yet it represents only one component of the broader, interconnected exposome.

The exposome encompasses the totality of environmental influences, from conception through late life [4–6]. Air pollution operates within a broader network of chemical, physical, social, behavioral, and policy-related exposures that collectively influence CVD risk, intersect across biological pathways, and generate cumulative and synergistic effects

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overlooked in single-pollutant models. However, existing CVD epidemiology has largely examined fine particulate matter (particles ≤ 2.5 microns in diameter, $PM_{2.5}$), nitrogen dioxide (NO_2), ozone (O_3), and other pollutants separately, with limited integration of the natural, built, and social context in which they occur. Key gaps persist in understanding how mixtures of pollutants co-occur with heat, noise, psychosocial stress, and neighborhood disadvantage; how structural inequities concentrate multiple hazards; and how biological processes, such as inflammation, oxidative stress, and epigenetic dysregulation, encode the impact of these exposures over time.

In 2026, the American Heart Association (AHA), American College of Cardiology (ACC), European Society of Cardiology (ESC), and World Heart Federation (WHF) issued a joint statement urging the field to address air pollution and related environmental stressors as urgent, preventable determinants of CVD [7]. Responding to this call, this review situates long-term air pollution exposure within the Public Health Exposome (PHE) framework [5] to synthesize evidence on CVD impacts and identify scientific, methodological, and policy gaps. The PHE framework organizes external exposures across the natural, built, social, and policy environments and links them to biological responses through the endo-exposome (Fig. 1). Grounding the review in this systems-oriented perspective allows for a more integrated evaluation of how complex, multilevel exposures contribute to CVD risk and where opportunities exist for prevention and policy action.

The Public Health Exposome Framework

The Public Health Exposome (PHE) framework places air pollution as one component within a multidimensional system of natural, built, social, and policy environments that collectively shape CVD risk across the lifecourse [4, 5, 8, 9]. This perspective moves beyond pollutant-specific analyses by emphasizing how exposures cluster and interact. Ambient pollution co-occurs with extreme temperatures, wildfire smoke, humidity, and traffic emissions, producing cumulative and synergistic cardiometabolic effects that are not captured when exposures are evaluated independently [10].

The built environment further structures exposure patterns and resilience. Walkability, green space, transit access, and housing quality influence both pollution levels and opportunities for health-promoting behaviors, whereas

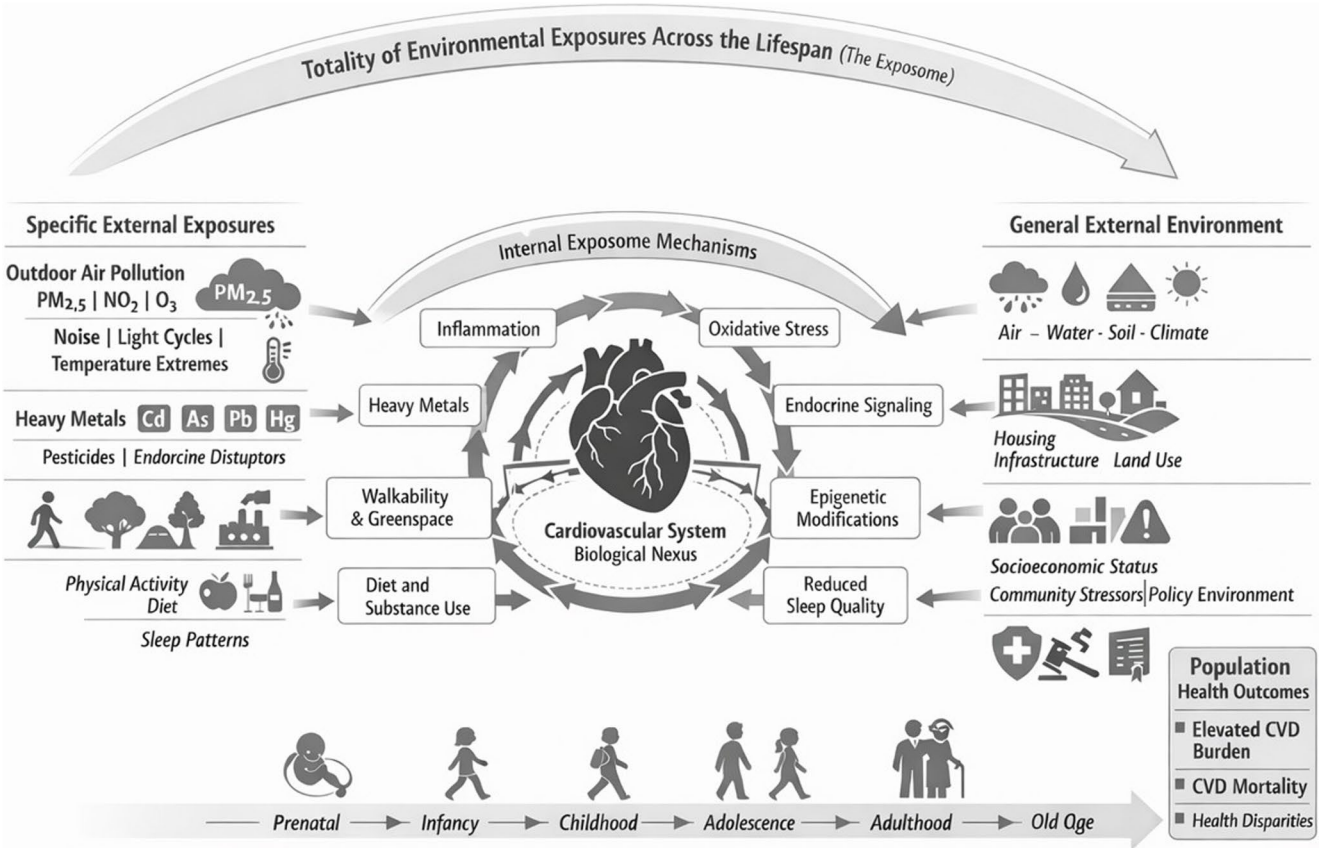


Fig. 1 The Public Health Exposome Framework for Cardiovascular Disease Risk

proximity to major roadways, and substandard housing increase exposure to $PM_{2.5}$, NO_2, and indoor combustion pollutants [11, 12]. These features intersect with longstanding socioeconomic inequities and discriminatory land-use practices that concentrate multiple hazards in historically marginalized communities. Such structural forces heighten extrinsic vulnerability and amplify biological susceptibility through chronic stress, heightened inflammation, and reduced adaptive capacity [13, 14].

The PHE framework also incorporates temporal dimensions, highlighting critical windows, from prenatal development through older adulthood, when environmental exposures may exert durable CVD effects [15]. By integrating the endo-exposome, the framework links external exposures to internal biological responses, supported by multi-omics tools [16] capable of characterizing pathways related to oxidative stress, immune activation, endothelial dysfunction, and epigenetic regulation. Finally, advances in measurement and analytics, including satellite-derived data, low-cost sensing, exposure network modeling, and machine-learning approaches, enhance the precision with which this complex environmental system can be characterized [17]. Applied within the PHE framework, these tools enable a more holistic understanding of cumulative environmental burden and help identify leverage points for targeted prevention and policy interventions.

Air Pollution

Air pollution arises from a mix of natural and human-made sources that emit primary pollutants such as PM, sulfur dioxide (SO_2), and nitrogen oxides (N_xO_x), and generate secondary pollutants like O_3, NO_2 and sulfates (SO_4) through atmospheric reactions [18–20]. Extensive evidence shows that even low concentrations of $PM_{2.5}$ contribute to premature mortality and CVD disease [21]. PM varies by size (PM_{10}, $PM_{2.5}$, ultrafine particles), with smaller particles penetrating deeper into the respiratory and vascular systems and driving systemic inflammation [13] and oxidative effects [22]. Toxicity is influenced by particle composition, size, oxidative potential, and meteorological conditions [20, 23]. In 2024, the U.S. Environmental Protection Agency (EPA) finalized new National Ambient Air Quality Standards (NAAQS) for fine particle pollution (soot), lowering the annual standard to 9 μg/m³ to improve public health, and set new standards for power plant emissions [24]. However, these moves were reversed one year later [25].

Anthropogenic sources, such as traffic emissions, industrial activities, and fossil fuel combustion, remain dominant contributors, while natural sources such as dust storms, wildfires, and sea spray increasingly shape regional air quality. Wildfire-related $PM_{2.5}$ is also harmful due to its high oxidative potential and long-range transport [26]. Traffic emissions generate ultrafine particles and reactive gases including NOx, while sulfur oxides arise from combustion of sulfur-rich fuels. Atmospheric chemistry involving NOx, volatile organic compounds, and humidity drives formation of secondary sulfates and nitrates, elevating $PM_{2.5}$ even in areas distant from emission sources [27, 28].

Exposure is further modified by features of the built and social environment. Poor housing quality, limited ventilation, and proximity to major roadways increase pollutant infiltration [29], while socioeconomic disadvantage [30] and discriminatory land-use patterns [31] concentrate exposures in historically marginalized communities. These multilevel influences underscore that air pollution is best understood as part of the broader exposome, interacting with co-occurring environmental and social stressors that shape CVD risk across the lifecourse.

As summarized in Table 1, these dynamics reflect a multidimensional exposure milieu in which chemical pollutants intersect with physical conditions, such as heat, humidity, and noise, as well as built environment factors, social stressors, and structural policy contexts. Together, these co-occurring exposures create interaction pathways, ranging from oxidative stress to autonomic and neuroendocrine disruption, that intensify vulnerability to ambient air pollution and contribute to persistent CVD disparities.

Table 1 Exposure Mixtures Matrix: Multidimensional Interactions With Ambient Air Pollution

Exposure Domain	Representative Exposures	Mechanistic Interaction With Air Pollution
Chemical	$PM_{2.5}$, NO_2, O_3, volatile organic compounds (VOCs)	Potentiates oxidative stress, promotes systemic inflammation, and exacerbates cardiopulmonary toxicity
Physical	Ambient heat, humidity, environmental noise	Heat amplifies pollutant toxicity via thermoregulatory strain; noise augments autonomic nervous system activation and stress-related susceptibility
Built Environment	Traffic density, substandard housing, indoor particulate sources	Increases cumulative exposure burden and alters time–activity patterns, intensifying chronic inhalation and contact pathways
Social Stressors	Structural discrimination, socioeconomic deprivation, community violence	Heightens allostatic load, dysregulates neuroendocrine stress pathways, and amplifies inflammatory responses to pollutants
Policy and Structural Factors	Zoning practices, regulatory enforcement gaps, land-use policies	Spatially concentrates multi-hazard exposures and perpetuates environmental inequities in marginalized communities

Epidemiologic Evidence Linking Long-Term Air Pollution Exposure with CVD

Well-established epidemiological evidence demonstrates that long-term exposure to air pollution, particularly $PM_{2.5}$, increases the risk for atherosclerotic ischemic heart disease, myocardial infarction, stroke, heart failure, hypertension, arrhythmia and dyslipidemia [32–37]. Meta-analyses consistently report that chronic $PM_{2.5}$ exposure increases CVD mortality by approximately 5–10% per 10 μg/m³ increase in $PM_{2.5}$ [34], with associations evident even at concentrations below current regulatory limits.

Long-term exposure to $PM_{2.5}$ contributes to ischemic heart disease [38], including higher incidence of myocardial infarction [34] and accelerated atherosclerotic plaque development [39]. Subclinical markers such as coronary artery calcium [40], carotid intima-media thickness [41], endothelial dysfunction [42] and arterial stiffness [43] provide strong mechanistic support for these associations. In addition, evidence for cerebrovascular outcomes shows that chronic $PM_{2.5}$ exposure increases risks of stroke incidence, stroke mortality and cerebral small vessel disease [44, 45], with heightened vulnerability among older adults [46] and individuals with metabolic conditions [36, 47].

Air pollution also plays a role in heart failure, with studies linking long-term exposure to increased incidence [48] and hospitalizations [49], likely through pathways involving systemic inflammation [50], autonomic imbalance [51], and ventricular remodeling [52]. Furthermore, long-term exposure contributes to cardiometabolic precursors of CVD, hypertension [33, 36], dyslipidemia [53], insulin resistance [54], obesity [55], and type 2 diabetes [55], highlighting early pathways through which pollution increases downstream CVD risk.

Although evidence for nitrogen dioxide (NO_2) and other co-pollutants varies, the overall body of research demonstrates that chronic air pollution exposure is a pervasive, multisystem contributor to CVD across the life course [56, 57].

Biological Mechanisms: Oxidative Stress, Inflammation, and Endothelial Injury

Environmental stressors across the exposome, including air pollutants, chemical toxicants, radiation, heat, and socioeconomic adversity, activate a cascade of biological pathways that converge on oxidative stress, inflammation, and endothelial dysfunction [58]. These exposures initiate neuroendocrine stress responses that elevate catecholamines and cortisol, contributing to allostatic load (AL), a multisystem marker of cumulative physiological strain. AL, also known as the "wear and tear" on the body over a lifetime, is an objective measure that quantifies the level of stress experienced throughout one's life.

Air pollution is a particularly potent driver: $PM_{2.5}$, NO_2, and ozone exposures have been linked to circadian rhythm disruption, dysregulation of stress hormones, and altered expression of circadian and metabolic genes [59]. Experimental evidence demonstrates that $PM_{2.5}$ induces insulin resistance, reduced energy expenditure, and disrupted thermogenesis, effects that reverse when exposure ceases, while human studies show strong correlations between $PM_{2.5}$ and components of the circadian-metabolic syndrome, including sleep disturbance and depression [59]. As a result, chronic environmental stress increases CVD vulnerability by impairing homeostatic balance and amplifying oxidative and inflammatory signaling.

These biological disturbances interact with chemical and physical pollutants such as lead, tobacco smoke [55], and ionizing radiation, which independently promote oxidative stress, immune activation, and endothelial damage. Long- and short-term epidemiologic studies, supported by imaging and experimental research, demonstrate that particulate matter promotes endothelial dysfunction, vascular stiffness, subclinical atherosclerosis, and development of vulnerable plaques through oxidative, inflammatory, thrombotic, and vasoconstrictive pathways. Cohort studies such as Heinz Nixdorf Recall, KORA, MESA and CARDIA [40, 41, 60] consistently link higher $PM_{2.5}$ and traffic-related pollutants with increased carotid intima–media thickness, arterial calcification, arterial inflammation, and major CVD events. Together, these findings underscore oxidative stress, inflammation, and endothelial injury as central, interconnected biological mechanisms through which the exposome exerts its CVD effects.

The Natural Environment

Heat and Humidity

Heat waves are associated with increased CVD mortality. Extreme heat activates sympathetic responses, dehydration-related electrolyte imbalances, and systemic inflammation, increasing the incidence of hypertension and acute myocardial infarction, particularly among those with existing disease [61, 62]. These physiologic stresses occur alongside shifts in ambient air pollution, a dominant natural exposome stressor [3]. Temperature-sensitive ozone (O_3) accelerates airway inflammation, oxidative stress, endothelial dysfunction, and atherosclerotic progression, with heat intensifying its photochemical formation [42]. Wildfire smoke, drought conditions, and acrolein-rich traffic emissions further compound pollutant toxicity and population exposure [26, 27].

Humidity adds an additional layer of CVD stress by modifying both thermoregulation and atmospheric chemistry [28]. Extremes of high and low relative humidity impair heat dissipation and elevate CVD mortality, while long-term exposure to higher summer specific humidity and its variability is associated with increased CVD hospitalization [49]. Humidity also influences O_3 dynamics, affecting radical formation and pollutant persistence in urban air masses [61]. Methodologic evidence from multi-city analyses indicates that apparent temperature is the strongest predictor of heat-related all-cause mortality, whereas absolute humidity frequently emerges as a top predictor across cause-specific mortality outcomes [62]. These metrics remain central to accurately characterizing heat–health relationships in a warming climate.

The Built Environment

The built environment, including transportation infrastructure, land-use patterns, green space distribution, and the local food environment, shapes CVD health through dynamic interactions with pollution exposures [63, 64]. Walkable, mixed-use neighborhoods encourage physical activity and reduce car dependence [11, 13, 63], yet residents often face higher exposure to traffic-related air pollution and noise, both of which drive oxidative stress, autonomic dysregulation, and endothelial injury [11]. Conversely, car-dependent areas may lower pollution exposure but contribute to sedentary behavior and social isolation [12, 64]. Food environments compound these spatial risks: neighborhoods with poor walkability and low greenness frequently lack supermarkets and affordable fresh foods, increasing food insecurity and reliance on calorie-dense ultra-processed foods [11]. These dietary constraints heighten inflammation, dyslipidemia, and insulin resistance, amplifying the biological effects of pollution. Evidence from an umbrella review [11] highlights strong, consistent relationships between air pollution, noise, and CVD, with the greatest burden borne by socially vulnerable communities where adverse built features, food insecurity, and environmental exposures co-occur. Understanding these interlocking pathways is essential for designing interventions that jointly address pollution, mobility, and nutrition.

Urban Green Spaces and Pollution Interactions

Urban green spaces, parks, street trees, community gardens, and biodiverse natural areas, modify CVD risk by simultaneously influencing physical activity, pollution exposure, thermal stress, and food access [12]. Green vegetation can buffer particulate matter, lower ambient temperatures, and reduce noise [63], thereby mitigating pollution-related endothelial dysfunction and autonomic stress. However, these benefits depend on quality, biodiversity, and spatial placement [65]: heavily trafficked parks or green corridors adjacent to major roadways may expose users to elevated $PM_{2.5}$ and NO_2, partly offsetting CVD gains. Studies from other countries consistently show lower CVD mortality in greener areas [11, 12]. However, analyses from vulnerable populations using CARDIA data reveal complexities [66], such as greater greenness lowering coronary artery calcification while proximity to poorly maintained parks in deprived neighborhoods predicts higher risk, likely reflecting safety, utilization, and pollution gradients. Urban agriculture and community gardens illustrate how green spaces can also improve the food environment by enhancing access to fresh produce [64], reducing reliance on ultra-processed foods, and bolstering dietary quality. The combined influence of greenery, pollution buffering, walkability, and food access underscores the need for integrated planning strategies that create safe, high-quality, and nutritionally supportive green spaces capable of reducing cumulative environmental CVD burdens.

The Social Environment

Socioeconomic Status

Socioeconomic status (SES), including education, occupation, income, and wealth, strongly shapes exposure and vulnerability to environmental pollution. Lower-SES populations are more likely to live near highways, industrial facilities, and waste sites, resulting in higher chronic exposure to $PM_{2.5}$, nitrogen oxides, and ozone [67]. Poor housing quality and limited air conditioning increase indoor pollutant infiltration, while socioeconomic adversity heightens biological susceptibility through chronic stress, nutritional deprivation, and reduced access to preventive care, amplifying inflammation and endothelial dysfunction [12, 58, 64]. Race and ethnicity intersect with SES [31, 68] through structural racism embedded in housing and zoning policies [14, 31, 68, 69]. Historical redlining and discriminatory land-use practices have concentrated pollution sources in communities of color, making race a dominant predictor of exposure independent of income. Pollution interacts with racism-related stress to accelerate vascular aging and reinforce cardiometabolic inequities.

Family Structure and Psychosocial Stressors

Family structure, psychosocial stress, and social support jointly shape exposure to and vulnerability from environmental pollution across the life course. Single-parent

households, overcrowding, and multigenerational caregiving are more prevalent in socioeconomically disadvantaged neighborhoods characterized by elevated ambient and indoor pollution [67, 68]. These contexts often coincide with substandard housing, proximity to traffic corridors, and limited residential mobility, increasing cumulative exposure. Early-life adversity and household instability may further sensitize neuroendocrine, immune, and metabolic pathways, rendering children and adolescents more susceptible to pollution-related cardiometabolic programming with persistent adult consequences [15, 46].

Psychosocial stressors, including job strain, neighborhood disorder, crime, noise, discrimination, and financial insecurity, operate synergistically with pollution through convergent biological mechanisms [70]. Chronic stress activates the sympathetic nervous system and hypothalamic–pituitary–adrenal axis, promoting cortisol dysregulation, oxidative stress, and systemic inflammation, pathways also triggered by air pollution [15, 71]. Population studies demonstrate interactive effects between neighborhood deprivation, adverse childhood experiences, and particulate matter on diabetes, stroke, and obesity, supporting a cumulative stress framework in which psychosocial adversity amplifies pollution-related CVD harm [10, 15, 71].

The Policy Environment

Federal regulations, especially the Clean Air Act and subsequent Environmental Protection Agency (EPA) standards, have significantly reduced ambient PM and improved population health [72]. Regions with stronger regulatory enforcement consistently show lower environment-related mortality. Yet CVD risk persists at pollution levels below current NAAQS, and millions remain exposed above recommended thresholds. Updating the standards based on emerging epidemiologic and clinical evidence, and ensuring strict enforcement, remains essential to further reduce CVD burden [73]. Although the EPA strengthened NAAQS for fine PM in 2024, these evidence-based standards were later reversed during the second Trump administration [74]. The agency's mission and capacity were significantly weakened through staffing reductions, closure of the Office of Research and Development, and a shift toward deregulation and energy production over environmental protection [25]. Similar political and structural barriers limit evidence-based air quality policies in many countries, despite clear scientific consensus on the benefits of emission reduction.

The global consequences of inaction are substantial. In India, long-term air pollution exposure contributed an estimated 1.8 million deaths in 2019, 18% of total mortality, relative to World Health Organization guideline levels [75]. Major sources include fossil fuel combustion, coal, and transportation. Economic losses are serious: air pollution cost India an estimated US$95 billion in 2019, or 3% of GDP, due to premature mortality, reduced productivity, and increased healthcare use [76]. Although multiple initiatives aim to improve air quality, major challenges remain in sustaining long-term pollution control.

Public awareness of air pollution's health and economic effects remains limited, particularly in marginalized communities. Risk-communication systems are underdeveloped, and many clinicians lack training on environmental exposures and their CVD implications [77]. Environmental stressors remain insufficiently integrated into global health education and CVD risk assessment tools [78], despite escalating burden from pollution and climate change.

Strengthening public health infrastructure is critical. Priorities include expanding environmental health education, improving community engagement, promoting renewable energy and sustainable transport, increasing access to heart-healthy foods, and supporting local food systems that reinforce nutrition and economic resilience. Health impact assessments should be incorporated into zoning and infrastructure decisions to prevent additional pollution sources in overburdened communities [79]. Ultimately, effective policy requires a strong evidence base and sustained political will. Recent U.S. policy reversals, including weakened environmental protections and retreat from international cooperation [80] threaten progress. Delays will increase future health, economic, and environmental costs and make solutions more difficult to achieve.

Lifecourse Windows of Susceptibility

A growing body of evidence indicates that CVD vulnerability to air pollution is not uniform across the lifespan but instead reflects critical windows of susceptibility during which exposures exert disproportionate and lasting effects [15, 46]. Prenatal exposure to $PM_{2.5}$ can disrupt fetal development through oxidative stress, inflammation, and epigenetic reprogramming, thereby predisposing offspring to lifelong cardiometabolic dysfunction [15]. During infancy and childhood [46], the heightened plasticity of the immune, pulmonary, and CVD systems amplifies sensitivity to ambient pollutants, shaping long-term trajectories of endothelial function, autonomic balance, and metabolic regulation. Adolescence represents a transitional phase [15] in which environmental exposures interact with behavioral, hormonal, and psychosocial changes, potentially accelerating subclinical vascular injury. In older adulthood [46], age-related declines in physiological reserve magnify pollutant-induced CVD stress, consistent with a "harvesting effect" that increases vulnerability to acute events [52].

Across these stages, cumulative and repeated exposures contribute to progressive atherosclerosis, left ventricular remodeling, and worsening cardiometabolic risk, thereby amplifying susceptibility to both chronic disease progression and acute pollution-related triggers [15, 40, 52]. Importantly, these biological processes are embedded within broader social and built environments, where socioeconomic disadvantage, neighborhood stressors, and limited environmental control further intensify exposure burdens. Adopting a lifecourse framework is therefore essential for identifying sensitive periods, elucidating mechanisms of cumulative risk, and guiding early, multilevel interventions to mitigate lifelong CVD disease burden.

Omics

Omics methods quantify cellular molecules and biological processes, including gene expression, metabolic activity, and protein levels. By capturing these molecular signatures, omics approaches enable the development of detailed exposure profiles that reveal pathways through which environmental exposures influence CVD risk across the life course. When integrated within the Public Health Exposome (PHE) framework, alongside data on the physical, social, and biological environments, these techniques can enhance risk assessment of environmental exposure [81, 82]. Emerging multi-omics studies [15, 16] show that air pollution, particularly $PM_{2.5}$, induces coordinated epigenomic, proteomic, and metabolomic disruptions involving inflammation, oxidative stress, endothelial dysfunction, and lipid metabolism [15, 83]. These alterations converge on pathways promoting CVD [15]. Omics also reveal heterogeneity in susceptibility shaped by socioeconomic and built environments [15, 16]. Incorporating lifecourse perspectives into multi-omics research [15] can enhance early risk stratification, improve identification of populations at heightened risk, and support the development of targeted prevention strategies within epidemiologic practice.

Multi-omics studies demonstrate that air pollution, particularly $PM_{2.5}$ and traffic-related emissions, induces coordinated disruptions across epigenomic, transcriptomic, proteomic, and metabolomic domains [15, 16, 83, 84]. Exposure has been linked to differential DNA methylation in genes regulating inflammation, oxidative stress, endothelial function, and DNA repair, driving transcriptional shifts that amplify pro-inflammatory and pro-atherogenic signaling [15, 84].

Proteomic profiles indicate elevated cytokine activity, acute-phase responses, and increased coagulation factors, consistent with systemic inflammation, endothelial injury, and thrombogenic potential [16]. Metabolomic profiles further reveal disruptions in lipid metabolism [15], mitochondrial function, and amino acid processing [83]. When examined jointly, these molecular layers converge on pathways implicated in vascular dysfunction and cardiometabolic disease and highlight variation in susceptibility shaped by socioeconomic and built environments [15, 16, 83, 84]. Incorporating a lifecourse perspective emphasizes how early-life exposures leave lasting molecular imprints, supporting the development of precision environmental cardiology approaches that enhance risk stratification and inform targeted prevention efforts.

Methodological Advances: Deep Learning and Other AI

Rapid advances in deep learning and other artificial intelligence (AI) techniques are creating new opportunities to strengthen and integrate the global evidence base linking environmental risk factors, such as air and water pollution, noise, and heat stress, to CVD. However, analyzing the exposome and its relationship to CVD is exceptionally complex, requiring integration of high-dimensional, time-varying, and spatially resolved data that capture the totality of lifetime environmental exposures rather than isolated factors [17, 85–87]. Traditional epidemiological models, which often assume linear relationships, are not well suited to address the strong correlations, nonlinear relationships, and mixture effects inherent in exposomic data, particularly given evidence that chemical pollution such as $PM_{2.5}$ can trigger systemic inflammation and oxidative stress, substantially increasing CVD morbidity. Integrating omics-based measures of the internal exposome with external environmental exposures poses additional challenges, including the alignment of temporal and spatial scales, the high dimensionality of molecular data, and the complexity of modeling joint associations with CVD risk. Persistent research gaps further hinder the operationalization of the PHE, as summarized in Table 2. These gaps include continued reliance on single-pollutant approaches, limited integration of built and social environments, insufficient characterization of molecular and endo-exposome pathways, inadequate life-course modeling, underutilization of flexible analytic methods, and challenges in translating exposomic evidence into effective policy.

To address these challenges, researchers are increasingly applying advanced machine-learning and deep-learning methodologies [88], including random forests [89], gradient-boosted decision trees, neural networks, and ensemble algorithms such as XGBoost, to improve exposure assessment and prediction of CVD events by detecting nonlinear patterns and synergistic pollutants effects [90]. Graph-theoretical approaches further characterize correlated pollutant clusters and exposure networks, while Exposome-Wide

Table 2 Summary of Key Research Gaps in Air Pollution and the Public Health Exposome

Domain	Persisting Gaps	Needed Advances
Environmental Mixtures	Focus on single pollutants; limited synergy models	Multi-exposure modeling, mixture toxicology
Contextual Factors	Limited integration of built/social environment	Multilevel exposure mapping; structural determinants
Molecular Integration	Incomplete endo-exposome signatures	Multi-omics, causal mediation
Lifecourse	Insufficient timing models	Window-specific susceptibility, cumulative burden
Methods	Linear models inadequate	ML/AI, graph analytics, high-resolution sensing
Policy Translation	Evidence–policy gap	Targeted public policy interventions

Association Studies (ExWAS) and federated learning expand the capacity to examine diverse exposures across decentralized datasets [91]. Concurrently, wearable sensors, personal air monitors, GPS-enabled technologies, and machine vision technologies generate real-time, individualized, and street-level exposure data to support fine-grained spatiotemporal analytics [92]. Collectively, these innovations are advancing an integrated, systems-oriented exposome science capable of quantifying cumulative environmental stressors, integrating internal and external exposures, and identifying populations at heightened CVD risk.

Conclusion

The transition to a PHE framework represents an essential evolution for contemporary CVD epidemiology. Traditional exposure–outcome approaches inadequately capture the complex intersection of the environmental, social, and structural determinants that shape CVD vulnerability in real-world settings. Individuals are not exposed to fine particulate matter in isolation; exposures co-occur with extreme heat, neighborhood deprivation, psychosocial stress, and the enduring effects of structural inequity. Emerging evidence indicates that these co-existing stressors act synergistically and produce spatially patterned risks across the life course.

By organizing natural, built, social, and policy environments into a cohesive systems structure, the PHE provides a framework to integrate complex mixtures, multilevel contextual influences, and biological response pathways. It underscores that CVD risk is shaped as much by structural and policy determinants as by biological susceptibility. Advances in high-resolution spatial modeling, satellite-based monitoring, machine learning, and causal inference approaches can further enhance the precision of risk characterization and the prediction of environmental stressors and CVD. The integration of exposomic science with robust, evidence-based policies offers a promising path toward reducing pollution-attributable CVD and improving health outcome for all.

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Data Availability No datasets were generated or analysed during the current study.

Declarations

Competing Interests The authors declare no competing interests.
Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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