Air Pollution and Cardiovascular Health: Mechanisms, Vulnerabilities, and Genetic Factors

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KEYWORDS
air pollution, cardiovascular health, genetic susceptibility, inflammation, oxidative stress, precision health, vulnerable populations.
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ABSTRACT:
Air pollution is a major environmental risk factor contributing to the global burden of cardiovascular diseases (CVDs) such as ischemic heart disease, hypertension, and stroke. This review examines how pollutants like particulate matter ($PM_{2.5}$), nitrogen dioxide (NO_2), ozone (O_3), sulfur dioxide (SO_2), and carbon monoxide (CO) impact cardiovascular health through mechanisms such as oxidative stress, systemic inflammation, and endothelial dysfunction. It emphasizes the role of genetic susceptibility in modulating responses to air pollution, particularly through polymorphisms in antioxidant and inflammatory pathways. The review suggests that precision health strategies, including genetic screening, could address disparities caused by genetic variability and environmental exposure. Incorporating these strategies into public health interventions could help identify vulnerable populations, such as the elderly or those with pre-existing conditions, and tailor interventions accordingly. This approach complements existing mitigation efforts like emission reductions and air quality standards. The integration of molecular mechanisms with public health practices highlights the urgent need for coordinated global policies to reduce the cardiovascular burden of air pollution and ensure equitable health solutions for all populations.

1. Introduction

Air pollution poses a serious risk to public health worldwide and is a major factor in the increased prevalence of cardiovascular diseases (CVDs), which remain the leading cause of death worldwide. Long-term exposure to pollutants such as fine particulate matter ($PM_{2.5}$), nitrogen dioxide (NO_2), and ozone (O_3) has been linked to adverse cardiovascular outcomes, including ischemic heart disease, stroke, and heart failure [1,2,3]. Recent studies have highlighted that **genetic susceptibility** plays a crucial role in modulating individual responses to these environmental exposures. Variations in genes related to oxidative stress, inflammation, and vascular repair mechanisms can enhance the severity of cardiovascular damage caused by air pollution, thereby exacerbating health disparities among populations [4,5].

This review aims to synthesize the latest evidence on **genetic susceptibility** and its role in the cardiovascular risks associated with air pollution. Given the growing evidence of genetic susceptibility to air pollution, the integration of **precision health** into public health strategies offers a timely and innovative approach to mitigating these risks. By incorporating both genetic factors and environmental exposures, precision health can lead to more personalized and effective public health interventions and policies [4,5,6]. This review uniquely integrates genetic variability with environmental risk assessments, providing a framework for implementing precision health strategies to address disparities in cardiovascular health caused by air pollution [4,5,6,7].

Moreover, it discusses how **elderly individuals**, those with **pre-existing cardiovascular conditions**, and populations living in **high-pollution areas** are disproportionately affected by the cardiovascular risks of air pollution. The review also explores intervention strategies, such as **low-emission zones** and **personalized health monitoring**, to reduce the cardiovascular burden of air pollution [8,9].

While extensive research has documented the cardiovascular effects of air pollution, much of the existing literature has focused primarily on environmental exposures without considering the role of genetic susceptibility [1,2,3,10,11,12]. Recent studies suggest that genetic variations in antioxidant and inflammatory pathways modulate individual responses to pollutants. Still, these findings have not been sufficiently integrated into public health policies or intervention strategies [4,5,6,7]. This review aims to fill this gap by synthesizing current evidence on gene-environment interactions and highlighting how precision health strategies, including genetic screening, could be employed to reduce disparities caused by environmental exposures.
This review emphasizes the interplay between genetics and environmental factors, highlighting the transformative potential of precision health strategies in shaping public health policy and practice, particularly for at-risk communities.

2. Methods

This review synthesizes evidence from studies published between 2015 and 2024 on the cardiovascular effects of air pollution, focusing on pollutants such as $PM_{2.5}$, NO_2, and O_3. Systematic searches were conducted across databases including PubMed, Scopus, and Web of Science, using keywords like "air pollution," "cardiovascular diseases," "genetic susceptibility," and "oxidative stress." Studies were selected based on their relevance, quality, and focus on understanding the interaction between genetic factors and environmental exposures. Meta-analyses and studies that explored **genetic susceptibility** about cardiovascular outcomes due to air pollution were prioritized to highlight the novelty of gene-environment interactions.

3. Review

3.1. Air pollutants and Sources

The ecology suffers from human-induced contamination of the soil, air, and water. Although society, technology, and the provision of many services saw significant advancements during the industrial revolution, it also produced a significant amount of airborne pollutants that are harmful to human health. The global issue of environmental contamination is unquestionably considered a complex public health issue [10,13,14].

Any substance that tampers with the qualities of the atmosphere and contaminates the indoor or outdoor environment is considered air pollution, whether it be chemical, physical, or biological. Automobiles, manufacturing, home combustion appliances, and forest fires are common sources of air pollution [10,13,14]. The primary causes of outdoor air pollution are human activities like industrial emissions, road traffic, residential heating, shipping, air traffic, construction, agricultural activities, war, and fire accidents, in addition to natural disasters like earthquakes, tsunamis, volcanic eruptions, spontaneous forest fires, and abnormally high temperatures. The primary causes of indoor air pollution are smoking, building materials, air conditioning, heating, lighting, using air fresheners or housecleaning products, and cooking with fuel such as coal or wood [10,13,14].

Particulate matter ($PM_{2.5}$), nitrogen dioxide (NO_2), ozone (O_3), sulfur dioxide (SO_2), and carbon monoxide (CO) are among the many dangerous pollutants that are included in air pollution and represent serious health hazards to the general public. These pollutants vary in their sources and mechanisms of action, with **$PM_{2.5}$** and **NO_2** contributing to systemic inflammation and endothelial dysfunction, while **CO** induces tissue hypoxia by forming carboxyhemoglobin, reducing oxygen delivery to vital organs. Each pollutant's distinct properties and mechanisms necessitate tailored mitigation strategies to reduce their cardiovascular burden [13,14].

Size-based particulate matter penetrates deeply into lung tissues, whereas nitrogen dioxide and ozone irritate airways and trigger inflammatory reactions. Both carbon monoxide and sulfur dioxide, which come from automobile emissions and industrial operations, respectively, have a major impact on respiratory health. Together, these contaminants significantly impair human health by causing a variety of respiratory issues and cardiovascular events [13,14].

3.2. Factors contributing to the severity or level of air pollution

The degree or severity of air pollution has a major effect on human health, especially on the cardiovascular systems. Elevated air pollution levels are linked to a higher risk of cardiovascular illnesses and other health problems [13,14,15].

This is a brief synopsis of the variables that contribute to the intensity or degree of air pollution:

3.2.1. Outdoor air pollution

Emissions from Combustion Sources (the burning of fossil fuels by industrial processes and transportation): There are numerous variables that can lead to a rise in outdoor air pollution. Waste management practices, including landfills and open burning of waste materials, emit pollutants. Agricultural practices, such as the use of pesticides and fertilizers, also contribute to air pollution. Additionally, deforestation and changes in land use, including forest fires, further exacerbate air quality issues. Energy Production: Power stations that burn fossil fuels emit pollutants such as nitrogen oxides and sulfur dioxide; Residential Heating and Cooking: Solid fuel combustion in homes results in air pollution both indoors and outdoors, **Volatile Organic Compounds (VOCs)** emitted from industrial processes, paints, and various sources contribute to environmental pollution. **Natural Sources** (Volcanic activity, wildfires, and biogenic emissions release pollutants into the atmosphere), **Climate Conditions** (Temperature inversions and other meteorological factors can trap pollutants), **Vehicle and Industrial Technologies** (Outdated technology in vehicles and industries can contribute to higher emissions), **Population Density and Urbanization** (Urban areas with high population density and industrial activities often experience elevated pollution levels), **Geographic Scope** (Topography: Mountainous areas, valleys, and wind patterns influence the dispersion and accumulation of pollutants, Meteorological Conditions: Climate zones, wind patterns, and temperature inversions impact pollution levels Proximity to Pollution Sources: Geographic location relative to industrial zones, highways, and pollution sources affects exposure) [15,16,17].

3.2.2. Indoor air pollution

Ventilation rates (inadequate ventilation un buildings causes indoor pollutants to accumulate) are among the factors that can exacerbate outdoor air pollution. **Building Design and Construction** (Pollutants can be trapped indoors by sealing and insulation techniques, **Fuel and Appliance Use** (Indoor pollution is caused by solid fuel use, combustion appliances, and poor venting), **Household chemicals**: Indoor air pollution is caused by volatile organic compounds (VOCs) found in paints, cleaning chemicals, and other items. **Smoking** (tobacco smoke lowers air quality by releasing toxic compounds indoors), **Mold and Moisture** (Mold development and indoor air pollution can result from excessive moisture and humid circumstances), **Practices for controlling pests** (using pesticides indoors without adequate ventilation can release hazardous chemicals), **Building Materials and Furniture** (Indoor pollution is caused by off-gassing from carpets, building materials, and furniture), **Occupant Behavior** (pollutants can be released indoors during cooking,

cleaning, and other activities), **Radon gas** is a naturally occurring radioactive gas that can penetrate homes and cause indoor air pollution [15,16,18,19].

3.3. Epidemiological evidence

A strong correlation between exposure to air pollution and a higher risk of cardiovascular illnesses (CVDs), such as ischemic heart disease, stroke, hypertension, and heart failure, has been repeatedly shown by several epidemiological studies. Of particular concern is **fine particulate matter ($PM_{2.5}$)**, which has been strongly linked to an elevated risk of heart attacks, strokes, and high blood pressure (Brook et al., 2010). Long-term exposure to pollutants such as **$PM_{2.5}$**, **NO_2**, **O_3**, **SO_2**, and **carbon monoxide (CO)** is associated with increased cardiovascular morbidity and mortality (Miller et al., 2020). **Carbon monoxide**, in particular, reduces the oxygen-carrying capacity of blood and impairs vascular function, contributing to myocardial infarction, arrhythmias, and other cardiovascular conditions [12,13,14].

The connection between ambient air pollution and cardiovascular diseases (CVDs) has been the subject of extensive research in recent years [18,19]. The epidemiological evidence currently available linking ambient air pollution and CVDs. De Bont evaluated the strength and caliber of the evidence. The outcomes that were most frequently studied among the 56 reviews that were included were morbidity, all-cause CVD death, and stroke (22 studies) [19]. There is a direct correlation between higher levels of ambient air pollution exposure, both short- and long-term, and the greatest rates of cardiovascular disease (CVD) mortality and morbidity, stroke, blood pressure, and ischemic heart disease (IHD). There is evidence linking short-term exposure to nitrogen oxides (NOx), particulate matter <2.5 μm (PM2.5), and particulate matter <10 μm (PM10) to an increased risk of stroke (both fatal and nonfatal), hypertension, and myocardial infarction (MI) [1,19]. Elevated atherosclerosis, MI incidents, hypertension, stroke occurrences, and stroke mortality have all been connected to prolonged exposure to PM2.5. Studies on other CVD-related outcomes, like arrhythmias, atrial fibrillation, or heart failure, have been conducted, although their findings have mostly been positive statistical correlations [1,19].

Exposure to pollution results in a range of diseases and fatalities. Cardiovascular disease is the cause of more than 60% of instances. These are the primary causes of both death and disability. Compared to metabolic, behavioral, and tobacco-related risk factors, environmental variables are responsible for a greater proportion of deaths from cardiovascular disease. The risk of cardiovascular disease is increased by airborne particulate matter, depending on its size, that is disseminated in the atmosphere. Elemental carbon, PM2.5, and PM10, as well as nitrogen oxide (NO2), have all been linked to heart attacks, variations in blood pressure [19,20,21].

Recent research suggests that **genetic susceptibility** plays a critical role in how individuals respond to these pollutants. **Genetic polymorphisms** in **antioxidant genes**, such as **superoxide dismutase (SOD)**, and in **inflammatory genes** like **TNF-α** can exacerbate the cardiovascular effects of air pollution, leading to increased risk of heart disease, stroke, and hypertension (Xie et al., 2022; Tan et al., 2021, Zhang et al., 2021). These pollutants, in combination with **genetic factors**, significantly impair public health by causing a variety of respiratory issues and cardiovascular events. Pollutants such as **NOx**, **$PM_{2.5}$**, and **PM_{10}** increased cardiovascular events like **stroke** and **myocardial infarction** has also highlighted the need for personalized health approaches based on **genetic susceptibility** (De Bont et al., 2020) [19,20,21].

3.4. Mechanisms of Action

The cardiovascular effects of air pollution are mediated by several interconnected mechanisms, including **oxidative stress**, **inflammatory activation**, and **endothelial dysfunction**. **Oxidative stress** results from the overproduction of reactive oxygen species (ROS), which damage endothelial cells and promote atherosclerosis. Similarly, **inflammation** occurs due to the upregulation of pro-inflammatory cytokines like TNF-α and IL-6, further exacerbating vascular injury. Additionally, air pollution disrupts **endothelial function**, contributing to blood vessel constriction, elevated blood pressure, and decreased blood flow. These mechanisms, along with autonomic dysfunction, heighten the risk of cardiovascular diseases (CVDs) like heart failure, ischemic heart disease, and stroke. The **genetic susceptibility** of individuals plays a key role, as polymorphisms in genes related to oxidative stress and inflammation, such as **Nrf2**, can increase vulnerability to these adverse effects. Prolonged exposure to pollutants like $PM_{2.5}$ and NO_2 thus exacerbates CVD outcomes, leading to increased morbidity and mortality in vulnerable populations [22,23,24].

Many intricate pathophysiological mechanisms link air pollution to a higher risk of cardiovascular diseases (CVD). Though the exact pathways are still unclear, a great deal of research has identified several significant ones that connect exposure to air pollution to CVD [19,20,21]. These mechanisms include:

Inflammation: The body can get inflamed by several gases, specifically fine particulate matter (PM2.5) and ozone (O3). Atherosclerosis, or the buildup of plaque in the arteries, is a major risk factor for CVD and can be made worse by blood vessel inflammation [3,23,24,25].

Oxidative Stress: The body may experience oxidative stress as a result of air pollution. An imbalance between the body's capacity to eliminate hazardous reactive oxygen species (ROS) and the generation of these molecules can lead to oxidative stress. This oxidative stress can lead to inflammation, damage blood vessel walls, and hasten the onset of CVD [3,23,24,25].

Endothelial Dysfunction: Air pollution exposure can lead to endothelial dysfunction, which affects the blood vessel's inner lining. Because endothelial dysfunction can result in blood vessel constriction, elevated blood pressure, and decreased blood flow, it is an important early event in the development of atherosclerosis [26,27,28].

Autonomic Nervous System Imbalance: The autonomic nervous system, which controls blood pressure and heart rate, can be impacted by air pollution. Pollution-induced changes in this system can increase the risk of arrhythmias (abnormal heart rhythms) and other CVD-related complications [28,29].

Blood Coagulation and Thrombosis: There is a correlation between increased blood coagulation and the development of thrombosis with exposure to air pollution. Due to thrombosis, or the formation of clots within blood arteries, this may raise the risk of heart attacks and strokes [30,31].

Blood Pressure Elevation: Acute and long-term elevations in blood pressure have been linked to air pollution, namely PM2.5. The cardiovascular system may be strained by this blood pressure rise, which also raises the possibility of hypertension, a significant risk factor for CVD [32,33].

Accelerated Atherosclerosis: Prolonged exposure to air pollution might hasten the artery-narrowing process of atherosclerosis, raising the risk of heart attacks and strokes [22,34].

Impaired Cardiac Function: It has been shown that being around air pollution increases the risk of cardiac arrhythmias and decreases heart rate variability, both of which compromise cardiac function. Sudden cardiac events may become more likely as a result of these impacts [35,36,37].

Systemic Effects: Air pollution affects not only the respiratory system but the entire body. This entails the release of substances like pro-inflammatory cytokines that can have an impact on the cardiovascular system [12,38].

It's vital to remember that different systems may work in different ways based on individual sensitivity, the kind and makeup of air pollutants, and the length and intensity of exposure. In addition, the risk of cardiovascular illnesses might be further increased by the combined effects of many contaminants and other risk factors (such as food and smoking). Reducing exposure to air pollution and addressing its sources remain essential public health goals in order to mitigate these detrimental cardiovascular effects [20,39].

3.5. Effects on specific cardiovascular system

All-cause CVD mortality and morbidity. Prolonged exposure to air pollution, including fine particulate matter (PM2.5) and ground-level ozone (O3), has been associated with heart-related death. Heart attacks, strokes, heart failure, and other cardiovascular conditions are included in this category of fatalities. Oxidative stress, inflammation, and the advancement of underlying cardiovascular illnesses are some of the elements at play [24,40,41].

In addition to raising the chance of dying from cardiovascular disease, air pollution also raises rates of morbidity. High exposure to air pollution increases the risk of non-fatal cardiovascular events, including angina (chest discomfort), heart attacks, strokes, and hospitalizations related to heart disease [24,40,41].

Ischemic heart disease and myocardial infarction. The body may experience oxidative stress and inflammation as a result of exposure to air pollutants, especially fine particulate matter (PM2.5) and ground-level ozone (O3). This could lead to the formation and rupture of arterial plaques, which could cause a heart attack [22,40,41].

Individuals who already have heart problems, such as congestive heart failure or coronary artery disease, are more likely to see an exacerbation of their symptoms when exposed to air pollution. Pollutants can strain the heart by reducing the availability of oxygen and increasing the burden on the heart [22,40,41].

Atherosclerosis and arterial stiffness. Atherosclerosis is the narrowing and hardening of arteries due to the accumulation of plaque, consisting of cholesterol, fat, calcium, and inflammatory cells. This narrowing reduces blood flow and can lead to the formation of blood clots [22,34].

Long-term exposure to air pollution, particularly fine particulate matter (PM2.5), might hasten atherosclerosis. Pollutants have the potential to damage the endothelium, the lining that coats blood vessels, and promote the accumulation of fatty deposits, which decreases the artery's flexibility and makes it more vulnerable to blockages [22,34].

Blood pressure and hypertension. Exposure to air pollution is linked to hypertension, or elevated blood pressure, which is a significant risk factor for ischemic heart disease. Because hypertension strains the heart more, heart disease is more likely to occur [32,33].

Heart failure. The development and aggravation of heart failure, a chronic cardiovascular disease characterized by a compromised heart's capacity to pump blood properly, can be attributed to air pollution [35,36,37]. Here's how air pollution is linked to heart failure:

1. **Inflammation and oxidative stress:** Ozone (O3) and fine particulate matter (PM2.5) are two types of air pollution that can put the body under oxidative stress and induce inflammation. These reactions can cause systemic inflammation, which can affect the heart and blood vessels. Prolonged inflammation and oxidative stress can damage the heart muscle and accelerate the development of heart failure.

2. **Worsening of pre-existing Conditions:** When exposed to air pollution, people who already have cardiovascular diseases such as hypertension and coronary artery disease are more likely to experience heart failure. Over time, air pollution can worsen these diseases and cause more damage to the heart muscle.
3. **Reduced oxygen supply:** Elevated air pollution, such as PM2.5, can lower the blood's ability to carry oxygen. This implies that in order to adequately supply oxygen to all of the body's tissues, including the heart muscle itself, the heart must beat stronger. Heart failure may eventually result from the heart's increased workload causing the heart's chambers to expand.
4. **Elevated blood pressure**: Air pollution is associated with elevated blood pressure (hypertension). Left ventricular hypertrophy, or the thickening of the left ventricle of the heart, can result from hypertension, which also increases the burden on the heart. Over time, this can impair the heart's ability to pump effectively and contribute to heart failure.
5. **Impaired endothelial function:** Air pollution can impair the function of the endothelial cells that line blood vessels. This endothelial dysfunction can lead to the constriction of blood vessels and reduction in blood flow to the heart muscle. Prolonged impaired endothelial function can contribute to heart failure.

6. **Arrhythmias:** Air pollution can disrupt the electrical signaling in the heart, leading to arrhythmias (irregular heart rhythms). Arrhythmias can reduce the heart's efficiency in pumping blood and increase the risk of heart failure [42,43].

Arrhythmias, atrial fibrillation, and cardiac arrest. Air pollution can cause arrhythmias, including atrial fibrillation, and may increase the risk of cardiac arrest through various mechanisms [42,43].
In particular, research on atrial fibrillation has demonstrated a connection between an increased risk of atrial fibrillation and exposure to air pollution. A common kind of arrhythmia called atrial fibrillation is characterized by fast and irregular heartbeats in the atria, the heart's upper chambers. The association between air pollution and atrial fibrillation may be due to a variety of causes, including inflammation, oxidative stress, dysregulation of the autonomic nervous system, and endothelial dysfunction [42,43].
Although there is no direct link between air pollution and cardiac arrest, the increased risk of arrhythmias caused by pollution can lead to cardiac arrest, particularly in people who already have heart problems. Cardiac arrest occurs when the heart's electrical activity becomes chaotic, leading to a sudden loss of effective blood circulation. Air pollution's impact on the heart's electrical system can play a role in triggering these life-threatening events [42,43].
Exacerbation of pre-existing cardiovascular conditions. Cardiovascular diseases can get worse due to air pollution. The negative consequences of air pollution are more likely to affect people who have heart disease, hypertension, or other cardiovascular disease risk factors. It may intensify heart failure symptoms or cause heart attacks [19,22].
Reduced exercise tolerance. Air pollution can reduce an individual's exercise capacity and tolerance. This can discourage physical activity, which is essential for cardiovascular health [44].
Reduced life expectancy. Prolonged exposure to air pollution can reduce life expectancy, with a portion of this reduction attributed to cardiovascular diseases [45].

3.6. Introduction to Vulnerability:

The differential effects of air pollution on cardiovascular health underscore the need to address the varying susceptibilities of specific popu-lations. Vulnerability arises from a combination of biological, environmental, social, and genetic factors, making targeted interventions es -sential to reduce health disparities [46,47,48].

3.6.1. Prenatal age (Unborn Babies and Pregnant Women).

Exposure to air pollution during pregnancy poses risks to both the fetus and the mother. Adverse outcomes, such as low birth weight, preterm birth, congenital heart defects, and impaired lung development, are linked to prenatal exposure to pollutants like $PM_{2.5}$ and NO_2. Furthermore, maternal immune dysregulation caused by pollutants has been associated with preeclampsia, gestational diabetes mellitus (GDM), and fetal growth restriction, highlighting the long-term implications for cardiovascular and overall health [49,50,51].

3.6.2. Children.

Children's developing cardiovascular and respiratory systems are particularly sensitive to environmental pollutants. Early-life exposure to $PM_{2.5}$, O_3, and NO_2 increases lifetime risks for hypertension, ischemic heart disease, and other cardiovascular diseases. Additionally, long-term exposure in childhood has been linked to reduced lung function, chronic inflammation, and an increased likelihood of developing cardiovascular comorbidities later in life [48,49,52].

3.6.3. The elderly.

Aging individuals often have compromised immune systems and reduced physiological reserves, making them more susceptible to the cardiovascular effects of air pollution. Prolonged exposure to pollutants exacerbates conditions such as atherosclerosis, arrhythmias, and heart failure, increasing morbidity and mortality among the elderly. Cardiovascular diseases are more common in older persons and can be made worse by exposure to air pollution [19,22].

3.6.4. Individuals with pre-existing health conditions.

People with pre-existing health conditions, including cardiovascular disorders (e.g., coronary artery disease, hypertension), diabetes, respiratory diseases (e.g., asthma, COPD), and obesity, experience heightened vulnerability. Air pollution exacerbates these conditions through inflammatory responses and oxidative stress, further compromising their health [20,53].

3.6.5. Low socioeconomic groups.

Populations in low-income areas often face disproportionate exposure to pollutants due to proximity to industrial zones, congested traffic, inadequate housing, lack of access to green spaces, and inadequate means for preventative actions.. Limited access to healthcare compounds their vulnerability, making it challenging to manage or mitigate the cardiovascular risks associated with air pollution [54,55].

3.6.6. Occupational groups, and outdoor workers.

Workers in industries such as construction, agriculture, and traffic control face prolonged exposure to pollutants like $PM_{2.5}$ and NO_2. Occupational exposure significantly increases the risk of cardiovascular conditions, including hypertension and heart disease, emphasizing the need for protective measures in these environments [56,57].

3.6.7. Athletes and outdoor enthusiasts.

Strenuous physical activity in polluted environments elevates cardiovascular risks. Exercise increases the inhalation of pollutants, which can impair lung function, exacerbate respiratory symptoms, and trigger cardiovascular events such as arrhythmias and myocardial infarction [58,59].

3.6.8. Communities near pollution sources.

Living near industrial complexes, coal-fired power plants, and highways exposes communities to higher concentrations of pollutants. Due to prolonged exposure to pollution, these populations often experience higher rates of respiratory and cardiovascular diseases due to chronic exposure [60,61].

3.6.9. Urban dwellers.

Urban areas are hotspots for air pollution due to vehicular emissions, industrial activity, and high population density. Urban residents face elevated risks of developing cardiovascular conditions linked to chronic exposure to pollutants such as $PM_{2.5}$ and NO_2 [62,63].

3.6.10. Immune-compromised individuals.

Individuals undergoing chemotherapy, organ transplant recipients, and people living with HIV/AIDS are particularly vulnerable. Impaired immune systems exacerbate oxidative stress and inflammation caused by pollutants, increasing cardiovascular risk [64,65].

3.6.11. Genetic susceptibility.

Genetic factors significantly modulate individual vulnerability to the cardiovascular effects of air pollution. Polymorphisms in genes such as **endothelin-1** and **angiotensin-converting enzyme (ACE)** heighten susceptibility to hypertension and ischemic heart disease when exposed to pollutants like $PM_{2.5}$ and NO_2. Understanding genetic susceptibility enables the development of targeted interventions, such as personalized therapies, to mitigate health risks [66,67,68].

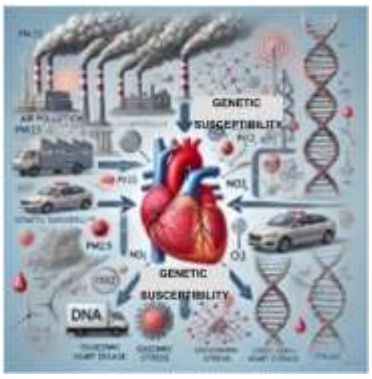

Figure 1. Air pollution, genetic susceptibility, and cardiovascular disease.

3.7. Genetic Factors:

Genetic susceptibility plays a crucial role in determining individual responses to air pollution, particularly in relation to oxidative stress and inflammatory pathways. Fifteen studies highlighted specific genetic polymorphisms in genes associated with oxidative stress (e.g., the NQO1 gene) and inflammation (e.g., TNF-α), which were found to enhance the cardiovascular risks associated with long-term exposure to air pollution. Variations in these genes may predispose individuals to more severe cardiovascular effects, particularly those who are already vulnerable due to age, pre-existing cardiovascular conditions, or high levels of environmental exposure.

3.8. Public Health Interventions Targeting Genetic Susceptibility:

Several studies emphasized the potential of precision health strategies, such as genetic screening, to improve public health interventions. By identifying individuals with specific genetic vulnerabilities, personalized interventions could be designed to mitigate the cardiovascular risks of air pollution.

For example, interventions could include targeted antioxidant therapies or lifestyle modifications for individuals with certain genetic variants. Public health policies, such as low-emission zones and personalized health monitoring, were also identified as key strategies to reduce exposure in at-risk populations, offering a more personalized approach to mitigating cardiovascular risks.

3.9. Holistic Interventions

Addressing vulnerabilities across life stages requires a **multifaceted approach**, including:

- **Policy interventions**: Enforcing stricter air quality standards and emission controls.
- **Community engagement**: Raising awareness about exposure risks and preventive measures.
- **Healthcare access**: Ensuring equitable access to medical care for at-risk populations.
- **Research on genetic susceptibility**: Advancing precision health strategies to tailor interventions for genetically vulnerable individuals.

Promoting environmental justice and protecting vulnerable populations are essential to safeguarding cardiovascular health and ensuring global health equity [69,70,71].

3.10. Mechanisms of impact

For a comprehensive understanding, it is necessary to clarify the manner in which air pollution adversely affects cardiovascular health. One of the main causes of inflammation and cellular damage is oxidative stress, which is brought on by an imbalance between antioxidant defenses and reactive oxygen species. Prolonged exposure to pollutants causes inflammation, a basic reaction to irritants and foreign invaders, to become dysregulated, which exacerbates respiratory symptoms and advances the course of disease. Damage to the tissue brought on by a series of oxidative stressors and inflammations reduces lung function and increases vulnerability to infections and diseases [22,72].

3.11. Mitigation and Intervention Strategies

Effective mitigation strategies include reducing industrial emissions, establishing low-emission zones, and improving air quality monitoring [73,74,75]. However, the integration of precision health approaches provides a new frontier for public health interventions. By incorporating genetic screening, individuals with increased susceptibility—such as those carrying polymorphisms in oxidative stress and inflammatory pathways—can be identified and targeted for personalized interventions, such as antioxidant therapies or anti-inflammatory drugs. Additionally, case studies of emission control policies demonstrate significant reductions in cardiovascular morbidity, emphasizing the role of policy-driven interventions in mitigating pollution-related health impacts [76].

4. Discussion

The findings of this review highlight the critical interplay between air pollution and cardiovascular health, mediated by mechanisms such as oxidative stress, systemic inflammation, and endothelial dysfunction. While considerable progress has been made in understanding these biological mechanisms, the variability in individual susceptibility due to genetic factors remains underexplored in current public health policies.

Our findings highlight the pivotal role of genetic susceptibility in modulating the cardiovascular risks associated with air pollution. While environmental factors such as particulate matter ($PM_{2.5}$)

and nitrogen dioxide (NO_2) have long been recognized as key contributors to cardiovascular disease, the genetic variability in individual responses to these pollutants has largely been overlooked in traditional risk assessments. By incorporating precision health approaches, such as genetic screening, public health interventions can be more targeted and effective, particularly for vulnerable populations with heightened genetic risk. This innovative approach could significantly reduce the cardiovascular burden of air pollution, bridging the gap between genetic research and public health practice.

Precision health offers a transformative approach to mitigating the cardiovascular effects of air pollution. By incorporating genetic data into public health strategies, we can tailor interventions to individuals' genetic profiles, which would not only improve efficacy but also reduce the overall cardiovascular burden of air pollution. For example, individuals with certain **polymorphisms in oxidative stress** and **inflammatory genes** may benefit from targeted antioxidant therapies or anti-inflammatory treatments. This approach can complement current environmental policies by making interventions more personalized and effective, ultimately reducing health disparities caused by air pollution exposure [77,78].

While substantial evidence links air pollution to cardiovascular diseases, many studies have predominantly focused on environmental exposures, often overlooking genetic susceptibility. A critical gap exists in understanding how genetic variations influence individual responses to pollutants. Notably, inconsistencies across studies regarding the specific genetic polymorphisms involved remain unexplored in depth. Additionally, while genetic factors such as polymorphisms in antioxidant and inflammatory pathways have shown potential to exacerbate the effects of air pollution, their integration into public health strategies remains minimal. This gap calls for more comprehensive studies that consider both genetic factors and environmental exposures to better target interventions for vulnerable populations.

The integration of **precision health** into public health interventions offers transformative potential in mitigating the cardiovascular risks associated with air pollution. Several countries have begun exploring the integration of genetic screening into public health strategies to address the cardiovascular effects of air pollution [77,78]. National programs like Genomics England demonstrate the feasibility of integrating large-scale genetic data into healthcare systems, providing valuable insights for advancing precision medicine. While not directly linked to air pollution reduction, these initiatives highlight the potential for leveraging genomic data to address disparities influenced by environmental exposures [79,80]. Similarly, the UCLA-Regeneron collaboration exemplifies efforts to integrate genetic profiling into healthcare systems, illustrating precision medicine's capacity to address health inequities [81,82]. Moving forward, large-scale programs like Genomics England and targeted initiatives in California offer a roadmap for incorporating genetic data into public health strategies for vulnerable populations [79,80,81,82].

Several countries have begun exploring the integration of genetic screening into public health strategies to address the cardiovascular effects of air pollution. For instance, the Genomic Health Alliance in the United Kingdom and targeted programs in California aim to identify individuals most at risk and tailor interventions to their genetic profiles. These initiatives highlight the promise of personalized health approaches but also underline challenges such as accessibility, cost, and ethical considerations.

Global initiatives, such as WHO's framework on air quality and health, provide essential guidelines for improving air quality and public health strategies, which can serve as platforms for developing more equitable and effective mitigation policies across countries [83]. Countries like the United Kingdom and California are already exploring how genetic screening can identify vulnerable

populations and guide tailored interventions. These examples illustrate the potential for precision health to complement traditional mitigation strategies by addressing disparities caused by genetic variability and environmental exposure.

However, challenges such as accessibility to genetic testing, ethical concerns, and cost must be addressed to ensure widespread adoption. Advancements in affordable sequencing technologies and community-based health initiatives offer potential solutions to reduce costs and improve access, particularly in resource-limited settings. Partnerships between global health organizations and national governments could accelerate the integration of genetic screening into primary healthcare systems.

Future studies should explore the cost-effectiveness of incorporating genetic screening into public health systems, particularly in low- and middle-income countries where both air pollution and cardiovascular disease burdens are highest. Additionally, research is needed to develop scalable frameworks that integrate genetic data with environmental health strategies, ensuring that these approaches are both accessible and equitable. For example, national programs like the UK's Genomics England have demonstrated the feasibility of large-scale genetic data integration, providing valuable lessons for other countries [79,80].

The translation of molecular insights into actionable public health interventions represents a critical frontier in addressing the global burden of air pollution. Collaborative efforts between researchers, policymakers, and healthcare providers will be essential to turn these insights into impactful solutions for at-risk populations.

Future research should focus on bridging the gap between molecular insights and public health applications, with an emphasis on developing scalable interventions that consider both genetic and environmental factors. For instance, partnerships between global health organizations and national governments could accelerate the integration of genetic screening into primary healthcare systems. Additionally, studies on the cost-effectiveness of genetic screening in public health systems are particularly needed in low- and middle-income countries, where both air pollution and cardiovascular disease burdens are highest. Such studies could inform policies that optimize resource allocation while maximizing health benefits for vulnerable populations. These steps will be critical to ensuring that the advances in genetic research are translated into actionable solutions for global health challenges.

5. Conclusions

This review underscores the urgent need for a multidisciplinary approach to addressing the cardiovascular burden of air pollution. By integrating knowledge of molecular mechanisms with genetic susceptibility, we can develop more effective public health interventions tailored to at-risk populations. Policies must move beyond one-size-fits-all approaches and incorporate **precision health strategies** that address the disparities in individual vulnerability caused by genetic and environmental interactions.

Moreover, the success of emission control policies in reducing CVD-related outcomes highlights the importance of continued investment in air quality improvements at both local and global levels. Cooperation amongst various sectors is crucial, including community involvement, environmental policy, and healthcare, to mitigate health effects of air pollution. Future initiatives should prioritize equitable access to interventions, particularly for vulnerable populations, while advancing research to translate genetic findings into actionable public health solutions.

Addressing these challenges will require global collaboration across policymakers, researchers, and healthcare providers. By prioritizing the integration of genetic screening into public health frameworks, particularly in regions with high cardiovascular burdens, policymakers can ensure that advances in genetic research translate into impactful and equitable health outcomes.

6. Future Directions

Future studies should explore the cost-effectiveness of incorporating genetic screening into public health systems, particularly in low- and middle-income countries, where both air pollution and cardiovascular disease burdens are highest. While large-scale genomic initiatives like Genomics England provide important insights, their cost-effectiveness and accessibility in low-resource settings need further investigation. Additionally, research is needed to develop scalable frameworks that integrate genetic data with environmental health strategies, ensuring that these approaches are both accessible and equitable. Governments should prioritize collaborations between health systems and genomics initiatives to make these technologies affordable and accessible, particularly for high-risk populations.

Investigating preventive measures tailored to genetic susceptibility—such as antioxidant or anti-inflammatory therapies—could complement existing air quality improvement efforts. Additionally, interdisciplinary collaboration and advancements in genomic technologies, such as AI-based genetic analysis, are essential to develop scalable, equitable solutions that reduce the cardiovascular burden of air pollution globally.

Author Contributions

Hari Krismanuel: Conceptualization, Resources, Methodology, Writing – original draft, Writing – review & editing, Validation, Supervision.

Publication Ethics Statement

This study complies with the ethical publishing standards of the International Journal of Environmental Research and Public Health (IJERPH). Author affirms that the manuscript is original, has not been published previously, and is not under consideration by another journal. The authors have adhered to ethical research and publication guidelines, including accurate reporting of data and acknowledgement of all contributors.

Research Ethics Statement

This research did not involve human or animal participants. Ethical considerations for secondary data analysis were followed, ensuring proper citation and compliance with copyright requirements.

Funding: None.

Institutional Review Board Statement

Ethics approval was not required for this article.

Data Availability Statement

The data associated with the articles included in this review are available in the original sources cited throughout the manuscript.

Acknowledgments
In this section, you can acknowledge any support given which is not covered by the author contribution or funding sections. This may include administrative and technical support, or donations in kind (e.g., materials used for experiments).

Conflicts of Interest
The author declares no conflict of interest.

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