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Reduction of environmental pollutants for prevention of cardiovascular disease

it's time to act

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CURRENT OPINION
Epidemiology and prevention

Reduction of environmental pollutants for prevention of cardiovascular disease: it's time to act

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Introduction

Cardiovascular disease (CVD) represents the result of underlying genetic predisposition and lifetime exposure to multiple environmental factors. The past century has seen a revolution in our understanding of the importance of modifiable risk factors such as diet, exercise, and smoking. Exposure to environmental pollutants, be it in the air, water, or physical environment, is increasingly recognized as a silent, yet important determinant of CVD.[1] The quote 'genetics loads the gun but the environment pulls the trigger', put forward by G.A. Bray and F. Collins, exemplifies the complex relationship between human disease and the environment. The cardiovascular system is highly vulnerable to a variety of environmental insults, including tobacco smoke, solvents, pesticides, and other inhaled or ingested pollutants, as well as extremes in noise and temperature. While our understanding of multiple environmental factors continues to evolve, it is estimated that environmental air pollution and noise pollution alone may contribute to a substantial burden attributable to environmental factors as we currently understand them. It is important to note that noise and air pollution can have many of the same sources such as heavy industry, road and aircraft vehicles. In a recent in-depth report, the European Commission acknowledged that the societal costs for the combination noise and air pollution are nearly 1 trillion Euros, while the costs for alcohol and smoking are considerably less (50–120 and 540 billion Euro, respectively, see https://ec.europa.eu/environment/integration/research/newsalert/pdf/air_noise_pollution_socioeconomic_status_links_IR13_en.pdf).

The World Health Organization (WHO) calculates that 12.6 million premature deaths per year are attributable to unhealthy environments, 8.2 million of which are due to non-communicable disease, with CVD (including stroke) being the largest contributor, accounting for nearly 5 million of these deaths.[2] Among all environmental pollutants, poor air quality is the most important risk factor, and ambient air pollution due to particulate matter <2.5 μm ($PM_{2.5}$) exposure ranks 5th among all global risk factors in 2015, leading to 4.2 million deaths annually as estimated by the Global Burden of Disease study.[3] Nine out of 10 people worldwide are exposed to ambient air pollutant levels above WHO guidelines (>10 μg/m).[3,4] Using a novel exposure-response hazard function (global estimate of exposure mortality model) to estimate global mortality attributable to air pollution, Burnett *et al.*[5] and Lelieveld *et al.*[6] found that around 9 million global premature deaths (790 000 excess deaths in Europe alone) were attributable to air pollution,[7] numbers that are well comparable to that of smoking.[6] These figures are substantially higher than those estimated by the WHO and Global Burden of Disease study.[2,3]

Ambient noise is the other omnipresent exposure with emerging data suggesting a large attributable burden of disability to this factor in many urban environments. In Western Europe, it is estimated that around 1.6 million healthy life years are lost every year due to noise. It is estimated that a large part of the European population is exposed to noise originating from road traffic at levels exceeding 55 decibels [dB(A), A-weighted decibel scale adapted to the human hearing frequencies]; 20% exposed to levels exceeding 65 dB(A) during the daytime; and 30% of the population is exposed to levels exceeding 55 dB(A) (see https://www.eea.europa.eu/publications/environmen

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tal-noise-in-europe). In this review, we will focus on the cardiovascular effects of ambient air pollution and noise pollution as prototypical environmental factors that provide important lessons to facilitate understanding of the outsize effects of the environment on susceptibility to CVD. The pathophysiology, epidemiology, mitigation measures, and future challenges for these two common yet pervasive environmental factors are discussed in detail.

In many parts of the world, a substantial portion of the urban population is exposed to road traffic noise at levels exceeding 55 dB(A).[8] In cities in Asia, the proportion of the population reaching L_{den} levels (day–evening–night level, i.e. the average sound pressure level measured over a 24 h period with adjustment for more detrimental health effects of nocturnal noise) of 60–64 dB is very high.[9] In contrast to the relatively straightforward classification of noise, air pollution is intrinsically complex and defy easy classification. From a regulatory perspective, 'criteria' air pollutants allow health-based and/or environmentally based guidelines for setting permissible levels.[10] These include carbon monoxide, lead, nitrogen oxides, ground-level ozone, particle pollution (often referred to as PM), and sulphur oxides. Particulate matter is categorized based on its aerodynamic diameter: ≤10 μm [thoracic particles (PM_{10})], ≤2.5 μm [fine particles ($PM_{2.5}$)], ≤0.1 μm [ultrafine particles (UFP)], and between 2.5 and 10 μm [coarse particles ($PM_{2.5–10}$)]. Although 'criteria' pollutants are regulated individually, it is anticipated that the effects of air pollution are driven by the complex interaction of particulate and gaseous components in mixtures and that smaller particles (e.g. UFP) are more detrimental then larger ones.

There is substantial spatial and temporal variation of both noise and air pollution. Traffic-related pollutants and noise often peaking during the late morning and evening rush hours. Gradients for both noise and air pollutants are also dependent upon meteorological conditions, including diurnal changes in vertical mixing height, wind speed, and temperature. In the case of noise, the gradients are substantial as the intensity of noise decreases exponentially with the distance from its source. The gradients for air pollution from their source may also differ depending upon the pollutant. Traffic factors, such as the speed, traffic load, etc., may also differentially affect noise and traffic-related air pollution. During traffic congestion, when traffic is at standstill or at lower engine speeds, noise levels may be lower, but emissions may be dramatically higher, contributing to marked surges in traffic-related air pollutants. In contrast, when traffic is moving well, noise levels may be higher, but emissions may be lower. Environmental factors such as road conditions, noise barriers, and surrounding buildings are well known to influence traffic noise but may not influence air pollution substantially.

The highly associated nature of traffic noise and air pollution makes it challenging to isolate their independent effects on cardiovascular events in epidemiological studies. A few studies have attempted to assess the independent contribution of noise from air pollution and vice versa. The results are, however, somewhat variable, with some studies demonstrating an independent effect of noise and/or air pollution on cardiovascular morbidity and mortality, while others find marked attenuation of effects after adjusting for the other. Whether noise and air pollution have differing, additive, synergistic, and/or confounding effects upon cardiovascular health is still incompletely understood. Also of great importance in all air pollution and noise exposure studies is the co-linearity of these risk factors to other confounders (e.g. lower socio-economic status, psychosocial stressors, other poorly understood environmental variables and adverse lifestyle factors) that often go hand-in-hand with pollutants.

Pathophysiology and epidemiology of noise and cardiovascular disease

Epidemiology

During the last decade, a number of epidemiological studies have investigated effects of transportation noise on risk for CVD. In 2018, a systematic review by WHO found that there was substantial evidence to conclude that road traffic noise increases the risk for ischaemic heart disease, with an 8% higher risk per 10 dB higher noise.[11] For stroke, the evidence was ranked as moderate, with only one study on incidence and four on mortality.[11] Subsequently, large population-based studies from Frankfurt, London, and Switzerland found road traffic noise to increase stroke incidence and/or mortality, especially ischaemic strokes,[12–14] whereas smaller cohort studies indicated no association.[15] Recently, road traffic noise has been found to increase the risk for other major CVD not evaluated by WHO, most importantly heart failure and atrial fibrillation.[14,16] Aircraft noise has also been associated with higher CVD incidence and mortality,[14,17] but due to a limited number of studies, the evidence is still rated low to moderate.[18]

Epidemiological studies have linked transportation noise with a number of major cardiovascular risk factors, most consistently obesity and diabetes.[19,20] Also, many studies investigated effects of noise on hypertension, and although a meta-analysis of 26 studies found that road traffic noise was associated with higher prevalence of hypertension,[11] studies on incidence are still few and inconsistent.

Ambient air pollution and traffic noise, especially from roads, are correlated and suspected of being associated with the same CVD, and therefore mutual adjustment is highly important. Most recent studies on noise and CVD adjust for air pollution and generally the results are found to be robust to the adjustment, suggesting that transportation noise is indeed an independent risk factor for CVD.[21]

Another noise source investigated in relation to CVD risk is occupational noise; an exposure mainly occurring during daytime. Most existing studies are cross-sectional, and results from a few prospective studies providing conflicting evidence, with some studies indicating an association with CVD,[22] whereas others finding no association,[23] stressing the need for more well-designed prospective studies.

Pathophysiology

According to the noise stress reaction model introduced by Babisch,[24] non-auditory health effects of noise have been demonstrated to activate a so-called 'indirect pathway', which in turn represents the cognitive perception of the sound, and its subsequent cortical activation is related to emotional responses such as annoyance and anger (reviewed in Ref. 25) This stress reaction chain can initiate physiological stress responses, involving the hypothalamus, the limbic system, and the autonomic nervous system with activation

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of the hypothalamus–pituitary–adrenal (HPA) axis and the sympathetic–adrenal–medulla axis, and is associated with an increase in heart rate and in levels of stress hormones (cortisol, adrenalin, and noradrenaline) enhanced platelet reactivity, vascular inflammation, and oxidative stress (see *Figure 1*). While the conscious experience with noise might be the primary source of stress reactions during daytime (for transportation and occupational noise), the subconscious biological response during night-time in sleeping subjects, at much lower transportation noise levels, is thought to play an important role in pathophysiology, particularly through disruption of sleep–wake cycle, diurnal variation, and perturbation of time periods critical for physiological and mental restoration. Recent human data provided a molecular proof of the important pathophysiological role of this 'indirect pathway' by identifying amygdalar activation (using ^{18}F-FDGPET/CT imaging) by transportation noise in 498 subjects, and its association with arterial inflammation and major adverse cardiovascular events.[27] These data are indeed consistent with animal experiments demonstrating an increased release of stress hormones (catecholamines and cortisol), higher blood pressure, endothelial dysfunction,[28] neuroinflammation, diminished neuronal nitric oxide synthase (nNOS) expression as well as cerebral oxidative stress in aircraft noise-exposed mice.[29] These changes were substantially more pronounced when noise exposure was applied during the sleep phase (reflecting night-time noise exposure) and was mostly prevented in mice with genetic deletion or pharmacological inhibition of the phagocytic NADPH oxidase (NOX-2).[29] These studies also revealed substantial changes in the gene regulatory network by noise exposure, especially within inflammatory, antioxidant defence, and circadian clock pathways (*Figure 1*).[28,29] The conclusions from these experiments are supportive of a role for shortened sleep duration and sleep fragmentation in cerebrovascular oxidative stress and endothelial dysfunction.

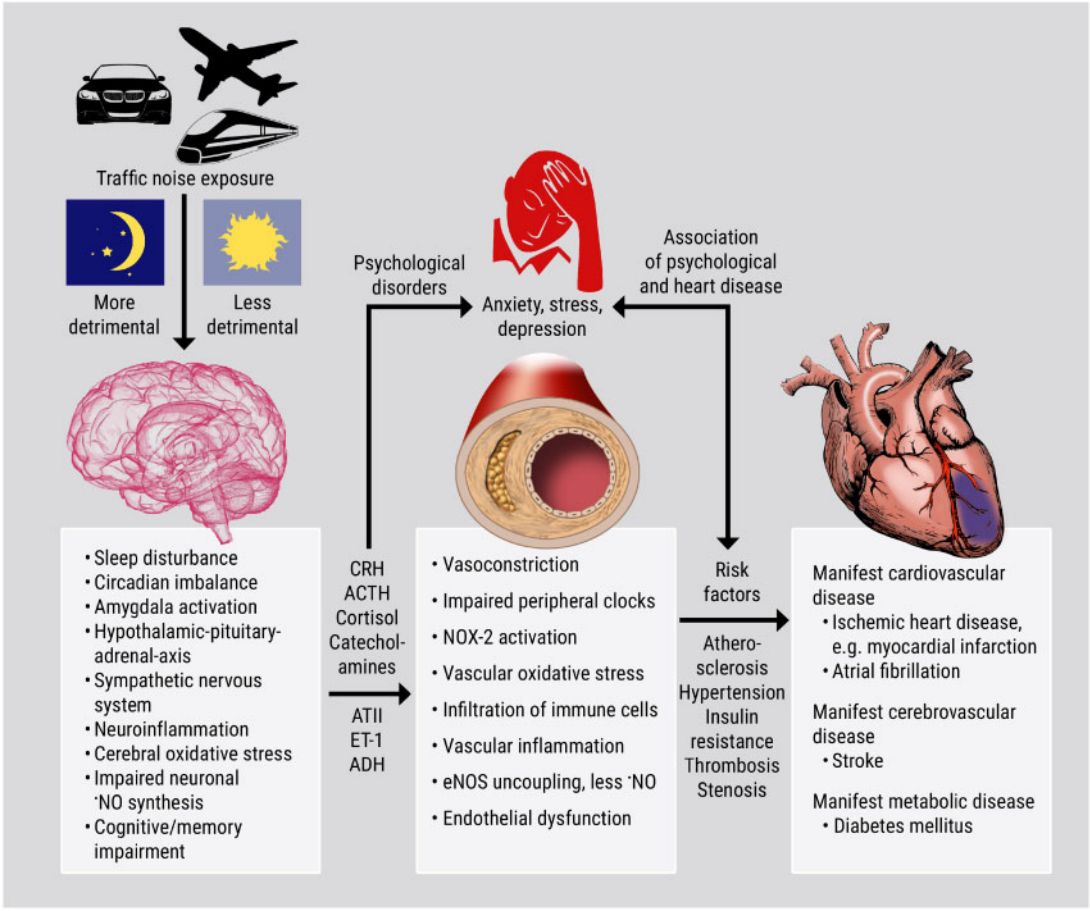

Figure 1 The key mechanisms of the adverse health effects of traffic noise exposure. Environmental noise exposure causes mental stress responses, a neuroinflammatory phenotype, and cognitive decline. This may lead to manifest psychological disorders and mental diseases or, via stress hormone release and induction of potent vasoconstrictors, to vascular dysfunction and damage. All of these mechanisms initiate cardio-metabolic risk factors that lead to manifest end organ damage. Of note, chronic cardio-metabolic diseases often are associated with psychological diseases and vice versa.[26] • ACTH, adrenocorticotropic hormone; ADH, antidiuretic hormone (vasopressin); ATII, angiotensin II; CRH, corticotropin-releasing hormone; eNOS, endothelial nitric oxide synthase; ET-1, endothelin-1;NO, nitric oxide; NOX-2, phagocytic NADPH oxidase (catalytic subunit).

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Likewise, we observed a significant degree of endothelial dysfunction, an increase in stress hormone release, blood pressure and a decrease in sleep quality in healthy subjects and patients with established coronary artery disease, in response to night-time aircraft noise (reviewed in Ref.[25]) Importantly, endothelial dysfunction was corrected by the antioxidant vitamin C indicating increased vascular oxidative stress in response to night-time aircraft noise exposure. The important role of oxidative stress and inflammation for noise-induced cardiovascular complications was also supported by changes of the plasma proteome, centred on redox, pro-thrombotic and proinflammatory pathways, in subjects exposed to train noise for one night [mean SPL 54 dB(A)].[30]

Pathophysiology and epidemiology of air pollution and cardiovascular disease

Since the publication of an American Heart Association Scientific Statement,[31] there has been a consistent stream of epidemiological and mechanistic evidence linking $PM_{2.5}$, the most frequently implicated air pollution component with CVD.[5,6] Mounting evidence suggests that health risks attributable to $PM_{2.5}$ persist even at low levels, below WHO air quality guidelines and European standards (annual levels <10 and <25 $\mu g/m^3$, respectively). Updated exposure-response dose curves suggest a robust supralinear concentration-response-curve for PM and CVD with no apparent safe threshold level.[32]

Epidemiology

Current estimates suggest air pollution is associated with around 9 million premature deaths, worldwide annually with ~40–60% of mortality attributed to cardiovascular causes.[5,33]Short-term exposure (over hours or days) is associated with increased risk for myocardial infarction, stroke, heart failure, arrhythmia, and sudden death by about 1–2% per 10 $\mu g/m^3$. Longer-term exposure over months or years, amplifies these risk associations, to 5–10% per 10 $\mu g/m^3$. Living in regions with poor air quality potentiates the atherosclerotic process and promotes the development of several chronic cardiometabolic conditions (e.g. diabetes, hypertension).

Although the strength of the association for criteria air pollutants is strongest for $PM_{2.5}$, there are data linking other pollutants such as nitrogen oxides (e.g. NO_2) and less consistently ozone (O_3) with cardiovascular events.[32] Pollutants from traffic and combustion sources are of high concern (due to high levels of ultrafine PM, toxicity of constituents, and penetration of pollutants systemically) although precise burden estimates have yet to be established for this source. Coarse PM_{10} air pollution from anthropogenic sources has been associated with cardiovascular disease although sources such as agricultural emissions and crustal material are less well studied.

Given the continuing links between $PM_{2.5}$ and adverse cardiovascular events, even at levels substantially below 10 $\mu g/m^3$, there is a need for a realistic lower limit that may strike the balance between what is reasonably possible and eliminating anthropogenic sources. It is important to keep in mind that complete elimination of all PM2.5 may not possible given that some $PM_{2.5}$ is natural. Calculations by Lelieveld *et al.*[33] of a complete phase-out of fossil fuel-related emissions (needed to achieve the 2°C climate change goal under the Paris Agreement) demonstrated a reduction in excess mortality rate of 3.61 million per year worldwide. The increase in mean life expectancy in Europe would be around 1.2 years indicating a tremendous health co-benefit from the phase-out of carbon dioxide emissions.

Pathophysiology

Mechanistic studies, using controlled exposure studies in humans and experimental models support a causal relationship between PM and CVD. Acute exposure to air pollutants induces rapid changes that include vasoconstriction, endothelial dysfunction, arterial stiffening, arrhythmia, exacerbation of cardiac ischaemia, increased blood coagulability, and decreased fibrinolytic capacity. Additionally, long-term exposure to PM accelerates the growth and vulnerability of atherosclerotic plaques.[34] A broad range of mechanisms accounts for pathophysiology at an organ and cellular level, with inflammation and oxidative stress playing key roles.[25] Additionally, several convincing pathways can account for the link between inhalation of pollutants and the cardiovascular system, including passage of inflammatory (and other) mediators into the circulation, direct passage of particles (or their constituents) into circulation, imbalance of autonomic nervous system activity, and changes to central control of endocrine systems. The contribution of individual pathways will depend on type of pollutant, the exposure (dose and duration), specific cardiovascular endpoints, and the health status of individual. Finally, the cardiovascular effects of pollutants occur in both healthy individuals and those with pre-existing cardiorespiratory disease, suggesting a potential contributory role on the induction, progression, and exacerbation of CVD.[32,34]

Mitigation strategies

Noise mitigation

In 2020, the European Environment Agency concluded that more than 20% of the EU population live with road traffic noise levels that are harmful to health and that this proportion is likely to increase in the future (see https://www.eea.europa.eu/publications/environmental-noise-in-europe [last accessed 17/09/2020]). European Environment Agency also estimated that in EU, 22 million live with high railway noise and 4 million with high aircraft noise.

The authorities can use different strategies to reduce levels of traffic noise (*Table 1*). For road traffic, the sound generated by the contact between the tires and the pavement is the dominant noise source, at speeds above 35 km/h for cars and above 60 km/h for trucks. Therefore, changing to electric cars will result in only minor reductions in road traffic noise. Generally applied strategies for reducing road traffic noise include noise barriers in densely populated areas, applying quiet road surfaces, and reducing speed, especially during night-time. Furthermore, there is a great potential in developing and using low-noise tires. As many of these mitigation methods result in only relatively small changes in noise (*Table 1*), a combination of different methods is important in highly exposed areas. For aircraft noise, mitigation strategies include to minimizing overlapping of air

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Table 1 Mitigation methods resulting in reduction in road traffic noise

Change in noise	Perceived change	Methods for noise reduction
1 dB	A very small change.	Reduce speed by 10 km/h
		Replace all cars with electric cars
		Shift traffic from night-time to day-time period
		Remove 25% of the traffic
3 dB	An audible, but small change.	Reduce speed by 30 km/h
		Apply quiet road surfaces
		Use low-noise emitting tires
		Remove 50% of the traffic
5 dB	A substantial change.	Build noise barriers
		Remove 65% of traffic
10 dB	A large change. Sounds like a halving of the sound.	Build high noise barriers
		Remove 90% of the traffic
		Sound-reducing windows

traffic routes and housing zones, introduction of night bans, and implementation of continuous descent arrivals, which require the aircraft to approach on steeper descents with lower, less variable throttle settings. For railway noise, replacing cast-iron block breaks with composite material, grinding of railway tracks and night bans, are among the preferred strategies for reducing noise. Lastly, installing sound-reducing windows and/or orientation of the bedroom towards the quiet side of the residence can reduce noise exposure.

Air pollution mitigation

Although it is widely recognized that legislation, policies, regulation, and technology, coupled with enforcement, are critical to reduction of air pollution levels, the political momentum required to accomplish this globally is currently limited. Thus, personal measures to mitigate risk take on a much greater importance. The current experience and lessons learned with personal protective equipment and mitigation in reducing exposure to SARS-CoV2 are highly reminiscent of their use in combating air pollution, albeit the protection provided varies depending on the pollutant.[35] Mitigation measures must be affordable and broadly applicable to the population, and the level of protection provided should match the risk of population that is being exposed (*Figure 2*). The latter would necessitate an understanding of the health risk of the patient/community and degree of exposure. The need and urgency plus intensity of any recommended intervention also need to be weighed against their potential benefits vs. risks for each individual (e.g. wasted effort, resources, unnecessary concern, or possible complacency of the user). Although no intervention to reduce air pollution exposure has as yet been shown to reduce cardiovascular events, the consistent link between increased levels of $PM_{2.5}$ and cardiovascular events, evidence for measures in lowering $PM_{2.5}$ levels, and the impact of several mitigation strategies in improving surrogate markers are highly suggestive that interventions could be correspondingly impactful in reducing cardiovascular events.

Current approaches to mitigate air pollution and their impact have been previously reviewed and can be broadly classified into: (i) Active personal exposure mitigation with home air cleaning and personal equipment (*Table 2*); (ii) Modification of human behaviour to reduce passive exposures; (iii) Pharmacologic approaches.[32] Studies on N95 respirator under ambient $PM_{2.5}$ exposure conditions at both high and low levels of exposures over a few hours have shown to reduce systolic blood pressure and improve heart rate variability.[32,36] In the only trial comparing exposure mitigation to both noise and air pollution, individual reduction of air pollution or noise with a respirator or noise-cancelling headphones, respectively, did not alter blood pressure. Heart rate variability indices were, however, variably improved with either intervention.[37] Face masks and procedural masks (e.g. surgical masks) are widely available but are not effective in filtering $PM_{2.5}$, especially if poorly fitting or worn during high activity,[38] and therefore cannot be recommended for widespread usage if N95 respirators are available. Closing car windows, air-conditioning, and cabin air filters represent approaches that could be important in those who are susceptible, but only in those spending large amounts of time in transportation microenvironments. Behavioural strategies such as air pollution avoidance by changing travel routes, staying indoors/closing windows, and modification of activity can help limit air pollution exposure, but unintended consequences in some instances have the potential of offsetting benefit. An example is closing windows to limit outdoor exposure but increasing the hazard for indoor air pollutants or limiting outdoor recreation/exercise to mitigate ambient exposures. The latter scenario of limiting outdoor exposure brings up some very practical questions about the risk/benefit of loss of cardiovascular benefits of exercise vs. potential gain from benefits secondary to air pollution mitigation. Health impact modelling and epidemiologic studies have demonstrated that the benefits of aerobic exercise nearly always exceed the risk of air pollution exposure across a range of concentrations, and for long durations of exercise for normal individuals (>75 min). Based on current evidence, guiding healthy people to avoid outdoor activity in areas with high $PM_{2.5}$ pollution has the potential to produce greater harm than benefit, given the low absolute risk for cardiovascular or respiratory events. On the other hand, advising patients with pre-established CVD to continue

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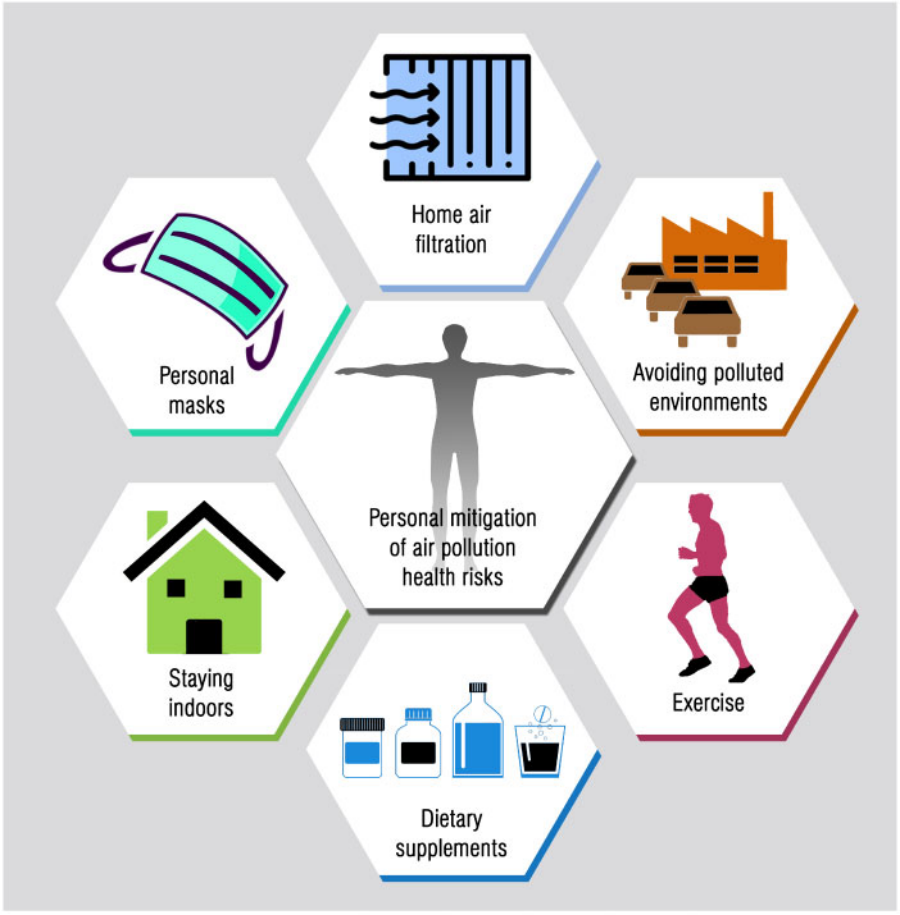

Figure 2 Mitigation measures to reduce air pollution exposure.

to remain >400 m away from major roadways to avoid exposure to traffic pollutants is a reasonable measure, despite the current lack of strong evidentiary support.

Although a variety of over the counter drugs and medications have been shown to mitigate association between air pollution and surrogates, almost none can be recommended to protect against air pollution mediated adverse health effects at this time. However, the use of medications for primary and secondary prevention of CHD should be encouraged if indicated for other reasons.

Housing and urban design to improve cardiovascular health

Two-third of the European population live in urban areas and this number continues to grow. A recent Statement on Air Quality Policy has discussed aspects in the built environment that may be targeted in order to reduce exposures to $PM_{2.5}$ (in press 2020). Briefly, built environment features may directly or indirectly modify adverse cardiovascular effects of air pollution through the indoor living environment, green spaces, roads, utilities, and transportation infrastructure. The design of communities has the potential of impacting exposures, by affecting the continuum of human existence across indoor living, commuting, working, and recreation (*Figure 3*). The layout of roads, sidewalks, green spaces, and the availability of cheap public transportation can affect travel behaviour and can help alleviate air quality.[39] Communities with proximity and compactness have been associated with higher life expectancy, improved air quality, and health.[40,41] Green environments can improve air quality, encourage physical activity, and promote social interactions, ultimately improving cardiovascular health. Indeed, there is evidence to support a protective association of green spaces on PM-associated CVD.[42,43] All-cause and ischaemic heart disease mortality related to income deprivation has been shown to be lower in populations who live in the greenest areas, vs. those who have less exposure to green space.[44] Recently, Giles-Corti identified eight integrated regional and local interventions that, when combined, encourage walking, cycling and public transport use, while reducing private motor vehicle use.[45] These eight interventions are directed to reduce traffic exposure, to reduce air pollution and noise, and to reduce the important public health issue loneliness and social isolation, to improve the safety from crime, to reduce physical inactivity and prolonged sitting, and to prevent the consumption of unhealthy diets.[45]

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Table 2 Personal active mitigation methods to reduce air pollution exposure

Type of intervention	Efficacy in reducing exposure	Considerations for use	Evidence in reducing surrogate outcomes
Personal air purifying respirators (reducing solid but not gaseous air pollutants).			
N95 respirators	Highly effective in reducing $PM_{2.5}$. Removes >95% inhaled particles at 0.3 μm in size	Fit and use frequency are key determinants of efficacy. A valve or microventilator fan may reduce humidity and enhance comfort. Uncomfortable to wear over long periods	Randomized controlled clinical trials over short durations (typically up to 48 h) with evidence for reducing blood pressure and improving heart rate variability indices.
Surgical and cloth masks	Not uniformly effective in reducing PM2.5 exposure	While few studies suggest that these may reduce exposure, highly variable in efficacy.	Not recommended owing to variability in reducing exposure to particles
Portable air cleaners (PAC)			
Portable devices with high efficiency-particulate airfilter (HEPA) Filters. Electrostatic PACs additionally ionize particles	Designed to clean air in a small area. Effective in reducing indoor particles but duration of use and volume of room, key determinants of efficacy.	Efficacy related to clean air delivery rate normalized by room volume, which must be competitive with ventilation and deposition (loss) rates. Electrostatic PACs may result in ozone production	Overall trend in studies suggest a benefit on blood pressure and heart rate variability
Heating ventilation and air-conditioning (HVAC)			
Installed centrally in homes with filters that reduce exposure.	Effective in reducing concentrations as long as filters replaced regularly.	Efficacy is variable with building and operational factors (i.e. open windows)	No data currently available

Figure 3 Urban design considerations to reduce exposure to noise and air pollution.

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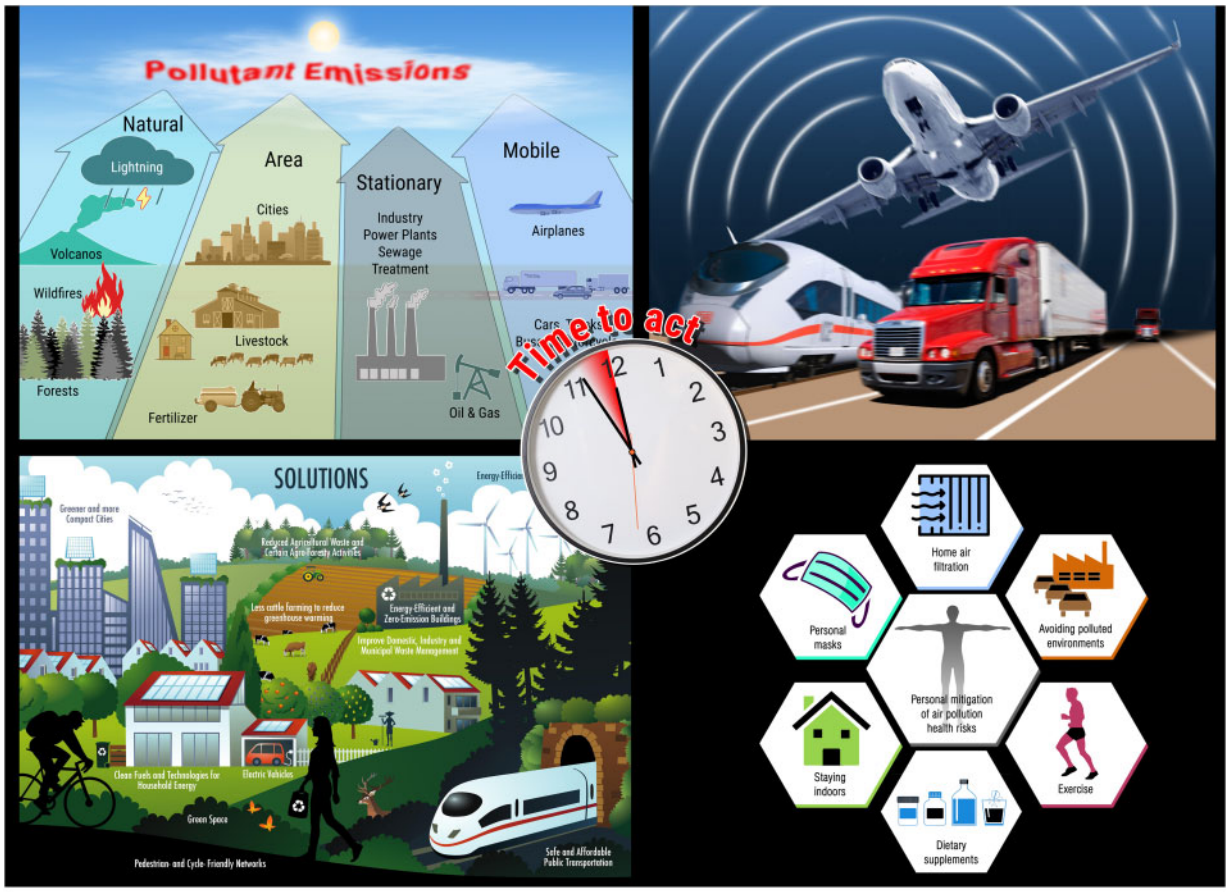

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Future perspectives: opportunities and challenges over the next decade

Efforts to mitigate air pollution and noise are endeavours that involve complex economic and geopolitical considerations. Measures such as transportation reform, shift to zero-emission fuels, urban landscape reform, and ecologically sound lifestyle changes may help simultaneously alleviate air/noise pollution while accomplishing climate change goals. However, reducing air pollution and noise may have short-term challenges due to economic incentives that are substantially misaligned with health and environmental priorities and thus opportunities to understand the importance of these factors in human health will sadly continue. An important avenue of investigation is convergent studies that look at the broad and collective impact and burden of air and noise pollution as archetypal environmental risk factors. The questions that need to be addressed are many and include the magnitude and time course of response of co-exposure, interactive effects of environmental factors on surrogate measures, duration of effect/time course of reversal, impact on circadian rhythm, and finally the effect of reversal as well as prevention and lifestyle approaches that may help mitigate risk (e.g. diet, stress, and exercise).

The rapid development of personalized technologies that provide multiple measures of health in fine temporal detail in conjunction with data on environmental exposure provide an unprecedented opportunity for research and may allow an extraordinary understanding of the interactions between environmental and non-environmental risk factors over long durations. Together with developments in next-generation sequencing technologies, and opportunities in big data, assimilative studies of this nature may finally provide a granular view of the environmental–genetic interactions leading to the development of CVD. However, the extent of these advances may be tempered by the need to manage subject burden and costs, and imprecise data on many environmental variables. Increased awareness of the societal burden posed by environmental risk factors and acknowledgement in traditional risk factor guidelines may pressurize politicians to intensify the efforts required for effective legislation.

The cardiovascular community has a responsibility to help promulgate the impact of, not only health lifestyle and diet, but also over the outsize impact of air and noise pollution on cardiovascular health. Individuals can apply political pressure through democratic means

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and lobbying to enact changes at regional and national levels that lead to reductions in noise/air pollution exposure. Patient organization can provide a strong voice in the call for action at governmental level. Importantly, air pollution was mentioned in the published guidelines for cardiovascular prevention, but the recommendations to reduce pollution were completely insufficient,[47] while prevention measures with respect to traffic noise were completely lacking. Noise and air pollution represent significant cardiovascular risk factors, it is important that these factors are included into the ESC guidelines, and others, for myocardial infarction, arterial hypertension, and heart failure.

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