Climate change and cardiovascular disease: implications for global health

Haitham Khraishah[1,2†], Barrak Alahmad[3,4], Robert L. Ostergard Jr[5], Abdelrahman AlAshqar[6], Mazen Albaghdadi[7], Nirupama Vellanki[2], Mohammed M. Chowdhury[8], Sadeer G. Al-Kindi[9], Antonella Zanobetti[3], Antonio Gasparrini[10,11,12] and Sanjay Rajagopalan[9]

[1]Division of Cardiovascular Medicine, University of Maryland School of Medicine, Baltimore, MD, USA.

[2]Department of Medicine, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, USA.

[3]Department of Environmental Health, Harvard T.H. Chan School of Public Health, Harvard University, Boston, MA, USA.

[4]Environmental & Occupational Health Department, Faculty of Public Health, Kuwait University, Hawalli, Kuwait.

[5]Department of Political Science, University of Nevada, Reno, NV, USA.

[6]Department of Obstetrics, Gynecology and Reproductive Sciences, Yale University School of Medicine, New Haven, CT, USA.

[7]Division of Cardiology, Peter Munk Cardiac Centre, Toronto General Hospital, University of Toronto, Toronto, Ontario, Canada.

[8]Department of Vascular and Endovascular Surgery, Department of Surgery, Addenbrooke's Hospital, University of Cambridge, Cambridge, UK.

[9]University Hospitals, Harrington Heart & Vascular Institute, Department of Medicine, Case Western Reserve University, Cleveland, OH, USA.

[10]Centre for Statistical Methodology, London School of Hygiene & Tropical Medicine, London, UK.

[11]Centre on Climate Change and Planetary Health, London School of Hygiene & Tropical Medicine, London, UK.

[12]Department of Public Health Environments and Society, London School of Hygiene & Tropical Medicine, London, UK.

[†]e-mail: hkhraishah@som.umaryland.edu

Abstract | Climate change is the greatest existential challenge to planetary and human health and is dictated by a shift in the Earth's weather and air conditions owing to anthropogenic activity. Climate change has resulted not only in extreme temperatures, but also in an increase in the frequency of droughts, wildfires, dust storms, coastal flooding, storm surges and hurricanes, as well as multiple compound and cascading events. The interactions between climate change and health outcomes are diverse and complex and include several exposure pathways that might promote the development of non-communicable diseases such as cardiovascular disease. A collaborative approach is needed to solve this climate crisis, whereby medical professionals, scientific researchers, public health officials and policymakers should work together to mitigate and limit the consequences of global warming. In this Review, we aim to provide an overview of the consequences of climate change on cardiovascular health, which result from direct exposure pathways, such as shifts in ambient temperature, air pollution, forest fires, desert (dust and sand) storms and extreme weather events. We also describe the populations that are most susceptible to the health effects caused by climate change and propose potential mitigation strategies, with an emphasis on collaboration at the scientific, governmental and policy levels.

[H1] Introduction

Over the past century, anthropogenic activities, particularly the burning of fossil fuels, have resulted in the release of excessive quantities of carbon dioxide (CO_2) and other greenhouse gases, which traps heat in the lower atmosphere to cause global warming[1]. The primary constituents of greenhouse gases include CO_2, methane (CH_4), nitrous oxide (N_2O), fluorinated gases and ground ozone (O_3). Greenhouse gases absorb and emit radiative energy, and excess release of greenhouse gases has contributed to droughts, the melting of permafrost, and the retreat of glaciers and sea ice, which have further led to a rise in the Earth's temperature owing to the loss of sunlight-reflecting snow[1]. Each of the past four decades has been successively warmer than any preceding decade since 1850[1].

In 2019, approximately 18.6 million people died from cardiovascular disease (CVD) worldwide[2]. Although environmental stress is a *sine qua non* for climate change, the extent to which conditions like CVD are attributable to climate change might not be fully appreciated. The DPSEEA (Driving Force, Pressure, State, Exposure, Effect and Action) framework (Fig. 1) helps to contextualize the range of factors that should be considered when conducting an assessment of the health effects of and adaptations to climate change[3]. Direct exposure to extreme weather events, ambient temperatures, heat waves, cold spells and a wide array of pollutants has the potential to exacerbate disease in individuals with underlying cardiovascular conditions and contribute to the development of disease in those without known CVD. The indirect effects of climate change on cardiovascular health involve multiple complex exposure pathways including access to healthy food and clean water, transportation, housing, electricity, communication systems, medical assistance and other social determinants of health, all of which are essential for the maintenance of cardiovascular health (Fig. 2). In this Review, we summarize the

environmental exposures associated with climate change and their interactions; explore the effect of air pollution, extreme temperatures and other extreme weather events on CVD; describe the subpopulations that are most at risk of climate change-induced CVD; and propose strategies to mitigate the cardiovascular effects mediated by climate change.

[H1] Interlinkage of environmental exposures

Climate change can affect health through multiple cascading and compound environmental events (Fig. 2). The most plausible mechanisms seem to relate to extremes in weather patterns and air pollution, each of which might have independent yet interlinked effects on cardiovascular health. Worsening air quality owing to increased pollutants can exacerbate the extreme fluctuations in temperature levels, and these changes might lead to further deteriorations in air quality[4]. Climate change disrupts meteorological and atmospheric conditions, including temperature, precipitation, humidity, wind speed and water vapour pressure levels[5]. These weather conditions can increase the levels of particulate matter (PM) and ground O_3, among other pollutants, a phenomenon known as weather or climate penalty[6]. Higher air temperatures contribute to increased levels of O_3 precursors and accelerate the chemical formation of O_3. Changing wind patterns, decreased rainfall and reduced humidity levels can lead to periods of air stagnation, which can promote the accumulation of O_3[7]. The association between temperature levels and fine particulate matter (particles ≤2.5 μm in diameter ($PM_{2.5}$)) is less straightforward because of the diversity of particle components. For example, rising temperatures increase the oxidizing potential of the atmospheric components to produce more sulfate particles, but can also reduce nitrate particle levels by increasing the volatility of solid particles[5]. Wildfires, which now

occur more frequently owing to climate change, have also been shown to increase O_3 and $PM_{2.5}$ formation[8].

Over the past two decades, the weather penalties from increased O_3 and $PM_{2.5}$ levels alone were responsible for >20,000 excess deaths between 1994 and 2012 in the USA[9], whereas weather penalties from excess PM_{10} levels resulted in >3,200 excess deaths between 1993 and 2017 in Spain[10]. However, none of these studies specifically characterized the effects of climate penalties on cardiovascular outcomes, despite the well-established adverse effects of excess O_3 and $PM_{2.5}$ levels on cardiovascular health.

[H1] Epidemiological study design

The association between short-term environmental exposures related to climate change (such as ambient temperature, PM and O_3 levels) and cardiovascular outcomes is generally assessed using time series or case–crossover studies, both of which have yielded similar results[9]. These epidemiological study designs are beneficial for the assessment of short-term associations because they can eliminate confounding related to time-invariant factors, including personal characteristics such as age, sex and smoking status[10,11]. Health effects of long-term (such as yearly or seasonal) temperature patterns are far less studied than the health effects of short-term extreme weather events, and the available data on the effects of long-term exposure to elevated or reduced ambient temperatures on cardiovascular outcomes are sometimes inconsistent[11]. Long-term effects of temperature (such as a change in mortality for every 1°C increase in mean temperature in the summer) or air pollution have been examined in longitudinal or survival epidemiological studies[12,13].

[H1] Air pollution and CVD

A sizeable body of evidence exists on the effects of air pollution on cardiovascular and cardiometabolic morbidity and mortality. Below, we summarize the main cardiovascular outcomes related to air pollution. Please refer to other published work on the effects of air pollution on the pathophysiology of CVD[14–16], because this topic is beyond the scope of this Review.

Air pollution is a defined as "a complex mixture that varies in concentration and composition according to time and place and is greatly influenced by weather"[14]. Primary air pollutants are emitted from natural or anthropogenic sources directly into the atmosphere, whereas secondary pollutants result from the chemical reactions or the physical interactions between the primary pollutants themselves or with other atmospheric components. Examples of primary pollutants include PM, carbon monoxide (CO), sulfur dioxide (SO_2) and nitrogen oxides such as nitrogen dioxide (NO_2). Secondary pollutants include secondary $PM_{2.5}$ and photochemical oxidants such as O_3. The exposure–response curve between either ground O_3 or PM levels with health outcomes is hyperbolic, with sharp increases at lower exposure levels that reach a plateau at higher levels[14] (Table 1).

[H2] Particulate matter

PM — usually measured in $\mu g/m^3$ (mass per volume) by regulatory and monitoring networks, but sometimes estimated at finer spatial resolutions using remote sensing data — is a mixture of solid and liquid substances that arise from natural sources (including crustal material like sand and salt), agricultural sources (such as from ammonia-based fertilizer) and anthropogenic sources (such as from the burning of fossil fuels)[17]. PM can be categorized according to size, whereby

PM_{10} refers to inhalable particles with an aerodynamic diameter of the particles of <10 μm, $PM_{2.5}$ to fine particles <2.5 μm and $PM_{0.1}$ to ultrafine particles <0.1 μm. PM size determines their fate and mode of transport, as well as the location within the respiratory tract where the particles will settle. Current evidence suggests that the level of $PM_{2.5}$ exposure that can mediate adverse health effects is well below the levels of $PM_{2.5}$ exposure recommended by the WHO air quality guidelines (<5 $\mu g/m^3$ for annual levels and <15 $\mu g/m^3$ for daily levels), with no evidence of a lower threshold below which $PM_{2.5}$ levels are considered safe[15,18] (Table 1).

[H2] Ozone

O_3 is a naturally occurring molecule in the Earth's stratosphere that acts as an important shield by absorbing ultraviolet radiation emitted by the sun. Ground-level O_3 is different from stratospheric O_3. At the ground level, O_3 is a major secondary pollutant, and its formation is promoted by photochemical reactions of nitrogen oxide and volatile organic compounds in a sunlit atmosphere. Volatile organic compounds are mostly emitted by anthropogenic activities, such as the burning of fossil fuels in industrial processes, homes and motor vehicles. The reactions that lead to O_3 formation are also heavily influenced by the meteorological fluctuations seen with climate change[19]. Normally, O_3 is rapidly generated and consumed without substantial accumulation over time, and O_3 levels are lowest in concentration during night-time. However, increasing ambient temperature leads to increases in ground-level O_3 concentration that might be difficult to mitigate given the relationship between ambient temperature and O_3 levels[20]. O_3 levels are measured as the 8 h maximum concentration in parts per million or billion by volume (ppm or ppb). Evidence from a 2017 study suggests a continued relationship between O_3 levels and mortality at concentrations <60 ppb, which is a lower range than that described by the US

National Ambient Air Quality Standards (70 ppb over 8 h)[21]. However, the effect estimates between O_3 levels and mortality are lower than that of $PM_{2.5}$[21]. By 2030, maximum daily O_3 concentrations are projected to soar up to 1–5 ppb throughout the USA, which, together with projected increases in average daily temperatures, would amount to an additional tens of thousands of O_3-related illnesses and premature deaths per year[22].

[H2] Epidemiology of air pollution and CVD

[H3] ***Cardiovascular risk factors*****.** The association between insulin resistance and air pollution has been extensively reviewed[23–25]. A 2020 meta-analysis reported a significant association between 10 μg/m^3 increments in $PM_{2.5}$ levels and the incidence and prevalence of type 2 diabetes mellitus[26]. The investigators also found a significant association between 10 μg/m^3 increments in NO_2 levels and the prevalence of type 2 diabetes[26].

Numerous systematic and narrative reviews have also highlighted the association between blood pressure and air pollution levels[15,27–30]. The prevalence of hypertension was linked to short-term (OR 1.07, 95% CI 1.00–1.14) and long-term (OR 1.1, 95% CI 1.07–1.14) exposure to 10 μg/m^3 increments of $PM_{2.5}$[29,31]. Short-term exposure to increments of 10 μg/m^3 in $PM_{2.5}$ has also been linked with 1–3 mmHg elevations in both systolic and diastolic blood pressure levels[32]. Personal strategies to limit air pollution exposure (such as use of face masks and indoor air purifiers) were shown to significantly reduce blood pressure levels, therby supporting strategies to reduce air pollution as a way to prevent and treat hypertension[24,33].

[H3] Cardiovascular mortality. Both short-term and long-term exposure to $PM_{2.5}$ and other pollutants increase the risk of cardiovascular events. Despite low $PM_{2.5}$ exposure levels in

Canada and the USA (9–11 μg/m^3), studies from these countries also demonstrated a positive association between long-term exposure to $PM_{2.5}$ and cardiovascular mortality. In a large US study (*n* = 517,043), long-term exposure (between 2000 and 2009) to $PM_{2.5}$ was linked to a 10% increase in cardiovascular mortality for every 10 μg/m^3 increase in $PM_{2.5}$ levels[34]. Furthermore, data from the 2001 Canadian Census Health and Environment Cohort showed that the 10-year hazard ratio estimates for cardiovascular mortality increased by 25% for every 10 μg/m^3 increase in $PM_{2.5}$ concentration[35]. A few cohort studies have also examined the association between long-term exposure to high levels of $PM_{2.5}$ and cardiovascular morbidity and mortality. In a prospective cohort study from China, researchers demonstrated that in the setting of high $PM_{2.5}$ levels (mean 43.7 μg/m^3), every 10 μg/m^3 increase in $PM_{2.5}$ levels was linked with a 12% increase in cardiovascular mortality[36]. A 2020 meta-analysis of 28 studies reported a modest but significant association between short-term exposure to $PM_{2.5}$ (measured as 24-h average concentration) and cardiovascular mortality[37]. With regard to the association between other pollutants and cardiovascular mortality, a 2021 meta-analysis that evaluated data from 398 cities in 22 countries, with a total of 19.7 million cardiovascular deaths between 1973 and 2018, showed that a 10 μg/m^3 increase in NO_2 exposure was associated with a 0.37% increase in cardiovascular mortality on the day after exposure[38]. At present, the relationship between ground-level O_3 concentration and cardiovascular mortality remains unclear[39,40].

[H3] Myocardial infarction. Numerous studies have investigated the relationship between short-term and long-term exposure to air pollutants and the incidence of fatal and non-fatal myocardial infarction (MI). In a meta-analysis of 34 studies, short-term exposure to the main air pollutants (CO, NO_2, SO_2, PM_{10} and $PM_{2.5}$, but not O_3) was associated with a marginal increase in the risk

of MI[41]. The investigators reported a 1.1% and 2.5% increase in the risk of MI associated with each 10 μg/m^3 increment in NO_2 and $PM_{2.5}$ concentrations, respectively[41]. In a pooled analysis of data from six population-based cohort studies from Denmark, Germany, the Netherlands and Sweden (*n* = 137,148), 10 μg/m^3 increments in long-term exposure to NO_2 was associated with a significant increase in the incidence of coronary artery disease (CAD; HR 1.04, 95% CI 1.01–1.07)[42]. However, long-term exposure to ground O_3 or $PM_{2.5}$ was not associated with an increase in the incidence of CAD[42]. Finally, a 2021 meta-analysis of 42 studies demonstrated that a 10 μg/m^3 incremental increase in long-term exposure to $PM_{2.5}$ was significantly associated with death from CAD (relative risk (RR) 1.23, 95% CI 1.15–1.31), but not the incidence of MI[43]. The repetitive, continuous exposure to air pollution over a lifetime might contribute to the development of high-risk coronary plaques and amplify the risk of atherosclerosis[44]. Patients with pre-existing CAD might, therefore, be at an increased risk of the detrimental effects of air pollution on the heart[15]. In summary, short-term exposure to $PM_{2.5}$ is associated with marginal increases in the incidence of MI, whereas the association between long-term exposure to $PM_{2.5}$ and the risk of MI is less clear, with a trend towards significance. Additional large-scale studies are needed to further elucidate this potential association.

[H3] Heart failure. Multiple studies have demonstrated a link between exposure to air pollution and heart failure (HF) hospitalizations. A meta-analysis of 35 studies showed that short-term exposure to the main air pollutants (CO, NO_2, SO_2, PM_{10} and $PM_{2.5}$, but not O_3) was associated with an increase in HF hospitalizations and mortality[45]. The analysis also demonstrated that 10 μg/m^3 incremental increases in $PM_{2.5}$ levels were associated with a 2.12% increase in HF hospitalizations or death, with the strongest associations noted on the day of exposure[45]. A study

of residents living in Ontario, Canada, also demonstrated a link between long-term exposure to major air pollutants and increased HF admissions; specifically, 5% and 3% increases in HF admissions were associated with each interquartile range increase in exposure to $PM_{2.5}$ and O_3, respectively[46]. Furthermore, using UK Biobank data, a prospective cohort study reported that long-term exposure to pollutants (as measured by air pollution score, a summation of each pollutant concentration weighted by regression coefficients) was associated with a 31% increase in the risk of incident HF in the highest quartile compared with the lowest quartile of air pollution score, after adjustment for possible confounders[47]. In addition, the relationship between air pollution and HF might be modified by genetic susceptibility[47]. Further studies are warranted to confirm the relationship between long-term exposure to air pollution and HF risk.

[H3] Stroke. The link between short-term and long-term air pollution exposure with increased risk of stroke is well established. A 2021 meta-analysis of 68 studies and >23 million participants reported an association between short-term exposure to $PM_{2.5}$ (as measured by an increase by 10 $\mu g/m^3$ in $PM_{2.5}$ concentration) and stroke hospitalizations, incidence of stroke and stroke mortality[48]. In addition, the analysis revealed a positive association between 10 $\mu g/m^3$ increments in short-term exposure to NO_2 and stroke hospitalizations, stroke incidence and stroke mortality[48]. Similarly, a 2021 meta-analysis of 42 studies showed that a 10 $\mu g/m^3$ increase in long-term exposure to $PM_{2.5}$ was linked with a 13% increased risk of incident stroke and a 24% increased risk of cerebrovascular death[43]. However, an analysis of 11 European cohorts from the ESCAPE project[49] (n = 99,446) did not show a significant association between long-term exposure to $PM_{2.5}$ and stroke incidence, but a 5 $\mu g/m^3$ incremental increase in annual $PM_{2.5}$ levels was associated with higher stroke incidence among individuals aged ≥60 years and those

who had never smoked[49]. A pooled analysis of six European cohorts from the ELAPSE project similarly demonstrated a link between a 5 $\mu g/m^3$ incremental increase in long-term exposure to $PM_{2.5}$ and the incidence of stroke[42]. Moreover, a 10 $\mu g/m^3$ increase in long-term exposure to NO_2 was associated with an 8% increase in the incidence of stroke[42]. The associations between cerebrovascular events and exposure to PM_{10} or ground-level O_3 are less consistent[42,48].

[H3] Cardiac arrhythmias. A majority of the studies in the literature that have assessed the potential link between air pollution and the incidence of arrhythmias have not explored specific subtypes of arrhythmias, which might be misleading because this disease group includes a wide range of pathologies with distinct pathophysiological mechanisms. In this section, we discuss only the studies that have investigated specific types of arrhythmias.

Short-term exposure to air pollution has been shown to increase the risk of atrial fibrillation. In meta-analysis of four observational studies (n = 461,441), a 10 $\mu g/m^3$ increase in $PM_{2.5}$ levels was associated with a 0.89% increase in the population-attributable risk of atrial fibrillation[50]. Furthermore, a study of 176 patients with an implantable cardioverter–defibrillator reported a 39% increased risk of a ventricular arrhythmia event with each interquartile range increase in $PM_{2.5}$ level[51]. Similar findings have also been observed in high-risk populations[52,53]. Finally, among healthy individuals and those with a history of CVD, both short-term and long-term exposure to $PM_{2.5}$ have been associated with an increased burden of premature ventricular contractions[53,54].

[H1] Temperature and cardiovascular events

Both low and high temperatures contribute to cardiovascular morbidity and mortality[55–57]. In 2019, the Global Burden of Disease Study[58] introduced non-optimal temperatures as a risk factor for death worldwide, with the greatest mortality burden associated with low rather than high temperatures. The *Lancet* Countdown on health and climate change summarized the effects of extreme temperatures, among many other consequences of climate change, on health and disease, including CVD[59]. A 2021 global analysis estimated that >5 million deaths annually are associated with non-optimal temperatures[60]. These trends are expected to worsen in the coming years given continual global warming and greater vulnerability of patients with multiple risk factors for CVD[61].

[H2] Temperature as an exposure

Temperatures are recorded at weather stations near or within residential areas. Although the variability of temperature extremes that might exist in each population or geographical region should be recognized, the actual temperature that individuals are exposed to is a function of thermally controlled indoor settings (heaters or air conditioners). An extensive review on the effect of short-term exposure to temperature on mortality showed that the exposure–response relationship is inherently non-linear and might produce U-shaped, V-shaped or J-shaped curves[9]. The optimum temperature (which refers to the mean daily temperature at which the lowest mortality occurs and is also known as the minimum mortality temperature) is the demarcation or the inflection point of the curves and can vary according to climate zones, geographical locations and population vulnerabilities[62,63] (Table 1). Another factor to consider is the delayed or 'lagged' effect over time of environmental stressors, such as extreme temperature or air pollution. The health effects of extreme cold temperature usually persist longer (up to 2 weeks or more),

whereas the effects of extreme heat events normally last for 2–3 days[64,65]. Importantly, the majority of the evidence on the effects of temperature on health focus on broad categories, such as overall CVD or respiratory hospitalization, and the association between short-term fluctuations in temperature and cause-specific aetiologies of CVD, such as MI, HF and stroke, are not as well studied.

[H2] Epidemiology of temperature-related CVD

[H3] Cardiovascular risk factors. Temperature extremes might have an influence on the risk of developing diabetes and might also be associated with poor glycaemic control in patients with underlying diabetes[66]. Exposure to cold stimulates energy use through activation of brown adipose tissue, which contributes to thermogenesis via uncoupling mechanisms[67]. Elevated brown adipose tissue activity has been linked with improved glycaemic control and insulin sensitivity in both healthy individuals and patients with type 2 diabetes[68–70]. At the population level, high mean annual temperature was associated with elevated fasting plasma glucose levels, insulin resistance, and increased incidence and prevalence of diabetes[71–73] (Supplementary Table 1).

Short-term fluctuations in temperature have also been linked with blood pressure levels. Studies across a range of climates and populations have demonstrated an inverse association between temperature and blood pressure levels on the same and/or preceding days[74,75]. A 2017 meta-analysis of 14 studies showed that a decrease in mean outdoor temperature of 1°C was associated with an increase in systolic blood pressure of 0.26 mmHg and in diastolic blood pressure of 0.13 mmHg[75]. The effect of temperature on blood pressure levels was larger in individuals with established CVD. Interestingly, night-time blood pressure has been shown to be

higher during the summer months than in the winter months, suggesting that a warming climate might have opposing effects and counteract traditional mechanisms of cardioprotection[76]. Warmer nights might lead to increased blood pressure levels several hours later during the following afternoon[77]. Reduced sleep duration or quality has also been suggested as a potential mechanism for the seemingly paradoxical elevation in night-time blood pressure levels during warmer weather[78]. In addition, increases in mean ambient temperature were associated with lower plasma HDL and higher plasma LDL levels[79]. In the 2021 report of the *Lancet* Countdown on health and climate change, hot climates and CVD were found to be linked through reductions in physical activity. High temperatures reduced the time spent exercising, which can potentially increase the risk of CVD in the long term[59].

[H3] Cardiovascular mortality. Globally, the relative risk of all-cause death and cardiovascular death increases sharply if the mean daily temperature goes above or below the optimum temperature[60,62] (Supplementary Table 2). In a meta-analysis of 18 studies, a 1°C increase or decrease in ambient temperature above or below the optimal temperature threshold for a certain region was associated with an increase in cardiovascular mortality by 3.44% and 1.66%, respectively[80]. However, these findings do not link the changes in temperature with specific causes of cardiovascular or cerebrovascular mortality, such as MI, HF or stroke. A time-series analysis in England and Wales during the summer months in 1993–2006 demonstrated an increase in cardiovascular mortality by 1.8% for every 1°C increase above the regional heat threshold[81]. A study from Kuwait, a region with a hot climate, reported a threefold increase in cardiovascular mortality when comparing the period with the most extreme temperature (99th percentile: 42.7°C) to the period with the optimal temperature for lowest cardiovascular

mortality (34.7°C) from 2010 to 2016[82]. Furthermore, a time-series analysis of individuals from 272 Chinese cities assessed during 2013–2015 demonstrated that cold temperatures had a greater association with cardiovascular mortality than high ambient temperatures[83]. Compared with the optimum temperature (22.8°C), extreme cold temperatures (<2.5th percentile: −1.4°C) increased cardiovascular mortality by 92%, with sustained effects lasting >14 days[83]. Conversely, extreme hot temperatures (>97.5th percentile: 29.0°C) increased cardiovascular mortality by 22%[83]. Similarly, the Eurowinter Group reported an increase in mortality from ischaemic heart disease and cerebrovascular disease for every 1°C drop in temperature among individuals living in Europe[84]. Finally, a study in Brisbane, Australia, during 1996–2004 estimated the effect of extreme temperatures on years of life lost owing to CVD. During this period, the deaths attributable to CVD (7 deaths per day) accounted for >40% of total mortality and equated to 65 years of life lost per day owing to CVD[85]. Compared with the optimum temperature of 24°C, days with a mean temperature of 10°C were associated with 31 years of life were lost owing to CVD, whereas days with a mean temperature of 32°C were associated with 45 years of life lost owing to CVD[85].

[H3] Ischaemic heart disease. Similar to cardiovascular mortality, both high and low temperature extremes are associated with an increased incidence of MI. Although the relationship between cold temperatures and MI hospitalization has been well described in the literature[86,87], the association between heat and MI hospitalization is less consistent[88] (Supplementary Table 3). The relative importance of heat-related MI hospitalizations is expected to become more evident under the current trajectory of climate change[88]. A 2019 study from Augsburg, Germany, compared the incidence of MI during the periods of 1987–2000 and 2001–

2014[89]. During the earlier period, MI was triggered by cold exposure only, but the relative risk of heat-related MI significantly increased during the latter period[89]. This increased susceptibility to heat was more evident in patients with diabetes and hyperlipidaemia, underscoring the importance of depicting non-optimal temperature as a risk factor for CVD, especially in vulnerable subgroups[89]. By contrast, two separate studies did not find an association between warmer temperatures and an increased incidence of MI in Madrid, Spain, during 2013–2017 and in England and Wales during 2003–2006[87,90]. However, a 2018 meta-analysis of 23 studies showed that the relative risk of MI hospitalization was 1.016 for each 1°C increase in ambient temperature and 1.014 for each 1°C decrease[90].

[H3] HF admissions. The majority of published studies evaluating the relationship between HF admissions and environmental exposures have focused on seasonality, rather than temperature extremes[91]. Several studies showed greater HF admissions and mortality during winter months, concomitant with an increase in mortality related to respiratory disease[91–93]. A greater diurnal temperature range (the difference between the maximal and minimal temperatures in a single day) has also been linked to greater HF admissions, even after adjusting for seasonality, mean temperature levels, humidity and air pollution[94]. However, studies that assess the relationship between daily ambient temperatures and HF admissions are lacking.

[H3] Arrhythmias. Given the broad range of arrhythmia subtypes and the heterogeneity of arrhythmia end points, the association between ambient temperature and cardiac arrhythmias is not well understood. A study of 31,629 arrhythmia-related emergency department visits in Seoul, South Korea, reported that each 1°C decrease in mean temperature and each 1°C increase in

diurnal temperature range was associated with an increase in the attributable risk of cardiac arrhythmias by 1.06% and 1.84%, respectively[95]. In a subgroup analysis, women and older individuals aged ≥65 years were more susceptible to changes in diurnal temperature range than their male and younger counterparts, respectively[95]. The types of cardiac arrhythmias assessed in the study included, but were not limited to, cardiac arrest, paroxysmal tachycardia, atrial fibrillation, and other atrial and ventricular arrhythmias[95]. In another study examining 5,038 implantable cardioverter–defibrillator activations in London, UK, during 1995–2003, the risk of ventricular arrhythmias increased by 1.2% for every 1°C decrease in ambient temperature[96]. The magnitude of the risk was greatest at very cold temperatures; the risk of implantable cardioverter–defibrillator shock events significantly increased by 11.2% for every 1°C decrease in temperatures below 2°C[96]. Interestingly, in this study, higher temperatures were not associated with ventricular arrhythmias. In addition, patients aged >65 years were most vulnerable to temperature-induced ventricular arrythmias[96]. In the Veterans Affairs Normative Aging cohort, a 10% increase in ventricular ectopy identified on an electrocardiogram was observed for each 1°C increase in ambient temperature[97]. Other studies from Germany and Brazil also found an increased risk of ventricular arrhythmias with both extremes of temperatures[98,99]. Although atrial fibrillation is one of the most commonly studied arrhythmias, no study so far has evaluated the relationship between ambient temperature and the incidence of this form of arrhythmia.

[H3] Stroke. Studies of the association between stroke (and its subtypes) and ambient temperature have yielded inconsistent findings. In a systematic review and meta-analysis of 20 studies and 2,070,923 events, an increase or a decrease of 1°C in ambient temperature increased the risk of stroke-related death by 1.5% and 1.2%, respectively[100]. As with other cardiovascular

outcomes, the effect of cold weather occurred 2–4 days after the exposure, whereas the effects of heat occurred on the same day[100]. In terms of the incidence of stroke, no association was found between hot temperatures and stroke in a meta-analysis of 20 studies, whereas lower temperatures increased the risk of stroke by 0.9%[100]. Similarly, a separate meta-analysis of 26 studies with a total of 19,736 patients with cerebrovascular accidents from 12 countries demonstrated that lower temperatures significantly correlated with higher risks of all subtypes of stroke, but found substantial heterogeneity in the magnitude of the effect depending on the geographical latitude and average temperatures at the study site, as well as the percentage of men included in the study[101]. The relationship between ischaemic stroke and ambient temperature levels is also unclear, with inconsistent results published in numerous meta-analyses[101,102].

[H2] Effect of heatwaves and cold spells on CVD

Although heatwaves are not a new phenomenon, their intensity, frequency and duration are expected to increase owing to climate change[1]. Using sensitivity analyses for different heatwave definitions, numerous studies have found that even a slight change in the definition of a heatwave had a demonstrable effect on estimated health outcomes. As such, comparison between studies or meta-analyses with conflicting definitions of a heatwave might not be appropriate or useful[103]. In a meta-analysis that pooled the effects of heatwaves on all-cause and cardiorespiratory mortality by different heatwave definitions, a heatwave definition of ≥35°C for ≥3 days revealed a 21%increased risk of cardiovascular death[104]. However, using cut-off points of temperatures ≥98th percentile for a duration of 2 days, heatwaves increased cardiovascular mortality by only 9%[104]. An individual-level meta-analysis of 400 communities in 18 countries examined the effect that differences in the definition of a heatwave had on estimates of

mortality[105]. The analysis found that heatwaves of all definitions had a significant association with all-cause mortality; however, the higher the temperature threshold used in the definition, the stronger the association. Modifying the duration of the heatwave definition did not have an effect on the strength of its association with mortality[105]. Another meta-analysis of 27 studies found that heatwaves (pooled results of different definitions) increased cardiovascular mortality by 15%[106]. Conversely, pooling of 18 studies (with different definitions of a heatwave) revealed no association between heatwaves and cardiovascular morbidity[106]. This finding could be attributable to the various ways in which cardiovascular outcomes were measured, because the studies relied on numerous data sources such as hospital admissions, emergency department visits, ambulance attendances, and call-outs or transport[107,108].

The heatwaves in July 1995 in Chicago, USA, and in the summer of 2003 in Europe were pivotal in providing insights into the adverse health effects of heatwaves. In Chicago, the 8-day heatwave event in July 1995 resulted in >600 excess deaths and 3,300 emergency room visits[109]. Daily temperatures during the heatwave ranged from 33.9°C to 40.0°C, with the heat index peaking at 48.3°C[109]. The relative risk of cardiovascular death was 2.39 on the day with the highest number of deaths[107]. An 11% increase in hospital admissions owing to dehydration, heat stroke and heat exhaustion was observed, especially in patients with underlying CVD (such as hypertension) and diabetes[110]. During the European heatwave in July and August of 2003, temperatures ranging from 35°C to 40°C were repeatedly recorded across multiple Western and Central European countries[111]. An analysis from 16 European countries reported 70,000 additional deaths during the summer of 2003 compared with summer reference periods from 1998–2002[112]. In July and August of 2010, Russia recorded a heatwave that produced temperatures >40°C[113]. The 44-day historic heatwave triggered numerous wildfires, resulting in

approximately 11,000 excess non-accidental deaths in Moscow compared with a similar time period in previous years[114]. Of note, approximately 2,000 deaths were attributed to the combined effects of heatwaves and air pollution from the wildfires.

To date, limited data exists on the association between heatwaves and the incidence of MI. A study from Spain showed no link between the risk of ST-segment elevation MI and heatwaves during the 66 days registered as a heatwave period in Madrid between June 2013 and June 2017[115]. Studies linking the effects of heatwaves and HF, arrhythmias and cerebrovascular accidents are scarce.

Cold spells are defined by a low temperature threshold lasting for a specific duration (usually >2 consecutive days). A meta-analysis of 8 studies reported that cold spells were associated with an 11% increase in cardiovascular mortality[116]. However, as with studies on heatwaves and CVD, substantial heterogeneity existed in the definition of a cold spell between the pooled studies, with intensity ranging from the first to fifth percentile of temperature levels, and a duration ranging from 2 to 5 days[116]. According to data from the British Regional Heart Study[117], cold spells (defined as a temperature $<10^{th}$ percentile for $\geq$4 consecutive days) increased the risk of death related to coronary heart disease or stroke by twofold. Of note, during cold winter months, a layer of warm air can trap a dense layer of cold air, which in turn can prevent atmospheric mixing and trap air pollutants near the cold surface. This phenomenon, known as 'temperature inversion', is associated with increased concentrations of air pollutants, and has been observed in the Utah Valley in the USA, where high levels of PM were measured near the valley floor[118,119].

Several meteorological variables can contribute to heat and cold vulnerability, including humidity, wind and solar radiation. Morbidity and mortality can increase with higher

temperatures, in part owing to its combination with elevated humidity levels, which places stress on the thermoregulatory system[120,121]. However, studies on the effect of these factors in isolation have reported contradictory results. For example, no link has been found between humidity levels and increased mortality[122]. One potential explanation is that weather is often the composite of a number of aggregate variables that collectively influence health events. Therefore, the estimation of the synergetic effects of these variables on health might be a much more important and practical framework to evaluate the health-related consequences of weather-related factors. The Spatial Synoptic Classification, which classifies weather into seven types (dry polar, dry moderate, dry tropical, moist polar, moist moderate, moist tropical and transition) has been used in biometeorological applications to estimate the effect of the entire suite of weather conditions on morbidity and mortality[123]. From a pragmatic standpoint, an extreme weather event, especially when protracted over several days, also encompasses a myriad of other weather-related elements; studies on the effects of these extreme weather events on cardiovascular health are therefore warranted[103].

[H2] Mechanistic insights

Although mechanistic links have been proposed between the effects of extreme temperatures on cardiovascular events, temperature extremes might not be experienced by individuals living in thermally controlled indoor environments. However, the possibility of cascading events in the context of climate change might have an effect on vulnerable populations who are directly exposed to extreme outdoor temperatures. At high temperatures, an elevated core body temperature might result in volume depletion and sympathetic activation, leading to tachycardia[124]. Hyperthermia causes dehydration, which results in haemoconcentration, as

evidenced by laboratory findings of thrombocytosis and leukocytosis among individuals exposed to extreme heat[125]. Haemoconcentration contributes to a hypercoagulable state, which might increase the risk of thrombosis and MI[124]. Hypothermia also causes hypercoagulability owing to increased viscosity, haemoconcentration owing to fluid shifting into the extravascular space, and clotting factor abnormalities[126]. A rising core body temperature might also lead to a hypermetabolic state and increased oxygen consumption. Heart rate can increase by an average of 8.5 bpm for every 1ºC increase in core body temperature[127]. In vulnerable individuals with pre-existing CVD, this sympathetic activation might lead to demand ischaemia or even plaque rupture, whereas volume depletion can lead to cardiogenic shock[88] (Fig. 3). A drop in core body temperature leads to an increase in sympathetic response, which results in vasoconstriction and elevated skeletal muscle tone to generate and conserve heat, as well as a catecholamine-driven rise in blood pressure levels and an increase in myocardial oxygen demand[128–130]. A fall in core body temperature can also lead to increased cholesterol crystallization in atherosclerotic plaques, increasing the risk of plaque rupture and MI in vulnerable individuals[131] (Fig. 3). Extreme heat might also affect cellular endothelial function and trigger conformational changes in proteins (especially the chaperone family of heat shock proteins), which can lead to systemic inflammation and multi-organ failure[132]. Extreme cases of hyperthermia and heatstroke can trigger a systemic inflammatory response, which is mediated by circulating mRNAs that activate inflammatory cytokines and the high mobility group protein B1 (HMGB1), leading to excessive activation of leukocytes and endothelial cells[133] (Fig. 4). Hyperthermia can trigger electrolyte disturbances such as hypokalaemia and hyperkalaemia, as well as hypomagnesaemia, which can increase the risk of arrhythmias[134,135]. Conversely, hypothermia can lead to bradycardia, with a study showing a 50% decrease in the heart rate of dogs with a core body temperature of 28ºC

compared with those with a core temperature of 37ºC[136]. This decrease is likely to be attributable to an increase in action potential duration and a reduction in His–Purkinje cell transmembrane resting potential, which leads to decreased conduction velocity and arrhythmias such as ventricular fibrillation or asystole[137]. Electrocardiogram changes observed in individuals with low core body temperature include J waves, QRS widening, QTc prolongation and T wave inversion[138,139].

[H1] Wildfires, desert dust and CVD

Wildfire smoke is an increasingly important contributor to air pollution in many parts of the world. Both the frequency and duration of wildfire events have dramatically increased in the past two decades as a consequence of climate change, with a resulting reinforcing feed-forward loop, whereby wildfires increase the propensity for climate change and climate change in turn increases the risk of wildfires[140]. Summer wildfire frequency increased approximately eightfold between 1972 and 2018 in California, resulting in a fivefold rise in the annual area burned[141]. Approximately 10.3 million individuals in the USA were estimated to have experienced unhealthy air quality levels (average daily fire-related $PM_{2.5}$ >35 μg/m^3) that were associated with exposure to wildfire for ≥10 days between 2008 and 2012[142]. Many studies have consistently demonstrated a link between short-term all-cause mortality and wildfires, whereby each 10 μg/m^3 increase in wildfire-related $PM_{2.5}$ exposure resulted in a 0.8–2.4% increase in all-cause mortality[143,144]. Although the evidence linking wildfire smoke exposure to respiratory outcomes (including hospitalizations) is robust[143–145], the data on the relationship between wildfire exposure and CVD are limited by the relatively smaller sample sizes. $PM_{2.5}$ exposure from wildfire smoke is associated with increased cardiovascular mortality and out-of-hospital

cardiac arrests, with effect estimates similar to those mediated by ambient $PM_{2.5}$ levels[143]. However, mixed results have been noted with cardiovascular hospitalizations. For example, studies examining the communities affected by the forest fires in 2003 in British Columbia, Canada[146,147], and during the 1990s in Australia[148] reported no increase in cardiovascular hospitalizations. However, the studies that assessed the wildfires in 2003 in southern California, USA[149], and in 1997 in Indonesia[150] reported higher cardiovascular hospitalization rates than in other years, although less pronounced than for respiratory illness. These studies are difficult to interpret in a larger context given that they include very different populations at different times with varying levels of exposure. Furthermore, these investigations did not rigorously examine the appropriate exposure window because hospitalizations for CVD were assessed for only a few months after the wildfire episode, with the exposure often lasting several weeks. Studying the outcomes for only a few weeks after a wildfire event might not fully capture the degree of health risk conferred by the wildfire. Given that forest fires are becoming an increasingly important contributor to air pollution, this source merits serious consideration as a risk factor for cardiovascular events. Wildfire smoke, for example, might contain a substantial proportion of ultrafine particles, which are an emerging risk factor for CVD[151]. Furthermore, wildfire smoke might also contain oxidative components such as polycyclic aromatic hydrocarbons that can exacerbate the adverse cardiovascular effects. In the immediate vicinity of wildfires, high temperatures and the release of other gaseous components might also exacerbate the adverse cardiovascular effects, particularly in individuals with pre-existing CVD.

Given that sand and dust storms affect >150 countries worldwide, billions of individuals are at risk of the health consequences of these storms[152]. However, only 30% of these countries are classified as sand and dust storm source areas, indicating that dust particles can spread widely

across national and international borders[153]. Sand and dust storms are strongly related to climate change and a series of interlinked factors. These factors include a warming climate, the El Niño phenomenon and larger differences in temperature between land and sea, resulting in larger pressure differentials that create strong winds, a reduction in rainfall, loss of soil moisture and deforestation[153]. These factors in various combinations create a fertile environment for dust storms. The main component of sand and dust storms is PM_{10}, but a substantial amount of coarse PM ($PM_{2.5–10}$) and $PM_{2.5}$ are also present. The association between an increase in dust particle concentration and mortality suggests the likelihood of a short-term increase in mortality during dust storms[154]. A systematic review of the health effects associated with desert dust reported a 0.27% increase in all-cause mortality on dust days compared with non-dust days[154]. In a 2020 meta-analysis of 21 studies on the health effects of dust exposure in Asia, a 2.33% increase in combined circulatory and respiratory mortality was observed during dust days compared with non-dust days at lag day 0 (the day of dust exposure) and a 3.99% increase at lag day 3 (3 days after the initial exposure)[155]. The majority of the studies assessing the effects of desert dust on cardiovascular morbidity evaluated data from emergency department admissions. In a study that examined the cardiovascular effects of dust that reached Taipei, Taiwan, from Asian desert storms, a 26%, 35% and 20% increase in emergency visits for overall CVD, ischaemic heart disease and cerebrovascular accidents, respectively, were observed during the storm-affected period compared with pre-storm periods. The differences in effect estimates between studies might be related to the various distances of locations studied in relation to dust sources (that is, the location of the desert), different exposure assessment strategies and epidemiological designs, and the different chemical composition of dust and carried particles in the various regions (for example, as a result of mixing with anthropogenic emissions)[156].

[H1] Vulnerable subpopulations

Climate change vulnerability is defined as the propensity to be adversely affected by climate change. Coastal and low-lying geographical areas, as well as densely packed cities with poor infrastructural amenities, offer less protection from the potential health risks associated with extreme climate change-related events. Similarly, other factors such as homelessness, type of housing and lack of green spaces contribute to climate change vulnerability. For example, during the heatwave in the summer months of 2003 in Europe, residents in old buildings with a lack of thermal insulation had a twofold increased risk of death compared with residents living in buildings with proper insulation[157].

Climate change has a differential effect across various demographic and socioeconomic subgroups living in different geographical areas. Age is the most consistent individual-level effect modifier of temperature-related cardiovascular mortality, with elderly individuals being most vulnerable to the adverse health effects mediated by temperature extremes[157,158]. During the heatwaves in 1995 in Chicago, USA, and in 2003 in Paris, France, mortality was the highest in bed-bound, elderly patients with comorbidities, such as obesity, CVD, and mental and neurological disorders[110,157]. Moreover, elderly individuals are also vulnerable to the effects of wildfire exposure and other climate-related extreme events that might place stress on the cardiovascular system. Individuals from ethnic minority groups might also be more susceptible to the adverse health effects mediated by temperature-related events. For example, African American individuals have an increased all-cause mortality during both heat-related and cold-related extreme weather events compared with white individuals, an effect that is driven by lower socioeconomic resources and numerous other socially disadvantageous circumstances

among the African American population[108,159]. Furthermore, a study examining ethnicity-related disparities on all-cause mortality from extreme heat events in four US cities showed a significant increase in mortality among Black American individuals compared with white individuals, which is likely to be related to the lower number of air conditioning units in African-American households than in houses of white individuals[160].

The type and nature of an individual's job can also alter their susceptibility to climate-related health effects. Manual and construction workers tend to work outdoors and are exposed to heat and pollution. During the 2003 heatwaves in Paris, France, manual workers had a twofold to threefold increase in all-cause mortality compared with individuals with an office job[157]. Refugees and immigrants are another subpopulation who are at increased risk of climate-related cardiovascular events. Language barriers, poor living conditions and socioeconomic disparities have been linked with increased heat-related vulnerability in refugees[161]. Migrant workers tend to take jobs with less pay and longer hours, are often unprotected by public policies, and work under unsafe conditions with little occupational safety and health training and high risk of occupational injuries[162]. In hot regions, migrant workers take on more demanding work and therefore have substantial outdoor exposure to extreme heat and air pollution[163,164]. In Kuwait, our group found a threefold increase in the risk of cardiovascular death from extreme heat among migrant workers compared with the host population[163]. Compromised mobility, reduced cognitive function, and other mental or behavioural factors might also increase susceptibility to climate-related health effects, particularly if no action is taken to mitigate these risks.

[H1] Mitigating climate change-related CVD

Climate change highlights the dilemma that medical professionals confront in addressing individual-level health problems that manifest from larger hierarchical and cross-systemic processes. Therefore, untargeted strategies or recommendations for personal-level intervention are unlikely to be the most effective approach from a cost, effort or equity standpoint. A multi-level intervention from an individual-level to a system or worldwide approach is urgently needed to address this existential problem. This intervention should involve cross-disciplinary collaboration between physicians, researchers, public health workers, political scientists, legislators and national leaders to mitigate the effects of climate change.

This understanding underlies the approach that countries have used to address the larger problem of climate change. The threats brought about through climate change propelled 190 countries to agree to the provisions of the Paris Agreement signed in 2015[165]. Under the agreement, countries would limit global warming to <2.0ºC above preindustrial levels (with a more ambitious target of <1.5ºC). The agreement further recognized the important role of sub-state actors such as local and regional authorities, civil society and the private sector in adapting to the different conditions that might affect regions, countries and local environments with climate change. A multi-regional analysis that included 451 locations in 23 countries evaluated heat-related and cold-related mortality under scenarios consistent with the Paris Agreement targets (1.5°C and 2.0°C) versus more extreme scenarios (3.0°C and 4.0°C increases)[166]. If global mean temperatures stay within the targets of the Paris Agreement, the analysis predicted that large increases in temperature-related mortality will be prevented. However, in the interests of the global health community, potential strategies to mitigate cardiovascular deaths under the 1.5°C and 2.0°C scenarios should be investigated. However, a key limitation of the Paris Agreement is that the agreement is not binding, meaning that there is no enforcement mechanism

to compel states to comply with the agreement's provisions. Indeed, the agreement does not mandate individual states to reduce greenhouse gas emissions; instead, the agreement allows countries to set their own emission targets that are in line with their developmental and technological standing. This situation means that policies that seek to address the relationship between climate change and CVDs might need to be implemented at multiple levels and involve various stakeholders for effective measures to emerge (Fig. 5). Therefore, mandatory regional or national policies to reduce fossil fuel emissions at the population level, particularly those that have both short-term climate and health co-benefits, are highly effective. Such short-term reductions in emissions can result in substantial reductions in cardiovascular events[167].

An assessment of patient-specific and community health risk and the degree of climate-related exposures is important for the implementation of any mitigation strategy (Fig. 1). A key focus of this strategy is climate adaptation that focuses on preparing for, coping with and responding to the effects of current and subsequent climate change problems[168]. The strategy is centrally focused on managing risks and uncertainties posed by climate change. Therefore, the adaptation process is particularly important to cardiovascular health given the variable effect that climate change will have at all levels, from individuals to communities, countries and regions. One clear area of focus is on climate-resilient buildings and infrastructure. Climate-resilient infrastructure is defined as a planned, designed, built and operated approach that anticipates, prepares for and adapts to substantial environmental stressors. This infrastructure should be designed and constructed to withstand, respond to and rapidly recover from disruptions caused by climate extremes, especially for vulnerable individuals with pre-existing CVDs. Healthy buildings should promote thermal comfort and have the potential to prevent adverse health outcomes[169]. Management (non-structural) adaptation measures include changing the timing of

maintenance to account for changing patterns of energy demand and supply, and investment in early warning systems that target vulnerable individuals. Individual-level climate change adaptation includes installation of air conditioning and heating systems and air purifiers. At the governmental level, local and regional governments can implement policies that are in accordance with the objectives of the Paris Agreement, given the reluctance on the part of the federal governments to move towards fulfilling these objectives[170]. Although federal governments have broad, sweeping powers that can bring about meaningful change, often the lack of political will to make such changes leaves local and regional governments with more autonomy to move forwards with their own climate change agendas. Heat–health action plans (HHAPs) (Supplementary Table 4) are an example of a framework that was developed by the WHO regional office for Europe in response to the 2003 summer heatwaves and were adopted by several regional and subnational authorities to direct their heat-prevention efforts[171]. HHAPs include guidance for a collaborative response to excessive heat conditions, timely alert systems, information dissemination, reduction in indoor heat exposure, emergency response of health-care systems and urban planning[171]. To date, the data on the effectiveness of HHAPs are limited and further studies are needed to assist decision-makers to select the most appropriate preventive measures and to improve HHAPs[172]. At the societal level, other stakeholders including non-governmental organizations and corporations have proved to be more willing than previously to enact mitigation policies that campaigners and consumers have demanded as a result of publicity on the problems associated with climate change[173].

[H1] Conclusions

Despite the improvements in primary and secondary prevention, CVD remains the leading cause of death globally. As we uncover the intricate links between environmental stressors and CVD, policymakers, public health officials and medical professionals must reconceptualize and integrate health within the context of the long-term objectives of environmental sustainability (Box 1). The effect of climate change on cardiovascular and overall health is a multifaceted problem that needs to be addressed at various levels. In the most favourable outlook for climate change in the future, alterations in temperature, air quality and extreme weather will still result in quantifiable and avoidable cardiovascular events. More work is needed to understand the adverse effects of environmental stressors on cardiovascular health, and further insights gleaned from these investigations should lead to a concerted effort to mitigate the effects of climate change on cardiovascular health.

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H.K. and A.A. researched data for the article. H.K., B.A., R.L.O. Jr, M.A., S.G.A.-K., A.G. and S.R. contributed to the discussion of its content. H.K., B.A., R.L.O. Jr, A.A., N.V., M.M.C., A.Z. and S.R. wrote the manuscript. H.K., B.A., R.L.O. Jr., A.A., M.A., M.M.C., S.G.A.-K., A.Z., A.G. and S.R. reviewed and edited the manuscript before submission.

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The authors declare no competing interests.

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Key points

Climate change is the greatest existential threat to humans and can adversely affect cardiovascular health.

Pollutants such as particulate matter and ozone show a hyperbolic exposure–response curve for different cardiovascular outcomes, whereas the relationship between temperature and cardiovascular outcomes seems to be U-shaped.

A multidisciplinary approach is needed to integrate cardiovascular health with the objectives from environmental sustainability frameworks.

Further research is needed to identify vulnerable subpopulations worldwide and to develop measures to mitigate the burden of climate change through health action plans and medical preparedness.

Table 1 | **Temperature and particulate matter as climate change-related health exposures**

Feature	**Ambient temperature**	**Particulate matter**
Unit of measurement	°F or °C	$\mu g/m^3$
Exposure assessment	Average daily outdoor air temperature, usually measured from meteorological stations	Average daily particulate matter ($PM_{2.5}$ and PM_{10}) levels, usually measured by regulatory monitoring networks or estimated from models with fine spatiotemporal resolution
Study design	Short-term effects: time-series and case–crossover studies; long-term effects: longitudinal cohort studies	Short-term effects: time-series and case–crossover studies; long-term effects: longitudinal cohort studies
Lag effect	Cold temperatures: up to 3 weeks; hot temperatures: up to 1 week	Up to 5 days (short-term effect)
Exposure–response curve	(NRCardio-Khraishah-t1.1.ai)	(NRCardio-Khraishah-t1.2.ai)

$PM_{2.5}$, fine particulate matter ≤2.5 μm in diameter; PM_{10}, particulate matter ≤10 μm in diameter.

Fig. 1 | **The DPSEEA framework.** The DPSEEA (Driving Force, Pressure, State, Exposure, Effect and Action) framework[3] provides a range of factors that should be considered when conducting a climate change assessment.

Fig. 2 | **The effect of climate change on the development of cardiovascular disease.** Anthropogenic-driven climate change has resulted in extreme temperature, altered meteorology and extreme weather events. Climate change can affect cardiovascular health both directly and indirectly. Direct pathways occur through exposure to extreme temperatures and poor air quality, which promote systemic inflammation and a hypercoagulable state and alter thermoregulatory processes. Indirect pathways include exposure to the byproducts of climate change, such as damaged health-care infrastructure, wildfires and secondary pollutants. CO_2, carbon dioxide; NO_2, nitrogen dioxide; PM, particulate matter.

Fig. 3 | **Pathophysiological pathways involved in mediating the effects of temperature on cardiovascular disease.** In order to reduce core body temperature, heat exposure triggers peripheral vasodilatation and sweating. These effects lead to potential dehydration, haemoconcentration and electrolyte imbalance, and mediate sympathetic activation and tachycardia. In susceptible individuals with pre-existing cardiovascular disease, these cascading events can result in demand ischaemia or atherosclerotic plaque rupture, causing myocardial infarction and/or stroke. Conversely, cold exposure leads to sympathetic activation, peripheral vasoconstriction and increased muscle tone, elevating blood pressure levels. Cold exposure can also promote cholesterol crystal deposition in atherosclerotic plaques. Sympathetic activation,

elevated blood pressure levels and cholesterol crystallization can lead to demand ischaemia and/or atherosclerotic plaque rupture.

Fig. 4 | **The effect of increased heat exposure on inflammatory and procoagulant cascades.** Heat exposure can lead to the release of endotoxins from the intestine and of IL-1 and IL-6 from the muscles to the systemic circulation, activating leukocytes and mounting an inflammatory response. The release of pro-inflammatory cytokines leads to a procoagulant state through increased expression of tissue factor, thrombomodulin and von Willebrand factor, as well as through inhibition of fibrinolysis and reduced levels of protein C, protein S and antithrombin III. TNF, tumour necrosis factor.

Fig. 5 | **Integrative climate change strategy.** An integrated approach to tackle climate change through adaptation and mitigation strategies involving multi-level policy stakeholders.

Box 1 | **Take-home messages for physicians and cardiologists**

Climate change, environmental exposures and occupational history should be considered major risk factors that can negatively affect cardiovascular and general health. Physicians should be able to provide guidance on how to mitigate these risk factors, particularly for patients with multiple cardiovascular risk factors or a history of cardiovascular disease. These recommendations can be divided into two broad categories that mitigate air pollution or extreme temperature induced by climate change. Examples of recommendations to reduce air pollution exposure include avoiding outdoor exercise activity on days with elevated pollution levels, use of N95 or fine particulate matter ($PM_{2.5}$) masks, use of indoor air purifiers, and installation of heating, ventilation and air conditioning units with a high-efficiency particulate air filter[174]. Vulnerable patients should also avoid using gas stoves, fireplaces and incense, which can all exacerbate indoor air pollution. To mitigate heat risks, patients should be counselled on avoiding outdoor activities during days with extreme heat conditions, on maintaining proper hydration, and on how to utilize indoor thermal control systems and reduce reliance on traditional air conditioning units that can themselves be contributors to greenhouse gas emissions[14].

The wider medical community must also engage in the conversation and debate on climate change, which begins fundamentally with training in medical school. Physicians must be conveyors of climate information during medical training, but also beyond medical school in policy forums. Calls have been made to integrate climate change and its effects on health in curricula across the spectrum of medical education. A framework that includes how climate change can harm health, necessitate adaptation in clinical practice and undermine health-care delivery should be adopted by the Accreditation Council for Graduate Medical Education in the USA, and by relevant councils in other countries, as core competencies for resident education[175].

Moreover, the medical community, especially cardiologists, must engage in the policy conversation. A multinational survey of 4,654 health professionals showed a consistent understanding of the health damage of climate change in their countries, and they felt a responsibility to educate the public and policymakers about the problem[176]. Despite this finding, less than half of the general public are personally concerned about the health effects of climate change[177]. These assessments are fed by a misperception that climate change does not affect everyone. Health-care professionals must be a conduit of education and information that emphasizes the individual consequences of the long-term detrimental effect that climate change can have on all people[177].

ToC

The relationship between climate change and health outcomes is complex. In this Review, Rajagopalan and colleagues describe the environmental exposures associated with climate change and provide an overview of the consequences of climate change, including air pollution and extreme temperatures, on cardiovascular health and disease.