American Journal of Preventive Cardiology 12 (2022) 100391

Contents lists available at ScienceDirect

American Journal of Preventive Cardiology

journal homepage: www.journals.elsevier.com/american-journal-of-preventive-cardiology

State-of-the-Art Review

Climate change and the prevention of cardiovascular disease

Alan P. Jacobsen [a,*], Yii Chun Khiew [b], Eamon Duffy [c], James O'Connell [d], Evans Brown [e], Paul G. Auwaerter [f], Roger S. Blumenthal [a], Brian S. Schwartz [g], John William McEvoy [a,h]

[a] Ciccarone Center for the Prevention of Cardiovascular Disease, Department of Medicine, Johns Hopkins University School of Medicine, Baltimore, MD, United States
[b] Division of Gastroenterology, Department of Gastroenterology, MedStar Georgetown University Hospital, Washington, DC, United States
[c] Division of Cardiology, Department of Medicine, Columbia University Irving Medical Center, New York, NY, United States
[d] Department of Public Health, Health Service Executive West, Galway, Ireland
[e] Department of Medicine, Division of Hospital Medicine, Johns Hopkins University School of Medicine, Baltimore, MD, United States
[f] Sherrilyn and Ken Fisher Center for Environmental Infectious Diseases, Department of Medicine, Johns Hopkins University School of Medicine, Baltimore, MD, United States
[g] Department of Environmental Health and Engineering, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, United States
[h] National Institute for Prevention and Cardiovascular Health, National University of Ireland Galway, Galway, Ireland

ABSTRACT

Climate change is a worsening global crisis that will continue negatively impacting population health and well-being unless adaptation and mitigation interventions are rapidly implemented. Climate change-related cardiovascular disease is mediated by air pollution, increased ambient temperatures, vector-borne disease and mental health disorders. Climate change-related cardiovascular disease can be modulated by climate change adaptation; however, this process could result in significant health inequity because persons and populations of lower socioeconomic status have fewer adaptation options. Clear scientific evidence for climate change and its impact on human health have not yet resulted in the national and international impetus and policies necessary to slow climate change. As respected members of society who regularly communicate scientific evidence to patients, clinicians are well-positioned to advocate on the importance of addressing climate change. This narrative review summarizes the links between climate change and cardiovascular health, proposes actionable items clinicians and other healthcare providers can execute both in their personal life and as an advocate of climate policies, and encourages communication of the health impacts of climate change when counseling patients. Our aim is to inspire the reader to invest more time in communicating the most crucial public health issue of the 21st century to their patients.

1. Introduction

Human activities, particularly the combustion of fossil fuels, have unequivocally warmed the earth's atmosphere, ocean, and land by increasing the atmospheric concentrations of greenhouse gasses (GHG) like carbon dioxide (CO_2) [1–5]. The big picture solution to climate change is that fewer climate forcing agents must be put into the atmosphere than are taken out, a process referred to as "mitigation" [6]. These mitigation strategies involve every energy-consuming human activity. Sustained reductions in total global CO_2 emissions have yet to occur. Several Western industrialized economies have managed to achieve small reductions in GHG emissions over the past two decades [7, 8]. Still, these reductions in GHG are inadequate to achieve emission goals to keep global warming below 1.5 °C this century. Furthermore, increased GHG production is expected from low- and middle-income countries, especially without appropriate assistance from high income countries [9].

1.1. The impact of climate change and planetary health on human health

Climate change affects human health through extreme weather events, heat stress, air pollution, infectious diseases, malnutrition, and other factors such as migration and displacement, outlined by the World Health organisation and The Lancet Countdown International Collaboration on Health and Climate Change [10–13]. The health effects of air pollution and increasing temperatures are particularly salient for those with or at increased risk of CVD [13–17]. In 2019, air pollution was responsible for 11.8% of deaths and 8.3% of disability-adjusted life years (DALYs), and high temperatures were responsible for 0.54% of death and 0.46% of DALYs globally [18,19]. Assuming no adaptation, the

The authors received no financial support for the research, authorship, and/or publication of this article. All authors have contributed sufficiently to merit authorship. There are no conflicts of interests or disclosures, financial or otherwise. APJ formulated the concept of the paper and drafted the initial review. YK, ED, JOC, EB, PGA, RSB, BSS, and JWM provided critical review, revision and editing of the paper.

* Corresponding author.
E-mail address: ajacob41@jhmi.edu (A.P. Jacobsen).

https://doi.org/10.1016/j.ajpc.2022.100391
Received 20 July 2022; Received in revised form 27 August 2022; Accepted 10 September 2022
Available online 11 September 2022

global climate change-attributable, heat-related excess mortality is expected to almost triple between 2030 and 2050 [20].

"Adaptation" is defined by the Intergovernmental Panel on Climate Change (IPCC) as the process of adjustment to actual or expected climate [21] (Table 2). This can be considered analogous to the secondary prevention of cardiovascular disease (CVD). It does not encompass the activities that prevent the onset of climate change itself but, rather, actions that minimize the impact of climate change when it has already occurred. Adaptation capacity is strongly linked to socioeconomic status. Climate change disproportionately harms those with the fewest resources. Health care and other inequities will soar unless there are definite steps to avert this [22]. Already, racial minorities experience greater exposure to air pollution due to proximity to large roads and urban redlined areas (with the latter tending to be hotter than neighboring areas due to a lack of tree cover) [23–26].

Planetary health is a related but different concept to climate change. It refers to the health impacts of disruption to the earth's natural systems caused by humans [27]. It expands the definition of environmental factors influencing health beyond climate change to include forest clearance, land degradation, biodiversity loss, freshwater depletion and damage to coastal reefs and ecosystems [28]. Climate change mitigation and adaptation strategies have widely differing planetary health implications. For example, afforestation and tree-planting programs, which create CO_2 sinks, also cause an imbalance in the water cycles of grasslands and their ecosystems [29,30]. Lithium mining in Chile, necessary for low carbon energy devices, has been criticized for depleting local groundwater resources across the Atacama Desert, destroying fragile ecosystems and converting meadows and lagoons into salt flats [31]. Considering the relationships among these global challenges may avoid the unintended consequences of addressing just one arm of planetary health.

1.2. The impact of climate change on cardiovascular disease

To date, review articles have centered primarily on the impact of pollution on CVD, with relatively few focusing on climate change as a broader topic [14,32–37]. This review broadens the focus of how climate change affects cardiac health beyond air pollution to include heat stress, infectious diseases, and other psychological and social factors (Fig. 1). Our specific aim is to evaluate, in the context of climate change, current CVD prevention lifestyle and pharmacological recommendations provided to patients by clinicians and other healthcare professionals and to conclude with practical suggestions for clinicians on how to use personal decisions, policy advocacy, and your role as a clinician communicator to help address climate change.

2. Air pollution

2.1. Epidemiology and pathophysiology of air pollution

Air pollution is defined as an unwanted, dangerous material introduced into the earth's environment due to human activity [38]. It is composed of a mixture of gasses and particles, and the dominant source is fossil fuel combustion [32]. Particulate matter (PM) is categorized into coarse particles (PM10), which have an aerodynamic diameter of <10 µm, fine particles (PM2.5, <2.5 µm in diameter), and ultrafine particles (PM0.1, <0.1 µm). PM2.5 is the principal air pollutant contributing to CVD. The gaseous components of pollution are composed of primary gasses such as nitrogen oxides, sulfur dioxide, and carbon monoxide, and secondary gaseous pollutants such as tropospheric ozone (found at

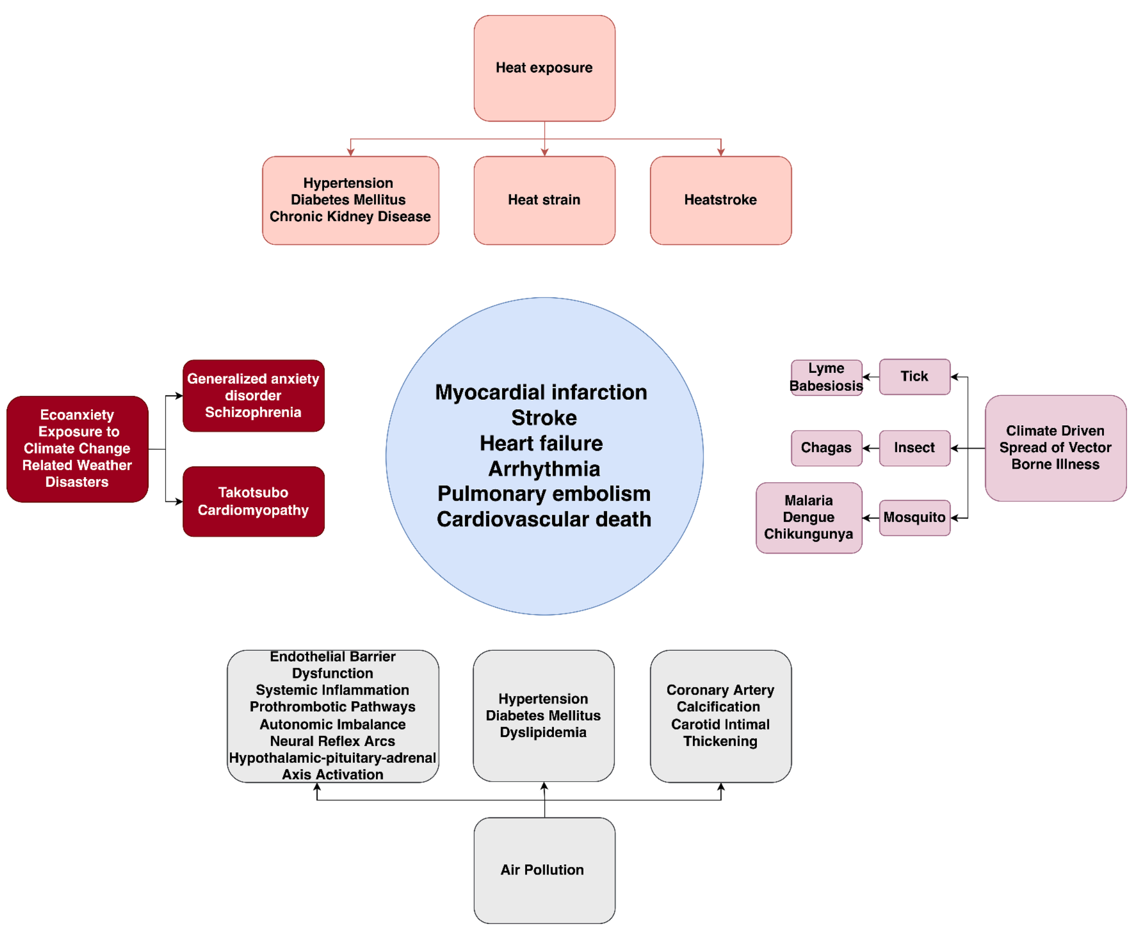

Fig. 1. Climate change and cardiovascular disease.

ground level and not a component of the stratospheric ozone layer) generated by nitrogen oxides and volatile organic compounds reacting in the presence of sunlight.

Air pollution and climate change are intrinsically linked [39]. Fossil fuel combustion including "natural" gas [40], is the major cause of both problems. Increased temperatures and dry conditions have extended the fire season and increased the risk of wildfires [41]. Temperature tightly correlates with tropospheric ozone concentrations [42,43]. Increased temperatures are associated with stagnant atmospheric conditions [44–46], whereby light winds and a stable lower atmosphere prevent horizontal and vertical dispersion of airborne pollutants, while an absence of precipitation prevents the washing away of pollutants [47]. Air conditioning can help prevent heat-related deaths, but the current technology leads to further fossil fuel combustion [48].

Furthermore, associations between particulate matter and mortality, including cardiovascular mortality, are more robust with higher mean annual temperatures [49].

Mechanistic frameworks linking the pathophysiological effects of air pollution to CVD health begin with the deposition of PM2.5 in the lungs, where it interacts with cells and endogenous structures, both locally in the lungs and systemically across various vascular beds to initiate oxidative stress, low-grade inflammation, and create harmful biological intermediates (e.g., modified phospholipids) [33]. These primary initiating pathways activate subsequent effector pathways such as (1) endothelial barrier dysfunction; (2) systemic inflammation; (3) pro-thrombotic pathways; (4) autonomic imbalance; (5) hypothalamic-pituitary-adrenal axis activation; and (6) neural reflex arcs, all of which progress to the development of CVD risk factors such as hypertension [50,51], diabetes mellitus [52], dyslipidemia[53], and subclinical atherosclerosis [54]. Ultimately, clinical outcomes, such as

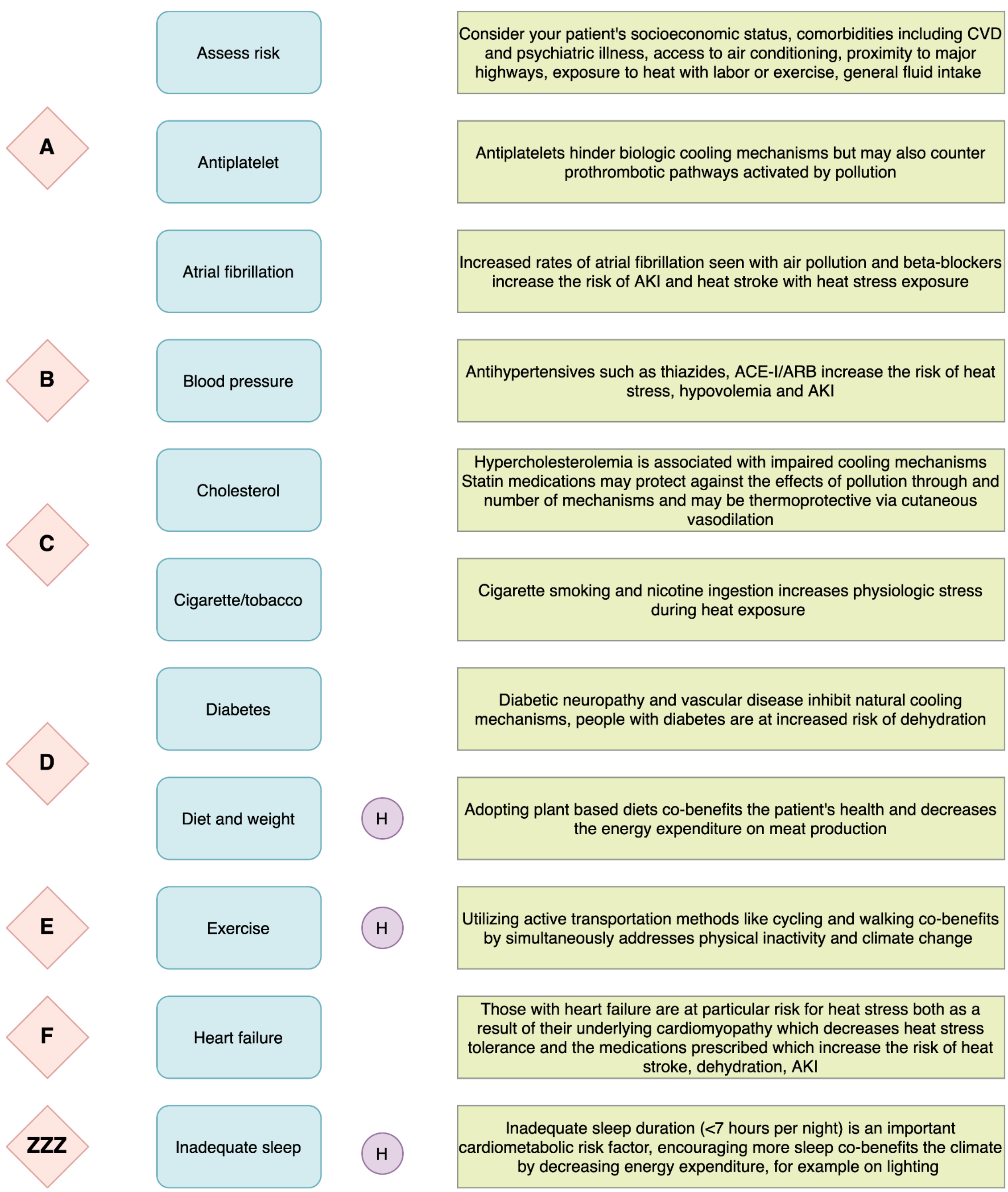

Fig. 2. Exposure-response curve for the relative risk of cardiovascular disease associated with long-term exposure to PM2.5.

cardiovascular death [55–57], myocardial infarction [58,59], stroke [60,61], arrhythmia[62] and heart failure[63] have all been linked to air pollution [32,33,38,64–68].

Three characteristics of air pollution are worth highlighting to aid in developing strategies to counteract its adverse cardiovascular effects:

- First, air pollution can be classified as ambient (outdoor) or household (indoor), which is vital in highlighting the differing sources, populations affected, and strategies required to improve health in these settings.
- Second, the exposure-response curve displaying CVD risk as a function of pollutant concentration rises steeply at low levels before flattening out at extreme concentrations, without a threshold below which exposure can be considered safe (Fig. 2) [33,69]. As a result, 99% of the global population breathes air pollution at levels that exceed the World Health Organization's air quality guidelines, with low- and middle-income countries experiencing the highest exposures [70].
- Third, while chronic exposure to air pollution is similar to traditional risk factors, like hypertension, instigating chronic pathophysiological processes that ultimately result in cardiovascular events, short-term (up to 7 days) exposure to even minimally increased concentrations of PM2.5 are also associated with increases in acute myocardial infarction (2.5% per 10 mg/m^3) and heart failure hospitalization or death [59,63].

The WHO interim targets (Its) are also highlighted. The Its are successive targets of 35, 25, and 15 μg/m3, which were set up to reduce mortality. Exceeding IT-1 levels is associated with increased mortality by 15%. IT-2 and IT-3 reduce mortality by 6% at or below each level. For typical days in U.S. cities, the levels range within 24-h standards (5 to 35 μg/m3). In India, peak daily levels exceeding 250 μg/m3 are common. Figure courtesy of Rajagopalan et al. [33,69].

2.2. Strategies to minimize the impact of air pollution on CVD

The Air Quality Index (AQI) is a tool for reporting air quality. It is calculated based on five major pollutants' ambient air concentrations: particle pollution and ground-level ozone are the main determinants, but nitrogen dioxide, sulfur dioxide and carbon monoxide are also considered [71]. The index ranges from 0 to 500, wh10ereby values at or below 100 are considered satisfactory. The index is subdivided into six categories, and graded activity recommendations are provided first to those particularly sensitive to air pollution, such as those with cardiovascular or pulmonary disease, and then to all individuals [72]. For example, when the AQI is 101–150, people with cardiopulmonary disease and diabetes, children and older adults are advised to reduce prolonged or heavy exertion (such activities include playing basketball or soccer, chopping wood, heavy manual labor, and vigorous running, cycling, or hiking).

The core intervention against air pollution requires societal and governmental changes in shifting to renewable energy sources. Until that can be achieved, alternative policy interventions such as the promotion of low/zero-emission transportation and urban landscape reform, in combination with personal interventions such as minimizing commuting during rush hour, and the use of face masks and air purifiers should be employed. Some studies, primarily from Asian megacities, have found the use of facemasks such as the N95 respirator and air-filters/cleaners to be associated with improvements in cardiopulmonary surrogate markers such as blood pressure [73,74]. There may be a particular benefit for those living near heavily trafficked highways and powerplants or during periods of poor air quality due to meteorological stagnation events or wildfires [75,76]. This initial data is promising and summarized elsewhere [77], but further trials of personal strategies to reduce air pollution exposure and improve health outcomes are warranted.

3. Heat

3.1. Epidemiology of increasing temperatures

The impact of increasing temperatures on human society is dependent on both vulnerability and the magnitude of exposure to heat. Vulnerability refers to the propensity to be adversely affected by climate change and encompasses a variety of elements, including susceptibility to harm and lack of capacity to cope and adapt [78]. Vulnerability differs within communities, across societies, regions and countries, and may also change over time. For example, vulnerability is modulated by population age, access to air conditioning, overall health expenditure, and rates of CVD, obesity and mental health disorders [35,79–81].

Regarding heat exposure, the overall temperature-attributable excess mortality related to climate change is determined by the net effect of increased heat-related mortality and decreased cold-related mortality [82,83]. The frequency of heat waves, which are responsible for more significant mortality than any other extreme weather event in the U.S. and other parts of the world [84], is increasing in concert with mean temperatures [85,86]. Extreme cold weather conditions that accompany climate change also contributes to an increase in temperature variability that is expected to increase clinical cardiovascular events [87–93]. Although high-income countries will be better placed to prevent harm from some health consequences of climate change – like undernutrition, diarrheal disease, malaria or dengue – heat mortality is expected to increase, even in wealthy countries [89]. The European heat wave of 2003 was a devastating example of this, with a death toll exceeding 30,000 [94].

3.2. Heat stress and wet bulb temperature

Heat stress refers to the environmental conditions, for example, temperature or humidity, that an individual is exposed to, whereas heat strain refers to the physiological response to these conditions [95]. The wet bulb temperature represents the temperature a thermometer (or the human body) may be cooled to by ventilation (convection of ambient air) and evaporation [96]. At 100% relative humidity, the wet bulb temperature is equal to the air temperature, so the human body can only be cooled by ventilation. The wet bulb temperature is lower than the air temperature at lower humidity, when the human body can be cooled by both ventilation and evaporation. Building on the wet bulb concept, the Universal Thermal Climate Index (UTCI) also incorporates wind and radiation [97].

According to the UTCI, mild heat strain starts at 23 °C with high humidity or 27 °C with low humidity. Exposures as short as 6 h to temperatures above 35 °C – just below body temperature – with high humidity can be lethal as neither ventilation nor evaporation is effective [98]. The National Weather Service issues Excessive Heat Warnings or Advisories based on the "Heat Index," which is the temperature at a reference humidity level that produces the same discomfort as the temperature and humidity of the actual environment [99]. However, there is mixed evidence that such alerts prevent excess death, which may relate to heterogeneity in heat response plans that facilitate individual behavior change in response to these alerts [100,101]. Public health officials must work with the weather service and behavioral scientists to develop an effective system for recognizing risks and implementing an effective plan that engages the public.

3.3. Physiology of heat stress

Humans cool themselves by dissipating heat with a combination of ventilation; conduction by direct contact with a surface; respiration by inhaling cool air and exhaling warm air; evaporation by sweating; and radiation. There is wide variation in an individual's capacity to tolerate heat stress. The primary physiologic response to increased temperature involves endothelial vasorelaxation with increased cutaneous blood flow [102,103]. This mechanism is blunted in the elderly and those with hypercholesterolemia; the latter is thought to occur due to atherosclerosis-mediated decreases in arterial smooth muscle responsiveness to nitrovasodilators [104,105]. The shift in blood flow from the core to the peripheral circulation results in a reduction of intracardiac filling pressures and systemic vascular resistance, necessitating an increased cardiac output [106–108].

An increase in ejection fraction is frequently seen with heat stress; however, diastolic function is often impaired such that stroke volume decreases, and cardiac output is augmented primarily by heart rate [109]. These hemodynamic changes may be less well tolerated in those with poor cardiovascular reserve, particularly those with underlying cardiomyopathy and valvular heart disease, and those who use cardiac medications that slow heart rate [110]. Acute rises in red cell and platelet counts, blood viscosity and plasma cholesterol may help explain the increased mortality from arterial thrombosis during heat stress [111].

Heatstroke is a specific pathology defined as hyperthermia associated with a systematic inflammatory response leading to a syndrome of multi-organ dysfunction in which encephalopathy predominates [112,113]. Classic heatstroke typically occurs in elderly, chronically ill patients whose physiologic reserves are overwhelmed by heat stress. Patients with underlying CVD or taking medications such as diuretics and beta-blockers are at increased risk of heatstroke. Exertional heatstroke occurs in otherwise healthy individuals performing strenuous outdoor activities, such as laborers, athletes, and soldiers.

Initial management includes rapid on-site cooling with cold-water immersion for exertional heatstroke (before transporting to the emergency department). Conductive or evaporative cooling is used for classic heatstroke as cold-water immersion is thought less well tolerated by elderly individuals, though data are limited [114]. Subsequent management requires monitoring for and addressing complications such as heart failure, arrhythmia, acute kidney injury, rhabdomyolysis, encephalopathy, disseminated intravascular coagulation (DIC), acute respiratory distress syndrome and liver failure.

3.4. Strategies to minimize the impact of rising temperatures on CVD

As patients with CVD are at the highest risk for dying in a heatwave, it is prudent for clinicians to provide such patients with practical advice for coping with heat exposure [115,116]. Advice that is supported by scientific evidence includes to: (1) increase fluid intake and not wait for thirst to trigger drinking, particularly amongst the elderly; (2) remain in a cool or air-conditioned environment and wear loose-fitting clothes; (3) reduce normal activity levels; and (4) provide patients with "heatwave rules" specific to their cardiovascular medications. Examples could include careful home monitoring of their weight, blood pressure and symptoms of presyncope and halving their diuretic or antihypertensive dose on particularly hot days [81].

Finally, there should be a greater emphasis on educating the public on the risks of heat waves. In particular, the first heatwave of the summer is usually the most dangerous for human health as individuals have not had the opportunity to develop thermal tolerance or acclimatize [35,117,118]. Thermal tolerance refers to cellular adaptation with the accumulation of heat-shock proteins caused by a single, severe, nonlethal heat exposure. In contrast, heat acclimation refers to physiologic adaptions such as improved sweating, cutaneous blood flow, fluid balance and altered metabolism. Consequently, there is greater resilience against heat stress [119–121]. Employing preventive measures such as those described above during this first heatwave can prevent substantial heat-related morbidity and mortality when humans are particularly vulnerable.

4. Vector-borne disease

Climate-driven vector-borne illness affects other specialties to a greater extent however the cardiovascular system may be involved [122]. The incidence of Lyme disease, a climate change indicator used by the Environmental Protection Agency, has doubled since 1990 [123]. The *Ixodes scapularis* deer tick that predominantly transmits the bacteria in North America is most active when temperatures and humidity are above 7°C and 85% respectively [124,125]. Lyme carditis is an uncommon manifestation, occurring when *Borrelia burgdorferi* disseminates from the tick bite site in the skin, infecting heart tissue and causing inflammation [126]. The predominant cardiac manifestation is partial heart block, which usually is mild and resolves, though rarely progresses to complete heart block, which may be permanent without antibiotic therapy. Lyme myocarditis or pericarditis may also occur and can be fatal [127]. The same *Ixodes* tick is also responsible for transmitting the *Babesia microti* parasite, which infects erythrocytes [128]. Up to 10% of individuals presenting with babesiosis have evidence of decompensated heart failure, presumably due to anemia [129]. Babesiosis-associated myocarditis has also been described [130].

Between 8 and 12 million people worldwide are estimated to have Chagas disease [131], which results from infection with the protozoan *Trypanosoma cruzi* endemic to Central and South America. The infection is becoming more common in the U.S. primarily due to migration [132,133]. However, autochthonous infection i.e., spread between individuals in the same place (as opposed to importation or migration), has been acquired Arizona, Arkansas, California, Louisiana, Mississippi, Missouri, Tennessee, and Texas [134]—suggesting expanded climate-driven range. The triatomine insects involved in transmitting *T. cruzi* are becoming more common in these southern U.S. states, tend to develop faster and feed more often to avoid dehydration when temperatures are >30 °C, resulting in this indigenous spread [135–137]. Manifestations of Chagas heart disease include dilated cardiomyopathy, ventricular aneurysm, ventricular arrhythmias and conduction disturbances (classically right bundle branch block) [109].

Temperature and humidity influence mosquito survival, frequency of blood feeding, and the development of parasites within mosquitos [138]. Malaria, caused by *Plasmodium* protozoa and transmitted by *Anopheles* mosquitoes [139], is endemic in sub-Saharan Africa, Asia, Oceania, South and Central America. Fluctuations in autochthonous transmission of malaria have also been seen in areas like Greece and the Anhui Province in China [140–142]. Cardiovascular involvement is not commonly reported in patients with malaria, but is associated with considerable morbidity when present modulated by a dysregulated inflammatory cytokine response, endothelial dysfunction and red blood cell sequestration [143,144].

The *Aedes* mosquito native to Southeast Asia is involved in the transmission of both chikungunya and dengue virus. Over the last two decades, climate conditions have developed such that much of Europe is increasingly suitable for breeding the Aedes mosquito [145]. Chikungunya disease typically presents with fever and disabling arthralgias but can present with systemic involvement and more severe disease [146]. When this is the case, cardiovascular involvement typically presents acutely with myocarditis and arrhythmia, which may progress to chronic dilated cardiomyopathy [147]. Similarly, most dengue infections are relatively benign; however, severe presentations include a dengue-associated vasculopathy with hemorrhage, endothelial dysfunction with capillary leak and hypovolemic shock, and organ dysfunction [148]. Direct effects of the dengue virus on the heart include myocardial impairment through circulating myocardial depressant factors, myocarditis, and arrhythmia, of which relative bradycardia is a notable feature [149,150].

Similar increases in the number of West Nile virus cases, are expected with current climate projections [135]. Atypical or particularly severe presentations of West Nile virus with cardiovascular involvement have been described [151], and cardiologists will need greater awareness of the clinical presentation and increasing prevalence of these infectious diseases.

5. Mental health disorders

"Solastalgia" refers to the distress that is produced by environmental change [152], while climate anxiety refers to typical anxiety symptoms such as obsessive thinking, insomnia and panic attacks related to the global climate crisis and the threat of environmental disaster [153–155]. Some climate-related exposures, including heat and humidity and disasters such as droughts, wildfires and floods, are associated with substance use disorders, schizophrenia, mood disorders, anxiety and vascular dementia [156,157]. This is pertinent because several psychiatric illnesses, including schizophrenia [158] and anxiety [159] have clear associations with CVD. For example, major psychiatric illness and atypical antipsychotic medications are components of cardiovascular risk prediction algorithms such as the QRISK3 risk calculator [160]. Beyond the more significant burden of CVD mediated by chronic mental health conditions, a greater incidence of Takotsubo cardiomyopathy has been documented in response to extreme weather events [161,162].

6. Ocean health and CVD

Climate change results in increasing ocean temperature, higher sea levels, more acidic seawater, and greater levels of salinity with knock-on effects on the cardiovascular system. First, increasing sea levels has resulted in increased soil and potable water salinity with multiple adverse effects including increased rates of hypertension [163]; second, loss of fisheries impede the public's ability to follow the American Heart Association's (AHA) recommendation to consume fish at least twice a week; third, microplastic accumulation such as bisphenol-A in our oceans is consumed by humans and is associated with increased CVD [164]. Addressing these impacts of climate change on our oceans may ultimately yield positive effects on cardiovascular health [165].

7. How climate change impacts a cardiologist's practice and recommendations

7.1. Lifestyle

Reviews have not gone beyond synthesizing evidence of harm from climate change. Here we go further to provide actionable recommendations regarding lifestyle, review what limited evidence exists regarding pharmacologic therapies, and discuss the bidirectional relationship between the cardiovascular healthcare system and climate change.

Certain "health co-benefits" may be experienced with climate change mitigation and adaptation strategies, particularly exercise and diet (Fig. 3) [34,166,167]. Adopting a low greenhouse gas emission diet through decreased meat consumption from methane-producing animals such as sheep and cows is associated with reduced mortality, ischemic heart disease, and stroke [168–170]. Mediterranean-type diets, which are high in plant foods and emphasize plant protein sources, simultaneously decrease the risk of CVD induced by air pollution and minimize greenhouse gas production [171–176].

Physical activity, including work and commuting-related, leisure, and fitness purposes, increases longevity [179] and decreases the risk of CVD [180], hypertension [181], obesity[182] and diabetes [183]. Active transportation methods such as cycling and walking simultaneously address physical inactivity and (by reducing CO_2 emissions) climate change [184–187]. Urban planning more conducive to active transportation with decreased emissions may result in better cardiovascular health and reduce heat exposure due to increased greenspace with less asphalt. There are some concerns regarding outdoor exercise when air quality is particularly poor [188]. However, the cardiometabolic health benefits of active commuting outweigh the increased health risks of traffic-related pollutants in all but the most extreme pollution cases [189,190]. High temperatures can also reduce the frequency and duration of physical exercise that can be tolerated [191,192]. As a result, sports medicine authorities in many countries, including the US, suggest postponing outdoor competitive events if the wet-bulb temperature is above 28 °C [193,194]. Cardiologists and primary care physicians should advocate for community designs that emphasize areas where individuals can exercise under natural foliage and away from polluting foci such as busy roads and industrial areas. Cigarette smoking and nicotine ingestion increase physiologic strain during heat exposure and may increase the risk of heat stress [195].

Finally, the AHA defines inadequate sleep duration as <7 h per night and is recognized as an important cardiometabolic risk factor [196,197]. In large prospective studies, healthy, nonobese adults, who reported <6 h of sleep a day were at increased risk of myocardial infarction, obesity, dyslipidemia, hypertension and elevated fasting glucose [198,199]. Sleep disruption has also been reported as a result of climate-related temperature changes and climate-related stress responses [200,201]. Sound pollution from industry and motor vehicles (particularly those

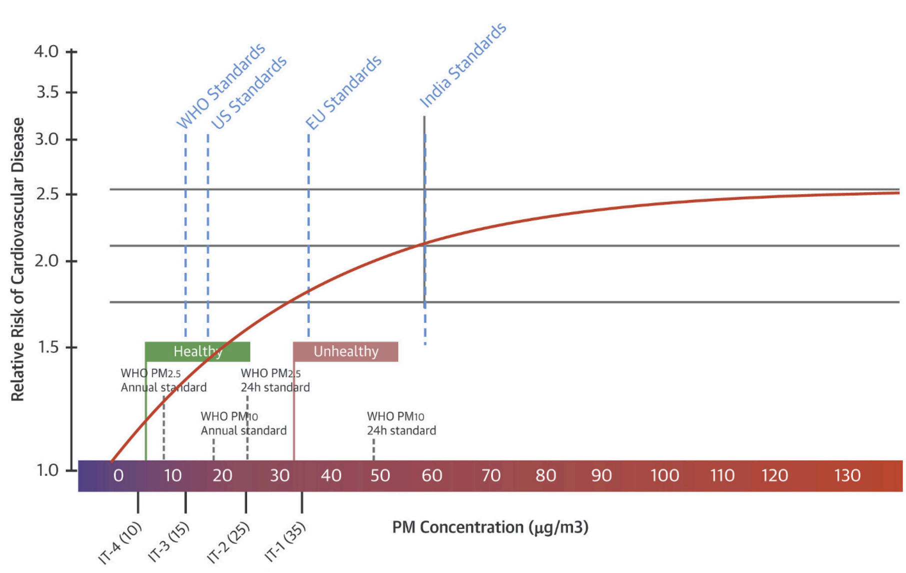

Fig. 3. The ABCs of cardiovascular disease prevention [177,178]: Climate change edit
H, Health co-benefit.

with combustion engines) further contributes to poor sleep. Encouraging adequate sleep is yet another health co-benefit in that our patients' metabolic health will benefit from more sleep. A sleeping human tends to consume less energy resulting in less GHG emissions.

7.2. Medications

Commonly prescribed cardiovascular medications impact our patients' susceptibility to heat-related illness [202–204]. Diuretics, angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, and sodium-glucose cotransporter-2 inhibitors increase the risk of hypovolemia and heatstroke [205–207]. Beta-blockers decrease blood flow to the skin and reduce cardiac output, also placing individuals at higher risk of heatstroke [208].

Aspirin and clopidogrel use results in attenuated reflex cutaneous vasodilation, which may elevate core temperatures in the setting of both passive and exertional heat stress [209]. Conversely, there is some evidence that aspirin may inhibit heat-induced platelet hyperaggregability involved in DIC secondary to heat stroke [210], and aspirin pretreatment has been found to prolong survival in rats who sustain heat stroke [211]. Aspirin does not appear to modify the effect of PM exposure on ischemic stroke [212].

Statin medications may be thermo-protective primarily via cutaneous vasodilation [213,214], achieved by stabilizing the essential cofactor tetrahydrobiopterin, necessary for nitric oxide production [215,216]. An analysis of a large U.S. Medicaid program found a protective association of statin use against all-cause mortality which strengthened as daily average and daily maximum temperature increased [217]. Preclinical studies have suggested that the inflammatory response induced by exposure to ambient air pollution may be nullified by statin therapy; however, this has not been borne out by observational data [218,219]. By understanding how medications impact heat and pollution sensitivity, clinicians can give individualized recommendations regarding their patient's risk during extreme exposures.

Certain medications are particularly heat-sensitive. For example, the efficacy of PCSK9-inhibitors significantly decreases when stored at temperatures higher than 25 °C for several hours [220], and insulin has long been recognized as a heat-sensitive medication that undergoes degradation at temperatures above 30 °C. With increasing temperature and temperature variability, those most disadvantaged will not have the resources to store their therapies correctly. Medicines stable at higher room temperatures are needed to avoid refrigeration, benefitting those without access to such appliances.

7.3. Preparing the healthcare system for climate change

Cardiovascular specialists need to work with hospital administrators in the healthcare system in which they practice to prepare for the increasing impact of climate change. Disruption of healthcare infrastructure, due to events such as wildfires, floods and hurricanes is already affecting a substantial amount of healthcare delivery [221]. Desertification, ocean warming and acidification threaten the availability of healthy diets. Health systems should invest in disaster planning and early warning systems to prepare for waves of patients in extreme weather events or climate refugees [34]. Plans to access and provide nutritious food should also be developed.

While climate change has significant impacts on health care delivery [222], the inverse is also true [223]. The U.S. healthcare system accounts for 8.5% of all U.S. GHG emissions and, if it were a country, would rank 13th in the world in terms of emissions [224]. Steps to eliminating GHG production in the healthcare sector include reducing demand through preventive care, use of clean energy, choosing medical supplies and equipment with lower carbon footprints, and employing telemedicine where possible [225,226]. Cardiac catheterization labs and intensive care units are particularly carbon intense environments that require significant sustainability assessment and, where we should be especially sensitive to the consequences of providing futile care [227].

7.4. Personal and policy action items

Climate health literature is dominated by impact research, however mitigation and adaptation responses remain niche topics [228]. Here we propose a list of actionable items that physicians may implement in their personal and professional capacity to reduce their impact on climate change (Table 1). Incorporating personal action items such as flying less and eating a plant based diet are important short term strategies to engage with other individuals and convince them of the important changes that need to occur. However, these actions alone are grossly inadequate, without wider communication or policy action [229]. Instigation of personal action items in the short term may also counter the "governance trap" wherein the public and governments each seek to attribute responsibility for instigating change to the other [230].

7.5. Climate change communication

We have an opportunity to adapt our practice to protect our patients in this changing climate and use our voice to influence the mitigation and adaptation strategies required to combat climate change. The public's prioritization of climate change fluctuates. At the beginning of the last decade, it has fallen below that of the 1980s [230,240]. The discrepancy between the increasing scientific certainty of anthropogenic climate change and a decreasing public concern for the issue is known as the "psychological climate paradox" [241]. An information deficit does not explain this, but rather cognitive biases and social influences that prevent the facts about climate change from being internalized and influencing behavior [242]. One such critical influence has been the

Table 1
Actionable items physicians can implement in their personal and professional capacity.

High Impact Personal Actions for Individuals in High-Income Countries [231]:*
- Fly less.
- Drive less, in a more efficient car, or do not drive.
- Eat a plant-based diet, be less wasteful with food.
- Make your home more energy efficient.
- Dress and shop sustainably.
- Consider having fewer children.
- Consider choosing carbon friendly pets.

Policy, Advocacy and Media Action [232]:
- Legislative advocacy: E-mail, call or meet with your local, state or federal representatives about the health effects of climate change. Support candidates committed to addressing climate change. Testify at hearings. Join or follow advocacy groups to keep informed in terms of legislation, such as "Physicians for Social Responsibility" [233] or the "Medical Society Consortium on Climate and Health" [234].
- Determine if your hospital system has a climate solution plan, and if not, advocate or work to ensure one is developed [235].
- Engage in non-violent social protests to address the climate emergency [236].
- Pen an Op-Ed or write letters to the Editor about the connection between climate change and health after extreme weather events.

Climate Change Communication [237]:
- Open up the conversation with patients or colleagues whenever there is a significant weather abnormality: flood, tropical storm, heatwave, wildfire.
- Highlight the health co-benefits of a low greenhouse gas lifestyle and diet.
- Discuss the health effects of climate change as a matter of routine when discussing other health maintenance.
- Encourage high-risk patients to make personal disaster action plans during hot-weather or disaster seasons (e.g., wildfire season, hurricane season).
- When a patient presents with a complication of climate change, alert them that this is the case.
  - Syncope due to heat.
  - Acute kidney injury due to hypovolemia.
  - Asthma or COPD flares due to worsening air pollution.
  - Myocardial infarction or heart failure exacerbation due to particulate matter or wildfire smoke exposure

Table 2
Glossary.

Term	Explanation
Air pollution	Unwanted, dangerous material that is introduced into the earth's environment as a result of human activity
Air Quality Index	A tool for reporting air quality and is calculated based on the ambient air concentrations of five major pollutants
Anthropocene	The most recent period in the earth's history when human activity significantly impacted the planet's climate and ecosystems.
Autochthonous transmission	Spread of a microorganism between individuals in the same place (as opposed to importation or migration)
Climate forcing	Any influence on climate that originates from outside the climate system itself, for example, GHG or surface reflectivity (as opposed to radiative forcing as below)
Climate change adaptation	The process of adjustment to actual or expected climate
Climate change mitigation	Actions that reduce the rate of climate change by decreasing the rate of GHG emissions and increasing the rate of GHG removal [6]
Health co-benefits	Climate change mitigation activities that also provide health gains
Heat acclimation	Physiologic adaptions including improved sweating, cutaneous blood flow, fluid balance and altered metabolism. and consequently, greater resilience against heat stress
Heat index	The temperature at a reference humidity level produces the same level of discomfort as the temperature and humidity of the actual environment.
Heat strain	The physiological response to environmental conditions that an individual is exposed to
Heat stress	The environmental conditions, for example, temperature or humidity, that an individual is exposed to
Heatstroke	A form of hyperthermia associated with a systematic inflammatory response leads to a multi-organ dysfunction syndrome in which encephalopathy predominates. An entirely separate entity to a cerebrovascular accident
Heatwave	A series of unusually hot days. Variably defined, but the EPA defines as two or more consecutive days when the daily minimum apparent temperature (the actual temperature adjusted for humidity) in a particular city exceeds the 85th percentile of historical July and August temperatures (1981–2010) for that city
Intergovernmental Panel on Climate Change (IPCC)	The international body set up by the United Nations provides reports on the scientific basis of climate change, its impacts and future risks, and options for adaptation and mitigation
Particulate matter (PM)	The particle component of air pollution is categorized based on the diameter of the particle
Planetary health	Refers to the health impacts of disruption to the earth's natural systems caused by humans
Psychological climate paradox	The discrepancy between the increasing scientific certainty of anthropogenic-driven climate change and a decreasing public concern for the issue
Radiative forcing	The difference between incoming and outgoing radiation is known as a planet's radiative forcing (as opposed to climate forcing as above)
Representative Concentration Pathway (RCP)	RCPs are pathways that provide time-dependent projections of atmospheric greenhouse gas (GHG) concentrations [238]
Shared Socioeconomic Pathway (SSP)	SSPs are reference pathways describing plausible alternative trends in the evolution of society and ecosystems over a century timescale, in the absence of climate change or climate policies [239]
The Universal Thermal Climate Index (UTCI)	Provides an assessment of thermal strain in humans incorporating temperature, humidity, wind and radiation
Thermal tolerance	Cellular adaptation with the accumulation of heat-shock proteins caused by a single, severe but nonlethal heat exposure
Tropospheric ozone	One of the gaseous components of air pollution found at ground level (as opposed to stratospheric ozone, which protects life on Earth from harmful ultraviolet radiation)
Vulnerability	Vulnerability refers to the propensity or predisposition to be adversely affected by climate change and encompasses a variety of concepts and elements, including sensitivity or susceptibility to harm and lack of capacity to cope and adapt [78]
Wet bulb temperature	The temperature to which a thermometer (or the human body) may be cooled by ventilation and evaporation

concerted efforts of high emitting industries to influence the discourse on climate change, similar to big tobacco and the risks of smoking [243].

Humans tend to struggle with future, uncertain (or perceived to be debatable), and costly to correct (both financially and non-financially) problems [244]. Unfortunately, climate change is all three, which partially explains our inability to confront the issue. Climate communication must address these barriers by making the climate issue more personal, nudging the public towards action to minimize cognitive dissonance and denial, providing a narrative of opportunity and giving meaningful indicators on progress, for example, the proportion of reduction in CO_2 emissions, or share of fossil fuels in total energy use [241,245].

Patients and the public respond to simple, clear messages repeated often and from trusted sources. Physicians have the experience and skills to communicate messages to influence their patients' behaviors. For example, convincing a patient to take a statin deals with an uncertain and potentially costly future cardiovascular event. Yet, patients will regularly leave their cardiologist's office assured that this is necessary.

In 2020 many clinicians embraced a new role by rapidly educating themselves on the health effects of COVID-19 to allow them to provide reliable public health information [246]. Up to 75% of physicians report that it is their responsibility to inform patients about the health impacts of climate change [232,247]. Changing current behaviors should be the immediate priority, while larger-scale policy and regulatory solutions should be the focus long-term [248]. This is our opportunity to impress upon our patients the health impacts of climate change and provide guidance on what needs to be done to address the greatest public health challenge of the 21st century [249,250].

8. Conclusion

Cardiovascular disease related to climate change can be prevented. This review has summarized the pathophysiology of cardiovascular disease associated with air pollution, heat and other medical conditions. Evidence-based recommendations relating to lifestyle, medication, cardiovascular care, and communication have been devised so that clinicians and other healthcare professionals may take action to prevent climate-change-associated heart disease among their patients.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

[1] Stocker T., Qin D., Plattner G., Tignor M., Allen S., Boschung J. Climate change 2013: the Physical Science Basis. Contribution of working group i to the fifth assessment report of the intergovernmental panel on climate change. In: IPCC, editor. United Kingdom and New York, NY, USA: Cambridge University Press Cambridge 2013.

[2] IPCC. Global warming of 1.5°C. An IPCC Special Report on the impacts of global warming of 1.5°C above pre-industrial levels and related global greenhouse gas emission pathways, in the context of strengthening the global response to the threat of climate change, sustainable development, and efforts to eradicate poverty. In: V. Masson-Delmotte PZ, H. O. Pörtner, D. Roberts, J. Skea, P.R. Shukla, A. Pirani, W. Moufouma-Okia, C. Péan, R. Pidcock, S. Connors, J. B. R. Matthews, Y. Chen, X. Zhou, M. I. Gomis, E. Lonnoy, T. Maycock, M. Tignor, T. Waterfield, editor. 2018.

[3] National Research Council 2020. Climate change: evidence and causes: update 2020. Washington, DC: The National Academies Press; 2020.

[4] Masson-Delmotte V., Zhai P., Pirani A., et al. IPCC 2021: climate change 2021: the physical science basis. contribution of working group i to the sixth assessment report of the intergovernmental panel on climate change. Cambridge: Cambridge University Press; 2021.

[5] United States Environmental Protection Agency. Inventory of U.S. greenhouse gas emissions and sinks 1990-2019. 2021.

[6] IPCC. Summary for policymakers. Climate Change 2022: Mitigation of climate change contribution of working group iii to the sixth assessment report of the intergovernmental panel on climate change. In: P.R. Shukla JS, R. Slade, A. Al Khourdajie, R. van Diemen, D. McCollum, M. Pathak, S. Some, P. Vyas, R. Fradera, M. Belkacemi, A. Hasija, G. Lisboa, S. Luz, J. Malley, (editors), editor. Cambridge, UK and New York, NY, USA: Cambridge University Press; 2022.

[7] European Environmental Agency. Total greenhouse gas emission trends and projections in Europe. Denmark 2019.

[8] United Nations Environment Programme. Emissions gap report 2021: the heat is on – a world of climate promises not yet delivered. Nairobi 2021.

[9] United Nations Framework Convention on Climate Change: Conference of the Parties serving as the meeting of the Parties to the Paris Agreement. Nationally determined contributions under the Paris Agreement. Glasgow 2021.

[10] Haines A, Ebi K. The imperative for climate action to protect health. N Engl J Med 2019;380(3):263–73. https://doi.org/10.1056/NEJMra1807873. 01.

[11] Rocque RJ, Beaudoin C, Ndjaboue R, et al. Health effects of climate change: an overview of systematic reviews. BMJ Open 2021;11(6):e046333. https://doi.org/10.1136/bmjopen-2020-046333. 06 09.

[12] World Health Organisation. COP24 special report: health and climate change. 2018.

[13] Romanello M, McGushin A, Di Napoli C, et al. The 2021 report of the Lancet Countdown on health and climate change: code red for a healthy future. Lancet 2021;398(10311):1619–62. https://doi.org/10.1016/S0140-6736(21)01787-6. Oct 30.

[14] Peters A, Schneider A. Cardiovascular risks of climate change. Nat Rev Cardiol 2021;18(1):1–2. https://doi.org/10.1038/s41569-020-00473-5. Jan.

[15] Lelieveld J, Klingmüller K, Pozzer A, et al. Cardiovascular disease burden from ambient air pollution in Europe reassessed using novel hazard ratio functions. Eur Heart J 2019;40(20):1590–6. https://doi.org/10.1093/eurheartj/ehz135. 05.

[16] Alahmad B, Khraishah H, Shakarchi AF, et al. Cardiovascular mortality and exposure to heat in an inherently hot region: implications for climate change. Circulation 2020;141(15):1271–3. https://doi.org/10.1161/CIRCULATIONAHA.119.044860. 04 14.

[17] Visseren FLJ, Mach F, Smulders YM, et al. 2021 ESC Guidelines on cardiovascular disease prevention in clinical practice. Eur Heart J 2021;42(34):3227–337. https://doi.org/10.1093/eurheartj/ehab484. Sep 07.

[18] Song J, Pan R, Yi W, et al. Ambient high temperature exposure and global disease burden during 1990-2019: an analysis of the Global Burden of Disease Study 2019. Sci Total Environ 2021;787:147540. https://doi.org/10.1016/j.scitotenv.2021.147540. Sep 15.

[19] Global Burden of Disease 2019 Risk Factors Collaborators. Global burden of 87 risk factors in 204 countries and territories, 1990-2019: a systematic analysis for the global burden of disease study 2019. Lancet 2020;396(10258):1223–49. https://doi.org/10.1016/S0140-6736(20)30752-2. Oct 17.

[20] World Health Organisation. Quantitative risk assessment of the effects of climate change on selected causes of death, 2030s and 2050s. 2014.

[21] IPCC, Mach K.J., Planton S., von Stechow C. Annex II: glossary. climate change 2014: synthesis report. contribution of working groups I, ii and iii to the fifth assessment report of the intergovernmental panel on climate change. Geneva, Switzerland 2014. p. 117–30.

[22] Salas R.N., Knappenberger P., Hess J. 2020 Lancet countdown on health and climate change brief for the United State of America. London, United Kingdom: Lancet Countdown; 2020. p. 32.

[23] Hoffman JS, Shandas V, Pendleton N. The effects of historical housing policies on resident exposure to intra-urban heat: a study of 108 US Urban areas. Climate 2020;8(1):12.

[24] Park YM, Kwan MP. Understanding racial disparities in exposure to traffic-related air pollution: considering the spatiotemporal dynamics of population distribution. Int J Environ Res Public Health 2020;17(3). https://doi.org/10.3390/ijerph17030908. 02 01.

[25] Jones MR, Diez-Roux AV, Hajat A, et al. Race/ethnicity, residential segregation, and exposure to ambient air pollution: the multi-ethnic study of atherosclerosis (MESA). Am J Public Health 2014;104(11):2130–7. https://doi.org/10.2105/AJPH.2014.302135. Nov.

[26] Salas RN. Environmental racism and climate change - missed diagnoses. N Engl J Med 2021. https://doi.org/10.1056/NEJMp2109160. Aug 18.

[27] Whitmee S, Haines A, Beyrer C, et al. Safeguarding human health in the anthropocene epoch: report of the rockefeller foundation-lancet commission on planetary health. Lancet 2015;386(10007):1973–2028. https://doi.org/10.1016/S0140-6736(15)60901-1. Nov 14.

[28] Chang AY, Barry M, Harrington RA. The need to expand the framework of environmental determinants of cardiovascular health from climate change to planetary health: trial by wildfire. Circulation 2021,;143(21):2029–31. https://doi.org/10.1161/CIRCULATIONAHA.120.051892. May 25.

[29] Schwärzel K, Zhang L, Montanarella L, Wang Y, Sun G. How afforestation affects the water cycle in drylands: a process-based comparative analysis. Glob Chang Biol 2020;26(2):944–59. https://doi.org/10.1111/gcb.14875. 02.

[30] Li R, Zheng H, O'Connor P, et al. Time and space catch up with restoration programs that ignore ecosystem service trade-offs. Sci Adv 2021;7(14). https://doi.org/10.1126/sciadv.abf8650. Mar.

[31] Sovacool BK, Ali SH, Bazilian M, et al. Sustainable minerals and metals for a low-carbon future. Science 2020;367(6473):30–3. https://doi.org/10.1126/science.aaz6003. 01 03.

[32] Rajagopalan S, Landrigan PJ. Pollution and the Heart. N Engl J Med 2021;385(20):1881–92. https://doi.org/10.1056/NEJMra2030281. Nov 11.

[33] Rajagopalan S, Al-Kindi SG, Brook RD. Air pollution and cardiovascular disease: JACC state-of-the-art review. J Am Coll Cardiol 2018;72(17):2054–70. https://doi.org/10.1016/j.jacc.2018.07.099. 10.

[34] Hadley MB, Vedanthan R, Ebi KL, Fuster V. Climate cardiology. BMJ Glob Health 2022;7(6). https://doi.org/10.1136/bmjgh-2022-008860. Jun.

[35] De Blois J, Kjellstrom T, Agewall S, Ezekowitz JA, Armstrong PW, Atar D. The effects of climate change on cardiac health. Cardiology 2015;131(4):209–17. https://doi.org/10.1159/000398787.

[36] Newby DE, Mannucci PM, Tell GS, et al. Expert position paper on air pollution and cardiovascular disease. Eur Heart J 2015;36(2):83–93b. https://doi.org/10.1093/eurheartj/ehu458. Jan.

[37] Brauer M, Casadei B, Harrington RA, Kovacs R, Sliwa K, Group WAPE. Taking a stand against air pollution-the impact on cardiovascular disease: a joint opinion from the world heart federation, american college of cardiology, American heart association, and the european society of cardiology. Circulation 2021;143(14):e800–4. https://doi.org/10.1161/CIRCULATIONAHA.120.052666. Apr.

[38] Landrigan PJ, Fuller R, Acosta NJR, et al. The lancet commission on pollution and health. Lancet 2018;391(10119):462–512. https://doi.org/10.1016/S0140-6736(17)32345-0. 02.

[39] Al-Kindi SG, Brook RD, Biswal S, Rajagopalan S. Environmental determinants of cardiovascular disease: lessons learned from air pollution. Nat Rev Cardiol 2020;17(10):656–72. https://doi.org/10.1038/s41569-020-0371-2. 10.

[40] Landrigan PJ, Frumkin H, Lundberg BE. The false promise of natural gas. N Engl J Med 2020;382(2):104–7. https://doi.org/10.1056/NEJMp1913663. Jan.

[41] Jolly WM, Cochrane MA, Freeborn PH, et al. Climate-induced variations in global wildfire danger from 1979 to 2013. Nat Commun 2015;6:7537. https://doi.org/10.1038/ncomms8537. Jul 14.

[42] Jacob DJ, Logan JA, Gardner GM, et al. Factors regulating ozone over the United States and its export to the global atmosphere. J Geophys Res Atmos 1993;98(D8):14817–26. https://doi.org/10.1029/98JD01224.

[43] Bloomer BJ, Stehr JW, Piety CA, Salawitch RJ, Dickerson RR. Observed relationships of ozone air pollution with temperature and emissions. Geophys Res Lett 2009;36(9). https://doi.org/10.1029/2009GL037308.

[44] Climate Central. Climate change is threatening air quality across the country. 2019.

[45] Horton DE, Harshvardhan, Diffenbaugh NS. Response of air stagnation frequency to anthropogenically enhanced radiative forcing. Environ Res Lett 2012;7(4). https://doi.org/10.1088/1748-9326/7/4/044034.

[46] Horton DE, Skinner CB, Singh D, Diffenbaugh NS. Occurrence and persistence of future atmospheric stagnation events. Nat Clim Chang 2014;4:698–703. https://doi.org/10.1038/nclimate2272. Aug.

[47] National Centers for Environmental Information. Air stagnation index. In: Administration NOaA, editor. 2021.

[48] Birol F. The future of cooling. In: Agency IE, editor. Paris2018.

[49] Liu C, Chen R, Sera F, et al. Ambient particulate air pollution and daily mortality in 652 cities. N Engl J Med 2019;381(8):705–15. https://doi.org/10.1056/NEJMoa1817364. 08 22.

[50] Yang BY, Qian Z, Howard SW, et al. Global association between ambient air pollution and blood pressure: a systematic review and meta-analysis. Environ Pollut 2018;235:576–88. https://doi.org/10.1016/j.envpol.2018.01.001. Apr.

[51] Cai Y, Zhang B, Ke W, et al. Associations of short-term and long-term exposure to ambient air pollutants with hypertension: a systematic review and meta-analysis. Hypertension 2016;68(1):62–70. https://doi.org/10.1161/HYPERTENSIONAHA.116.07218. 07.

[52] Bowe B, Xie Y, Li T, Yan Y, Xian H, Al-Aly Z. The 2016 global and national burden of diabetes mellitus attributable to PM. Lancet Planet Health 2018;2(7):e301–12. https://doi.org/10.1016/S2542-5196(18)30140-2. 07.

[53] Bell G, Mora S, Greenland P, Tsai M, Gill E, Kaufman JD. Association of air pollution exposures with high-density lipoprotein cholesterol and particle number: the multi-ethnic study of atherosclerosis. Arterioscler Thromb Vasc Biol 2017;37(5):976–82. https://doi.org/10.1161/ATVBAHA.116.308193. 05.

[54] Kaufman JD, Adar SD, Barr RG, et al. Association between air pollution and coronary artery calcification within six metropolitan areas in the USA (the Multi-

Ethnic Study of Atherosclerosis and Air Pollution): a longitudinal cohort study. Lancet 2016;388(10045):696–704. https://doi.org/10.1016/S0140-6736(16)00378-0. Aug 13.
[55] Weichenthal S, Villeneuve PJ, Burnett RT, et al. Long-term exposure to fine particulate matter: association with nonaccidental and cardiovascular mortality in the agricultural health study cohort. Environ Health Perspect 2014;122(6):609–15. https://doi.org/10.1289/ehp.1307277. Jun.
[56] Pope CA, Burnett RT, Thun MJ, et al. Lung cancer, cardiopulmonary mortality, and long-term exposure to fine particulate air pollution. JAMA 2002;287(9):1132–41. https://doi.org/10.1001/jama.287.9.1132. Mar 06.
[57] Pope CA, Lefler JS, Ezzati M, et al. Mortality risk and fine particulate air pollution in a large, representative cohort of U.S. adults. Environ Health Perspect 2019;127(7):77007. https://doi.org/10.1289/EHP4438. 07.
[58] Cesaroni G, Forastiere F, Stafoggia M, et al. Long term exposure to ambient air pollution and incidence of acute coronary events: prospective cohort study and meta-analysis in 11 European cohorts from the ESCAPE Project. BMJ 2014;348:f7412. https://doi.org/10.1136/bmj.f7412. Jan 21.
[59] Mustafic H, Jabre P, Caussin C, et al. Main air pollutants and myocardial infarction: a systematic review and meta-analysis. JAMA 2012;307(7):713–21. https://doi.org/10.1001/jama.2012.126. Feb 15.
[60] Shah AS, Lee KK, McAllister DA, et al. Short term exposure to air pollution and stroke: systematic review and meta-analysis. BMJ 2015;350:h1295. https://doi.org/10.1136/bmj.h1295. Mar 24.
[61] Rhinehart ZJ, Kinnee E, Essien UR, et al. Association of fine particulate matter and risk of stroke in patients with atrial fibrillation. JAMA Netw Open 2020;3(9):e2011760. https://doi.org/10.1001/jamanetworkopen.2020.11760. 09.
[62] Shao Q, Liu T, Korantzopoulos P, Zhang Z, Zhao J, Li G. Association between air pollution and development of atrial fibrillation: a meta-analysis of observational studies. Heart Lung 2016;45(6):557–62. https://doi.org/10.1016/j.hrtlng.2016.08.001. Nov - Dec 2016.
[63] Shah AS, Langrish JP, Nair H, et al. Global association of air pollution and heart failure: a systematic review and meta-analysis. Lancet 2013;382(9897):1039–48. https://doi.org/10.1016/S0140-6736(13)60898-3. Sep 21.
[64] Kim JB, Prunicki M, Haddad F, et al. Cumulative lifetime burden of cardiovascular disease from early exposure to air pollution. J Am Heart Assoc 2020;9(6):e014944. https://doi.org/10.1161/JAHA.119.014944. 03 17.
[65] Münzel T, Sørensen M, Gori T, et al. Environmental stressors and cardio-metabolic disease: part I-epidemiologic evidence supporting a role for noise and air pollution and effects of mitigation strategies. Eur Heart J 2017;38(8):550–6. https://doi.org/10.1093/eurheartj/ehw269. Feb.
[66] Münzel T, Sørensen M, Gori T, et al. Environmental stressors and cardio-metabolic disease: part II-mechanistic insights. Eur Heart J 2017;38(8):557–64. https://doi.org/10.1093/eurheartj/ehw294. Feb.
[67] Hadley MB, Baumgartner J, Vedanthan R. Developing a clinical approach to air pollution and cardiovascular health. Circulation 2018;137(7):725–42. https://doi.org/10.1161/CIRCULATIONAHA.117.030377. 02.
[68] Cosselman KE, Navas-Acien A, Kaufman JD. Environmental factors in cardiovascular disease. Nat Rev Cardiol 2015;12(11):627–42. https://doi.org/10.1038/nrcardio.2015.152. Nov.
[69] Burnett RT, Pope CA, Ezzati M, et al. An integrated risk function for estimating the global burden of disease attributable to ambient fine particulate matter exposure. Environ Health Perspect 2014;122(4):397–403. https://doi.org/10.1289/ehp.1307049. Apr.
[70] World Health Organisation. WHO global air quality guidelines: particulate matter (PM 2.5 and PM 10), ozone, nitrogen dioxide, sulfur dioxide and carbon monoxide. 2021.
[71] United States Environmental Protection Agency. Air quality - national summary. 2021.
[72] United States Environmental Protection Agency. Air quality guide for particle pollution. In: Radiation OoAQa, editor. 2015.
[73] Langrish JP, Li X, Wang S, et al. Reducing personal exposure to particulate air pollution improves cardiovascular health in patients with coronary heart disease. Environ Health Perspect 2012;120(3):367–72. https://doi.org/10.1289/ehp.1103898. Mar.
[74] Chen R, Zhao A, Chen H, et al. Cardiopulmonary benefits of reducing indoor particles of outdoor origin: a randomized, double-blind crossover trial of air purifiers. J Am Coll Cardiol 2015;65(21):2279–87. https://doi.org/10.1016/j.jacc.2015.03.553. Jun.
[75] Xu R, Yu P, Abramson MJ, et al. Wildfires, global climate change, and human health. N Engl J Med 2020;383(22):2173–81. https://doi.org/10.1056/NEJMsr2028985. 11 26.
[76] Rajagopalan S, Brook RD. Personalizing your airspace and your health. J Am Coll Cardiol 2015;65(21):2288–90. https://doi.org/10.1016/j.jacc.2015.04.010. Jun.
[77] Newman JD, Bhatt DL, Rajagopalan S, et al. Cardiopulmonary Impact of particulate air pollution in high-risk populations: JACC state-of-the-art review. J Am Coll Cardiol 2020;76(24):2878–94. https://doi.org/10.1016/j.jacc.2020.10.020. 12 15.
[78] IPCC. Climate change 2022: impacts, adaptation, and vulnerability. In: Contribution of working group ii to the sixth assessment report of the intergovernmental panel on climate change H.O. Pörtner DCR, M. Tignor, E.S. Poloczanska, K. Mintenbeck, A. Alegría, M. Craig, S. Langsdorf, S. Löschke, V. Möller, A. Okem, B. Rama (eds.). editor. United Kingdom: Cambridge Press; 2022.
[79] Lee JY, Kim H, Gasparrini A, et al. Predicted temperature-increase-induced global health burden and its regional variability. Environ Int 2019;131:105027. https://doi.org/10.1016/j.envint.2019.105027. 10.
[80] Semenza JC, Rubin CH, Falter KH, et al. Heat-related deaths during the July 1995 heat wave in Chicago. N Engl J Med 1996;335(2):84–90. https://doi.org/10.1056/NEJM199607113350203. Jul 11.
[81] Hajat S, O'Connor M, Kosatsky T. Health effects of hot weather: from awareness of risk factors to effective health protection. Lancet 2010;375(9717):856–63. https://doi.org/10.1016/S0140-6736(09)61711-6. Mar 06.
[82] Gasparrini A, Guo Y, Sera F, et al. Projections of temperature-related excess mortality under climate change scenarios. Lancet Planet Health 2017;1(9):e360–7. https://doi.org/10.1016/S2542-5196(17)30156-0. Dec.
[83] Argacha JF, Bourdrel T, van de Borne P. Ecology of the cardiovascular system: a focus on air-related environmental factors. Trends Cardiovasc Med 2018;28(2):112–26. https://doi.org/10.1016/j.tcm.2017.07.013. 02.
[84] Vaidyanathan A., Malilay J., Schramm P., Saha S. Heat-related deaths — United States, 2004–2018. In: Rep MMMW, editor. 2020. p. 729–34.
[85] Philip S.Y., Kew S.F., Jan van Oldenborgh G., Yang W., al e. Rapid attribution analysis of the extraordinary heatwave on the pacific coast of the us and canada. The Netherlands: World Weather Attribution; 2021.
[86] Schiermeier Q. Climate change made North America's deadly heatwave 150 times more likely. Nature 2021. https://doi.org/10.1038/d41586-021-01869-0. Jul 08.
[87] Guerra F, Bonelli P, Flori M, et al. Temporal trends and temperature-related incidence of electrical storm: the TEMPEST study (temperature-related incidence of electrical storm). Circ Arrhythm Electrophysiol 2017;10(3). https://doi.org/10.1161/CIRCEP.116.004634. Mar.
[88] Zhao Q, Coelho MSZS, Li S, et al. Temperature variability and hospitalization for cardiac arrhythmia in Brazil: a nationwide case-crossover study during 2000-2015. Environ Pollut 2019;246:552–8. https://doi.org/10.1016/j.envpol.2018.12.063. Mar.
[89] Organisation WH. Quantitative risk assessment of the effects of climate change on selected causes of death, 2030s and 2050s. 2014.
[90] Kang Y, Tang H, Zhang L, et al. Long-term temperature variability and the incidence of cardiovascular diseases: a large, representative cohort study in China. Environ Pollut 2021;278:116831. https://doi.org/10.1016/j.envpol.2021.116831. Jun 01.
[91] Yang J, Zhou M, Li M, et al. Vulnerability to the impact of temperature variability on mortality in 31 major Chinese cities. Environ Pollut 2018;239:631–7. https://doi.org/10.1016/j.envpol.2018.04.090. Aug.
[92] Zanobetti A, O'Neill MS, Gronlund CJ, Schwartz JD. Summer temperature variability and long-term survival among elderly people with chronic disease. Proc Natl Acad Sci U S A 2012;109(17):6608–13. https://doi.org/10.1073/pnas.1113070109. Apr 24.
[93] Mercer JB. Cold–an underrated risk factor for health. Environ Res 2003;92(1):8–13. https://doi.org/10.1016/s0013-9351(02)00009-9. May.
[94] De Bono A, Peduzzi P, Kluser S, Giuliani G. Impacts of summer 2003 heat wave in Europe. Environ Alert Bull 2004;2:4.
[95] Asseng S, Spänkuch D, Hernandez-Ochoa IM, Laporta J. The upper temperature thresholds of life. Lancet Planet Health 2021;5(6):e378–85. https://doi.org/10.1016/S2542-5196(21)00079-6. 06.
[96] Schär C. The worst heat waves to come.: Nature Climate Change; 2016. p. 128–9.
[97] Bröde P, Błazejczyk K, Fiala D, et al. The universal thermal climate index UTCI compared to ergonomics standards for assessing the thermal environment. Ind Health 2013;51(1):16–24. https://doi.org/10.2486/indhealth.2012-0098.
[98] Sherwood SC, Huber M. An adaptability limit to climate change due to heat stress. Proc Natl Acad Sci U S A. 2010,;107(21):9552–5. https://doi.org/10.1073/pnas.0913352107. May 25.
[99] Havenith G, Fiala D. Thermal indices and thermophysiological modeling for heat stress. Compr Physiol 2015;6(1):255–302. https://doi.org/10.1002/cphy.c140051. Dec 15.
[100] Weinberger KR, Zanobetti A, Schwartz J, Wellenius GA. Effectiveness of national weather service heat alerts in preventing mortality in 20 US cities. Environ Int 2018;116:30–8. https://doi.org/10.1016/j.envint.2018.03.028. 07.
[101] Benmarhnia T, Bailey Z, Kaiser D, Auger N, King N, Kaufman JS. A difference-in-differences approach to assess the effect of a heat action plan on heat-related mortality, and differences in effectiveness according to sex, age, and socioeconomic status (Montreal, Quebec). Environ Health Perspect 2016;124(11):1694–9. https://doi.org/10.1289/EHP203. Nov.
[102] Charkoudian N. Skin blood flow in adult human thermoregulation: how it works, when it does not, and why. Mayo Clin Proc 2003;78(5):603–12. https://doi.org/10.4065/78.5.603. May.
[103] Sessler DI. Thermoregulatory defense mechanisms. Crit Care Med 2009;37(7 Suppl):S203–10. https://doi.org/10.1097/CCM.0b013e3181aa5568. Jul.
[104] Creager MA, Cooke JP, Mendelsohn ME, et al. Impaired vasodilation of forearm resistance vessels in hypercholesterolemic humans. J Clin Invest 1990;86(1):228–34. https://doi.org/10.1172/JCI114688. Jul.
[105] Holowatz LA, Kenney WL. Peripheral mechanisms of thermoregulatory control of skin blood flow in aged humans. J Appl Physiol 2010;109(5):1538–44. https://doi.org/10.1152/japplphysiol.00338.2010 (1985)Nov.
[106] Rowell LB. Cardiovascular aspects of human thermoregulation. Circ Res 1983;52(4):367–79. https://doi.org/10.1161/01.res.52.4.367. Apr.
[107] Rowell LB, Brengelmann GL, Blackmon JR, Murray JA. Redistribution of blood flow during sustained high skin temperature in resting man. J Appl Physiol 1970;28(4):415–20. https://doi.org/10.1152/jappl.1970.28.4.415. Apr.
[108] Rowell LB, Brengelmann GL, Murray JA. Cardiovascular responses to sustained high skin temperature in resting man. J Appl Physiol 1969;27(5):673–80. https://doi.org/10.1152/jappl.1969.27.5.673. Nov.
[109] Nelson MD, Haykowsky MJ, Petersen SR, DeLorey DS, Cheng-Baron J, Thompson RB. Increased left ventricular twist, untwisting rates, and suction

maintain global diastolic function during passive heat stress in humans. Am J Physiol Heart Circ Physiol 2010;298(3):H930–7. https://doi.org/10.1152/ajpheart.00987.2009. Mar.
[110] Cui J, Sinoway LI. Cardiovascular responses to heat stress in chronic heart failure. Curr Heart Fail Rep 2014;11(2):139–45. https://doi.org/10.1007/s11897-014-0191-y. Jun.
[111] Keatinge WR, Coleshaw SR, Easton JC, Cotter F, Mattock MB, Chelliah R. Increased platelet and red cell counts, blood viscosity, and plasma cholesterol levels during heat stress, and mortality from coronary and cerebral thrombosis. Am J Med 1986;81(5):795–800. https://doi.org/10.1016/0002-9343(86)90348-7. Nov.
[112] Epstein Y, Yanovich R. Heatstroke. N Engl J Med 2019;380(25):2449–59. https://doi.org/10.1056/NEJMra1810762. Jun 20.
[113] Cheng J, Xu Z, Bambrick H, et al. Cardiorespiratory effects of heatwaves: a systematic review and meta-analysis of global epidemiological evidence. Environ Res 2019;177:108610. https://doi.org/10.1016/j.envres.2019.108610. 10.
[114] Bouchama A, Dehbi M, Chaves-Carballo E. Cooling and hemodynamic management in heatstroke: practical recommendations. Crit Care 2007;11(3): R54. https://doi.org/10.1186/cc5910.
[115] Basu R, Ostro BD. A multicounty analysis identifying the populations vulnerable to mortality associated with high ambient temperature in California. Am J Epidemiol 2008;168(6):632–7. https://doi.org/10.1093/aje/kwn170. Sep 15.
[116] Baccini M, Biggeri A, Accetta G, et al. Heat effects on mortality in 15 European cities. Epidemiology 2008;19(5):711–9. https://doi.org/10.1097/EDE.0b013e318176bfcd. Sep.
[117] Basu R, Samet JM. Relation between elevated ambient temperature and mortality: a review of the epidemiologic evidence. Epidemiol Rev 2002;24(2):190–202. https://doi.org/10.1093/epirev/mxf007.
[118] Anderson GB, Bell ML. Heat waves in the United States: mortality risk during heat waves and effect modification by heat wave characteristics in 43U.S. communities. Environ Health Perspect 2011;119(2):210–8. https://doi.org/10.1289/ehp.1002313. Feb.
[119] Moseley PL. Heat shock proteins and heat adaptation of the whole organism. J Appl Physiol 1997;83(5):1413–7. https://doi.org/10.1152/jappl.1997.83.5.1413 (1985). Nov.
[120] Tupling AR. Protection of heart and skeletal muscle by heat shock proteins. Appl Physiol Nutr Metab 2008;33(5):1021–2. https://doi.org/10.1139/H08-066. Oct.
[121] Périard JD, Racinais S, Sawka MN. Adaptations and mechanisms of human heat acclimation: applications for competitive athletes and sports. Scand J Med Sci Sports 2015;25(Suppl 1):20–38. https://doi.org/10.1111/sms.12408. Jun.
[122] Rocklöv J, Dubrow R. Climate change: an enduring challenge for vector-borne disease prevention and control. Nat Immunol 2020;21(5):479–83. https://doi.org/10.1038/s41590-020-0648-y. 05.
[123] Ostfeld RS, Brunner JL. Climate change and Ixodes tick-borne diseases of humans. Philos Trans R Soc Lond B Biol Sci 2015;370(1665). https://doi.org/10.1098/rstb.2014.0051. Apr 05.
[124] Centers for Disease Control and Prevention (CDC). Lyme disease data tables: historical data. 2021.
[125] Leighton PA, Koffi JK, Pelcat Y, Lindsay LR, Ogden NH. Predicting the speed of tick invasion: an empirical model of range expansion for the Lyme disease vector Ixodes scapularis in Canada. J Appl Ecol 2012;49(2):457–64. https://doi.org/10.1111/j.1365-2664.2012.02112.x.
[126] Krause PJ, Bockenstedt LK. Cardiology patient pages. Lyme disease and the heart. Circulation 2013;127(7):e451–4. https://doi.org/10.1161/CIRCULATIONAHA.112.101485. Feb 19.
[127] Centers for Disease Control and Prevention. Three sudden cardiac deaths associated with lyme carditis. In: MMWR, editor. United States 2013.
[128] Centers for Disease Control and Prevention (CDC). Babesiosis. USA 2021.
[129] White DJ, Talarico J, Chang HG, Birkhead GS, Heimberger T, Morse DL. Human babesiosis in New York State: review of 139 hospitalized cases and analysis of prognostic factors. Arch Intern Med 1998;158(19):2149–54. https://doi.org/10.1001/archinte.158.19.2149. Oct 26.
[130] Kandalaft O, Craig C, Pervaiz A, Hiser WB. Abesiosis associated myocarditis. J Am Coll Cardiol 2019;73(9_Supplement_1):2487. https://doi.org/10.1016/S0735-1097(19)33093-1. 2487.
[131] Bonney KM. Chagas disease in the 21st century: a public health success or an emerging threat? Parasite 2014;21:11. https://doi.org/10.1051/parasite/2014012.
[132] Nunes MCP, Beaton A, Acquatella H, et al. Chagas cardiomyopathy: an update of current clinical knowledge and management: a scientific statement from the American Heart association. Circulation 2018;138(12):e169–209. https://doi.org/10.1161/CIR.0000000000000599. 09 18.
[133] Mora G. Chagas cardiomyopathy. e-J Cardiol Pract 2016.
[134] Beatty NL, Klotz SA. Autochthonous chagas disease in the United States: how are people getting infected? Am J Trop Med Hyg 2020;103(3):967–9. https://doi.org/10.4269/ajtmh.19-0733. 09.
[135] Short EE, Caminade C, Thomas BN. Climate change contribution to the emergence or re-emergence of parasitic diseases. Infect Dis 2017;10:1178633617732296. https://doi.org/10.1177/1178633617732296 (Auckl).
[136] Asin S, Catalá S. Development of Trypanosoma cruzi in Triatoma infestans: influence of temperature and blood consumption. J Parasitol 1995;81(1):1–7. Feb.
[137] Garza M, Feria Arroyo TP, Casillas EA, Sanchez-Cordero V, Rivaldi CL, Sarkar S. Projected future distributions of vectors of Trypanosoma cruzi in North America under climate change scenarios. PLoS Negl Trop Dis 2014;8(5):e2818. https://doi.org/10.1371/journal.pntd.0002818. May.
[138] Medlock JM, Leach SA. Effect of climate change on vector-borne disease risk in the UK. Lancet Infect Dis 2015;15(6):721–30. https://doi.org/10.1016/S1473-3099(15)70091-5. Jun.
[139] Organisation WH. Malaria. Geneva 2021.
[140] Gao HW, Wang LP, Liang S, et al. Change in rainfall drives malaria re-emergence in Anhui Province, China. PLoS One 2012;7(8):e43686. https://doi.org/10.1371/journal.pone.0043686.
[141] Andriopoulos P, Economopoulou A, Spanakos G, Assimakopoulos G. A local outbreak of autochthonous Plasmodium vivax malaria in Laconia, Greece–a re-emerging infection in the southern borders of Europe? Int J Infect Dis 2013;17(2): e125–8. https://doi.org/10.1016/j.ijid.2012.09.009. Feb.
[142] Martens WJ, Niessen LW, Rotmans J, Jetten TH, McMichael AJ. Potential impact of global climate change on malaria risk. Environ Health Perspect 1995;103(5): 458–64. https://doi.org/10.1289/ehp.95103458. May.
[143] Gupta S, Gazendam N, Farina JM, et al. Malaria and the heart: JACC state-of-the-art review. J Am Coll Cardiol 2021;77(8):1110–21. https://doi.org/10.1016/j.jacc.2020.12.042. 03 02.
[144] Colomba C, Trizzino M, Gioè C, et al. Malaria and the heart: two rare case reports of. J Vector Borne Dis 2017;54(4):372–4. https://doi.org/10.4103/0972-9062.225845. 2017 Oct-Dec.
[145] Caminade C, Medlock JM, Ducheyne E, et al. Suitability of European climate for the Asian tiger mosquito Aedes albopictus: recent trends and future scenarios. J R Soc Interface 2012;9(75):2708–17. https://doi.org/10.1098/rsif.2012.0138. Oct 07.
[146] Cotella JI, Sauce AL, Saldarriaga CI, et al. Chikungunya and the heart. Cardiology 2021;146(3):324–34. https://doi.org/10.1159/000514206. 2021.
[147] Alvarez MF, Bolívar-Mejía A, Rodriguez-Morales AJ, Ramirez-Vallejo E. Cardiovascular involvement and manifestations of systemic Chikungunya virus infection: a systematic review. F1000Res 2017;6:390. https://doi.org/10.12688/f1000research.11078.2.
[148] Yacoub S, Wertheim H, Simmons CP, Screaton G, Wills B. Cardiovascular manifestations of the emerging dengue pandemic. Nat Rev Cardiol 2014;11(6): 335–45. https://doi.org/10.1038/nrcardio.2014.40. Jun.
[149] Lateef A, Fisher DA, Tambyah PA. Dengue and relative bradycardia. Emerg Infect Dis 2007;13(4):650–1. https://doi.org/10.3201/eid1304.061212. Apr.
[150] Carta KAG, Mendoza_Britto IJ, Finizola V, et al. Abstract 13292: bradycardia as a Manifestation of Chikungunya Myocarditis. A new threat to America. Circulation 2016;134(suppl_1):A13292. https://doi.org/10.1161/circ.134.suppl_1.13292. A13292.
[151] Kushawaha A, Jadonath S, Mobarakai N. West nile virus myocarditis causing a fatal arrhythmia: a case report. Cases J 2009,;2:7147. https://doi.org/10.1186/1757-1626-2-7147. May 27.
[152] Albrecht G, Sartore GM, Connor L, et al. Solastalgia: the distress caused by environmental change. Australas Psychiatry 2007;15(Suppl 1):S95–8. https://doi.org/10.1080/10398560701701288.
[153] Clayton S. Climate anxiety: psychological responses to climate change. J Anxiety Disord 2020;74:102263. https://doi.org/10.1016/j.janxdis.2020.102263. 08.
[154] Clayton S., Manning C., Speiser M., Hill A.N. Mental health and our changing climate: impacts, inequities, responses. In: American Psychological Association a, ecoAmerica., editors. Washington D.C. 2021.
[155] Wu J, Snell G, Samji H. Climate anxiety in young people: a call to action. Lancet Planet Health 2020;4(10):e435–6. https://doi.org/10.1016/S2542-5196(20)30223-0. 10.
[156] Liu J, Varghese BM, Hansen A, et al. Is there an association between hot weather and poor mental health outcomes? A systematic review and meta-analysis. Environ Int 2021;153:106533. https://doi.org/10.1016/j.envint.2021.106533. 08.
[157] Charlson F, Ali S, Benmarhnia T, et al. Climate change and mental health: a scoping review. Int J Environ Res Public Health 2021;18(9). https://doi.org/10.3390/ijerph18094486. 04 23.
[158] Nielsen RE, Banner J, Jensen SE. Cardiovascular disease in patients with severe mental illness. Nat Rev Cardiol 2021;18(2):136–45. https://doi.org/10.1038/s41569-020-00463-7. 02.
[159] Richardson S, Shaffer JA, Falzon L, Krupka D, Davidson KW, Edmondson D. Meta-analysis of perceived stress and its association with incident coronary heart disease. Am J Cardiol 2012;110(12):1711–6. https://doi.org/10.1016/j.amjcard.2012.08.004. Dec 15.
[160] Hippisley-Cox J, Coupland C, Brindle P. Development and validation of QRISK3 risk prediction algorithms to estimate future risk of cardiovascular disease: prospective cohort study. BMJ 2017;357:j2099. https://doi.org/10.1136/bmj.j2099. May.
[161] Templin C, Ghadri JR, Diekmann J, et al. Clinical features and outcomes of Takotsubo (Stress) cardiomyopathy. N Engl J Med 2015;373(10):929–38. https://doi.org/10.1056/NEJMoa1406761. Sep 03.
[162] Itoh T, Toda N, Yoshizawa M, et al. Impact of the Great East Japan Earthquake and Tsunami on the Incidence of Takotsubo Syndrome using a multicenter, long-term regional registry. Circ J 2021. https://doi.org/10.1253/circj.CJ-20-1044. Jun 12.
[163] Talukder MRR, Rutherford S, Phung D, Islam MZ, Chu C. The effect of drinking water salinity on blood pressure in young adults of coastal Bangladesh. Environ Pollut 2016;214:248–54. https://doi.org/10.1016/j.envpol.2016.03.074. Jul.
[164] Lang IA, Galloway TS, Scarlett A, et al. Association of urinary bisphenol A concentration with medical disorders and laboratory abnormalities in adults. JAMA 2008;300(11):1303–10. https://doi.org/10.1001/jama.300.11.1303. Sep 17.

[165] AE J. Our oceans brim with climate solutions. We need a blue new deal. Washington DC: Washington Post; 2019.
[166] Haines A, McMichael AJ, Smith KR, et al. Public health benefits of strategies to reduce greenhouse-gas emissions: overview and implications for policy makers. Lancet 2009;374(9707):2104–14. https://doi.org/10.1016/S0140-6736(09)61759-1. Dec 19.
[167] Jennings N, Fecht D, De Matteis S. Mapping the co-benefits of climate change action to issues of public concern in the UK: a narrative review. Lancet Planet Health 2020;4(9):e424–33. https://doi.org/10.1016/S2542-5196(20)30167-4. 09.
[168] Milner J, Green R, Dangour AD, et al. Health effects of adopting low greenhouse gas emission diets in the UK. BMJ Open 2015;5(4):e007364. https://doi.org/10.1136/bmjopen-2014-007364. Apr 30.
[169] Thurston GD, De Matteis S, Murray K, et al. Maximizing the public health benefits from climate action. Environ Sci Technol 2018;52(7):3852–3. https://doi.org/10.1021/acs.est.8b00859. Apr 03.
[170] Pan A, Sun Q, Bernstein AM, et al. Red meat consumption and mortality: results from 2 prospective cohort studies. Arch Intern Med 2012;172(7):555–63. https://doi.org/10.1001/archinternmed.2011.2287. Apr 09.
[171] Lim CC, Hayes RB, Ahn J, et al. Mediterranean diet and the association between air pollution and cardiovascular disease mortality risk. Circulation 2019;139(15):1766–75. https://doi.org/10.1161/CIRCULATIONAHA.118.035742. 04 09.
[172] Anand SS, Hawkes C, de Souza RJ, et al. Food consumption and its impact on cardiovascular disease: importance of solutions focused on the globalized food system: a report from the workshop convened by the world heart federation. J Am Coll Cardiol 2015;66(14):1590–614. https://doi.org/10.1016/j.jacc.2015.07.050. Oct 06.
[173] Magkos F, Tetens I, Bügel SG, et al. A perspective on the transition to plant-based diets: a diet change may attenuate climate change, but can it also attenuate obesity and chronic disease risk? Adv Nutr 2020;11(1):1–9. https://doi.org/10.1093/advances/nmz090. 01 01.
[174] Mendoza-Vasconez AS, Landry MJ, Crimarco A, Bladier C, Gardner CD. Sustainable diets for cardiovascular disease prevention and management. Curr Atheroscler Rep 2021;23(7):31. https://doi.org/10.1007/s11883-021-00929-0. May 10.
[175] Estruch R, Ros E, Salas-Salvadó J, et al. Primary prevention of cardiovascular disease with a mediterranean diet supplemented with extra-virgin olive oil or nuts. N Engl J Med 2018;378(25):e34. https://doi.org/10.1056/NEJMoa1800389. Jun 21.
[176] de Lorgeril M, Salen P, Martin JL, Monjaud I, Delaye J, Mamelle N. Mediterranean diet, traditional risk factors, and the rate of cardiovascular complications after myocardial infarction: final report of the Lyon diet heart study. Circulation 1999;99(6):779–85. https://doi.org/10.1161/01.cir.99.6.779. Feb 16.
[177] Arps K, Pallazola VA, Cardoso R, et al. Clinician's guide to the updated ABCs of cardiovascular disease prevention: a review part 1. Am J Med 2019;132(6):e569–80. https://doi.org/10.1016/j.amjmed.2019.01.016. 06.
[178] Arps K, Pallazola VA, Cardoso R, et al. Clinician's guide to the updated ABCs of cardiovascular disease prevention: a review part 2. Am J Med 2019;132(7):e599–609. https://doi.org/10.1016/j.amjmed.2019.01.031. 07.
[179] Arem H, Moore SC, Patel A, et al. Leisure time physical activity and mortality: a detailed pooled analysis of the dose-response relationship. JAMA Intern Med 2015;175(6):959–67. https://doi.org/10.1001/jamainternmed.2015.0533. Jun.
[180] Kyu HH, Bachman VF, Alexander LT, et al. Physical activity and risk of breast cancer, colon cancer, diabetes, ischemic heart disease, and ischemic stroke events: systematic review and dose-response meta-analysis for the global burden of disease study 2013. BMJ 2016;354:i3857. https://doi.org/10.1136/bmj.i3857. Aug 09.
[181] Whelton SP, Chin A, Xin X, He J. Effect of aerobic exercise on blood pressure: a meta-analysis of randomized, controlled trials. Ann Intern Med 2002;136(7):493–503. https://doi.org/10.7326/0003-4819-136-7-200204020-00006. Apr 02.
[182] Villareal DT, Aguirre L, Gurney AB, et al. Aerobic or resistance exercise, or both, in dieting obese older adults. N Engl J Med 2017;376(20):1943–55. https://doi.org/10.1056/NEJMoa1616338. 05 18.
[183] Sigal RJ, Kenny GP, Boulé NG, et al. Effects of aerobic training, resistance training, or both on glycemic control in type 2 diabetes: a randomized trial. Ann Intern Med 2007;147(6):357–69. https://doi.org/10.7326/0003-4819-147-6-200709180-00005. Sep 18.
[184] Alessio HM, Bassett DR, Bopp MJ, et al. Climate change, air pollution, and physical inactivity: is active transportation part of the solution? Med Sci Sports Exerc 2021;53(6):1170–8. https://doi.org/10.1249/MSS.0000000000002569. Jun 01.
[185] Manson JE, Greenland P, LaCroix AZ, et al. Walking compared with vigorous exercise for the prevention of cardiovascular events in women. N Engl J Med 2002;347(10):716–25. https://doi.org/10.1056/NEJMoa021067. Sep 05.
[186] Celis-Morales CA, Lyall DM, Welsh P, et al. Association between active commuting and incident cardiovascular disease, cancer, and mortality: prospective cohort study. BMJ 2017;357:j1456. https://doi.org/10.1136/bmj.j1456. Apr 19.
[187] Barengo NC, Hu G, Lakka TA, Pekkarinen H, Nissinen A, Tuomilehto J. Low physical activity as a predictor for total and cardiovascular disease mortality in middle-aged men and women in Finland. Eur Heart J 2004;25(24):2204–11. https://doi.org/10.1016/j.ehj.2004.10.009. Dec.
[188] Kim SR, Choi S, Kim K, et al. Association of the combined effects of air pollution and changes in physical activity with cardiovascular disease in young adults. Eur Heart J 2021;42(25):2487–97. https://doi.org/10.1093/eurheartj/ehab139. Jul.
[189] Tainio M, de Nazelle AJ, Götschi T, et al. Can air pollution negate the health benefits of cycling and walking? Prev Med 2016;87:233–6. https://doi.org/10.1016/j.ypmed.2016.02.002. 06.
[190] Cepeda M, Schoufour J, Freak-Poli R, et al. Levels of ambient air pollution according to mode of transport: a systematic review. Lancet Public Health 2017;2(1):e23–34. https://doi.org/10.1016/S2468-2667(16)30021-4. 01.
[191] Heaney AK, Carrión D, Burkart K, Lesk C, Jack D. Climate change and physical activity: estimated impacts of ambient temperatures on bikeshare usage in New York City. Environ Health Perspect 2019;127(3):37002. https://doi.org/10.1289/EHP4039. 03.
[192] An R, Shen J, Li Y, Bandaru S. Projecting the influence of global warming on physical activity patterns: a systematic review. Curr Obes Rep 2020;9(4):550–61. https://doi.org/10.1007/s13679-020-00406-w. Dec.
[193] Armstrong LE, Casa DJ, Millard-Stafford M, et al. American college of sports medicine position stand. Exertional heat illness during training and competition. Med Sci Sports Exerc 2007;39(3):556–72. https://doi.org/10.1249/MSS.0b013e31802fa199. Mar.
[194] Casa DJ, DeMartini JK, Bergeron MF, et al. National athletic trainers' association position statement: exertional heat illnesses. J Athl Train 2015;50(9):986–1000. https://doi.org/10.4085/1062-6050-50.9.07. Sep.
[195] Druyan A, Atias D, Ketko I, Cohen-Sivan Y, Heled Y. The effects of smoking and nicotine ingestion on exercise heat tolerance. J Basic Clin Physiol Pharmacol 2017;28(2):167–70. https://doi.org/10.1515/jbcpp-2016-0065. Mar 01.
[196] St-Onge MP, Grandner MA, Brown D, et al. Sleep duration and quality: impact on lifestyle behaviors and cardiometabolic health: a scientific statement from the American Heart association. Circulation 2016;134(18):e367–86. https://doi.org/10.1161/CIR.0000000000000444. Nov.
[197] Ai S, Zhang J, Zhao G, et al. Causal associations of short and long sleep durations with 12 cardiovascular diseases: linear and nonlinear Mendelian randomization analyses in UK Biobank. Eur Heart J 2021;42(34):3349–57. https://doi.org/10.1093/eurheartj/ehab170. 09 07.
[198] Deng HB, Tam T, Zee BC, et al. Short sleep duration increases metabolic impact in healthy adults: a population-based cohort study. Sleep 2017;40(10). https://doi.org/10.1093/sleep/zsx130. 10 01.
[199] Daghlas I, Dashti HS, Lane J, et al. Sleep duration and myocardial infarction. J Am Coll Cardiol 2019;74(10):1304–14. https://doi.org/10.1016/j.jacc.2019.07.022. 09 10.
[200] Rifkin DI, Long MW, Perry MJ. Climate change and sleep: a systematic review of the literature and conceptual framework. Sleep Med Rev 2018;42:3–9. https://doi.org/10.1016/j.smrv.2018.07.007. 12.
[201] Obradovich N, Migliorini R, Mednick SC, Fowler JH. Nighttime temperature and human sleep loss in a changing climate. Sci Adv 2017;3(5):e1601555. https://doi.org/10.1126/sciadv.1601555. May.
[202] Layton JB, Li W, Yuan J, Gilman JP, Horton DB, Setoguchi S. Heatwaves, medications, and heat-related hospitalization in older medicare beneficiaries with chronic conditions. PLoS One 2020;15(12):e0243665. https://doi.org/10.1371/journal.pone.0243665.
[203] Kalisch Ellett L, Pratt N, Le Blanc V, K W, Roughead EE. Increased risk of hospital admission for dehydration or heat-related illness after initiation of medicines: a sequence symmetry analysis. J Clin Pharm Ther 2016.
[204] Sommet A, Durrieu G, Lapeyre-Mestre M, Montastruc JL, Association of French Pharmaco Vigilance Centres. A comparative study of adverse drug reactions during two heat waves that occurred in France in 2003 and 2006. Pharmacoepidemiol Drug Saf 2012;21(3):285–8. https://doi.org/10.1002/pds.2307. Mar.
[205] Schoolwerth AC, Sica DA, Ballermann BJ, Wilcox CS, Association CotKiCDatCfHBPRotAH. Renal considerations in angiotensin converting enzyme inhibitor therapy: a statement for healthcare professionals from the council on the kidney in cardiovascular disease and the council for high blood pressure research of the American Heart association. Circulation 2001;104(16):1985–91. https://doi.org/10.1161/hc4101.096153. Oct 16.
[206] Rose BD. Clinical physiology of acid-base and electrolyte disorders (Clinical physiology of acid base & electrolyte disorders). 5th ed. McGraw-Hill Education; 2001.
[207] Milder TY, Stocker SL, Day RO, Greenfield JR. Potential safety issues with use of sodium-glucose cotransporter 2 inhibitors, particularly in people with type 2 diabetes and chronic kidney disease. Drug Saf 2020;43(12):1211–21. https://doi.org/10.1007/s40264-020-01010-6. 12.
[208] Freund BJ, Joyner MJ, Jilka SM, et al. Thermoregulation during prolonged exercise in heat: alterations with beta-adrenergic blockade. J Appl Physiol 1987;63(3):930–6. https://doi.org/10.1152/jappl.1987.63.3.930 (1985)Sep.
[209] Bruning RS, Dahmus JD, Kenney WL, Alexander LM. Aspirin and clopidogrel alter core temperature and skin blood flow during heat stress. Med Sci Sports Exerc 2013;45(4):674–82. https://doi.org/10.1249/MSS.0b013e31827981dc. Apr.
[210] Gader AM, al-Mashhadani SA, al-Harthy SS. Direct activation of platelets by heat is the possible trigger of the coagulopathy of heat stroke. Br J Haematol 1990;74(1):86–92. https://doi.org/10.1111/j.1365-2141.1990.tb02543.x. Jan.
[211] Song XD, Chen AH, Luo BD, Zou F. [Pretreatment with aspirin for protection against heat stroke in rats]. Di Yi Jun Yi Da Xue Xue Bao 2004;24(6):631–5. Jun.
[212] Fisher JA, Puett RC, Laden F, et al. Case-crossover analysis of short-term particulate matter exposures and stroke in the health professionals follow-up study. Environ Int 2019;124:153–60. https://doi.org/10.1016/j.envint.2018.12.044. 03.
[213] Greaney JL, Stanhewicz AE, Kenney WL. Chronic statin therapy is associated with enhanced cutaneous vascular responsiveness to sympathetic outflow during

passive heat stress. J Physiol 2019;597(18):4743–55. https://doi.org/10.1113/JP278237. 09.
[214] Holowatz LA, Santhanam L, Webb A, Berkowitz DE, Kenney WL. Oral atorvastatin therapy restores cutaneous microvascular function by decreasing arginase activity in hypercholesterolaemic humans. J Physiol 2011;589(Pt 8):2093–103. https://doi.org/10.1113/jphysiol.2010.203935. Apr 15.
[215] Alexander LM, Kutz JL, Kenney WL. Tetrahydrobiopterin increases NO-dependent vasodilation in hypercholesterolemic human skin through eNOS-coupling mechanisms. Am J Physiol Regul Integr Comp Physiol 2013;304(2):R164–9. https://doi.org/10.1152/ajpregu.00448.2012. Jan 15.
[216] Holowatz LA, Kenney WL. Oral atorvastatin therapy increases nitric oxide-dependent cutaneous vasodilation in humans by decreasing ascorbate-sensitive oxidants. Am J Physiol Regul Integr Comp Physiol 2011;301(3):R763–8. https://doi.org/10.1152/ajpregu.00220.2011. Sep.
[217] Nam YH, Bilker WB, Leonard CE, Bell ML, Alexander LM, Hennessy S. Publisher correction: effect of statins on the association between high temperature and all-cause mortality in a socioeconomically disadvantaged population: a cohort study. Sci Rep 2019;9(1):11010. https://doi.org/10.1038/s41598-019-46259-9. Jul 24.
[218] Hartiala J, Breton CV, Tang WH, et al. Ambient air pollution is associated with the severity of coronary atherosclerosis and incident myocardial infarction in patients undergoing elective cardiac evaluation. J Am Heart Assoc 2016;5(8). https://doi.org/10.1161/JAHA.116.003947. 07 28.
[219] Alexeeff SE, Coull BA, Gryparis A, et al. Medium-term exposure to traffic-related air pollution and markers of inflammation and endothelial function. Environ Health Perspect 2011;119(4):481–6. https://doi.org/10.1289/ehp.1002560. Apr.
[220] Kongmalai T, Chuanchaiyakul N, Sripatumtong C, et al. The effect of temperature on the stability of PCSK-9 monoclonal antibody: an experimental study. Lipids Health Dis 2021;20(1):21. https://doi.org/10.1186/s12944-021-01447-3. Feb 25.
[221] Solomon CG, Salas RN, Malina D, et al. Fossil-fuel pollution and climate change - a new NEJM group series. N Engl J Med 2022;386(24):2328–9. https://doi.org/10.1056/NEJMe2206300. 06 16.
[222] Salas RN, Solomon CG. The climate crisis - health and care delivery. N Engl J Med 2019;381(8):e13. https://doi.org/10.1056/NEJMp1906035. Aug.
[223] Dzau VJ, Levine R, Barrett G, Witty A. Decarbonizing the U.S. health sector - a call to action. N Engl J Med 2021;385(23):2117–9. https://doi.org/10.1056/NEJMp2115675. Dec 02.
[224] Eckelman MJ, Huang K, Lagasse R, Senay E, Dubrow R, Sherman JD. Health care pollution and public health damage in the United States: an update. Health Aff 2020;39(12):2071–9 (Millwood)12.
[225] Salas RN, Maibach E, Pencheon D, Watts N, Frumkin H. A pathway to net zero emissions for healthcare. BMJ 2020;371:m3785. https://doi.org/10.1136/bmj.m3785. 10 01.
[226] Holmner A, Ebi KL, Lazuardi L, Nilsson M. Carbon footprint of telemedicine solutions–unexplored opportunity for reducing carbon emissions in the health sector. PLoS One 2014;9(9):e105040. https://doi.org/10.1371/journal.pone.0105040.
[227] Bein T, Koch S, Schulz C. What's new in intensive care: environmental sustainability. Intensive Care Med 2021;47(8):903–5. https://doi.org/10.1007/s00134-021-06455-6. Aug.
[228] Berrang-Ford L, Sietsma AJ, Callaghan M, et al. Systematic mapping of global research on climate and health: a machine learning review. Lancet Planet Health 2021;5(8):e514–25. https://doi.org/10.1016/S2542-5196(21)00179-0. 08.
[229] Mann ME. Lifestyle changes aren't enough to save the planet. here's what could. USA: TIME; 2019.
[230] Pidgeon N. Public understanding of, and attitudes to, climate change: UK and international perspectives and policy. Taylor and Francis; 2012.
[231] Wynes S, Nicholas KA. The climate mitigation gap: education and government recommendations miss the most effective individual actions. Environ. Res. Lett. 2017.
[232] Rudolph L., Harrison C. A physician's guide to climate change, health and equity. In: Institute PH, editor. Oakland, CA2016.
[233] Physicians for Social Responsibility. Environment and Health Program. United States of America 2021.
[234] The Medical Society Consortium on Climate and Health. 10/2/21, 2021. https://medsocietiesforclimatehealth.org/.
[235] Salas RN, Friend TH, Bernstein A, Jha AK. Adding a climate lens to health policy in the United States. Health Aff 2020;39(12):2063–70 (Millwood)12.
[236] Horton R. Offline: extinction or rebellion? Lancet 2019;394(10205):1216. https://doi.org/10.1016/S0140-6736(19)32260-3. 10 05.
[237] Bernstein A., Salas R.N., Solomon C. The climate crisis and clinical practice symposium. Boston, MA 2020.
[238] Moss RH, Edmonds JA, Hibbard KA, et al. The next generation of scenarios for climate change research and assessment. Nature 11 2010;463(7282):747–56. https://doi.org/10.1038/nature08823. Feb.
[239] O'Neill BC, Kriegler E, Riahi K, et al. A new scenario framework for climate change research: the concept of shared socioeconomic pathways. Clim Change 2014;122(3):387–400. https://doi.org/10.1007/s10584-013-0905-2. 2014/02/01.
[240] Brulle RJ, Carmichael J, Jenkins JC. Shifting public opinion on climate change: an empirical assessment of factors influencing concern over climate change in the U.S., 2002–2010. Clim Change 2012;114(2):169–88. https://doi.org/10.1007/s10584-012-0403-y. 2012/09/01.
[241] Stoknes PE. Rethinking climate communications and the "psychological climate paradox. Energy Res Soc Sci 2014.
[242] Cinner J. How behavioral science can help conservation. Science 2018;362(6417):889–90. https://doi.org/10.1126/science.aau6028. 11 23.
[243] Supran G. Fueling their own climate narrative. Science 2021;374(6568):702. https://doi.org/10.1126/science.abm3434. Nov 05.
[244] Marshall G. Hear no climate evil. New Scientist; 2014.
[245] Peters GP, Andrew RM, Canadell JG, et al. Key indicators to track current progress and future ambition of the Paris agreement. Nat Clim Change 2017;7(2):118–22. https://doi.org/10.1038/nclimate3202. 2017/02/01.
[246] Ledford CJW, Anderson LN. Communication strategies for family physicians practicing throughout emerging public health crises. Fam Med 2020;52(5):48–50. https://doi.org/10.22454/FamMed.2020.960734. 05.
[247] Salas RN, Knappenberger P, Hess J. 2018 Lancet countdown on health and climate change brief for the United State of America. London, United Kingdom: Lancet Countdown; 2018. p. 32.
[248] Schwartz BS, Parker C, Glass TA, Hu H. Global environmental change: what can health care providers and the environmental health community do about it now? Environ Health Perspect 2006;114(12):1807–12. https://doi.org/10.1289/ehp.9313. Dec.
[249] Climate Health Action. U.S. call to action on climate, health, and equity: a policy action agenda. USA 2019.
[250] Salas RN, Malina D, Solomon CG. Prioritizing health in a changing climate. N Engl J Med. 2019;381(8):773–4. https://doi.org/10.1056/NEJMe1909957. 08 22.