Circulation Research

COMPENDIUM ON ENVIRONMENTAL IMPACTS ON CARDIOVASCULAR HEALTH AND BIOLOGY

Heat and Cardiovascular Mortality: An Epidemiological Perspective

Nidhi Singh,* Ashtyn Tracy Areal,* Susanne Breitner, Siqi Zhang, Stefan Agewall, Tamara Schikowski,† Alexandra Schneider†

ABSTRACT: As global temperatures rise, extreme heat events are projected to become more frequent and intense. Extreme heat causes a wide range of health effects, including an overall increase in morbidity and mortality. It is important to note that while there is sufficient epidemiological evidence for heat-related increases in all-cause mortality, evidence on the association between heat and cause-specific deaths such as cardiovascular disease (CVD) mortality (and its more specific causes) is limited, with inconsistent findings. Existing systematic reviews and meta-analyses of epidemiological studies on heat and CVD mortality have summarized the available evidence. However, the target audience of such reviews is mainly limited to the specific field of environmental epidemiology. This overarching perspective aims to provide health professionals with a comprehensive overview of recent epidemiological evidence of how extreme heat is associated with CVD mortality. The rationale behind this broad perspective is that a better understanding of the effect of extreme heat on CVD mortality will help CVD health professionals optimize their plans to adapt to the changes brought about by climate change and heat events. To policymakers, this perspective would help formulate targeted mitigation, strengthen early warning systems, and develop better adaptation strategies. Despite the heterogeneity in evidence worldwide, due in part to different climatic conditions and population dynamics, there is a clear link between heat and CVD mortality. The risk has often been found to be higher in vulnerable subgroups, including older people, people with preexisting conditions, and the socioeconomically deprived. This perspective also highlights the lack of evidence from low- and middle-income countries and focuses on cause-specific CVD deaths. In addition, the perspective highlights the temporal changes in heat-related CVD deaths as well as the interactive effect of heat with other environmental factors and the potential biological pathways. Importantly, these various aspects of epidemiological studies have never been fully investigated and, therefore, the true extent of the impact of heat on CVD deaths remains largely unknown. Furthermore, this perspective also highlights the research gaps in epidemiological studies and the potential solutions to generate more robust evidence on the future consequences of heat on CVD deaths.

Key Words: cardiovascular diseases ■ climate change ■ extreme heat ■ mortality ■ population dynamics

Cardiovascular diseases (CVDs) remain the leading cause of death worldwide, claiming 18 million lives every year, despite significant achievements in public health in reducing risk factors such as tobacco use, nutritional interventions, and physical activities.[1] However, evidence has accumulated recently on the adverse effects of environmental and meteorological factors, including heat, on cardiovascular morbidity and mortality.[2,3]

Climate change is the biggest environmental threat to human health in the 21st century.[4] Climate change is a dynamic phenomenon that is accompanied by increasing global temperatures worldwide and an increase in extreme weather events such as wildfires, heat waves, and droughts. The most recent report from The Intergovernmental Panel on Climate Change reaffirms the mounting threat of climate change worldwide,[5]

Correspondence to: Tamara Schikowski, PhD, MPH, IUF - Leibniz Research Institute for Environmental Medicine GmbH, Auf'm Hennekamp 50, 40225 Düsseldorf, Germany. Email tamara.schikowski@IUF-duesseldorf.de
*Shared first authorship.
†T. Schikowski and A. Schneider contributed equally as last authors.
For Sources of Funding and Disclosures, see page 1110.

Nonstandard Abbreviations and Acronyms

CVD	cardiovascular disease
GBD	Global Burden of Diseases, Injuries, and Risk Factors Study
GDP	gross domestic product
HF	heart failure
IHD	ischemic heart disease
LMIC	lower middle-income countries
MI	myocardial infarction
SES	socioeconomic status

with solid evidence that carbon dioxide (CO_2) emissions will lead to further temperature increases and extreme heat and cold events. Additionally, the frequency of extreme heat waves is expected to increase in a warmer climate, resulting in greater variability of surface temperatures.[4,5]

While the effects of cold, air pollution, and seasonal variation on cardiovascular health have been well studied, the effects of heat on CVD are understudied.[6]

The GBD (Global Burden of Diseases, Injuries, and Risk Factors Study) 2019 included high temperature as a risk factor to human health, accounting for 11.7 million years of healthy life lost (disability-adjusted life years) globally.[7] In particular, extreme heat and heat stress can lead to severe health effects due to the acute exacerbation of illnesses.[4,7]

Heat is of concern as exposure to heat can lead to heat exhaustion or heat stroke if the internal body temperature is not adequately regulated by the thermoregulatory mechanisms. Such thermal dysregulation in turn increases the demand placed on the heart to supply enough blood and oxygen to the body, causing cardiac stress.[6,8,9] Although extreme heat can be a risk factor for all ages, older people, pregnant women, and people with chronic morbidities, more specifically those with impaired cardiovascular health, are particularly at risk of mortality and morbidity associated with (extreme) heat.[6,8,9]

This overview provides a summary of epidemiological evidence on the effect of heat on CVD mortality in the general population and vulnerable groups of people. The review also summarizes how the association between heat and CVD mortality may have changed over time and how different environmental factors influence the association between heat and CVD mortality. Last, we discuss the potential underlying biological mechanisms of how heat increases the risk of CVD mortality and existing research gaps. This review will help provide a simplified and better understanding of the effect of extreme heat on CVD mortality. It aims to provide stakeholders with the necessary information for targeted mitigation, strengthening early warning systems, and developing better adaptation strategies. It should also support cardiologists in engaging in heat-health action plans and delivering informed and effective care to their patients during heat exposure.

SHORT-TERM EFFECTS OF HEAT ON CVD MORTALITY

The GBD Study reported that heat has led to ≈93 000 CVD deaths worldwide in 2019 alone.[10,11] Several studies have shown that short-term exposure, that is, hour-to-hour or day-to-day variations (on an hourly to daily basis) to high temperatures and heat waves increase the risk of CVD mortality and that the association's strength varies from region to region (Table 1).[8,12,13] Similar evidence comes from a recent meta-analysis based on existing evidence from different climate zones throughout the world, which showed an increase of 2.1% in CVD-related mortality for every 1 °C rise in temperature (relative risk

Table 1. Definitions of Exposure Metrics in the Discussed Studies

Exposure metric	Definition
Tmean; mean temperature (°C)	The daily average ambient temperature.
Tmax; maximum temperature (°C)	The daily maximum ambient temperature.
Tmin; minimum temperature (°C)	The daily minimum ambient temperature.
Apparent temperature (°C)	Temperature exposure that accounts for the effect of temperature (°C), vapor pressure, RH (%), and WS (m/s).
WBGT (°C)	Temperature exposure that accounts for the effect of temperature (°C), RH (%), solar insolation (kW/m²), and WS (m/s).
HI (°C)	Temperature exposure that accounts for the effect of temperature and RH (%).
UTCI (°C)	Temperature exposure that accounts for the effect of temperature (°C), RH (%), WS (m/s), and mean radiant temperature (function of temperature and cloud coverage)
PET (°C)	Temperature exposure that accounts for the effect of temperature (°C), altitude and latitude of the area under study, RH (%), WS (m/s) and cloudiness (octas) and individual variables such as height, weight, age, sex, clothing, and physical activity of the people.
Heat wave definition (low heat wave intensity)	Daily Tmean/Tmax/Tmin/AT exceeding the temperature threshold ≥90–93th percentiles of their mean annual values for 0–4 consecutive days.
Heat wave definition (middle-intensity heat wave)	Daily Tmean/Tmax/Tmin/AT exceeding the temperature threshold ≥94–96th percentiles of their mean annual values for 0 to 3 consecutive days.
Heat wave definition (high-intensity heat wave)	Daily Tmean/Tmax/Tmin/AT exceeding the temperature threshold ≥97–99th percentiles of their mean annual values for 0 to 2 consecutive days.

HI indicates heat index; PET, physiological equivalent temperature index; UTCI, universal thermal climate index; and WBGT, wet bulb global temperature.

[RR], 1.021 [95% CI, 1.020–1.023]) and an increased risk of 11·7% in CVD mortality associated with heat waves (RR, 1.117 [95% CI, 1.093–1.141]).[12]

Different studies using different definitions of heat waves (the details about the use of different exposure metrics and criteria are described in Table 2) have reported that the effect of heat wave days showed a higher risk of CVD-related mortality than more moderate high-temperature days; the effect increases further with an increase in heat wave intensity.[12,19,22]

The evidence of the association between CVD and heat is primarily from high-income country (HIC) regions like Australia,[37] Europe,[23,38,39] and the United States.[40] Substantial evidence is also available from China[12]; at the same time, only a few studies were conducted in lower-middle-income countries (LMICs), which include a large part of Asia, Africa, Latin America, and some parts of East Europe.[15,41–44] Many of the LMICs have seen a remarkable series of record-breaking heat waves, which are not unexpected as per the latest Intergovernmental Panel on Climate Change Assessment Report, showing that the frequency and intensity of heat waves have increased.[5] The health burden is immense since many LMICs are not better adapted to such high temperatures/heat waves and have fewer resources and infrastructure to cope with heat compared with HICs.[5] The same was reported in the GBD study, showing higher CVD deaths in LMICs in South-East Asia, the Eastern Mediterranean region, and the African region, combined accounting for ≈75 000 deaths alone in 2019 due to high temperature against ≈13 000 deaths in the Western Pacific region, and ≈5000 deaths in the American and European regions combined.[45]

The risk of heat-attributable CVD mortality can vary depending upon the specific causes of CVD deaths. For example, some studies showed a higher heat-related mortality risk for stroke followed by myocardial infarction (MI) or ischemic heart disease (IHD) and heart failure (HF).[12] The same was observed in the GBD 2019 study, which showed higher deaths due to stroke (≈48 000), followed by IHD (≈43 000) and hypertensive heart disease (≈2000) on exposure to high temperatures.[45] However, a different trend was observed in recent evidence from Germany, which showed an increased risk due to HF mortality, followed by MI.[25] Unlike high temperatures, the association between heat waves and CVD-specific deaths was higher for IHD, followed by stroke and HF.[13] These findings highlight that although a general trend in cause-specific CVD deaths due to high temperature is observed globally, regional discrepancies exist between the studies. Therefore, any assumptions concerning a general order in cause-specific CVD deaths related to high temperature/heat waves for a specific region should be carefully interpreted. The discrepancies between the studies could arise because of several reasons, such as different criteria used to determine the causes of death, different study regions, population structure, genetics, and nutrition, among others.[8,46] Since the available evidence on cause-specific deaths is limited and highly heterogeneous, there is a need for more studies on cause-specific heat-attributable CVD deaths so that mitigating cause-specific CVD mortality can be prioritized.

High temperature/heat waves can affect CVD deaths on the same day and several subsequent days after exposure, this is called a lag effect.[47] This so-called lag time can differ depending on the specific cause of death, geographic location, climatic conditions, environmental factors, socioeconomic status (SES), and health infrastructure. Nevertheless, the lag time associated with the heat effect is often short (between 0 and 10 days)—in most cases, the effects last for 3 to 4 days[12,48] (Table 1).

Since temperature is not the only environmental risk factor that contributes to CVD-related mortality, it is imperative to account for the effect of other factors like meteorologic variables (wind speed: WS, air pressure, and relative humidity: RH) or air pollution, as well as for seasonal and long-term trends, day of the week, and public holidays to quantify the effect only due to heat.[6,12] Some of these parameters are often referred to as confounding factors, so studies should consider the potential confounding effect of these variables. However, there is a growing debate about whether air pollution should be considered a confounder or a mediator in short-term temperature-health studies without clarifying the causal assumption.[49] Nevertheless, most of the studies included air pollution as a confounding variable or effect modifier and found specific impacts on the temperature-health association, while other studies found no effect, indicating the role of air pollution neither as a confounder nor modifier.[49] Studies showing the mediating role of air pollution are scarce.

The time series study design, which associates time-varying exposures to time-varying event counts, is the most popular approach for studying short-term effects. At the same time, some studies adopted the case-crossover study design, a modification of the matched case-control design where each case acts as its control.[8,25,27,35] Time series studies use a log-linear regression model that adjusts for potential confounding of other time-varying factors like weather, day of the week, and temporal trends. In contrast, case-crossover studies control for time-invariant subject-specific covariates such as sex and race, and temporal trends by its design and, therefore, avoid control through statistical modeling.[50,51] The selection of the study design is, of course, often dependent on the data available.

Assessing the exposure-response relationship helps to understand how the changes in levels of exposure will affect the risk of specific mortality. The information is essential for risk assessors as different exposure-response curves could imply other causal inferences and

Table 2. Characteristics of Included Studies in the Presented Perspective

ID	Author, year (Ref)	Location	Study period	Study design	Exposure	Season	Air pollution-AD/EM/SA	Adjusted for other covariates	Outcome (ICD-10); Ages	Subgroup analysis	Lags (days)	Association	Significant
Short-term studies													
1	Achebak et al, 2019[14]	Spain and the Balearic Islands	1980–2016, 15-y moving periods (1980–94, 1981–95, 2002–16)	TS, QPR, DLNM, REMA	Tmean/ MMT	Annual		DOW, long-term trend and seasonality	CVD (I00–I99)	Age (60–74, 75–89, 90, 90+), sex	0–21	+	Yes
2	Alahmad et al, 2020[15]	Kuwait	2010–2016	TS, DLNM, NBR	Ambient Tmean, MMT	Annual, warm season	AD (PM_{10}, O_3)	Time trends, Seasonality, DOW	CVD (I00–I99)	Sex, Age (15–64, 65+)	0–30	+	Yes
3	Alahmad et al, 2023[8]	27 countries across 5 continents	1979–2019	TS, QPR, DLNM	MMT	Annual	SA (O_3, NO_2, PM_{10}, and $PM_{2.5}$)	SA (RH), DOW, month, year. In meta regression-seasonal temperature, and country-level GDP per capita	CVD (I00–I99), IHD (I20–I25), CVA (I60–I69), HF (I50), arrhythmia (I47–I49); all ages		0–15	+	Yes
4	Chen et al, 2019[16]	Augsburg, Germany	1987–2014 (1987–2000 and 2001–14)	CC, DLNM, comparison of exposure-response curves, multivariate Wald test	Tmean/ MMIT	Annual	EM (PM_{10}, NO_2, and O_3)	RH, BP, population	MI (ICD-10: I21)	Age, sex, place of residence, living alone, history of hypertension, and diabetes, education, smoking, and obesity	0–1	+	Yes
5	Fang et al, 2023[17]	353 locations, China	2006–2017	TS, DLNM, REMA	Tmean	Warm (June to August)	AD (PM_{10})	RH, WS, RF, DOW, long-term trends	CVD (I00–I99), CVA (I60–I69); all ages	…	0–3	+	No
6	Gu et al, 2022[18]	Mianyang City, China	2013–2019	TS, QPR, DLNM	Tmean	Annual	…	DOW, seasonal and long-term trends	CVD (I00–I99); all ages	Age (<65, 65+), sex	0–30	+	Yes
7.	He et al, 2022[3]	Shandong Province, China	2013–2019	TS, QPR, DLNM, REMA	Tmean	Annual	AD ($PM_{2.5}$, SO_2, NO_2 and CO)	RH, DOW, Holidays, long-term trends and seasonality	CVA (I60–I67); All ages	…	0–3 0–7 0–14	+	Yes
8.	Jahan et al, 2022[19]	Malta	1992–2017	TS, QPR, DLNM	HW	Annual	…	RH, DOW, holidays, seasonal and long-term trends and population	CVD (I00–I99); IHD (I20–I25); CVA (I60–I69); all ages	Age (0 to <15, 15 to <65, 65+), sex and time periods	0–5	+	No
9.	Kephart et al, 2022[20]	326 Latin American cities	2002–2015	TS, PR, DLNM. REMA	Tmean	Annual	…	DOW, month, year and season	CVD (I00–I99); all ages	Age (<65, 65+)	0–21	+	Yes
10	Majeed et al, 2022[21]	England and Wales; King County, Washington, United States	2001–2015	NBR, QPR	Tmean	Warm (June to July)	AD ($PM_{2.5}$)	Time trend, season, mental and behavioral mortality rates	CVD (I00–I99); adults aged 60 to 69 y	Age (60–64, 65–69) and sex		+	Yes

(*Continued*)

Table 2. Continued

ID	Author, year (Ref)	Location	Study period	Study design	Exposure	Season	Air pollution-AD/EM/SA	Adjusted for other covariates	Outcome (ICD-10); Ages	Subgroup analysis	Lags (days)	Association	Significant
11	Moraes et al, 2022[22]	São Paulo, Brazil	2006–2015	TS, QPR, DLNM	HW	Warm (September to March)	AD (PM_{10})	RH, DOW, holidays, long-term trends, Season	CVD (I00–I99); IHD (I20–I25), CVA (I60–I69), aged ≥65 y	Age (≥65), sex	0–10	+	Yes
12	Murage et al, 2017[23]	London, The United Kingdom	1993–2015	TS, DLNM, QPR	Tmean/ Tmax/ Tmin	Summer (June to September)	AD (PM_{10}, O_3)	Seasonality, long-term trend, DOW, specific humidity	CVD (I00–I99), CVA (I60–I69), IHD (I25), MI (I22–123), HF (I50), S (I60–I69). All Aged	Age (0–64, 65–74, 75+)	0–7	+	Yes
13	Rahman et al, 2022[24]	California, United States	2014–2019	CC, CLR	Tmax/ Tmin	Annual	Co-exposure ($PM_{2.5}$)	Tmax, Tmin, RH	CVD (I00–I99); all ages	Age (<75, 75+)	0–3	+	Yes
14	Rai et al, 2023[25]	15 cities, Germany	1993–2016	TS, PR, DLNM, MMAM	Tmean	Warm (April to September)	…	DOW, long-term trends, and season	CVD (I00–I99), IHD (I20–I25), MI (ICD-10: I21), CVA (I60–I69), HF (I50); all ages	Age (0–64, 65–74, 75+), sex	0–14	+	Yes
15	Rai et al, 2023[26]	482 locations, 24 countries.	2000–2018	QPR	Tmean	Warm (6 consecutive hottest months)	EM (PM_{10}, $PM_{2.5}$, O_3, NO_2)	DOW and season	CVD (I00–I99): all ages	…	0–1	+	Yes
16	Saucy et al, 2021[27]	Zurich, Switzerland	2000–2015	CC, CLR, DLNM	Tmean	Annual	AD (NO_2 and $PM_{2.5}$)	RF, aircraft noise before deaths, and holidays	CVD (I00–I99), HD (I10–I15), IHD (I20–I25), MI (I21, I22), CVA (I60–I64), HF (I50), and arrhythmias (I44–I49); all ages	Age (≤75, 75–85, 85+), sex, education, level of urbanization. women (75+), SES, marriage	0–7	+	Yes
17	de Schrijver et al, 2023[28]	Switzerland	1990–2010, RCP/ SSP scenario (1980–2100)	TS, QPR, DLNM, REMA, Projection	Tmean/ MMT	Annual		DOW, long-term trend and seasonality	all-cause mortality	Age (<75, 75+)	0–21	+	Yes
18	Shrikhande et al, 2023[29]	Puducherry, India	2011–2020	CC, BLD, DLNM	AT	Annual	…	WS, RH	CVD (I00–I99); IHD, CVA (I60–I69); all ages	Age (<60, 60+) and sex	5–16	+	Yes
19	Silveira et al, 2023[30]	Rio de Janeiro, Brazil	2012–2017	CC, DLNM	HW	Warm (November to March)	…	AH and holidays	CVD (I00–I99): All ages	Age (0–64, 65+), sex	0–5	+	Yes
20	Wang et al, 2023[31]	136 cities, China	2006–2019	TS, QPR, DLNM, REMA	HW	warm (May to September)	…	Tmean, DOW, RH, long-term trend, season	CVD (I00–I99): all ages	Age (0–64, 65–74, 75+), sex, working conditions (outdoor or indoor)	0–4	+	Yes

(*Continued*)

Table 2. Continued

ID	Author, year (Ref)	Location	Study period	Study design	Exposure	Season	Air pollution-AD/EM/SA	Adjusted for other covariates	Outcome (ICD-10); Ages	Subgroup analysis	Lags (days)	Association	Significant
21	Xia et al, 2023[32]	Chengdu City, China	2016–2020	TS, DLNM, PR	Tmean	Annual	AD ($PM_{2.5}$, O_3)		CVD (I00–I99), CVA (I60–I69), IHD (I20–25); All ages	Age (65–74, 75–84, 85+), sex, education level, and marital status	0–3	+	Yes
22	Xu et al, 2023[33]	Jiangsu province, China	2015–2020	CC, CLR	Tmean	Annual	Interactive effect ($PM_{2.5}$): SA (SO_2, NO_2, CO, and O_3)		MI (I21, I22): all ages	Age (<80, 80+), sex, SES		+	Yes
23	Yan et al, 2023[34]	102 counties, China	2014–2017	PR	HW	Annual	SA (O_3, $PM_{2.5}$)	Tmax, RH, DOW, year, population, County	CVD (I00–I99), HD (I10–I15), IHD (I20–I25), MI (I21–I23), arrhythmia (I44–I49), CVA (I60–I69); all ages	Age (0–64 65–74>74) and sex	0–4	+	Yes
24	Zhang et al, 2023[35]	Norway, England and Wales, and Germany	1996–2018.	CC, QPR, DLNM, REMA	Tmean	Warm (May to September)	EM ($PM_{2.5}$ and O_3)	4-way interaction (area, DOW, month, year)	CVD (I00–I99); all ages	Age (65+, 75+) and sex	0–1	+	Yes
Long term study													
1	Hu et al, 2022[36]	China	2006–2017	DID, GAM, PR	Tmean	Annual, Summer (June to August)	AD (PM_{10})	RH, temperature deviation, Urbanization, education attainment, GDP	CVD (I00–I99)	Age (0–64, 65+), Sex,		…	Yes

AD indicates adjusted in the main model; AH, absolute humidity; AT, apparent temperature; BLD, binomial likelihood distribution; BP, barometric pressure; CC, case cross over; CLR, conditional logistic regression; CVA, cerebrovascular disease; CVD, cardiovascular disease; DID, difference-in-difference approach; DLNM, distributed lag nonlinear model; DOW, day of the weak; EM, effect modification; ETE, extreme temperature event; GDP, gross domestic product; HD, heart disease; HF, heart failure; HW, heat wave; IHD, ischemic heart disease; MI, myocardial infarction; MMAM, multivariate meta-analytical model; MMIT, minimum myocardial infarction temperature; MMT, minimum mortality temperature; NBR, negative binomial regression; NO_2, nitrogen dioxide; O_3, ozone; PM_{10}, particulate matter with an aerodynamic diameter of <10 µm; $PM_{2.5}$, particulate matter with an aerodynamic diameter of < 2.5 µm; PR, Poisson regression; QPR, quasi poisson regression; REMA, random effect meta-analysis; RF, rainfall; RH, relative humidity; SA, sensitivity analysis; Tmax, maximum temperature; Tmean, mean temperature; Tmin, minimum temperature; TS, time series; and WS, wind speed.

require different risk management strategies, decision-making, and policy development.[52]

Despite several reasons mentioned above that led to heterogeneity in evidence, for example, different study designs, exposure classification and exposure metrics, statistical methods, population diversity, susceptibility, and climate, the link between heat and CVD mortality was strongly reported in several studies.

LONG-TERM EFFECTS OF HEAT ON CVD MORTALITY

A systematic review by Zafeiratou et al[53] only identified 3 studies that investigated the long-term effects of heat on CVD. They found that the results were inconsistent and not statistically significant. We have identified 1 additional paper by Hu et al[36] who examined the association between long-term exposure to ambient temperature and mortality risk from 364 communities across China using the difference-in-differences approach to control for unmeasured confounding, which addresses many of the concerns related to the time series design[36] (Table 1). Overall, this study concluded that while there was an increase in CVD mortality annually, this was most likely due to cold exposure as seasonal analysis found a decrease in CVD mortality per 1 °C decrease in mean temperature.[36]

The long-term heat effects on CVD mortality have not been well understood compared with the short-term heat effects. There are several reasons why it is complex to perform long-term studies. First, long-term exposure studies require significant time and resources. Second, confounding factors are difficult to control for

over extended periods. Third, performing long-term heat-controlled exposure studies presents many ethical challenges. Finally, the effects of long-term heat exposure are often subtle and cumulative which makes identifying the specific effects of heat challenging. However, it is imperative that researchers must start to investigate the long-term impacts of heat as understanding the long-term heat effects on CVD is imperative for the development of mitigation strategies and health action plans.

SUSCEPTIBLE GROUPS FOR CLIMATE EFFECTS

Existing epidemiological studies have shown that the risk of CVD mortality due to heat can be predominantly higher in older people (aged 65 years and above), people with underlying health conditions (eg, hypertension, diabetes, hyperlipidemia, and coronary artery disease) and in socioeconomically deprived groups,[54,55] see Table 3. It was reported that ≈50 000 people above the age of 70 years died due to heat exposure in 2019, and about 33 000 people between 50 and 69 years against ≈9000 deaths below the age of 50.[45] With an increase in age, the body's ability to maintain thermoregulation is challenged and therefore, exposure to mild or moderate hyperthermia or exposure to a very hot and humid environment (42 °C, 30%–72% humidity) increases the CVD risk in older people.[14]

A recent meta-analysis shows a 0.8% higher RR in people aged ≥65 years than in people aged 0 to 64 years per 1 °C increase in temperature (1.7%; RR, 1.017 [95% CI, 1.016–1.019] versus 0.9%; RR, 1.009 [95% CI, 1.004–1.014]; *P*=0.03).[12] Another piece of evidence comes from Germany (2005–2016), where Rai et al[25] showed 5% higher mortality in people aged 65 to 74 years and 17% higher mortality in people aged 75 years and above compared with people aged 64 years and below due to the effect of heat. Similar results were also reported from China, Europe, Australia, and Latin America.[18,20,56] However, not all studies confirm this age-dependency of heat effects.[57,58]

Although both sexes have an increased risk of CVD mortality on high-temperature/ heat wave days, the magnitude can differ among males and females due to differences in their behavioral patterns, mobility associated with occupation and, foremost, the physiological differences.[30,59,60] As of 2019, 50 000 males died due to high temperatures versus 42 000 females.[45] However, the differences in the risk based on sex are not well studied, and the results are heterogeneous. Although some studies have shown a higher risk in males,[21] several studies have found higher susceptibility in females.[19,22,29] A study from India showed that females both above and below 60 years of age, on average, have a higher risk of CVD mortality from heat than men.[29] Similarly, a study from São Paulo, Brazil, showed a higher risk of overall CVD-related deaths in females during heat waves compared with men.[22] Other evidence was also reported from European countries,[25,35] United States,[19] China,[18,34] and Australia,[56]

A greater risk of heat-related CVD mortality was also observed in studies from LMICs than in upper

Table 3. Groups Vulnerable to the Adverse Effects of High Temperatures and Heat Waves and the Reasons These Groups Are at Increased Risk

Vulnerable population group	Reason	Pictorial representation
Children and the elderly	More susceptible to heat-related illnesses due to limited adaptive capabilities.	
Pregnant women	More susceptible to heat-related illness due to strained thermoregulatory systems	
Outdoor workers	More likely to be constantly exposed to adverse climate conditions.	
People with chronic diseases	Less likely to be able to sense and respond to changes in temperature. Some medications can exacerbate the adverse effects of heat.	
Lower-middle-income countries/communities	Higher exposure to environmental risks and limited access to health care.	
Indigenous communities	Profound cultural, social, and economic impacts from climate-induced changes.	

middle-income countries and HICs.[61] Importantly, these countries also witness very high summer temperatures or intense heat wave events, which adds to the standing vulnerability.[61] The population from LMICs often lack the proper infrastructure to cope with the heat, such as electricity, air conditioners, cold waters, and inefficient health care services during heat wave events,[62] which increases their vulnerability to CVD-related deaths. For example, recent evidence shows a 9% higher risk of CVD mortality per 1 °C increase in temperature in LMICs than in upper middle-income countries.[12] Similar evidence comes from a multi-country analysis by Alahmad et al,[8] which showed higher heat-related mortality due to stroke and HF for countries with low gross domestic product (GDP) per capita compared with high GDP per capita countries; however, the opposite was observed for IHD with higher heat-related mortality in high GDP countries than in low GDP countries. Similarly, a study from China showed a higher CVD mortality risk associated with high temperature in older people with low educational levels than with high education levels; however, the same is not necessarily reflected in CVD deaths due to specific causes.[32] Since the evidence from LMICs is scarce, any generalization about the strength of the association between CVD mortality and high temperature/heat waves should be made with caution.[12]

In contrast, evidence from European countries (Norway, England, Wales, and Germany) showed a significantly higher risk of CVD mortality in areas with high GDP and employment rates.[35] The same was observed in Switzerland, where middle and high SES groups showed a higher risk of CVD mortality than low SES groups.[27] Since these countries are flat economies and offer efficient health care services to their residents, people with low SES still have access to proper health care facilities; therefore, high CVD mortality risk in high GDP areas can be explained by differences in behavioral or dietary habits or preexisting disease conditions.[63] In addition, these countries have a proportionately higher percentage of older people. These factors might increase their risk during high temperature/heat wave events. Besides, people living in areas of high population density and more urbanized areas, those with comorbidities, and those working primarily in outdoor environments are mostly at higher risk (Table 3).[31,35]

TEMPORAL TRENDS

Existing evidence confirms the association between heat and CVD-related mortality. With the rising temperature driven by climate change, the CVD mortality burden may also rise. It was very apparent from the GBD 2019 data that CVD deaths due to high temperatures increased linearly between 1990 (13 000) and 2019 (93 000).[45] Therefore, for effective mitigation and adaptation strategy, it is essential to understand the change in present and future trends in the temperature-CVD mortality association.

A handful of studies have studied the changes in the temporal trend of temperature-CVD mortality association, and the nonuniform inferences from these studies make it complex to generalize the evidence.[16,64–67] A study from Queensland, Australia, reported a nonsignificant change in the effect of heat on CVD mortality in 2013 compared with 1997.[68] However, the subgroup analysis showed a significant rising trend of heat effect on CVD mortality in men, adults ≤85 years, residents of LMICs and hot climate regions, although a declining trend was noted for people ≥85 years and in areas of high SES.[68] In contrast, studies from Spain and the Balearic Islands reported a reduction in heat-attributable CVD deaths for the summer months between 1980 and 2015/2016[14] for both men and women across all age groups. For example, a decline in heat-attributable fraction by 42.06% (95% empirical CI, 41.06–4439) was reported for men between 1980 to 1994 and 2002 to 2016 and by 36.64% (36.04–36.70) for women.[14] Similarly, a study on the elderly US population reported a decreased risk for heat-related CVD mortality from 4.7% in 1987 to 0.4% in 2000.[67]

Nevertheless, some studies have reported an increased heat-CVD mortality risk over time. For example, a study from Augsburg, Germany, reported a significant increase in trend in the heat-related MI risk during 2001 to 2014 to 1.14 (95% CI, 1.00–1.29) from 0.93 (95% CI, 0.78–1.12) during 1987 to 2000. Noticeably, people with preexisting conditions like diabetes and hyperlipidemia, people living in rural counties, and current smokers were driving this increase in risk.[16] In another study based on 15 large German cities, the temperature-mortality associations showed an increasing heat effect on CVD, comparing the period 1993 to 2004 to 2005 to 2016, although the differences were insignificant.[25] The same was visible for the modifying effect by age and sex.[26] A study based on 136 Chinese cities also showed an increase in the effects of heat on CVD-related mortality between 2006 and 2019, and the effect was mostly prominent in females and elderly aged 65 to 74.[31]

Some studies have attempted to predict the trend of heat-associated mortality in the future and showed an overall rise in heat-associated mortality in different future scenarios.[28,69–72] However, a noticeable geographic difference was observed. Temperate regions are projected to witness a net decline in combined heat and cold-related mortality in 2090 to 2099 compared with 2010 to 2019 due to less intense warming and a substantial decrease in cold-related deaths.[73] Conversely, warmer regions are likely to witness a sharp rise in heat-related mortality, causing a net increase in overall mortality.[73] However, projections related to cause-specific mortality, such as CVD, are lacking. Considering that the world population is aging, making the vulnerable

subpopulation larger, and the climate is getting warmer, there is likely an increase in heat-related mortality in the future.[73] However, this would also depend on changes in medical treatment and its efficiency in preventing CVD disease and mortality. Therefore, future studies should be devoted to better understanding change in the temporal trend of heat-CVD mortality association to reduce heterogeneity and obtain robust projections of temperature-mortality impacts.

INFLUENCE OF OTHER ENVIRONMENTAL EXPOSURES ON HEAT EFFECT

Temperature is not the sole environmental factor that affects health. There is often an interplay between temperature, humidity, wind, radiation, precipitation, and air pollution.[74] This interactive effect happens when other environmental factors influence the relationship between high temperature/heat wave and CVD mortality. These joint effects could be synergistic, which means being more than just the sum of the two independent effects. Although incorporating the interaction effect in a model could be complex, the real-world scenario behaves as such. Therefore, interaction is an important aspect to consider in studies investigating temperature or heat effects (Figure 1).

For example, humidity changes how humans perceive temperature and can affect thermoregulation.[17] The study by Fang et al[17] investigated the effect of heat exposure on days with low humidity (dry days) and high humidity (wet days). This study reported that both hot-dry and hot-wet exposure exacerbates CVD mortality; however, this effect was much stronger with hot-dry exposures, with the difference between hot-dry exposure and hot-wet exposure being statistically significant.[17] He et al[3] looked at the modifying effects of greenspace on heat exposure; they found a decrease in heat-related CVD mortality with increased greenspace, which was defined using the normalized difference between vegetation index. This finding points to the protective effects of greenspace on heat.

The studies by Rahman et al,[24] Rai et al,[26] and Xu et al[33] all investigated the effect of high temperatures on CVD mortality modified by air pollution. All 3 studies looked specifically at how fine particles ($PM_{2.5}$) modified the impact of high temperature on CVD mortality. Rai et al[26] and Xu et al[33] found that increasing levels of $PM_{2.5}$ and increasing temperatures were associated with an increased risk of cardiovascular mortality. However, when they looked at the interactive effect between $PM_{2.5}$

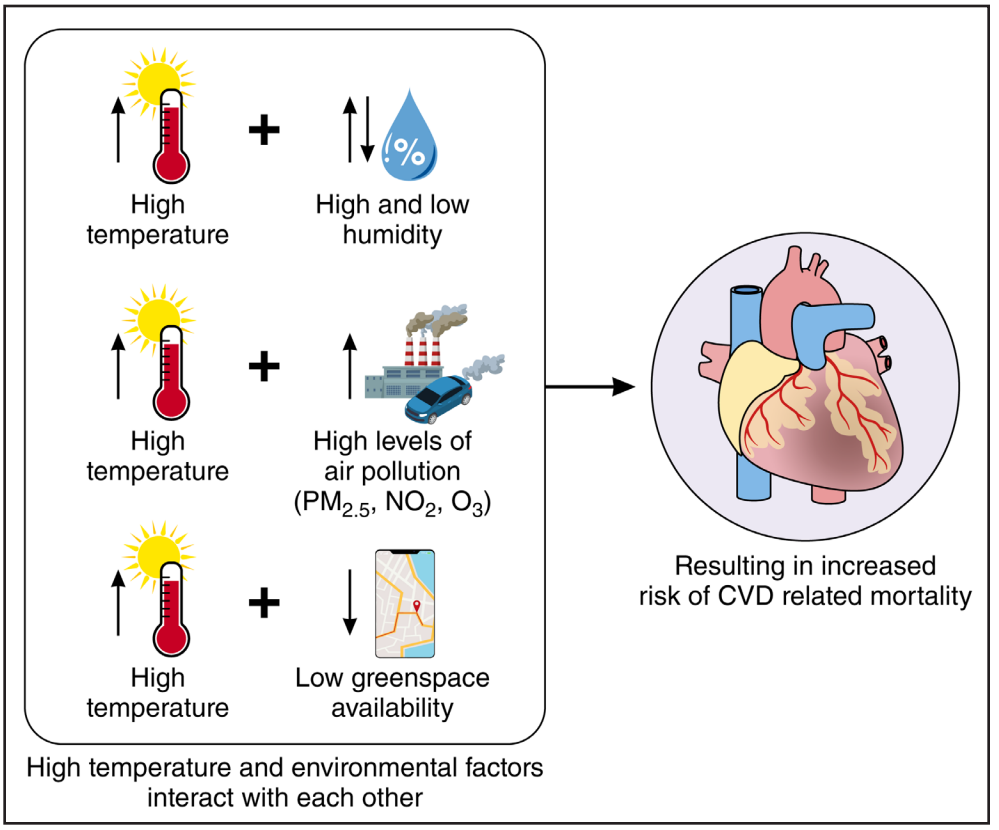

Figure 1. The interaction between temperature and other environmental factors increases the risk of cardiovascular disease (CVD)-related mortality.
Image Credit: Sceyence Studios.

and high temperatures, they reported that the interactive effect between $PM_{2.5}$ and temperature exceeded that of the individual effects. Rahman et al[24] found that the individual effects of extreme $PM_{2.5}$ and heat increased the risk of CVD mortality. However, interactive effects were inconsistent, with some of the discussed studies finding significant results and others finding no effect. Furthermore, Rai et al[26] looked at the association between high temperature and cardiovascular disease modified by PM_{10}, O_3, and NO_2. All 3 pollutants increased the risk of heat-related CVD mortality; however, this effect was most apparent for O_3 and NO_2. Generally, higher air pollution was found to amplify the adverse effects of high temperatures on CVD mortality.

POTENTIAL BIOLOGICAL PATHWAYS

How environmental factors impact the human body and the related mechanisms that facilitate this are still poorly understood; however, several biological pathways are hypothesized by epidemiological studies mentioned in this perspective, to be involved in the association between heat and CVD mortality (Figure 2).[15]

During periods of high-temperature exposure or extreme heat events, thermoregulatory mechanisms increase vasodilation, which increases blood flow to the skin to ameliorate heat through sweat.[9,15] However, these thermoregulatory processes can become exhausted, causing core body temperatures to rise and leading to disrupted homeostasis[15]; this, in turn, can lead to dehydration, which can then trigger hemoconcentration, a hypercoagulable state, electrolyte derangements, hypotension, systematic inflammatory responses and an unsustainable increase in cardiac output.[9,15,75]

A study by Lim et al[76] investigated the association of dehydration markers, temperature, and CVD mortality and found that temperature-related changes in hydration status may underlie increased CVD mortality. This conclusion was supported by other epidemiological studies, which suggested that dehydration was the most probable biological mechanism as dehydration activates the sympathetic nervous system as well as causes hemoconcentration, that is, an increase in red blood cells in the blood[9,15,75]; this cascade causes an increase in cardiac output and heart rate.[9,15,75] Cardiac output increases due to several related reasons: vasodilation causes hypovolemia, pulmonary pressure, systemic pressure, and peripheral resistance to decrease, which in turn increases systolic function and heart rate[75]; this increase in cardiac output can trigger myocardial ischemia, MI, HF, and stroke in susceptible individuals, which can then lead to cardiac death.[9]

Additionally, sex differences in heat vulnerability can be partly explained by their physiological differences in coping with excessive heat. For instance, a higher percentage of body fat and contrasts in skin conductance decreases the heat dissipation capacity in women.[60] Women's thermoregulatory response can also be influenced by hormones associated with the menstrual cycle, resulting in elevated body temperature. Similarly, changes in hormone levels in postmenopausal women, such as decreased estrogen levels, can also affect the thermoregulatory response associated with inflammation and contribute to CVD-related mortality in older women.[35,77,78]

Animal studies have largely focused on investigating the effects of heat on biomarkers related to oxidative stress, inflammatory mediators, heat-shock proteins, and thrombotic or vasomotor factors. A literature review by Mol et al[79] assessed evidence of climatic heat events on CVD in animal models. In this review, it was suggested that exposure to heat was associated with an increase in oxidative stress, vasoconstriction, coagulation, inflammation, and denaturing of proteins, which in turn were all associated with adverse CVD as much as myocardial

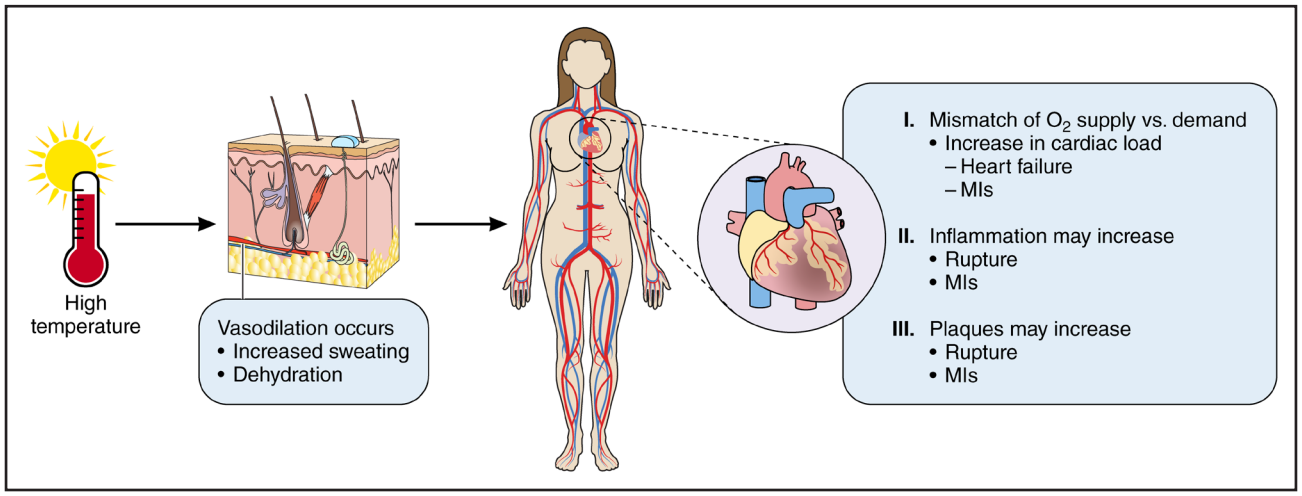

Figure 2. Potential biological pathway of heat on the cardiovascular system.
Image Credit: Sceyence Studios.

ischemia, MI, HF, thrombosis, and stroke. These animal studies largely support the conclusions suggested by epidemiological studies.

RESEARCH GAPS

The rising intensity and frequency of extreme temperatures due to global warming might have notable effects on CVD health. Still, the underlying biological mechanisms mediating the association between extreme heat and adverse cardiovascular outcomes are poorly understood. This limited policy interventions aiming at reducing CVD-related health risks from heat.[80] In turn, there is a lack of evidence, which shows the effectiveness of the so far performed policy interventions (eg, heat-health action plans), especially for vulnerable groups (people with low SES, elderly ≥65 years, people with preexisting disease conditions).[81,82]

It is a fact that the threshold temperature might vary from 1 region to another depending on the geographic location, climatic pattern, and population adaptation level: for example, a high temperature in 1 region could fall under the normal range in another. Nevertheless, a region-specific definition would be a prerequisite for better planning of health interventions and monitoring of the health effects before and after the onset of high-temperature days.

Another critical point adding to heterogeneity is the choice of study designs, which differ from time-series to case-crossover, case-control, or cross-sectional study designs. The major drawbacks of such studies are the lack of consideration for individual-level risk factors such as preexisting cardiovascular diseases, other comorbidities, use of medication, smoking and drinking habits, physical activity, and SES, among others.[6,12] Therefore, research should focus on longitudinal study designs like cohort studies with more individual-specific information. Such information will also help in establishing a causal pathway. Conducting random control trials is not possible for many logistical and ethical reasons.

Various environmental factors besides temperature, such as humidity, air pollution, and season, can influence CVD mortality. Therefore, these factors must be considered while assessing the association between heat and CVD mortality. However, consideration for these factors is often neglected. The combination of extreme heat and high air pollution levels is complex and can severely affect CVD mortality, therefore, the role of air pollution in temperature-CVD mortality association should be investigated as a potential confounder/modifier/mediator through secondary analysis. Similarly, the combination of heat and high humidity can be more detrimental than the individual effect of temperature. Therefore, instead of merely adjusting for these covariates, possible interactions should be investigated between these parameters.

An important limitation mentioned in most studies is the lack of high-resolution, reliable exposure data. The sources of data acquisition varied highly from 1 study to another. The sources of exposure data are so heterogeneous that it adds significant biases in the estimates and reduces the comparability of risks across countries. Therefore, efforts should be made toward expanding the network of ground monitoring stations and strengthening the quality of exposure data, specifically in LMICs, where access to heat prevention technology is not as easily accessible. Also, using high-resolution exposure data that has been modeled similarly for many cities would enhance the comparability of the estimated health effects across these cities.

Similarly, most existing studies use outdoor air temperature to indicate personal exposure, which might result in misclassification of individual exposure.[83] Since most of the studies consider populations living in cities and spending most of their time indoors,[84] indoor exposure to temperatures should be a better index of personal exposure than outdoor temperature. Therefore, any inferences based on outdoor exposure to heat should be carefully examined.[85]

It is important to highlight those countries or regions that top the climate change vulnerability index list, showed an absence of studies from these regions.[86] To date, studies on heat-related CVD mortality are scarce for regions like Africa, South Asia, and Eastern Europe, among which several countries topped the Global Climate Risk Index 2021 list.[86] However, the population characteristics, baseline CVD rates, health care infrastructure and housing characteristics, population susceptibility, and adaptive capacity could be markedly different in these countries. Therefore, future emphasis should be given to research from these regions.[12]

Besides, the rising issue of climate change and extreme weather events can expound environmental injustices, which are primarily caused by the unequal distribution of resources and are particularly apparent, for example, in racial and ethnic minorities, less educated people, outdoor workers, females, children, older adults, the elderly, and people living in vulnerable housing.[87] However, there is a research gap on how environmental justice affects the risk of exposure to heat and CVD. Nevertheless, constant efforts are rising towards improving social inequity in exposure to heat waves.[87]

Most studies available on the association between heat and CVD mortality are primarily from urban areas, and evidence from suburban or rural areas is still missing to a large extent. Since the physiological exposure to heat can vary widely based on an individual's capacity to access green vegetation, air-conditioning or other cooling mechanisms, housing material, and occupation, evidence based on rural background is imperative to understand the differences in risk between urban and rural settings.[88]

Furthermore, most of the studies are focused on all causes of CVD deaths, and only a handful of studies

have considered cause-specific CVD deaths, which warrant further research.[12,13] IHD and stroke, which are globally estimated to be the leading causes of death,[77,78] are unsatisfactorily studied. Similarly, evidence of the association between heat and other CVD-specific diseases like HF and arrhythmia is minimal.[8] Additional challenges are presented due to differently coded CVD deaths across sites and people with multiple CVDs, leading to misclassification bias. Therefore, the CVD responses during heat exposure in individuals with other heart diseases and medication use should also be characterized.

It is also essential to expand the understanding of how heat can impact different sexes, older age groups, and people with comorbidities.[20] The result should also be focused on other unmeasured factors that might contribute to the CVD risk, warranting future research. Since the response toward certain levels of exposure differs based on population adaptation processes, such as behavioral and physiological changes that they adapt over time, it should also be considered when investigating the risk of heat on health in general. The list of Identified research gaps and potential solutions are summarized in Table 4

Table 4. Identified research gaps and potential solutions for heat-CVD research

S. No.	Research gap	Potential solutions
11	Temporal shifts in exposure-response functions of heat and overall/cause-specific morbidity/mortality.	More studies with e.g., longer time series should be made to understand the temporal shifts in association.
2.2	Exposure-response relationships for temperature and more cause-specific CVD mortality and hospital admissions	Unsatisfactory evidence on cause-specific CVD deaths like IHD and stroke, which are globally estimated to be the leading causes of death makes efficient policy intervention difficult and therefore should be focused more.
3.3	Interaction effect due to simultaneous interplay of ambient temperature with other environmental factors (eg, climatic factors, air pollution, green space, biodiversity) as well as with social factors (environmental justice)	The combination of extreme heat and high humidity/ air pollution levels is complex and can be more detrimental than the individual effect of temperature. Therefore, instead of merely adjusting for these covariates, Possible interactions should be investigated between environmental factors and social factors.
4.4	The interplay of both outdoor and indoor exposure to temperature as a proxy for personal exposure	Studies should include both outdoor and indoor exposure as a better index of personal exposure to temperature.
5.5	The underlying biological mechanisms for the impact of temperature on CVD-related morbidity and mortality.	More studies are needed that go beyond mere mortality or hospital admission outcomes to improve knowledge of specific biological responses which can improve mechanistic understanding of the effect of exposures on health and can be used to mitigate adverse health outcomes
66	Long-term impacts of nonoptimal temperatures on CVD-related morbidity and mortality	The studies on the potential effects of prolonged exposure to high temperatures will help provide clear evidence of the disease burden of high temperatures to recommend effective measures.
77	More insight into adaptation processes (behavioral and physiological)	Since the response towards certain levels of exposure differs based on population adaptation processes, both behavioral and physiological changes, this aspect needs to be considered more in future studies.
8.7	Effectiveness of policy interventions, especially for vulnerable groups (people with low SES, elderly ≥65 y, people with preexisting disease conditions)	The studies should focus on evaluating the effectiveness of policy interventions for vulnerable subgroups so that more specific improvements can be made.
9.8	Region-specific definition of high temperature days, heat wave days	Based on climate type, racial composition, population and SES structure, an attempt could be made to define standard criteria for hot days or heat wave days.
10.9	Lack of accountability on vulnerable subgroups and individual-level risk factors such as age, preexisting cardiovascular diseases, other comorbidities, use of medication, smoking and drinking habits, physical activity, and SES, among others	Research should focus on longitudinal study designs like cohort studies with more individual-specific information. Such information will also help in establishing a causal pathway
11.10	Lack of high-resolution, reliable exposure data.	Efforts should be made toward reducing exposure misclassification and heterogeneity in the sources of exposure data by expanding the network of ground monitoring stations and strengthening the quality of exposure data, specifically in LMICs
12.11	Lack of evidence on the effect of nonoptimal temperature on human health in general from LMICs.	Future emphasis should be given to research from regions like Africa, South Asia, and Eastern Europe, which are highly vulnerable to climate change so that required mitigation and adaptation policies can be enacted.
13.	Differences in risk between urban and rural settings	Since the physiological exposure to heat can vary widely based on an individual's SES as well as the built environment in different settings, evidence based on rural background is imperative to understand the differences in risk between urban and rural settings.
14.	Differently coded CVD deaths and people with multiple CVD led to misclassification bias.	The cardiovascular responses during heat exposure in individuals with other heart diseases and medication use should also be characterized.

This table was adapted from the EXHAUSTION White Paper - Exposure to heat and air pollution in Europe. Important findings and recommendations.[89] CVD indicates cardiovascular diseases; IDH, ischemic heart disease; and LIMC, lower middle-income countries.

PUBLIC HEALTH IMPLICATIONS

Climate change and its impacts, including increased ambient temperatures and extreme weather events, are among the most significant risks to human health. Quantifying and generalizing the effects of climate variables on human health is complex. However, articles that assist public and global health stakeholders in understanding the consequences of climate-related meteorologic variables on health are of great importance. Along these lines, this review is the most up-to-date synthesis of data related to the impact of heat on cardiovascular disease mortality. Ultimately, this review will inform and enable decision-makers to make better-informed decisions when selecting effective and equitable adaptation measures to minimize climate change-induced health impacts. Moreover, by giving an up-to-date evidence base, we want to inform and raise awareness among health care practitioners in addressing climate change during patient conversations. This can support implementing preventive measures and improving adaptation measures, for example, heat warning systems linked to specific recommendations, for better protection of the population from climate change.

CONCLUSIONS

The present perspective on epidemiological evidence shows that a diverse range of CVD health outcomes can be affected by exposure to heat. Therefore, focus should be shifted towards the cause-specific CVD outcomes in addition to total CVD deaths. Besides, the risk of CVD mortality is substantially greater in the elderly, adults with preexisting CVDs, and socioeconomically deprived. A major emphasis on conducting heat-CVD research in LMICs would be a prerequisite considering the existing lack of evidence from LMICs, given, that these regions account for a majority of vulnerable population. Furthermore, the biological mechanism through which extreme temperature affects CVD mortality remains to be fully elucidated. Therefore, in light of rising climate change issues, the present study advocates that more studies should be focused on LMICs and vulnerable groups and that more studies should be dedicated to a better understanding of the potential biological pathways. Such evidence will be helpful not only in more informed and efficient care for CVD patients but also in better planning of policy interventions, mitigation and adaptation strategies, and early warning systems aimed at reducing CVD-related mortality from heat, particularly in vulnerable groups directly before and after the onset of high-temperature/heat wave days.

ARTICLE INFORMATION

Affiliations

IUF-Leibniz Research Institute for Environmental Medicine, Düsseldorf, Germany (N.S., A.T.A., T.S.). Medical Research School, Heinrich Heine University Düsseldorf, Germany (A.T.A.). Institute of Epidemiology, Helmholtz Zentrum München – German Research Center for Environmental Health, Neuherberg, Germany (S.B., A.S.). IBE-Chair of Epidemiology, Faculty of Medicine, LMU Munich, Neuherberg, Germany (S.B.). Institute of Clinical Medicine, University of Oslo, Norway (S.A.). Department of Clinical Sciences, Danderyd University Hospital, Karolinska Institutet, Stockholm, Sweden (S.A.).

Sources of Funding

S. Breitner, S. Zhang, S. Agewall, and A. Schneider: this work was supported by the European Union's Horizon 2020 Project Exhaustion (Grant ID: 820655). N. Singh, A.T. Areal, and T. Schikowski: The IUF is funded by the federal and state governments—the Ministry of Culture and Science of North Rhine-Westphalia (MKW) and the Federal Ministry of Education and Research (BMBF).

Disclosures

None.

REFERENCES

1. Roth GA, Johnson C, Abajobir A, Abd-Allah F, Abera SF, Abyu G, Ahmed M, Aksut B, Alam T, Alam K, et al. Global, regional, and national burden of cardiovascular diseases for 10 causes, 1990 to 2015. *J Am Coll Cardiol.* 2017;70:1–25. doi: 10.1016/j.jacc.2017.04.052
2. Al-Kindi SG, Brook RD, Biswal S, Rajagopalan S. Environmental determinants of cardiovascular disease: lessons learned from air pollution. *Nat Rev Cardiol.* 2020;17:656–672. doi: 10.1038/s41569-020-0371-2
3. He F, Wei J, Dong Y, Liu C, Zhao K, Peng W, Lu Z, Zhang B, Xue F, Guo X, et al. Associations of ambient temperature with mortality for ischemic and hemorrhagic stroke and the modification effects of greenness in Shandong Province, China. *Sci Total Environ.* 2022;851:158046. doi: 10.1016/j.scitotenv.2022.158046
4. Romanello M, Di Napoli C, Drummond P, Green C, Kennard H, Lampard P, Scamman D, Arnell N, Ayeb-Karlsson S, Ford LB, et al. The 2022 report of the Lancet Countdown on health and climate change: health at the mercy of fossil fuels. *Lancet.* 2022;400:1619–1654. doi: 10.1016/S0140-6736(22)01540-9
5. IPCC. *Climate Change 2023: Synthesis Report. Contribution of Working Groups I, II and III to the Sixth Assessment Report of the Intergovernmental Panel on Climate Change*. Geneva, Switzerland: IPCC; 2023.
6. Chaseling GK, Iglesies-Grau J, Juneau M, Nigam A, Kaiser D, Gagnon D. Extreme heat and cardiovascular health: what a cardiovascular health professional should know. *Can J Cardiol.* 2021;37:1828–1836. doi: 10.1016/j.cjca.2021.08.008
7. Murray CJ, Aravkin AY, Zheng P, Abbafati C, Abbas KM, Abbasi-Kangevari M, et al. 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;396:1223–1249.
8. Alahmad B, Khraishah H, Royé D, Vicedo-Cabrera AM, Guo Y, Papatheodorou SI, Achilleos S, Acquaotta F, Armstrong B, Bell ML, et al. Associations between extreme temperatures and cardiovascular cause-specific mortality: results from 27 countries. *Circulation.* 2023;147:35–46. doi: 10.1161/CIRCULATIONAHA.122.061832
9. Desai Y, Khraishah H, Alahmad B. Focus: climate change and environmental health: heat and the heart. *Yale J Biol Med.* 2023;96:197. doi: 10.59249/HGAL4894
10. Le H, Yan MM, Zhang YQ, Kai W, Wang YQ, Luo SQ, Wang F. Global burden of cardiovascular disease attributable to high temperature in 204 countries and territories from 1990 to 2019. *Biomed Environ Sci.* 2023;36:222–230. doi: 10.3967/bes2023.025
11. Liu JM, Liu T, Burkart KG, Wang HD, He GH, Hu JX, Xiao J, Yin P, Wang L, Liang X, et al. Mortality burden attributable to high and low ambient temperatures in China and its provinces: Results from the Global Burden of Disease Study 2019. *Lancet Reg Health West Pac.* 2022;24:100493. doi: 10.1016/j.lanwpc.2022.100493
12. Liu J, Varghese BM, Hansen A, Zhang Y, Driscoll T, Morgan G, Dear K, Gourley M, Capon A, Bi P. Heat exposure and cardiovascular health outcomes: a systematic review and meta-analysis. *Lancet Planet Health.* 2022;6:e484–e495. doi: 10.1016/S2542-5196(22)00117-6
13. Cheng J, Xu Z, Bambrick H, Prescott V, Wang N, Zhang Y, Su H, Tong S, Hu W. Cardiorespiratory effects of heatwaves: a systematic review and meta-analysis of global epidemiological evidence. *Environ Res.* 2019;177:108610. doi: 10.1016/j.envres.2019.108610
14. Achebak H, Devolder D, Ballester J. Trends in temperature-related age-specific and sex-specific mortality from cardiovascular diseases in Spain: a

national time-series analysis. *Lancet Planet Health*. 2019;3:e297–e306. doi: 10.1016/S2542-5196(19)30090-7
15. Alahmad B, Khraishah H, Shakarchi AF, Albaghdadi M, Rajagopalan S, Koutrakis P, Jaffer FA. Cardiovascular mortality and exposure to heat in an inherently hot region: implications for climate change. *Circulation*. 2020;141:1271–1273. doi: 10.1161/CIRCULATIONAHA.119.044860
16. Chen K, Breitner S, Wolf K, Hampel R, Meisinger C, Heier M, von Scheidt W, Kuch B, Peters A, Schneider A; KORA Study Group. Temporal variations in the triggering of myocardial infarction by air temperature in Augsburg, Germany, 1987-2014. *Eur Heart J*. 2019;40:1600–1608. doi: 10.1093/eurheartj/ehz116
17. Fang W, Li Z, Gao J, Meng R, He G, Hou Z, Zhu S, Zhou M, Zhou C, Xiao Y, et al. The joint and interaction effect of high temperature and humidity on mortality in China. *Environ Int*. 2023;171:107669. doi: 10.1016/j.envint.2022.107669
18. Guo H, Du P, Zhang H, Zhou Z, Zhao M, Wang J, Shi X, Lin J, Lan Y, Xiao X, et al. Time series study on the effects of daily average temperature on the mortality from respiratory diseases and circulatory diseases: a case study in Mianyang City. *BMC Public Health*. 2022;22:1001. doi: 10.1186/s12889-022-13384-6
19. Jahan S, Cauchi JP, Galdies C, Wraith D. Effects of ambient temperatures and extreme weather events on circulatory mortality in a high population density area: exploring mortality data from Malta. *Clim Risk Manage*. 2022;38:100463. doi: 10.1016/j.crm.2022.100463
20. Kephart JL, Sánchez BN, Moore J, Schinasi LH, Bakhtsiyarava M, Ju Y, Gouveia N, Caiaffa WT, Dronova I, Arunachalam S, et al. City-level impact of extreme temperatures and mortality in Latin America. *Nat Med*. 2022;28:1700–1705. doi: 10.1038/s41591-022-01872-6
21. Majeed H, Floras JS. Warmer summer nocturnal surface air temperatures and cardiovascular disease death risk: a population-based study. *BMJ Open*. 2022;12:e056806. doi: 10.1136/bmjopen-2021-056806
22. Moraes SLD, Almendra R, Barrozo LV. Impact of heat waves and cold spells on cause-specific mortality in the city of São Paulo, Brazil. *Int J Hyg Environ Health*. 2022;239:113861. doi: 10.1016/j.ijheh.2021.113861
23. Murage P, Hajat S, Kovats R. Effect of night-time temperatures on cause and age-specific mortality in London. *Environ Epidemiol*. 2017;1:e005. doi: 10.1097/EE9.0000000000000005
24. Rahman MM, McConnell R, Schlaerth H, Ko J, Silva S, Lurmann FW, Palinkas L, Johnston J, Hurlburt M, Yin H, et al. The effects of coexposure to extremes of heat and particulate air pollution on mortality in California implications for climate change. *Am J Respir Crit Care Med*. 2022;206:1117–1127. doi: 10.1164/rccm.202204-0657OC
25. Rai M, Breitner S, Huber V, Zhang S, Peters A, Schneider A. Temporal variation in the association between temperature and cause-specific mortality in 15 German cities. *Environ Res*. 2023;229:115668. doi: 10.1016/j.envres.2023.115668
26. Rai M, Stafoggia M, de'Donato F, Scortichini M, Zafeiratou S, Vazquez Fernandez L, Zhang S, Katsouyanni K, Samoli E, Rao S, et al. Heat-related cardiorespiratory mortality: effect modification by air pollution across 482 cities from 24 countries. *Environ Int*. 2023;174:107825. doi: 10.1016/j.envint.2023.107825
27. Saucy A, Ragettli MS, Vienneau D, de Hoogh K, Tangermann L, Schaffer B, Wunderli J-M, Probst-Hensch N, Röösli M. The role of extreme temperature in cause-specific acute cardiovascular mortality in Switzerland: a case-crossover study. *Sci Total Environ*. 2021;790:147958. doi: 10.1016/j.scitotenv.2021.147958
28. de Schrijver E, Sivaraj S, Raible CC, Franco OH, Chen K, Vicedo-Cabrera AM. Nationwide projections of heat- and cold-related mortality impacts under various climate change and population development scenarios in Switzerland. *Environ Res Lett*. 2023;18:094010. doi: 10.1088/1748-9326/ace7e1
29. Shrikhande SS, Pedder H, Roeoesli M, Dalvie MA, Lakshmanasamy R, Gasparrini A, Utzinger J, Cissé G. Non-optimal apparent temperature and cardiovascular mortality: the association in Puducherry, India between 2011 and 2020. *BMC Public Health*. 2023;23:291. doi: 10.1186/s12889-023-15128-6
30. Silveira IH, Cortes TR, Bell ML, Junger WL. Effects of heat waves on cardiovascular and respiratory mortality in Rio de Janeiro, Brazil. *PLoS One*. 2023;18:e0283899. doi: 10.1371/journal.pone.0283899
31. Wang Y, Lin L, Xu Z, Wang L, Huang J, Zhou M, Li G. Have residents adapted to heat wave and cold spell in the 21st century? Evidence from 136 Chinese cities. *Environ Int*. 2023;173:107811. doi: 10.1016/j.envint.2023.107811
32. Xia Y, Shi C, Li Y, Jiang X, Ruan S, Gao X, Chen Y, Huang W, Li M, Xue R, et al. Effects of ambient temperature on mortality among elderly residents of Chengdu city in Southwest China, 2016-2020: a distributed-lag non-linear time series analysis. *BMC Public Health*. 2023;23:149. doi: 10.1186/s12889-022-14931-x
33. Xu R, Huang S, Shi C, Wang R, Liu T, Li Y, Zheng Y, Lv Z, Wei J, Sun H, et al. Extreme temperature events, fine particulate matter, and myocardial infarction mortality. *Circulation*. 2023;148:312–323. doi: 10.1161/CIRCULATIONAHA.122.063504
34. Yan M, Xie Y, Zhu H, Ban J, Gong J, Li T. Cardiovascular mortality risks during the 2017 exceptional heatwaves in China. *Environ Int*. 2023;172:107767. doi: 10.1016/j.envint.2023.107767
35. Zhang S, Breitner S, Rai M, Nikolaou N, Stafoggia M, De' Donato F, Samoli E, Zafeiratou S, Katsouyanni K, Rao S, et al. Assessment of short-term heat effects on cardiovascular mortality and vulnerability factors using small area data in Europe. *Environ Int*. 2023;179:108154. doi: 10.1016/j.envint.2023.108154
36. Hu J, Zhou M, Qin M, Tong S, Hou Z, Xu Y, Zhou C, Xiao Y, Yu M, Huang B, et al. Long-term exposure to ambient temperature and mortality risk in China: a nationwide study using the difference-in-differences design. *Environ Pollut*. 2022;292:118392. doi: 10.1016/j.envpol.2021.118392
37. Wang XY, Barnett AG, Yu W, FitzGerald G, Tippett V, Aitken P, Neville G, McRae D, Verrall K, Tong S. The impact of heatwaves on mortality and emergency hospital admissions from non-external causes in Brisbane, Australia. *Occup Environ Med*. 2012;69:163–169. doi: 10.1136/oem.2010.062141
38. Fouillet A, Rey G, Laurent F, Pavillon G, Bellec S, Guihenneuc-Jouyaux C, Clavel J, Jougla E, Hémon D. Excess mortality related to the August 2003 heat wave in France. *Int Arch Occup Environ Health*. 2006;80:16–24. doi: 10.1007/s00420-006-0089-4
39. Basagaña X, Sartini C, Barrera-Gómez J, Dadvand P, Cunillera J, Ostro B, Sunyer J, Medina-Ramón M. Heat waves and cause-specific mortality at all ages. *Epidemiology*. 2011;22:765–772. doi: 10.1097/ede.0b013e31823031c5
40. Sheridan SC, Lin S. Assessing variability in the impacts of heat on health outcomes in New York City over time, season, and heat-wave duration. *Ecohealth*. 2014;11:512–525. doi: 10.1007/s10393-014-0970-7
41. Burkart K, Breitner S, Schneider A, Khan MMH, Krämer A, Endlicher W. An analysis of heat effects in different subpopulations of Bangladesh. *Int J Biometeorol*. 2014;58:227–237. doi: 10.1007/s00484-013-0668-5
42. Yatim ANM, Latif MT, Sofwan NM, Ahamad F, Khan MF, Mahiyuddin WRW, Sahani M. The association between temperature and cause-specific mortality in the Klang Valley, Malaysia. *Environ Sci Pollut Res Int*. 2021;28:60209–60220. doi: 10.1007/s11356-021-14962-8
43. Ferreira LCM, Nogueira MC, Pereira RVB, de Farias WCM, Rodrigues MMS, Teixeira MTB, Carvalho MS. Ambient temperature and mortality due to acute myocardial infarction in Brazil: an ecological study of time-series analyses. *Sci Rep*. 2019;9:13790.
44. Nada Hamadeh CVR, Eric M, Shwetha GE. New World Bank country classifications by income level: 2022-2023 2022. https://blogs.worldbank.org/opendata/new-world-bank-country-classifications-income-level-2022-2023
45. *Institute for Health Metrics and Evaluation (IHME).* GBD Results Seattle, WA: IHME, University of Washington. 2020. https://vizhub.healthdata.org/gbd-results/
46. Livingstone KM, Abbott G, Ward J, Bowe SJ. Unhealthy lifestyle, genetics and risk of cardiovascular disease and mortality in 76,958 individuals from the UK Biobank cohort study. *Nutrients*. 2021;13:4283. doi: 10.3390/nu13124283
47. Rocklöv J, Forsberg B. The effect of temperature on mortality in Stockholm 1998–2003: a study of lag structures and heatwave effects. *Scand J Public Health*. 2008;36:516–523. doi: 10.1177/1403494807088458
48. Guo Y, Gasparrini A, Armstrong BG, Tawatsupa B, Tobias A, Lavigne E, de Sousa Zanotti Stagliorio Coelho M, Pan X, Kim H, Hashizume M, et al. Heat wave and mortality: a multicountry, multicommunity study. *Environ Health Perspect*. 2017;125:087006. doi: 10.1289/EHP1026
49. Buckley JP, Samet JM, Richardson DB. Commentary: does air pollution confound studies of temperature? *Epidemiology*. 2014;25:242–245. doi: 10.1097/EDE.0000000000000051
50. Maclure M, Mittleman MA. Should we use a case-crossover design? *Annu Rev Public Health*. 2000;21:193–221. doi: 10.1146/annurev.publhealth.21.1.193
51. Fung KY, Krewski D, Chen Y, Burnett R, Cakmak S. Comparison of time series and case-crossover analyses of air pollution and hospital admission data. *Int J Epidemiol*. 2003;32:1064–1070. doi: 10.1093/ije/dyg246
52. Cox LA Jr. What is an exposure-response curve? *Glob Epidemiol*. 2023;6:100114. doi: 10.1016/j.gloepi.2023.100114

53. Zafeiratou S, Samoli E, Dimakopoulou K, Rodopoulou S, Analitis A, Gasparrini A, Stafoggia M, De' Donato F, Rao S, Monteiro A, et al; EXHAUSTION project team. A systematic review on the association between total and cardiopulmonary mortality/morbidity or cardiovascular risk factors with long-term exposure to increased or decreased ambient temperature. *Sci Total Environ*. 2021;772:145383. doi: 10.1016/j.scitotenv.2021.145383
54. Peters A, Schneider A. Cardiovascular risks of climate change. *Nat Rev Cardiol*. 2020;18:1–2. doi: 10.1038/s41569-020-00473-5
55. Vu A, Rutherford S, Phung D. Heat health prevention measures and adaptation in older populations—A systematic review. *Int J Environ Res Public Health*. 2019;16:4370. doi: 10.3390/ijerph16224370
56. Wang XY, Guo Y, FitzGerald G, Aitken P, Tippett V, Chen D, Wang X, Tong S. The impacts of heatwaves on mortality differ with different study periods: a multi-city time series investigation. *PLoS One*. 2015;10:e0134233. doi: 10.1371/journal.pone.0134233
57. Tian Z, Li S, Zhang J, Guo Y. The characteristic of heat wave effects on coronary heart disease mortality in Beijing, China: a time series study. *PLoS One*. 2013;8:e77321. doi: 10.1371/journal.pone.0077321
58. Dong W, Zeng Q, Ma Y, Li G, Pan X. Impact of heat wave definitions on the added effect of heat waves on cardiovascular mortality in Beijing, China. *Int J Environ Res Public Health*. 2016;13:933. doi: 10.3390/ijerph13090933
59. Son J-Y, Liu JC, Bell ML. Temperature-related mortality: a systematic review and investigation of effect modifiers. *Environ Res Lett*. 2019;14:073004. doi: 10.1088/1748-9326/ab1cdb
60. van Steen Y, Ntarladima A-M, Grobbee R, Karssenberg D, Vaartjes I. Sex differences in mortality after heat waves: are elderly women at higher risk? *Int Arch Occup Environ Health*. 2019;92:37–48. doi: 10.1007/s00420-018-1360-1
61. Campbell S, Remenyi TA, White CJ, Johnston FH. Heatwave and health impact research: a global review. *Health Place*. 2018;53:210–218. doi: 10.1016/j.healthplace.2018.08.017
62. Michelozzi P, Accetta G, De Sario M, D'Ippoliti D, Marino C, Baccini M, Biggeri A, Anderson HR, Katsouyanni K, Ballester F, et al; PHEWE Collaborative Group. High temperature and hospitalizations for cardiovascular and respiratory causes in 12 European cities. *Am J Respir Crit Care Med*. 2009;179:383–389. doi: 10.1164/rccm.200802-217OC
63. Grasgruber P, Cacek J, Hrazdíra E, Hřebíčková S, Sebera M. Global correlates of cardiovascular risk: a comparison of 158 countries. *Nutrients*. 2018;10:411. doi: 10.3390/nu10040411
64. Yang C, Meng X, Chen R, Cai J, Zhao Z, Wan Y, Kan H. Long-term variations in the association between ambient temperature and daily cardiovascular mortality in Shanghai, China. *Sci Total Environ*. 2015;538:524–530. doi: 10.1016/j.scitotenv.2015.08.097
65. Chung Y, Noh H, Honda Y, Hashizume M, Bell ML, Guo YL, Kim H. Temporal changes in mortality related to extreme temperatures for 15 cities in Northeast Asia: adaptation to heat and maladaptation to cold. *Am J Epidemiol*. 2017;185:907–913. doi: 10.1093/aje/kww199
66. Carson C, Hajat S, Armstrong B, Wilkinson P. Declining vulnerability to temperature-related mortality in London over the 20th century. *Am J Epidemiol*. 2006;164:77–84. doi: 10.1093/aje/kwj147
67. Barnett AG. Temperature and cardiovascular deaths in the US elderly: changes over time. *Epidemiology*. 2007;18:369–372. doi: 10.1097/01.ede.0000257515.34445.a0
68. Lu P, Xia G, Zhao Q, Xu R, Li S, Guo Y. Temporal trends of the association between ambient temperature and hospitalisations for cardiovascular diseases in Queensland, Australia from 1995 to 2016: a time-stratified case-crossover study. *PLoS Med*. 2020;17:e1003176. doi: 10.1371/journal.pmed.1003176
69. Wang Y, Wang A, Zhai J, Tao H, Jiang T, Su B, Yang J, Wang G, Liu Q, Gao C, et al. Tens of thousands additional deaths annually in cities of China between 1.5 °C and 2.0 °C warming. *Nat Commun*. 2019;10:3376. doi: 10.1038/s41467-019-11283-w
70. Jenkins K, Kennedy-Asser A, Andrews O, Lo YTE. Updated projections of UK heat-related mortality using policy-relevant global warming levels and socio-economic scenarios. *Environ Res Lett*. 2022;17:114036. doi: 10.1088/1748-9326/ac9cf3
71. Petkova EP, Vink JK, Horton RM, Gasparrini A, Bader DA, Francis JD, Kinney PL. Towards more comprehensive projections of Urban heat-related mortality: estimates for New York City under multiple population, adaptation, and climate scenarios. *Environ Health Perspect*. 2017;125:47–55. doi: 10.1289/EHP166
72. Lee JY, Lee WS, Ebi KL, Kim H. Temperature-Related summer mortality under multiple climate, population, and adaptation scenarios. *Int J Environ Res Public Health*. 2019;16:1026. doi: 10.3390/ijerph16061026
73. Gasparrini A, Guo Y, Sera F, Vicedo-Cabrera AM, Huber V, Tong S, de Sousa Zanotti Stagliorio Coelho M, Nascimento Saldiva PH, Lavigne E, Matus Correa P, et al. Projections of temperature-related excess mortality under climate change scenarios. *Lancet Planet Health*. 2017;1:e360–e367. doi: 10.1016/S2542-5196(17)30156-0
74. Davis RE, McGregor GR, Enfield KB. Humidity: a review and primer on atmospheric moisture and human health. *Environ Res*. 2016;144:106–116. doi: 10.1016/j.envres.2015.10.014
75. Giorgini P, Di Giosia P, Petrarca M, Lattanzio F, Stamerra CA, Ferri C. Climate changes and human health: a review of the effect of environmental stressors on cardiovascular diseases across epidemiology and biological mechanisms. *Curr Pharm Des*. 2017;23:3247–3261. doi: 10.2174/1381612823666170317143248
76. Lim Y-H, Park M-S, Kim Y, Kim H, Hong Y-C. Effects of cold and hot temperature on dehydration: a mechanism of cardiovascular burden. *Int J Biometeorol*. 2015;59:1035–1043. doi: 10.1007/s00484-014-0917-2
77. Nappi RE, Chedraui P, Lambrinoudaki I, Simoncini T. Menopause: a cardiometabolic transition. *Lancet Diabetes Endocrinol*. 2022;10:442–456. doi: 10.1016/S2213-8587(22)00076-6
78. Charkoudian N. Skin blood flow in adult human thermoregulation: how it works, when it does not, and why. *Mayo Clin Proc*. 2003;78:603–612. doi: 10.4065/78.5.603
79. Mol N, Priya A, Singh AK, Mago P, Shalimar, Ray AK. "Unravelling the impacts of climatic heat events on cardiovascular health in animal models.". *Environ Res*. 2024;248:118315.
80. 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;124:1694–1699. doi: 10.1289/EHP203
81. Bassil KL, Cole DC. Effectiveness of public health interventions in reducing morbidity and mortality during heat episodes: a structured review. *Int J Environ Res Public Health*. 2010;7:991–1001. doi: 10.3390/ijerph7030991
82. Baaghideh M, Mayvaneh F. Climate change and simulation of cardiovascular disease mortality: a case study of Mashhad, Iran. *Iran J Public Health*. 2017;46:396–407.
83. White-Newsome JL, Sánchez BN, Jolliet O, Zhang Z, Parker EA, Dvonch JT, O'Neill MS. Climate change and health: indoor heat exposure in vulnerable populations. *Environ Res*. 2012;112:20–27. doi: 10.1016/j.envres.2011.10.008
84. Höppe P, Martinac I. Indoor climate and air quality: review of current and future topics in the field of ISB study group 10. *Int J Biometeorol*. 1998;42:1–7. doi: 10.1007/s004840050075
85. Nguyen JL, Schwartz J, Dockery DW. The relationship between indoor and outdoor temperature, apparent temperature, relative humidity, and absolute humidity. *Indoor Air*. 2014;24:103–112. doi: 10.1111/ina.12052
86. Index GCR. *Who Suffers Most from Extreme Weather Events? Weather related loss events in 2019 and 2000–2019*. German Watch; 2021.
87. Zeng P, Sun F, Liu Y, Chen C, Tian T, Dong Q, Che Y. Significant social inequalities exist between hot and cold extremes along urban-rural gradients. *Sustainable Cities Soc*. 2022;82:103899. doi: 10.1016/j.scs.2022.103899
88. Guo Y, Li S, Zhang Y, Armstrong B, Jaakkola JJ, Tong S, Pan X. Extremely cold and hot temperatures increase the risk of ischaemic heart disease mortality: epidemiological evidence from China. *Heart*. 2013;99:195–203. doi: 10.1136/heartjnl-2012-302518
89. Kristin Aunan HAA, Mikael SA, Roxana B, Susanne B, Sourangsu C, Antonio G, Risto H, Ulas I, Lin M, Pierre M, et al. EXHAUSTION White Paper - Exposure to heat and air pollution in Europe. Important findings and recommendations. [White paper]. White Paper. 2024.