

World Journal of *Cardiology*

World J Cardiol 2022 March 26; 14(3): 108-189



REVIEW

- 108 Fundamentals of percutaneous coronary bifurcation interventions
Kirat T
- 139 Arrhythmic risk stratification in ischemic, non-ischemic and hypertrophic cardiomyopathy: A two-step multifactorial, electrophysiology study inclusive approach
Arsenos P, Gatzoulis KA, Tsiachris D, Dilaveris P, Sideris S, Sotiropoulos I, Archontakis S, Antoniou CK, Kordalis A, Skiadas I, Toutouzas K, Vlachopoulos C, Tousoulis D, Tsioufis K
- 152 Climatic influences on cardiovascular diseases
Abrignani MG, Lombardo A, Braschi A, Renda N, Abrignani V

MINIREVIEWS

- 170 Predictors of persistence of functional mitral regurgitation after cardiac resynchronization therapy: Review of literature
Russo E, Russo G, Braccio M, Cassese M

ORIGINAL ARTICLE

Retrospective Study

- 177 Risk profiles and outcomes of patients receiving antibacterial cardiovascular implantable electronic device envelopes: A retrospective analysis
Woodard DA, Kim G, Nilsson KR

LETTER TO THE EDITOR

- 187 Electrocardiographic alterations in patients with chronic obstructive pulmonary disease
Eyuboglu M

ABOUT COVER

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Climatic influences on cardiovascular diseases

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Abstract

Classical risk factors only partially account for variations in cardiovascular disease incidence; therefore, also other so far unknown features, among which meteorological factors, may influence heart diseases (mainly coronary heart diseases, but also heart failure, arrhythmias, aortic dissection and stroke) rates. The most studied phenomenon is ambient temperature. The relation between mortality, as well as cardiovascular diseases incidence, and temperature appears graphically as a "U" shape. Exposure to cold, heat and heat waves is associated with an increased risk of acute coronary syndromes. Other climatic variables, such as humidity, atmospheric pressure, sunlight hours, wind strength and direction and rain/snow precipitations have been hypothesized as related to fatal and non-fatal cardiovascular diseases incidence. Main limitation of these studies is the unavailability of data on individual exposure to weather parameters. Effects of weather may vary depending on other factors, such as population disease profile and age structure. Climatic stress may increase direct and indirect risks to human health *via* different, complex pathophysiological pathways and exogenous and endogenous mechanisms. These data have attracted growing interest because of the recent earth's climate change, with consequent increasing ambient temperatures and climatic fluctuations. This review evaluates the evidence base for cardiac health consequences of climate conditions, and it also explores potential further implications.

Key Words: Weather; Climate; Meteorology; Cardiovascular diseases; Myocardial infarction; Angina pectoris

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Core Tip: Climatic stress may determine some risks to human health *via* complex pathophysiological pathways. Meteorological factors may influence coronary heart diseases, but also heart failure, arrhythmias, aortic dissection and stroke rates. The most studied phenomenon is temperature. The relation between mortality, as well as cardiovascular diseases incidence, and temperature appears graphically as a “U” shape. Other variables, such as humidity, atmospheric pressure, sunlight hours, wind strength and direction and rain/snow precipitations have been studied. These data have attracted growing interest because of the recent earth’s climate change. This review evaluates the evidence for cardiac health consequences of climate conditions.

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INTRODUCTION

Despite considerable advances in identifying the conditions that may predispose to atherosclerosis, less information is known about the incident events leading to plaque rupture. Classical risk factors only partially account for variations in cardiovascular disease incidence and mortality. Therefore, also other so far unknown features, among which meteorological factors, may influence cardiovascular diseases rates.

AMBIENT TEMPERATURE AND MORTALITY

Seasonal peaks in respiratory, cardiovascular, and cerebrovascular mortality, with a winter increase in deaths, have been reported in different countries, referred to as “excess winter mortality”[1-3]. This phenomenon has been strongly linked to changes in temperature[4-8].

The relation between environmental temperature and health has been known for a very long time. Several disorders, such as heat stroke and hypothermia, are directly linked to temperature extremes. Low seasonal temperatures increase the odds of mortality[9,10]. An association between extreme high temperatures and mortality has also been demonstrated[11,12], as confirmed by recent data[13-16]. Actually, a number of ecological time-series studies suggest that the relation between mortality and ambient temperature appears graphically as a “U” shape, with mortality rates lower on days in which the average temperatures range between 15° to 25°C, rising progressively as the ambient temperature becomes hotter or colder[17-20]. Most of mortality linked to heat occurs during first days after temperature increase, while the effect of cold has been prolonged for several weeks[21-23]. Spatial and temporal differences have been described in this phenomenon[24-27]. Many heat-related deaths occur in people before they come to medical attention[28]. Investigations carried out in a large number of cities have shown that temperature level corresponding to the minimum mortality varies from place to place and country to country according to the usual climate (heat thresholds were generally higher in communities closer to the equator), probably reflecting adaptations of the population to the usual range of temperature[29]. High respiratory, cardiovascular and influenza mortality in winter leads to lower temperature effects in the following summer[30]. There was a progressive reduction in temperature related deaths over the 20th century, despite an aging population[31-33]. This trend is likely to reflect improvements in social, environmental, behavioural, and health-care factors[34,35]. In the recent COVID-19 pandemic, there was a negative correlation between the cumulative relative risk of death and temperature[36]. Table 1 shows main studies on the relations between weather and general mortality.

In particular, various epidemiological studies have reported greater coronary heart disease (CHD) and acute myocardial infarction (AMI) mortality both in winter[37-40] and in extremely hot summers [25,41,42]. Many authors have postulated that weather-related variables may also explain these seasonal trends, as well as substantial geographic variations in CHD mortality. Cold climate is independently associated to coronary mortality[43-45], but a U-shaped relationship between ambient temperature and cardiovascular mortality has been also described even in milder regions, where either low temperatures or heat waves are exceptional[46-48], with few exceptions[49]. Consensus is lacking, however, on whether this phenomenon reflects variations in incidence or in case fatality rate. Cold effect seems delayed, whereas heat effect is acute, both of which last for several days[34,46,50]. The delay between peak of cold is lower for all-cause mortality and CHD causes than for respiratory ones[51]. Mean temperature had better predictive ability than minimum and maximum one[35,46]. Table 2 shows main studies on the relations between weather and cardiovascular mortality.

Table 1 Main studies on the relations between weather and general mortality

Ref.	Setting and population	Year	Main results
Chung <i>et al</i> [11]	Fifteen cities in Northeast Asia	1972-2010	Cold effects had longer time lags (5–11 d) than heat effects, which were immediate (1–3 d). Both cold and heat effects were more significant for cardiorespiratory mortality than for other causes of death
Curriero <i>et al</i> [4]	Eleven large eastern United States cities	1973-1994	Current and recent days' temperatures were the weather components most strongly predictive of mortality. Mortality risk generally decreased as temperature increased from the coldest days to a certain threshold temperature, which varied by latitude, above which mortality risk increased as temperature increased. Strong association of the temperature-mortality relation with latitude, with a greater effect of colder temperatures on mortality risk in more-southern cities and of warmer temperatures in more-northern cities
Fernández-Raga <i>et al</i> [18]	Castile-León, Spain	1980-1988	Temperatures with lower death risk for patients with cardiovascular diseases (16.8°C) are apparently lower than those for patients with respiratory diseases (18.1°C)
Achebak <i>et al</i> [31]	47 major cities in Spain	1980-2015	Reduction in relative risks of cause-specific and cause-sex mortality across the whole range of summer temperatures
Gemmel <i>et al</i> [2]	Scotland, United Kingdom	1981-1993	A 1°C decrease in mean temperature was associated with a 1% increase in deaths 1 wk later
Guo <i>et al</i> [15]	400 communities from 18 countries/regions	1984-2013	Heat waves had significant cumulative associations with mortality but varied by community. The higher the temperature threshold used to define heat waves, the higher heat wave associations on mortality. The association between heat waves and mortality appeared acutely and lasted for 3 and 4 d. Heat waves had higher associations with mortality in moderate areas than in cold and hot areas
Gasparrini <i>et al</i> [22]	305 locations in 9 countries: Australia, Canada, China, Italy, Japan, South Korea, Spain, United Kingdom, and United States	1985-2012	Strong evidence of a reduction in risk over the season. Relative risks for the 99 th percentile versus the minimum mortality temperature were in the range of 1.15–2.03 in early summer. In late summer, the excess was substantially reduced or abated, with relative risks in the range of 0.97–1.41
Gasparrini <i>et al</i> [27]	384 locations in Australia, Brazil, Canada, China, Italy, Japan, South Korea, Spain, Sweden, Taiwan, Thailand, United Kingdom, and United States	1985-2012	7.71% (95%CI: 7.43–7.91) of mortality was attributable to non-optimum temperature in the selected countries within the study period, with substantial differences between countries, ranging from 3.37% (3.06 to 3.63) in Thailand to 11.00% (9.29 to 12.47) in China. The temperature percentile of minimum mortality varied from roughly the 60 th percentile in tropical areas to about the 80–90 th percentile in temperate regions
Aylin <i>et al</i> [5]	Great Britain	1986-1996	Significant association between mortality and temperature with 1.5 higher odds of dying for every 1°C reduction in winter temperature
The Eurowinter Group [1]	Men and women aged 50–59 and 65–74 in north Finland, south Finland, Baden-Württemberg, the Netherlands, London, and north Italy	1988-1992	Percentage increases in all-cause mortality per 1°C fall in temperature below 18°C were greater in warmer regions than in colder regions. High indices of cold-related mortality were associated with high mean winter temperatures ($P < 0.01$ for all-cause mortality and respiratory mortality; $P > 0.05$ for mortality from ischaemic heart disease and cerebrovascular disease)
Rocklöv <i>et al</i> [30]	Stockholm, Sweden	1990-2002	A high rate of respiratory and cardiovascular mortality in winter reduced the heat effect the following summer. The cumulative effect per 1°C increase was 0.95% below and 0.89% above a threshold (21.3°C) after a winter with low cardiovascular and respiratory mortality, but -0.23% below and 0.21% above the threshold after a winter with high cardiovascular and respiratory mortality
Ragettli <i>et al</i> [32]	Switzerland	1995-2013	Significant temperature-mortality relationships were found for maximal (1.15; 1.08–1.22); mean (1.16; 1.09–1.23), and minimal (1.23; 1.15–1.32) temperature. Mortality risks were higher at the beginning of the summer. Recent non-significant reduction in the effect of high temperatures on mortality
Chen <i>et al</i> [10]	All deaths among residents in Ontario, Canada	1996-2010	In warm seasons, each 5°C increase in daily mean temperature was associated with a 2.5% increase in nonaccidental deaths (95%CI: 1.3%–3.8%) on the day of exposure (lag 0). In cold seasons, each 5°C decrease in daily temperature was associated with a 3.0% (95%CI: 1.8%–4.2%) increase in nonaccidental deaths, which persisted over 7 d. Cold-related effects were stronger for cardiovascular-related deaths (any cardiovascular death: 4.1%, 95%CI: 2.3%–5.9%; CHD: 5.8%, 95%CI: 3.6%–8.1%). Each 5°C change in daily temperature was estimated to induce 7 excess deaths per day in cold seasons and 4 excess deaths in warm seasons
Oudin Åström <i>et al</i> [24]	Eastern Esthonia	1997-2013	Immediate increase in mortality associated with temperatures exceeding the 75 th percentile of summer maximum temperatures, corresponding to approximately 23°C. This increase lasted for a couple of days
Bell <i>et al</i> [21]	Mexico City, Mexico; Sao Paulo, Brazil; Santiago, Chile	1998-2002	Elevated temperatures (in particular same and previous day apparent temperature) are associated with mortality risk
Chan <i>et al</i> [12]	Hong Kong, China	1998-2006	An average 18°C increase in daily mean temperature above 28.2°C was associated with a 1.8% increase in mortality. Non-cancer related causes such as cardiovascular and respiratory infection-related deaths were more sensitive to high temperature

Xu <i>et al</i> [34]	Barcelona, Spain	1999-2006	The effect of three consecutive hot days was a 30% increase in all-cause mortality (RR = 1.30, 95%CI: 1.24-1.38)
Guo <i>et al</i> [23]	Chiang Mai city, Thailand	1999-2008	Both hot and cold temperatures resulted in immediate increase in all mortality types and age groups. Generally, the hot effects on all mortality types and age groups were short-term, while the cold effects lasted longer. The relative risk of mortality associated with cold temperature (19.35°C, 1 st centile) relative to 24.7°C (25 th centile) was 1.29 (95%CI: 1.16, 1.44) for lags 0-21. The relative risk of mortality associated with high temperature (31.7°C, 99 th centile) relative to 28°C (75 th centile) was 1.11 (95%CI: 1.00, 1.24) for lags 0-21
Oudin Åström <i>et al</i> [24]	Population over 50 years in Rome, Italy, and Stockholm, Sweden	2000-2008	The percent increase in daily mortality during heat waves as compared to normal summer days was 22% (95%CI: 18%-26%) in Rome and 8% (95%CI: 3%-12%) in Stockholm
Zafeiratou <i>et al</i> [8]	42 Municipalities within the Greater Athens Area, Greece	2000-2012	Significant effects of daily temperature increase on all-cause, cardiovascular, and respiratory mortality (<i>e.g.</i> , for all ages 4.16% (95%CI: 3.73%, 4.60%) per 1 °C increase in daily temperature (lags 0-3)
Fu <i>et al</i> [14]	India	2001-2013	Mortality from all medical causes, stroke, and respiratory diseases showed excess risks at moderately cold temperature and hot temperature. Moderately cold temperature was estimated to have higher attributable risks [6.3% (95% empirical CI 1.1 to 11.1) for all medical deaths, 27.2% (11.4 to 40.2) for stroke, 9.7% (3.7 to 15.3) for IHD, and 6.5% (3.5 to 9.2) for respiratory diseases] than extremely cold, moderately hot, and extremely hot temperatures
Zeng <i>et al</i> [9]	15973 elderly residents of 866 counties and cities, China	2002-2005	Low seasonal temperatures increase the odds of mortality
Argaud <i>et al</i> [25]	Lyon, France	2003	Independent contribution to mortality from heatstroke if patients used long-term antihypertensive medication (HR, 2.17; 95%CI: 1.17-4.05), or presented at admission with cardiovascular failure (HR, 2.43; 95%CI: 1.14-5.17)
Zhang <i>et al</i> [35]	Wuhan, China	2003-2006	U-shaped relationship between temperature and mortality. Cold effect was delayed, whereas hot effect was acute, both of which lasted for several days. For cold effects over lag 0-21 d, a 1°C decrease in mean temperature below cold thresholds was associated with a 2.39% (95%CI: 1.71, 3.08) increase in non-accidental mortality, 3.65% (95%CI: 2.62, 4.69) increase in cardiovascular mortality, 3.87% (95%CI: 1.57, 6.22) increase in respiratory mortality, 3.13% (95%CI: 1.88, 4.38) increase in stroke mortality, and 21.57% (95%CI: 12.59, 31.26) increase in CHD mortality. For hot effects over lag 0-7 d, a 1 °C increase in mean temperature above the hot thresholds was associated with a 25.18% (95%CI: 18.74, 31.96) increase in non-accidental mortality, 34.10% (95%CI: 25.63, 43.16) increase in cardiovascular mortality, 24.27% (95%CI: 7.55, 43.59) increase in respiratory mortality, 59.1% (95%CI: 41.81, 78.5) increase in stroke mortality, and 17.00% (95%CI: 7.91, 26.87) increase in CHD mortality
Gómez-Acebo <i>et al</i> [7]	Cantabria (northern Spain)	2003-2006	Raising maximum or minimum temperatures by 1°C was associated with a 2% excess in mortality risk throughout the warm period. No effect in mortality on the cold season
Gómez-Acebo <i>et al</i> [17]	Cantabria (northern Spain)	2004-2005	The higher OR for cancer mortality was seen on the first day of exposure (OR = 4.91; 95%CI: 1.65-13.07 in the whole population). Cardiovascular (OR = 2.63; 95%CI: 1.88-3.67) and respiratory mortality (OR = 2.72; 95%CI: 1.46-5.08) showed a weaker effect
Analitis <i>et al</i> [26]	9 European cities	2004-2010	In the warm season, the percentage increase in all deaths from natural causes per °C increase in ambient temperature tended to be greater during high ozone days. For the cold period, no evidence for synergy was found.
McMichael <i>et al</i> [19]	Urban populations in Delhi, Monterrey, Mexico City, Chiang Mai, Bangkok, Salvador, Sao Paulo, Santiago, Cape Town, Ljubljana, Bucharest and Sofia.	2007	Most cities showed a U-shaped temperature-mortality relationship, with clear evidence of increasing death rates at colder temperatures and with increasing heat. Heat thresholds were generally higher in cities with warmer climates, while cold thresholds were unrelated to climate
Rabczenko <i>et al</i> [20]	Warsaw, Poland	2008-2013	Analysis of dependence between temperature and mortality for whole population as well as for subpopulations with respect to sex and age demonstrated its similar U-shape. Comfort varied between 20 and 24°C, with slight tendency to be higher for woman
Can <i>et al</i> [13]	Istanbul, Turkey	2013-2017	Three extreme heat waves in summer months of 2015, 2016, and 2017, which covered 14 days in total, significantly increased the mortality rate and caused 419 excess deaths in 23 d of exposure
Oray <i>et al</i> [16]	Izmir province, Turkey	2016	During the study period, the mean number of ED visits and mortality rates were significantly higher than the previous year's same period [320 ± 30/d <i>vs</i> 269 ± 27/d, (<i>P</i> < 0.01), and 1.6% <i>vs</i> 0.7%, (<i>P</i> < 0.01)]. Although the admission rate was similar between the study period and the other 21 d of June 2016 [320 ± 30/d <i>vs</i> 310 ± 32/d, (<i>P</i> = 0.445)] in-hospital mortality rate was significantly higher [1.6% <i>vs</i> 0.7%, (<i>P</i> < 0.01)]

CHD: Coronary heart disease; CI: Confidence interval; OR: Odds ratio.

AMBIENT TEMPERATURE AND CARDIOVASCULAR AND NON-CARDIOVASCULAR DISEASES

Weather exposure beyond certain thresholds affects human health negatively[52]. Both cold and heat temperature significantly increased risk of hospitalization for several diseases[53]. However, heat waves have documented a higher impact on mortality than on morbidity (hospital admissions)[41,54,55]. This phenomenon could be explained by the hypothesis that deaths from circulatory disease occur rapidly patients reach a hospital[56]. There are relationships between temperature (in particular its short-term variability) and hospital admissions due to various forms of heart disease[57-61]. Hot and cold temperature are a risk factor for a wide range of cardiovascular, respiratory, and psychiatric illness; yet, in few studies, the increase in temperature reduced the risk of hospital admissions for pulmonary embolism and angina pectoris[62]. Table 3 shows main studies on the relations between weather and hospital admissions.

AMBIENT TEMPERATURE AND ACUTE CORONARY SYNDROMES

Seasonal variations in emergency admission rates and trial recruitment of patients suffering from acute coronary syndromes (ACS) are well described[37], and a number of epidemiological studies have reported a greater winter ACS incidence, with similar seasonal trends in all studied cohorts, including men and women, middle-aged and elderly patients, and patients from northern and southern hemispheres[4].

Over the past few decades, a growing body of epidemiological studies found the effects of ambient temperature on cardiovascular disease, including risk for ACS[63-66]. Inverse relationship between temperature and ACS is well known[67-71], even regardless of season[37,72,73]. In a previous study, we correlated the daily number of AMI cases admitted to a western Sicily hospital and weather conditions on a day-to-day basis over twelve years, showing a significant association between daily number of ACS hospital admission and minimal daily temperature[74]. Effects of low temperature on total ACS cases were more pronounced in years with higher average temperatures and also during summer, suggesting not a pure “cold effect” but an influence of unusual temperature decreases[64,75].

This relation, moreover, could be actually U-shaped, with higher short-term risk of ACS also in extremely hot summer[67,76-79]. Very few studies failed to demonstrate an association between temperature and ACS incidence[80]. A recent meta-analysis, however, confirmed that cold exposure, heat exposure, and exposure to heat waves were associated with an increased risk of ACS[81].

It has been hypothesized that angina’s worsening occurs in cold weather, but few studies have investigated variations in hospitalizations due to angina pectoris in relation to climatic variables[3,59]. We showed a significant association between daily number of angina hospital admission and temperature [82]. Table 4 shows main studies on the relations between weather and hospital admissions for ACS.

Main limitation of these studies is the unavailability of data on individual exposure to temperature variability[57]. These seasonal changes, besides, do not seem universal[43,76], as they are absent near the equator or in subpolar regions, with less temperature fluctuations than in temperate regions. For this reason, it seems inadequate to extrapolate results to different environments.

ACS AND OTHER METEOROLOGICAL PHENOMENA BEYOND TEMPERATURE

Ambient humidity

We observed a negative significant relationship between the number of ACS admissions and maximal humidity[74]. This was confirmed as regards angina admissions only in males, in whom we showed also a positive significant relationship between angina and minimal humidity[82]. Previous data for ACS were confounding: although some studies showed an association with low humidity[83,84], and other no association[69], more researches showed high humidity being related to CHD in northern countries[68,76] and in other Mediterranean[48,78], Asian[75], and Oceanian[54] settings. Fernández-Raga *et al*[18] suggested as the optimal relative humidity 24% for patients with respiratory diseases, and 45% for cardiovascular ones.

Atmospheric pressure.

Consequences of atmospheric pressure on cardiovascular diseases have been studied less frequently. Associations between an increase in CHD occurrence and low atmospheric temperatures have been reported from mortality data and hospital admission registries. A morbidity registry (Lille-WHO MONICA Project) detected a linear V-shaped relationship with a minimum at 1016 mbar: a 10-mbar decrease and a 10-mbar increase were associated with significant 12% and 11% increase in event rates, respectively[73]. Ambient pressure had a statistical impact on the incidence of angina or ACS also in Sweden[72], Serbia[83], Slovenia[68], Lithuania[85], and Switzerland[86], but in Mediterranean

Table 2 Main studies on the relations between weather and cardiovascular mortality

Ref.	Population and setting	Year	Main results
Gyllerup <i>et al</i> [44]	Men aged 40–64 from 259 municipalities in Sweden	1975–1984	Coronary mortality is more strongly associated with cold climate than with other explanatory factors such as cholesterol, socioeconomic factors, or tobacco
Crawford <i>et al</i> [43]	Deaths in Northern Ireland, United Kingdom	1979–1998	Low temperature is associated with highest mortality rates from myocardial infarction
Gerber <i>et al</i> [45]	Olmsted County, Minnesota, United States	1979–2002	RR of sudden death, but not of myocardial infarction, was increased in low temperatures (1.20, 95%CI: 1.07–1.35, for temperatures below 0°C vs 18°C–30°C). These associations were stronger for unexpected sudden death ($P < 0.05$)
Wichmann <i>et al</i> [49]	Gothenburg, Sweden	1985–2010	No evidence of association between temperature and CHD deaths in the entire year, warm or cold periods
Enquesselassie <i>et al</i> [3]	Australian community-based register of heart disease (the WHO MONICA Project)	1992	Coronary deaths were more likely to occur on days of low temperature (and to a much lesser extent, of high temperature. Patterns of sudden and non-sudden deaths were not associated with weather conditions. Both longer-term seasonal effects and daily temperature effects exist
Dilaveris <i>et al</i> [48]	AMI deaths in Athens, Greece	2001	The best predictor was the average temperature of the previous 7 d; the relation between daily myocardial infarction deaths and 7-d average temperature (R^2 0.109, $P < 0.001$) was U-shaped
Zhang <i>et al</i> [35]	District of Wuhan, China	2003–2010	For cold effects over lag 0–21 d, a 1°C decrease in mean temperature below the cold thresholds was associated with a 3.65% (95%CI: 2.62, 4.69) increase in cardiovascular mortality and 21.57% (95%CI: 12.59, 31.26) increase in CHD mortality. For hot effects over lag 0–7 d, a 1°C increase in mean temperature above the hot thresholds was associated with a 34.10% (95%CI: 25.63, 43.16) increase in cardiovascular mortality and 17.00% (95%CI: 7.91, 26.87) increase in CHD mortality
Wang X <i>et al</i> [47]	Beijing and Shanghai, China	2007–2009	The cold effects on cause-specific cardiovascular mortality reached the strongest at lag 0–27, while the hot effects reached the strongest at lag 0–14
Yang J <i>et al</i> [6]	Nine Chinese mega-cities	2007–2013	Statistically significant nonlinear associations between temperature and mortality were observed, with a total of 50658 deaths from myocardial infarction attributable to non-optimal temperatures
Yin Q, Wang J [50]	Beijing, China	2010–2012	When extremely high temperatures occur continuously, at varying temperature thresholds and durations, adverse effects on CVD mortality vary significantly. The longer the heat wave lasts, the greater the mortality risk is. When the daily maximum temperature exceeded 35 °C from the fourth day onward, the RR attributed to consecutive days' high temperature exposure saw an increase to about 10% ($P < 0.05$), and at the 5 th day, the RR reached 51%

AMI: Acute myocardial infarction; CHD: Coronary heart disease; CVD: Cardiovascular diseases; CI: Confidence Interval; OR: Odds ratio; RR: Relative risk.

population we did not observe any significant relation[82].

Sunlight

The amount of sunlight hours seems inversely related to winter mortality and ACS risk[72]. Our study in a Mediterranean area did not confirm any relation between sunlight hours and ACS daily admissions [74].

Wind, rain, and snow

ACS incidence during southern wind periods seems significantly greater than during the northern ones [75]. Also, the amount of rain and wind speed seems inversely related to winter mortality and ACS incidence[72,75,85,86]. We, however, failed to observe any significant relationship between wind force and direction, rain, and the number of hospital ACS admissions[74], suggesting these variables are not strong triggers, according to other authors[43]. It is likely that rain intermixed with snow may trigger increased mortality from cardiovascular disease. Snow is somewhat more significant in triggering deaths from heart disease than is air temperature, influencing mortality, mainly in males[87,88]. Snow fall exceeding 2 cm/d was identified as a significant predictor for ACS admission rates[89]. Snow- and rainfall had inconsistent effects in another study[87].

Combination of weather factors

The assessment of air temperature does not allow evaluation of actual discomfort perception caused by the combination of different meteorological parameters. Alternative biometeorological approaches consider Apparent Temperature Index in summer and New United States/Canada Wind Chill Temperature Index in winter, which combine air temperature, relative humidity and wind velocity[90], the presence of anticyclonic and cyclonic air mass[91], as well as specific local climatic conditions, such as the Arctic Oscillation[92].

Table 3 Main studies on the relations between weather and hospital admissions

Ref.	Population and setting	Year	Main results
Ebi <i>et al</i> [59]	Three Californian regions, United States	1983-1998	Association between temperature and hospitalizations varied by region, age, and gender
Michelozi <i>et al</i> [41]	Twelve European cities participating in the Assessment and Prevention of Acute Health Effects of Weather Conditions in Europe (PHEWE) project	1990-2001	For an 18°C increase in maximum apparent temperature above a threshold, respiratory admissions increased by 14.5% (95%CI: 1.9-7.3) and 13.1% (95%CI: 0.8-5.5) in Mediterranean and North-Continental cities, respectively. In contrast, the association between temperature and cardiovascular and cerebrovascular admissions tended to be negative and did not reach statistical significance
Vaneckova and Bambrick [52]	Sidney, Australia	1991-2009	On hot days, hospital admissions increased for all major categories. This increase was not shared homogeneously across all diseases. Admissions due to some major categories increased one to three days after a hot day (e.g., respiratory and cardiovascular diseases) and on two and three consecutive days
Goldie <i>et al</i> [54]	Darwin, Australia	1993-2011	Nighttime humidity was the most statistically significant predictor ($P < 0.001$), followed by daytime temperature ($P < 0.05$). Hot days appeared to have higher admission rates when they were preceded by high nighttime humidity
Linares and Diaz[28]	Daily emergency admissions between May and September in the Hospital General Universitario Gregorio Marañón, Madrid, Spain	1995-2000	The temperature above which hospital admissions soar coincides with the temperature limit above which mortality sharply rises, which, in turn, coincides with 95 th percentile of the maximum daily temperature series
Chan <i>et al</i> [53]	Hong Kong, China	1998-2009	During summer, admissions increased by 4.5% for every increase of 1°C above 29°C; during winter, admissions increased by 1.4% for every decrease of 1°C within the 8.2-26.9 °C range. Admissions for respiratory and infectious diseases increased during extreme heat and cold, but cardiovascular disease admissions increased only during cold temperatures. During winter, for every decrease of 1°C within the 8.2-26.9 °C range, admissions for cardiovascular diseases rose by 2.1%
Yitshak-Sade <i>et al</i> [61]	Respiratory, cardiac and stroke admissions of adults ≥ 65 (2015660), New England, United States	2001-2011	The short-term temperature effect was higher in months of higher temperature variability as well. For cardiac admissions, the PM2.5 effect was larger on colder days (0.56% versus -0.30%) and in months of higher temperature variability (0.99% <i>vs</i> -0.56%)
van Loenhout <i>et al</i> [55]	the Netherlands	2002-2007	Positive relationship between increasing temperatures above 21 °C and the risk for urgent emergency room admissions for respiratory diseases. For admissions for circulatory diseases, there is only a small significant increase of risk within the 85+ age group for moderate heat, but not for extreme heat
Ponjoan <i>et al</i> [58]	Catalonia, Spain	2006-2016	The overall incidence of cardiovascular hospitalizations significantly increased during cold spells (RR = 1.120; 95%CI: 1.10-1.30) and the effect was even stronger in the 7 d after the cold spell (RR = 1.29; 95%CI: 1.22-1.36). Conversely, cardiovascular hospitalizations did not increase during heatwaves
Shiue <i>et al</i> [60]	Ten percent of daily hospital admissions across Germany	2009-2011	Admissions due to diseases of pericardium, nonrheumatic mitral and aortic valve disorders, cardiomyopathy, atrioventricular block, other conduction disorders, atrial fibrillation and flutter, and other cardiac arrhythmias peaked when physiologically equivalent temperature was between 0 and 10°C
Tian <i>et al</i> [57]	184 cities in China	2014-2017	a 1°C increase in short-term temperature variability (calculated from the SD of daily minimum and maximum temperatures) at 0-1 days was associated with a 0.44% (0.32%-0.55%), 0.31% (0.20%-0.43%), 0.48% (0.01%-0.96%), 0.34% (0.01%-0.67%), and 0.82% (0.59%-1.05%) increase in hospital admissions for cardiovascular disease, ischemic heart disease, heart failure, heart rhythm disturbances, and ischemic stroke, respectively

CHD: Coronary heart disease; CVD: Cardiovascular diseases; CI: Confidence interval; PM: Particulate matter; RR: Relative risk; SD: Standard deviation.

WEATHER AND OTHER CARDIOVASCULAR DISEASE BEYOND CHD

Heart failure

Environmental exposure is an important, but underappreciated, risk factor contributing to development and severity of heart failure. In European warm period (from June to October), there are significant less admissions than that in the cold period (from December to March). Air temperature is the most significant environmental factor related to heart failure hospital admissions, showing an inversed correlation[93,94]. Heart failure admissions peaked when temperature was between 0 and -10°C[68]. Every 1°C decrease in mean temperature and every 1hPa decrease in air pressure were associated, respectively, with an increase in the daily number of emergency admissions for heart failure by 7.83% (95%CI: 2.06-13.25) and 3.56% (95%CI: 1.09-5.96)[71]. Some other features, such as precipitation, are also relevant[94].

Table 4 Main studies on the relations between weather and acute coronary syndromes

Ref.	Population and setting	Year	Main results
Mirić <i>et al</i> [78]	Coastal part of middle Dalmatia (Croatia)	1981-1987	Significant association of acute myocardial infarction incidence with increased air temperature four days before, and on the day of the incident ($P < 0.05$)
Danet <i>et al</i> [73]	Morbidity registry (Lille-WHO MONICA Project) monitoring 257000 men Aged 25-64 years.	1985-1994	The events rate decreased linearly with increasing atmospheric temperature: a 10°C decrease was associated with a 13% increase in event rates
Wichmann <i>et al</i> [49]	AMI hospitalisations in Gothenburg, Sweden	1985-2010	A linear exposure-response corresponding to a 3% and 7% decrease in AMI hospitalisations was observed for an inter-quartile range increase in the 2-d cumulative average of temperature during the entire year and the warm period, respectively
Abrignani <i>et al</i> [74]	Hospital admissions for acute myocardial infarction in Trapani, Italy	1987-1998	Significant association as regards the incidence relative ratio between daily number of myocardial infarction hospital admission and minimal daily temperature
Abrignani <i>et al</i> [82]	Hospital admissions for angina pectoris in Trapani, Italy	1987-1998	Significant association between daily number of angina hospital admission and temperature. Significant incidence relative ratios (95%CI) were, in males, 0.988 (0.980-0.996) ($P < 0.004$) for minimal temperature. The corresponding values in females were 0.973 (0.951-0.995) ($P < 0.017$) for maximal temperature and 1.024 (1.001-1.048) ($P < 0.037$) for minimal temperature
Marchant <i>et al</i> [37]	633 consecutive patients with myocardial infarction admitted to a coronary care unit in London, United Kingdom	1988-1991	Excess of infarctions on colder days in both winter and summer
Bayentin <i>et al</i> [77]	Quebec, Canada	1989-2006	Cold temperatures during winter and hot episodes during summer are associated with an increase of up to 12% in the daily hospital admission rate for CHD. In most regions, exposure to a continuous period of cold or hot temperature was more harmful than just one isolated day of extreme weather
Wolf <i>et al</i> [64]	Myocardial infarctions and coronary deaths in the Monitoring Trends and Determinants on Cardiovascular Diseases/ Cooperative Health Research in Augsburg (MONICA/KORA) Registry, Germany	1995-2004	A 10°C decrease in 5-d average temperature was associated with a relative risk of 1.10 (95%CI: 1.04-1.15). Effect of temperature on the occurrence of nonfatal events showed a delayed pattern, whereas the association with fatal forms was more immediate
Madrigano <i>et al</i> [70]	Patients with a possible discharge diagnosis of AMI in 11 acute care general hospitals serving residents of the Worcester metropolitan area (Worcester Heart Attack Study), United Kingdom	1995, 1997, 1999, 2001, 2003	A decrease in an interquartile range in apparent temperature was associated with an increased risk of acute myocardial infarction on the same day [HR = 1.15 (95%CI: 1.01-1.31)]. Extreme cold during the 2 d prior was associated with an increased risk of acute myocardial infarction [1.36 (1.07-1.74)]. Exposure to heat increased the risk of dying after an AMI
Mohammad <i>et al</i> [72]	All myocardial infarctions reported to the Swedish Web-System for Enhancement and Development of Evidence-Based Care in Heart Disease Evaluated According to Recommended Therapies (SWEDEHEART)	1998-2013	The most pronounced association was observed for air temperature, where a 1-SD increase (7.4°C) was associated with a 2.8% reduction in risk of myocardial infarction (incidence ratio, 0.972; 95%CI: 0.967-0.977; $P < 0.001$). Results were consistent for non-ST-elevation as well as ST-elevation myocardial infarction and across a large range of subgroups and health care regions
Messner <i>et al</i> [76]	Subarctic area of Northern Sweden	2001	A 1°C temperature rise was associated with an 1.5% increase in the number of nonfatal acute myocardial infarctions
Chang <i>et al</i> [69]	Myocardial infarctions among women aged 15-49 from 17 different countries in Africa, Asia, Europe, Latin America, and the Caribbean	2003	Overall, a 5°C drop in temperature was associated with a 12% increase in admissions for heart attack (incidence rate ratio 0.88 (95%CI: 0.8-0.97)
Misailidou <i>et al</i> [65]	Five rural Greek regions (Karditsa, Lamia, Chalkida, Kalamata and Zakynthos)	2003-2004	For an 18°C decrease in temperature there was a 1.6% (95%CI: 0.9%-2.2%) increase in admissions for CHD
Bhaskaran <i>et al</i> [63]	84010 hospital admissions for myocardial infarction in the Myocardial Ischaemia National Audit Project (15 conurbations in England and Wales, United Kingdom)	2003-2006	Broadly linear relation between temperature and myocardial infarction, without a threshold: each 1°C reduction in daily mean temperature was associated with a 2.0% (95%CI: 1.1%-2.9%) cumulative increase in risk of myocardial infarction over the current and following 28 d, the strongest effects being estimated at intermediate lags of 2-7 and 8-14 d. Heat had no detrimental effect
Nastos <i>et al</i> [80]	Crete, Greece	2004-2007	The impact of weather variability on the ACS incidence is not statistically significant
Ravljén <i>et al</i> [68]	ACS treated with coronary emergency catheter interventions in Slovenia	2008-2011	Daily average temperature, atmospheric pressure and relative humidity all have relevant and significant influences on ACS incidences for the entire population. However, the ACS incidence for population over 65 is only affected by daily average temperature

Hori <i>et al</i> [71]	Japan	2010	Every 1°C decrease in mean temperature was associated with an increase in the daily number of emergency admissions for ACS by 7.83% (95%CI: 2.06-13.25)
García-Lledó <i>et al</i> [66]	Madrid, Spain	2013-2017	The minimum incidence rate of myocardial infarction was observed at the maximum temperature of 18°C. Warmer temperatures were not associated with a higher incidence (RR, 1.03; 95%CI: 0.76-1.41), whereas colder temperatures were significantly associated with an increased risk (IRR, 1.25; 95%CI: 1.02-1.54)
Lin <i>et al</i> [67]	Hospitalizations for CHD in New York State, United States	2015	Extremely low universal apparent temperature in winter was associated with increased risk of AMI, especially during lag4-lag6
Sharif Nia <i>et al</i> [75]	Hospital admission for AMI in Mazandaran Province, Iran	2015-2016	Daily minimum temperature correlated with ACS events [RR = 0.942 (95%CI: 0.927-0.958), <i>P</i> < 0.001]

ACS: Acute coronary syndromes; AMI: Acute myocardial infarction; CHD: Coronary heart disease; CI: Confidence interval; RR: Relative risk; SD: Standard deviation.

Arrhythmias

Current paradigm in sudden cardiac death (SCD) requires an abnormal myocardial substrate and an internal or external transient factor (such as a cold spell, an unusually cold weather event) that triggers cardiac arrest. An increased risk of ischaemic SCD was significantly associated with a preceding cold spell[95], and cardiac arrest admissions peaked when temperatures were between 0° and -10°C[60]. These associations were stronger for unexpected SCD than for SCD with prior CHD[45]. However, also higher average daily temperature and larger variation in humidity were associated with increase in appropriate ICD interventions in patients with arrhythmogenic right ventricular dysplasia/cardiomyopathy[96].

Aortic dissection

Days with spontaneous type A aortic dissections were significantly colder than those without dissections[97]. There appears to be a significant correlation between mean low monthly pressures and rupture incidence[98].

Stroke

Significant associations between temperature and hospital admission rates for stroke were apparent and generally stronger than in other cardiovascular disease[99-101]. Both increases and decreases in temperature had a marked relationship with stroke deaths, while hospital admissions were only associated with low temperature[102,103]. Overall, a 5°C drop in temperature was significantly associated with a 7% increase in admissions for stroke[69]. Every 1°C increase in mean temperature during the preceding 24 h was associated with a significant 2.1% increase in ischaemic stroke admissions. A fall in atmospheric pressure over the preceding 48 h was associated with increased rate of haemorrhagic stroke admissions. Higher maximum daily temperature gave a significant increase in lacunar stroke admissions than in other ischaemic strokes[100]. In another study, every 1°C decrease in mean temperature was associated with an increase in the daily number of emergency admissions by 35.57% for intracerebral haemorrhage and by 11.71% for cerebral infarction. An increase of emergency admissions due to intracerebral haemorrhage was observed at every 1 hPa decrease in air pressure[71]. A recent metanalysis, finally, confirmed that lower mean ambient temperature is significantly associated with the risk of intracerebral haemorrhage, but not with ischemic stroke and subarachnoid haemorrhage [104].

AGE, SEX, OTHER FACTORS AND CLIMATIC VARIABLES

Effects of weather vary depending on other factors, such as the population disease profile and age structure[19,74]. People with pre-existing medical conditions such as cardiovascular disease or carrying out physically demanding work, and the elderly, particularly those in nursing and care homes, are particularly vulnerable[68,105-108].

Mortality's increase with cold or heat was greater for older age groups[21,63,109]. Diurnal temperature range are related to hospital admissions for all cardiovascular and cerebrovascular disease among elderly, namely in males[59,83,110]. In the elderly, cardiovascular disease curve was U-shaped, showing higher values for cold stress than for heat one[107,109,111,112]. In general, longer duration of heat waves increases the risks of cardiovascular mortality for the elderly[113]. Main predictors of death are: The use of home public-integrated assistance, a higher comorbidity, a higher degree of disability [114], lack of thermal insulation and sleeping right under the roof[113], being confined to bed or unable to care for oneself and pre-existing cardiovascular diseases[115]. Home air-conditioning, visiting cool

environments, dressing lightly, and increasing social contact were instead strongly associated with better outcomes[113,115]. Weak correlation between atmospheric air wind speed and ACS morbidity in older populations was determined[111].

Diurnal temperature range was significantly associated with hospital admissions for all cardiovascular disease, ischemic heart disease and cerebrovascular disease among elderly females[110]. We showed that, in females, a reduction in maximal temperature is associated with more hospital angina admissions[82], whereas the number of angina admissions is positively correlated with an increase in minimal temperature, as observed also by Ebi[59]. Increased outside temperature and sunshine hours were identified as strong positive predictors for ACS occurrence in women[89], as they tend to present with AMI at a later age than men, they will tend to exhibit a more marked seasonal variation[107-109]. A weak correlation between atmospheric air wind speed and MI morbidity in women was determined[111]. Snow fall was identified as a positive predictor for ACS admission rates with a significant effect in men, but not in women[89]. Other studies failed to detect significant difference according to sex[65].

Risk of heat-related death was significantly higher among Black people[112,116] and Australian indigens[105].

Heat-related mortality varied with sociodemographic characteristics such as in people living in low socioeconomic districts[12,106,107,117].

People living in areas with high PM2.5 concentration showed higher vulnerabilities to cold-ACS effects than other groups did[67].

MECHANISMS

Up to date, there are not clear pathophysiological links between weather and cardiovascular diseases. Climatic stress may increase direct and indirect risks to human health *via* different, complex pathophysiological pathways and exogenous and endogenous mechanisms. The pattern of well-known conventional risk factors (such as blood pressure, serum lipids, haematological and coagulation factors, body weight, glucose tolerance), a number of hormones including steroids, environmental factors (such as air pollution) as well as acute infections shows a marked seasonal variation, with a winter clustering of peak values[118,119]. In addition, humans display different seasonal behaviour in diet, activity, housing and smoking habits, psychosocial factors and mood disorders in winter[120]. Other factors, such as overindulgence, or stress on Christmas holidays, might also contribute[121].

Cold

Mechanisms leading to possible influence of cold on ACS or angina onset are most likely multifactorial. Different heart and circulation adjustments occur when humans are acutely exposed to low outdoor temperatures. Increase in circulating levels of catecholamines, secondary to cutaneous thermoreceptor activation[122], lead to peripheral vasoconstriction and then to increase in blood pressure[123], heart rate, and left ventricular end-diastolic pressure and volume[3,124,125] with, in turn, increased cardiac work and peripheral resistance, greater heart oxygen requirement and reduction of ischemic threshold [3]; they may be clinically relevant when coronary circulation is already compromised[126]. People with normal cardiovascular function, in fact, are unaffected by cold stress, whereas those with IHD may be crippled, although rarely, by exposure to cold, especially if they perform physical work[122]. At the same time, reduced myocardial perfusion may lead to earlier ischemia, angina, and impaired performance. Also having a heart failure deteriorates submaximal and maximal performance in cold conditions[127]. In cold conditions also a greater sodium intake lead to an increase in blood pressure. Cold-induced vasoconstriction results in an early return of reflected pressure waves from the periphery and an increase in central aortic systolic pressure, with increase of central aortic augmentation index [128]. Endothelial dysfunction may be another mechanism. Brachial flow-mediated dilation would vary by temperature (in the Framingham Offspring cohort it was highest in the warmest and lowest in the coldest outdoor temperature quartiles)[129]. Moreover, coronary artery spasm could occur if vasoconstriction extends to the heart vessels. Cold-intolerant patients had a steeper heart rate response in cold conditions and developed ischemia and angina earlier. In cold-tolerant patients, this increase may be offset by a reduction in heart rate if baroreceptor function is normal. Baroreceptor function was impaired in cold-intolerant patients. If baroreceptor function is abnormal, heart rate may not decrease in response to a cold-induced increase in blood pressure. This mechanism may account for some of the variability in tolerance to cold exposure that affects patients with exertional angina[124].

More dramatic events, such as sudden death, may be due to increased frequency of cardiac arrhythmias, or, perhaps through rises in blood pressure, to abrupt rupture of atherosclerotic plaques [3].

Cold, besides, exerts other biological negative effects on inflammatory markers, haemostasis, rheological factors, and lipids (probably related to haemoconcentration), alcohol consumption, and body weight gain[40,124,125,130,131]. A 10°C decrease in temperature led to an increase in platelet counts and fibrinogen and a decrease in C-reactive protein in CHD patients[131]. In cold weather, a

greater tendency to clot in circulatory system has been demonstrated[119,132,133]. This could be related to plasma volume contraction (haemoconcentration) [119,126,134], induced by peripheral vasoconstriction, which can in part also explain the increase in serum lipids. These acute responses to cold conditions could trigger ACS.

Cold conditions may increase also the risk of respiratory infections through suppression of immune responses and direct effects on respiratory tree, and although no association can be claimed between respiratory infections and coronary deaths during cold season[124], a theory links pulmonary inflammation to stroke[99].

Finally, other causes hypothesized to explain the impact of cold are socioeconomic, mainly housing conditions[12,34].

Heat

During summer, ACS patients working outdoors show abnormal hemorheology (high haematocrit and blood viscosity)[135], as dehydration is more likely to occur[29]. Outdoor heat is associated with decreasing blood pressure, and cardiovascular vulnerability may vary primarily by central air conditioning[136]. Higher ambient temperature is associated with decreases in heart rate variability during warm season but not during cold one[137]. Hot weather is associated with an increase in systolic pressure at night in treated elderly hypertensive subjects, likely because of a nocturnal blood pressure escape from effects of a lighter summertime drug regimen[133].

Humidity

When air contains a high percentage of humidity, perspiration and the processes of temperature homeostasis may be hindered, making more difficult the automatic processes of internal temperature control, thus increasing respiratory fatigue and heart rate. However, this mechanism may be important only in more severe ischemic forms.

Rain and wind

A reduction of outdoor excursions when it is raining and windy prevents outdoor cold stress.

Sunshine

Several studies have demonstrated significantly lower levels of vitamin D, synthesized by skin following exposure to ultraviolet radiation, in subjects with CHD, particularly in winter[138]. It has been suggested that vitamin D may be a confounding factor in the association between cholesterol, structurally like it, and CHD risk. This is corroborated by findings of a strong, positive association between latitude and mean blood cholesterol, and a strong negative association between hours of sunshine and CHD mortality[120]. Association between vitamin D levels and CHD, however, has been shown to be independent of total serum cholesterol[138].

Age

With increasing age, winter peak increased. This is likely to reflect a combination of factors: poorer temperature autonomic control, lower physical activity levels, less use of protective clothing, greater time spent at home, more sensitivity to seasonal influenza and blood pressure changes, and poorer household heating and insulation. The predominance of effects of meteorological factors in the elderly could be also explained by the lower impact of genetic AMI determinants.

Sex

Different effects of weather on women may be related to different coronary anatomy in the female sex, as woman have less extensive coronary atherosclerosis, lower coronary size, and lower collateral circulation than males.

Pollution

Interaction between air pollution and weather is often missed in literature[139]. Studies show that ambient temperature and air pollution may interact to affect cardiovascular events *via* autonomic nervous system dysfunction[137]. Much higher PM10 effects on mortality were observed during warmer days[26,140-142], and the hypothesis that such an effect is attributable to enhanced exposure to particles in summer could not be rejected[143].

CONCLUSION

Implications and conclusions

Weather influences on heart diseases remind us that climatic stress can be considered as a new potential risk factor for cardiovascular events and even mortality[3,125]. Such an understanding has several potential implications for developing civil protection policy towards allocation of public healthcare

resources and planning appropriate measures to prevent cardiovascular events[59,116]. Weather-related health effects have sharply attracted growing interest because of the recent observed and predicted earth's climate change, with consequent increasing ambient temperatures and climatic fluctuations, extremes of precipitation (floods and droughts), air pollution, and infectious diseases. Contrary to current predictions, this may mean a paradoxical increase in seasonal cycle of events with greater winter peaks, even as overall global temperatures rise[93]. Thus, increases in heat-related mortality due to global warming are unlikely to be compensated by decreases in cold-related mortality[112]. In a global environment of rapid and extreme climatic events, more populations will be exposed to conditions they are not readily adapted to from a bio-behavioural perspective[60,144]. Adaptation to such changes, that are expected to further increase, would seem to be imperative for medical professionals, health institutions, and general public[41,70].

Public health educational, behavioural and social measures[28,43] have been proposed to reduce adverse cardiovascular consequences of climate variability. We wish here to summarize the most important ones.

High risk identification: Prevention programs must be based around rapid identification of high-risk conditions and people, such as frailties with cardiovascular disease, or the elderly[53,107]. Protective measures, in fact, should be directed towards susceptible groups, rather than the population as a whole, with the creation of an up-to-date database and care of vulnerable high-risk individuals[21,24,110,114].

Specific interventions: In the community, at home, and in institutions that care for elderly or vulnerable people, such as hospitals, a comfortable temperature should be granted[63,65]. Educational measures should be suggested to high-risk people. During the passing atmospheric front, as well as in extreme ambient temperature periods, *i.e.*, coronary patients should stay at home, and avoid both physical and psychological stress[78].

Provision of targeted advice: Many weather-related diseases may be preventable by and appropriate response to emergencies. Operative health weather watch/warning systems link public health actions to meteorological forecasts of dangerous weather. We need development of a short-term forecast system of daily demand using weather variables.

Remodulation of health services offer: During severe climatic conditions, it should be granted a greater deployment of ambulance services and an adequate reinforcement of health personnel in order to meet the unexpected increase in demands, and to avoid potential mismatch between the occurrence of acute cardiovascular events and medical service capacities[108].

Future perspectives: In the long term, improvements in infrastructures, residential architecture, working environment and urban planning must be adapted[113].

In conclusion, the problem of climate change is serious, urgent and getting worse[144]. Fairly obvious connections between climate change and cardiovascular health have been outlined in this article. Medical professionals, and societies of medical professionals, easily capable of understanding the physical and statistical methods used by climatologists, are in a good position to give politicians and leaders in industry and agriculture their necessary support[144].

Further large, exhaustive, population-based cohort research with consistent methodology over long periods in geographical areas with homogeneous meteorological variables should be carried out to further clarify climatic influences on CHD occurrence, to identify underlying pathophysiological mechanisms, to show vulnerable populations and individuals and to develop cost-effective strategies to promote resilience against provocations of climate change[86,113].

FOOTNOTES

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