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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 <sup>th</sup> 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 <sup>th</sup> percentile in tropical areas to about the 80–90 <sup>th</sup> 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 <sup>th</sup> 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 <sup>st</sup> centile) relative to 24.7°C (25 <sup>th</sup> 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 <sup>th</sup> centile) relative to 28°C (75 <sup>th</sup> 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
Analtis <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 vs 269 ± 27/d, ( <i>P</i> < 0.01), and 1.6% vs 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 vs 310 ± 32/d, ( <i>P</i> = 0.445)] in-hospital mortality rate was significantly higher [1.6% vs 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 <sup>th</sup> 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
Michelozzi <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 <sup>th</sup> 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
Ravljien <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 meta-analysis, 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].

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## MECHANISMS

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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].

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## **CONCLUSION**

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### **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].

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## FOOTNOTES

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## REFERENCES

- 1 Cold exposure and winter mortality from ischaemic heart disease, cerebrovascular disease, respiratory disease, and all causes in warm and cold regions of Europe. The Eurowinter Group. *Lancet* 1997; **349**: 1341-1346 [PMID: 9149695 DOI: 10.1016/S0140-6736(96)12338-2]
- 2 Gemmell I, McLoone P, Boddy FA, Dickinson GJ, Watt GC. Seasonal variation in mortality in Scotland. *Int J Epidemiol* 2000; **29**: 274-279 [PMID: 10817125 DOI: 10.1093/ije/29.2.274]
- 3 Enquesselassie F, Dobson AJ, Alexander HM, Steele PL. Seasons, temperature and coronary disease. *Int J Epidemiol* 1993; **22**: 632-636 [PMID: 8225736 DOI: 10.1093/ije/22.4.632]
- 4 Curriero FC, Heiner KS, Samet JM, Zeger SL, Strug L, Patz JA. Temperature and mortality in 11 cities of the eastern United States. *Am J Epidemiol* 2002; **155**: 80-87 [PMID: 11772788 DOI: 10.1093/aje/155.1.80]
- 5 Aylin P, Morris S, Wakefield J, Grossinho A, Jarup L, Elliott P. Temperature, housing, deprivation and their relationship to excess winter mortality in Great Britain, 1986-1996. *Int J Epidemiol* 2001; **30**: 1100-1108 [PMID: 11689529 DOI: 10.1093/ije/30.5.1100]
- 6 Yang J, Zhou M, Ou CQ, Yin P, Li M, Tong S, Gasparrini A, Liu X, Li J, Cao L, Wu H, Liu Q. Seasonal variations of temperature-related mortality burden from cardiovascular disease and myocardial infarction in China. *Environ Pollut* 2017; **224**: 400-406 [PMID: 28222981 DOI: 10.1016/j.envpol.2017.02.020]
- 7 Gómez-Acebo I, Llorca J, Rodríguez-Cundín P, Dierssen-Sotos T. Extreme temperatures and mortality in the North of Spain. *Int J Public Health* 2012; **57**: 305-313 [PMID: 21229285 DOI: 10.1007/s00038-010-0229-1]
- 8 Zafeiratou S, Analitis A, Founda D, Giannakopoulos C, Varotsos KV, Sismanidis P, Keramitsoglou I, Katsouyanni K. Spatial Variability in the Effect of High Ambient Temperature on Mortality: An Analysis at Municipality Level within the Greater Athens Area. *Int J Environ Res Public Health* 2019; **16** [PMID: 31575034 DOI: 10.3390/ijerph16193689]
- 9 Zeng Y, Gu D, Purser J, Hoenig H, Christakis N. Associations of environmental factors with elderly health and mortality in China. *Am J Public Health* 2010; **100**: 298-305 [PMID: 20019314 DOI: 10.2105/AJPH.2008.154971]
- 10 Chen H, Wang J, Li Q, Yagouti A, Lavigne E, Foty R, Burnett RT, Villeneuve PJ, Cakmak S, Copes R. Assessment of the effect of cold and hot temperatures on mortality in Ontario, Canada: a population-based study. *CMAJ Open* 2016; **4**: E48-E58 [PMID: 27280114 DOI: 10.9778/cmajo.20150111]
- 11 Chung Y, Lim YH, Honda Y, Guo YL, Hashizume M, Bell ML, Chen BY, Kim H. Mortality related to extreme temperature for 15 cities in northeast Asia. *Epidemiology* 2015; **26**: 255-262 [PMID: 25643105 DOI: 10.1097/EDE.0000000000000229]
- 12 Chan EY, Goggins WB, Kim JJ, Griffiths SM. A study of intracity variation of temperature-related mortality and socioeconomic status among the Chinese population in Hong Kong. *J Epidemiol Community Health* 2012; **66**: 322-327 [PMID: 20974839 DOI: 10.1136/jech.2008.085167]
- 13 Can G, Şahin Ü, Sayılı U, Dubé M, Kara B, Acar HC, İnan B, Aksu Sayman Ö, Lebel G, Bustinza R, Küçükali H, Güven U, Gosselin P. Excess Mortality in Istanbul during Extreme Heat Waves between 2013 and 2017. *Int J Environ Res Public Health* 2019; **16** [PMID: 31703402 DOI: 10.3390/ijerph16224348]
- 14 Fu SH, Gasparrini A, Rodriguez PS, Jha P. Mortality attributable to hot and cold ambient temperatures in India: a nationally representative case-crossover study. *PLoS Med* 2018; **15**: e1002619 [PMID: 30040816 DOI: 10.1371/journal.pmed.1002619]
- 15 Guo Y, Gasparrini A, Armstrong BG, Tawatsupa B, Tobias A, Lavigne E, Coelho MSZS, Pan X, Kim H, Hashizume M, Honda Y, Guo YL, Wu CF, Zanobetti A, Schwartz JD, Bell ML, Scortichini M, Michelozzi P, Punnasiri K, Li S, Tian L, Garcia SDO, Seposo X, Overcenco A, Zeka A, Goodman P, Dang TN, Dung DV, Mayvaneh F, Saldiva PHN, Williams G, Tong S. Heat Wave and Mortality: A Multicountry, Multicommunity Study. *Environ Health Perspect* 2017; **125**: 087006 [PMID: 28886602 DOI: 10.1289/EHP1026]
- 16 Oray NC, Oray D, Aksay E, Atilla R, Bayram B. The impact of a heat wave on mortality in the emergency department. *Medicine (Baltimore)* 2018; **97**: e13815 [PMID: 30593174 DOI: 10.1097/MD.00000000000013815]
- 17 Gómez-Acebo I, Llorca J, Dierssen T. Cold-related mortality due to cardiovascular diseases, respiratory diseases and cancer: a case-crossover study. *Public Health* 2013; **127**: 252-258 [PMID: 23433803 DOI: 10.1016/j.puhe.2012.12.014]
- 18 Fernández-Raga M, Tomás C, Fraile R. Human mortality seasonality in Castile-León, Spain, between 1980 and 1998: the influence of temperature, pressure and humidity. *Int J Biometeorol* 2010; **54**: 379-392 [PMID: 20107841 DOI: 10.1007/s00484-009-0289-1]
- 19 McMichael AJ, Wilkinson P, Kovats RS, Pattenden S, Hajat S, Armstrong B, Vajanapoom N, Niciu EM, Mahomed H, Kingkeow C, Kosnik M, O'Neill MS, Romieu I, Ramirez-Aguilar M, Barreto ML, Gouveia N, Nikiforov B. International study of temperature, heat and urban mortality: the 'ISOTHERM' project. *Int J Epidemiol* 2008; **37**: 1121-1131 [PMID: 18522981 DOI: 10.1093/ije/dyn086]
- 20 Rabczenko D, Wojtyniak B, Kuchcik M, Szymalski W, Seroka W, Żmudzka E. Association between high temperature and mortality of Warsaw inhabitants, 2008-2013. *Przegl Epidemiol* 2016; **70**: 629-640 [PMID: 28233965]
- 21 Bell ML, O'Neill MS, Ranjit N, Borja-Aburto VH, Cifuentes LA, Gouveia NC. Vulnerability to heat-related mortality in Latin America: a case-crossover study in Sao Paulo, Brazil, Santiago, Chile and Mexico City, Mexico. *Int J Epidemiol* 2008; **37**: 796-804 [PMID: 18511489 DOI: 10.1093/ije/dyn094]

- 22 **Gasparrini A**, Guo Y, Hashizume M, Lavigne E, Tobias A, Zanobetti A, Schwartz JD, Leone M, Michelozzi P, Kan H, Tong S, Honda Y, Kim H, Armstrong BG. Changes in Susceptibility to Heat During the Summer: A Multicountry Analysis. *Am J Epidemiol* 2016; **183**: 1027-1036 [PMID: 27188948 DOI: 10.1093/aje/kwv260]
- 23 **Guo Y**, Punnasiri K, Tong S. Effects of temperature on mortality in Chiang Mai city, Thailand: a time series study. *Environ Health* 2012; **11**: 36 [PMID: 22613086 DOI: 10.1186/1476-069X-11-36]
- 24 **Oudin Åström D**, Schifano P, Asta F, Lallo A, Michelozzi P, Rocklöv J, Forsberg B. The effect of heat waves on mortality in susceptible groups: a cohort study of a mediterranean and a northern European City. *Environ Health* 2015; **14**: 30 [PMID: 25889290 DOI: 10.1186/s12940-015-0012-0]
- 25 **Argaud L**, Ferry T, Le QH, Marfisi A, Ciorba D, Achache P, Ducluzeau R, Robert D. Short- and long-term outcomes of heatstroke following the 2003 heat wave in Lyon, France. *Arch Intern Med* 2007; **167**: 2177-2183 [PMID: 17698677 DOI: 10.1001/archinte.167.20.10147]
- 26 **Analtis A**, De' Donato F, Scortichini M, Lanki T, Basagana X, Ballester F, Astrom C, Paldy A, Pascal M, Gasparrini A, Michelozzi P, Katsouyanni K. Synergistic Effects of Ambient Temperature and Air Pollution on Health in Europe: Results from the PHASE Project. *Int J Environ Res Public Health* 2018; **15** [PMID: 30154318 DOI: 10.3390/ijerph15091856]
- 27 **Gasparrini A**, Guo Y, Hashizume M, Lavigne E, Zanobetti A, Schwartz J, Tobias A, Tong S, Rocklöv J, Forsberg B, Leone M, De Sario M, Bell ML, Guo YL, Wu CF, Kan H, Yi SM, de Sousa Zanotti Stagliorio Coelho M, Saldiva PH, Honda Y, Kim H, Armstrong B. Mortality risk attributable to high and low ambient temperature: a multicountry observational study. *Lancet* 2015; **386**: 369-375 [PMID: 26003380 DOI: 10.1016/S0140-6736(14)62114-0]
- 28 **Linares C**, Díaz J. Impact of high temperatures on hospital admissions: comparative analysis with previous studies about mortality (Madrid). *Eur J Public Health* 2008; **18**: 317-322 [PMID: 18045814 DOI: 10.1093/eurpub/ckm108]
- 29 **Rocklöv J**, Ebi K, Forsberg B. Mortality related to temperature and persistent extreme temperatures: a study of cause-specific and age-stratified mortality. *Occup Environ Med* 2011; **68**: 531-536 [PMID: 20962034 DOI: 10.1136/oem.2010.058818]
- 30 **Rocklöv J**, Forsberg B, Ebi K, Bellander T. Susceptibility to mortality related to temperature and heat and cold wave duration in the population of Stockholm County, Sweden. *Glob Health Action* 2014; **7**: 22737 [PMID: 24647126 DOI: 10.3402/gha.v7.22737]
- 31 **Achebak H**, Devolder D, Ballester J. Heat-related mortality trends under recent climate warming in Spain: A 36-year observational study. *PLoS Med* 2018; **15**: e1002617 [PMID: 30040838 DOI: 10.1371/journal.pmed.1002617]
- 32 **Ragettli MS**, Vicedo-Cabrera AM, Schindler C, Röösli M. Exploring the association between heat and mortality in Switzerland between 1995 and 2013. *Environ Res* 2017; **158**: 703-709 [PMID: 28735231 DOI: 10.1016/j.envres.2017.07.021]
- 33 **Bobb JF**, Peng RD, Bell ML, Dominici F. Heat-related mortality and adaptation to heat in the United States. *Environ Health Perspect* 2014; **122**: 811-816 [PMID: 24780880 DOI: 10.1289/ehp.1307392]
- 34 **Xu Y**, Dadvand P, Barrera-Gómez J, Sartini C, Mari-Dell'Olmo M, Borrell C, Medina-Ramón M, Sunyer J, Basagaña X. Differences on the effect of heat waves on mortality by sociodemographic and urban landscape characteristics. *J Epidemiol Community Health* 2013; **67**: 519-525 [PMID: 23443960 DOI: 10.1136/jech-2012-201899]
- 35 **Zhang Y**, Li C, Feng R, Zhu Y, Wu K, Tan X, Ma L. The Short-Term Effect of Ambient Temperature on Mortality in Wuhan, China: A Time-Series Study Using a Distributed Lag Non-Linear Model. *Int J Environ Res Public Health* 2016; **13** [PMID: 27438847 DOI: 10.3390/ijerph13070722]
- 36 **Zhu G**, Zhu Y, Wang Z, Meng W, Wang X, Feng J, Li J, Xiao Y, Shi F, Wang S. The association between ambient temperature and mortality of the coronavirus disease 2019 (COVID-19) in Wuhan, China: a time-series analysis. *BMC Public Health* 2021; **21**: 117 [PMID: 33430851 DOI: 10.1186/s12889-020-10131-7]
- 37 **Marchant B**, Ranjadayan K, Stevenson R, Wilkinson P, Timmis AD. Circadian and seasonal factors in the pathogenesis of acute myocardial infarction: the influence of environmental temperature. *Br Heart J* 1993; **69**: 385-387 [PMID: 8518058 DOI: 10.1136/hrt.69.5.385]
- 38 **Wilkinson P**, Pattenden S, Armstrong B, Fletcher A, Kovats RS, Mangtani P, McMichael AJ. Vulnerability to winter mortality in elderly people in Britain: population based study. *BMJ* 2004; **329**: 647 [PMID: 15315961 DOI: 10.1136/bmj.38167.589907.55]
- 39 **Meal AG**, Pringle M, Hammersley V. Time changes in new cases of ischaemic heart disease in general practice. *Fam Pract* 2000; **17**: 394-400 [PMID: 11021898 DOI: 10.1093/fampra/17.5.394]
- 40 **Pell JP**, Cobbe SM. Seasonal variations in coronary heart disease. *QJM* 1999; **92**: 689-696 [PMID: 10581331 DOI: 10.1093/qjmed/92.12.689]
- 41 **Michelozzi P**, Accetta G, De Sario M, D'Ippoliti D, Marino C, Baccini M, Biggeri A, Anderson HR, Katsouyanni K, Ballester F, Bisanti L, Cadum E, Forsberg B, Forastiere F, Goodman PG, Hojs A, Kirchmayer U, Medina S, Paldy A, Schindler C, Sunyer J, Perucci CA; 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 [PMID: 19060232 DOI: 10.1164/rccm.200802-217OC]
- 42 **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 [PMID: 24098818 DOI: 10.1371/journal.pone.0077321]
- 43 **Crawford VL**, McCann M, Stout RW. Changes in seasonal deaths from myocardial infarction. *QJM* 2003; **96**: 45-52 [PMID: 12509648 DOI: 10.1093/qjmed/hcg005]
- 44 **Gyllerup S**, Lanke J, Lindholm LH, Schersten B. Cold climate is an important factor in explaining regional differences in coronary mortality even if serum cholesterol and other established risk factors are taken into account. *Scott Med J* 1993; **38**: 169-172 [PMID: 8146634 DOI: 10.1177/003693309303800604]
- 45 **Gerber Y**, Jacobsen SJ, Killian JM, Weston SA, Roger VL. Seasonality and daily weather conditions in relation to myocardial infarction and sudden cardiac death in Olmsted County, Minnesota, 1979 to 2002. *J Am Coll Cardiol* 2006; **48**: 287-292 [PMID: 16843177 DOI: 10.1016/j.jacc.2006.02.065]
- 46 **Zhang Y**, Peng M, Wang L, Yu C. Association of diurnal temperature range with daily mortality in England and Wales: A nationwide time-series study. *Sci Total Environ* 2018; **619-620**: 291-300 [PMID: 29154047 DOI: 10.1016/j.scitotenv.2018.05.001]

- 10.1016/j.scitotenv.2017.11.056]
- 47 **Wang X**, Li G, Liu L, Westerdahl D, Jin X, Pan X. Effects of Extreme Temperatures on Cause-Specific Cardiovascular Mortality in China. *Int J Environ Res Public Health* 2015; **12**: 16136-16156 [PMID: 26703637 DOI: 10.3390/ijerph121215042]
  - 48 **Dilaveris P**, Syntetos A, Giannopoulos G, Gialafos E, Pantazis A, Stefanadis C. CLimate Impacts on Myocardial infarction deaths in the Athens Territory: the CLIMATE study. *Heart* 2006; **92**: 1747-1751 [PMID: 16840509 DOI: 10.1136/hrt.2006.091884]
  - 49 **Wichmann J**, Rosengren A, Sjöberg K, Barregard L, Sallsten G. Association between ambient temperature and acute myocardial infarction hospitalisations in Gothenburg, Sweden: 1985-2010. *PLoS One* 2013; **8**: e62059 [PMID: 23646115 DOI: 10.1371/journal.pone.0062059]
  - 50 **Yin Q**, Wang J. The association between consecutive days' heat wave and cardiovascular disease mortality in Beijing, China. *BMC Public Health* 2017; **17**: 223 [PMID: 28228117 DOI: 10.1186/s12889-017-4129-7]
  - 51 **Chen K**, Wolf K, Breitner S, Gasparrini A, Stafoggia M, Samoli E, Andersen ZJ, Bero-Bedada G, Bellander T, Hennig F, Jacquemin B, Pekkanen J, Hampel R, Cyrus J, Peters A, Schneider A; UF&HEALTH Study Group. Two-way effect modifications of air pollution and air temperature on total natural and cardiovascular mortality in eight European urban areas. *Environ Int* 2018; **116**: 186-196 [PMID: 29689465 DOI: 10.1016/j.envint.2018.04.021]
  - 52 **Vaneckova P**, Bambrick H. Cause-specific hospital admissions on hot days in Sydney, Australia. *PLoS One* 2013; **8**: e55459 [PMID: 23408986 DOI: 10.1371/journal.pone.0055459]
  - 53 **Chan EY**, Goggins WB, Yue JS, Lee P. Hospital admissions as a function of temperature, other weather phenomena and pollution levels in an urban setting in China. *Bull World Health Organ* 2013; **91**: 576-584 [PMID: 23940405 DOI: 10.2471/BLT.12.113035]
  - 54 **Goldie J**, Sherwood SC, Green D, Alexander L. Temperature and Humidity Effects on Hospital Morbidity in Darwin, Australia. *Ann Glob Health* 2015; **81**: 333-341 [PMID: 26615068 DOI: 10.1016/j.aogh.2015.07.003]
  - 55 **van Loenhout JAF**, Delbiso TD, Kiriliouk A, Rodriguez-Llanes JM, Segers J, Guha-Sapir D. Heat and emergency room admissions in the Netherlands. *BMC Public Health* 2018; **18**: 108 [PMID: 29304777 DOI: 10.1186/s12889-017-5021-1]
  - 56 **Mastrangelo G**, Hajat S, Fadda E, Buja A, Fedeli U, Spolaore P. Contrasting patterns of hospital admissions and mortality during heat waves: are deaths from circulatory disease a real excess or an artifact? *Med Hypotheses* 2006; **66**: 1025-1028 [PMID: 16413137 DOI: 10.1016/j.mehy.2005.09.053]
  - 57 **Tian Y**, Liu H, Si Y, Cao Y, Song J, Li M, Wu Y, Wang X, Xiang X, Juan J, Chen L, Wei C, Gao P, Hu Y. Association between temperature variability and daily hospital admissions for cause-specific cardiovascular disease in urban China: A national time-series study. *PLoS Med* 2019; **16**: e1002738 [PMID: 30689640 DOI: 10.1371/journal.pmed.1002738]
  - 58 **Ponjoan A**, Blanch J, Alves-Cabreros L, Martí-Lluch R, Comas-Cufí M, Parramon D, Del Mar Garcia-Gil M, Ramos R, Petersen I. Effects of extreme temperatures on cardiovascular emergency hospitalizations in a Mediterranean region: a self-controlled case series study. *Environ Health* 2017; **16**: 32 [PMID: 28376798 DOI: 10.1186/s12940-017-0238-0]
  - 59 **Ebi KL**, Exuzides KA, Lau E, Kelsh M, Barnston A. Weather changes associated with hospitalizations for cardiovascular diseases and stroke in California, 1983-1998. *Int J Biometeorol* 2004; **49**: 48-58 [PMID: 15138867 DOI: 10.1007/s00484-004-0207-5]
  - 60 **Shiue I**, Perkins DR, Bearman N. Relationships of physiologically equivalent temperature and hospital admissions due to I30-I51 other forms of heart disease in Germany in 2009-2011. *Environ Sci Pollut Res Int* 2016; **23**: 6343-6352 [PMID: 26620859 DOI: 10.1007/s11356-015-5727-5]
  - 61 **Yitshak-Sade M**, Bobb JF, Schwartz JD, Kloog I, Zanobetti A. The association between short and long-term exposure to PM<sub>2.5</sub> and temperature and hospital admissions in New England and the synergistic effect of the short-term exposures. *Sci Total Environ* 2018; **639**: 868-875 [PMID: 29929325 DOI: 10.1016/j.scitotenv.2018.05.181]
  - 62 **de Miguel-Diez J**, Jiménez-García R, López de Andrés A, Hernández-Barrera V, Carrasco-Garrido P, Monreal M, Jiménez D, Jara-Palmares L, Álvaro-Meca A. Analysis of environmental risk factors for pulmonary embolism: A case-crossover study (2001-2013). *Eur J Intern Med* 2016; **31**: 55-61 [PMID: 27012471 DOI: 10.1016/j.ejim.2016.03.001]
  - 63 **Bhaskaran K**, Hajat S, Haines A, Herrett E, Wilkinson P, Smeeth L. Short term effects of temperature on risk of myocardial infarction in England and Wales: time series regression analysis of the Myocardial Ischaemia National Audit Project (MINAP) registry. *BMJ* 2010; **341**: e3823 [PMID: 20699305 DOI: 10.1136/bmj.e3823]
  - 64 **Wolf K**, Schneider A, Breitner S, von Klot S, Meisinger C, Cyrus J, Hymer H, Wichmann HE, Peters A; Cooperative Health Research in the Region of Augsburg Study Group. Air temperature and the occurrence of myocardial infarction in Augsburg, Germany. *Circulation* 2009; **120**: 735-742 [PMID: 19687361 DOI: 10.1161/CIRCULATIONAHA.108.815860]
  - 65 **Misailidou M**, Pitsavos C, Panagiotakos DB, Chrysohou C, Stefanadis C. Short-term effects of atmospheric temperature and humidity on morbidity from acute coronary syndromes in free of air pollution rural Greece. *Eur J Cardiovasc Prev Rehabil* 2006; **13**: 846-848 [PMID: 17001228 DOI: 10.1097/01.hjr.0000221857.04168.06]
  - 66 **García-Lledó A**, Rodríguez-Martín S, Tobias A, Alonso-Martín J, Ansedo-Cascudo JC, de Abajo FJ. Heat waves, ambient temperature, and risk of myocardial infarction: an ecological study in the Community of Madrid. *Rev Esp Cardiol (Engl Ed)* 2020; **73**: 300-306 [PMID: 31678071 DOI: 10.1016/j.rec.2019.05.016]
  - 67 **Lin S**, Soim A, Gleason KA, Hwang SA. Association Between Low Temperature During Winter Season and Hospitalizations for Ischemic Heart Diseases in New York State. *J Environ Health* 2016; **78**: 66-74 [PMID: 26867294]
  - 68 **Ravljien M**, Bilban M, Kajfež-Bogataj L, Hovelja T, Vavpotič D. Influence of daily individual meteorological parameters on the incidence of acute coronary syndrome. *Int J Environ Res Public Health* 2014; **11**: 11616-11626 [PMID: 25396770 DOI: 10.3390/ijerph111111616]
  - 69 **Chang CL**, Shipley M, Marmot M, Poulter N. Lower ambient temperature was associated with an increased risk of hospitalization for stroke and acute myocardial infarction in young women. *J Clin Epidemiol* 2004; **57**: 749-757 [PMID: 15358404 DOI: 10.1016/j.jclinepi.2003.10.016]
  - 70 **Madrigano J**, Mittleman MA, Baccarelli A, Goldberg R, Melly S, von Klot S, Schwartz J. Temperature, myocardial infarction, and mortality: effect modification by individual- and area-level characteristics. *Epidemiology* 2013; **24**: 439-

- 446 [PMID: 23462524 DOI: 10.1097/EDE.0b013e3182878397]
- 71 **Hori A**, Hashizume M, Tsuda Y, Tsukahara T, Nomiya T. Effects of weather variability and air pollutants on emergency admissions for cardiovascular and cerebrovascular diseases. *Int J Environ Health Res* 2012; **22**: 416-430 [PMID: 22384943 DOI: 10.1080/09603123.2011.650155]
- 72 **Mohammad MA**, Koul S, Rylance R, Fröbert O, Alfredsson J, Sahlén A, Witt N, Jernberg T, Muller J, Erlinge D. Association of Weather With Day-to-Day Incidence of Myocardial Infarction: A SWEDEHEART Nationwide Observational Study. *JAMA Cardiol* 2018; **3**: 1081-1089 [PMID: 30422202 DOI: 10.1001/jamacardio.2018.3466]
- 73 **Danet S**, Richard F, Montaye M, Beauchant S, Lemaire B, Graux C, Cottel D, Marécaux N, Amouyel P. Unhealthy effects of atmospheric temperature and pressure on the occurrence of myocardial infarction and coronary deaths. A 10-year survey: the Lille-World Health Organization MONICA project (Monitoring trends and determinants in cardiovascular disease). *Circulation* 1999; **100**: E1-E7 [PMID: 10393689 DOI: 10.1161/01.cir.100.1.e1]
- 74 **Abrignani MG**, Corrao S, Biondo GB, Renda N, Braschi A, Novo G, Di Girolamo A, Braschi GB, Novo S. Influence of climatic variables on acute myocardial infarction hospital admissions. *Int J Cardiol* 2009; **137**: 123-129 [PMID: 18694607 DOI: 10.1016/j.ijcard.2008.06.036]
- 75 **Sharif Nia H**, Chan YH, Froelicher ES, Pahlevan Sharif S, Yaghoobzadeh A, Jafari A, Goudarzian AH, Pourkia R, Haghdoost AA, Arefinia F, Nazari R. Weather fluctuations: predictive factors in the prevalence of acute coronary syndrome. *Health Promot Perspect* 2019; **9**: 123-130 [PMID: 31249799 DOI: 10.15171/hpp.2019.17]
- 76 **Messner T**, Lundberg V, Wikström B. A temperature rise is associated with an increase in the number of acute myocardial infarctions in the subarctic area. *Int J Circumpolar Health* 2002; **61**: 201-207 [PMID: 12369109 DOI: 10.3402/ijch.v61i3.17453]
- 77 **Bayentin L**, El Adlouni S, Ouarda TB, Gosselin P, Doyon B, Chebana F. Spatial variability of climate effects on ischemic heart disease hospitalization rates for the period 1989-2006 in Quebec, Canada. *Int J Health Geogr* 2010; **9**: 5 [PMID: 20144187 DOI: 10.1186/1476-072X-9-5]
- 78 **Mirić D**, Rumboldt Z. The impact of meteorological factors on the onset of myocardial infarction in the coastal region of middle Dalmatia. *G Ital Cardiol* 1993; **23**: 655-660 [PMID: 8405831]
- 79 **Bhaskaran K**, Hajat S, Haines A, Herrett E, Wilkinson P, Smeeth L. Effects of ambient temperature on the incidence of myocardial infarction. *Heart* 2009; **95**: 1760-1769 [PMID: 19635724 DOI: 10.1136/hrt.2009.175000]
- 80 **Nastos PT**, Giaouzaki KN, Kampanis NA, Matzarakis A. Acute coronary syndromes related to bio-climate in a Mediterranean area. The case of Ierapetra, Crete Island, Greece. *Int J Environ Health Res* 2013; **23**: 76-90 [PMID: 22774800 DOI: 10.1080/09603123.2012.699031]
- 81 **Sun Z**, Chen C, Xu D, Li T. Effects of ambient temperature on myocardial infarction: A systematic review and meta-analysis. *Environ Pollut* 2018; **241**: 1106-1114 [PMID: 30029319 DOI: 10.1016/j.envpol.2018.06.045]
- 82 **Abrignani MG**, Corrao S, Biondo GB, Lombardo RM, Di Girolamo P, Braschi A, Di Girolamo A, Novo S. Effects of ambient temperature, humidity, and other meteorological variables on hospital admissions for angina pectoris. *Eur J Prev Cardiol* 2012; **19**: 342-348 [PMID: 21450571 DOI: 10.1177/1741826711402741]
- 83 **Bijelović S**, Dragić N, Bijelović M, Kovačević M, Jevtić M, Ninković Mrdenovački O. Impact of climate conditions on hospital admissions for subcategories of cardiovascular diseases. *Med Pr* 2017; **68**: 189-197 [PMID: 28345679 DOI: 10.13075/mp.5893.00606]
- 84 **Cheng TO**. Myocardial infarction and the weather: a significant positive correlation between the onset of heart infarct and 28 KHz atmospheric--a pilot study. *Clin Cardiol* 1985; **8**: 510 [PMID: 4053428 DOI: 10.1002/clc.4960081002]
- 85 **Vencloviene J**, Babarskiene R, Dobožinskas P, Siurkaite V. Effects of weather conditions on emergency ambulance calls for acute coronary syndromes. *Int J Biometeorol* 2015; **59**: 1083-1093 [PMID: 25344902 DOI: 10.1007/s00484-014-0921-6]
- 86 **Goerre S**, Egli C, Gerber S, Defila C, Minder C, Richner H, Meier B. Impact of weather and climate on the incidence of acute coronary syndromes. *Int J Cardiol* 2007; **118**: 36-40 [PMID: 16904213 DOI: 10.1016/j.ijcard.2006.06.015]
- 87 **Baker-Blocker A**. Winter weather and cardiovascular mortality in Minneapolis-St. Paul. *Am J Public Health* 1982; **72**: 261-265 [PMID: 7058966 DOI: 10.2105/ajph.72.3.261]
- 88 **Auger N**, Potter BJ, Smargiassi A, Bilodeau-Bertrand M, Paris C, Kosatsky T. Association between quantity and duration of snowfall and risk of myocardial infarction. *CMAJ* 2017; **189**: E235-E242 [PMID: 28202557 DOI: 10.1503/cmaj.161064]
- 89 **Gebhard C**, Gebhard CE, Stähli BE, Maafi F, Bertrand MJ, Wildi K, Fortier A, Galvan Onandia Z, Toma A, Zhang ZW, Smith DC, Spagnoli V, Ly HQ. Weather and risk of ST-elevation myocardial infarction revisited: Impact on young women. *PLoS One* 2018; **13**: e0195602 [PMID: 29630673 DOI: 10.1371/journal.pone.0195602]
- 90 **Morabito M**, Modesti PA, Cecchi L, Crisci A, Orlandini S, Maracchi G, Gensini GF. Relationships between weather and myocardial infarction: a biometeorological approach. *Int J Cardiol* 2005; **105**: 288-293 [PMID: 16274770 DOI: 10.1016/j.ijcard.2004.12.047]
- 91 **Morabito M**, Crisci A, Grifoni D, Orlandini S, Cecchi L, Bacci L, Modesti PA, Gensini GF, Maracchi G. Winter air-mass-based synoptic climatological approach and hospital admissions for myocardial infarction in Florence, Italy. *Environ Res* 2006; **102**: 52-60 [PMID: 16460725 DOI: 10.1016/j.envres.2005.12.007]
- 92 **Messner T**, Lundberg V, Wikström B. The Arctic Oscillation and incidence of acute myocardial infarction. *J Intern Med* 2003; **253**: 666-670 [PMID: 12755963 DOI: 10.1046/j.1365-2796.2003.01153.x]
- 93 **Stewart S**, Moholdt TT, Burrell LM, Sliwa K, Mocumbi AO, McMurray JJ, Keates AK, Hawley JA. Winter Peaks in Heart Failure: An Inevitable or Preventable Consequence of Seasonal Vulnerability? *Card Fail Rev* 2019; **5**: 83-85 [PMID: 31179017 DOI: 10.15420/cfr.2018.40.2]
- 94 **Escobar V**, Lozano A, Larburu N, Kerexeta J, Álvarez R, Juez B, Echebarria A, Azcona A, Artola G. Impact of environmental factors on heart failure decompensations. *ESC Heart Fail* 2019; **6**: 1226-1232 [PMID: 31483570 DOI: 10.1002/ehf2.12506]
- 95 **Ryti NR**, Mäkiyö EM, Antikainen H, Junttila MJ, Hookana E, Ikäheimo TM, Kortelainen ML, Huikuri HV, Jaakkola JJ. Cold spells and ischaemic sudden cardiac death: effect modification by prior diagnosis of ischaemic heart disease and

- cardioprotective medication. *Sci Rep* 2017; **7**: 41060 [PMID: 28106161 DOI: 10.1038/srep41060]
- 96 **Chung FP**, Li HR, Chong E, Pan CH, Lin YJ, Chang SL, Lo LW, Hu YF, Tuan TC, Chao TF, Liao JN, Lin WY, Shaw KP, Chen SA. Seasonal variation in the frequency of sudden cardiac death and ventricular tachyarrhythmia in patients with arrhythmogenic right ventricular dysplasia/cardiomyopathy: the effect of meteorological factors. *Heart Rhythm* 2013; **10**: 1859-1866 [PMID: 24080066 DOI: 10.1016/j.hrthm.2013.09.069]
- 97 **Benouaich V**, Soler P, Gourraud PA, Lopez S, Rousseau H, Marcheix B. Impact of meteorological conditions on the occurrence of acute type A aortic dissections. *Interact Cardiovasc Thorac Surg* 2010; **10**: 403-406 [PMID: 20008897 DOI: 10.1510/icvts.2009.219873]
- 98 **Kordzadeh A**, Askari A, Panayiotopoulos Y. Atmospheric pressure and infra-renal abdominal aortic aneurysm rupture: a single observational study and a comprehensive review of literature. *Int J Surg* 2013; **11**: 458-462 [PMID: 23619334 DOI: 10.1016/j.ijssu.2013.04.008]
- 99 **Low RB**, Bielory L, Qureshi AI, Dunn V, Stuhlmiller DF, Dickey DA. The relation of stroke admissions to recent weather, airborne allergens, air pollution, seasons, upper respiratory infections, and asthma incidence, September 11, 2001, and day of the week. *Stroke* 2006; **37**: 951-957 [PMID: 16527994 DOI: 10.1161/01.STR.0000214681.94680.66]
- 100 **Dawson J**, Weir C, Wright F, Bryden C, Aslanyan S, Lees K, Bird W, Walters M. Associations between meteorological variables and acute stroke hospital admissions in the west of Scotland. *Acta Neurol Scand* 2008; **117**: 85-89 [PMID: 18184342 DOI: 10.1111/j.1600-0404.2007.00916.x]
- 101 **Matsumoto M**, Ishikawa S, Kajii E. Cumulative effects of weather on stroke incidence: a multi-community cohort study in Japan. *J Epidemiol* 2010; **20**: 136-142 [PMID: 20037258 DOI: 10.2188/jea.je20090103]
- 102 **Royé D**, Zarrabeitia MT, Riancho J, Santurtún A. A time series analysis of the relationship between apparent temperature, air pollutants and ischemic stroke in Madrid, Spain. *Environ Res* 2019; **173**: 349-358 [PMID: 30953949 DOI: 10.1016/j.envres.2019.03.065]
- 103 **Ravljien M**, Bajrović F, Vavpotič D. A time series analysis of the relationship between ambient temperature and ischaemic stroke in the Ljubljana area: immediate, delayed and cumulative effects. *BMC Neurol* 2021; **21**: 23 [PMID: 33446129 DOI: 10.1186/s12883-021-02044-8]
- 104 **Wang X**, Cao Y, Hong D, Zheng D, Richtering S, Sandset EC, Leong TH, Arima H, Islam S, Salam A, Anderson C, Robinson T, Hackett ML. Ambient Temperature and Stroke Occurrence: A Systematic Review and Meta-Analysis. *Int J Environ Res Public Health* 2016; **13** [PMID: 27420077 DOI: 10.3390/ijerph13070698]
- 105 **Webb L**, Bambrick H, Tait P, Green D, Alexander L. Effect of ambient temperature on Australian northern territory public hospital admissions for cardiovascular disease among indigenous and non-indigenous populations. *Int J Environ Res Public Health* 2014; **11**: 1942-1959 [PMID: 24531121 DOI: 10.3390/ijerph110201942]
- 106 **Kwon BY**, Lee E, Lee S, Heo S, Jo K, Kim J, Park MS. Vulnerabilities to Temperature Effects on Acute Myocardial Infarction Hospital Admissions in South Korea. *Int J Environ Res Public Health* 2015; **12**: 14571-14588 [PMID: 26580643 DOI: 10.3390/ijerph121114571]
- 107 **Hajat S**, Kovats RS, Lachowycz K. Heat-related and cold-related deaths in England and Wales: who is at risk? *Occup Environ Med* 2007; **64**: 93-100 [PMID: 16990293 DOI: 10.1136/oem.2006.029017]
- 108 **Wong HT**, Lai PC. Weather inference and daily demand for emergency ambulance services. *Emerg Med J* 2012; **29**: 60-64 [PMID: 21030546 DOI: 10.1136/emj.2010.096701]
- 109 **Grech V**, Aquilina O, Pace J. Gender differences in seasonality of acute myocardial infarction admissions and mortality in a population-based study. *J Epidemiol Community Health* 2001; **55**: 147-148 [PMID: 11154255 DOI: 10.1136/jech.55.2.147]
- 110 **Zheng S**, Wang M, Li B, Wang S, He S, Yin L, Shang K, Li T. Gender, Age and Season as Modifiers of the Effects of Diurnal Temperature Range on Emergency Room Admissions for Cause-Specific Cardiovascular Disease among the Elderly in Beijing. *Int J Environ Res Public Health* 2016; **13** [PMID: 27128931 DOI: 10.3390/ijerph13050447]
- 111 **Radišauskas R**, Bernotienė G, Bacevičienė M, Ustinavičienė R, Kirvaitienė J, Krančiukaitė-Butylkinienė D. Trends of myocardial infarction morbidity and its associations with weather conditions. *Medicina (Kaunas)* 2014; **50**: 182-189 [PMID: 25323547 DOI: 10.1016/j.medic.2014.08.003]
- 112 **Medina-Ramón M**, Zanobetti A, Cavanagh DP, Schwartz J. Extreme temperatures and mortality: assessing effect modification by personal characteristics and specific cause of death in a multi-city case-only analysis. *Environ Health Perspect* 2006; **114**: 1331-1336 [PMID: 16966084 DOI: 10.1289/ehp.9074]
- 113 **Vandentorren S**, Bretin P, Zeghnoun A, Mandereau-Bruno L, Croisier A, Cochet C, Ribéron J, Siberan I, Declercq B, Ledrans M. August 2003 heat wave in France: risk factors for death of elderly people living at home. *Eur J Public Health* 2006; **16**: 583-591 [PMID: 17028103 DOI: 10.1093/eurpub/ckl063]
- 114 **Faroni M**, Salvioli G, Rielli R, Goldoni CA, Orlandi G, Zauli Sajani S, Guerzoni A, Maccaferri C, Daya G, Mussi C. A retrospective study on heat-related mortality in an elderly population during the 2003 heat wave in Modena, Italy: the Argento Project. *J Gerontol A Biol Sci Med Sci* 2007; **62**: 647-651 [PMID: 17595422 DOI: 10.1093/gerona/62.6.647]
- 115 **Bouchama A**, Dehbi M, Mohamed G, Matthies F, Shoukri M, Menne B. Prognostic factors in heat wave related deaths: a meta-analysis. *Arch Intern Med* 2007; **167**: 2170-2176 [PMID: 17698676 DOI: 10.1001/archinte.167.20.ira70009]
- 116 **Kaiser R**, Le Tertre A, Schwartz J, Gotway CA, Daley WR, Rubin CH. The effect of the 1995 heat wave in Chicago on all-cause and cause-specific mortality. *Am J Public Health* 2007; **97** Suppl 1: S158-S162 [PMID: 17413056 DOI: 10.2105/AJPH.2006.100081]
- 117 **Marí-Dell'Olmo M**, Tobías A, Gómez-Gutiérrez A, Rodríguez-Sanz M, García de Olalla P, Camprubi E, Gasparrini A, Borrell C. Social inequalities in the association between temperature and mortality in a South European context. *Int J Public Health* 2019; **64**: 27-37 [PMID: 29577171 DOI: 10.1007/s00038-018-1094-6]
- 118 **Crawford VL**, McNerlan SE, Stout RW. Seasonal changes in platelets, fibrinogen and factor VII in elderly people. *Age Ageing* 2003; **32**: 661-665 [PMID: 14600009 DOI: 10.1093/ageing/afg113]
- 119 **Ockene IS**, Chiriboga DE, Stanek EJ 3rd, Harmatz MG, Nicolosi R, Saperia G, Well AD, Freedson P, Merriam PA, Reed G, Ma Y, Matthews CE, Hebert JR. Seasonal variation in serum cholesterol levels: treatment implications and possible mechanisms. *Arch Intern Med* 2004; **164**: 863-870 [PMID: 15111372 DOI: 10.1001/archinte.164.8.863]

- 120 **Sher L.** Seasonal distribution of myocardial infarction and seasonal mood changes. *J Am Coll Cardiol* 1999; **33**: 2088-2089 [PMID: 10362222 DOI: 10.1016/s0735-1097(99)00124-2]
- 121 **Kloner RA,** Poole WK, Perritt RL. When throughout the year is coronary death most likely to occur? *Circulation* 1999; **100**: 1630-1634 [PMID: 10517734 DOI: 10.1161/01.cir.100.15.1630]
- 122 **Houdas Y,** Deklunder G, Lecroart JL. Cold exposure and ischemic heart disease. *Int J Sports Med* 1992; **13** Suppl 1: S179-S181 [PMID: 1483767 DOI: 10.1055/s-2007-1024632]
- 123 **Giacconi S,** Ghione S, Palombo C, Genovesi-Ebert A, Marabotti C, Fommei E, Donato L. Seasonal influences on blood pressure in high normal to mild hypertensive range. *Hypertension* 1989; **14**: 22-27 [PMID: 2737734 DOI: 10.1161/01.hyp.14.1.22]
- 124 **Marchant B,** Donaldson G, Mridha K, Scarborough M, Timmis AD. Mechanisms of cold intolerance in patients with angina. *J Am Coll Cardiol* 1994; **23**: 630-636 [PMID: 8113545 DOI: 10.1016/0735-1097(94)90747-1]
- 125 **Cheng X,** Su H. Effects of climatic temperature stress on cardiovascular diseases. *Eur J Intern Med* 2010; **21**: 164-167 [PMID: 20493415 DOI: 10.1016/j.ejim.2010.03.001]
- 126 **De Lorenzo F,** Kadziola Z, Mukherjee M, Saba N, Kakkar VV. Haemodynamic responses and changes of haemostatic risk factors in cold-adapted humans. *QJM* 1999; **92**: 509-513 [PMID: 10627870 DOI: 10.1093/qjmed/92.9.509]
- 127 **Ikäheimo TM.** Cardiovascular diseases, cold exposure and exercise. *Temperature (Austin)* 2018; **5**: 123-146 [PMID: 30377633 DOI: 10.1080/23328940.2017.1414014]
- 128 **Edwards DG,** Gauthier AL, Hayman MA, Lang JT, Kenefick RW. Acute effects of cold exposure on central aortic wave reflection. *J Appl Physiol (1985)* 2006; **100**: 1210-1214 [PMID: 16223975 DOI: 10.1152/jappphysiol.01154.2005]
- 129 **Widlansky ME,** Vita JA, Keyes MJ, Larson MG, Hamburg NM, Levy D, Mitchell GF, Osypiuk EW, Vasan RS, Benjamin EJ. Relation of season and temperature to endothelium-dependent flow-mediated vasodilation in subjects without clinical evidence of cardiovascular disease (from the Framingham Heart Study). *Am J Cardiol* 2007; **100**: 518-523 [PMID: 17659939 DOI: 10.1016/j.amjcard.2007.03.055]
- 130 **Hiramatsu K,** Yamada T, Katakura M. Acute effects of cold on blood pressure, renin-angiotensin-aldosterone system, catecholamines and adrenal steroids in man. *Clin Exp Pharmacol Physiol* 1984; **11**: 171-179 [PMID: 6378465 DOI: 10.1111/j.1440-1681.1984.tb00254.x]
- 131 **Hampel R,** Breitner S, Rückerl R, Frampton MW, Koenig W, Phipps RP, Wichmann HE, Peters A, Schneider A. Air temperature and inflammatory and coagulation responses in men with coronary or pulmonary disease during the winter season. *Occup Environ Med* 2010; **67**: 408-416 [PMID: 19884649 DOI: 10.1136/oem.2009.048660]
- 132 **Elwood PC,** Beswick A, O'Brien JR, Renaud S, Fifield R, Limb ES, Bainton D. Temperature and risk factors for ischaemic heart disease in the Caerphilly prospective study. *Br Heart J* 1993; **70**: 520-523 [PMID: 7506563 DOI: 10.1136/hrt.70.6.520]
- 133 **Modesti PA,** Morabito M, Bertolozzi I, Massetti L, Panci G, Lumachi C, Giglio A, Bilo G, Caldara G, Lonati L, Orlandini S, Maracchi G, Mancia G, Gensini GF, Parati G. Weather-related changes in 24-hour blood pressure profile: effects of age and implications for hypertension management. *Hypertension* 2006; **47**: 155-161 [PMID: 16380524 DOI: 10.1161/01.HYP.0000199192.17126.d4]
- 134 **Hassi J,** Rintamäki H, Ruskoaho H, Leppäluoto J, Vuolteenaho O. Plasma levels of endothelin-1 and atrial natriuretic peptide in men during a 2-hour stay in a cold room. *Acta Physiol Scand* 1991; **142**: 481-485 [PMID: 1835249 DOI: 10.1111/j.1748-1716.1991.tb09183.x]
- 135 **Kolar J,** Bhatnagar SK, Hudak A, Smid J, al-Yusuf AR. The effect of a hot dry climate on the haemorrhology of healthy males and patients with acute myocardial infarction. *J Trop Med Hyg* 1988; **91**: 77-82 [PMID: 3379656]
- 136 **Gronlund CJ,** Sheppard L, Adar SD, O'Neill MS, Auchincloss A, Madrigano J, Kaufman J, Diez Roux AV. Vulnerability to the Cardiovascular Effects of Ambient Heat in Six US Cities: Results from the Multi-Ethnic Study of Atherosclerosis (MESA). *Epidemiology* 2018; **29**: 756-764 [PMID: 30113342 DOI: 10.1097/EDE.0000000000000910]
- 137 **Ren C,** O'Neill MS, Park SK, Sparrow D, Vokonas P, Schwartz J. Ambient temperature, air pollution, and heart rate variability in an aging population. *Am J Epidemiol* 2011; **173**: 1013-1021 [PMID: 21385834 DOI: 10.1093/aje/kwq477]
- 138 **Scragg R,** Jackson R, Holdaway IM, Lim T, Beaglehole R. Myocardial infarction is inversely associated with plasma 25-hydroxyvitamin D3 levels: a community-based study. *Int J Epidemiol* 1990; **19**: 559-563 [PMID: 2262248 DOI: 10.1093/ije/19.3.559]
- 139 **Ren C,** Williams GM, Mengersen K, Morawska L, Tong S. Temperature enhanced effects of ozone on cardiovascular mortality in 95 large US communities, 1987-2000: Assessment using the NMMAPS data. *Arch Environ Occup Health* 2009; **64**: 177-184 [PMID: 19864220 DOI: 10.1080/19338240903240749]
- 140 **Burkart K,** Canário P, Breitner S, Schneider A, Scherber K, Andrade H, Alcoforado MJ, Endlicher W. Interactive short-term effects of equivalent temperature and air pollution on human mortality in Berlin and Lisbon. *Environ Pollut* 2013; **183**: 54-63 [PMID: 23941745 DOI: 10.1016/j.envpol.2013.06.002]
- 141 **Willers SM,** Jonker MF, Klok L, Keuken MP, Odink J, van den Elshout S, Sabel CE, Mackenbach JP, Burdorf A. High resolution exposure modelling of heat and air pollution and the impact on mortality. *Environ Int* 2016; **89-90**: 102-109 [PMID: 26826367 DOI: 10.1016/j.envint.2016.01.013]
- 142 **Scortichini M,** De Sario M, deDonato FK, Davoli M, Michelozzi P, Stafoggia M. Short-Term Effects of Heat on Mortality and Effect Modification by Air Pollution in 25 Italian Cities. *Int J Environ Res Public Health* 2018; **15** [PMID: 30126130 DOI: 10.3390/ijerph15081771]
- 143 **Qin RX,** Xiao C, Zhu Y, Li J, Yang J, Gu S, Xia J, Su B, Liu Q, Woodward A. The interactive effects between high temperature and air pollution on mortality: A time-series analysis in Hefei, China. *Sci Total Environ* 2017; **575**: 1530-1537 [PMID: 28029451 DOI: 10.1016/j.scitotenv.2016.10.033]
- 144 **Faergeman O.** Climate change and preventive medicine. *Eur J Cardiovasc Prev Rehabil* 2007; **14**: 726-729 [PMID: 18043291 DOI: 10.1097/HJR.0b013e3282f30097]



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