



## Effects of Extreme Ambient Temperature on Cardiovascular Outcomes: A Systematic Review

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### ABSTRACT

**Introduction:** Extreme weather or climate, including heat waves and cold waves, is considered a health issue causing adverse effects on health, such as cardiovascular diseases (CVDs), mortality and morbidity. Thus, this systematic review aimed to study the impacts of extreme ambient temperature on cardiovascular outcomes.

**Material and Methods:** This study was carried out based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) protocol. Papers about the ambient temperature and cardiovascular outcomes were searched in the scientific database, including ISI, PubMed, Scopus, and Google Scholar, from January 1970 up to the end of 2020. We used the key terms, such as “heat wave”, “cold wave”, “extreme event”, “cardiovascular disease”, “mortality”, and “morbidity”. The thematic analysis method was used to determine all themes and analyze the data.

**Results:** Among the 7631 searched and extracted papers, 20 articles met the eligibility criteria for including the process of final analysis. Effects of extreme events included mortality, morbidity, and hospitalization due to CVD. A relationship between extreme events and CVD mortality was confirmed for cerebrovascular diseases, including congestive heart failure (CHF), ischemic heart diseases (IHD), myocardial infarction (MI), cardiac arrhythmia, coronary heart disease (CHD), out-of-hospital cardiac arrest (OHCA), acute coronary syndrome (ACS), and blood pressure.

**Conclusion:** The present study indicated the impact of extreme ambient temperature on CVD outcomes. The findings provided adaptation and preventive measures and strategies which can be used for CVD patients and managers to prevent CVD due to ambient temperature.

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### Introduction

Extreme weather or extreme climate, including heat waves and cold waves, related to excessive extreme temperatures in cold and warm season, is expected to impact health, such as increased cardiovascular diseases (CVDs), mortality, and morbidity<sup>1, 2</sup>. CVD sharing the characteristics of

acute attack and hard recovery, has become an main health issue<sup>3</sup>. CVDs are a group of diseases that include both the heart and blood vessels<sup>4</sup>. CVDs are one of the main causes of global mortality. According to estimation of World Health Organization (WHO), more than 17.9 million people die from cardiovascular, annually<sup>5</sup>.

CVDs cause adverse economic effects, such as disability, affect the productivity of active labor force, and result in reduced gross domestic product (GDP) and national income<sup>6</sup>. One of the main factors of CVD is exposure to extreme events, such as cold and heat waves. Both cold and heat temperatures are related to increased death due to CVDs. In addition, insignificant excess hospital emergency admissions due to CVDs are considered on both heat and cold waves<sup>7</sup>. Based on the latest measurement of CVD mortality rate vs. GDP per capita, 2017, CVD mortality rate is measured as the number of deaths per 100,000 individuals versus GDP per capita<sup>8</sup>.

The relation between heat wave and hospitalization is urgent and of short-term period, whereas that of cold waves is postponed but would last longer. Extreme ambient temperature events, especially heat waves, have been proved as the most hazardous of all environmental hazards and claim the largest numbers of patients<sup>7</sup>. The World Meteorological Organization (WMO) described heat wave as the daily maximum temperature that is higher than 32 °C and period of more than 3 days<sup>9</sup>. Exposure to heat waves composed with physical exertion can at the same time effect in systems of sympathetic and parasympathetic, increasing the possibility of atrial fibrillation<sup>10</sup>. Dehydration, raised hypotension and even endothelial cell damage, blood viscosity, and a higher possibility of thromboembolic diseases are the major pathophysiological mechanisms of the heat impacts on health<sup>11</sup>. Moreover, heat waves may impair the endothelial function, enhancing the risk for cardiovascular events<sup>12</sup>.

Cold waves can affect CVD stress due to blood pressure, vasoconstriction, rising in blood viscosity and count of red blood cell, plasma fibrinogen and cholesterol<sup>13</sup>. Cold stress is associated with increased blood pressure and platelet aggregation; raised vasoconstriction; increased blood viscosity and count of red blood cell, plasma fibrinogen and cholesterol; and higher hem concentration, all of which could causes thrombosis<sup>7</sup>. Numerous researches have proven

extreme ambient temperature to be related to raise CVD mortality and morbidity. Several research studies have confirmed the effect of extreme events, such as cold and heat waves on cardiovascular mortality<sup>14-16</sup>. All of studies have evaluated the raised risk of CVD outcomes under various conditions, such as duration and intensity<sup>16</sup>. Vulnerable group, including elderly people, women, and outdoor employees are at higher risk than the other groups. Harmful impacts of heat waves among the older people and women are more severe than younger people and males<sup>16</sup>. The present systematic review aimed to study the effects of ambient temperature (heat and cold waves) on CVD outcomes, such as mortality, morbidity, and hospitalization.

### Materials and Methods

In this research, the systematic review of papers related to ambient temperature and CVD was conducted based on the PRISMA guidelines<sup>17</sup>.

#### *Strategy of search and data sources*

Strategy of search was conducted based on the Cochrane protocol<sup>18</sup>. The key terms were firstly selected by authors based on the Medical Subject Headings (MeSH). Then, the syntax of search strategy was designed in partnership with an academic librarian expert. The scientific international databases included ISI, PubMed, Cochrane Library, and Scopus, within the period of Jan 1<sup>st</sup>, 1970 to Dec 31<sup>st</sup>, 2020. Furthermore, the gray literature was searched through the Open Grey online database and Google Scholar. As well as, the reference lists of the retrieved papers were checked to identify any further studies. Finally, the EndNote was used to screen and control the whole searched paper followed by the removal of duplicate and irrelevant papers.

Syntax of search strategy was as follows: ("Heat Wave" OR "Cold Wave" OR "Extreme Event" OR "Ambient temperature" OR "Cold Temperature", "Hot temperature" OR "climate change" AND "cardiovascular disease" OR "Heart Diseases" OR "Cardiovascular Infections" OR "Cardiovascular Abnormalities" OR "acute coronary syndrome" OR "acute myocardial infarction" OR "coronary event"

OR "heart attack" OR "heart failure" OR "hospital admissions" "congestive heart failure" OR "heart infarct\*" OR hospitalization)

### **Criteria for Eligibility**

In this research, the papers were selected and remained based on the criteria as follows:

- 1) The papers apparently addressing the ambient temperature and CVD.
- 2) Full texts of papers are available freely.
- 3) The papers published in English language.
- 4) The studies that included in all types of methodologies published in peer-reviewed journals.
- 5) The papers encompassing all types of CVD associated in ambient temperature.

The exclusion criteria were as follows:

- 1) The books, letters to the editor, editorials, clinical studies, abstracts, conference papers, presentations, theses, and commentaries.
- 2) The studies with irrelevant subjects and duplicate data.
- 3) The studies with ambiguous methodology or without results.
- 4) The studies including the association between ambient temperature with other diseases, such as respiratory or renal.

### **Study selection**

Initially, duplicate studies were removed using the EndNote software. Remaining studies were assessed based on titles and abstracts and some irrelevant articles were removed. In the next step, two authors assessed the full texts of the retrieved studies critically based on eligibility criteria, independently. Then, the results of assessment were compared and in the case of any disagreement, they were resolved through consensus. In case of any disagreement of opinions between the two previous authors, a third author was requested independently for final decision.

### **Data extraction**

The determined information was extracted from the selected final studies using standard data extraction form. The collected data included 1) first author name 2) publication year 3) title 4)

location 5) purpose of study 6) study design 7) exposure (heat wave/cold wave) 8) types of CVD 9) outcome 10) key results of articles along with the corresponding standard deviations were exploited from the selected studies.

### **Quality assessment and risk of bias**

Assessment of quality for the final studies was conducted to separate low-quality articles from others and to avoid risk of bias. Given that the low-quality studies were of high level of bias, they were all removed from this study. Quality assessment or risk of bias for all of the assessed full texts of articles was independently and critically performed by two authors through the critical appraisal skills program (CASP)<sup>19</sup>, the strengthening the reporting of observational studies in epidemiology (STROBE) tools<sup>20</sup>, and checklists.

### **Ethical Issue**

This research was completed in accordance with the ethical principles of, and was approved by, the research ethics committee of Iran University of Medical Sciences (IR.IUMS.REC. 1397.1376).

### **Results**

A total of 7631 studies were found from the scientific databases and 8 articles were identified from other sources. Firstly, 2378 papers were removed using the EndNote because of duplication. Then, 5253 papers were assessed based on titles and abstracts for eligibility and 5127 papers were excluded. Then, full texts of the 126 remained papers were reviewed. Finally, 20 papers met the eligibility criteria for including the process of systematic review after considering type of articles and quality assessment as shown in Table 1. This table reveals first author name, publication year, title, location, aim of study, study design, exposure (heat wave/cold wave), types of CVD, outcome and key results of articles. Figure 1 demonstrates PRISMA flowchart encompassing study identification and selection process. PRISMA primarily focuses on review reports evaluating the study selection process. This process includes number of records

identified through searching databases and additional documents searched through other database, records removed after duplicates,

records screened, full-text papers reviewed for eligibility, full-text papers excluded with causes, and final studies included in article.

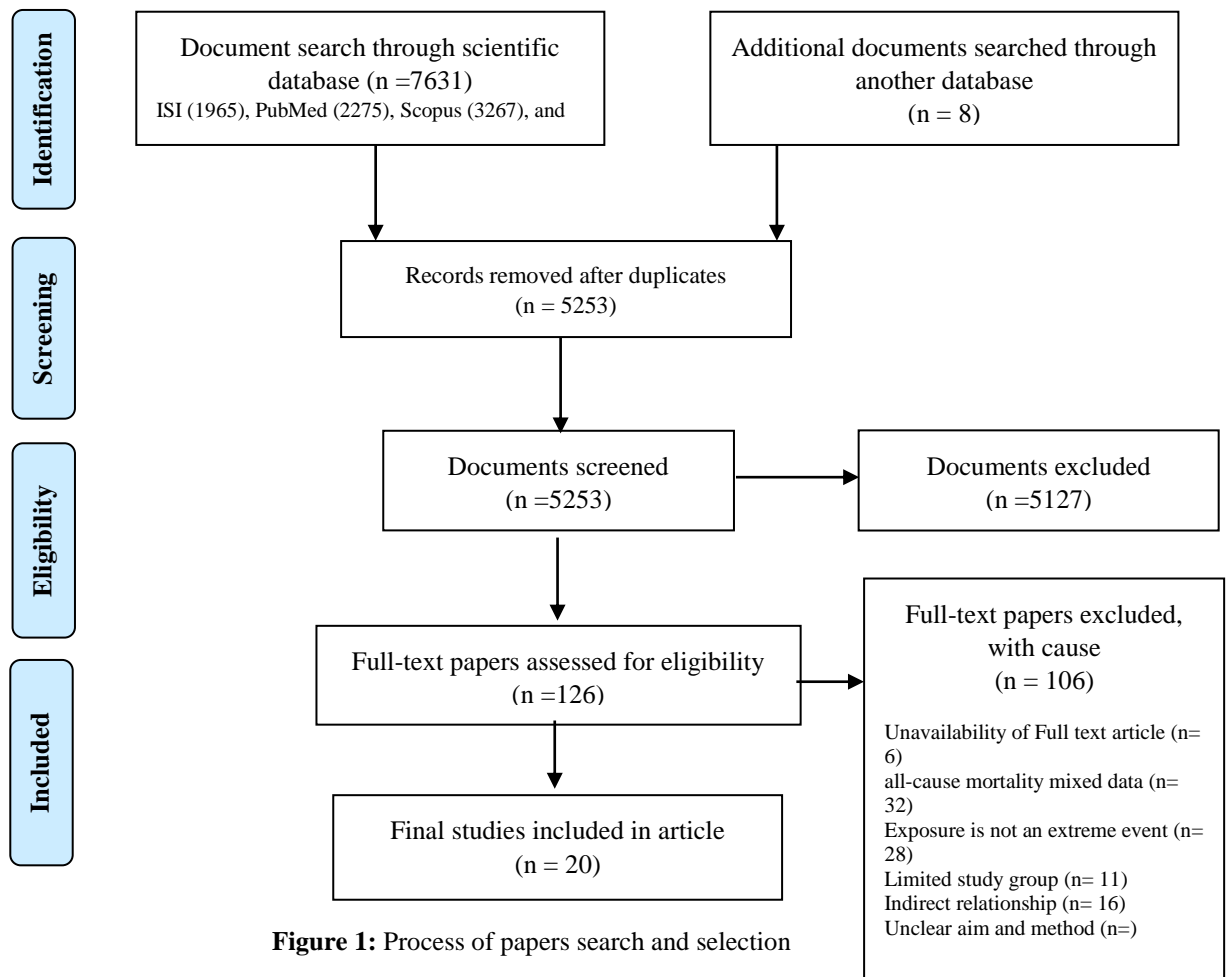


Figure 1: Process of papers search and selection

Table 1: Characteristics of the final included studies

Reference Number	First author	Year	Study methods and design	Exposure (heat wave/cold wave)	Location	Outcome	Period	Key results
[14]	A. CAGLE	2005	Cross sectional	Cold wave	USA	cardiac mortality	1980–2001	Cold waves may be a main factor in bringing on the onset of CVD, even in mild winters region. Public health measures highlighting cold exposure while out of homes may play a main role in encouraging the decrease of cold stress, especially among elderly and those already at higher risk of CVD.
[30]	Dilaveris	2006	Cross sectional	Heat and cold	Greece	MI	2001	Ambient temperature is a main factor of AMI death even in the mild weather of a Mediterranean region, its effects being predominantly evident in the older people.
[48]	Liang	2008	Longitudinal study	Heat and cold	Taiwan	acute coronary syndrome	2000-2003	A direct relationship between the daily temperature range and ACS admissions was highlighted.
[48]	Stefanie Kolb	2010	Case-crossover design	Heat and cold	Canada	Congestive Heart Failure	1984-1993	Relationship between heat waves with increases in short-term risk of CVD mortality was confirmed. But relationship between cold waves with increased risk of CVD was not found.
[31]	Krishnan Bhaskaran	2012	Case-crossover study	Heat	England and Wales	MI	2003-09	Heat waves higher of 20°C was related to increased risk of MI after 1-6 hours exposure.
[33]	Vasconcelos	2013	Poisson regression	Cold wave	Portugal	MI	2003-2007	Cold waves have no effect on acute MI.
[27]	Stefan Zacharias	2014	Time series	Heat waves	Germany	Ischemic heart diseases	2001–2010	Mortality due to IHD is associated to heat waves. But heat wave no effect on hospital admissions due to IHD.
[15]	Lubczyńska	2015	Non-linear model	Heat wave	Cyprus	Cardiovascular mortality	2004-2010	Heat waves is associated to CVD mortality in Cyprus. Therefore, proper interventions should be developed.
[54]	LingYang	2015	Cross sectional	cold	China	Blood pressure	2004-2008	Mortality due to CVD is associated to higher blood pressure.
[45]	Yue Niu	2016	Time-series	Heat and cold	China	Out-of-hospital cardiac Arrest	2008-2012	Heat and cold waves are related to high risk of OHCA in China.
[37]	Jayeun Kim	2016	Cross sectional	Heat and cold	South Korea	Cardiac arrhythmias	2008-2011	Cold and heat waves and higher DTR are associated to arrhythmia exacerbations. Thus, proper measures should be performed with aim of risk reduction for vulnerable groups to reduce cold waves exposure.

Reference Number	First author	Year	Study methods and design	Exposure (heat wave/cold wave)	Location	Outcome	Period	Key results
[52]	Lina Madaniyazi	2016	Regression model	Heat and cold	China	Blood pressure	2006-2011	Heat and cold waves were effects on the blood pressure.
[16]	Qian Yin	2017	A generalized additive model (GAM)	Heat wave	China	Cardiovascular disease mortality	2010- 2012	Heat wave is associated to mortality due to CVD in Beijing, China.
[35]	Fisher	2017	Case-crossover	Extreme heat events	USA	Acute MI hospitalizations	1960–1989	Heat and cold waves are associated to increasing of hospitalization due to AMI.
[23]	Goggins	2017	Time-series	Heat and cold	Hong Kong	HF	2002- 2011	Heat and cold wave have direct relationship with hospitalization due to heart failure in Hong Kong.
[41]	Li Bai	2017	Cross sectional	Heat and cold	Canada	Coronary heart disease	1996- 2013	Heat and cold waves are associated to increasing of hospitalization due to AMI in Ontario.
[49]	Moghadamnia	2018	Time-series	Heat and cold	Iran	ACS	2005 -2014	Heat and cold waves have direct relationship with increasing risk of ACS hospital admission in Rasht, Iran.
[53]	Dandan Xua	2019	Lag nonlinear model	Heat and cold	China	Blood pressure	2013-2016	Heat and cold waves have direct association to higher blood pressure. Thus, appropriate protective measures should be conducted during cold wave especially.
[34]	Thu Dang	2019	Time-series	Heat and cold	Vietnam	Hospital admissions for acute MI	2008–2015	Heat and cold and AMI have direct relationship in Vietnam.
[38]	Qi Zhao	2019	Case-crossover	Heat and cold	Brazil	Cardiac arrhythmia	2000–2015	Heat and cold are associated to hospitalization due to cardiac arrhythmia in Brazil.

## Discussion

The purpose of present study was to systematic review and summarize key findings related to the impact of extreme events on cardiovascular outcomes, including mortality, CVD, and hospitalization attributed to CVD. The systematic review of the 20 included publications demonstrated that extreme events play a significant role in the cardiovascular outcomes. Several studies have proved increased risk of cardiovascular outcomes, such as mortality, CVD, and hospitalization. An association between extreme events and CVD mortality was observed for cerebrovascular diseases, congestive heart failure, ischemic heart disease, myocardial infarction, cardiac arrhythmia, coronary heart disease, out-of-hospital cardiac arrest, acute coronary syndrome, and blood pressure. (Figure 2)

### ***Congestive Heart Failure***

A syndrome in which the heart is not able to pump blood sufficiently named Heart failure (HF) that causes MI and hypertension<sup>21</sup>. CHF is a disease that results in pulmonary vascular congestion and decreased heart output. CHF is a chronic status that the pumping power of cardiac muscle is affected<sup>22</sup>. One of the risk factors of CHF is weather, especially heat wave. Many papers have studied relation between extreme temperature events and morbidity, mortality, and hospitalizations raise during heat and cold waves<sup>23</sup>. Based on some studies, the mortality rate due to CHF increased significantly at ambient high temperature<sup>24, 25</sup>.

### ***Ischemic Heart Disease (IHD)***

The inadequate condition of oxygen within the heart muscles due to an imbalance between oxygen supply and demand, named IHD. This illness determined by reduced blood supply to the cardiac muscle. This event results from the obstruction in coronary arteries by atherosclerosis and thrombus<sup>26</sup>. Many research studies have shown the impact of heat wave on death due to IHD. Intensity and duration of heat waves feature stronger influences on IHD deaths. The period of heat waves has main effects on mortality. Heat waves

with a period of three days shown an average IHD mortality raise of about 10%, days during longer heat waves are related to higher death rate of up to 19%.<sup>27</sup>

### ***Myocardial infarction***

MI, or heart attack, is due to an atherosclerotic plaque rupture, leading to partial or complete thrombotic vessel occlusion<sup>28</sup>. Acute MI is one of the leading reasons of death worldwide. An MI causes impairment in diastolic and systolic function, making the patient prone to arrhythmias<sup>29</sup>. Ambient temperature is a major risk factor of AMI mortality<sup>30</sup>. Heat waves with temperature of above a threshold of 20°C to be related to an raised risk of MI 1-6 hours after exposure<sup>31</sup>. In cold weather the blood pressure decreases in the peripheral parts of the body. It increases viscosity and concentration of blood which may leading to higher clotting and, so, a greater rate of thrombosis<sup>32</sup>. Negative effects of cold wave on acute MI have been demonstrated in some studies<sup>33</sup>. Furthermore, some studies have shown that exposure to extremely high and extremely low temperature increases the rate of hospitalization due to AMI. Risks of heat waves may be different in population subgroups<sup>34, 35</sup>.

### ***Cardiac arrhythmia***

Cardiac arrhythmia is considered a major risk factor for mortality due to CVDs, especially in the older people, in whom disorder heart function may aggravate pre-existing abnormalities.<sup>36</sup>

Cardiac arrhythmias, including atrial fibrillation and flutter, are one of the types of CVDs in which the heartbeat is abnormal, very rapid, or slow. Some arrhythmias have no symptoms, and their particular reason may sometimes be unknown<sup>37</sup>. Based on recent evidence, acute exposure to heat and cold raise the possibility of cardiac arrhythmia, which is mainly due to paroxysmal tachycardia and other cardiac arrhythmias<sup>38</sup>. Also, emergency department (ED) visits due to arrhythmia is strongly related extreme ambient temperature. Arrhythmia-related emergency department visits decrease during fall and winter<sup>37</sup>.

**Coronary heart disease**

CHD is one of the types of CVD that creates when the arteries of the cardiac cannot transfer sufficient oxygen-rich blood to the cardiac. CHD is developed by the buildup of plaque, a waxy substance, inside the lining of larger coronary arteries. This buildup can partially or totally block blood flow in the large arteries of the cardiac<sup>39, 40</sup>. Risks of CHD hospitalizations with both heat and cold waves were investigated and confirmed<sup>41</sup>. Also, there are limited epidemiological studies quantifying the ambient temperature-related burden of CVD death, especially CHD<sup>42</sup>.

**Out-of-hospital cardiac arrest**

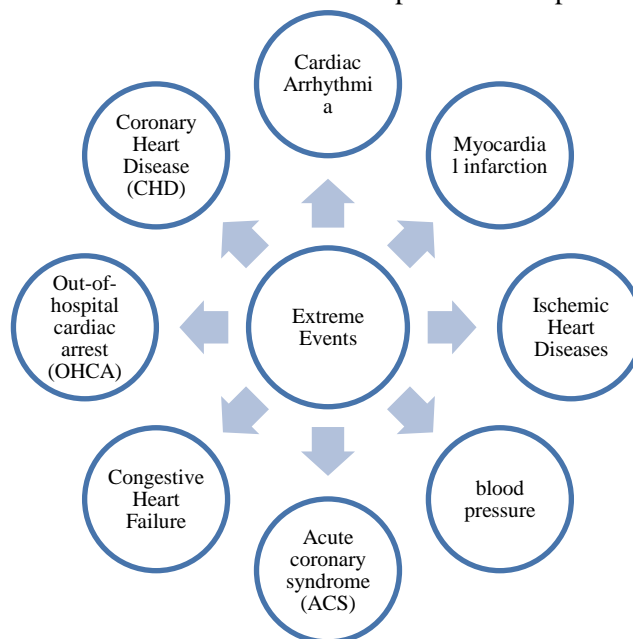
OHCA is considered an important global human health challenge. The loss of mechanical heart function and the absence of systemic circulation are described as OHCA<sup>43</sup>. Cessation of cardiac mechanical activity that occurs outside of the hospital is named OHCA and is approved by the absence of symptom of circulation<sup>44</sup>. The potential effects of seasonal variation and ambient temperature on OHCA were investigated<sup>45</sup>. Some studies have shown that both cold and heat waves were significantly related to raised hospital emergency admission and death due to OHCA<sup>45</sup>.

**Acute coronary syndrome**

ACS is one of the types CVD and leading numerous mortalities globally. ACS often shown a level of destruction to the coronary arteries by atherosclerosis; plaque rupture, thrombosis, and inflammation<sup>46, 47</sup>. There was a significant seasonal fluctuation in the rate of ACS, and extreme ambient temperature may affect the onset of ACS<sup>48</sup>. Ambient temperature range associated significantly with daily emergency hospitalization due to ACS<sup>48, 49</sup>. Diurnal ambient temperature fell below 17.0°C or the diurnal temperature range exceeded a threshold of 5.8°C. The risk level of ACS was higher than baseline data<sup>48</sup>.

**Blood Pressure**

Hypertension or blood pressure is one of the most important risk factors for CVD and is a one of the main causes of precocious death globally. Blood pressure is a crucial medical status that significantly raises the risks of heart, brain, kidney, and other illness. Based on the estimation of the WHO 1.13 billion people worldwide have hypertension<sup>50</sup>. Cold wave leading to vasoconstriction and tachycardia, both of which contribute to raised blood pressure and heart load<sup>51</sup>. Several studies have confirmed that blood pressure changes with temperature and extreme ambient temperature imparts a very short-term impact on blood pressure<sup>52-54</sup>.



**Figure 2:** Cardiovascular outcomes due to extreme ambient temperature



### **Recommendation and measures**

CVD patients should be made aware of the raised risk of ambient temperatures. Health system especially, hospitals and emergency department should take into account the raised load of patients and demand of specific facilities during heat and cold waves<sup>48</sup>. Timely protective measures and adaptation strategies, such as identification of susceptible populations to heat-related CVD, using air conditioners in summer, avoiding outdoor activities, wearing light clothing, adequate hydration, development of heat shelters, also a well-developed early warning system and emergency service seem to decrease the burden of CVD outcomes<sup>15, 49, 53</sup>. Public information of impending cold waves, may be a way to encourage people especially vulnerable group, including the elderly and people with underlying heart disease to dress warmly<sup>55</sup>. The outcomes of heat and cold waves could be concerned in mass media and social media weather predicates when improper status is possible. Recommendation and warning on preventive behavior change should be given to CVD patients, before and during heat and cold days<sup>41</sup>.

### **Conclusion**

The present systematic review demonstrated the impact of extreme ambient temperature on CVD outcome, including mortality, morbidity, and hospital admission. According to the results, extreme ambient temperature had a significant association to the CVD outcomes. Moreover, heat exposure and extreme ambient temperature, including cold and heat waves were related to a raised risk of CVD. Through identification of these effects, measures and strategies can be developed to have an impact on this major global health challenge. This comprehensive systematic review study presents a potential adaptation and preventive strategies for the relationship with extreme weather on CVD, and can also be used in the prevention of CVD due to ambient temperature. The results of this research can help policy-makers and administrators in developing standards for cold and heat waves, conduct

necessary prevention, mitigation and preparations, developing more exact heat alarms, and taking activities to prevent or decrease temperature-related mortality and morbidity, to ultimately contribute to better human health.

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### **Conflict of interest**

The authors declare that there is no competing interest.

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