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Association of heat and cold waves with cause-specific mortality in Iran: a systematic review and meta-analysis

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Despite the frequent occurrence of heat waves in the Middle East, there is a lack of evidence regarding the overall estimates for the effect of heat waves on mortality in this region. This study aimed to review the effect of exposure to heat and cold waves and daily cause-specific mortality. Four electronic databases were searched. The titles, abstracts, and full-texts of the articles were carefully reviewed by two researchers. Once eligible studies were identified, the required data were extracted. Separate meta-analyses were conducted based on gender, age group, and health endpoint combinations. According to the meta-analysis, heat waves had a statistically significant effect on all-cause mortality with an RR of 1.23 (CI 95%: 1.08, 1.39). Cardiovascular mortality significantly increased in heat waves with an RR of 1.08 (CI 95%: 1.05, 1.10). However, the increase in respiratory mortality was not statistically significant. Compared to young people (age < 65 years old) and women, elderly and men were more vulnerable to heat waves with RRs of 1.31 (95% CI: 1.05, 1.57) and 1.33 (95% CI: 1.08, 1.58), respectively. This study can be beneficial in developing response or adaptation plans for heat waves. Future studies should focus on other specific health endpoints like ischemic heart disease, chronic obstructive pulmonary diseases, etc., and other outcomes such as hospitalization and emergency visits.

Keywords Heat wave, Temperature, Death, Climate change, Public health, Abnormal temperature

Extreme weather conditions are defined as weather events that are significantly different from the average, usual weather patterns[1,2]. They can include heat waves, cold wave, droughts, floods, wildfires, and hurricanes. Extreme weather conditions can cause widespread injuries, adverse health outcomes, and loss of life[1]. A heat wave (HW) is a period of abnormally hot weather, which may be accompanied by high humidity. There is no standard definition for heat waves, since various studies apply different criteria to identify these events[3]. Heat waves can occur in any climate, but they are more common in hot, dry climates. Climate change is causing an alteration in long-term weather patterns leading to increased frequency and intensity of heat waves around the world[4]. The number of heat wave days is expected to increase by 4–34 days per season for every °C of global warming[5]. If the temperature increases by 5 °C, some tropical regions could experience up to 120 extra heat wave days per season[5]. The intensity of heat waves is generally expected to increase by 0.5–1.5 °C above a given global warming threshold, but this increase is higher over the Mediterranean and Central Asian regions[5]. Between warming thresholds of 1.5 °C and 2.5 °C, the return intervals of intense heat waves are expected to reduce by 2–3 fold. Heat wave duration is projected to increase by 2–10 days per °C, with larger changes over lower latitudes[5].

HWs can have serious health impacts on humans. They can cause dehydration, heat exhaustion, and heat stroke[6–8]. The elderly, children, and people with pre-existing medical conditions are particularly vulnerable

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to the effects of heat waves[4]. According to a study in US, heat waves are associated with an increased risk of mortality. The study found that for every 1 °C increase in temperature above a threshold temperature (defined as the 95th percentile of daily mean temperature), there was a 3.74% increase in mortality risk[9]. Another study investigated the associations between heat waves and daily hospital admissions for cardiovascular (CVD) and respiratory (RD) diseases in Vietnam. Associations between hospital admissions for respiratory diseases and heat waves were observed at lag-day 2, with excess risk (ER = 8.31%, 95% CI 0.64, 16.55%)[10]. In another study on mortality, heat waves were associated with a 5% increase in all-cause mortality compared to deaths on non-HW days[11].

Cold waves (CWs), described as rapid and prolonged temperature reductions, present a complex interaction with climate change that is intricate and region-dependent[12]. Although a warming planet might imply fewer cold extremes, research has shown that climate change can potentially weaken the polar vortex, a low-pressure area located in the polar regions, causing severe cold waves[13]. Conversely, certain areas might experience a decrease in cold wave frequency and intensity due to an overarching warming trend[14]. Predicting future cold wave trends remains uncertain due to the complexities of atmospheric dynamics and climate change influences[14]. However, many climate models anticipate fewer cold waves with increasing global temperatures[15].

Exposure to prolonged cold can lead to hypothermia, frostbite, cardiovascular complications, and respiratory problems[16,17]. In some cases, these complications can be severe, leading to increased morbidity and mortality rates during cold wave periods[16]. Comparatively, while both cold and heat waves pose significant health threats, some studies suggest that cold waves may have a greater impact on mortality rates than heat waves[18]. Cold weather conditions often last longer, potentially leading to more persistent health effects than shorter-lived heatwaves[19]. Additionally, certain populations may be better equipped or acclimated to deal with extreme heat rather than cold although this ability may vary across different geographic and demographic contexts[20]. Thus given this likely variability, it is important to develop region-specific public health measures to combat extreme temperature events.

Iran is located in the Middle East and Western Asia. This country mainly consists of arid and semi-arid areas. Previous studies have indicated a high frequency of heat and cold waves in Iran[21]. Since these episodes are likely linked to climate change, the future situation will likely worsen. Iran is one of the countries in the Middle East and North Africa region to be most affected by climate change[22]. Another study predicted that Iran will experience increase temperatures and decreased precipitation in the future due to climate change[23]. These shifts could produce more frequent and severe droughts, water shortages, and heat waves in the country.

Some studies about the effect of heat and cold waves on mortality have been previously conducted in Iran[21,24]. They only investigated one city. Therefore, no overall estimate of the effect of heat waves on mortality is currently available for Iran. Similar gaps in knowledge exist in other Middle Eastern countries[25,26]. Due to the uncertainty of the results related to the effect of heat waves on human health and the lack of sufficient studies in Iran and other Middle Eastern countries, conducting a study to pool the results of studies on the association between heat and cold waves and mortality could be beneficial for the whole region. The outcome of such a study quantifies the likely health burden attributed to heat and cold waves, and helps policy-makers to prepare programs to reduce exposures during these events.

This systematic review and meta-analysis study was designed to review all the studies conducted in Iran regarding the effects of short-term exposure to heat and cold waves on daily cause-specific mortality.

Materials and methods

Search strategy

Four electronic databases namely Scopus, PubMed, Web of Science, and Embase, were searched on October 4th, 2022 to identify the relevant documents. Documents of interest were peer-reviewed articles investigating the effect of heat waves (HWs) and cold waves (CWs) on mortality due to any cause of death. The keywords used for the systematic search included "heatwave*", "coldwave*", "warm spell", "cold spell", "hot wave", "extreme temperature", "extreme weather", "temperature", "weather", "climate", "season", "heat", "wet bulb", "mortality", "death", "health effect", "years of life lost", "life expectancy", "YLL, "hyperthermia", "heat stroke", "thermal stress", and "Iran". The complete list of keywords is provided in the Supplementary Materials. The search was limited to the title, abstract and keywords of documents published in English. After the searches in the four databases, all results were pooled, and duplicate records were removed.

Screening and selection of studies

In this study, we aimed to collect evidence about the effect of heat and cold waves on cause-specific mortality in Iran. A systematic process including search in online databases, screening, assessing eligibility, data extraction, and meta-analysis was followed (Fig. 1).

The title, abstract and full-text of articles were carefully reviewed by two independent researcher. Disagreements were resolved upon discussion or a third party decision. The studies having following criteria were included in this study: (1) original peer-reviewed articles, (2) quantitative observational studies, (3) investigating the general population or a hospital population representative for the whole community, (4) investigating mortality due to any cause of death based on the International Classification of Diseases (ICD), 9th or 10th revision, (5) investigating at least one city of Iran, and (6) investigating heat and cold waves with any definition, since there is no standard definition of these episodes, and (7) having a time-series design, case-crossover design, case control design or a single episode analyses.

The exclusion criteria were as follows: (1) review articles, books, proceedings, etc. (2) qualitative studies, (3) investigating other health outcomes rather than mortality such as hospitalization, and (4) investigating the seasonal effects of temperature, not the HW and CW.

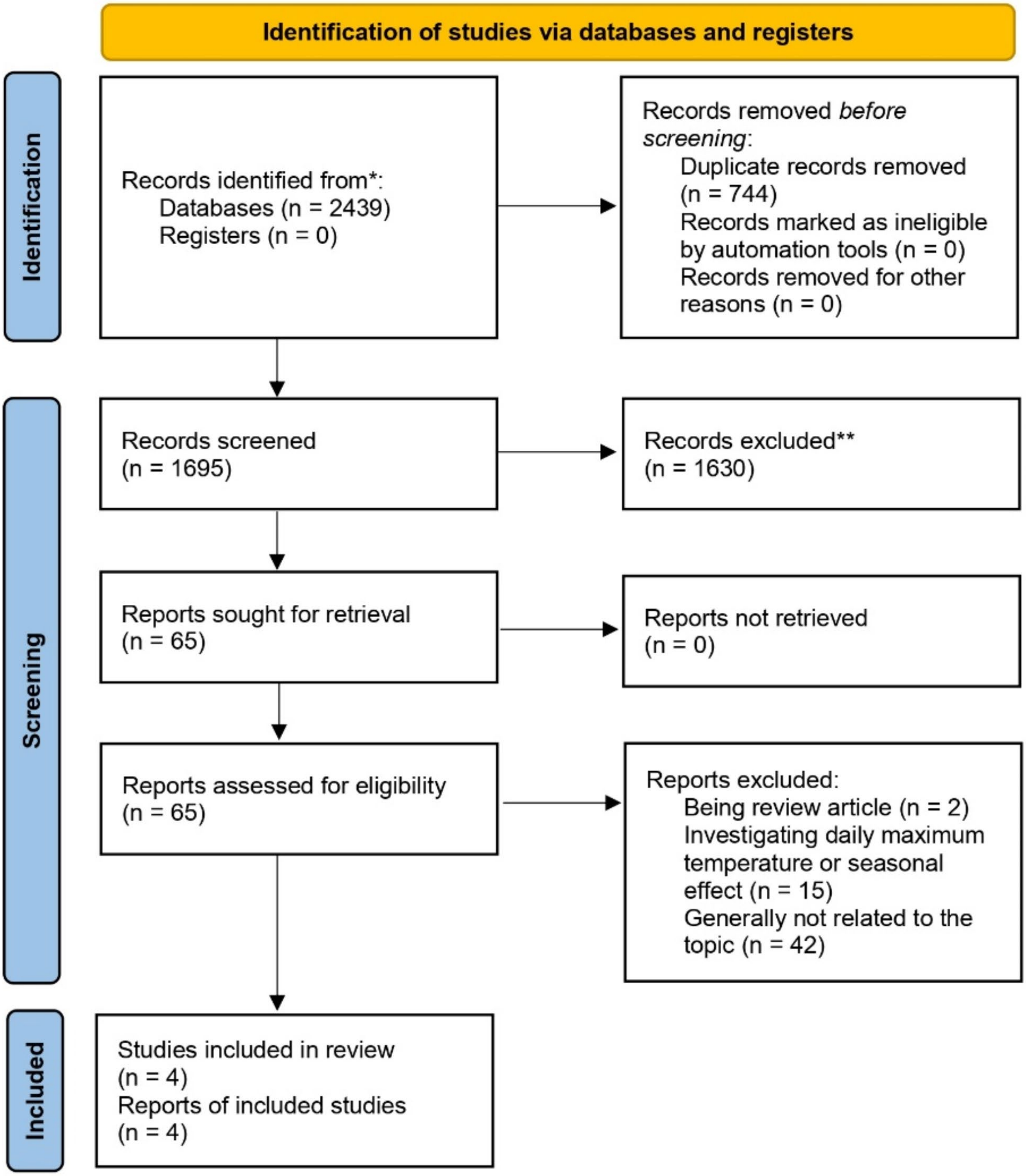

Fig. 1. PRISMA diagram of the systematic review.

The systematic process including search in online databases, screening, assessing eligibility, data extraction and meta-analysis was followed is shown in Fig. 1.

Data extraction

Once the eligible studies were identified, the data were extracted from them. This information included first author, publication year, cities studied, study duration, gender group(s), age group(s), sample size, definition of HW/CW used in the study, statistical model, model specification, health endpoint(s) of interest, lag-day, type of risk measure, value of risk measure (and its 95% confidence intervals), and model adjustments.

Assessment of risk of bias

The risk of bias in individual studies was evaluated using a rating tool developed by the Office of Health Assessment and Translation (OHAT) and modified by Dimitrova et al. to be suitable for time-series environmental health study designs. The rating tool consisted of seven domains, including selection, confounding, exposure assessment, outcome assessment, selective reporting and other bias (appropriateness of statistical methods). Each article was rated based on each of the seven domains as definitely low, probably low, probably high, and definitely high. As mentioned by Dimitrova et al., a conservative approach has been followed in developing this tool since it tends to report a high risk of bias in case of inadequate information in any specific domain[27]. Two independent reviewers assessed the risk of bias. In case of conflicts, a third impartial person was asked to adjudicate.

Meta-analysis

Separate meta-analyses were considered based on the gender, age group, and health endpoint combinations with at least three studies. Finally, seven sets of meta-analyses were conducted, including for (1) both genders, all ages, all-cause mortality, (2) both genders, all ages, cardiovascular mortality, (3) both genders, all ages, respiratory mortality, (4) females, all ages, all-cause mortality, (5) males, all ages, all-cause mortality, (6) both genders, people aged < 65 years, all-cause mortality, and (7) both genders, people aged 65 years and older, all-cause mortality.

Some studies had reported several risk estimates mainly due to considering various lags and different HW definitions. In this case, only one risk estimate was selected from each study and entered the meta-analysis. For selecting the risk estimate, we followed the procedure previously applied in the meta-analysis of time-series studies[28,29]. To select one risk estimate from each study, the most statistically significant estimate or the largest estimate were chosen.

Relative risk (RR) was chosen as the risk measure of interest. Therefore, results of studies reported in other measure types were converted to RR. For this, percent change in mortality were converted to RR using this equation:

$$\mathrm{RR} = 1 + (\text{percent change}/100).$$

STATA v.17 (STATA Corp., College Station, TX) was used for the meta-analyses. First, the inconsistency index (I^2) test was estimated to explore the heterogeneity across the studies. The I^2 statistic estimates the percentage of total variation across studies due to heterogeneity rather than chance[30]. In our study, when I^2 exceeded 50%, a random effect model using the Sidik–Jonkman method was used; otherwise, a fixed-effect model was applied. Funnel plot and Egger test were used to evaluate the publication bias. A significance level of 0.05 was set in all analyses.

Results

Qualitative assessment

From a total of 1695 unique documents found, 65 articles were assessed for eligibility and four were included in the qualitative and quantitative evaluation. Table 1 presents the characteristics of the studies included in our systematic review. From a total of 1695 unique documents found, 65 articles were assessed for eligibility and four were included in the qualitative and quantitative evaluation. Each study evaluated one specific city. Three out of these four studies had focused only on HWs, but Sharafkhani et al. investigated both HWs and CWs[24].

As can be seen in Table 1, the study durations span from 6 to 13 years. Maximum sample size of studies ranged from about 1100 to 46,000 people. All studies investigated the effect of HWs on males, females, and both genders in aggregate. Also, all studies had reported age-specific estimates in addition to the overall estimates for all age groups. Cause-specific mortality was all-cause, cardiovascular, respiratory, and cerebrovascular mortality. The variables adjusted in the statistical models were mainly air pollutants, meteorological parameters, day of week, holidays, seasonality, and long-term trends. Results of the risk of bias assessment are presented in Table S2 (Supplementary Materials). No significant risk of bias was found in the studies.

Only four studies were found that attempted to assess the association of HWs with mortality. This result shows that research in this field needs to be expanded by future studies. However, these four studies had an appropriate geographical distribution across Iran, covering all main areas of the country and different climatic zones. While Tehran is located in central Iran, Kerman with a hot and dry climate is in the southeastern part of

Author	Cities	Years	Gender	Age group	Sample size	Health outcome	Lag-day	Risk measure	Adjustment*
Aboubakri et al. (2019)	Kerman	13	Both, male and female	All, < 65 and > 65 years	46,200	All-cause	0–14	RR	SO_2, PM_{10}, O_3, day of week, holidays
Ahmadnezhad et al. (2013)	Tehran	11	Both, male and female	All and > 65 years	1069	All-cause, CVD, respiratory, and cerebrovascular	0	RR	Ozone, PM_{10} and $PM_{2.5}$
Sharafkhani et al. (2020)	Urmia	6	Both, male and female	All, < 64, 65–74, > 75 years	12,702	All-cause, CVD, respiratory	0 to 0–30	Excess risk (%)	NO_2, PM_{10}, SO_2, RH, WS, season, time, DOW, holidays
Aghababaeian et al. (2023)	Dezful	7	Both, male and female	All, < 14, 15–64, 65–74, > 75	13,441	All-cause, CVD and respiratory	0 to 0–13	Excess risk (%)	Time, season, DOW, holiday, PM_{10}, $PM_{2.5}$, RH

Table 1. Characteristics of studies included in our systematic review. *DOW* day of the week, *RH* relative humidity, *WS* wind speed.

the country. Urmia with cold and humid and Dezful with hot and humid climates are located in the northwest and southwest areas of Iran, respectively. Cheng et al. conducted a global systematic review of the studies investigating the cardiopulmonary effects of HWs and identified 54 studies conducted in 20 countries[3]. At the time of Cheng et al.'s study, only one relevant article had been published from Iran, i.e. Ahmadinezhad et al.[21]. Dimitrova et al. found five studies investigated the effect of HWs on health in Southern Asia, and declared that studies were limited geographically, with half of the countries in the region not represented and two countries covered by only one study[27].

Risk of bias

Results of the risk of bias assessment are presented in Table S2 (Supplementary Materials). No significant risk of bias was found in the study.

Effect of HWs on cause-specific mortality

Figure 2 illustrates the overall RRs related to the effect of heat waves on all-cause, CVD and respiratory mortality. In case of the all-cause and respiratory mortality, the heterogeneity between the studies were high enough to perform a random-effect model ($I^2 > 50\%$). In addition, funnel plots and Egger test showed that there is publication bias for all-causes mortality ($p < 0.05$) (Supplementary Materials). According to the results of the meta-analysis, heat waves had a statistically significant effect on all-cause mortality with an RR of 1.23 (CI 95% 1.08, 1.39), indicating that mortality rate is increased by 23% during heat waves compared to normal days in Iran. Cardiovascular mortality significantly increased in heat waves with an RR of 1.08 (CI 95% 1.05, 1.10). However, although the increase in respiratory mortality was positive, it was not statistically significant (1.09; CI 95% 0.84, 1.34). This result suggests that cardiovascular diseases are more affected by heat waves than respiratory outcomes.

Our findings are generally consistent with previous studies in other countries. Dimitrova et al. pooled the estimates reported from studies conducted in South Asia on the association between HWs and mortality. They found a statistically significant association at higher temperatures, i.e., above 31 °C and 34 °C[27]. Cheng et al. conducted a meta-analysis on heat waves and cardiorespiratory outcomes, reporting significant associations with cardiovascular mortality (RR: 1.149, 95% CI 1.090–1.210) and respiratory mortality (RR: 1.183, 95% CI 1.092–1.282). These associations varied by countries and studies, indicating an average increase of 15% in cardiovascular and 18% in respiratory mortality during heat waves[3]. However, these estimates are based on studies conducted in multiple countries.

Because many climatic, demographic, and socioeconomic parameters which are involved in the relationship between HWs and health outcomes vary from one country to another[31]. Mason et al. assessed all the evidence on the health effects of HWs in Australia from a health service demand point of view. Significant associations were found for hospital admission, emergency department visits, ambulance call outs, and mortality due to exposure to heat waves. In case of mortality, death due to CVD, nervous system, mental and behavioral disorders and diabetes were statistically associated with HWs[32].

Previous studies have shown that extended exposure to high temperatures could lead to acclimation, and thus reduce the risk of HWs[33]. In our study, stronger associations of HWs with mortality were found in cities with lower mean temperatures on normal days. The RRs for all-cause mortality in Kerman (1.45; 95% CI 1.13, 1.76) and Urmia (1.31; 95% CI 1.00, 1.61) were higher than in Dezful (1.29; 95% CI 1.08, 1.50)[24,34,35]. However, the average temperatures in Kerman (17.32 ± 8.87 °C) and Urmia (11.8 ± 9.6 °C) were lower than in Dezful (24.6 ± 9.3 °C). Similar patterns were observed in the case of CVD and respiratory mortality, where RRs in Dezful were lower than those reported in Tehran and Urmia which had lower average temperatures[21].

In a study in Italy, Conti et al. reported mortality rates during the 2003 summer heat wave in 21 different regions of this country. They found that areas in northern Italy were at higher risk of being affected by HWs. For example, the elderly mortality rate was highest in Turin (44.9%), Trento (35.2%), Milan (30.6%), and Genoa (22.2%), which are generally known for colder weather than areas further south. The authors hypothesized that since hot weather in the aforementioned cities is less common, thus, the inhabitants are less likely to be tolerant to the high temperatures[36].

Effect of CWs

Sharafkhani et al. found no significant correlation between cold waves (CWs) and respiratory or cardiovascular mortality. However, when considering the other effects, there was a notable decrease in the risk of non-accidental death during the initial lag days (days 0–2) of a cold wave event (cumulative excess risk = − 19 (95% CI − 35, − 2))[24]. However, numerous other studies have reported increased rates of respiratory and cardiovascular-related mortality during cold waves[16,37]. The difference in findings may be attributed to various factors including differences in study design, geographical location, demographic profiles, and the definition of cold waves[38].

The observed decrease in non-accidental deaths could be due to a short-term displacement effect, often referred to as "harvesting". This effect suggests that some of the individuals most vulnerable to cold wave conditions may die in the initial stages, leading to an apparent reduction in mortality rates immediately after the onset of cold weather[18]. It is also plausible that the prompt implementation of public health measures and emergency responses to extreme cold weather could play a role in the observed reduction in non-accidental deaths[19]. Further research is needed to fully elucidate these complex relationships and potential mitigating factors.

HWs and modifying effects of age

Figure 3 presents the results of association between exposure to heat waves and death due to all causes in people aged less than 65 years and elderly people (≥ 65 years old). Significant heterogeneity was found between the

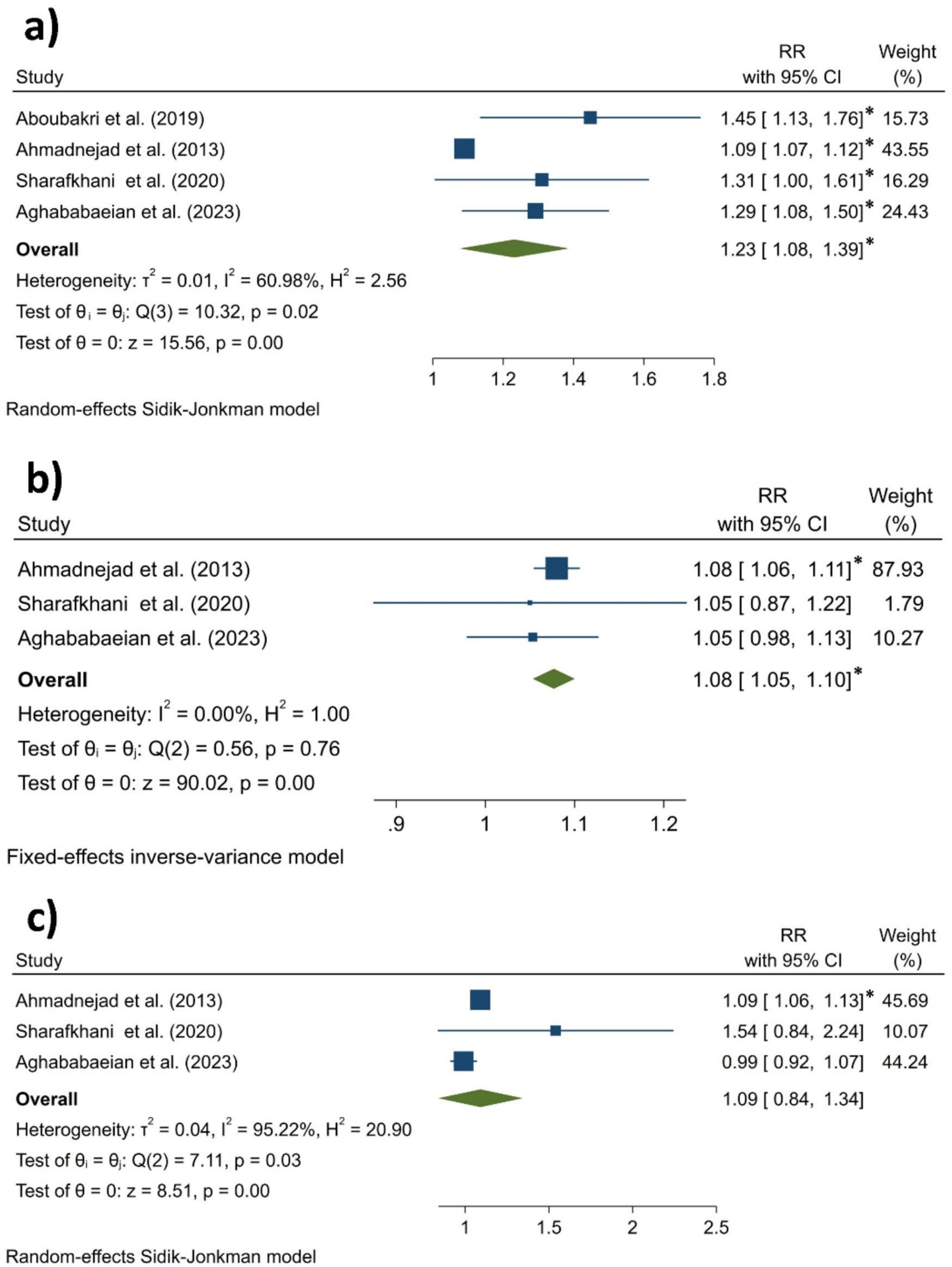

Fig. 2. Meta-analysis results regarding the effect of heat waves on (**a**) all-cause mortality, (**b**) cardiovascular mortality, and (**c**) respiratory mortality (asterisks indicate statistical significance at 0.05 level).

results reported for > 65 years old people. Also, publication bias was found in the case of both sets of meta-analyses (Supplementary Materials). Heat waves had a positive but not significant effect on people aged < 65 years (RR: 1.07; 95% CI 0.90, 1.25). However, the effect of heat waves on elderly was statistically significant with a high RR of 1.31 (95% CI 1.05, 1.57). This result indicates that heat waves in Iran affect older individuals more than the younger age groups. Also, heat waves increase the average death rate in elderly by 30% compared to normal days.

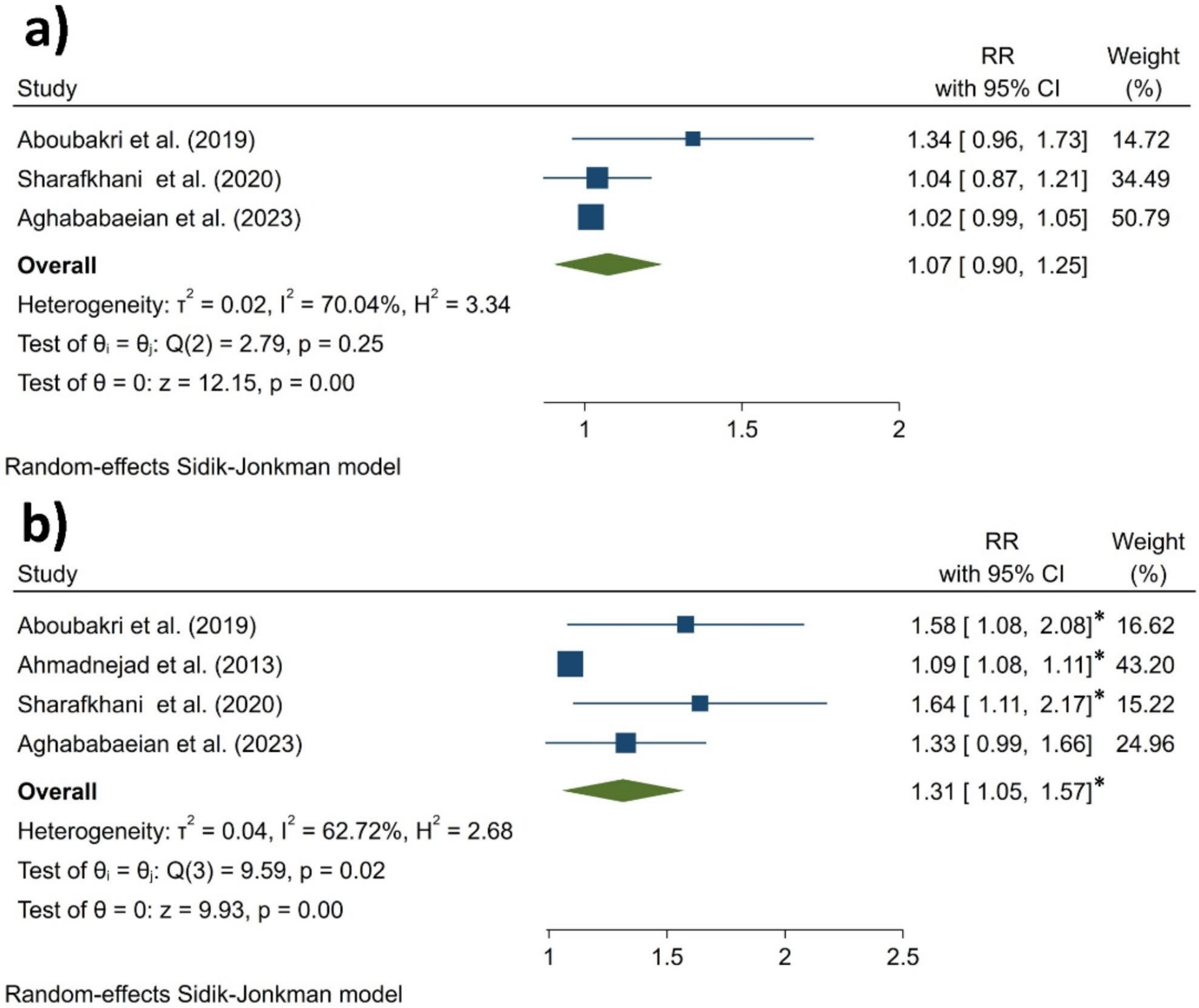

Fig. 3. Meta-analysis results regarding the effect of heat waves on all-cause mortality among (**a**) people aged < 65 years, and (**b**) elderly people (asterisks indicate statistical significance at 0.05 level).

Our results are consistent with previous studies. Cheng et al. reported HWs were directly associated with CVD mortality among young people (RR: 1.03; 95% CI 0.98, 1.09) and elderly (RR: 1.20; 95% CI 1.08, 1.32). However, the association was only significant for the elderly[3]. Similar effects were found for respiratory mortality, where the relative risks for young and old people were 1.29 (95% CI 0.85, 1.95) and 1.33 (95% CI 1.16, 1.53), respectively[3]. These results indicate that elderly people are more affected by heat waves on a global scale. Similar findings have been reported in other studies[27,39,40]. One major reason for higher mortality rates in older people is that pre-existing health conditions are very common among this age group making them more vulnerable such that exposures to even short periods of heat can aggravate their health conditions by worsening disease-specific symptoms[41]. This information can be of practical benefit to health authorities when informing the public on upcoming HWs. However, Kaltsatou et al. declared that although current advances in technology permit scientists to predict HWs and enable health agencies to alert the public with heat advisories, the number of HW-related deaths remains high. The explanations for these increased deaths remain uncertain[33].

HWs and modification effect of gender

The effect of heat waves on all-cause mortality among females and males is presented in Fig. 4. Significant heterogeneity was found among the results of the reported studies. Also, publication bias was found only for studies reporting effects in women (Supplementary Materials). The results indicated a gender difference in the effect of HWs on mortality. While HWs had an insignificant association with all-cause mortality among women with an RR of 1.14 (95% CI 0.95, 1.33), the same exposure led to a significant increase in mortality in men (1.33; 95% CI 1.08, 1.58). This result implies that men are more affected by the HW episodes than women in Iran.

Other studies have also investigated the vulnerability of HWs. In a 2019 global assessment, positive and protective impacts of HWs on CVD mortality were observed among men and women, respectively. However,

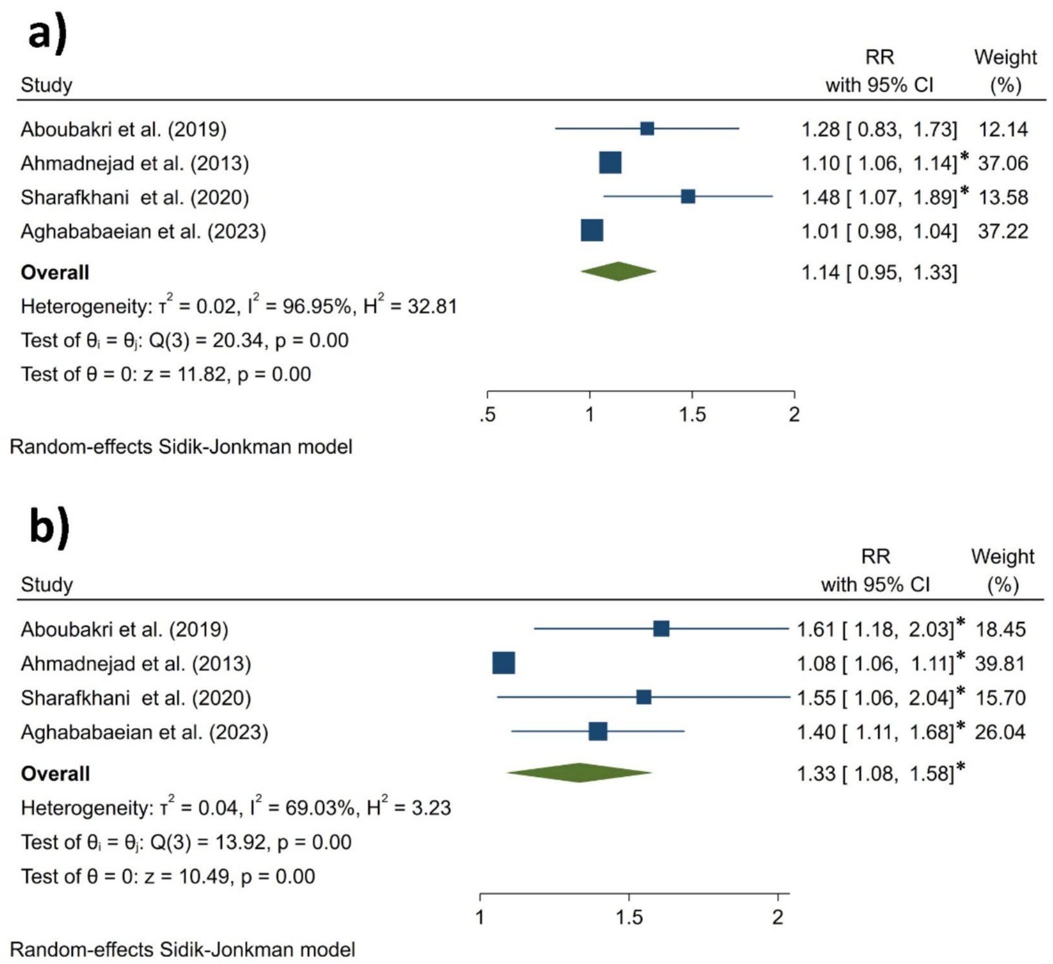

Fig. 4. Meta-analysis results regarding the effect of heat waves on all-cause mortality among (**a**) women, and (**b**) men (asterisks indicate statistical significance at 0.05 level).

both associations were statistically insignificant[3]. In the study by Ingole et al., an increase in total mortality was observed among men at lag 0 days (RR = 1.38; CI 1.05–1.83), which was higher than that for women[42]. These results contradict the findings of Navas-Martín et al. In a comprehensive review of gender differences in the effect of heat waves in Spain, they found that despite some evidence of greater minimum mortality temperature (MMT) in men especially in the case of CVD, and circulatory and respiratory mortality, the body of evidence suggested that women were more vulnerable to the heat exposure[43]. The physiological reasons may be lower heat loss from evaporation through sweat, a greater presence of adipose tissue (body fat), and decreased peripheral blood perfusion in women. These conditions could be intensified after menopause[44]. However, physiological differences cannot be the only reason for any gender difference, and cultural, socioeconomic, climatic, and demographic factors may also be involved[43,45].

Strengths and limitations
The strength of this study is that it is the first systematic review in the Middle East to evaluate the effect of HWs and CWs on mortality. Second, the overall estimates obtained from the meta-analysis should be beneficial for quantifying the health burden attributed to HWs in Iran. Also, the patterns found can be applied in preparing any emergency responses or adaptation plans against these events.

This study also has some limitations. First, the number of articles included in the quantitative analysis was very limited. However, obtaining the overall estimates even based on a few studies is more beneficial than not having any estimates at all. Second, the meta-analysis was only conducted on all-cause, total CVD, and total respiratory mortality. Other causes of death could also provide valuable insights too. Finally, only one study was retrieved for cold waves in which it was reported that cold waves have higher rates of adverse health outcomes. Additional studies are needed and should consider the effects of both hot and cold waves on health.

Conclusions
In this study, articles reporting the health consequences of heat and cold waves in Iran were systematically identified, and their results were pooled to obtain overall estimates. The results showed that HWs significantly

increased death due to all causes and cardiovascular diseases, but not respiratory mortality. These results indicate that HWs impose significant health and economic burdens on Iran. Therefore, measures should be employed to reduce public exposure to anomalous temperatures during the HWs. Specifically, people aged over 65 years and men were more vulnerable to heat waves. These findings can provide practical implications for developing response or adaptation plan to mitigate the effects of these events. Future studies could focus on specific health endpoints like ischemic heart disease, chronic obstructive pulmonary diseases, etc. and other outcomes such as hospitalization and emergency calls and visits as well as expanding work on cold periods.

Data availability

The authors confirm that the data supporting the findings of this study are available within the article and its supplementary materials.

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Author contributions
MH and AO participated in all stages of the study. PKH participated in conceptualization, methodology, supervision, validation, and roles/writing. HA and SF participated in methodology, investigation, software, visualization, and roles/writing. MHF participated in review and editing.

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Declarations

Competing interests
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