Journal of Thermal Biology 82 (2019) 76–82

Contents lists available at ScienceDirect

Journal of Thermal Biology

journal homepage: www.elsevier.com/locate/jtherbio

Attributable risk of mortality associated with heat and heat waves: A time-series study in Kerman, Iran during 2005–2017

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ARTICLE INFO

Keywords:
Heat
Heat wave
Mortality
Attributable risk

ABSTRACT

The association between heat or heat waves and mortality should often be reported in a way that makes it sensible by health policymakers. In this study we aimed to assess the effect of heat and heat waves on mortality using attributable risks during 2005–2017. Nine heat waves were defined using a combination of severity and duration of mean daily temperature. Heat wave effects were assessed using added and main effects. Added effects were assessed as a binary variable and main effects were assessed by comparing the median temperature (in heat wave days) to Minimum Mortality Temperature (MMT). The effects of heat, mild heat and extreme heat on mortality were also assessed. Distributed Lag Non-linear Models were used to assess the relations in a bi-dimensional perspective in which the quadratic b-spline was chosen as the basis function for the dimension of the exposure and the natural cubic b-spline was chosen for lag dimension. The backward perspective was used to estimate the attributable risks. The total mortality attributed to non-optimal temperatures for all days was 1.91% (CI 95%: -6.36, 8.47). The attributable risks (AR) were 2.23%, 2.02% and 0.25% for heat, mild heat and extreme heat days, respectively. AR was more for females and the above 65 years old groups than other groups in heat, mild heat and extreme heat days. While the stronger heat waves defined based on temperature above the 95 and 98th percentile had a significant attributable risk for total mortality in the added effects; the weaker heat waves (defined based on temperature above of the 90th percentile (HW1, HW2, HW3) had higher attributable risks, significant for HW1 and HW2, in the main effects. Apparently weaker heat waves show more immediate effects, while stronger heat waves increase mortality over several days.

1. Introduction

Increasing mortality due to weather conditions has become a public health concern. Heat is one of the important factors affecting human mortality in many countries (Dadbakhsh et al., 2017; Deng et al., 2018; Kalankesh et al., 2015; Sharafkhani et al., 2017). Several studies have assessed the effect of heat on mortality using modern time series analysis (Stafoggia et al., 2006; Zheng et al., 2018; Zhong et al., 2018; Miao et al., 2017). An immediate effect of heat on mortality has been shown in many studies and some subgroups are more vulnerable. For example a multicity study in Italy found higher heat-related mortality for women than men (Stafoggia et al., 2006). Also some epidemiological evidence have shown that elderly people are more at risk than younger people (Ishigami et al., 2008).

One of the extreme weather events is heat waves, that are likely to become more frequent and more intense in the coming decades (Song et al., 2018; Sharafkhani et al., 2019; Aboubakri et al., 2018). Also human heat related mortality has increased with global warming (Pachauri et al., 2014; Dadbakhsh et al., 2018; Sharafkhani et al., 2018). Previous research have studied the effects of heat in two manners: the "main and the added effect". The former is the independent effect of daily temperature levels that is estimated by the usual exposure-response function from the temperature-health relation including both heat wave and non-heat wave days, while the latter is the added risk due to the duration of sustained heat for some consecutive days that is commonly estimated by an indicator (Chen et al., 2015; Gasparrini and Armstrong, 2011).

It is important to report the association between heat or heat wave and mortality in a way that makes it understandable by lay people and policymakers. Most researchers have examined the association in terms of ratio measures, such as relative risk (RR) and OR. These measures provide useful information on the burden of exposure, but relative

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https://doi.org/10.1016/j.jtherbio.2019.03.013
Received 2 February 2019; Received in revised form 17 March 2019; Accepted 19 March 2019
Available online 22 March 2019
0306-4565/

attributable measures, such as attributable fraction or attributable number are more helpful for evaluating the potential benefits of preventive interventions. The attributable fraction (AF) is the amount of death that can be attributed to a specific risk factor and has an important role in public health evaluations. The AF combines relative risk and the prevalence of exposure to measure the public health burden of a risk factor (Steenland and Armstrong, 2006). There are few studies evaluating the effect of heat wave on mortality using the attributable fraction. In this study we aimed to assess the effect of heat and heat waves on mortality using the attributable fraction/number approach.

2. Methods

2.1. Data and area under study

Kerman city has a population of about 740,000 people and is located in Kerman province in southeastern Iran. It is located at 56°52′30″–57°07′30″E and 30°07′30″–30°22′30″N and in a flat plain that has an altitude of 1754 m. It is a semi-arid to dry region that has hot summers and cold winters. The temperature range is wide and varies from −8 to 37 °C throughout the year (Hamzeh et al., 2011; Atapour, 2015).

Meteorological and mortality data from January 2005 to March 2017 were inquired from the Iran Meteorological Organization and the Death Registry of the Health Deputy of Kerman University of Medical Sciences, respectively. Ambient air pollution data (PM_{10}, SO_2, O_3, NO_2, CO, NO and $PM_{2.5}$), as potential confounders, were inquired from the Kerman Department of Environment.

2.2. Heat wave definition

There is no worldwide agreement on the standard definition of heat waves. In the literature, intensity and duration of temperature has been used as the definition of heat waves (Song et al., 2018; Lee et al., 2016). Also, some previous studies have suggested that defining the heat wave based on one parameter is not suitable for different climates. However, many studies have used daily mean temperature, as a better predictor for mortality than the minimum or maximum daily temperature (Xu et al., 2016; Xu et al., 2018; Xu and Tong, 2017). In the models used in present study, the AIC for daily mean temperature was less than minimum or maximum daily temperature. Therefore, the heat wave was defined using a combination of severity and duration of mean daily temperature. Nine definitions of a heat wave were used that have been listed in Table 1.

Heat wave effects were assessed using two effects of heat including added and main effects. Main effects shows the independent effects of daily temperature, while the excess risk due to sustained high temperatures for several consecutive days is considered as the added effect (17). Added effect was assessed using a binary variable. Nine binary variables were constructed, in which code 1 was assigned to heat wave days and 0 to non-heat wave. Main effect was assessed by comparing the median temperature (in heat wave days) to the Minimum Mortality Temperature (MMT). The median temperatures are shown in Table 1. MMT was found using methods used in recent papers (Tobías et al., 2017).

Table 1
Different definitions of heat wave using percentile and duration of mean temperature along with median temperature.

Heat wave	Definition		Median temperature (°C)
	Percentile	Duration of high temperature	
HW1	≥90th percentile of temperature	≥2 consecutive days	30.10
HW2		≥3 consecutive days	30.10
HW3		≥4 consecutive days	30.20
HW4	≥95th percentile of temperature	≥2 consecutive days	30.80
HW5		≥3 consecutive days	30.90
HW6		≥4 consecutive days	30.95
HW7	≥98th percentile of temperature	≥2 consecutive days	31.70
HW8		≥3 consecutive days	31.70
HW9		≥4 consecutive days	31.75

2.3. Heat definition

In addition to heat wave, the effects of heat, mild heat and extreme heat on mortality were also assessed in this study. Temperature above MMT was defined as heat. Temperature between the MMT and the 99th percentile and over the 99th percentile were defined as mild and extreme heat respectively.

2.4. Modeling strategy

Distributed Lag Non-linear Models were used to assess the relations in a bi-dimensional perspective which can vary non-linearly along the space of the predictors and lags (Gasparrini, 2013). The quadratic b-spline was chosen as the basis function for the dimensions of exposure and the natural cubic b-spline was chosen for lag dimensions. Spline knots were placed at equal spaces for both dimensions. They were placed in log scale for lag dimensions. The MMT value was selected as the reference value. There was uncertainty about the MMT point in this study and it was strongly dependent on the model used. It was 22.7 °C for the model presented in this study. The maximum lag of 14 was used because previous studies have suggested that hot temperature effects are limited to the 2 first weeks of exposure (Ma et al., 2014).

Initially generalized linear models and Poisson models were applied. The model is shown in equation (1). In this equation, Y_t refers to the number of deaths on day t. Temp (temperature) and HW (Heat Wave) are the main exposure variables at time t, α is the intercept, Cb is the cross-basis function in DLNM framework that shows the exposure value at time t and lag time ℓ and is a matrix including 14 lags in this study. NS and ε_t represent the natural spline function and the residual at time t, respectively. According to the lowest Akaike information criterion (AIC), the degree of freedom = 3 was selected for the natural spline. The time variable with a degree of freedom = 5 per year was selected in order to control the trend and seasonal effects. The degree of freedom = 5 was also selected based on the lowest AIC. In the model, DOW and Holiday are the days of the week and the public holidays, respectively. Holiday was entered as a binary variable into the model. The DOW variable is a qualitative variable with 7 categories, and Friday (the weekend in Muslim countries) was considered as the reference.

$$\log(Y_t) = \alpha + \text{Cb1temp}_{t\ell} + \text{Cb2HW}_{t\ell} + \text{NS}(SO_2,\ 3) + \text{NS}(PM_{10},\ 3) + \text{NS}(O_3,\ 3) + \text{NS}(\text{Time},\ 5^*\text{year}) + \text{DOW} + \text{Holiday} + \varepsilon_t \quad (1)$$

$Y_t \sim \text{Poisson}(\mu_t)$.

2.4.1. Attributable risk

The attributable risk measure within DLNM is produced in two perspectives; backward and forward. Both perspectives have been suggested by Gasparrini et al. (Gasparrini and Leone, 2014). The forward perspective is likely to produce some bias, therefore the backward perspective was used in this study.

The risk in DLNM can be described by exposure-response function f(x) and lag-response function w(ℓ). Two sets of basis functions are independently selected to represent f(x) and w(ℓ), respectively. Cross-basis is a bi dimensional space of functions obtained by the combination of the two sets integrated over the lag dimension. The details have been presented by Gasparrini et al. (Gasparrini et al., 2010, 2014; Gasparrini, 2014).

$$w_{x,t}^{T}\eta = \sum_{\ell=\ell 0}^{L} \beta_{x_{t-\ell}}, \ell \quad (2)$$

The $w_{x,t}^{T}\eta$ in equation (2) is a cross-basis that combines two functions (the risk of exposure-response and risk of lag-response) and it shows the overall cumulative effect along $\ell = \ell_0$ and L, that are minimum and maximum lags respectively. The minimum and maximum lags were 0 and 14 respectively in this study. Here t refers to time, ℓ is lag time, x is the exposure experienced in past period ℓ and $\beta x,\ell$ represents the association with an exposure x at lag ℓ versus the reference value x0 (counterfactual situation). The added effect of heat wave was assessed using the binary variable. Thus the counterfactual condition was non-heat wave days and for temperature it was the MMT point. The sum of contributions of βx from exposures $x_{t-\ell 0},\ldots, x_{t-L}$ experienced within the lag period make the overall cumulative effect ($w_{x,t}^{T}\eta$).

$$AF_{x,t} = 1 - e^{-\sum_{\ell=\ell 0}^{L} \beta_{x_{t-\ell}},\ell} \quad (3)$$

In equation (3), AF is Attributable Fraction that basically comes from "(RR-1)/RR" and then "1-exp (-Bx)". Here the coefficient β is replaced with the overall cumulative effect calculated from ($w_{x,t}^{T}\eta$) in DLNM, so the $AF_{x,t}$ represents the related fraction at time t attributable to past exposures to x in the period $t\text{-}\ell_{0,\ \ldots,}L$ compared to a constant exposure X_0 throughout the same period.

The attributable number of deaths for each day due to past exposure to x can also be calculated through equation (4):

$$AN_{x,t} = AF_{x,t}.\ n_t \quad (4)$$

where $AN_{x,t}$ represents the number of deaths at day t attributed to exposure x. It is calculated by multiplying the attributable fraction to the number of deaths in each day (n_t).

The above formula can be developed to break up the attributable components related to special exposures or exposure ranges. The range used in this study were between the MMT (22.7 °C) to the maximum temperature, MMT to the 99th percentile, and 99th percentile to the maximum temperature that were considered as heat, mild heat and extreme heat respectively. The range was restricted to heat wave days and median temperature observed in heat wave days in order to evaluate the added and main effect of heat waves respectively.

An estimate of the total attributable number AN_{total} and fraction AF_{total} is calculated using equations (5) and (6) respectively. In equation (5), the attributable number that was calculated for each day by equation (4) is arithmetically summed. Finally, dividing the total attributable number of deaths to the deaths in all observations (number of death on all days) gives the total attributable fraction (equation (6)). In the formulas, i is the observation in the data set and m is the maximum observation.

$$AN_{total} = \sum_{i=1}^{m} AN_{x,t_i} \quad (5)$$

$$AF_{total} = \frac{AN_{total}}{\sum_{i=1}^{m} n_{t_i}} \quad (6)$$

The 95% confidence intervals for the AFs was estimated using Monte Carlo simulations.

The analysis were performed using Excel 2013 and R software version 3.3.2. The values were considered significant if the confidence interval excluded 0.

2.5. Ethical consideration

All information was inquired as aggregated and without individual identity. The research proposal was approved by the Ethics Committee of Kerman University of Medical Sciences. Ethics Code IR. KMU.REC.1396.2374.

Table 2
Summary of descriptive statistics of daily temperature and mortality by different age and sex groups.

Variable	Group	Mean	Standard Deviation	Percentile		
				25	50	75
Mortality	Male	6.20	3.05	4	6	8
	Female	4.30	2.42	3	4	6
	< 65 years	5.43	2.92	3	5	7
	> =65 years	5.13	2.67	3	5	7
	Total	10.54	4.31	8	10	13
Mean temperature	–	17.32	8.87	9.9	18.1	25

3. Results

About 46,200 deaths due to all-causes occurred during 2005–2017. The average daily mortality was 10.54 (± 4.31) deaths that was greater for men (6.20) than women (4.30) and the daily mean temperature was 17.32 (± 8.87)°C. Table 2 shows the daily mean, and the 25, 50 and 75th percentile of mortality and temperature.

The total mortality attributed to non-optimal temperatures for all days was 1.91% in Kerman and was not significant.

Fig. 1 shows the overall cumulative relative risk along temperature distribution with the minimum mortality temperature point and the cutoffs to define extreme temperatures over the period of 2005–2017. While there was no significant effect of cold temperature on mortality in any temperature value in the cold range, the cumulative relative risk was significant for hot temperatures.

The attributable risks of total mortality were significant for heat, mild heat and extreme heat days and were 2.23%, 2.02% and 0.25% respectively. Table 3 shows the mortality attributable to the days by different subgroups. The attributable risk was more for females and the above 65 years old groups in heat, mild heat and extreme heat days. But, it was only significant in heat and mild heat.

Table 4 shows the mortality attributable risk to main and added effects of heat waves by 9 different definitions and different sex and age groups. While the heat waves defined based on temperature above the 95 and 98th percentile had a significant attributable risk in total mortality in the added effects, the weaker heat wave (defined based on temperature above of the 90th percentile (HW1, HW2, HW3) had higher attributable risks in the main effect, significant in HW1 and HW2. Table 4 also shows those aged > 65 years old have higher AF than youngers in both effects.

Fig. 2 shows the frequency of heat wave days (the blue bars) and the frequency of days with median temperature during the study time frame (the orange bars). The cumulative relative risk (red lines) for total mortality in main (the right half of Fig. 2) and added (the left half of Fig. 2) effects for all definitions of heat waves has also been shown. The cumulative relative risk was significant for the strong heat waves (temperature above 98th percentile, HW 7, HW8, HW9) in the added effect. However, the frequency of these heat wave days were less than the weaker heat waves. In main effect, the cumulative relative risks were significant for all definitions. However, the attributable risk were lower for all definitions in main effect than added effect (Table 4).

For easier comparison between the two effects, we have shown the attributable number of total mortality in Fig 3. There are obviously higher attributable numbers (AN) in the added effects than main effects.

4. Discussion

As far as we know, this was the first study to explore all-cause mortality attributable to temperature range and heat waves in Iran. The attributable risk was higher for heat (2.23 percent) than all other non-optimum temperature. Also, the result showed that the attributable risk of females and over 65 years age groups mortality associated with heat

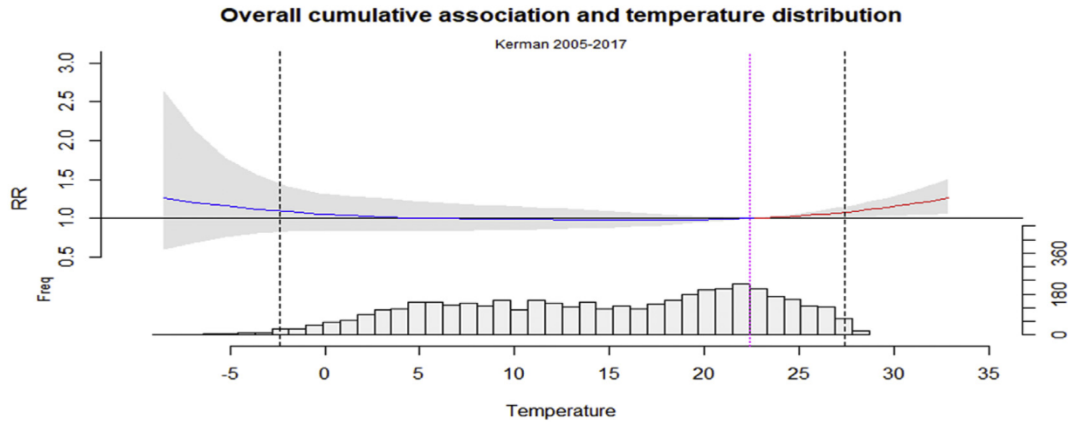

Fig. 1. The graph above shows the overall cumulative relative risk of temperature on total mortality over 0–14 day lags. The graph below shows the frequency of temperature. The pink line is the reference value. The dashed lines are the 1st and 99th temperature percentile and show the cut -off points for extreme cold and heat temperatures respectively.

were higher than males and under 65 years olds. While weaker heat waves had higher and significant attributable deaths in main effect, strong heat waves (defined based on temperature above the 95 and 98th percentile) had higher and significant attributable death in added effects. The attributable death calculated for the added effects of heat waves were considerably more than main effects in all definitions.

Some studies have measured the attributable mortality related to heat using similar approaches. For example, Yang et al. investigated cardiovascular mortality risk attributable to ambient temperature in China (Yang et al., 2015). They found that 17.1% (95% CI 14.4%–19.1%) of CVD mortality (330,352 deaths) was attributable to ambient temperature. There was substantial differences among cities, from 10.1% in Shanghai to 23.7% in Guangzhou. This value in Kerman was 1.91%. The attributable risk to heat was 1.3% in the above mentioned study that was approximately similar to our study. Yang's study had considered 21 days as their maximum lag, because they focused on both cold and heat effect and they only investigated mortality due to cardiovascular diseases.

The most important similar study conducted about this topic was done by Gasparrini et al. (Gasparrini et al., 2015). They calculated attributable deaths for heat and cold in 13 countries. In their study, 7.71% of mortality was attributable to non-optimum temperature and was more due to cold than heat (7.29% vs 0.42%). Also extreme temperatures (both cold or hot) were responsible for a small fraction of deaths, and corresponded to only 0.86% (95% CI 0·84%–0·87%). Another study looking for the association of all-cause mortality with high temperature in a temperate climate was conducted by Armstrong et al. (Armstrong et al., 2011) in 10 governmental regions of England and Wales. The attributable death due to heat was 1% (23,982 deaths). They used different methods to calculate the attributable risk.

The small difference in death attributed to heat in our study and previous studies may be justified by differences in the temperature distribution and period of studies. People usually adapt to the climate and temperature range of their own region. In the study conducted by Gasparrini et al. (Gasparrini et al., 2015), the hot days, had a high RR, but these days were only a small proportion of days under investigation. In our study hot and cold days had an approximately equal proportion, but hot days had a higher cumulative relative risk.

Several epidemiological studies have shown the adverse effects of heat wave on mortality. Lee et al. (Lee et al., 2016) evaluated the main and added effects of heat wave on mortality in Korea, using heat wave definitions similar to this study. They showed that the added effect of heat waves caused higher mortality rates as the temperature threshold increased. For instance, in heat waves above the 90th percentile, the effect of heat wave on mortality was minimal (3.7–5.8%), but above the 95th percentile, mortality increased by 8.6–11.3%. These results were similar to our study, and there was a higher cumulative relative risk above higher percentiles in both effects (Fig. 2, red line). However, these authors considered 30 days as the maximum lag, but the methodology was similar to our study.

Hajat et al. (Hajat et al., 2006) investigated the effect of high temperature and the added effects of heat waves on mortality in a 28 year period in London (1976–2003), 31 years in Budapest (1970–2000), and 18 years in Milan (1985–2002). In London, 0.37% of all mortality was attributed to heat, and slightly less than half of this fraction was attributable to the added effects of heat waves (0.16% as defined by the 99th percentile). The fraction of mortality attributable to heat was higher in Milan and Budapest, but less than one third of these were attributed to heat waves defined by the 98th percentile (less than one fifth of heat waves were defined by the 99th percentile). The analysis used in the study was different from our study and they considered 2 days as maximum lag. As heat, the minor difference in the estimations between some studies and our results can probably be due to the difference in methodologies.

There are a few studies about the attributable risk of mortality related to the main effect of heat waves. But there are some studies, evaluating the effect using ratio measures, such as relative risk. For example, one study showed that the relative risks of the main effects of heat waves increased with the increase in the temperature thresholds from the 95th to the 99th percentile, and a hot heat wave defined as above the 99th percentile for 4 days, had the highest risk (RR = 1.93, 95% CI: 1.46–2.55) (Song et al., 2018). We observed such a pattern in our study as well. In our study, the weaker heat waves, defined as above the 90th percentile, in the main effect had a lower cumulative relative

Table 3
The mortality fraction (%) attributable to heat, mild and extreme heat over lag 0–14 days, stratified by gender and age groups in Kerman.

Day	Total	Male	Female	< 65years old	≥65years old
Heat	**2.23(0.34,3.87)**	1.72(-0.83,4.05)	**2.94(0.11,5.44)**	0.7(-1.82,3.43)	**3.73(1.26,5.82)**
Mild heat	**2.02(0.3,3.69)**	1.49(-0.71,3.59)	**2.74(0.04,5.06)**	0.63(-2.05,2.98)	**3.38(1.04,5.34)**
Extreme heat	**0.25(0.06,0.41)**	0.22(-0.04,0.45)	0.27(-0.04,0.51)	0.06(-0.23,0.29)	**0.44(0.15,0.69)**
All days (except reference)	1.91(-6.36,8.47)	5.7(-3.57,13.26)	−3.99(-19.9,8.01)	−3.7(-15.78,5.89)	7.72(-3.81,16.58)

Table 4
The mortality fraction (%) attributable (with confidence interval 95%) to heat wave over lag 0–14 days, stratified by gender and age groups in Kerman.

Heat wave	Definition	Total	Male	Female	< 65 year old	≥65 year old
Main effect	Hw1[a]	**0.04(0.01,0.06)**	0.03(-0.01,0.06)	0.05(0,0.09)	0.01(-0.03,0.04)	**0.07(0.03,0.11)**
	Hw2[a]	**0.04(0.01,0.06)**	0.03(-0.01,0.06)	0.05(0,0.09)	0.01(-0.03,0.04)	**0.07(0.03,0.11)**
	Hw3	0.04(0,0.09)	0.02(-0.04,0.08)	0.07(-0.01,0.14)	0(-0.07,0.06)	**0.09(0.03,0.16)**
	Hw4	0.02(-0.01,0.05)	0.02(-0.03,0.06)	0.04(-0.01,0.08)	−0.01(-0.06,0.04)	**0.05(0.01,0.09)**
	Hw5	0.02(-0.01,0.04)	0(-0.04,0.03)	0.03(-0.01,0.07)	−0.01(-0.05,0.03)	**0.06(0.02,0.09)**
	Hw6	0.02(-0.01,0.04)	0(-0.05,0.04)	0.04(0,0.07)	−0.01(-0.05,0.03)	**0.05(0.01,0.09)**
	Hw7[b]	0.02(0,0.04)	0.01(-0.02,0.04)	0.03(-0.01,0.05)	0(-0.04,0.03)	**0.05(0.01,0.08)**
	Hw8[b]	0.02(0,0.04)	0.01(-0.02,0.04)	0.03(-0.01,0.05)	0(-0.04,0.03)	**0.05(0.01,0.08)**
	HW9	0.02(0,0.03)	0.01(-0.01,0.03)	0.03(0,0.05)	0.01(-0.02,0.02)	0.03(0,0.05)
Added effect	Hw1	0.48(-0.36,1.28)	0.76(-0.32,1.68)	0.18(-1.24,1.37)	0.09(-1.16,1.13)	0.85(-0.32,1.81)
	Hw2	0.55(-0.19,1.27)	0.88(-0.13,1.8)	0.18(-1.19,1.33)	0.24(-0.85,1.3)	0.84(-0.28,1.9)
	Hw3	0.44(-0.31,1.14)	0.78(-0.12,1.64)	0.03(-1.21,1.17)	0.25(-0.93,1.23)	0.6(-0.51,1.53)
	Hw4	**0.53(0.01,1.01)**	**0.77(0.04,1.41)**	0.26(-0.56,1.06)	0.28(-0.56,1.01)	0.77(-0.02,1.45)
	Hw5	**0.59(0.11,1.05)**	**0.79(0.14,1.41)**	0.36(-0.5,1.11)	0.43(-0.35,1.11)	**0.73(0.02,1.39)**
	Hw6	**0.45(0.01,0.89)**	**0.71(0.11,1.23)**	0.16(-0.63,0.79)	0.22(-0.44,0.79)	**0.67(0.04,1.24)**
	Hw7	**0.57(0.25,0.87)**	**0.77(0.36,1.14)**	0.3[a]-0.28,0.76)	**0.47(0.01,0.88)**	**0.63(0.17,1.05)**
	HW8	**0.56(0.28,0.8)**	**0.69(0.3,0.99)**	0.4(-0.06,0.8)	0.38(-0.03,0.75)	**0.7(0.28,1.06)**
	Hw9	**0.4(0.15,0.63)**	**0.54(0.23,0.81)**	0.23(-0.19,0.56)	0.33(-0.04,0.62)	**0.47(0.19,0.7)**

[a] The median points were identical.
[b] The median points were identical.

risk (Fig. 2) and there was higher attributable risk/number of deaths in the weak heat waves (Table 4 and Fig. 3, orange bars). Probably, because the frequency of days with the median temperature (temperatures shown in Table 1) was higher in weaker heat waves than others, in the main effect, attributable risks were higher in weaker heat waves.

Some previous studies have reported that more heat wave-related mortality is seen in main effects than added effects (Gasparrini and Armstrong, 2011; Zeng et al., 2014). Similar to these studies, the cumulative relative risk in main effect were significant for all definitions in our study, however they were higher for some definitions (stronger heat waves) in added effect. The small differences in the results of studies can be because of several reasons. One maybe the different definition of heat wave. A systematic review conducted by Xu et al. (22) on heat waves and mortality under different definitions showed that the adverse effect of heat wave on mortality can be obviously influenced by heat wave definition, and especially heat wave intensity. The two above mentioned studies didn't calculate the attributable risk that was much more for added effect than main effect in our study. Generally, because of different methods used in different studies in order to calculate attributable risk, comparison is not easy, especially considering the fact that we estimated the relations with non-linear lag models.

Khanjani et al. conducted a study in Kerman, Iran based on 2004–2008 data. Their results showed decreases in temperature were associated with increased cardiovascular and respiratory mortality. These results are in contrary with our results which show increased mortality with hot temperatures. The reason might be that linear

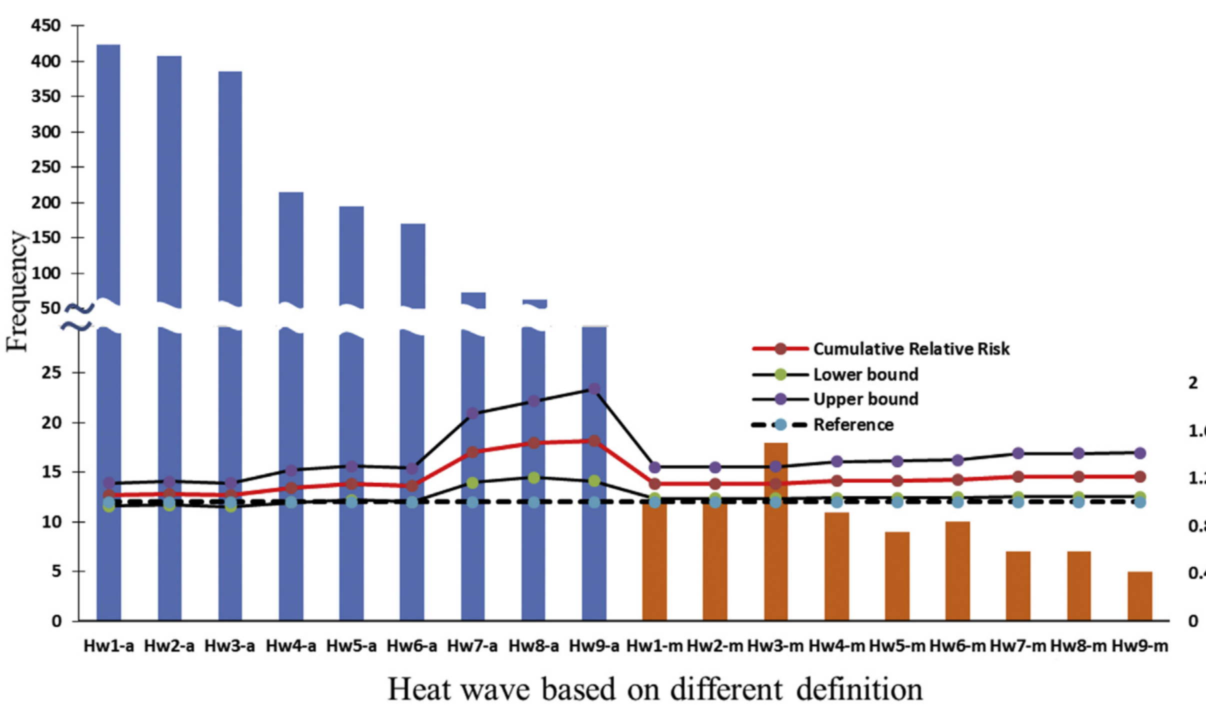

Fig. 2. The vertical bars show the frequency of exposure. The blue bars shows the number of days that heat waves happened, according to 9 definitions (Hw-a means added effect) and the orange bars shows the number of days with the median temperature that happened during heat wave days (Hw-m means main effect). The horizontal red line represents cumulative relative risk for total mortality in added (the left half) and main (the right half) effects for all definitions of heat waves along with its 95% confidence interval (the solid black lines). The dashed, black horizontal line is the reference line for the cumulative relative risk.

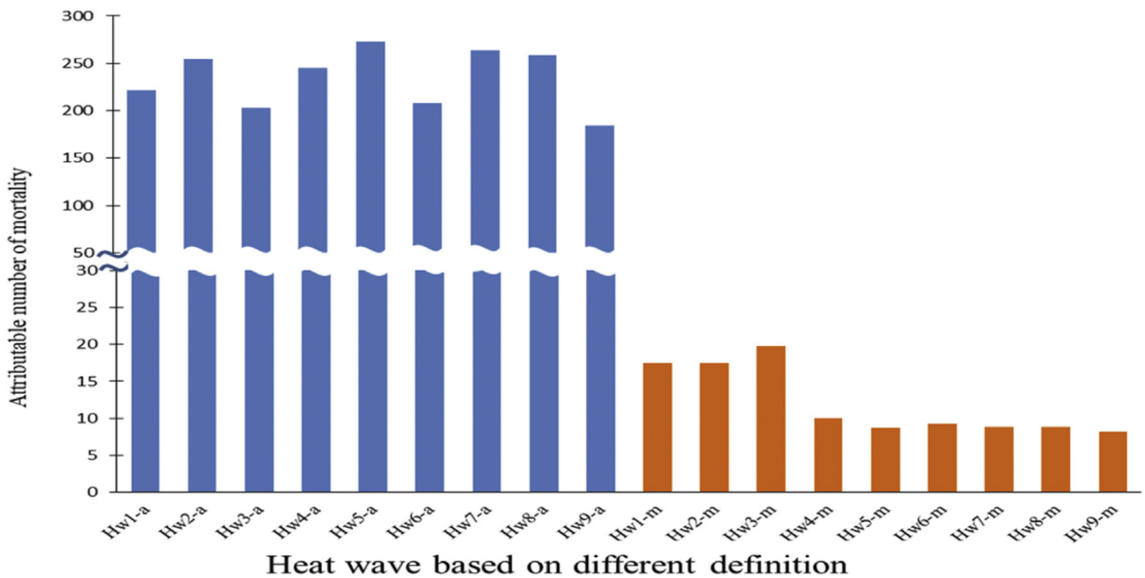

Fig. 3. Number of total mortality attributable to heat wave with 9 definitions over lag 0–14 days; the blue shows number of total mortality attributable to added effect and the orange shows number of total mortality attributable to main effect.

models not considering lag effects were used in their study, which might have caused bias in the estimations(Khanjani and Bahrampour, 2013).

4.1. Strength and limitations

Although, there are some studies that have evaluated the effect of heat on mortality using the attributable risk such as absolute excess (numbers) or relative excess (fraction) of deaths, but these studies have not considered the delayed effect of exposure or the non-linear relation between exposure and outcome. A strength of the study was that we applied a method that took into account non-linearity in the relation of exposure and its lags with outcome. This method gives us more stable and flexible estimation of the relation between heat or heat wave and mortality than non-linear models, and it also estimates less biased coefficients. One finding of our study, by using this method was that attributable fraction for the elderly was more than the young. This finding is meaningful from a public health perspective, because it has profound implications for heat-warning systems and projections for the effect of climate change on human health.

Missing data was one of the limitations in our study. The missing percentage was high for two confounder variables (PM_{10} and O_3) , and we could not apply a method to predict missing data. Eventually, we entered the two variables in the model because sensitivity analysis showed that they should better be in the model and the model without imputation had a better goodness of fit (lower AIC). The samples (about 4500 days of observation) were also enough to maintain the power of the study. Fortunately, there was low missing in the outcome data and main exposures.

In Iran, all deaths and their date, gender, and age are recorded in the death database of the Health Deputy of the Province's University of Medical Sciences. People are not allowed to bury the corpse without recording their death. However, the cause of death might be recorded inaccurately by health staff, and cause-specific mortality might be under or over reported. But, in this study we did not use cause-specific mortality.

5. Conclusion

The highest significant attributable risk/numbers was associated with the heat waves defined based on temperature above the 95 and 98th percentile in added effect and the weakest heat waves in main effect. The adverse health effects of heat waves should mainly be prevented through public health education and alert systems.

Conflicts of interest

Authors state no conflict of interest.

Acknowledgments

This study was financially supported by Kerman University of Medical Sciences through Grant No 96000792. The authors thank the Kerman Bureau of Meteorology and the Deputy of Health of Kerman University of Medical Sciences for providing the data for this study.

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