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Review

# Ambient temperature and risk of cardiovascular hospitalization: An updated systematic review and meta-analysis

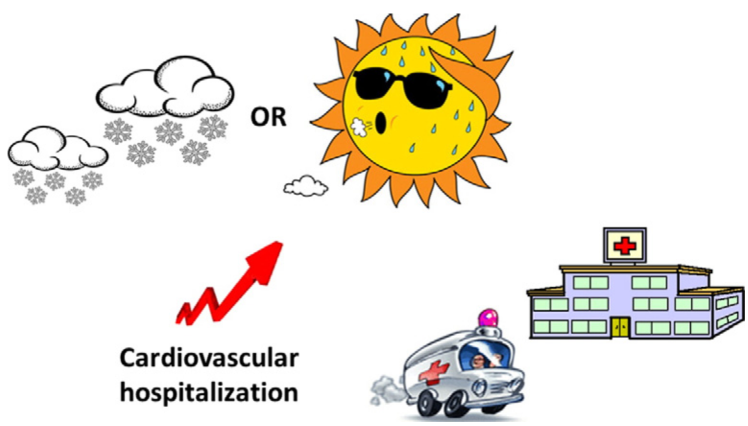
Dung Phung [a,*], Phong K. Thai [b,**], Yuming Guo [c], Lidia Morawska [b], Shannon Rutherford [a], Cordia Chu [a]

[a] Centre for Environment and Population Health, Griffith University, Australia
[b] International Laboratory for Air Quality & Health, Queensland University of Technology, Australia
[c] Division of Epidemiology and Biostatistics, School of Public Health, University of Queensland, Australia

## HIGHLIGHTS

- There are significant short-term effects of cold, heatwave to CDV hospitalization.
- Similar association was observed for diurnal temperature variation.
- There is an inconsistent effect of heat exposure on CDV hospitalizations.
- Future studies need to focus on specific geographical and climate areas.

## GRAPHICAL ABSTRACT

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## ABSTRACT

The association between temperatures and risk of cardiovascular mortality has been recognized but the association drawn from previous meta-analysis was weak due to the lack of sufficient studies. This paper presented a review with updated reports in the literature about the risk of cardiovascular hospitalization in relation to different temperature exposures and examined the dose–response relationship of temperature-cardiovascular hospitalization by change in units of temperature, latitudes, and lag days. The pooled effect sizes were calculated for cold, heat, heatwave, and diurnal variation using random-effects meta-analysis, and the dose–response relationship of temperature-cardiovascular admission was modelled using random-effect meta-regression. The Cochrane Q-test and index of heterogeneity ($I^2$) were used to evaluate heterogeneity, and Egger's test was used to evaluate publication bias. Sixty-four studies were included in meta-analysis. The pooled results suggest that for a change in temperature condition, the risk of cardiovascular hospitalization increased 2.8% (RR, 1.028; 95% CI, 1.021–1.035) for cold exposure, 2.2% (RR, 1.022; 95% CI, 1.006–1.039) for heatwave exposure, and 0.7% (RR, 1.007; 95% CI, 1.002–1.012) for an increase in diurnal temperature. However no association was observed for heat exposure. The significant dose–response relationship of temperature — cardiovascular admission was found with cold exposure and diurnal temperature. Increase in one-day lag caused a marginal reduction in risk of cardiovascular hospitalizations for cold exposure and diurnal variation, and increase in latitude was associated

* Correspondence to: D. Phung, Griffith University, Australia.
** Correspondence to: P. K. Thai, Queensland University of Technology, Australia.
*E-mail addresses:* d.phung@griffith.edu.au (D. Phung), phong.thai@qut.edu.au (P.K. Thai).

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with a decrease in risk of cardiovascular hospitalizations for diurnal temperature only. There is a significant short-term effect of cold exposure, heatwave and diurnal variation on cardiovascular hospitalizations. Further research is needed to understand the temperature-cardiovascular relationship for different climate areas.



**Contents**



## 1. Introduction

There is increasing evidence that on-going global climate change has generated more frequent and intense extreme weather events such as heatwaves and cold spells (IPCC, 2013). Such extreme temperatures have been associated with significant health impacts. For example, excessive hospitalizations due to a range of morbidity such as heat stroke, cardiovascular and respiratory diseases have been recorded during heatwave episodes (Empana et al., 2009; Knowlton et al., 2009; Ma et al., 2011; Semenza et al., 1999; Turner et al., 2013). The serious impacts of heatwaves on human health have led to the first guidance for a Heat-Health Warning system jointly developed by the World Meteorological Organization and World Health Organization (McGregor et al., 2015). On the other hand, episodes of extreme cold are major health threat in high-latitude countries (Huynen et al., 2001; Kysely et al., 2009; Pattenden et al., 2003; Shaposhnikov et al., 2014). Previous studies have indicated that one of the predominant causes of hospitalizations associated with extreme temperature is cardiovascular diseases (CVD) (Bayentin et al., 2010; Ebi et al., 2004; Oshige et al., 2006; Schwartz et al., 2004; Turner et al., 2012a) which can cause a large burden for the health system. Nevertheless, most environmental-related research to date has concentrated on the relationship between temperature and cardiovascular mortality (Baccini et al., 2008; Basu, 2009; Gasparrini et al., 2015; Guo et al., 2014; Huang et al., 2012; McMichael et al., 2008; Son et al., 2015; Yang et al., 2015).

Some systematic reviews have been recently conducted to evaluate the relationship between ambient temperature and morbidity, in which cardiovascular hospitalization has been involved as one of the morbidity causes (Astrom et al., 2011; Bhaskaran et al., 2009; Turner et al., 2012b; Ye et al., 2012). However, these studies have limitations which might result in inconclusive findings about temperature-CVD hospitalization relationship. Turner et al. (2012b) conducted a meta-analysis to evaluate the association between temperature and cardiorespiratory morbidity using a small number of studies, and the influences of cold exposure, heat waves, and variation of diurnal temperature on CVD hospitalizations were not analysed in this study. Bhaskaran et al. (2009) conducted a systematic review of the influence of temperature on the incidence of myocardial infarction with findings about the effects of both hot and cold weather on the risk of Myocardial infarction. Ye et al. (2012) systematically reviewed epidemiological evidence on temperature-morbidity relationship and indicated that there was a significant short-term effect of ambient temperature on total and cause-specific morbidities, including cardiovascular diseases. These two studies nevertheless did not quantify the pooled effect sizes of temperature–CDV hospitalization relationship. Another review by Astrom et al. (2011) found that the evidence of temperature-cardiovascular morbidity relationship among elderly people was inconclusive, and this study also did not quantify the pooled effects of temperature-CVD hospitalizations.

It is thus important to address this gap of information with newly published works in the literature. This study aims to conduct extensive search with the objectives to: (i) investigate the risk of cardiovascular hospitalization in relation to different temperature exposures (cold, heat, heatwaves, and diurnal temperature), and (ii) examine the dose–response of temperature-CVD relationship by change in units of temperature, latitudes, and lag days.

## 2. Method

This meta-analysis was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (Moher et al., 2009) and the recommendations of the meta-analysis of Observational Studies in Epidemiology group (MOOSE) (Stroup et al., 2000).

### 2.1. Study selection

The PubMed electronic database was used to search published studies examining the relationship between ambient temperature and cardiovascular morbidity. In order to avoid missing relevant studies, the keywords and Medical Sub-Heading (MeSH) terms in the initial search were set in two categories with 'or' operand used within a group and later 'and' or 'not' operands used between groups. The two categories comprised: (i) exposure variables, namely: climate change, temperature, heat wave, heatwave, cold, cold spells; (ii) outcome variables, namely: health effects, morbidity, hospitalization, emergency department visit, death, mortality. Our search was limited to 'English' and 'Human' studies. Then a further screening was conducted through the abstract review to identify the studies concerning the temperature-cardiovascular relationship (Fig. 1).

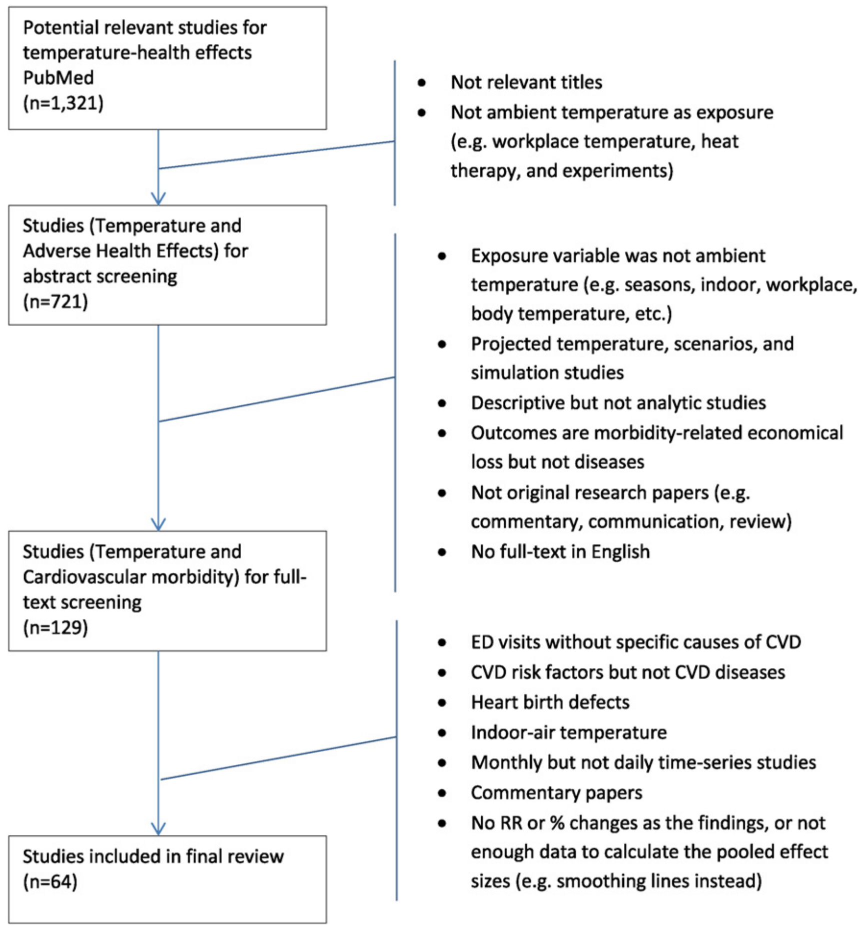


**Fig. 1.** Flow diagram for inclusion and exclusion of studies.

Three criteria for eligibility were used. First, published analytic studies needed to be based on one of the following calculations: regression coefficient, percentage change, relative risk (RR), and odds ratio (OR) on the relationship between ambient temperature and cardiovascular morbidity. Second, the study designs were required to be appropriate for examining the short-term effects of changes in temperature on cardiovascular morbidity (daily timescale), so each study had to contain an outcome measure related to hospitalizations for either all-cause or specific-cause cardiovascular diseases. Third, exposure to temperature was based on at least one of the following conditions:

- *Cold exposure*: number of degrees below the defined threshold or average value, or comparison between extreme cold condition and the reference value (e.g. 5th vs. 90th percentiles);
- *Heat exposure*: number of degrees above the defined threshold or average value but NOT during the cold season (e.g. winter), or comparison between extreme hot condition and the reference value (e.g. 99th vs. 75th percentiles);
- *Cold spells*: ≥2 days of extreme low temperature (e.g. 5th percentiles);
- *Heat wave*: ≥2 days of extreme high temperature (e.g. 95th percentiles);
- Variation in *diurnal temperature*: number of degrees between maximum and minimum temperature during the day.

The evidence from previous studies (Barnett et al., 2010; Basu et al., 2008; Hajat and Kosatky, 2010) demonstrated that the influence of temperature on mortality does not vary substantially with the temperature measures used. Therefore, all temperature measures were allowed in this study.

Criteria for exclusion included: (i) studies providing qualitative evaluation; (ii) studies providing only non-linear curves of temperature–outcome relationship because we cannot extract the effect sizes from these studies; (iii) studies using indoor or workplace temperature as the exposure variable; (iv) reviewing or commentary papers; (v) published papers with only English abstracts but without full texts in English.

The screening of potentially eligible studies was carried out using the tier approach with sequential steps (Fig. 1). First, the potential relevant studies for temperature-health effect relationship were obtained from a search of a wider study in temperature-health effects. Second, all obtained papers were title reviewed to check if their titles were relevant to the inclusion criteria or met exclusion criteria. Third, abstracts of selected papers were reviewed against the inclusion criteria. Fourth, the full texts of the papers selected from step 3 were reviewed against the inclusion criteria, and additional papers were identified and reviewed using manual searching in the references of full-text candidate papers.

### 2.2. Quality assessment

The criteria for evaluating the quality of the selected studies was modified from the criteria recommended by the BioMed Central for study assessment (Berman and Parker, 2002) (Table S2). The criteria used for evaluating quality of the studies comprise: (i) sources of the information including the time of data collection; (ii) study design, including clarity, appropriateness of, clear measurement of exposure variables, statistical packages, controls for confounding factors, and the clear definition of health outcomes; (iii) valid interpretation of results; and (iv) discussion. We developed a score scheme corresponding to the assessment criteria, and each study was evaluated using this score system. The quality score could range from 1 to 27. A cut-off point of 13 was used for a study to be included in this meta-analysis. As indicated in Table S2, a study that has score of more than 50% (13) was published in a peer-review journal, has well-described study design (clear research questions and descriptions in temperature exposures), and its results properly answered the research questions with presented measurements (RR, OR).

### 2.3. Data extraction

The data which were extracted from each of the included studies comprise: first author last name and publication year, country and location in which the study was performed, study design and time-span, temperature measures as exposure variables, threshold or reference temperature, day lags of the effect, outcome (% change in risk/RR/OR and 95% CI, cardiovascular diseases diagnosed), and controlled variables.

### 2.4. Data synthesis and analysis

Statistical analyses involved a two-step approach: (i) computing pooled effect sizes for each type of temperature exposure using a random-effect meta-analysis approach; (ii) modelling the dose–response pattern of temperature-cardiovascular relationship using a random-effect meta-regression analysis.

In step 1, effect estimates were converted to a relative risk (RR) reflecting a change in hospitalizations due to a change in the condition of temperature exposures (cold, heat, heat wave, and variation in diurnal temperature). Standard errors for the relative risk were derived from associated confidence intervals. Because studies were conducted in different populations, resulting in considerable heterogeneity of findings, the random effects methodology (Borenstein et al., 2010) was applied to calculate for within-study and between-study variation and generate pooled effect sizes. The pooled effect sizes were calculated separately for each type of temperature exposure: cold, heat, cold spell, heatwave, and variation in diurnal temperature. Due to the high variability of involved factors such as lags, latitude, and population, the use of effect size from each included study may not fully represent the relative magnitude of underlying risk. We applied the Empirical Bayesian (EB) approach (Clayton and Kaldor, 1987) to adjust the effect sizes of the included studies by incorporating data from other spatial settings using the following equations:

$$\theta_j = \gamma_j \bar{y}_j + \left(1 - \gamma_j\right)\bar{y} \tag{1}$$

$$\gamma_j = \frac{\tau^2}{\tau^2 + \sigma_j^2} \tag{2}$$

where, $\theta_j$ is the effect size of each included study $j$; $\gamma_j$is the shrinkage factor; $\tau^2$ is the variance between studies; and $\sigma_j^2$ is the variance within each included study $j$. Then the pooled effect sizes were computed and compared with those obtained from the normal meta-analysis.

Heterogeneity between studies was quantified using Cochran's Q-statistics by summing the squared deviations of each study's estimate from the overall meta-analytic estimate, and weighting each study's contribution in the same manner as in the meta-analysis. $P < 0.05$ was deemed significant (Cochran, 1954). However, the $Q$-statistics is susceptible to the number of studies included in meta-analysis. Therefore, we used the coefficient of inconsistency ($I^2$) recommended by Higgins et al. (2003), which can provide a measure of the degree of inconsistency in the studies' findings by describing the percentage of total variation across studies that is due to heterogeneity (Higgins et al., 2003). The heterogeneity degree ranged from 0 to 100%. The results were categorized as low (<25%), moderate (25–75%) and high (≥75%) heterogeneity. To investigate the possibility of publication bias, we used the approaches recommended by Egger et al. (1997); Sterne and Egger (2001) and Sterne et al. (2001). We first inspected the Begg's funnel plot with pseudo 95% confidence limits, which plots a measure of study precision (standard error as a function of effect size). Visual inspection of a funnel plot provides an indication of publication bias when larger and smaller studies are asymmetrically distributed across the combined effect size (Rothstein et al., 2005). The existing publication bias was further tested using Egger's test which evaluates the bias captured by the funnel plot by regression of the standard normal deviation on precision, defined as the inverse of the standard error.

In step 2, for the meta-regression analysis, we modelled the change in effect sizes (risk of cardiovascular hospitalizations) by the change in temperature degrees, lag days, and absolute latitude of the population using Eq. (1):

$$\theta_{ij} = \beta_0 T_{ij} + \beta_1 Lag_{ij} + \beta_2 Lat_{ij} + \varepsilon \tag{3}$$

where, $\theta_{ij}$ is the effect size of each study; $T_{ij}$ is the change in temperature measures (°C); $Lag_{ij}$ is the lag days; $Lat_{ij}$ is the latitude; and $\varepsilon$ is the residue. If the study compared the effect sizes between two specific temperature conditions (e.g. 0 °C vs. 15 °C, or 5th vs. 75th), the difference value between the two compared points was used as the continuous change in temperature measures. For the cumulative lags (e.g. 0–1, 2–15, 16–27), the midpoint (arithmetic mean) was assigned as the continuous change in lag days. A previous study (Turner et al., 2012b) found that a polynomial model for the lag effect did not perform better, so a linear term was used. Separate analyses were performed on studies related to cold and heat exposure using random-effect regression with empirical Bayesian technique.

Some sensitivity analyses were also performed. First, the pooled effect size was calculated after excluding the lower quality studies which have an assessment score of less than 75% of the total maximum score. Second, the pooled effect sizes were computed for the same-day effect only (lag 0), since the temperatures have been observed to have immediate and short-term effects on hospitalizations. Finally, the pooled effect size of hospitalizations only was estimated after excluding the hospital consultations and CVD biomarkers as the health outcome.

## 3. Result

### 3.1. Included and excluded studies

A total of 1321 papers in temperature-health effects were identified from our systematic search using the defined MeSH terms and keywords (Fig. 1). The first screening with brief title review excluded 600 papers. Most of the excluded papers were non-relevant titles and accorded with the criteria for exclusion. The second screening, abstract review, left us with 129 papers as full-text review candidates. The most common reasons for excluding studies were: ambient temperature not used as exposure variable, use of projected and simulated temperatures, morbidity related economic loss as the outcome, comment and review papers, and non-English full text. In fact, data obtained from the abstracts of non-English papers were not sufficient for the extraction criteria described in Data Extraction. The full-text screening resulted in 64 papers remaining for inclusion in the meta-analysis. The reasons for exclusion from the study in the third screening are shown in Fig. 1.

The sixty-four studies included in the meta-analysis were summarized according to the temperature exposure in Table 1. Most of the studies in temperature-cardiovascular hospitalizations have been done in more developed and temperate countries, and the top countries that have high research intensity in temperature-cardiovascular hospitalizations are United States of America, United Kingdom, Australia, and China. Few studies have been conducted in developing and tropical

**Table 1**
Summaries of studies included in this review.

| Authors/year | City/country | Study design/time-span | Exposure | Lags (days) | Outcome | | | Controlled variables |
|---|---|---|---|---|---|---|---|---|
| | | | | | RR/OR (95% CI) | Correspondent change in temperature/threshold | Cardiovascular morbidity | |
| **Cold effects** | | | | | | | | |
| Hajat and Haines (2002) | England-London/≥65 year-old | TS/1992–1995 | Mean temperature | 6–15 | 0.978 (0.93–1.028) | 1 °C decrease in temp. below 5 °C | Consultation with CVD (ICD-9, 390–403, 410–416, 420–429, 785) | Season, trend, air pollution, DOW, Christmas, New Year, Easter and bank holidays, and thunderstorm effects, consultation for influenza, humidity, interaction: temp.-humid-DOW. |
| Hong et al. (2003) | Incheon/Korea | Case-crossover/ 1998–2000 | Mean temperature (winter) | 1 | 2.9 (1.5–5.3) | 17.4 °C decreased (One interquartile) | Ischemic stroke | Humidity, air pressure |
| Panagiotakos et al. (2004) | Athens/Greece | TS/2001–2002 | Mean temperature<br>Minimum temp. | 0 | 1.05 (−0.91–3.01) | 1 °C decrease in mean temperature | Acute coronary syndrome | DOW, season, holidays, humidity, barometric pressure, gender, age groups |
| Kyobutungi et al. (2005) | Heidelberg/Germany | Case-crossover/ 1998–2000 | Mean temperature | 3 | 2.3 (0.7–7.3) | >5 °C decrease | Ischemic Stroke | Hypertension, diabetes, smoking, previous stroke, family history of stroke, atrial fibrillation |
| Misailidou et al. (2006) | Multi-city/Greece | 2003–2004 | Mean temperature | 0 | 1.016 (1.009–1.022) | | Acute coronary syndrome | humidity |
| Liang et al. (2008) | Taichung/Taiwan | TS/2000–2003 | Mean temperature | 0 | 1.539 (1.16–2.1) | 17 °C compared with 27–29 °C | Acute coronary syndrome | Air pollution, season, holidays |
| Wolf et al. (2009) | Ausburg/Germany | TS/1995–2004 | Mean temperature | 0<br>0–4 | 1.04 (0.97–1.12)<br>1.10(1.01–1.18) | 10 °C decrease | Myocardial Infarction | Trend, season, Monday, humidity, influenza |
| Lee et al. (2010) | Daegu/Korea | TS/2005–2007 | Mean temperature<br>Maximum<br>Minimum | 0<br>0<br>0 | 1.056 (−0.98–3.04)<br>1.047 (−0.91–3)<br>1.061 (1.04–1.09) | Decreased by 5 °C | Acute Myocardial infarction | DOW, season, holidays, humidity, wind speed, sunshine duration, thermos-hydrological index |
| Bhaskaran et al. (2010) | Multi-conurbation/ England & Wales | TS/2003–2006 | Mean temperature | 0–28<br>2–7<br>8–14 | 1.02 (1.011–1.029)<br>1.006 (1.002–1.011)<br>1.007 (1.003–1.011) | 1 °C reduction. | Myocardial infarction | Humidity, DOW, holidays, influenza, air pollution |
| Turner et al. (2012) | Brisbane/Australia | TS/2000–2007 | Mean temperature | 0–1<br>2–15<br>16–27 | 0.994 (0.988–1)<br>1.016 (1.006–1.026)<br>0.989 (0.979–0.998) | 22 °C | CVD Ambulance attendances | Season, trend, DOW, holidays, air pollutants |
| Goggins et al. (2012) | Hong Kong/China | TS/1999–2006 | Mean temperature | 0–13<br>0–13<br><br>0–4 | 1.016 (1.0–2.2)<br>1.11 (1.06–1.15)<br><br>1.027 (1.02–1.034) | 1 °C decrease from average<br>6.3 °C decrease from below 22<br>1 °C decrease from average | Ischemic Stroke<br>Ischemic Stroke<br><br>Hemorrhagic Stroke | Season, trend, DOW, holidays, other climate factors, and air pollutants, influenza |
| Wang et al. (2012) | Taiwan | TS/2000–2009 | Mean temperature | 0–3 | 1.07 (1.01–1.13) | 18 °C vs. mean | ERV risk for circulatory diseases | Humidity, air pollutants |
| Vasconcelos et al. (2013) | Lisbon/Portugal<br>Oporto/Portugal | TS/2003–2007 | Physiologically Equivalent Temperature (PET) | 0 | 1.022 (1.009–1.033)<br>1.017 (1.009–1.025) | 1 °C decrease in PET during winter | Acute myocardial infarctions | DOW, holidays, season, trend, influenza, PM10 |
| Wang et al. (2013b) | Jinan/China | TS/1990–2009 | Mean temperature | 0<br>10<br>0–2 | 1.43 (1.1–1.85)<br>1.08 (1.01–1.16)<br>1.53 (1.21–1.94) | 0 °C vs. 15 °C<br>−10 °C vs. 15 °C<br>0 °C vs. 15 °C | Ischemic stroke | Season, trend, DOW, holidays |
| Tanigawa-Sugihara et al. (2013) | Osaka/Japan | Cross-sectional analysis of prospective cohort | Mean temperature | 1 | 1.11 (1.08–1.13)<br><br>1.16 (1.14–1.19) | 5 °C decrease from 18 °C | Out-hospital Cardiac Arrest in <74 year-olds<br>Out-hospital Cardiac Arrest in ≥74 year-olds | Humidity, pressure |
| Googins et al. (2013) | HongKong<br>Taipaei<br>Kaohsiung | TS/2000–2009 | Mean temperature | 0–13 | 1.039 (1.032–1.046)<br>1.029 (1.021–1.037)<br>1.045 (1.025–1.065) | 1 °C decrease from 24 °C | Acute myocardial infarctions | Season, trend, DOW, holidays, air pollutants |
| Son et al. (2014) | Multi-city/Korean | TS/2003–2008 | Mean temperature | 0–32 | 0.932 (0.857–1.014) | 10th (2) vs. 50th (15) | CVD | Season, trend, humidity, DOW |
| Webb et al. (2014) | Northern Territory/Australian | Cohort/ 1992–2011 | Minimum temp. | 0 | 1.003 (1–1.006)<br>1.006 (0.999–1.016) | 5th vs. 90th<br>5th vs. 90th | IHD<br>Heart failure | Non-Indigenous men<br>Indigenous females |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | 1.006 (1–1.012) | 5th vs. 90th | Heart failure | Non-indigenous females |
| Mostofky et al. (2014) | Boston/USA | Case-crossover/ 1999–2008 | Mean apparent temp. | 2 | 1.09 (1.01–1.18) | 5 °C decrease from the average | Ischemic stroke | Humidity, Air pollution |
| Giang et al. (2014) | Thai Nguyen/Vietnam | TS/2008–2012 | Mean temperature | 0–30 | 1.12 (1.01–1.25) | 26 °C | Myocardial infarction, angina pectoris, congestive heart failure, hypertension, stroke. | Trend, DOW, holidays |
| Wang and Lin (2014) | Taipei/Taiwan | TS/2000–2009 | Mean temperature | 0–3 | 1.56 (1.23–1.97)<br>1.78 (1.37–2.34) | 14 vs. 26 | Cerebrovascular diseases<br>Hypertensive diseases | Humidity, season, trend, wind speed, DOW, holidays, influenza |
| Lee et al. (2014) | Korea | TS/2006–2010 | Minimum temp. | 5 | 1.01 (1–1.02) | −1.5 | Acute Myocardial infarction | Season, trend, other meteorological factors, air pollution |
| Urban et al. (2014) | Prague/Czech | Comparison | Mean temperature | 0 | 1.09 (1.003–1.19) | 10% coldest days | Phlebitis, throbophlebitis | |
| Gomes et al. (2015) | Mabuto/Mozambique | Case-crossover/ 2005–2006 | Minimum temp. | Within 7 days | 1.39 (1.11–1.74) | Declines higher than 2.4 °C in minimum temp. | Stroke | Humidity, precipitation, age, smoking, cholesterol, diabetes |
| **Cold spells** | | | | | | | | |
| Ma et al. (2011) | Shanghai/China | Cold-spells vs. Non-Cold spell | Maximum & Mean temperature | 0 | 1.33 (1.28–1.37) | Maximum & average ≤3rd & 7 days | CV | |
| Shaposhnikov et al. (2014) | Russia | TS/1992–2005 | Mean temperature | 0–2 | 1.91 (1.07–3.41) | ≤3rd & ≥5 days | Brain stroke | DOW, season, trend |
| **Heat Effects** | | | | | | | | |
| Ye et al. (2001) | Tokyo/Japan | TS/1980–1995 | Maximum temperature | 0 | 0.986 (0.98–0.996) | 1 °C increase | Hypertension | Season, trend, air pollution |
| Konken et al. (2003) | Denver, Colorado/USA | TS/1993–1997 | Maximum temperature | 0<br>1<br>1 | 1.175 (1.029–1.343)<br>0.875 (0.811–0.945)<br>1.132 (1.029–1.244) | 1 °C increase | Acute myocardial infarction<br>Coronary atherosclerosis<br>Congestive heart failure | Trends, DOW, air pollution |
| Schwartz et al. (2004) | Multi-city/USA | TS/1986–1994 | Mean temperature | 0<br>6 | 1.003 (0.999–1.007)<br>0.999 (0.997–1.000) | | ICD-codes for CV and MI | DOW, season, humidity, atmospheric pressure |
| Kovats et al. (2004) | England/1994–2000 | TS/GLM | Mean temperature | 0 | 1.17 (0.973–1.063) | 24 °C | ICD-10 codes for CV | Autocorrelation, season, humidity, air pollution, influenza count |
| Ebi et al. (2004) | USA | TS/1983–1998 | Maximum temperature | 7 | 1.008 (1–1.017)<br>0.979 (0.966–0.992)<br>0.966 (0.949–0.984)<br>1.009 (1.005–1.012)<br>0.988 (0.986–0.990)<br>0.974 (0.958–0.991)<br>1.004 (0.999–1.010)<br>0.965 (0.956–0.974)<br>0.978 (0.965–0.992)<br>1.009 (1.007–1.011)<br>0.975 (0.972–0.977)<br>0.968 (0.948–0.988)<br>1.015 (0.994–1.038)<br>0.993 (0.987–0.998)<br>0.953 (0.922–0.984)<br>1.001(1–1.002)<br>0.988 (0.988–0.989)<br>0.955(0.943–0.967)<br>0.999 (0.995–1.002)<br>0.962 (0.960–0.964)<br>0.967(0.947–0.987)<br>1.002 (0.999–1.004)<br>0.970 (0.964–0.978)<br>0.970 (0.964–0.978)<br>0.982 (0.970–0.994) | 1 °C increase | Stroke | Season, trend |

(continued on next page)

**Table 1** (*continued*)

| Authors/year | City/country | Study design/time-span | Exposure | Lags (days) | Outcome | | | Controlled variables |
|---|---|---|---|---|---|---|---|---|
| | | | | | RR/OR (95% CI) | Correspondent change in temperature/threshold | Cardiovascular morbidity | |
| Kyobutungi et al. (2005) | Heidelberg/Germany | Case-crossover | Mean temperature | 0 | 1.04 (0.98–1.09)<br>2.0 (0.7–5.9) | Increase 1 °C<br>Increase 5 °C | Stroke | Hypertension, diabetes, smoking, previous stroke, family history of stroke, atrial fibrillation |
| Barnett et al. (2005) | 24 countries | TS/1980–1995 | Mean temperature | 0–3 | 0.992 (0.988–0.996) | 1 °C increase from Mean temperature | Coronary events | Humidity |
| Misailidou et al. (2006) | Greece | 2003–2004 | Mean temperature | 0 | 0.984 (0.978–0.991) | Change in 1 °C | Acute coronary syndrome | Humidity, region, DOW, interaction |
| Ren et al. (2006) | Brisbane/Australia | TS/1996–2001 | Minimum temperature | 0 | 0.995 (0.979–1.010) | 19.3 °C | CVD hospital admissions | Season, trend, DOW, year, rain, humid, ozone, flu, PM |
| | | | | 0 | 0.996 (0.949–0.983) | | | |
| | | | | 1 | 1.001 (0.985–1.014) | | | |
| | | | | 1 | 0.992 (0.974–1.011) | | | |
| | | | | 2 | 1.015 (1.001–1.027) | | | |
| | | | | 2 | 0.986 (0.968–1.005) | | | |
| | | | | 0 | 0.996 (0.974–1.015) | | | |
| | | | | 0 | 1.005 (0.982–1.029) | | | |
| | | | | 1 | 1.012 (0.992–1.028) | | | |
| | | | | 1 | 0.992 (0.968–1.015) | | | |
| | | | | 1 | 1.012 (0.993–1.029) | | | |
| | | | | 2 | 0.979 (0.956–1.003) | | | |
| Dawson et al. (2008) | Scotland | TS/1990–2005 | Maximum temperature | 0 | 0.995 (0.987–1.003) | 1 °C increase from average | IS | Season, year, DOW, pressure |
| | | | | 0 | 0.979 (0.957–1.002) | | HS | |
| | | | | 0 | 1.011 (1.001–1.022) | | Lacunar and other ischemic stroke | |
| | | | Min temperature | 0 | 1.001 (0.993–1.008) | | IS | |
| | | | | 0 | 0.993 (0.974–1.014) | | HS | |
| | | | | | 1.007 (0.996–1.018) | | Lacunar and other ischemic stroke | |
| | | | Mean temperature | 0 | 0.997 (0.989–1.006) | | IS | |
| | | | | 0 | 0.983 (0.96–1.007) | | HS | |
| | | | | 0 | 1.01 (0.999–1.022) | | | |
| | | | Mean temperature | 2 | 1.014 (0.993–1.035) | | Ischemic stroke (IS) | |
| | | | | 2 | 1.028 (0.971–1.089) | | Haemorrhagic stroke (HS) | |
| | | | | 1 | 1.021 (1.007–1.035) | | Ischemic stroke | |
| | | | | 1 | 0.994 (0.957–1.033) | | Haemorrhagic stroke | |
| | | | | 2 | 0.979 (0.939–1.02) | | Lacunar and other ischemic | |
| | | | | 1 | 1.006 (0.979–1.034) | | stroke | |
| Michelozzi et al. (2009) | 12 European cities | TS/GLM 1990–2004 | Maximum apparent temperature | 0 | 0.994 (0.982–1.005)<br>0.994 (0.988–1.001) | 32.3 | ICD-9 codes for CV | Holidays, DOW, calendar month, air<br>pollution, other meteorological factors |
| Wang et al. (2009) | Brisbane/Australia | TS/1996–2005 | Maximum temperature | 0 | 1 (0.970–1.020) | 21 | CV (stroke) | Air pollutants, humidity |
| Lin et al. (2009) | USA/Temperate | TS/1991–2004 | Mean temperature | 0 | 0.997 (0.987–1.007) | 29.4(27.9–31) | ICD-9 codes for CVD from admissions records | Holidays, DOW, long-term trend, air pollution, atmospheric pressure |
| | | | | 1 | 1.006 (0.996–1.017) | | | |
| | | | | 2 | 1.006 (0.996–1.016) | | | |
| | | | | 3 | 1.036 (1.003–1.069) | | | |
| | | | | 4 | 1.007 (0.985–1.030) | | | |
| | | | Mean apparent temperature | 0 | 1.002 (0.961–1.043) | 35.6(32.5–38.6) | | |
| | | | | 1 | 1.025 (1.006–1.044) | | | |
| | | | | 2 | 1.022 (1.005–1.039) | | | |
| | | | | 3 | 1.036 (1.019–1.053) | | | |
| | | | | 4 | 1.014 (0.996–1.032) | | | |
| Green et al. (2010) | USA/Temperate | Case-crossover/ 1999–2005 | Mean apparent temperature | 0 | 1 (0.998–1.002)<br>1.003 (0.999–1.007)<br>0.999 (0.993–1.005) | Not reported | All CVD<br>Ischemic heart disease<br>Acute myocardial infarction | Season, DOW, air pollution, non-linear effects |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | 0.981 (0.974–0.987)<br>0.997 (0.977–1.017) | | Hemorrhagic stroke<br>All celebrovascular disease | |
| Ostro et al. (2010) | California/USA | Case-crossover/ 1999–2005 | Apparent temperature | 0 | 1.002 (1.001–1.004)<br>1.003 (1–1.006)<br>1.001 (0.997–1.004) | Not reported | CV<br>CV (Stroke)<br>CV (MI) | Season, trend, family income, socio-economic factors |
| Wichmann et al. (2011) | Copenhagen/Denmark | Case-crossover/ 2002–2006 | Max Apparent temperature | 0–5 | 0.989 (0.983–0.995) | 8 °C increase (1 IQR) | CVD | air pollutants, public holidays, influenza |
| Pudpong and Hajat (2011) | Thailand/ Tropical | Time-series/ 2002–2006 | Mean temperature | 0–13 | 0.979 (0.867–1.105) | 29 °C | ICD-10 codes for CV | Season, long-term trend, number of hospital involved, month, day of week, holiday, influenza, air pollution, humidity, rainfall. |
| Alessandrini et al. (2011) | Emilia-Romagna/ Italia | TS/2002–2006 | Mean apparent | 0 | 1.079 (1.038–1.12) | 30 | Emergency ambulance dispatches | Air pollution, season, trend, holidays & weekend |
| Wilker et al. (2012) | Boston/USA | Repeated measure analysis | Mean apparent temperature | 0–3<br>0–4<br>0–4 | 1.113 (1.11–1.225)<br>1.114 (1.012–1.225)<br>1.216 (1.025–1.442) | 5 °C increase | Biomarkers of Heart failure | Humidity, pressure, Ozone, PM2.5 |
| Bhaskaran et al. (2012) | Multi-conurbation/- England & Wales | Case-crossover | Mean temperature | 1–6 h<br>7–12 h<br>13–18 h<br>19–24 h<br>25–48 h<br>49–192 h<br>193–360 h | 1.019(1.005–1.033)<br>1.002 (0.991–1.014)<br>1.011 (0.997–1.026)<br>0.989 (0.997–1.001)<br>0.991 (0.981–1.001)<br>0.996 (0.986–1.006)<br>0.991 (0.981–1.002) | 1 °C increase above 20 °C | Acute myocardial infarction | Air pollution |
| Basu et al. (2012) | California/USA | Case-crossover | Apparent temperature | 0 | 1.017 (1–1.033)<br>1.028 (1.009–1.047)<br>1.028 (1.009–1.049)<br>1.127 (1.083–1.174)<br>0.9 (0.87–0.94)<br>0.916 (0.851–0.986)<br>0.864 (0.775–0.962) | 10 °F increase | Ischemic heart disease<br>Ischemic stroke<br>Cardiac dysrhythmia<br>Hypotension<br>Hypertension<br>Hemorrhagic stroke<br>Aneurysm | Air pollution |
| Turner et al. (2012a) | Brisbane/Australia | TS/2000–2007 | Mean temperature | 0–1<br>2–15<br>16–27 | 1.005 (0.997–1.012)<br>0.982 (0.969–0.994)<br>−0.35 (−1.51,0.81) | 1 °C increased above 22 | CVD Ambulant attendances | Season, trend, DOW, holidays, air pollution |
| Hori et al. (2012) | ?/Japan | TS/ | Mean temperature | 0 | 1.078 (1.021–1.133)<br>1.36 (1.16–1.59)<br>1.117 (1.004–1.199) | | Acute coronary syndrome<br>Intracerebral haemorrhage<br>Cerebral infarction | Season, tend, DOW, holidays, influenza |
| Williams et al. (2012) | Perth/Australia | TS/1994–2008 | Max temp.<br>Min temp. | 0<br>0 | 1.022 (0.991–1.054)<br>1.014 (0.990–1.039) | 10 °C increase | CVD ED | Air pollution |
| Monteiro et al. (2013) | Porto/Portugal | TS/2002–2007 | Apparent temperature | 0 | 0.975 (0.957–0.993) | | Circulatory morbidity | Ozone, PM |
| Radisauskas et al. (2013) | Kaunas/Lithuania | TS/2000–2007 | Mean temperature | 0 | 0.97 (0.96–0.98) | 5 °C increase | Acute Myocardial infarction | Atmospheric pressure |
| Wang et al. (2013a, 2013b) | China | TS/1990–2009 | Mean temperature | 0 | 0.43 (0.31–0.59) | 30 °C vs. 15 °C | Ischemic stroke | Season, trend, DOW, holidays |
| Tanigawa-Sugihara et al. (2013) | Japan | Cross-sectional analysis of prospective cohort | Mean temperature | 1 | 1.016 (0.978–1.055)<br>0.912 (0.876–0.950) | 5 °C increase from 18 °C | Out-hospital Cardiac Arrest in <74 year-olds<br>Out-hospital Cardiac Arrest in ≥74 year-olds | Humidity, pressure |
| Son et al. (2014) | Multi-city/Korea | TS/2003–2008 | Mean temperature | 0 | 4.5% (0.7–8.5) | 99th (25) vs. 90th (15) | CVD | Season, trend, humidity, DOW |
| Giang et al. (2014) | Hanoi/Vietnam | Time-series/2008–2012 | Mean temperature | 0–30 | 1.17 (0.9–1.52) | 26 °C | Myocardial infarction, angina pectoris, congestive heart failure, hypertension, stroke. | Trend, DOW, holidays |
| Das et al. (2014) | Multi-countries | Case-crossover/ 2007–2010 | Maximum temperature<br>Mean temperature | 1–3<br>1–3 | 1.18 (1.06–1.30)<br>1.21 (1.1–1.32) | | Acute heart failure | |
| Ravljen et al. (2014) | Slovenia | TS/2008–2011 | Mean temperature | 0 | 0.993 (0.988–0.998) | | Acute coronary syndrome | Humidity, season, atmospheric pressure |

(continued on next page)

**Table 1** (*continued*)

| Authors/year | City/country | Study design/time-span | Exposure | Lags (days) | Outcome | | | Controlled variables |
|---|---|---|---|---|---|---|---|---|
| | | | | | RR/OR (95% CI) | Correspondent change in temperature/threshold | Cardiovascular morbidity | |
| Sheridan and Lin (2014) | New York/USA | TS/1991–2004 | Hot days | 0 | 1.002 (0.989, 1.014) | | ICD-10 for CVD | |
| Wang and Lin (2014) | Taipei/Taiwan | TS/2000–2009 | Mean temperature | 0–3<br>0 | 2.36 (1.33–4.19)<br>1.69 (1.01–3.58) | 32 vs. 26 | Cerebrovascular diseases | Humidity, season, trend, wind speed, DOW, holidays, influenza |
| Gronlund et al. (2014) | Multi-city/USA | Case-crossover | Mean apparent temperature | 0–1<br>0–7<br>0–1<br>0–3<br>0–5<br>0–7 | 0.996 (0.994–0.998)<br>0.987 (0.984–0.99)<br>0.984 (0.973–0.994)<br>0.98 (0.971–0.99)<br>0.98 (0.97–0.99)<br>0.982 (0.973–0.992) | 90th vs. 75th<br><br>99th vs. 75th | ICD-10 codes for CVD | |
| Lee et al. (2014) | Korea | TS/2006–2010 | Maximum temperature<br>Mean temperature | 4<br>0 | 1.07 (1.05–1.10)<br>1.26 (1.08–1.46) | 31.5<br>28.5 | Acute Myocardial infarction | Season, trend, other meteorological factors, air pollution |
| Urban et al. (2014) | Prague/Czech | TS/1994–2009 | Mean temperature | 0 | 1.064 (1.004–1.128) | 10% warmest days | Atherosclerosis | |
| Shaposhnikov et al. (2014) | Moscow/Russia | TS/<br>1992–2005 | Mean temperature | 0–1 | 1.16 (1.02–1.3) | 10 °C increase | Brain stroke | Season, trend, weekends, holidays |
| Webb et al. (2014) | Australian | Cohort/1992–2011 | Maximum temperature | 0 | 1.32 (1.1–1.56) | 95th vs. 90th | IDH | Indigenous females |
| **Heatwave effects** | | | | | | | | |
| Semenza et al. (1999) | Chicago/USA | Comparison/heatwave vs. non-heatwave | Mean temperature | 0 | 1.23 (1.07–1.38) | Specific time | ICD-9 codes of CVD | |
| Mastrangelo et al. (2007) | Veneto/Italy | Comparison/GEE model | Mean temperature | 0 | 1.0 (0.99–1.01) | Specific heatwave periods | Circulatory | DOW |
| Empana et al. (2009) | Paris/France | Heatwave vs. non-heatwave | Mean temperature | 0 | 2.34 (1.6–3.41) | Specific time (>38.1 °C) | Out-of-hospital cardiac arrest | Age, gender |
| Knowlton et al. (2009) | California/USA | Heatwave vs. non-heatwave | Specific time defined by the meteorologist | 0 | 1.02 (1.01–1.03)<br>1.01 (1–1.02)<br>1.02 (0.96–1.07)<br>1.02 (0.97–1.06)<br>1.05 (1.02–1.09) | | ED visits for CVD<br>Hospitalizations<br>Acute MI, ED visits<br>Acute MI, hospitalizations<br>CVD, ED visits | State wide<br><br><br><br>Central Coast region |
| Wang et al. (2012) | Taiwan | TS/2000–2009 | Mean temperature | 0 | 1.23 (0.98–1.54) | 99th & >3 days | Circulatory diseases | Air pollution |
| Williams et al. (2012) | Perth/Australia | Heatwave vs. non-heatwave | Maximum temperature | 0 | 1.017 (0.953–1.086) | ≥35 °C & ≥3 days | CVD EDs | Air pollution |
| Vaneckova and Bambrick (2013) | Sydney/Australia | Case-crossover | Mean temperature | 0 | 1.01 (1–1.02)<br>1 (0.98–1.03) | 95th & 2–3 days<br>99th & 2–3 days | CVD | Ozone, humidity, PM |
| Turner et al. (2013) | Brisbane/Australia | TS/2000–2007 | Maximum temperature | 0 | 1.295 (1.004–1.67) | Max. temp > 37 °C for ≥2 days | Ambulance attendances | Other climates & air pollution |
| Sheridan and Lin (2014) | New York/USA | TS/1991–2004 | Apparent temperature | 0 | 0.981 (0.959–1.002) | Specific time | ICD-10 for CVD | |
| Ma et al. (2011) | China/Shanghai | Heatwave vs. non-heatwave | Maximum temperature | 0 | 1.08 (1.05–1.11) | Maximum temp. >35 & mean temp >97th & ≥7 days. | ICD-10 codes for CVD | |
| Bobb et al. (2014) | USA/temperate | TS/1999–2010 | ≥99th & ≥2 days | | 0.979 (0.970–0.987) | 99th & ≥2 days | CVD | Season, trend |
| Gronlund et al. (2014) | Multi-city/USA | Case-crossover | Apparent temperature | 0<br>0<br>0<br>0 | 0.996 (0.987–1.005)<br>1.006 (0.994–1.018)<br>0.994 (0.976–1.012)<br>0.991 (0.965–1.018) | Temp ≥95th & 2 days<br>≥95th & 4 days<br>≥95th & 6 days<br>≥95th & 8 days | ICD-10 codes for CVD | |
| Son et al. (2014) | Korea | TS/2003–2008 | Mean temperature | 0 | 0.957 (0.856–1.07) | 98th & ≥2 days | CVD | Season, trend, humidity, DOW |
| Shaposhnikov et al. (2014) | Moscow/Russia | TS/1992–2005 | Mean temperature | 1 | 0.68 (0.48–0.95) | ≥97th & ≥5 days | MI | DOW, season, trend |
| Ma et al. (2011) | China/Shanghai | Compare incidence/<br>2005–2008 | Maximum & mean temperature | 0 | 1.33 (1.28–1.37) | ≤3rd & ≥7 days | ICD-10 codes for CVD | |
| Phung et al, 2015 | Ho Chi Minh City/<br>Vietnam | TS/ 2004-2013 | Mean temperature | 0 | 1.129 (0.972-1.311) | ≥99th & ≥2 days | ICD-10 codes for CVD | Season, trend, humidity, DOW |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| **Diurnal temperature** | | | | | | | | |
| Lee et al. (2010) | Korea | TS/2005–2007 | Mean temperature | 0 | 1.068 (1.005–1.13) | Increased by 5 °C | Acute myocardial infarction | DOW, season, holidays, other climate factors |
| Lim et al. (2012) | Korea | TS/2003–2006 | DTR | 0 | 1.03 (1.014–1.046) | | Cardiac failure | |
| Wang et al. (2013a) | China | TS/2009–2011 | Mean temperature | 0 | 1.004 (0.999–1.046) | 1 °C increase in DRT | CVD | Season, trend, weather, air pollution |
| | | | | 1 | 1.004 (0.99–1.046) | | | |
| | | | | 2 | 1.002 (0.998–1.007) | | | |
| | | | | 3 | 1.0007 (0.997–1.005) | | | |
| | | | | 4 | 1.0001 (0.996–1.004) | | | |
| | | | | 5 | 0.997 (0.993–1.001) | | | |
| | | | | 6 | 0.997 (0.993–1) | | | |
| | | | | 7 | 1.001 (0.972–1.005) | | | |
| | | | | 0–1 | 1.006 (1–1.012) | | | |
| | | | | 0–2 | 1.008 (1.001–1.015) | | | |
| | | | | 0–3 | 1.007 (1–1.015) | | | |
| | | | | 0–4 | 1.007 (0.999–1.015) | | | |
| | | | | 0–5 | 1.004 (0.996–1.013) | | | |
| | | | | 0–6 | 1.001 (0.993–1.01) | | | |
| | | | | 0–7 | 1.002 (0.993–1.01) | | | |
| Shaposhnikov et al. (2014) | Russia | TS/ 1992–2005 | Mean temperature | 0–5 | 1.26 (1.02–1.57) | 10 °C increase in DRT | Brain stroke | DOW, season, trend |
| Qiu et al. (2013) | China | TS/2000–2007 | DTR | 0 | 1.009 (1.003–1.014) | 1 °C increase | Heart failure | Season, trend, mean temperature, humidity, air pollution |
| | | | | 1 | 1.009 (1.003–1.014) | | | |
| | | | | 2 | 1.008 (1.003–1.013) | | | |
| | | | | 3 | 1.009 (1.004–1.014) | | | |
| | | | | 4 | 1.006 (1.001–1.011) | | | |
| | | | | 5 | 1.006 (1.003–1.011) | | | |
| | | | | 0–5 | 1.038 (1.034–1.042) | Cumulative effect | | |
| Liang et al. (2008) | Taiwan | TS/2000–2003 | Mean temperature | 0 | 1.34 (1–1.8) | DTR > 9.6 compared with DTR < 5.8 | Emergency room admissions for ACS | Season, holidays, air pollution |

TS: time-series, DTR: diurnal temperature; DOW: day of week; CVD: cardiovascular diseases; RR: relative risk; OR: odds ratio.

countries (Fig. 2). Of the included studies, 11 reported the effects of cold only (Bhaskaran et al., 2010; Goggins et al., 2013; Goggins et al., 2012; Gomes et al., 2015; Hajat and Haines, 2002; Hong et al., 2003; Mostofsky et al., 2014; Panagiotakos et al., 2004; Vasconcelos et al., 2013; Wang et al., 2012; Wolf et al., 2009). Among them, only two studies reported the effects of cold spells. Therefore, cold spells were not involved in further analysis. Twenty four studies reported the effects of heat only (Alessandrini et al., 2011; Barnett et al., 2005; Basu et al., 2012; Bhaskaran et al., 2012; Das et al., 2014; Dawson et al., 2008; Ebi et al., 2004; Green et al., 2010; Hori et al., 2012; Konken et al., 2003; Kovats et al., 2004; Lin et al., 2009; Michelozzi et al., 2009; Monteiro et al., 2013; Ostro et al., 2010; Pudpong and Hajat, 2011; Radisauskas et al., 2013; Ravljen et al., 2014; Ren et al., 2006; Schwartz et al., 2004; Wang et al., 2009; Wichmann et al., 2011; Wilker et al., 2012; Ye et al., 2001), and nine studies provided evidence on heatwave-cardiovascular relationship (Bobb et al., 2014; Empana et al., 2009; Knowlton et al., 2009; Ma et al., 2011; Mastrangelo et al., 2007; Semenza et al., 1999; Turner et al., 2013; Vaneckova and Bambrick, 2013; Wang et al., 2012) while two studies reported the effects of variation in diurnal temperature only (Lim et al., 2012; Qiu et al., 2013). Seventeen studies reported the effects of multiple temperature exposure, of which nine studies examined the effects of both cold and heat exposure (Giang et al., 2014; Kyobutungi et al., 2005; Lee et al., 2014; Misailidou et al., 2006; Tanigawa-Sugihara et al., 2013; Turner et al., 2012a; Urban et al., 2014; Wang and Lin, 2014; Webb et al., 2014), two studies examined cold and diurnal temperature exposure (Lee et al., 2010; Liang et al., 2008), one study examined cold, heat and diurnal temperature exposure (Wang et al., 2013a), one study examined cold, heat and heatwave exposure (Webb et al., 2014), 3 studies examined heat and heatwave exposure (Gronlund et al., 2014; Sheridan and Lin, 2014; Williams et al., 2012), and only one study examined heat, heatwave and diurnal temperature (Shaposhnikov et al., 2014). The most commonly used temperature measurements were daily mean and maximum temperature, although some studies used minimum, apparent, and physiologically equivalent temperature (PET).

Some explicit threshold values were provided from the included studies. The mean temperature associated with cold effect ranged from 5 to 26 °C while that associated with heat effect ranged from 24 to 35.6 °C. In absence of a derived threshold, the remaining studies used average value or a specific percentile of temperature to test for the presence of temperature effect. The cold spell and heatwave definitions varied in the included studies; however the most common definitions the investigator used for these events were the long lasting extremes of temperature (e.g. ≤5th or ≥95th percentile for ≥2 days). The lag effects that were investigated in the included studies ranged from 0 to 30 days. One study, exceptionally, examined the lag effect by hours (Bhaskaran et al., 2012). Among the 64 included studies, 30 examined effect estimates for general cardiovascular diseases, and the rest examined effects for cause-specific cardiovascular diseases, including acute coronary syndrome, ischemic stroke, myocardial infarction, heart failure, hypertension, cerebrovascular disease, cardiac arrest. One study provided results in biomarkers of heart failure (Wilker et al., 2012). The most common method used to examine the relationship between temperature and cardiovascular hospitalizations was time-series using either generalized linear models (GLM) or generalized additive models (GAM) (e.g. Alessandrini et al., 2011; Barnett et al., 2005; Bhaskaran et al., 2010; Bobb et al., 2014; Dawson et al., 2008) while some studies used case-crossover design (e.g. Basu et al., 2012; Bhaskaran et al., 2012; Wichmann et al., 2011). Comparison of groups (e.g. Empana et al., 2009; Urban et al., 2014) and cohort studies (Tanigawa-Sugihara et al., 2013; Webb et al., 2014) were also employed. The most common confounding factors considered in exposure–outcome analyses comprised season and long-term trends using spline functions, days of the week, holidays, and air pollutants (Table 1). The reported OR/RR of incident cardiovascular hospitalizations in individual studies ranged from 0.93–2.9 (cold effect), 0.43–2.36 (heat effect), 0.68–2.34 (heatwave), and 0.99–1.34 (diurnal temperature). However, the means of OR/RR are all above unity (1.19, 1.03, 1.1, and 1.03, respectively). According to our quality criteria described in Table S2, the quality score of the included papers ranged from 15 to 26, corresponding to the range of 55–96% quality criteria met by papers. This result indicated that all papers included in the meta-analysis satisfied the quality criteria (score > the cut-off points of 13) and thus possess high research value.

### 3.2. Temperature and risk of cardiovascular hospitalizations

The pooled effect sizes of relationship between temperature exposure and risk of cardiovascular hospitalizations are separately reported for each of the temperature exposures: cold exposure, heat exposure, heatwave, and diurnal temperature. The pooled effect size for the relationship between the change in temperature condition and the change in risk of cardiovascular hospitalizations was a 2.8% increase (RR, 1.028; 95% CI, 1.021–1.035) for cold exposure (Fig. 3), 2.2% increase (RR, 1.022; 95% CI, 1.006–1.039) for heatwave exposure (Fig. 4), and 0.7% increase (RR, 1.007; 95% CI, 1.002–1.012) for an increase in diurnal temperature (Fig. 6). In contrast, no effect of heat exposure on the risk of cardiovascular hospitalizations was observed when all studies were included (RR, 0.997; 95% CI, 0.994–0.999) (Fig. 5). However, when incorporating the variation of effect sizes from different settings using the EB approach, the pooled effect sizes were increased for all types of temperature exposure (Fig. 7), comprising: 7.8% (RR, 1.078; 95% CI, 1.074–1.081) for cold exposure, 1% (RR, 1.01; 95% CI, 1.008–1.011) for heat exposure, 6.1% (RR, 1.061; 95% CI, 1.053–1.07) for heatwave exposure, and 1.5% (RR, 1.015; 95% CI, 1.011–1.02) for an increase in diurnal temperature. The significant heterogeneity between studies was found with all of the temperature exposure categories. The percentages of total variation across these studies caused by heterogeneity were high: $I^2$, 92.2% for cold exposure, 95.7% for heat exposure, 92.6% for heatwave, and 92.5% for diurnal temperature. These reflected inconsistent results of ORs/RRs among the included studies. The Begg's funnel plot with pseudo 95% confidence limits and Egger's test revealed potential publication bias for cold exposure (Egger's bias, 2.5, $p < 0.05$) while no evidence of publication bias was found for the heat exposure, heatwave, or diurnal temperature (Egger's bias, 2.5, $p = 0.4$; Egger's bias, 0.43, $p = 0.4$; Egger's bias, 1.95, $p = 0.9$; Egger's bias, 1.08, $p = 0.5$, respectively).

The dose–response effects of temperature, lag and latitude on the risk of cardiovascular hospitalizations are shown in Table 2. The results showed that the risk of cardiovascular hospitalizations significantly increase with each degree (1 °C) decrease in temperature in cold exposure (0.8%, 95% CI: 0.08–1.5) and with each degree (1 °C) increase in diurnal temperature (1.9%, 95% CI: 0.5–3.3), whereas the risk of cardiovascular hospitalizations decreased with each degree (1 °C) increase in temperature in heat exposure (−0.5, 95% CI: −0.9–0.04). However, this dose–response relationship was not statistically significant. An increase in one-day lag was associated with a borderline statistically significant (at 92% & 93%) reduction in risk of cardiovascular hospitalizations for cold exposure (−0.6%, 95% CI: −1.2–0.08) and diurnal temperature (−0.2%, 95% CI: −0.4–0.01) while no significant effect was seen in heat exposure. The increase of one-degree in latitude was found to statistically associate with a decrease in risk of cardiovascular hospitalizations (−0.05, 95% CI: −0.09–0.01) for diurnal temperature only. For all temperature exposures, $I^2$ values were mostly on the order of 88% to 100%, indicating large between-study heterogeneity, and supporting the use of random effect models.

Sensitivity analysis with the exclusion of studies with quality score of less than 20 points shows a very subtle change in the effects of cold exposure (RR, 1.029 vs. 1.028) and no difference for heat, heatwave, and diurnal temperature exposure. Subgroup analysis, which was performed for lag 0-day only, provided a higher risk of cardiovascular hospitalizations for heatwave exposure (RR, 1.024, 95% CI: 1.008–1.040)

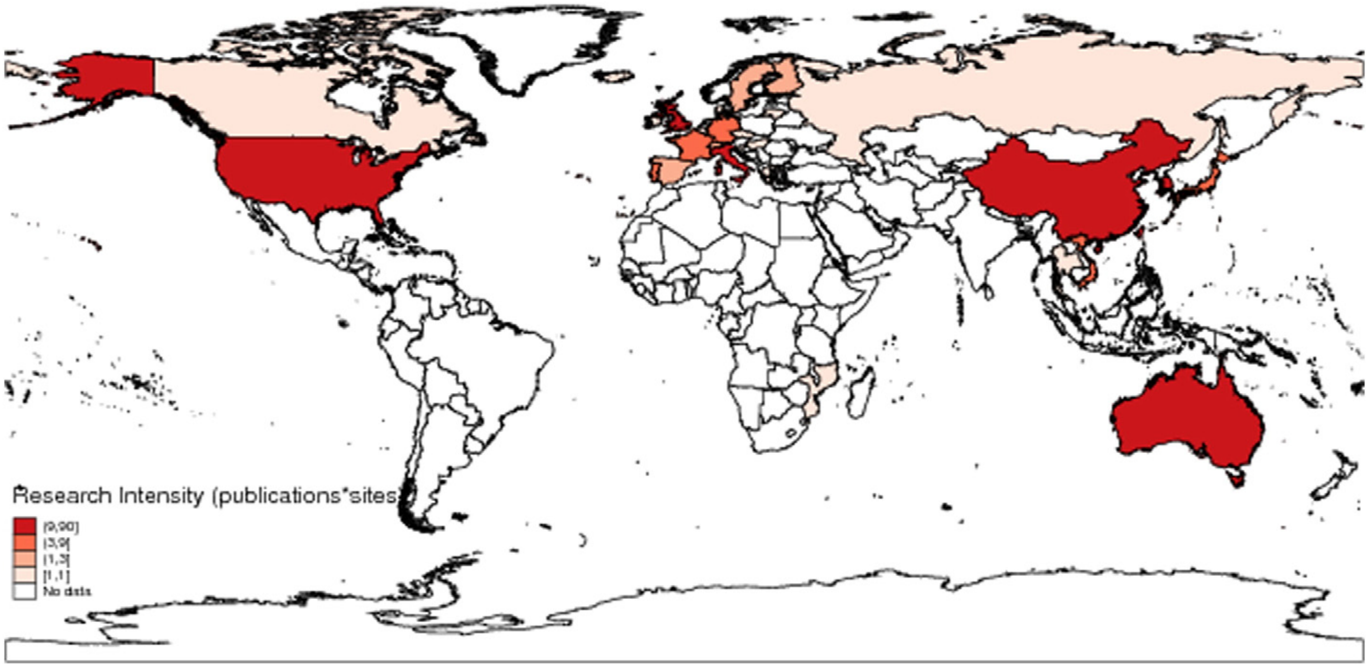


**Fig. 2.** Research Intensity (number of publications x number of sites) on the relationship between ambient temperature and cardiovascular morbidity in the world.

and diurnal temperature (RR, 1.019, 95% CI: 1.001–1.036) in comparison with the overall pooled effect sizes, whereas the lag-0 effect was lower for cold exposure (RR, 1.015, 95% CI: 1.008–1.023). The sensitivity analysis with the exclusion of the studies using CVD consultation and CVD-biomarkers as the outcomes provided the same results as those obtained for overall pooled effect sizes (the results are not shown).

## 4. Discussion

This meta-analysis offers an updated quantitative examination of the effects of different ambient temperature conditions, including cold, heat, heatwave, and diurnal exposure on risk of cardiovascular hospitalizations. The strength of the study is to fill the gaps of knowledge about temperature-cardiovascular morbidity reported from previous studies (Astrom et al., 2011; Bhaskaran et al., 2009; Turner et al., 2012b; Ye et al., 2012) which did not provide the quantitative pooled effect sizes of the temperature-cardiovascular morbidity relationship for separated temperature exposure conditions. In this study, we found the significantly increased risk of cardiovascular hospitalizations in relation to cold, heatwave exposure, and variation in diurnal temperature. However, the relationship between heat exposure and cardiovascular hospitalizations was found to be inconsistent. A reduction in risk of cardiovascular hospitalizations has been found when lags are longer. Heatwave exposure causes more immediate effects than cold exposure. Latitude modifies the temperature-cardiovascular hospitalization relationship with variation in diurnal temperature only.

The significant effect of cold exposure on elevated risk of cardiovascular diseases is consistent with the findings of a majority of previous studies, in which increased risk of cardiovascular hospitalizations was associated with a reduction in temperature during the cold seasons. The risk of ischemic stroke (IS) increases by 2%–53% with each 1 °C decrease from the average and threshold temperature (Goggins et al., 2012; Mostofsky et al., 2014; Wang et al., 2013b), and the risk of IS elevated from 130% (Kyobutungi et al., 2005) to 190% (Hong et al., 2003) when the temperature reduces from 5 °C to 17 °C. A decrease of 1 °C in average temperature causes an increase of 1.6–6% in risk of acute coronary syndrome (ACS) (Misailidou et al., 2006; Panagiotakos et al., 2004), and a decrease of 10 °C causes an increase of up to 54% in risk of ACS (Liang et al., 2008). Likewise, the risk of myocardial infarction (MI) rises by 0.6–12% for each 1–5 °C decrease from average and threshold temperature (Bhaskaran et al., 2010; Giang et al., 2014; Goggins et al., 2013; Lee et al., 2014; Vasconcelos et al., 2013; Wolf et al., 2009). The risk of emergency admissions due to cerebrovascular and hypertensive diseases increases by 56–78% when the temperature decreases 12 °C from the threshold temperature (26 °C) (Wang and Lin, 2014). The risk of cardiac arrest among the elder population was found to increase by 11–16% when the temperature went down by 5 °C from a threshold of 18 °C in Japan (Tanigawa-Sugihara et al., 2013). Several plausible mechanisms are potentially involved in increasing the risk of cardiovascular hospitalizations due to cold exposure. A potential pathological mechanism is that cold exposure causes different effects on the cardiovascular system, possibly mediated by stimulation of both sympathetic nervous activity and the coagulation system (DASH Collaborative Research Group et al., 2002; Kawahara et al., 1989; Keatinge et al., 1984; Touitou et al., 1986; Wilmshurst, 1994). The low air temperatures produce vasoconstriction leading to an increase in arterial pressure and in circulating levels of catecholamines, which can increase heart rate and cardiac work. These phenomena result in a greater oxygen demand and a potentially ischemic reaction in the vulnerable myocardium (Opie, 1998). Furthermore, cold temperatures are associated with an increase in blood pressure variability, resulting in higher cardiovascular hospitalizations and mortality (DASH Collaborative Research Group et al., 2002). In addition, the association between temperature and ACS may be indirectly causal as indoor smoking, lowliness and bodyweight increase during the winter (Wilmshurst, 1994).

In this study, we found that the heat exposure is inconsistently associated with risk of cardiovascular hospitalizations. However heatwaves, extended periods of heat exposure, are significantly associated with elevated risk of cardiovascular hospitalizations. The finding of the relationship between heat exposure and cardiovascular hospitalization is in lines with the recent review conducted by Turner et al. (2012b), in which the result of a meta-analysis indicated no apparent association between increased ambient temperature and cardiovascular morbidity (−0.5% change in risk of cardiovascular morbidity, 95%CI: −3%–2.1%) (Turner et al., 2012b). The inconsistent findings in this relationship were also reported in many original studies which suggested weak or absent association between heat exposure and cardiovascular morbidity (Barnett et al., 2005; Basu et al., 2012; Bhaskaran et al., 2012; Dawson et al., 2008; Ebi et al., 2004; Green et al., 2010; Gronlund et al., 2014; Konken et al., 2003; Lin et al., 2009; Michelozzi et al., 2009; Ostro et al., 2010; Radisauskas et al., 2013; Ren et al., 2006; Schwartz et al., 2004; Tanigawa-Sugihara et al., 2013; Turner et al., 2012a; Wang et al., 2009; Wichmann et al., 2011; Ye et al., 2001). One possible explanation for the difference between cold- and heat-cardiovascular morbidity is that decreased cardiovascular performance is less prevalent in the warmer months of the year (Turner et al., 2012b). Moreover, the CVD diseases inconsistently reacted to an increase in temperature. For example, the study by Konken et al. (2003) illustrated that higher temperatures are associated with increasing the frequency of hospitalization for acute myocardial infarction and congestive heart failure but did not influence visits for cardiac dysrhythmias. In contrast, higher temperature appeared to be a protective factor for coronary atherosclerosis and pulmonary heart diseases. This may be because people with chronic cardiovascular conditions avoid outdoor exposure during periods of peak heat. In addition, other factors such as age, gender and geographic region, which may modify the relationship between heat exposure and cardiovascular morbidity, were much varied among the included studies.

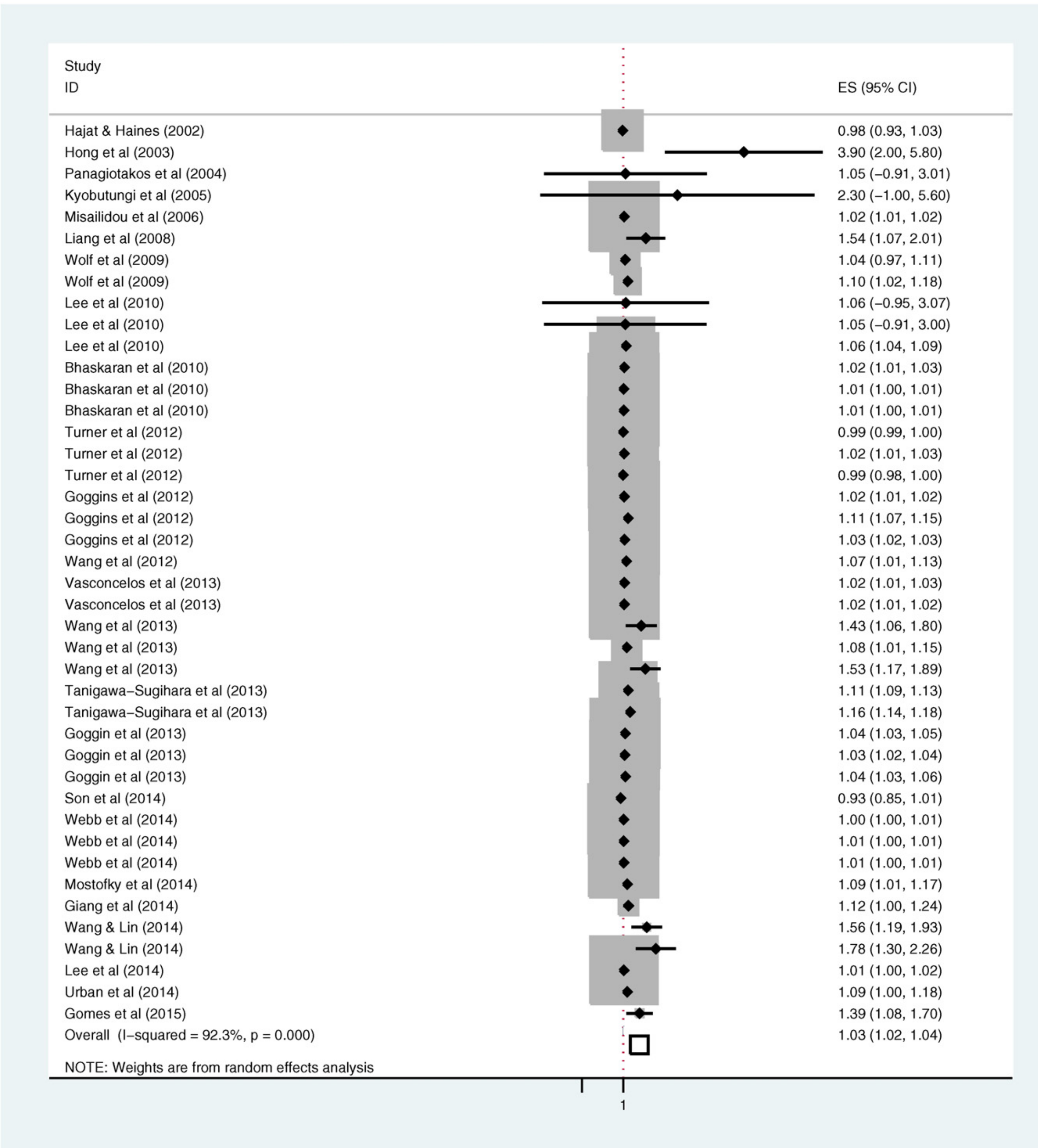


**Fig. 3.** Meta-analysis of cold exposure (defined as number of degrees below the defined threshold or average value, or comparison between extreme cold condition and the reference value, e.g. 5th vs. 90th) on the risk of cardiovascular hospitalization (Relative Risk & 95%CI).

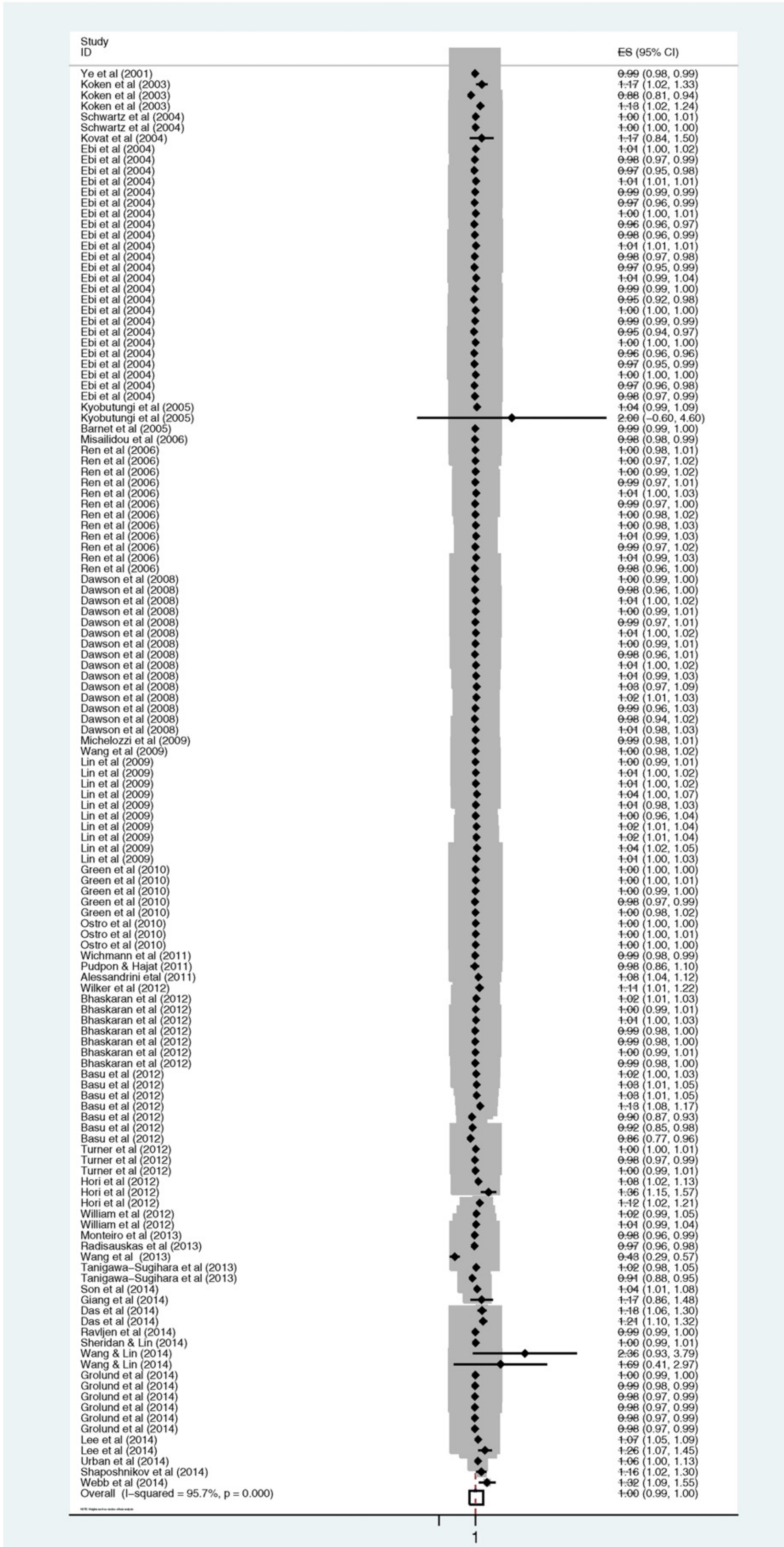


**Fig. 4.** Meta-analysis of heat exposure [defined as number of degrees above the defined threshold or average value but NOT during the cold season (e.g. winter), or comparison between extreme hot condition and the reference value (e.g. 99$^{th}$ vs. 75$^{th}$)] on the risk of cardiovascular hospitalization (Relative Risk & 95%CI).

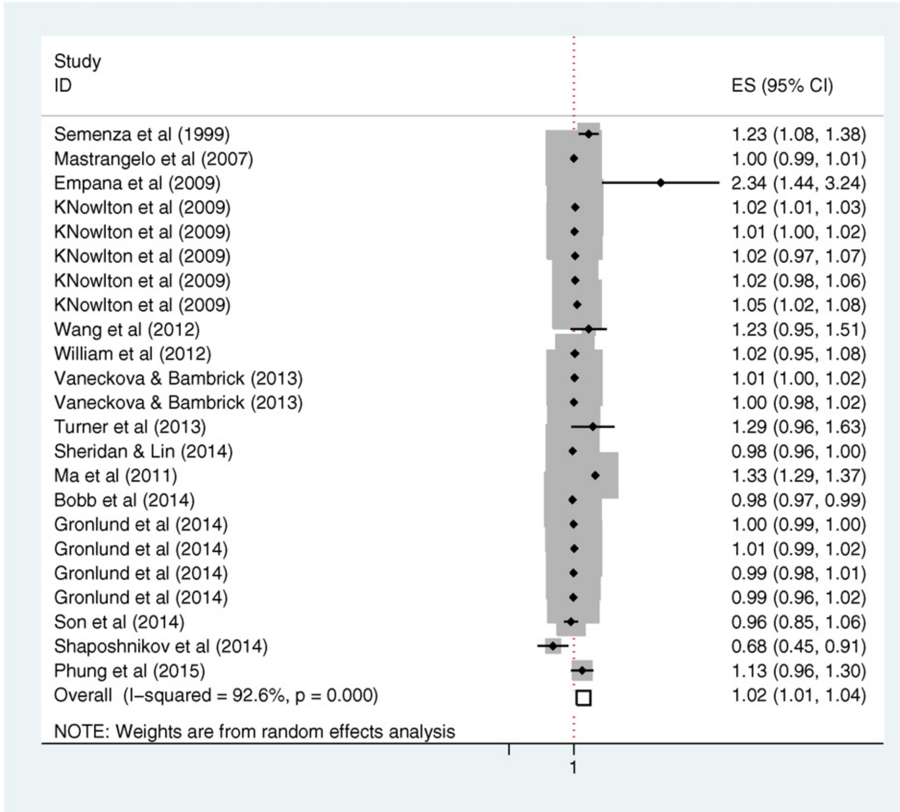


**Fig. 5.** Meta-analysis of heatwave exposure (defined as ≥ 2 days of extreme high temperature, e.g. 95$^{th}$) on the risk cardiovascular hospitalizations (Relative Risk & 95%CI).

In contrast to heat exposure, this study found a positive effect on the risk of cardiovascular hospitalizations from heatwave. This finding is consistent with the results of previous studies which found that long lasting extremely high temperatures were associated with the elevated risk of cardiovascular hospitalizations (Empana et al., 2009; Knowlton et al., 2009; Ma et al., 2011; Semenza et al., 1999; Turner et al., 2013; Wang et al., 2012; Williams et al., 2012). However, the previous study indicated that the cardiovascular disease was not a primary cause for admission, but as a pre-existing condition it was a risk factor for hospitalization, since diagnoses of chronic cardiovascular diseases (e.g. hypertensive disease) were more common than acute cardiac events (e.g. myocardial infarction). Elderly people (>65 year-olds) were more susceptible than other age groups. This can be explained by the physiological mechanisms of chronic heart insufficiency and/or the inability to increase cutaneous circulation, which can impede dissipation of extreme heat, resulting in increased risk of hospitalization. In addition, left ventricular diastolic filling declines with age as do cardiac output and heart rate (Schulman et al., 1992; Semenza et al., 1999).

The variation in diurnal temperature was found to significantly influence the risk of cardiovascular hospitalization in this study. This was consistent with the evidence provided from the original studies in different populations and settings. The studies (Qiu et al., 2013; Wang et al., 2013a) indicated that a one degree increase in diurnal temperature causes an increase by 0.35–3.8% in risk of cardiovascular hospitalization. The risk of cardiovascular hospitalization could rise by 6.8–34% if the diurnal temperature increases more than 5 °C (Lee et al., 2010; Liang et al., 2008; Shaposhnikov et al., 2014). Previous studies also found a significant association between diurnal temperature and cardiovascular mortality (Kan et al., 2007; Tam et al., 2009). These previous studies indicated that the most vulnerable group to diurnal temperature was people aged >40 years with pre-existing cardiovascular conditions (e.g. hypertension, high serum cholesterol level) (Shinkawa et al., 1990). The biological mechanism explaining this relationship is that a large change in temperature within one day may cause a sudden change in the heart rate and circulation of elderly people, and this phenomenon can act to increase the risk of cardiopulmonary and other diseases, even resulting in fatalities (Kenney and Hodgson, 1987).

In terms of latitude effect, this study found small negative effect of latitude on the risk of cardiovascular hospitalization for diurnal temperature exposure but not for cold and heat exposure. That means higher latitude countries show lower effects of diurnal temperature on the risk of cardiovascular hospitalization. This finding does not support the evidence from the previous review (Turner et al., 2012b) which indicated that there was an association with increased heat exposure at higher latitudes (colder climates) and risk of cardiovascular hospitalizations. The reasons for the latitude effect in colder climates were that the adaptive capacity of cold climate population is lower because the population is less acclimatized to high temperatures, live in houses that are unsuitable for hot weather, and have a lack of adaptive measures such as conditioning (Turner et al., 2012b). In terms of lag effect, this study found that the effects of exposure to hot temperatures were more immediate than for cold temperatures since the lag-0 effect of heatwave exposure was bigger than the overall effect (including all lags in analysis), whereas for cold exposure the lag-0 effects were the opposite. This finding was consistent with the results of the previous review conducted by Ye et al. (2012) which demonstrated more immediate effects of heat exposure in comparison with cold exposure. Most of the recent studies provided evidence on the short-term effects of high temperature on the same day and the 3 days following heat exposure (Green et al., 2010; Konken et al., 2003; Lin et al., 2009) while the effects of a longer lag were not clearly demonstrated from the studies (Ye et al., 2012). The more immediate effect of hot temperatures could also be an explanation for inconsistent findings in the relationship between heat exposure and cardiovascular hospitalizations, since heat exposure might cause an increase in out-of-hospital deaths before medical

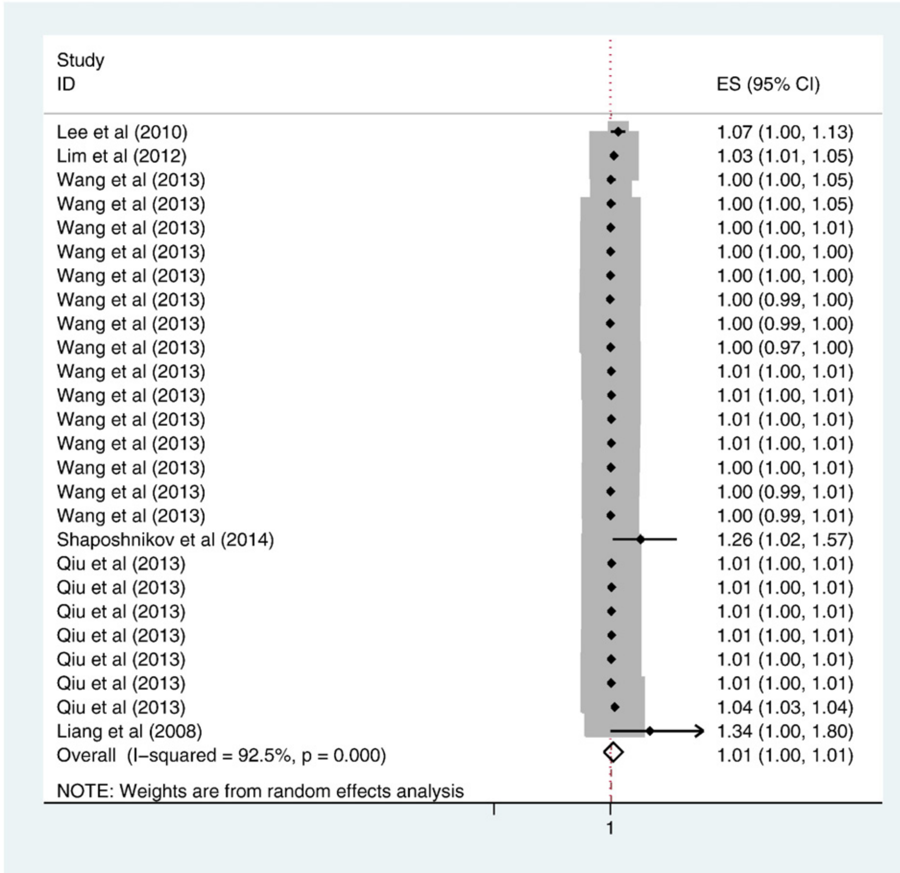


**Fig. 6.** Meta-analysis of diurnal temperature (defined as number of degrees between maximum and minimum temperature during the day) on the risk cardiovascular hospitalizations (Relative Risk & 95%CI).

treatment for acute cardiovascular events (Michelozzi et al., 2009; O'Neill and Ebi, 2009).

This study has some limitations. First, although an increased number of studies of the relationship between temperature and cardiovascular morbidity have been conducted recently, they were conducted predominantly in developed and temperate areas. Therefore, the pooled effect sizes could not be computed for specific geographical areas or for a limited range of climatic conditions, specifically for developing and tropical countries. Second, the variety of definitions in temperature exposure in individual included studies prevented the computation of normalized effect estimates for all exposures in step 1. Third, the number of included studies is not sufficient to examine the cause-specific cardiovascular disease but only all-cause cardiovascular hospitalizations. The previous review (Hajat and Haines, 2002) suggested that general practitioner consultations should be considered as the outcome for better strategies in early detection of temperature-related morbidity. Nevertheless, only one study using such outcome has been conducted since 2002. Fourth, the variety of latitudes, lags, temperature measurements and thresholds used in the included studies make the pooled estimates highly heterogeneous. However, this study used a Bayesian approach to incorporate

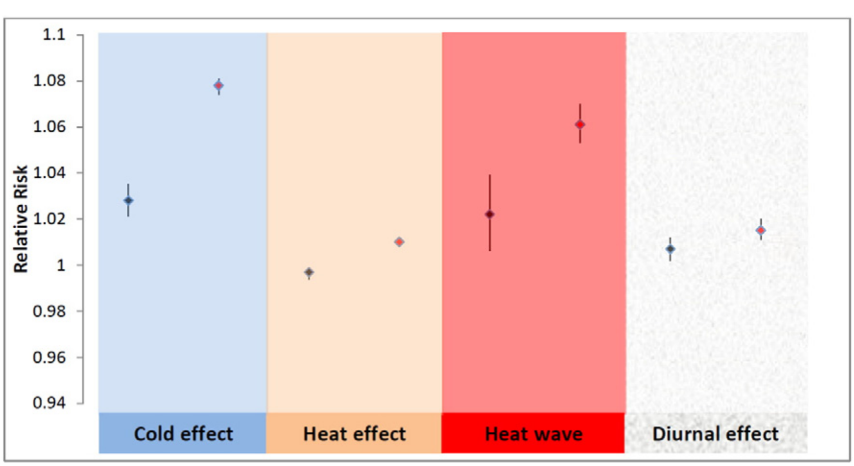


**Fig. 7.** Pooled effect sizes estimated by the normal and Empirical Bayesian approaches (blue: normal; red: Bayesian).

**Table 2**
The dose–response relationship between the risk of cardiovascular hospitalizations (%) and temperature, lag and latitude.

| Temperature exposure | One-degree change in temperature[a] | 95%CI | One-day increase in lag | 95%CI | One-degree increase in latitude | 95% CI |
|---|---|---|---|---|---|---|
| Cold exposure | **0.8**[b] | 0.08–1.5 | **−0.6**[c] | −1.2–0.08 | −0.07 | −0.2–0.1 |
| Heat exposure | −0.5 | −0.9–0.04 | −0.2 | −0.4–0.1 | −0.005 | −0.04–0.04 |
| Diurnal temperature | **1.9**[b] | 0.5–3.3 | **−0.2**[c] | −0.4–0.01 | **−0.05**[b] | −0.09–(−0.01) |

[a] One-degree decrease for cold exposure, and one-degree increase for heat and diurnal exposure.
[b] Statistically significant at 95%.
[c] Statistically significant at 92%.

the variation of these factors of included studies into the meta-analysis. Fifth, there is a lack of data on socioeconomic factors and adaptive capacity which can modify the relationship between temperature and cardiovascular morbidity to an important degree. A future study should be conducted to examine temperature-cardiovascular admissions queried by more potential variables such as geographical regions, age, sex, and other socio-economic factors.

For dose–response relationship between temperature and risk of CVD admissions, one-degree change for each temperature condition (cold, heat, diurnal) may have different meaning in different climate regions, and adjusting for latitude only might not completely remove the effects of different geographical difference. Future studies are needed to better understand the dose–response relationship in different climate regions. As the findings of this study indicated that heatwaves significantly associated with elevated risk of cardiovascular admission, it would be valuable to explore and to comment on the sensitivity of the result to selected metrics (such as maximum or minimum daily temperature), and derived indexes, such as apparent temperature, as well as the lag duration. Finally, the review may not be entirely comprehensive because non-English publications elsewhere such as Central-America, Middle East were not evaluated.

## 5. Conclusion

This study has demonstrated the significant relationship between cold exposure, heat waves, and variation in diurnal temperature and the elevated risk of cardiovascular hospitalization. However there is an inconsistent effect of heat exposure on cardiovascular hospitalizations. Such findings have not been quantitatively estimated from the previous reviews. Based on the evidence reviewed, there is need for future studies to focus on specific geographical and climate areas, particularly in developing and tropical countries. Additionally, temperature measurements and thresholds need to be standardized for all studies in temperature and health-related effect. For example, definitions of heat waves should be homogenous for different research populations and settings. The modification effects of socio-economic factors also need to be considered more thoroughly in future studies. In terms of intervention, early warning models for temperature-related cause-specific morbidity should be developed as an effective measure for climate change adaptation strategies and heat-related morbidity prevention.

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## Appendix A. Supplementary data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.scitotenv.2016.01.154.

## References


Alessandrini, E., Sajani, S.Z., Scotto, F., Miglio, R., Marchesi, S., Lauriola, P., 2011. Emergency ambulance dispatches and apparent temperature: a time series analysis in Emilia-Romagna, Italy. Environ. Res. 111, 1192–1200.

Astrom, D.O., Forsberg, B., Rocklov, J., 2011. Heat wave impact on morbidity and mortality in the elderly population: a review of recent studies. Maturitas 69, 99–105.

Baccini, M., Biggeri, A., Accetta, G., Kosatsky, T., Katsouyanni, K., Analitis, A., et al., 2008. Heat effects on mortality in 15 European cities. Epidemiology 19, 711–719.

Barnett, A.G., Dobson, A.J., McElduff, P., Salomaa, V., Kuulasmaa, K., Sans, S., 2005. Cold periods and coronary events: an analysis of populations worldwide. J. Epidemiol. Community Health 59, 551–557.

Barnett, A.G., Tong, S., Clements, A.C., 2010. What measure of temperature is the best predictor of mortality. Environ. Res. 110, 604–611.

Basu, R., 2009. High ambient temperature and mortality: a review of epidemiologic studies from 2001 to 2008. Environ. Heal. 8, 40.

Basu, R., Feng, W.Y., Ostro, B.D., 2008. Characterizing temperature and mortality in nine California counties. Epidemiology 19, 138–145.

Basu, R., Pearson, D., Malig, B., 2012. The effect of high ambient temperature on emergency room visits. Epidemiology 23, 813–820.

Bayentin, L., Adlouni, S.E., Ouarda, T.B., Gosselin, P., Doyon, B., Chebana, F., 2010. Spatial variability of climate effects on ischemic heart disease hospitalization rates for the period 1989–2006 in Quebec, Canada. Int. J. Health Geogr. 9, 5.

Berman, N.G., Parker, R.A., 2002. Meta-analysis: neither quick nor easy. BMC Med. Res. Methodol. 2, 1–9.

Bhaskaran, K., Hajat, S., Haines, A., Herrett, E., Wilkinson, P., Smeeth, L., 2009. Effects of ambient temperature on the incidence of myocardial infarction. Heart 95, 1760–1769.

Bhaskaran, K., Hajat, S., Haines, A., Herrett, E., Wilkinson, P., Meeth, L., 2010. 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 341, c3823.

Bhaskaran, K., Hajat, S., Haines, A., Herrett, E., Wilkinson, P., Meeth, L., 2012. Heat and risk of myocardial infarction: hourly level case-crossover analysis of MINAP database. BMJ 345, e8050.

Bobb, J.F., Obermeyer, Z., Wang, Y., Dominici, F., 2014. Cause-specific risk of hospital admission related to extreme heat in older adults. JAMA 312, 2659–2667.

Borenstein, M., Hedges, L.V., Higgins, J.P.T., Rothstein, H.R., 2010. A basic introduction to fixed-effects and random-effects models for meta-analysis. Research Syrnthesis Methods 1, 97–111.

Clayton, D., Kaldor, J., 1987. Empirical Bayesian estimates of age-standardized relative risks for use in disease mapping. Biometrics 43, 671–681.

Cochran, W.G., 1954. The combination of estimates from different experiments. Biometrics 10, 101–129.

Das, D., Bakal, J.A., Westerhout, C.M., Hernandez, A.F., O'Connor, C.M., Atar, D., et al., 2014. The association between meteorological events and acute heart failure: new insights from ASCEND-HF. Int. J. Cardiol. 177, 819–824.

DASH Collaborative Research Group, Jehn, M., Appel, L.G., Sacks, F.M., Miller, E.R., 2002. The effect of ambient temperature and barometric pressure on ambulatory blood pressure variability. Am. J. Hypertens. 15, 941–945.

Dawson, J., Weir, C., Wright, F., Bryden, C., Aslanyan, S., Lees, K., et al., 2008. Associations between meteorological variables and acute stroke hospital admissions in the west of Scotland. Acta Neurol. Scand. 117, 85–89.

Ebi, K.L., Exuzides, K.A., Lau, E., Kelsh, M., Barnston, A., 2004. Weather changes associated with hospitalizations for cardiovascular diseases and stroke in California, 1983–1998. Int. J. Biometeorol. 49, 48–58.

Egger, M., Smith, G.D., Schneider, M., Minder, C., 1997. Bias in meta-analysis detected by a simple, graphical test. BMJ 315, 629–634.

Empana, J., Sauval, P., Ducimetiere, P., Tafflet, M., Carli, P., Jouven, X., 2009. Increase in out-of-hospital cardiac arrest attended by the medical mobile intensive care units, but not myocardial infarction, during the 2003 heat wave in Paris, France. Crit. Care Med. 37, 3079–3084.

Gasparrini, A., Guo, Y., Hashizume, M., Laviqne, E., Anobetti, A., Swartz, J., et al., 2015. Mortality risk attributable to high and low ambient temperature: a multicountry observational study. Lancet SO140-6736, 62114-0.

Giang, P.N., Dung, D.V., Giang, K.B., Vinh, H.V., Rocklov, J., 2014. The effect of temperature on cardiovascular disease hospital admission among elderly people in Thai Nguyen Province, Vietnam. Global Health Action 7, 23649.

Goggins, W.B., Woo, J., Ho, S., Chan, E.Y.Y., Chau, O.H., 2012. Weather, season, and daily stroke admissions in Hong Kong. Int. J. Biometeorol. 56, 865–872.

Goggins, W.B., Chan, E.Y.Y., Yang, C., 2013. Weather, pollution, and acute myocardial infarction in Hong Kong and Taiwan. Int. J. Cardiol. 168, 243–249.

Gomes, J., Damasceno, A., Carrilho, C., Lobo, V., Lopoes, H., Madele, T., et al., 2015. Triggering of stroke by ambient temperature variation: A case-crossover study in Maputo, Mozambique. Clin. Neurol. Neurosurg. 129, 72–77.
Green, R.S., Basu, R., Malig, B., Broadwin, R., Kim, J.J., Ostro, B., 2010. The effects of temperature on hospital admissions in nine California counties. Int. J. Public Health 55, 113–121.
Gronlund, C.J., Zanobetti, A., Schwartz, J.D., Wellenius, G.A., O'Neill, M.S., 2014. Heat, heat waves, and hospital admissions among the elderly in the United States, 1992–2006.
Guo, Y., Gasparrini, A., Amstrong, B., Li, S., Tawatsupa, B., Tobias, A., et al., 2014. Global variation in the effects of ambient temperature on mortality: a systematic evaluation. Epidemiology 25, 781–789.
Hajat, S., Haines, A., 2002. Associations of cold temperatures with GP consultations for respiratory andcardiovascular disease amongst the elderly in London. Int. J. Epidemiol. 31, 825–830.
Hajat, S., Kosatky, T., 2010. Heat-related mortality: a review of exploration of heterogeneity. J. Epidemiol. Community Health 64, 753–760.
Higgins, J.P.T., Thompson, S.G., Deeks, J.J., Altman, D.G., 2003. Measuring inconsistency in meta-analyses. BMJ 327, 557–560.
Hong, Y., Rha, J., Lee, J., Ha, E., Kwon, H., Kim, H., 2003. Ischemic stroke associated with decrease in temperature. Epidemiology 14, 473–477.
Hori, A., Hashizume, M., Tsuda, Y., Tsukahara, T., Nomiyama, T., 2012. Effects of weather variability and air pollutants on emergency admission for cardiovascular diseases. Int. J. Environ. Health Res. 22, 416–430.
Huang, C., Barnett, A.G., Wang, X., Tong, S., 2012. Effects of extreme temperatures on years of life lost for cardiovascular deaths: a time-series study in Brisbane, Australia. Circulation 5, 609–614.
Huynen, M.M., Martens, P., Schram, D., Weijenberg, M.P., Kunst, A.E., 2001. The impact of heatwaves and cold spells on mortality rates in the Dutch population. Environ. Health Perspect. 109, 463–470.
IPCC, 2013. Intergovernmental Panel on Climate Change (IPCC, 2013) Climate Change 2013: The physical science basis. www.ipcc.ch (Accessed 16/06/2015) .
Kan, H., London, S.J., Chen, H., Song, G., Chen, G., Jiang, L., et al., 2007. Diurnal temperature range and daily mortality in Shanghai, China. Environ. Res. 103.
Kawahara, J., Sano, H., Fukuzaki, H., Saito, K., Hirouchi, H., 1989. Acute effects of exposure to cold on blood pressure, platelet function and sympathetic nervous activity in humans. Am. J. Hypertens. 2, 724–726.
Keatinge, W.R., Coleshaw, S.R., Cotter, F., Mattock, M., Murphy, M., Chelliah, R., 1984. Increases in platelet and red cell counts, blood viscosity, and arterial pressure during mild surface cooling: factors in mortality from coronary and cerebral thrombosis in winter. Br. Med. J. (Clin. Res. Ed.) 289, 1405–1408.
Kenney, W.L., Hodgson, J.L., 1987. Heat tolerance, thermoregulation and ageing. Sports Med. 4, 446–456.
Knowlton, K., Rotkin-Ellman, M., King, G., Margolis, H.G., Smith, D., Solomon, G., et al., 2009. The 2006 California heat wave: impacts on hospitalizations and emergency department visits. Environ. Health Perspect. 117, 61–67.
Konken, P.J., Piver, W.T., Ye, F., Elixhauser, A., Olsen, L.M., Portier, C.J., 2003. Temperature, air pollution, and hospitalization for cardiovascular diseases among elderly people in Denver. Environ. Health Perspect. 111, 1312–1317.
Kovats, R.S., Hajat, S., Wilkinson, P., 2004. Contrasting patterns of mortality and hospital admissions during hot weather and heat waves in Greater London. Occup. Environ. Med. 61, 893–898.
Kyobutungi, C., Grau, A., Stieglbauer, G., Becher, H., 2005. Absolute temperature, temperature changes and stroke risk: a case-crossover study. Eur. J. Epidemiol. 20, 393–398.
Kysely, J., Pokorna, L., Kyncl, J., Kriz, B., 2009. Excess cardiovascular mortality associated with cold spells in the Czech Republic. BM Public Health 9, 9–19.
Lee, J.H., Chae, S.C., Yang, D.H., Park, H.S., Chi, Y., Jun, J., et al., 2010. Influence of weather on daily hospital admissions for acute myocardial infarction (from the Korea Acute Myocardial Infarction Registry). Int. J. Cardiol. 144, 16–21.
Lee, S., Lee, E., Park, M.S., Kwon, B.Y., Kim, H., Jung, D.H., et al., 2014. Short-term effect of temperature on daily emergency visits for acute myocardial infarction with threshold temperatures. Plos ONE 9, e94070.
Liang, W.M., Liu, W.P., Chou, S.Y., Huo, H.W., 2008. Ambient temperature range and emergency room admissions for acute coronary syndrome in Taiwan. Int. J. Biometeorol. 52, 223–229.
Lim, Y., Hong, Y., Kim, H., 2012. Effects of diurnal temperature range on cardiovascular and respiratory hospital admissions in Korea. Sci. Total Environ. 417-418, 55–60.
Lin, S., Luo, M., Walker, R.J., Liu, X., Hwang, S.A., Chinery, R., 2009. Extreme high temperatures and hospital admissions for respiratory and cardiovascular diaseas. Epidemiology 20, 738–746.
Ma, W., Xu, X., Peng, L., Kan, H., 2011. Impacts of extreme temperature on hospital admission in Shanghai, China. Sci. Total Environ. 409, 3634–3637.
Mastrangelo, G., Fedeli, U., Visentin, C., Milan, G., Fadda, E., Spolaore, P., 2007. Pattern and determinants of hospitalization during heat waves: an ecologic study. BMC Public Health 7, 1–8.
McGregor, G.R., Bessemoulin, P., Ebi, K., Menne, B. (Eds.), 2015. Heatwaves and Health: Guidance on Warning-System Development. World Meteorological Organization and World Health Organization.
McMichael, A.J., Wilkinson, P., Kovats, R.S., Pattenden, S., Hajat, S., Amstrong, B., et al., 2008. International study of temperature, heat and urban mortality: the 'ISOTHURM' project. Int. J. Epidemiol. 37, 1121–1131.
Michelozzi, P., Accetta, G., Desario, M., et al., 2009. High temperature and hospitalizations for cardiovascular and respiratory causes in 12 European cities. American of Respiratory and Critical Care Medicine 179, 383–389.
Misailidou, M., Pitsavos, C., Panagiotakos, D.B., Chrysohoou, C., Stefanadis, C., 2006. 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. 13, 846–848.
Moher, D., Liberati, A., Tetzlaff, J., Altman, D.G., 2009. Preferred reporting items for systematic reviews and meta-analysis: the PRISMA statement. J. Clin. Epidemiol. 62, 1006–1012.
Monteiro, A., Carvalho, V., Oliveira, T., 2013. Excess mortality and morbidity during the July 2006 heat wave in Porto, Portugal. Int. J. Biometeorol. 2013, 155–167.
Mostofsky, E., Wilker, E.H., Schwartz, J., Zanobetti, A., Gold, D.R., Wellenius, G.A., et al., 2014. Short-term changes in ambient temperature and risk of Ischemic stroke. Cerebrovasc. Dis. 4, 9–18.
O'Neill, M.S., Ebi, K.L., 2009. Temperature extremes and health: impacts of climate variability and change in the United States. J. Occup. Environ. Med. 51, 13–25.
Opie, L., 1998. The Heart. 51. Lippincott-Raven Publishers, Philadelphia.
Oshige, K., Hori, Y., Tochikubo, O., Sugiyama, M., 2006. Influence of weather on emergency transport events coded as stroke: population-based study in Japan. Int. J. Biometeorol. 50, 305–311.
Ostro, B., Rauch, S., Green, R., Malig, B., Basu, R., 2010. The effects of temperature and use of air conditioning on hospitalizations. Am. J. Epidemiol. 172, 1053–1061.
Panagiotakos, D.B., Chrysohoou, C., Pitsavos, C., Nastos, P., Anadiotis, A., Tentolouris, C., et al., 2004. Climatological variations in daily hospital admissions for acute coronary syndromes. Int. J. Cardiol. 94, 229–233.
Pattenden, S., Nikiforov, B., Armstrong, B.G., 2003. Mortality and temperature in Sofia and London. J. Epidemiol. Community Health 57, 628–633.
Phung, D., Guo, Y., Thai, P., Rutherford, S., Wang, X., Nguyen, M., et al., 2015. The effects of high temperature on cardiovascular admissions in the most populous tropical city in Vietnam. Environ. Pollut. (in press).
Pudpong, N., Hajat, S., 2011. High temperature effects on out-patient visits and hospital admissions in Chiang Mai, Thailand. Sci. Total Environ. 2011, 5260–5267.
Qiu, H., Yu, I., Tse, L.A., Tian, L., Wang, X., Wong, T.W., 2013. Is greater temperature change within a day associated with increased emergency hospital admissions for heart failure? Circulation 2013, 930–935.
Radisauskas, R., Vaiciulis, V., Ustinaviciene, R., Bernotiene, G., 2013. The effect of atmospheric temperature and pressure on the occurrence of acute myocardial infarction in Kaunas. Public Health 49, 447–452.
Ravljen, M., Bilban, M., Kajfez-Bogataj, L., Hovelja, T., Vavpotie, D., 2014. Influence of daily individual meteorological parameters on the incidence of acute coronary syndrome. Int. J. Environ. Res. Public Health 11, 11616–11626.
Ren, C., Williams, M.G., Tong, S., 2006. Does particulate matter modify the association between temperature and cardiorespiratory diseases. Environ. Health Perspect. 114, 1690–1696.
Rothstein, H., Sutton, A.J., Borenstein, M., 2005. Publication Bias in Meta-analysis: Prevention, Assessment and Adjustment. John Wiley & Sons Inc., Hoboken, NJ.
Schulman, S.P., Lakatta, E.G., Fleg, J.I., Lakatta, L., Becker, L.C., Gerstenblith, G., 1992. Age related decline in left ventricular filling at rest and exercise. Am. J. Phys. 263, H1932–H1938.
Schwartz, J., Samet, J.M., Patz, J.A., 2004. Hospital admission for heart disease: the effects of temperature and humidity. Epidemiology 15, 755–761.
Semenza, J.C., McCullough, J.E., Flanders, W.D., McGeehin, A.A., Lumpkin, J.R., 1999. Excess hospital admissions during the July 1995 heat wave in Chicago. Am. J. Prev. Med. 16, 270–277.
Shaposhnikov, D., Revich, B., Gurfinkel, Y., Naumova, E., 2014. The influence of meteorological and geomagnetic factors on acute myocardial infarction and brain stroke in Moscow, Russia. Int. J. Biometeorol. 58, 799–808.
Sheridan, S.C., Lin, S., 2014. Assessing variability in the impacts of heat on health outcomes in New York City over time, season, and heat-wave duration. EcoHealth 11, 512–525.
Shinkawa, A., Ueda, K., Hasuo, Y., Kiyohara, Y., Fujishima, M., 1990. Seasonal variation in stroke incidence in Hisayama, Japan. Stroke 21.
Son, J., Bell, M.L., Lee, J., 2014. The impact of heat, cold, and heat waves on hospital admissions in eight cities in Korea. Int. J. Biometeorol. 2014, 1893–1903.
Son, Y.J., Gouveia, N., Bravo, M.A., de Freitas, C.U., Bell, M.L., 2015. The impact of temperature on mortality in a subtropical city: effects of cold, heat, and heat waves in São Paulo, Brazil. Int. J. Biometeorol. 2015.
Sterne, J.A.C., Egger, M., 2001. Funnel plots for detecting bias in meta-analysis: guidelines on choices of axis. J. Clin. Epidemiol. 54, 1046–1055.
Sterne, J.A.C., Egger, M., Smith, G.D., 2001. Investigating and dealing with publication and other biases in meta-analysis. BMJ 323, 101–105.
Stroup, D.F., Berlin, J.A., Morton, S.C., Olkin, I., Williamson, G.D., Rennie, D., et al., 2000. Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis of Observational Studies in Epidemiology (MOOSE) group. JAMA 283, 2008–2012.
Tam, W.W.S., Wong, T.W., Chair, S.Y., Wong, A.H.S., 2009. Diurnal temperature range and daily cardiovascular mortalities among the elderly in Hong Kong. Arch. Environ. Occup. Health Policy and Ethics 64.
Tanigawa-Sugihara, K., Iwami, T., Nishiyama, C., Kitamura, T., Goto, M., Ando, M., et al., 2013. Association between atmospheric conditions and occurrence of out-of-hospital cardiac arrest. Circ. J. 77, 2073–2078.
Touitou, Y., Touitou, C., Bogdan, A., et al., 1986. Differences between young and elderly subjects in seasonal and circadian variations of total plasma proteins and blood volume as reflected by hemoglobin, hematocrit, and erythrocyte counts. Clin. Chem. 32, 801–804.
Turner, L., Connell, D., Tong, S., 2012a. Exposure to hot and cold temperatures and ambulance attendances in Brisbane, Australia: a time-series study. BMJ Open 2, e001074.
Turner, L.R., Barnett, A.G., Connell, D., Tong, S., 2012b. Ambient temperature and cardiorespiratory morbidity: a systematic review and meta-analysis. Epidemiology 23, 594–606.

Turner, L.R., Connell, D., Tong, S., 2013. The effect of heat waves on ambulance attendances in Brisbane, Australia. Prehosp. Disaster Med. 28, 482–487.
Urban, A., Davidkovova, H., Kysely, J., 2014. Heat- and cold-stress effects on cardiovascular mortality and morbidity among urban and rural populations in the Czech Republic. Int. J. Biometeorol. 2014, 1057–1068.
Vaneckova, P., Bambrick, H., 2013. Cause-specific hospital admissions on hot days in Sydney, Australia. Plos ONE 8, e55459.
Vasconcelos, J., Freire, E., Almendra, R., Silva, G.L., 2013. The impact of winter cold weather on acute myocardial infarctions in Portugal. Environ. Pollut. 183, 14–18.
Wang, Y., Lin, Y., 2014. Association between temperature and emergency room visits for cardiorespiratory diseases, metabolic syndrome-related diseases, and accidents in metropolitan Taipei. Plos ONE 9, e99599.
Wang, X.Y., Barnett, A.G., Hu, W., Tong, S., 2009. Temperature variation and emergency hospital admissions for stroke in Brisbane, Australia, 1996–2005. Int. J. Biometeorol. 53, 535–541.
Wang, Y., Lin, Y., Chuang, C., Li, M., Chou, C., Liao, C., et al., 2012. Associating Emergency Room Visits With First and Prolonged Extreme Temperature Event in Taiwan: A Population-based Cohort Study.
Wang, M., Zheng, S., He, S., Li, B., Teng, H., Wang, S., et al., 2013a. The association between diurnal temperature range and emergency room admissions for cardiovascular, respiratory, digestive and genitourinary disease among the elderly: a time series study. Sci. Total Environ. 456-457, 370–375.
Wang, Q., Gao, C., Wang, H., Lang, L., Yue, T., Lin, H., 2013b. Ischemic stroke hospital admission associated with ambient temperature in Jinan, China. Plos ONE 8, e80381.
Webb, L., Bambrick, H., Tait, P., Green, D., Alexander, L., 2014. 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 11, 1942–1959.
Wichmann, J., Andersen, Z., Ketzel, M., Ellermann, T., Loft, S., 2011. Apparent temperature and cause-specific emergency hospital admissions in Greater Copenhagen, Denmark. Plos ONE 6, e22904.
Wilker, E.H., Yeh, G., Wellenius, G.A., Davis, R.B., Phillips, R.S., Mittlemen, M.A., 2012. Ambient temperature and biomarkers of heart failure: a repeated measures analysis. Environ. Health Perspect. 120, 1083–1087.
Williams, S., Nitschke, M., Weinstein, P., Pisaniello, D.L., Parton, K.A., Bi, P., 2012. The impact of summer temperatures and heatwaves on mortality and morbidity in Perth, Australia 1994–2008. Environ. Int. 40, 33–38.
Wilmshurst, P., 1994. Temperature and cardiovascular mortality. BMJ 309, 1029–1030.
Wolf, K., Schneider, A., Breitner, S., Klot, S., Meisinger, C., Cyrys, J., et al., 2009. Air temperature and the occurrence of myocardial infarction in Augsburg, Germany. Circulation 120, 735–742.
Yang, X., Li, L., Wang, J., Huang, J., Lu, S., 2015. Cardiovascular mortality associated with low and high temperatures: determinants of inter-region vulnerability in China. Int. J. Environ. Res. Public Health 12, 1918–1933.
Ye, F., Piver, W.T., Ando, M., Portier, C.J., 2001. Effects of temperature and air pollutants on cardiovascular and respiratory diseases for males and females older than 65 years of age in Tokyo, July and August 1980–1995. Environ. Health Perspect. 109, 355–359.
Ye, X., Wolff, R., Yu, W., Vaneckova, P., Pan, X., Tong, S., 2012. Ambient temperature and morbidity: a review of epidemiological evidence. Environ. Health Perspect. 120, 19–27.