Effects of ambient temperature on the incidence of myocardial infarction

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ABSTRACT
Context: While the effects of weather and, in particular, ambient temperature on overall mortality are well documented, the strength of the evidence base for the effects on acute myocardial infarction (MI) are less clear.
Objective: To systematically review studies specifically focusing on the effects of temperature on MI.
Data sources: Medline, Embase, and GeoBase publication databases, as well as reference lists, and the websites of a number of relevant public organisations.
Study selection: Studies of original data in which ambient temperature was an exposure of interest and MI a specific outcome were selected.
Data extraction: The reported effects of ambient temperature on the risk of MI, including effect sizes and confidence intervals, where possible, were recorded. Methodological details were also extracted, including study population, location and setting, ascertainment of MI events, adjustment for potential confounders and consideration of lagged effects.
Results: 19 studies were identified, of which 14 considered the short-term effects of temperature on a daily timescale, the remainder looking at longer-term effects. Overall, 8 of the 12 studies which included relevant data from the winter season reported a statistically significant short-term increased risk of MI at lower temperatures, while increases in risk at higher temperatures were reported in 7 of the 13 studies with relevant data. A number of differences were identified between studies in the population included demographics, location, local climate, study design and statistical methodology.
Conclusion: A number of studies, including some that were large and relatively well controlled, suggested that both hot and cold weather had detrimental effects on the short-term risk of MI. However, further research with consistent methodology is needed to clarify the magnitude of these effects and to show which populations and individuals are vulnerable.

In the light of global climate change, there is increasing interest in the effects of meteorological factors on health outcomes. A number of studies have found that ambient outdoor temperatures have a short-term effect on overall mortality, with many describing a U- or V-shaped relationship; for example, a large study in 11 US cities described a decreasing mortality risk as the temperature increased from the coldest days to a certain threshold temperature, above which mortality risk increased with temperature. A similar pattern has been seen in Europe, and in a number of lower- and middle-income countries. Periods of extreme cold or heat have also been associated with mortality peaks.

Evidence suggests that cardiovascular effects of differences in ambient temperature may contribute to the increased mortality risk. Ambient outdoor temperature has been linked to mortality specifically from cardiovascular diseases (CVDs); similar U-shaped relationships have been described, and studies have shown increases in CVD mortality associated both with cold and hot outdoor temperatures.

The effects of temperature on morbidity and mortality from myocardial infarction (MI) specifically have not been investigated as commonly as the effects on broader outcomes. We aimed to review the evidence for an effect of temperature on the risk of MI, hypothesising that MI risk would increase at both the upper and lower extremes of temperature. The motivation for a focused review on MI outcomes was twofold: first, mortality, though investigated frequently as an outcome, is likely to reflect only a small proportion of the total health impact of environmental exposure since many events do not directly result in death. Second, since MI is a specific outcome with a specific pathophysiology, a clearer description of the effects of temperature on MI may lead to a better understanding of the potential triggering mechanisms at work among those at high risk of an ischaemic event.

METHODS
Databases and sources
We searched two large databases covering health and medical literature: Medline (1950 to the present) and Embase. Since meteorological exposures were being considered, we also included the specialist database GeoBase to capture any relevant studies that might have been published in the geographical/geographical rather than the medical literature. Reference lists of all relevant studies were scanned to identify any further studies, and if these showed that search terms had been missed, extra terms were added to the main database searches. The searches were performed by a statistician/epidemiologist (KB), initially in July 2008, with the main database searches updated in May 2009.

In order to capture important “grey literature” we searched the websites of the following organisations for relevant reports: World Health Organization; European Union; Health Effects Institute (USA); Environmental Protection Agency (USA); National Institutes of Health (USA); Department of Health (UK); and Department for Environment, Food, and Rural Affairs (UK). As well as searching for original research, we examined the reference lists of any...
relevant reviews appearing in their reports. Conference abstracts and unpublished studies were not included in this review.

Search keywords and terms

Medline (accessed via OvidSP) is indexed according to MeSH terms. Our primary search used the following MeSH keywords: (“weather” or “climate”) and “myocardial infarction” and “humans”. All subterms were also included, and we limited the search to studies of adult humans, published in English. We performed equivalent searches in Embase (using equivalent headings in the Embase indexing system) and GeoBase (using keywords).

To identify studies in which a temperature effect on MI was reported as a specific secondary outcome within a broader study, we performed a secondary Medline search, as above but using the broader MeSH term “cardiovascular diseases” in place of “myocardial infarction”; we then limited the results to reports where “myocardial infarction” or an equivalent term was present in the title, abstract, or keywords (equivalent terms were defined as “myocardial infarct”*, “coronary event”, “heart attack”, “Q wave infarct”*, “non-Q wave infarct”*, “STEMI”, “coronary infarct”*, “heart infarct”*, “myocardial thrombosis”*, or “coronary thrombosis”, where * indicates any word ending).

Inclusion and exclusion criteria

In order to examine the hypothesis that temperature is associated with MI risk, studies of any relevant design were included provided that they presented original data, and included at least one analysis where ambient temperature (or a composite measure incorporating this) was an exposure of interest, and MI was the specific outcome; we did not include studies looking only at broader CVD outcomes and not considering MI specifically. Studies were excluded if the authors did not control for (or stratify by) any potential confounding factors, or did not report measures of precision or p values for the analysis of interest.

Procedure

Titles and abstracts were screened for relevance, and full-text versions obtained where appropriate for assessment with reference to the inclusion and exclusion criteria; we were able to obtain full-text papers in all cases where required and it was not necessary to contact specific authors. For each study included, the following information was recorded based on prior beliefs about key aspects of study methodology and in order to summarise study quality: study population, event of interest, number included, age range included, location and setting, time period, exposure variables, ascertainment of MI, spatial resolution, temporal resolution, adjustment for air pollution and other potential confounders, lags considered. In addition, main results were recorded, in particular the effects of temperature on risk of MI, including effect sizes and confidence intervals where possible. Where authors reported several relevant results (eg, for different lag days or for different subgroups), it was necessary to decide which result(s) to record; where a main or final model could be identified, this was chosen, otherwise we recorded results from the analysis on which the authors focused or that which best represented the overall conclusions of the study. Though this was a somewhat subjective process, in all cases, we also noted any important differences in the effect estimates between different analyses. For context, the temperature range for the location studied was recorded where given. Finally, effects of other meteorological variables were also noted.

To explore the role of local climate, we considered the 10-year average of the mean annual temperature and temperature range, using data from the Goddard Institute for Space Studies (GISS) surface temperature data.12 We obtained monthly mean temperatures over the period 1991–2000 from the nearest available monitoring station to each study location. The 10-year mean was calculated as the mean of the monthly temperatures, and we also calculated the 10-year mean of the minimum and maximum monthly temperatures to give an average annual temperature range. Multinational studies were excluded from this exploratory analysis.

RESULTS

After running the search strategy and screening abstracts for relevance, a total of 57 full text articles were obtained for further inspection, and 42 met the primary inclusion criteria. We then excluded 22 studies, four of which reported no direct effect estimates, and 18 that did not control for any potential confounding factors or did not report measures of precision or p values for the results of interest (online supplementary table A1); one further research paper was excluded because the same data were reported in a later paper, leaving a total of 19 in the review (fig 1). The majority looked at short-term effects of daily temperature levels (n = 14).10–26 A further two studies investigated temperature effects over the longer term (ie, on a monthly or yearly timescale),27,28 while three looked at more complex weather parameters designed to capture the effects of overall weather patterns not restricted to ambient temperature.29–31

Figure 1 Flow diagram of search strategy.
### Systematic review

#### Short-term effects of temperature

Thirteen studies used daily time-series data to investigate the short-term effect of temperature on MI risk (tables 1–3). Only one study used a different design: Hirasaki et al. looked at the effectiveness of 10 meteorological parameters in discriminating between days with and without MI events in Hokkaido, Japan; however, this small study identified no useful discriminating factors. The 13 daily time-series studies are now considered in more detail.

#### Methodological considerations

Variations in methodological aspects of the 13 daily time-series studies occurred in three main areas: ascertainment and validation of MI outcome events; adjustment for potential confounding factors; and flexibility of the fitted temperature effect in terms of allowance for non-linear and delayed (or ‘lagged’) effects.

MI data came from a variety of sources, the primary sources being hospital, clinic or medical care databases (n = 6), morbidity registries (n = 3), ambulance data (n = 1) and death certificate/mortality data (n = 3). Most studies, including all of those concentrating purely on mortality data, generally took the cause of death as coded in the source data. However, five studies, with access to symptom, ECG, and biomarker records, validated potential MI events using specific diagnostic criteria (table 1).

Adjustment for regular seasonal patterns within years, and for long-term trends over a number of years, was performed to varying degrees in a number of studies and may, where performed, lead to more reliable estimates of short-term temperature effects. Without such adjustment, estimated temperature effects are likely to include these seasonal and long-term changes in temperature and outcome, and any other factors which vary on these timescales could confound associations. A few studies included more specific potential confounders. Potential confounders for the relationship between temperature and MI, since they must by definition be associated with temperature, are usually other time-varying external factors, such as other meteorological parameters, pollution levels such as ambient particulate matter and ozone, and levels of infectious diseases such as influenza. Of note, only three studies⅓ ⅚ ⅚ made any adjustment for daily pollution levels, which are likely to be associated with daily temperature, and which a number of studies have suggested may affect short-term risk of MI.

Finally, there was variation in the way temperature relationships were investigated. Six of the 13 studies appeared to investigate temperature only as a linear effect, meaning that U-shaped relationships similar to those reported in some mortality studies could not have been detected. In addition, only 7/13 studies investigated the possibility of the effects of temperature on MI being delayed (‘lagged’) by one or more days: this is a potentially important consideration if the effects of temperature on MI incidence extend beyond same-day effects; for example, an extremely cold day may lead to an increase in the incidence of MI over the next several days. Even among studies that considered this, the potential lagged effects investigated varied widely, ranging from 1 to 30 days.

#### Effects of lower temperatures

Overall, eight of the 12 studies which included data from the winter season reported a statistically significant increased risk of MI at colder temperatures, either overall or for some subgroup (tables 2–3), including three of the five studies in which MI outcomes were validated against specified diagnostic criteria, as well as the only multinational study included, which estimated negative associations between temperature and MI risk for the majority of the 24 populations in Europe, China, the USA and Australia that were included (combined RR = 1.008 (95% CI 1.004 to 1.012) per 1°C drop in the temperature averaged over the current and previous 5 days). Estimated effect sizes varied between studies, however; for example, one study based in Sao Paulo, Brazil estimated a relative risk for MI mortality of 1.31 (1.19 to 1.44) for temperature in the lowest decile (11–15°C) compared with the nadir mortality at 22–23°C; this was consistent with two other studies which reported large effects on fatal MI outcomes.⅓ ⅙ ⅛

#### Effects of higher temperatures

Statistically significant increases in MI risk with higher temperatures were reported in seven out of the 13 studies (tables 2 and 3), including all three with MI mortality outcomes, though of note, only one of the five studies in which the MI outcomes were validated against diagnostic criteria found a heat effect. Four studies reported separate effects of both heat and cold, including the earlier-mentioned Brazilian study by Sharovsky et al. (RR = 1.11 (95% CI 1.06 to 1.16) for 2-day average temperature 24–27°C compared with 22–23°C). As with cold effects, there were differences in the way in which effects were reported, and in their sizes. Of interest, a study in northern Sweden found no effect of absolute temperature, but reported an increase in the risk of non-fatal MI when the temperature was higher than the previous day (RR = 1.015 (1.008 to 1.027) per 1°C increase). Morabito et al. found a 3% increase in MI risk associated with an extra 2 hours of “heat discomfort” in Florence, Italy (heat discomfort hours were defined as those above the 90th centile on an apparent temperature index incorporating temperature, humidity and wind velocity). It should be noted that the largest study to find no effect of heat was one of those investigating temperature only as a linear effect; since the authors found a cold effect, by design they could not have also reported a separate effect of heat on the same lag days.

#### Role of local climate

Barnett et al. considered heterogeneity in the temperature effect across the 24 populations (from 21 countries) included in their study. There was some variation in the estimated size of the risk increase associated with a drop in temperature (ranging from a 0 to 1.8% increase in risk per 1°C). Interestingly, 28% of this variation was explained by local mean temperature (rising to 54% when two outliers were excluded); in general, locations with higher mean temperatures were more vulnerable to cold days.

We explored this further in the remaining single-location studies by considering the 10-year mean temperature and the average annual range of temperatures (table 2). Studies in the six “warmest” regions all reported a detrimental effect of cold;⅓ ⅛ ⅝ ⅝ ⅝ ⅝ ⅝ of note, these warmer regions also tended to have smaller average annual temperature ranges (<20°C in five of six cases). In contrast, considering studies in the six “coldest” regions, which tended to experience a greater range of temperatures across the year (average range >20°C in four of six cases), only one of five investigating cold effects reported a significant effect of cold (⅝ ⅝ ⅝ ⅝ ⅝ ⅝ ⅝ with one further study using data from the summer months only).
<table>
<thead>
<tr>
<th>First author and year of publication</th>
<th>Population/data source</th>
<th>Location and time period</th>
<th>Number of MI events included (mean MIs/day)</th>
<th>Main temperature exposure variable(s)</th>
<th>Potential confounders included</th>
<th>MI ascertainment</th>
<th>Lags considered (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gerber 2006</td>
<td>County medical care registers</td>
<td>Olmsted County, USA 1979–2002</td>
<td>2676 (0.3)</td>
<td>Maximum temperature</td>
<td>Annual population, calendar year, season, rain, snowfall</td>
<td>Diagnoses compatible with MI extracted and validated using cardiac pain, biomarker, and ECG criteria</td>
<td>None</td>
</tr>
<tr>
<td>Wang 2006</td>
<td>Ambulance service centre data</td>
<td>Hiroshima, Japan 1993–2002</td>
<td>3755 (1.0)</td>
<td>Mean temperature, humidity-adjusted temperature</td>
<td>Atmospheric pressure</td>
<td>Diagnosis based on anamnestic, clinical, laboratory and ECG criteria</td>
<td>None</td>
</tr>
<tr>
<td>Enquselassie 1993</td>
<td>MONICA morbidity registry (covering ages &lt;70 years)</td>
<td>Hunter region, New South Wales, Australia 1985–90</td>
<td>3889 (1.9)</td>
<td>Maximum temperature</td>
<td>Calendar month, rainfall</td>
<td>Non-fatal definite MI and fatal MI/sudden coronary death, based on MONICA ECG, symptom and enzyme criteria[42]</td>
<td>None</td>
</tr>
<tr>
<td>Ohlson 1991</td>
<td>Single clinic diagnosis register (ages &lt;70)</td>
<td>Orebro, Sweden 1985–7 (cold seasons only)</td>
<td>357 (0.6)</td>
<td>Windchill-adjusted temperature (as measured at 7 pm)</td>
<td>Day of week, snowfall, atmospheric pressure</td>
<td>Records with ICD8 code 410.10, 410.99, or ICD9 code 410A/B/W/X</td>
<td>None</td>
</tr>
<tr>
<td>Barnett 2005</td>
<td>24 MONICA morbidity registries (covering ages 35–64 years)</td>
<td>Europe, China, USA, Australia 1980–95</td>
<td>87 410 (0.4–2.8 by location)</td>
<td>Mean temperature</td>
<td>Season and trend, day of week, humidity</td>
<td>Non-fatal definite MI and fatal definite/possible MI/unclassifiable event based on MONICA ECG, symptom and enzyme criteria[42]</td>
<td>0–14 inclusive</td>
</tr>
<tr>
<td>Morabito 2005</td>
<td>Hospitalisations database (Florentine area)</td>
<td>Florence, Italy 1998–2002</td>
<td>2683 (1.5)</td>
<td>Hours of severe discomfort (based on extremes of apparent and windchill temperature indices)</td>
<td>Stratified by season</td>
<td>Records with ICD9 = 410–410.92</td>
<td>0–3 inclusive</td>
</tr>
<tr>
<td>Ebi 2004</td>
<td>Hospitalisations data (covering all non-federal hospitals)</td>
<td>Three counties in California, USA 1993–8</td>
<td>283 031 (4.5–39.4 by location)</td>
<td>Minimum and maximum temperature</td>
<td>Season and trend</td>
<td>Records with ICD9 code 410</td>
<td>0, 7, 14, 30</td>
</tr>
<tr>
<td>Koken 2003</td>
<td>Hospital admissions data (11 hospitals, covering ages 65+ years)</td>
<td>Denver county, USA 1993–7 (July and August only)</td>
<td>Not reported</td>
<td>Maximum temperature, dew point temperature</td>
<td>Season and trend, day of week, air pollution variables</td>
<td>Primary discharge diagnosis (ICD9 = 410.XX)</td>
<td>0–4 inclusive</td>
</tr>
<tr>
<td>Messner 2002</td>
<td>Hospital and GP records, and death certificates data (ages 25–64)</td>
<td>Northern Sweden 1985–92</td>
<td>3322 (approx 0.91)</td>
<td>Temperature, change in temperature from previous day</td>
<td>Season, humidity, air pressure, change in humidity and air pressure from previous day</td>
<td>Suspected cases validated using symptom, ECG, and enzyme marker data</td>
<td>None</td>
</tr>
<tr>
<td>Danet 1999</td>
<td>Lille-WHO MONICA morbidity registry (covering ages 25–64 years)</td>
<td>Nord district, France 1985–94</td>
<td>3314 (approx 0.91)</td>
<td>Mean temperature</td>
<td>Annual population, mean atmospheric pressure, calendar year</td>
<td>Non-fatal definite MIs and fatal definite/possible MIs, based on MONICA ECG, symptom and enzyme criteria[42]</td>
<td>None</td>
</tr>
</tbody>
</table>

**Fatal events only**

<table>
<thead>
<tr>
<th>First author and year of publication</th>
<th>Population/data source</th>
<th>Location and time period</th>
<th>Number of MI events included (mean MIs/day)</th>
<th>Main temperature exposure variable(s)</th>
<th>Potential confounders included</th>
<th>MI ascertainment</th>
<th>Lags considered (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dilaveris 2006</td>
<td>Death certificate data</td>
<td>Athens territory, Greece 2001</td>
<td>3126 (8.6)</td>
<td>Daily mean/minimum/maximum temperature</td>
<td>Atmospheric pressure, relative humidity, season (based on calendar date)</td>
<td>Death certificates with ICD10 codes of 120.0–4, 121.9, I22.0, I22.1, I22.8, I22.9</td>
<td>Mean of 0, 7</td>
</tr>
</tbody>
</table>

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**continued**
Table 1 Continued

<table>
<thead>
<tr>
<th>First author and year of publication</th>
<th>Population/data source</th>
<th>Location and time period</th>
<th>Number of MI events included (mean MIs/day)</th>
<th>Main temperature exposure variable(s)</th>
<th>Potential confounders included</th>
<th>MI ascertainment</th>
<th>Lags considered (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sharovsky 2004&lt;sup&gt;26&lt;/sup&gt;</td>
<td>Death registry data</td>
<td>Sao Paulo, Brazil 1996–8</td>
<td>12 007 (16.4)</td>
<td>Mean temperature</td>
<td>Season and trend, relative humidity, atmospheric pressure, day of week, holidays, influenza levels, air pollution variables</td>
<td>Death certificates with MI (ICD10 = I21) listed as primary cause</td>
<td>0, and moving average of up to previous 7 days</td>
</tr>
<tr>
<td>Rossi 1999&lt;sup&gt;24&lt;/sup&gt;</td>
<td>Vital statistics department mortality data</td>
<td>Milan, Italy 1985–9</td>
<td>Approx 1600* (0.9)</td>
<td>Mean temperature</td>
<td>Season and trend, relative humidity, day of week, holidays, respiratory infection epidemics, pollution variables</td>
<td>Deaths with ICD9 codes of 410</td>
<td>Different lags considered, exact strategy unclear</td>
</tr>
</tbody>
</table>

*Derived from reported mean daily rate, and length of period under study; †derived from reported total number of events, and reported length of study.

No such pattern could be detected for heat effects; indeed, the studies based in the regions with the coolest and warmest mean temperatures (northern Sweden and Sao Paulo, Brazil, respectively) both reported detrimental effects of heat.

**Vulnerability among subgroups**

A few studies investigated vulnerability to temperature effects according to individual-level characteristics. Among those considering the effects of temperature separately for different age groups, there were inconsistent results; two studies, both of which had found significant detrimental effects of cold, reported that analyses restricted to the oldest age group gave similar effect size estimates to those including all patients,<sup>16</sup> though it should be noted that in the former study the oldest age group accounted for over half of the events, while in the latter the age structure of the study population was not reported. Morabito et al.<sup>16</sup> on the other hand, reported that correlations between “cold discomfort hours” and MI rates in winter were larger among those aged >65 years, while correlations between “heat discomfort hours” and MI rates in summer were larger among those aged <65 years. Age appeared to affect the magnitude of temperature effects in one study in California though the direction of the association was not consistent across the three regions studied.<sup>26</sup> In the same study, analyses were also presented stratified by sex: the estimated increase in risk of MI for a 3°C decrease in maximum temperature was greater among women in the Sacramento region (15.7% (4.9% to 27.6%) compared with 10.9% (5.1% to 16.9%) for men, among those aged 55–69 years), whereas the increase in MI risk following an equivalent temperature drop in San Francisco was larger among men (6.6% compared with 2.2% in women). Barnett et al.<sup>26</sup> reported that the increase in event rates in cold periods was greater among women than men (OR = 1.07 (1.03 to 1.11)), averaging over all 24 included populations. The same study found no difference between those with and without previous MI. Similarly, Enquelsassie et al.<sup>26</sup> reported that the effects of heat and cold among subjects with a prior history of ischaemic heart disease were similar to the effects among all study participants.

**Long-term effects of temperature**

Two studies considered the effect of temperature on MI risk over timescales of >1 month. Results from a monthly time-series study among 369 women aged 20–44 years, hospitalised for MI in 24 centres covering four continents, appeared to show an adverse effect of cold on a monthly timescale (RR = 1.14 (1.03 to 1.25) per 5°C temperature decrease).<sup>27</sup> A long-term effect of cold was also reported by Gyllerup, who compared MI mortality across 284 municipalities in Sweden, each of which was assigned a cold index based on the number of times the windchill-adjusted temperature in the municipality fell below −10°C in a 10-year period.<sup>28</sup> Municipalities in the three coldest deciles (based on this cold index) were reported to have standardised mortality ratios (SMRs) of >1 (SMR = 1.4 in the coldest decile), while those in the seven least cold deciles all had SMRs <1 (SMR = 0.9 for those in the least cold decile), with the effect persisting after adjustment for socioeconomic factors.

**Effects of composite weather parameters**

Three studies considered the effects of composite weather parameters: air mass type,<sup>29</sup> arctic oscillation index<sup>30</sup> and weather fronts<sup>31</sup> were all associated with short-term risk of MI. Results of such analyses can be difficult to interpret and compare; indeed two of these studies present two contrasting effects: Morabito et al., using hospitalisation data from Italy, found that an anticyclonic continental air mass, representing cold and clear weather, significantly increased the risk of MI compared with a mixed air mass representing mild, humid, cloudy weather (RR = 1.28, p<0.05, 1-day lagged effect), while Messner et al., in a study based in northern Sweden, found that MI risk increased with increasing arctic oscillation index, which corresponds to higher levels of temperature, humidity, and cloudiness (RR = 1.038 (1.015 to 1.062) per unit increase in arctic oscillation index, lagged by 3 days), though this apparent contradiction could simply represent the broadly U-shaped relationship between weather and MI that has been reported by other studies investigating temperature effects directly.

**DISCUSSION**

To our knowledge, this study is the first systematic review to specifically focus on the effects of ambient temperature on MI. Our search strategy is likely to have identified the majority of major studies focusing on this question, and we have also taken steps to include studies in which our specific outcome of interest was investigated as a subanalysis within a broader study.
### Table 2  Daily time-series studies with temperature exposures and myocardial infarction (MI) outcomes: summary/interpretation

<table>
<thead>
<tr>
<th>First author and year</th>
<th>MIs (n)</th>
<th>Long-term local mean temperature and annual range* (°C)</th>
<th>Detrimental effect of cold?</th>
<th>Detrimental effect of heat?</th>
<th>Adjusted for season and trend?</th>
<th>MI events: validation or specified criteria</th>
<th>Adjusted for humidity</th>
<th>Adjusted for atmospheric pressure</th>
<th>Adjusted for infectious disease levels</th>
<th>Adjusted for air pollution</th>
<th>Adjusted for day of week?</th>
<th>Allowance for non-linear temperature effects?</th>
<th>Investigated lag effects?</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Studies of fatal and non-fatal events</strong></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gerber 2006*</td>
<td>2676</td>
<td>7 (-10.8 to 21.2)</td>
<td>No</td>
<td>No</td>
<td>✓</td>
<td>✓</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>✓</td>
<td>x</td>
</tr>
<tr>
<td>Wang 2006*</td>
<td>3755</td>
<td>16.7 (5.6 to 28.3)</td>
<td>Yes</td>
<td>No</td>
<td>x</td>
<td>✓</td>
<td>✓</td>
<td>x</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Engussehissie 1993*</td>
<td>3889</td>
<td>17.9 (11.9 to 23.7)</td>
<td>Yes (fatal MIs only)</td>
<td>No</td>
<td>x†</td>
<td>✓</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>✓</td>
<td>x</td>
</tr>
<tr>
<td>Ohlson 1991*</td>
<td>357</td>
<td>6.3 (-3.9 to 17.3)</td>
<td>No</td>
<td>N/A</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>x</td>
</tr>
<tr>
<td>Barnett 2005*</td>
<td>87410</td>
<td>—</td>
<td>Yes</td>
<td>No</td>
<td>✓</td>
<td>✓</td>
<td>x</td>
<td>x</td>
<td>✓</td>
<td>✓</td>
<td>x</td>
<td>✓</td>
<td>x</td>
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<tr>
<td>Marabito 2005*</td>
<td>2683</td>
<td>14.1 (5.8 to 23.5)</td>
<td>Yes</td>
<td>Yes (for increased hours of discomfort)</td>
<td>✓</td>
<td>✓</td>
<td>x</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>x</td>
</tr>
<tr>
<td>Ebi 2004*</td>
<td>283031</td>
<td>14.7 (10.1 to 18.6)</td>
<td>Certain regions only (1/3 regions for night temperature; 2/3 regions for day temperature)</td>
<td></td>
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<tr>
<td>Koken 2003**</td>
<td>Not reported</td>
<td>9.7 (-1.4 to 21.9)</td>
<td>Yes</td>
<td>N/A</td>
<td>✓</td>
<td>✓</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>✓</td>
<td>✓</td>
<td>x</td>
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<tr>
<td>Messner 2002**</td>
<td>3222</td>
<td>-1.4 (-15.6 to 13.5)</td>
<td>No</td>
<td>Yes (change from previous day, non-fatal MIs only)</td>
<td>✓†</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Danet 1999*</td>
<td>3314</td>
<td>10.6 (2.0 to 19.1)</td>
<td>Yes</td>
<td>No</td>
<td>✓</td>
<td>✓</td>
<td>x</td>
<td>✓</td>
<td>x</td>
<td>✓</td>
<td>✓</td>
<td>x</td>
<td>x</td>
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<tr>
<td><strong>Fatal events only</strong></td>
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<td></td>
</tr>
<tr>
<td>Dilaveris 2006*</td>
<td>3126</td>
<td>18.0 (8.6 to 28.4)</td>
<td>Yes</td>
<td>Yes</td>
<td>✓†</td>
<td>✓</td>
<td>x</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Sharovsky 2004**</td>
<td>12007</td>
<td>18.0 (13.9 to 21.8)</td>
<td>Yes</td>
<td>Yes</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Rossi 1999**</td>
<td>Approx 1600</td>
<td>12.8 (3.8 to 22.9)</td>
<td>Not mentioned</td>
<td>Yes</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>

*10-Year average of the monthly mean temperatures, and of the minimum and maximum monthly mean temperature in the study area, as recorded at the nearest available monitoring station included in the Goddard Institute for Space Studies (GISS) surface temperature data, using data from the years 1991–2000 inclusive; †authors adjusted for calendar month, which should have approximately captured any seasonal effect; ‡authors performed a basic adjustment for season in a sensitivity analysis, which did not change the conclusions; §authors adjusted for annual population and calendar year, which should have approximately captured any long-term trend.
### Table 3  Daily time-series studies with temperature exposures and myocardial infarction (MI) outcomes: study results

<table>
<thead>
<tr>
<th>First author and year</th>
<th>Temperature variable*, range (if reported) (°C)</th>
<th>Relative risk (RR) or rate ratio for temperature (95% CI if reported)</th>
<th>(Change in temperature variable to which RR refers)</th>
<th>Subgroup to which RR refers (if applicable)</th>
<th>Lag for temp effect (days)</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Studies of fatal and non-fatal events</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gerber 2006&lt;sup&gt;13&lt;/sup&gt;</td>
<td>$t_{\text{max}}$ – 29 to 39</td>
<td>0.93 (0.73 to 1.14)&lt;br&gt;1.00 (reference)&lt;br&gt;0.97 (0.89 to 1.06)&lt;br&gt;1.03 (0.92 to 1.14)</td>
<td>$&gt;30$ °C&lt;br&gt;18–30 °C&lt;br&gt;0–17 °C&lt;br&gt;&lt;0 °C</td>
<td>0</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>Wang 2006&lt;sup&gt;15&lt;/sup&gt;</td>
<td>$t_{\text{mean}}$ – 0.9 to 32.7</td>
<td>1.00 (reference)&lt;br&gt;1.12 (0.99 to 1.27)&lt;br&gt;1.17 (1.01 to 1.35)</td>
<td>$&gt;20$ °C&lt;br&gt;10–20 °C&lt;br&gt;&lt;10 °C</td>
<td>0</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>Enquselassie 1993&lt;sup&gt;16&lt;/sup&gt;</td>
<td>$t_{\text{max}}$, 16 to 30</td>
<td>1.2 (0.9 to 1.5)&lt;br&gt;1.0 (reference)&lt;br&gt;1.4 (1.1 to 1.8)&lt;br&gt;1.2 (0.9 to 1.4)&lt;br&gt;1.0 (reference)&lt;br&gt;1.0 (0.8 to 1.3)&lt;br&gt;</td>
<td>$&gt;30$ °C&lt;br&gt;23–27 °C&lt;br&gt;&lt;16 °C&lt;br&gt;30–30 °C&lt;br&gt;23–27 °C&lt;br&gt;&lt;16 °C&lt;br&gt;</td>
<td>Fatal MIs&lt;br&gt;Fatal MIs&lt;br&gt;Fatal MIs&lt;br&gt;Non-fatal MIs&lt;br&gt;Non-fatal MIs&lt;br&gt;Non-fatal MIs&lt;br&gt;</td>
<td>0</td>
<td>–</td>
</tr>
<tr>
<td>Ohlson 1991&lt;sup&gt;17&lt;/sup&gt;</td>
<td>$t_{\text{wint}}$, 2 to 0</td>
<td>1.00 (reference)&lt;br&gt;1.09 (0.82 to 1.44)&lt;br&gt;1.07 (0.79 to 1.52)&lt;br&gt;1.10 (0.67 to 1.85)&lt;br&gt;</td>
<td>$&gt;0$ °C&lt;br&gt;10 to –1 °C&lt;br&gt;20 to –11 °C&lt;br&gt;&lt;–20 °C&lt;br&gt;</td>
<td>2</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>Barnett 2005&lt;sup&gt;18&lt;/sup&gt;</td>
<td>$t_{\text{mean}}$, 1.5 to 23.0</td>
<td>1.008 (1.004 to 1.012)&lt;br&gt;</td>
<td>Per 1 °C decrease&lt;br&gt;</td>
<td>Average 0–3&lt;br&gt;</td>
<td>Only a linear temperature effect appears to have been considered</td>
<td></td>
</tr>
<tr>
<td>Morabito 2005&lt;sup&gt;19&lt;/sup&gt;</td>
<td>$t_{\text{mean}}$, discomfort hours</td>
<td>1.03 (p&lt;0.01)&lt;br&gt;1.06 (p&lt;0.01)&lt;br&gt;</td>
<td>Per extra two heat discomfort hours&lt;br&gt;Per extra two cold discomfort hours</td>
<td>Summer, men, &lt;65 years&lt;br&gt;Winter, women, &lt;65 years&lt;br&gt;</td>
<td>0</td>
<td>Only linear effects of the exposure variables appear to have been considered. However, discomfort hours analysis was performed separately for winter and summer</td>
</tr>
<tr>
<td>Ebi 2004&lt;sup&gt;20&lt;/sup&gt;</td>
<td>$t_{\text{min}}$, $t_{\text{max}}$, 1 to 37 (tmin)</td>
<td>1.072 (1.057 to 1.086)&lt;br&gt;1.008 (1.004 to 1.012)&lt;br&gt;1.223 (1.083 to 1.381)&lt;br&gt;1.025 (1.000 to 1.052)&lt;br&gt;1.066 (1.023 to 1.111)&lt;br&gt;1.109 (1.051 to 1.169)&lt;br&gt;</td>
<td>Per 3 °C decrease (tmin)&lt;br&gt;Per 3 °C increase (tmin)&lt;br&gt;Per 3 °C increase (tmin)&lt;br&gt;Per 3 °C decrease (tmax)&lt;br&gt;Per 3 °C decrease (tmax)&lt;br&gt;Per 3 °C decrease (tmax)&lt;br&gt;</td>
<td>Men, 55–69 years, LA&lt;br&gt;Men, 55–69 years, SF&lt;br&gt;Men, 55–69 years, Sa&lt;br&gt;Men, 55–69 years, SA&lt;br&gt;Men, 55–69 years, SF&lt;br&gt;Men, 55–69 years, Sa&lt;br&gt;</td>
<td>7</td>
<td>Only linear temperature effects appears to have been considered. Effects for age &gt;70 years and for women were all in the same direction as those shown here</td>
</tr>
<tr>
<td>Koken 2003&lt;sup&gt;21&lt;/sup&gt;</td>
<td>$t_{\text{max}}$, 16.7 to 30.8</td>
<td>1.175 (1.029 to 1.343)&lt;br&gt;</td>
<td>Per 5.9 °C increase&lt;br&gt;</td>
<td>&gt;65 years&lt;br&gt;</td>
<td>0</td>
<td>Analysis was for July/August only</td>
</tr>
<tr>
<td>Messner 2002&lt;sup&gt;22&lt;/sup&gt;</td>
<td>$t_{\text{temp}}$, change –38 to 30 (temp)</td>
<td>1.001 (0.993 to 1.008)&lt;br&gt;1.000 (0.997 to 1.003)&lt;br&gt;1.003 (0.979 to 1.028)&lt;br&gt;1.015 (1.003 to 1.027)&lt;br&gt;</td>
<td>Per 1 °C decrease (temp)&lt;br&gt;Per 1 °C increase (temp)&lt;br&gt;Per 1 °C increase (tchange)&lt;br&gt;Per 1 °C increase (tchange)&lt;br&gt;</td>
<td>Fatal MIs&lt;br&gt;Non-fatal MIs&lt;br&gt;Fatal MIs&lt;br&gt;Non-fatal MIs&lt;br&gt;</td>
<td>0</td>
<td>Only linear temperature effects appears to have been considered</td>
</tr>
<tr>
<td>Danet 1999&lt;sup&gt;23&lt;/sup&gt;</td>
<td>$t_{\text{mean}}$, –15 to 28</td>
<td>1.05 (1.02 to 1.09)&lt;br&gt;</td>
<td>Per 5 °C decrease&lt;br&gt;</td>
<td>0</td>
<td>Only linear temperature effects appears to have been considered</td>
<td></td>
</tr>
<tr>
<td><strong>Fatal events only</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dilaveris 2006&lt;sup&gt;24&lt;/sup&gt;</td>
<td>$t_{\text{mean}}$, 1 to 39</td>
<td>1.13†&lt;br&gt;1.00 (reference)&lt;br&gt;1.40† (p&lt;0.001)&lt;br&gt;</td>
<td>30 °C&lt;br&gt;23.3 °C&lt;br&gt;10 °C&lt;br&gt;</td>
<td>Mean of last 7 days&lt;br&gt;</td>
<td>Results are from the regression line, which shows minimum event rate at 23.3 °C, with the event rate increasing smoothly above and below this temperature (levelling off at mean temperatures below 10 °C)</td>
<td></td>
</tr>
<tr>
<td>Sharovsky 2004&lt;sup&gt;25&lt;/sup&gt;</td>
<td>$t_{\text{mean}}$, 11 to 27</td>
<td>1.11 (1.06 to 1.16)&lt;br&gt;1.00 (reference)&lt;br&gt;1.16 (1.05 to 1.27)&lt;br&gt;</td>
<td>23.8–27.3 °C&lt;br&gt;21.6–22.6 °C&lt;br&gt;16.4–17.3 °C&lt;br&gt;</td>
<td>2-Day average&lt;br&gt;</td>
<td>–</td>
<td></td>
</tr>
</tbody>
</table>

Continued
We identified 19 relevant studies, with a total of 14 investigating short-term (day-to-day) effects of temperature on MI risk. A number of large and relatively well-controlled studies have reported a statistically significant effect of ambient temperature on MI risk. The vast majority of studies reported main effects on the same day or up to 3 days later, with no study reporting substantial effects lagging by more than 1 week. Over half of the time-series regression studies reported detrimental effects of cold and over half reported detrimental effects of heat; indeed a few studies found a U-shaped relationship, with MI risk increasing at both ends of the temperature scale. The size of temperature effects varied. Three studies of MI mortality outcomes were among those estimating the largest temperature effects—as much as a 31–44% increase in risk at the extremes of the local temperature scale compared with intermediate local temperatures. The larger size of these mortality effects might reflect an inherent lack of specificity in studies with mortality outcomes; some deaths are likely to have been coded as MI based on limited information, leading to potential misclassification, and if such misclassified causes of death were more strongly associated with temperature, results may have been exaggerated. On the other hand, studies based on hospital admissions may have underestimated the true temperature effects if difficulties in getting to hospital during temperature extremes led to more out-of-hospital MI deaths occurring which would not have been included. Although studies including non-fatal events generally estimated effects that were smaller in magnitude, detrimental effects of both heat and cold were still found in a number of these studies; considering the five studies in which MI outcomes were validated against diagnostic criteria, one and three studies found significant effects of heat and cold, respectively.

Various mechanisms have been suggested through which cold exposure might act as a trigger for MI, and it is possible that a number of parallel processes contribute to the effect. Experimental studies have found increased arterial pressure and blood viscosity during cold exposure, as well as an increased need for oxygen and consequently an increase in the cardiac workload. Furthermore, red cell counts, plasma cholesterol and fibrinogen concentrations, all of which may be thrombogenic, appear to be raised on exposure to cold. Heat exposure has also been shown under controlled conditions to lead to increases in red blood cell counts, platelet counts, and blood viscosity, as well as increases in heart rate. However, there is a lack of more recent data about the effects of temperature on an updated range of clotting measures and more research is needed in this area.

The majority of studies included used data sources such as hospital databases and registries, which would have had the potential to capture events across the local population, thus their findings should have good generalisability within the local settings. There might be a number of reasons for the heterogeneity in results between studies. One must consider that the studies included here cover a wide range of populations with differing demographic profiles, as well as a wide range of geographical locations. In each location, it is likely that various factors such as quality of housing, prevalence of air conditioning, central heating and insulation could have all influenced the strength and direction of the observed association between outdoor temperature and health outcomes at the population level. There were also many methodological differences across the studies included: MI events were identified from sources of various types; modelling strategies varied; different definitions of temperature were used as the main exposure (such as minimum, maximum, mean, windchill-adjusted); different allowances for non-linear temperature effects were made; and different lag days considered. There was also variation in the level of adjustment for potential confounding factors such as air pollution (which was only controlled for in a handful of studies).

In addition, local climate may have a role in the vulnerability to temperature effects. One study which incorporated data from 21 countries found that local mean temperature explained much of the variation in the magnitude of the detrimental effect of cold on MI risk, and we correspondingly found that, among single-location studies, those conducted in areas with higher long-term mean temperatures tended more frequently to report detrimental effects of cold than those conducted in warmer areas, and indeed tended to report effect estimates with larger magnitude. We did not observe such a pattern for the effect of heat, despite the differing effects of heat that have been reported local climate to be a strong modifier of temperature effects. Such effect modification may simply reflect better established adaptive measures in colder countries; the Eurowinter Group found that, at the same outdoor temperatures, people in Finland were more likely to have bedroom heating, keep their indoor temperatures higher, and were more likely to wear hats, gloves, anoraks, and (among women) trousers, than people in Athens, Greece; the potential benefits of such adaptive measures are suggested by the improvements in blood pressure achieved on installing home heating in a UK study. Others have suggested that there may be some
biological adaptation to cold,\textsuperscript{39} and cold-adapted subjects have been shown to have reduced activity of the sympathetic nervous system in response to cold stress.\textsuperscript{39}

Our review inevitably has some limitations. First, our search strategy might have missed some studies. However, by searching a number of different databases, with different indexing systems, and, furthermore, checking reference lists and the websites of major organisations, we believe that all major studies with MI as the primary outcome should have been picked up. We also took steps to include studies of CVDs more broadly, where an analysis of MI was also performed separately. Our decision to include only papers analysing specific MI outcomes might also have led to some informative studies of related outcomes being excluded, though we believe that this is outweighed by the advantage in interpretability from the very specific focus on MI. Second, as with any review of the literature, there might have been publication bias: studies finding effects may have been more likely to be published. The extent of publication bias is difficult to assess in studies with such varied methodology and reporting. Though such concerns should always be borne in mind, our goal was not to produce a definitive numerical estimate of the effects of temperature on MI risk, but rather to give an overview of the evidence available. Finally, we did not include non-English-language citations owing to resource limitations, but we believe that this is unlikely to have led to the omission of any major papers in the area.

There is some public health motivation for further clarifying the effects of temperature. Weather forecasting is reasonably accurate up to a few days in advance, and with a well-understood relationship between temperature and MI, those most vulnerable could be warned before the risk of MI was likely to increase, and given advice to reduce their personal risk. The UK Met Office recently set up a similar targeted warning system for people with chronic obstructive pulmonary disease, in which patients are alerted by an automated telephone call when the risk of disease exacerbation is elevated based on the ambient temperature; they are given advice on keeping warm, avoiding low temperatures and watching for warning signs of their condition worsening. It is claimed that a 20.5–48% reduction in hospital admissions has been achieved among practices signing up to the scheme.\textsuperscript{43} Health service providers could also be warned in advance where rates of MI were likely to increase, to aid the short-term allocation of resources.

A number of suggestions arise for future research. Though the majority of the studies included were of similar basic design (daily time-series studies), there was wide variation in the methodology and reporting used. More consistent adjustment for potential confounders such as season, long-term trend and air pollution; allowance for non-linear and delayed temperature effects; and more consistent reporting standards would make future studies in this area easier to compare and interpret. More large studies with this kind of consistent methodology and reporting will be required in a number of geographical locations to characterise the short-term effects of temperature on MI risk, and the relationship of such effects to local climate. There is also a need for more studies which take account of potential effect modifiers: though a few studies have presented stratified or age-restricted data, there is little direct evidence on how age, and other individual-level factors such as previous disease, affect a person’s vulnerability to temperature effects. In addition, individual-level studies collecting detailed information on such factors as clothing, air conditioning and home heating, though expensive and difficult to design, would provide valuable data to assess the role of adaptive measures. Finally, though the role of more complex weather indicators, such as air mass type, remains unclear and difficult to interpret, the effects of such factors are worthy of further investigation, since weather effects on human health may not be captured fully by investigating only specific parameters such as temperature and humidity; indeed interactions between the various aspects of weather may, in part, help to explain some of the variation in results across studies included in this review.

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Effects of ambient temperature on the incidence of myocardial infarction

K Bhaskaran, S Hajat, A Haines, E Herrett, P Wilkinson and L Smeeth

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