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Global variation in the effects of ambient temperature on mortality: a systematic evaluation

Yuming Guo^{1,*}, Antonio Gasparrini², Ben Armstrong³, Shanshan Li¹, Benjawan Tawatsupa⁴, Aurelio Tobias⁵, Eric Lavigne^{6,7}, Micheline de Sousa Zanotti Stagliorio Coelho⁸, Michela Leone⁹, Xiaochuan Pan¹⁰, Shilu Tong¹¹, Linwei Tian¹², Ho Kim¹³, Masahiro Hashizume¹⁴, Yasushi Honda¹⁵, Yue-Liang Leon Guo¹⁶, Chang-Fu Wu¹⁷, Kornwipa Punnasiri⁴, Seung-Muk Yi¹³, Paola Michelozzi⁹, Paulo Hilario Nascimento Saldiva⁸, and Gail Williams¹

¹Department of Epidemiology and Biostatistics, School of Population Health, The University of Queensland, Brisbane, Australia ²Department of Medical Statistics, London School of Hygiene & Tropical Medicine, London, United Kingdom ³Department of Social and Environmental Health Research, London School of Hygiene & Tropical Medicine, London, United Kingdom ⁴Health Impact Assessment Division, Department of Health, Ministry of Public Health, Thailand ⁵Institute of Environmental Assessment and Water Research, Spanish Council for Scientific Research, Barcelona, Spain ⁶Environmental Issues Division, Public Health Agency of Canada, Ottawa, Canada ⁷Department of Epidemiology and Community Medicine, University of Ottawa, Ottawa, Canada ⁸Laboratory of Experimental Air Pollution, Department of Pathology, School of Medicine, University of São Paulo, São Paulo, Brazil ⁹Department of Epidemiology of the Lazio Regional Health Service, Rome, Italy ¹⁰Department of Occupational and Environmental health, School of Public Health, Peking University, Beijing, China ¹¹School of Public Health and Social Work and Institute of Health and Biomedical Innovation, Queensland University of Technology, Brisbane, Australia ¹²The Jockey Club School of Public Health and Primary Care, The Chinese University of Hong Kong, Hong Kong, China ¹³Graduate School of Public Health, Seoul National University, Seoul, Republic of Korea ¹⁴Department of Pediatric Infectious Diseases, Institute of Tropical Medicine, Nagasaki University, Nagasaki, Japan ¹⁵Faculty of Health and Sport Sciences, University of Tsukuba, Tsukuba, Japan ¹⁶Department of Environmental and Occupational Medicine, National Taiwan University, Taipei, Taiwan ¹⁷Department of Public Health, National Taiwan University, Taipei, Taiwan

Abstract

*Corresponding author: Yuming Guo, Department of Epidemiology and Biostatistics, School of Population Health, The University of Queensland, Brisbane, QLD 4006, Australia; Telephone: +61 7 3346 5265; y.guo1@uq.edu.au.

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Background—Studies have examined the effects of temperature on mortality in a single city, country or region. However, less evidence is available on the variation in the associations between temperature and mortality in multiple countries, analyzed simultaneously.

Methods—We obtained daily data on temperature and mortality in 306 communities from 12 countries/regions (Australia, Brazil, Thailand, China, Taiwan, Korea, Japan, Italy, Spain, United Kingdom, United States and Canada). Two-stage analyses were used to assess the non-linear and delayed relationship between temperature and mortality. In the first stage, a Poisson regression allowing over-dispersion with distributed lag non-linear model was used to estimate the community-specific temperature-mortality relationship. In the second stage, a multivariate meta-analysis was used to pool the non-linear and delayed effects of ambient temperature at the national level, in each country.

Results—The temperatures associated with the lowest mortality were around the 75th percentile of temperature in all the countries/regions, ranging from 66th (Taiwan) to 80th (UK) percentiles. The estimated effects of cold and hot temperatures on mortality varied by community and country. Meta-analysis results show that both cold and hot temperatures increased the risk of mortality in all the countries/regions. Cold effects were delayed and lasted for many days, while hot effects appeared quickly and did not last long.

Conclusions—People have some ability to adapt to their local climate type, but both cold and hot temperatures are still associated with the risk of mortality. Public health strategies to alleviate the impact of ambient temperatures are important, in particular in the context of climate change.

Periods of low and high ambient temperatures have been found associated with high mortality in a wide range of climates and countries.¹⁻⁶ However, most previous studies have examined temperature effects only by community or country.^{2,4,7} Although some evidence of adaptation to local climates is clear from studies within large countries^{5,7} and the limited number of international studies⁸⁻¹⁰, there are no studies with a wide range of globally diverse communities and climates. The different analytic approaches adopted in studies on single countries or regions, in particular considering different lag periods, makes it difficult to assess how associations differ across climates and societies. In addition, some studies examined the effects of only high temperatures or only cold temperatures, which makes it difficult to define whether people have the ability to adapt to their local climates.^{11,12} Considering the global ambient temperature changes that are expected in the context of climate change, an international perspective on the temperature health effects carries with it important public health implications.

This study aims to examine how temperature-mortality relationships estimated using consistent methods vary across a wide range of communities in twelve countries/regions.

METHODS

Data Collection

In this study, we obtained daily data on non-accidental mortality and weather conditions in 306 communities from twelve countries/regions: Australia (3 cities during 1988-2008), Brazil (18 cities during 1997-2011), Thailand (62 provinces during 1999-2008), China (6

cities during 2002–2011), Taiwan (3 cities during 1994–2007), South Korea (7 cities during 1992–2010), Japan (7 cities during 1972–2009), Italy (10 cities during 1987–2010), Spain (51 cities during 1990–2010), United Kingdom (10 regions during 1993–2006), USA (108 cities during 1987–2000), and Canada (21 cities during 1986–2009) (see eFigure 1 for location and eTable 1 for community-specific information). Weather data included daily minimum, mean and maximum temperatures, and relative humidity. We used mean temperature to assess the effects of temperature on mortality, as it represents the exposure throughout the entire day and night and can be easily interpreted for decision-making purposes. The details for data collection are described in the supplemental material (eAppendix).

This study was approved by the Behavioural & Social Sciences Ethical Review Committee, University of Queensland.

Data analysis

Analysis plan—The temperature-mortality association was investigated with a two-stage analysis using time series data from the 306 communities in the twelve countries/regions. In the first stage, we applied a time series model to each community data in order to estimate the city-specific temperature–mortality relationship, allowing for non-linearity and delayed effects. These estimated relationships were then pooled in the second stage at country level with a multivariate meta-analysis. This approach has been illustrated in previous publications.^{13,14}

Although the temperature-mortality association in individual cities is naturally considered with temperature on a degrees scale, this makes for difficulties when combining curves across cities with non-overlapping temperature ranges (eTable 1). Also, because several studies suggested the adaptation of populations to their own climate,^{5,9} we hypothesized that health effects might be more consistent in terms of temperature percentiles than in the absolute scale of temperature.⁷ Therefore, we developed an approach by defining the temperature-mortality relationship on a relative scale, following methods previously described.¹³ Specifically, we standardized the community-specific absolute temperatures to community-specific percentiles. The results are expressed in terms of temperature percentiles, which correspond to different community-specific absolute temperatures. If curves on this scale are similar across communities, this implies that relative risks across percentiles are similar. Conversely, if curves on the original degree scale are similar, on the relative scale they would differ across communities with different climates.

First stage of analysis—In the first stage, for each community, we used a regression model to obtain community-specific estimates assuming a quasi-Poisson distribution allowing for over-dispersed death counts, which follows a standard analytical approach for time-series environmental health data.¹⁵ The community-specific Poisson time series model is given as the following:

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

$$\log(\mu_t) = \alpha + \beta T_{t,1} + NS(\text{time}, df) + \lambda \text{DOW}_t.$$

where Y_t is the observed daily death count on day t ; α is the intercept; $T_{t,l}$ is a matrix of variables obtained by the transformation of standardized temperature, β is vector of coefficients for $T_{t,l}$, and l is the lag days; $NS(time, df)$ is natural cubic spline of time, and df is degree of freedom per year for time, which was used to control for long-term trend and seasonality. 10 df per year for time was used to control seasonality and long-term trend, with the exception of Thailand where, because there were fewer cases per day, we used 7 df per year to avoid possible over control; DOW_t is a categorical variable for day of the week, and λ is vector of coefficients.

For each community, we modelled the non-linear and delayed effect of temperatures using the term $\beta T_{t,l}$ which is parameterized using a cross-basis function expressing a distributed lag non-linear model.¹⁶ In this study, a flexible cross-basis was defined by a natural cubic spline for the space of temperature, and a natural cubic spline with intercept for the space of lags, with the maximum lag up to 21 days. We placed three internal knots at equally-spaced temperature percentiles (25th, 50th, and 75th) and two internal knots at equally spaced log-values of lag (approximately 1.4, and 5.5 days), respectively, plus intercept. The spline for temperature was centered at the 75th percentile, representing the average point of minimum mortality in preliminary analyses. These choices defined spline basis with four degrees of freedom for temperature and four degrees of freedom for lag. The choice of 21 days for the lag period was motivated by previous studies showing that effects of cold temperature appeared only after some delay and lasted for several days, while effects of hot temperatures were more acute and possibly affected by mortality displacement.^{2,14}

Reduction of distributed lag non-linear models—The 16 community-specific parameters of the cross-basis function expressed the non-linear and delayed temperature-mortality association in each community. The association was then reduced to three summaries expressing the overall cumulative exposure-response relationship and the lag-response relationships specific to the 1st and 99th percentiles, compared with the percentile corresponding to the minimum-mortality temperature. The two last summaries represent the lag pattern of cold and hot temperatures, respectively. The reduction was performed for each summary by computing transformed parameters γ for the uni-dimensional natural cubic splines for the space of temperature or lag, accordingly, from the original parameters β of the cross-basis above. This method has been previously described.¹⁴

Second stage of analysis—At the second stage, a multivariate meta-analysis was used to pool the three sets of community-specific parameters γ obtained from the reduction of the first-stage model.¹⁴ The multivariate meta-analyses were fitted using a random effects model by maximum likelihood, and was applied in each country, obtaining national pooled estimates. Heterogeneity was assessed through a multivariate extension of the I^2 index, which quantifies the percentage of variability due to true differences across cities.

Estimating minimum-mortality temperature—Many individual cities had very imprecisely estimated temperature at which mortality was the lowest (“minimum-mortality temperature”), which would lead to problems if using these as baselines for estimating heat and cold relative risks. However, multivariate meta-analysis showed that most variation in

temperature-mortality associations was explained by country (I-sq = 52.7% reduced to 28.2%) when temperature was expressed on a percentile scale. We therefore used the country average minimum-mortality temperature percentile as baseline for calculation of heat and cold relative risks for all cities in that country.

Summary of the results—We plotted the estimated pooled overall cumulative exposure-response relationship at the national level. To represent the lag pattern of cold and hot temperatures on mortality, we also plotted the estimated pooled lag-response relationship for cold temperature (1st versus minimum-mortality temperature) and hot temperature (99th versus minimum-mortality temperature).

To obtain an easily interpretable estimate of the effects of cold and hot temperatures on mortality, we also calculated the overall cumulative relative risks of death associated with cold temperature (1st percentile) and with hot temperature (99th percentile), both relative to the minimum-mortality temperature. These effect estimates were computed from the nonlinear exposure-response curves; thus, they reflected a portion of the true temperature-mortality association.⁷ To obtain a comparison with previously published studies,⁷ we also calculated the overall cumulative relative risks of death associated (1) with cold temperature (1st percentile of temperature) compared with the 10th percentile of temperature and (2) with hot temperature (99th percentile of temperature) relative to 90th percentile of temperature.

We also plotted the associations of average temperature and latitude, with the minimum-mortality temperature in twelve countries/regions, to understand whether the minimum-mortality temperatures varied by country climate and latitude.

Sensitivity analyses were performed on the parameters for the community-specific model to test the robustness of our results. We changed lag days to 28 days to examine whether using 21 lag days was enough to capture the temperature effects on mortality. We modified the degrees of freedom for temperature (3–6 *df*). We included relative humidity into the analyses. We included air pollutants (PM₁₀, SO₂ and NO₂) in the analyses using China data.

The residuals were examined to evaluate the adequacy of the community-specific models. R software (version 3.0.1, R Development Core Team 2009) was used to do data analysis. The “dlnm” package was used to create the distributed lag non-linear model¹⁶ and the “mvmeta” package to fit the multivariate meta-analyses¹³.

RESULTS

Table 1 shows the summary of the study period, death count and mean temperature in the twelve countries/regions. This study included 306 communities. The study period covered 1972 to 2011. The total death counts were over 38 million. Thailand had the hottest climate pattern, while Canada had the coldest one. A summary for daily deaths and temperature in 306 communities, ordered by latitude within each country is presented in eTable 1. The average deaths and temperatures varied greatly by community, consistently with the range of different climates.

The pooled relationships between temperature and mortality were non-linear at the national level, with minimum-mortality temperature close to 75th percentile of temperature in all countries/regions (Figure 1). Both cold and hot temperatures were significantly associated with the increased risk of mortality in all countries/regions.

The relative risks of deaths associated with cold (1st percentile versus minimum-mortality temperature) and hot (99th percentile versus minimum-mortality temperature) temperatures differed by community and country (Figure 2; see eTable 2 for the values of relative risks).

The minimum-mortality temperatures were higher in countries with high temperature or in countries close to equator (Figure 3). But the minimum-mortality temperatures distributed around 75th percentile of temperature in all countries, ranging from 66th (Taiwan) to 80th (UK) percentiles (Table 2). The multivariate I^2 statistic suggested that 52.7% of the variation in temperature-mortality curves is attributable to true heterogeneity among communities. The estimate decreased to 28.2% when allowing for country effects.

In general, the effects of cold temperature (1st percentile versus the minimum-mortality temperature) were delayed by about two days and lasted for at least ten days at the national level (Figure 4), with some evidence of longer lags in Taiwan, Italy, Spain and to some extent the United Kingdom.

The effects of hot temperature (99th percentile versus the minimum-mortality temperature) appeared immediately and generally lasted only three or four days (Figure 5), though again in Italy and Spain risks persisted longer. There was a period of relative risk below 1.0 at longer lags, consistent with mortality displacement after exposure to hot temperatures in UK and South Korea, and to a lesser extent in Canada and Japan, which was not found in other countries.

Table 2 shows the pooled overall cumulative relative risks of cold and hot effects on mortality over lags of 0–21 days in the twelve countries/regions. In summary, effect estimates for cold effects using the 1st percentile versus the minimum-mortality temperature were higher than hot effects using the 99th percentile versus the minimum-mortality temperature in all the countries/regions. In general, people living in Taiwan, Italy and Spain were more sensitive to both cold and hot temperatures compared with people in other countries.

For comparability with some other publications,⁷ we also calculated relative risks for 1st versus 10th and 99th versus 90th percentiles of temperature as alternative indices of cold and heat risks. These estimates were lower, as expected. Results for each community were shown in eTable 2.

Sensitivity analyses showed that the results were broadly similar when we used 28 lag days (eFigure 2), changed the degrees of freedom for temperature (3–6 *df*) (eFigure 3), or included relative humidity in the analyses (eFigure 4). When we included selected air pollutants (PM₁₀, SO₂ and NO₂), the temperature effects on mortality were changed only very slightly (eFigure 5).

DISCUSSION

We have examined temperature-mortality associations using consistent methods for a much wider range of communities than has previously been investigated in a single study. In total, we studied 306 communities across twelve countries/regions, including countries from both developing and developed regions with various climate patterns (i.e., tropical, subtropical and temperate). We found evidence that in all countries/regions both cold and hot temperatures were associated with the increased risks of deaths. The effects of cold temperatures appeared after a couple of days but lasted at least ten days, while the effects of hot temperatures appeared immediately and lasted usually only three or four days. Despite widely ranging climates, the minimum-mortality temperatures were close to the 75th percentile of temperature in all twelve countries/regions, suggesting that people have adapted to some extent to their local climates.

Some of our findings, such as the broadly U-shaped temperature-mortality associations, have been strongly indicated by the ensemble of previous national or regional studies.^{4,5,7} However, our use of consistent methods across a wide range of communities removes doubt as to whether comparisons may be confused by differences in methods. Previous studies have used a wide variety of daily temperature indices, lags, mathematical forms for the association and methods to control for time-varying confounders, each of which can change the estimates of temperature-mortality associations.

The consistency of the minimum-mortality temperature around the 75th percentile across such a range of climates and levels of development is remarkable, although similar results were reported previously in national or regional studies.^{1,5,17} This finding is consistent with minimum-mortality temperatures in communities with colder climates being lower than in communities with warmer climates, with mortality increasing as temperature becomes unusual for the community. This suggests that, over the long term, people partially adapt to their local climates via a range of physiological, behavioral, and technological adaptations.¹⁸

That the minimum-mortality temperatures are close to the 75th percentile of temperature across varying climates suggests a degree of long-term adaptation, but from this it cannot be inferred that such adaptation would occur over a few decades, such as following climate change. Also, the fact that minimum-mortality temperatures are higher in warmer climates does not imply complete adaptation, as the degree of risk associated with hot and cold might still vary with climate. For these reasons we believe that it would be premature to use these results to make assumptions about adaptation to – and hence impact of – future climate change. We believe that our results can inform investigations that do so, but these would have to consider other factors as well.¹⁹ Based on our large dataset, we plan to explore the potential impacts of future climate change on mortality in future studies, following pioneering more local estimates.²⁰⁻²² Whatever the impact of future climate change, we found that both cold and hot temperatures increase the risk of mortality in all countries/regions. Thus, effective interventions to reduce vulnerability to both hot and cold temperatures would benefit population health.

Our finding that the minimum-mortality temperature was consistently around the 75th percentile suggests this as the most suitable reference temperature for both heat and cold summary relative risks, as it will more fully reflect the relationships between cold/hot temperatures and mortality – compared with alternatives such as the common 1st versus 10th and 99th versus 90th percentile contrasts. By this measure, cold effects (1st versus minimum-mortality temperature) were higher than hot effects (99th versus minimum-mortality temperature) in all the countries/regions. Relative risks using the 1st versus 10th and 99th versus 90th percentile contrasts were substantially lower, especially for cold, and underestimate both cold and hot effects. Our results estimated by using 1st versus 10th and 99th versus 90th percentile were comparable with previous studies conducted in USA ⁷.

There were substantial variations in the extent of risk elevation at the 1st (cold) and 99th (heat) percentiles relative to the minimum-mortality temperature – about equally between and within countries/regions. While it is the objective of this paper to describe, rather than fully explore, reasons for this variation (e.g., climatic or societal), some between-country patterns are noteworthy. Communities in Taiwan, Italy and Spain had higher temperature-related (cold and heat) mortality risks than those in other countries. This finding is not consistent with our prior hypothesis that developing countries (Brazil, Thailand and China) would be more sensitive to temperatures than wealthy countries, but it would be premature to consider this as strong evidence against that hypothesis. The variation in the impact of temperatures on mortality might be modified by climatic factors or by socioeconomic, demographic and infrastructure factors that are unrelated to whether a country is developing or developed.²³ For example, air conditioning is protective to heat-related deaths,²⁴ while poor heating and insulation affect cold-related deaths, especially in countries with a mild winter climate.²⁵ We found that cold-related mortality was delayed while hot-related mortality was acute at the national level. The effects of cold temperatures typically lasted for 10 days, compared with about 3 days for hot temperatures. Similar patterns of time lag have been observed in previous studies,^{7,14,26} but our observations across such a wide range of countries using the same methods is new. Our findings confirm that only timely preventive measures are helpful to reduce the health effects of hot temperatures, while several days' protection should be implemented to reduce the health impacts of cold temperatures.

We used flexible analytic techniques—in particular, multivariate meta-analysis with distributed lag non-linear model—to estimate and pool the non-linear and delayed relationship between temperature and mortality. These fairly new but established approaches offer flexibility for the assessment of the temperature-mortality relationship, without making strong prior assumptions about the exposure-mortality shape or lag structure. Most previous studies used only conventional linear exposure-responses and univariate meta-analysis that describe the relationship less completely or ignore correlated variables in the meta-analysis.²⁷

This study has some limitations. The data for the United States covered only the period of 1987–2000, which is earlier than other countries. This might have some impact on the comparisons, as the impacts of temperature on mortality have decreased in the US over recent years.²⁸ However, this issue is unlikely to have a major influence on our overall conclusions. As in other similar time series studies, we used the data on temperature from

fixed sites, rather than individual exposure, which will create measurement error in exposure to some extent. However, these measurement errors are likely to be random, which would usually result in an underestimation of the relative risks.²⁹ Air pollutants were not adjusted for in this study, because the data were not available for some countries. That air pollutants might be on the causal path between temperature and health can also complicate interpretation of adjusted models. However, the sensitivity analysis suggests that results were changed only slightly when we put air pollutants into the models. The study was restricted in various ways to avoid cluttering the paper with many results. For this reason we investigated only non-accidental mortality and did not formally explore reasons for variation on temperature-mortality associations between communities.

In conclusion, our results provide strong evidence that both cold and hot temperatures increase the risk of mortality in different countries in different climatic zones. The temperature at which mortality was lowest was close to the 75th percentile of temperature in all countries/regions, suggesting at least partial adaptation to local climate. However, the degree of risk associated with both cold and heat differed by community and country. In all countries/regions, the effects of cold temperatures appeared after a couple of days but lasted at least ten days, while the effects of hot temperatures appeared immediately and lasted usually only three or four days.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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REFERENCES

1. Martin SL, Cakmak S, Hebborn CA, Avramescu ML, Tremblay N. Climate change and future temperature-related mortality in 15 Canadian cities. *International journal of biometeorology*. 2012; 56(4):605–19. [PubMed: 21597936]
2. Guo Y, Barnett AG, Pan X, Yu W, Tong S. The impact of temperature on mortality in Tianjin, China: a case-crossover design with a distributed lag nonlinear model. *Environmental health perspectives*. 2011; 119(12):1719–25. [PubMed: 21827978]
3. Huynen MM, Martens P, Schram D, Weijenberg MP, Kunst AE. The impact of heat waves and cold spells on mortality rates in the Dutch population. *Environ Health Perspect*. 2001; 109(5):463–70. [PubMed: 11401757]

4. Tawatsupa B, Dear K, Kjellstrom T, Sleight A. The association between temperature and mortality in tropical middle income Thailand from 1999 to 2008. *International journal of biometeorology*. 2014; 58:203–215. [PubMed: 23100101]
5. Curriero FC, Heiner KS, Samet JM, Zeger SL, Strug L, Patz JA. Temperature and mortality in 11 cities of the eastern United States. *American Journal of Epidemiology*. 2002; 155(1):80–87. [PubMed: 11772788]
6. Armstrong BG, Chalabi Z, Fenn B, Hajat S, Kovats S, Milojevic A, Wilkinson P. Association of mortality with high temperatures in a temperate climate: England and Wales. *J Epidemiol Community Health*. 2011; 65(4):340–5. [PubMed: 20439353]
7. Anderson BG, Bell ML. Weather-related mortality: how heat, cold, and heat waves affect mortality in the United States. *Epidemiology*. 2009; 20(2):205–13. [PubMed: 19194300]
8. Analitis A, Katsouyanni K, Biggeri A, Baccini M, Forsberg B, Bisanti L, Kirchmayer U, Ballester F, Cadum E, Goodman PG, Hojs A, Sunyer J, Tiittanen P, Michelozzi P. Effects of cold weather on mortality: results from 15 European cities within the PHEWE project. *American journal of epidemiology*. 2008; 168(12):1397–408. [PubMed: 18952849]
9. McMichael AJ, Wilkinson P, Kovats RS, Pattenden S, Hajat S, Armstrong B, Vajanapoom N, Niciu EM, Mahomed H, Kingkeow C, Kosnik M, O'Neill MS, Romieu I, Ramirez-Aguilar M, Barreto ML, Gouveia N, Nikiforov B. International study of temperature, heat and urban mortality: the 'ISOTHURM' project. *International journal of epidemiology*. 2008; 37(5):1121–31. [PubMed: 18522981]
10. Baccini M, Biggeri A, Accetta G, Kosatsky T, Katsouyanni K, Analitis A, Anderson HR, Bisanti L, D'Ippoliti D, Danova J, Forsberg B, Medina S, Paldy A, Rabczenko D, Schindler C, Michelozzi P. Heat effects on mortality in 15 European cities. *Epidemiology*. 2008; 19(5):711–9. [PubMed: 18520615]
11. Basu R, Samet JM. Relation between elevated ambient temperature and mortality: A review of the epidemiologic evidence. *Epidemiologic Reviews*. 2002; 24(2):190–202. [PubMed: 12762092]
12. Basu R. High ambient temperature and mortality: a review of epidemiologic studies from 2001 to 2008. *Environmental Health*. 2009; 8
13. Gasparrini A, Armstrong B, Kenward MG. Multivariate meta-analysis for non-linear and other multi-parameter associations. *Stat Med*. 2012; 31(29):3821–39. [PubMed: 22807043]
14. Gasparrini A, Armstrong B. Reducing and meta-analysing estimates from distributed lag non-linear models. *BMC Med Res Methodol*. 2013; 13:1. [PubMed: 23297754]
15. Dominici F, Sheppard L, Clyde M. Health effects of air pollution: A statistical review. *International Statistical Review*. 2003; 71(2):243–276.
16. Gasparrini A, Armstrong B, Kenward M. Distributed lag non-linear models. *Statistics in medicine*. 2010; 29(21):2224–2234. [PubMed: 20812303]
17. Chung JY, Honda Y, Hong YC, Pan XC, Guo YL, Kim H. Ambient temperature and mortality: an international study in four capital cities of East Asia. *The Science of the total environment*. 2009; 408(2):390–6. [PubMed: 19853280]
18. Kovats RS, Hajat S. Heat stress and public health: a critical review. *Annu. Rev. Public Health*. 2008; 29:41–55. [PubMed: 18031221]
19. Kinney PL, O'Neill MS, Bell ML, Schwartz J. Approaches for estimating effects of climate change on heat-related deaths: challenges and opportunities. *Environmental Science and Policy*. 2008; 11(1):87–96.
20. Astrom DO, Forsberg B, Ebi KL, Rocklov J. Attributing mortality from extreme temperatures to climate change in Stockholm, Sweden. *Nature Climate Change*. 2013; 3(12):1050–1054.
21. Huang CR, Barnett AG, Wang XM, Tong SL. The impact of temperature on years of life lost in Brisbane, Australia. *Nature Climate Change*. 2012; 2(4):265–270.
22. Ballester J, Robine JM, Herrmann FR, Rodo X. Long-term projections and acclimatization scenarios of temperature-related mortality in Europe. *Nature Communications*. 2011; 2
23. Ebi KL, Kovats RS, Menne B. An approach for assessing human health vulnerability and public health interventions to adapt to climate change. *Environ Health Perspect*. 2006; 114(12):1930–1934. [PubMed: 17185287]

24. Bouchama A, Dehbi M, Mohamed G, Matthies F, Shoukri M, Menne B. Prognostic factors in heat wave-related deaths - A meta-analysis. *Archives of Internal Medicine*. 2007; 167(20):2170–2176. [PubMed: 17698676]
25. Dear KBG, McMichael AJ. The health impacts of cold homes and fuel poverty. *British Medical Journal*. 2011; 342
26. Goodman PG, Dockery DW, Clancy L. Cause-specific mortality and the extended effects of particulate pollution and temperature exposure. *Environmental health perspectives*. 2004; 112(2): 179–85. [PubMed: 14754572]
27. Jackson D, Riley R, White IR. Multivariate meta-analysis: Potential and promise. *Stat Med*. 2011
28. Guo Y, Barnett AG, Tong S. High temperatures-related elderly mortality varied greatly from year to year: important information for heat-warning systems. *Scientific reports*. 2012; 2
29. Guo Y, Barnett AG, Tong S. Spatiotemporal model or time series model for assessing city-wide temperature effects on mortality? *Environ Res*. 2013; 120:55–62. [PubMed: 23026801]

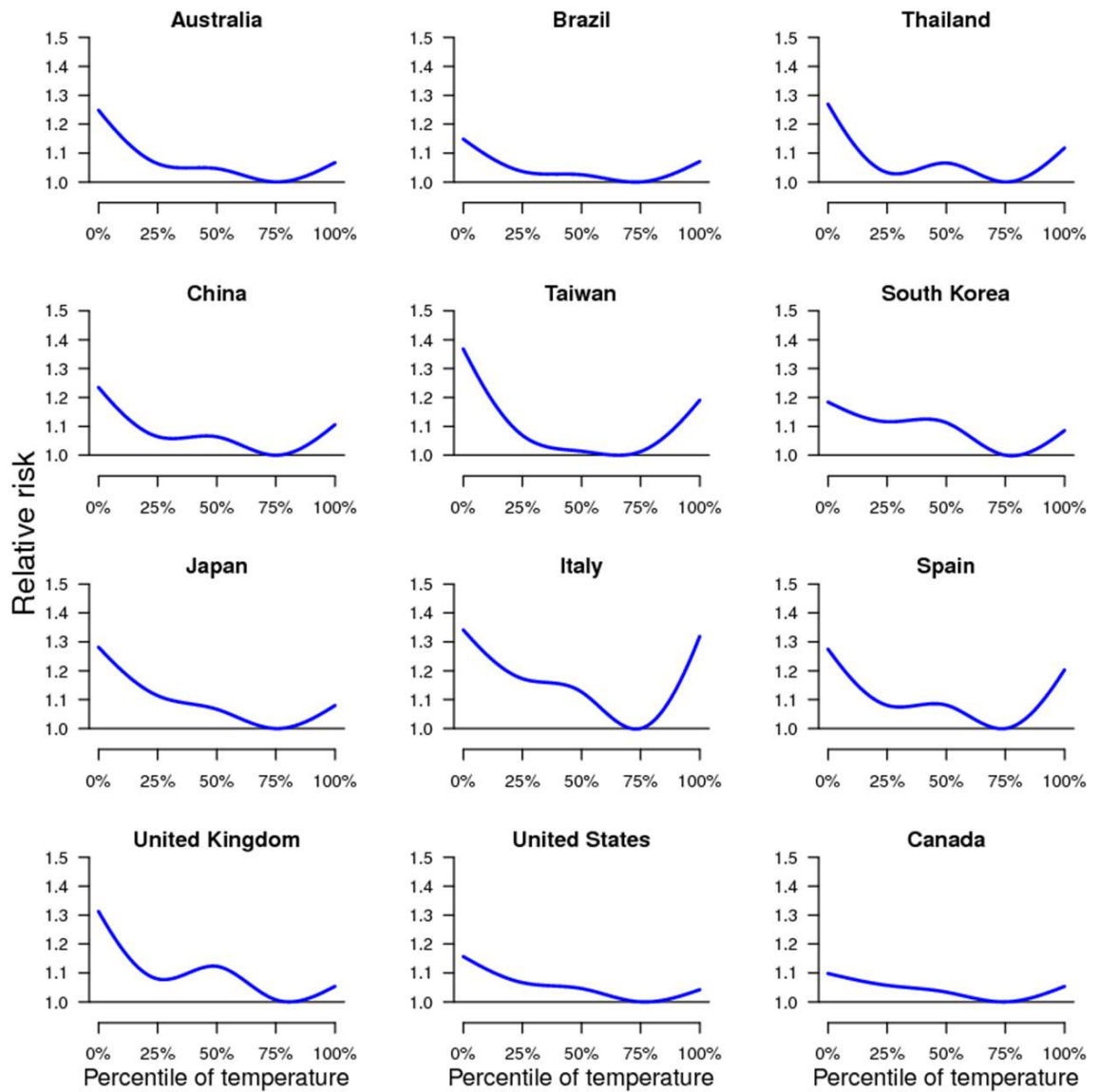


Figure 1. The pooled overall cumulative relationship between temperature and deaths over lags of 0-21 days in the twelve countries/regions.

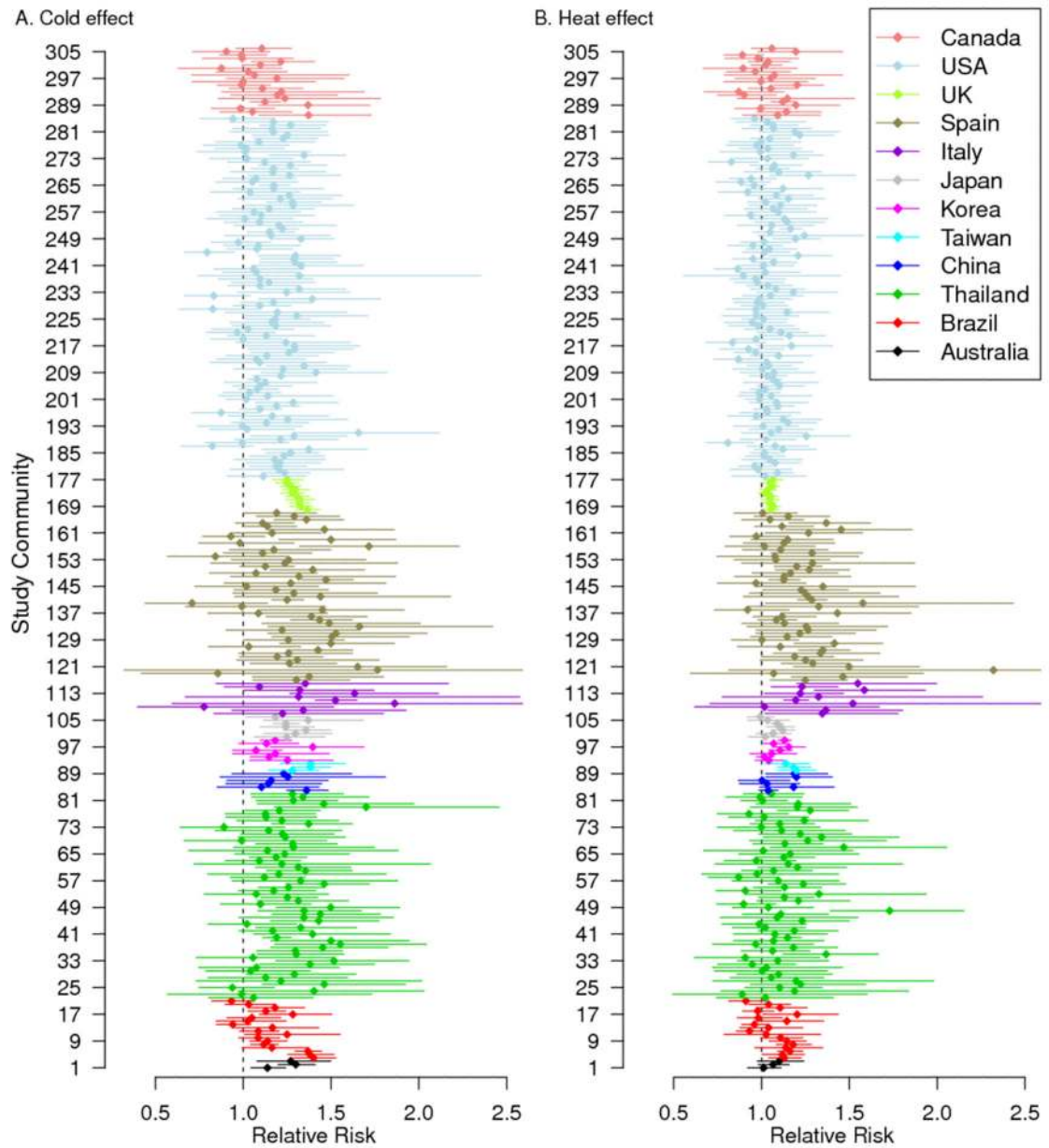


Figure 2. The relative risks of (A.) cold temperature (1st percentile versus minimum-mortality temperature) and (B.) hot temperature (99th percentile versus minimum-mortality temperature) on deaths cumulated over lags of 0–21 days in each community of the twelve countries/regions. The estimates are ordered by latitude within each country. (Community names are given in eTable 1.)

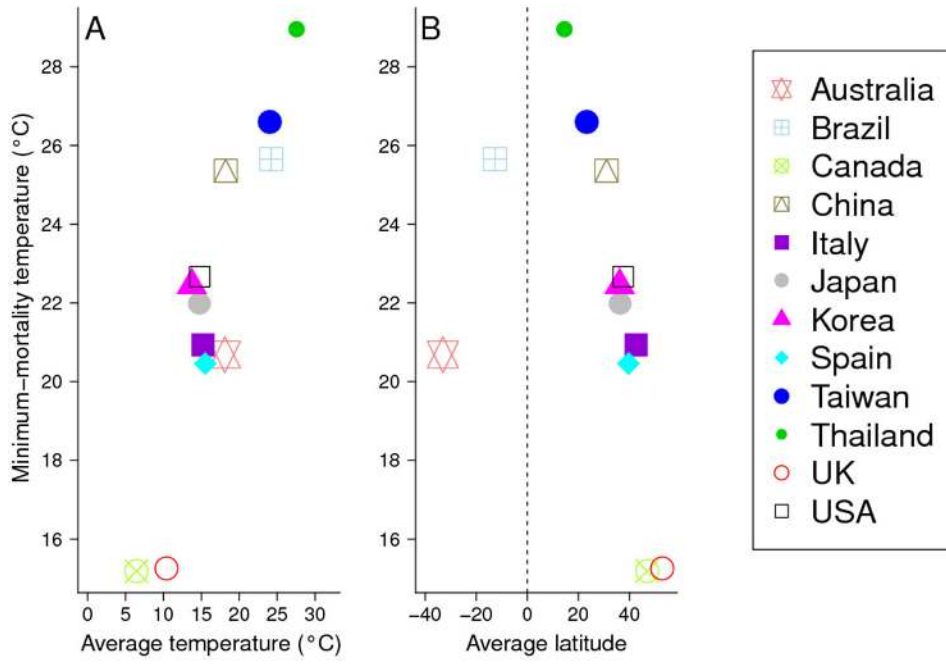


Figure 3. The associations of (A.) average temperature and of (B.) latitude, with minimum-mortality temperature in twelve countries/regions.

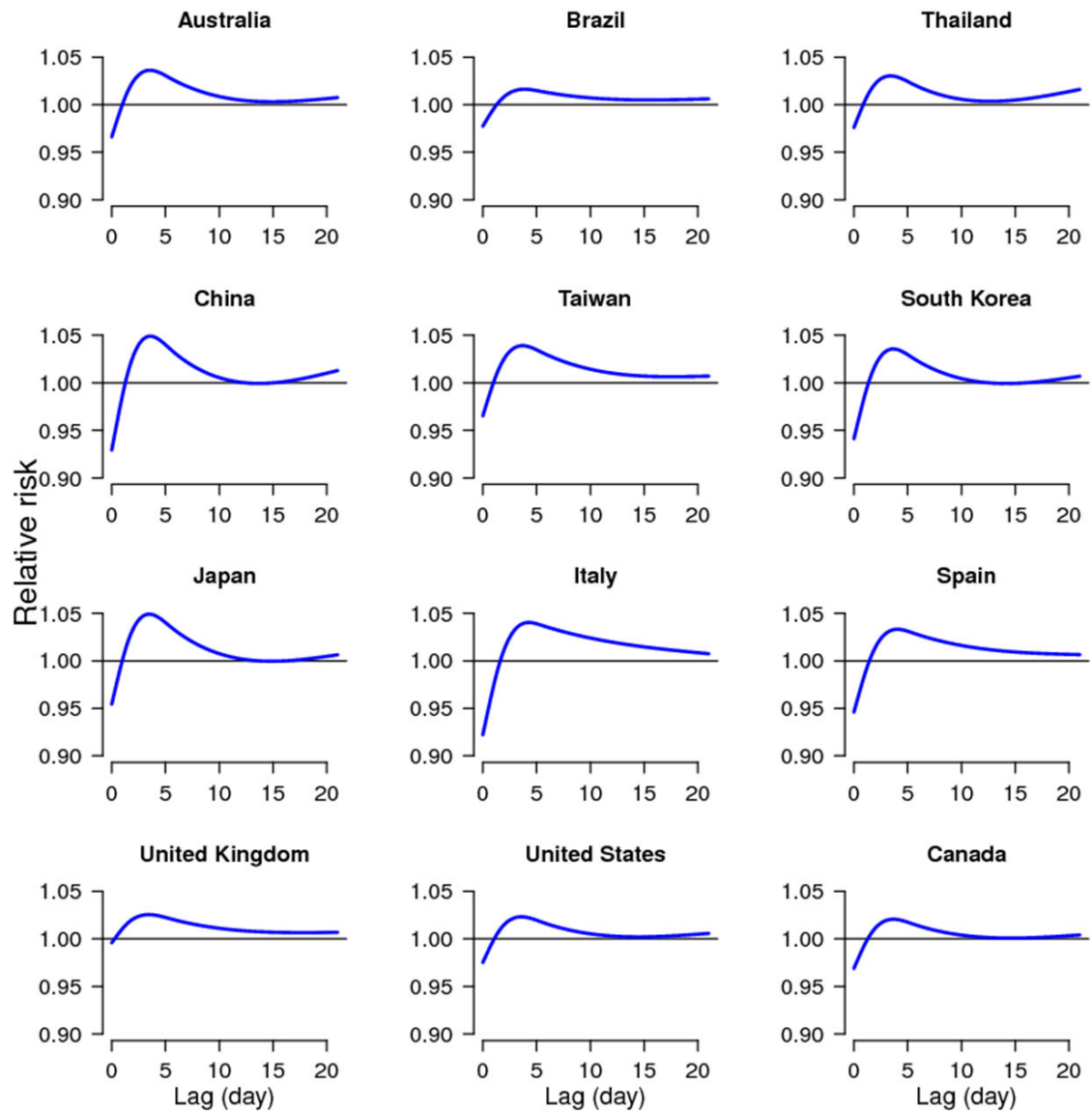


Figure 4. The pooled lag-response relationship associated with cold temperature (1st percentile versus minimum-mortality temperature) on deaths along lags of 0–21 days in the twelve countries/regions.

The percentiles of minimum-mortality temperatures are shown in Table 2.

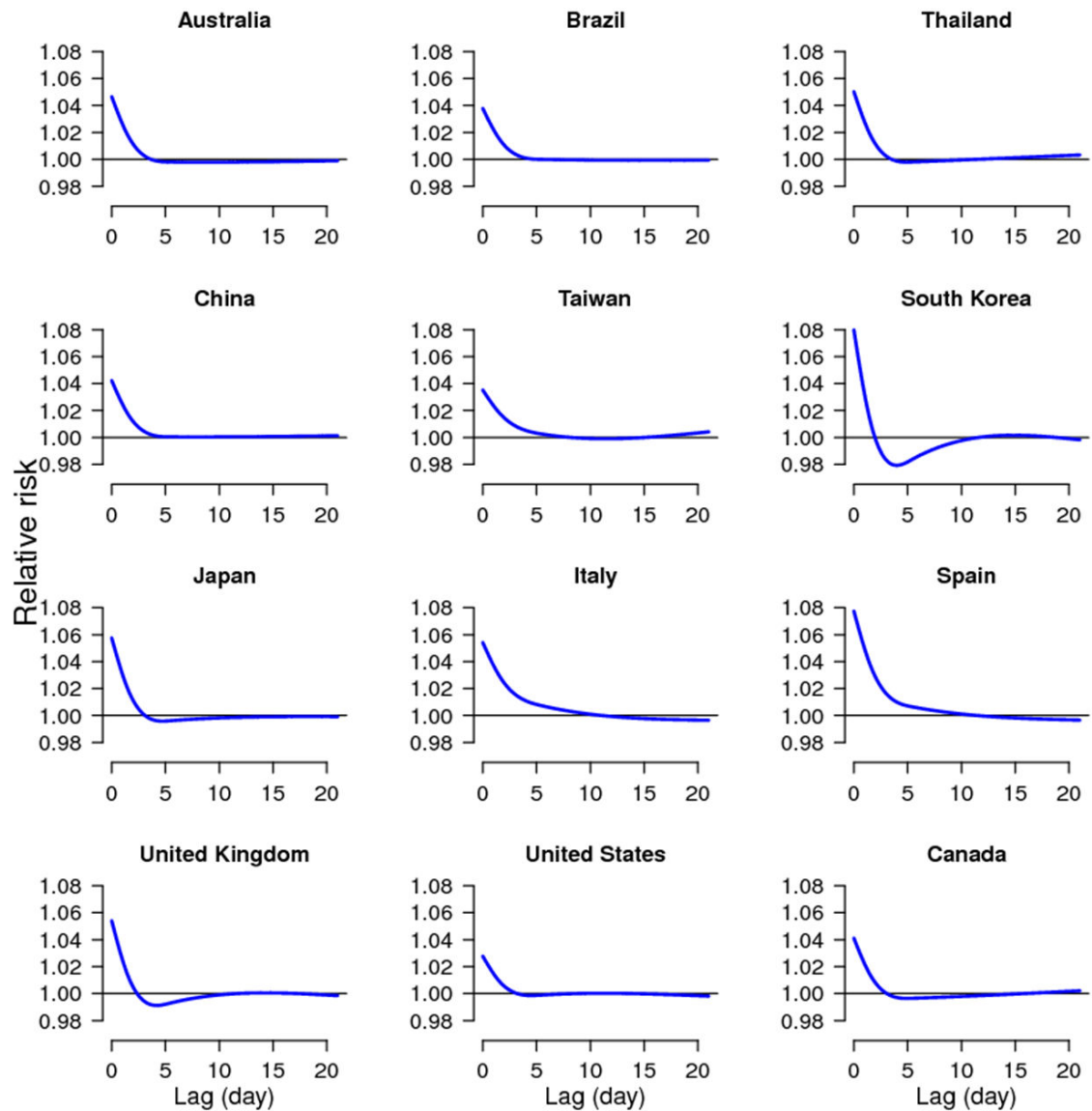


Figure 5. The pooled lag-response relationship associated with hot temperature (99th percentile versus minimum-mortality temperature) along lags of 0–21 days in the twelve countries/regions. The percentiles of minimum-mortality temperatures are shown in Table 2.

Table 1
Summary of the study periods, number of deaths and temperature distributions in the 12 countries/regions.

Country/region	Number of communities	Period	No. Deaths	Mean temperature (°C)	
				Mean	Standard deviation
Australia	3	1988–2009	1,184,154	18.1	4.3
Brazil	18	1997–2011	3,435,535	24.2	2.2
Thailand	62	1999–2008	1,827,853	27.6	2.1
China	6	2002–2011	639,348	18.2	8.6
Taiwan	3	1994–2007	688,394	24.0	4.6
South Korea	7	1992–2010	1,511,996	13.7	9.2
Japan	7	1972–2009	4,023,393	14.8	8.3
Italy	10	1987–2010	816,478	15.2	7.3
Spain	51	1990–2010	3,480,531	15.5	6.2
United Kingdom	10	1993–2006	7,573,716	10.4	5.2
United States	108	1987–2000	10,395,583	14.8	8.5
Canada	21	1986–2009	2,517,428	6.5	10.5
International	306	1972–2011	38,094,409	---	---

Table 2
The pooled relative risks of cold temperature and hot temperature on deaths cumulated over lags of 0–21 days in the 12 countries/regions: 1st versus 10th percentile and 1st versus minimum-mortality temperature percentile.

Estimates were calculated from the distributed lag non-linear model (Figure 1).

County/region	Cold effects			Hot effects		
	RR (95% CI)			RR (95% CI)		
	1 st versus 10 th	1 st versus minimum-mortality temperature percentile	Minimum-Mortality Temperature Percentile	99 th versus minimum-mortality temperature percentile	99 th versus 90 th	
Australia	1.07 (1.03-1.12)	1.24 (1.14-1.35)	76	1.06 (1.00-1.13)	1.03 (1.00-1.07)	
Brazil	1.05 (1.02-1.07)	1.14 (1.08-1.21)	72	1.07 (1.02-1.11)	1.03 (1.01-1.06)	
Thailand	1.10 (1.08-1.12)	1.25 (1.22-1.29)	76	1.11 (1.08-1.14)	1.06 (1.04-1.07)	
China	1.07 (1.03-1.11)	1.22 (1.12-1.34)	76	1.10 (1.03-1.17)	1.05 (1.02-1.09)	
Taiwan	1.11 (1.09-1.13)	1.35 (1.27-1.44)	66	1.18 (1.12-1.25)	1.07 (1.05-1.10)	
South Korea	1.03 (1.02-1.04)	1.18 (1.11-1.25)	78	1.08 (1.04-1.12)	1.05 (1.03-1.07)	
Japan	1.06 (1.04-1.08)	1.27 (1.21-1.33)	76	1.07 (1.04-1.11)	1.04 (1.03-1.06)	
Italy	1.06 (1.03-1.09)	1.33 (1.20-1.48)	74	1.30 (1.22-1.39)	1.14 (1.11-1.17)	
Spain	1.08 (1.07-1.09)	1.26 (1.22-1.32)	74	1.19 (1.16-1.23)	1.09 (1.08-1.11)	
United Kingdom	1.10 (1.09-1.11)	1.30 (1.27-1.33)	80	1.05 (1.04-1.06)	1.03 (1.03-1.04)	
United States	1.04 (1.03-1.04)	1.15 (1.13-1.18)	76	1.04 (1.02-1.06)	1.02 (1.01-1.03)	
Canada	1.02 (1.00-1.03)	1.10 (1.05-1.14)	74	1.05 (1.01-1.09)	1.03 (1.01-1.05)	