



A multi-country analysis on potential adaptive mechanisms to cold and heat in a changing climate



Ana M. Vicedo-Cabrera^{a,*}, Francesco Sera^a, Yuming Guo^b, Yeonseung Chung^c, Katherine Arbuthnott^a, Shilu Tong^{d,e,f}, Aurelio Tobias^g, Eric Lavigne^h, Micheline de Sousa Zanotti Stagliorio Coelhoⁱ, Paulo Hilario Nascimento Saldiva^j, Patrick G. Goodman^k, Ariana Zeka^k, Masahiro Hashizume^l, Yasushi Honda^m, Ho Kimⁿ, Martina S. Ragettli^{o,p}, Martin Röösli^{o,p}, Antonella Zanobetti^q, Joel Schwartz^q, Ben Armstrong^a, Antonio Gasparrini^a

^a Department of Social and Environmental Health Research, London School of Hygiene and Tropical Medicine, London, United Kingdom

^b Department of Epidemiology and Preventive Medicine, School of Public Health and Preventive Medicine, Monash University, Melbourne, Australia

^c Department of Mathematical Sciences, Korea Advanced Institute of Science and Technology, Daejeon, South Korea

^d Department of Clinical Epidemiology and Biostatistics, Children's Medical Center, Shanghai Jiao-Tong University, Shanghai, China

^e School of Public Health and Institute of Environment and Population Health, Anhui Medical University, Hefei, China

^f School of Public Health and Social Work, Queensland University of Technology, Brisbane, Australia

^g Institute of Environmental Assessment and Water Research (IDAEA), Spanish Council for Scientific Research (CSIC), Barcelona, Spain

^h Department of Epidemiology and Community Medicine, University of Ottawa, Ottawa, Canada

ⁱ Institute of Advanced Studies, University of São Paulo, São Paulo, Brazil

^j School of Physics, Dublin Institute of Technology, Dublin, Ireland

^k Institute for Environment, Health and Societies, Brunel University London, London, United Kingdom

^l Department of Pediatric Infectious Diseases, Institute of Tropical Medicine, Nagasaki University, Nagasaki, Japan

^m Faculty of Health and Sport Sciences, University of Tsukuba, Tsukuba, Japan

ⁿ Graduate School of Public Health, Seoul National University, Seoul, Republic of Korea

^o Swiss Tropical and Public Health Institute, Basel, Switzerland

^p University of Basel, Basel, Switzerland

^q Department of Environmental Health, Harvard T.H. Chan School of Public Health, Boston, MA, USA

ARTICLE INFO

Keywords:

Climate change
Heat
Cold
Adaptation
Mortality

ABSTRACT

Background: Temporal variation of temperature–health associations depends on the combination of two pathways: pure adaptation to increasingly warmer temperatures due to climate change, and other attenuation mechanisms due to non-climate factors such as infrastructural changes and improved health care. Disentangling these pathways is critical for assessing climate change impacts and for planning public health and climate policies. We present evidence on this topic by assessing temporal trends in cold- and heat-attributable mortality risks in a multi-country investigation.

Methods: Trends in country-specific attributable mortality fractions (AFs) for cold and heat (defined as below/above minimum mortality temperature, respectively) in 305 locations within 10 countries (1985–2012) were estimated using a two-stage time-series design with time-varying distributed lag non-linear models. To separate the contribution of pure adaptation to increasing temperatures and active changes in susceptibility (non-climate driven mechanisms) to heat and cold, we compared observed yearly-AFs with those predicted in two counterfactual scenarios: trends driven by either (1) changes in exposure-response function (assuming a constant temperature distribution), (2) or changes in temperature distribution (assuming constant exposure-response relationships). This comparison provides insights about the potential mechanisms and pace of adaptation in each population.

Results: Heat-related AFs decreased in all countries (ranging from 0.45–1.66% to 0.15–0.93%, in the first and last 5-year periods, respectively) except in Australia, Ireland and UK. Different patterns were found for cold

Abbreviations: DLNMs, distributed lags non-linear models; Q-AIC, quasi-Akaike score; BLUP, best linear unbiased prediction; MMT, minimum mortality temperature; MMP, minimum mortality percentile; AF, attributable mortality fractions; CI, confidence interval; RR, relative risk

* Corresponding author at: Department of Social and Environmental Health Research, London School of Hygiene and Tropical Medicine, 15-17 Tavistock Place, London WC1H 9SH, United Kingdom.

E-mail address: ana.vicedo-cabrera@lshtm.ac.uk (A.M. Vicedo-Cabrera).

<https://doi.org/10.1016/j.envint.2017.11.006>

Received 12 June 2017; Received in revised form 9 November 2017; Accepted 9 November 2017

Available online 20 December 2017

0160-4120/ © 2017 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

(where AFs ranged from 5.57–15.43% to 2.16–8.91%), showing either decreasing (Brazil, Japan, Spain, Australia and Ireland), increasing (USA), or stable trends (Canada, South Korea and UK). Heat-AF trends were mostly driven by changes in exposure-response associations due to modified susceptibility to temperature, whereas no clear patterns were observed for cold.

Conclusions: Our findings suggest a decrease in heat-mortality impacts over the past decades, well beyond those expected from a pure adaptation to changes in temperature due to the observed warming. This indicates that there is scope for the development of public health strategies to mitigate heat-related climate change impacts. In contrast, no clear conclusions were found for cold. Further investigations should focus on identification of factors defining these changes in susceptibility.

1. Introduction

As global warming has become more evident, public health and other sectors have turned their attention to climate change adaptation. Recent work examining the analysis of the historical impact of temperature on mortality in different locations has provided valuable insights on whether populations have adapted or, in general terms, become more or less susceptible to non-optimal temperatures, and which potential mechanisms and factors were involved (Arbuthnott et al., 2016). All this evidence is critical to inform current public health policy and protection of vulnerable populations (Hess et al., 2014). And, at the same time, knowledge of such changes can improve projections on future temperature-related health impacts under climate change scenarios.

Still, our current understanding on this subject is limited. First, a comprehensive assessment requires evidence on potential changes in susceptibility across the whole temperature spectrum (Arbuthnott et al., 2016). Most studies assessing temporal variations have focused on heat-mortality associations, reporting a substantial attenuation in risk in several locations (Åström et al., 2013; Barreca et al., 2016; Bobb et al., 2014; Carson et al., 2006; Coates, 2014; Ekamper et al., 2009; Guo et al., 2012; Heo et al., 2016; Nordio et al., 2015; Petkova et al., 2014). However, despite cold being responsible for a relatively large proportion of the overall temperature-related health burden (Gasparrini et al., 2015b), temporal variation in cold-mortality associations have only been investigated in a limited number of studies, with conflicting results (Åström et al., 2013; Barnett, 2007; Carson et al., 2006).

Second, and more importantly, most previous studies have relied on measures of relative risk (RR), and few have reported estimates in terms of impact (i.e. attributable risks), a measure shown to be more informative for policy planning and implementation (Gasparrini and Leone, 2014). Assessment of temporal variation in RR provides information on the extent of the change in susceptibility to heat or cold, although conclusions about the potential drivers for such change cannot be directly derived. For example, a reduction in heat-mortality risk can be driven by either ‘pure adaptation’, referred to here as any physiological acclimatisation of the population to a changing climate, or by an attenuation in risk due to extrinsic mechanisms, such as infrastructural changes or improved health care, which can happen simultaneously but independently from the changing climate (Arbuthnott et al., 2016). In contrast, attributable impact measures depend on both susceptibility, defined in terms of RR, and the prevalence of exposure (Gasparrini and Leone, 2014), and account for both adaptation to changes in exposure and autonomous attenuation. In the context of climate change, disentangling the temporal changes in attributable mortality driven through these two pathways can provide a more comprehensive picture of the evolution of the temperature-related health burden and is important in determining the contribution of different adaptive mechanisms to this evolution, and the potential for populations to adapt to global warming.

This study aims to address this issue by providing a comprehensive assessment of the potential adaptive mechanisms to non-optimal ambient temperatures during recent decades across different locations, characterized by different climates. Specifically, we illustrate the trends in both cold- and heat-attributable mortality in ten countries, and

differentiate between the potential contribution of ‘pure adaptation’ to changes in temperature and other non-climate driven mechanisms of attenuation in risk.

2. Material and methods

2.1. Data

Time series daily data including mortality and weather variables were collected through the Multi-Country Multi-city (MCC) Collaborative Research Network (<http://mccstudy.lshtm.ac.uk/>). We analysed data from 305 locations in 10 countries in largely overlapping periods ranging from 1st of January 1985 to 31st December 2012. Specifically, the data was from: Australia (3 cities, 1988–2008), Brazil (18 cities, 1997–2011), Canada (25 cities, 1986–2011), Island of Ireland (All-island data, 6 regions, 4 in the Republic of Ireland, and 2 in the Northern Ireland, 1985–2007), Japan (47 prefectures, 1985–2012), South Korea (7 cities, 1992–2010), Spain (50 cities, 1990–2010), Switzerland (8 cities, 1995–2012), the United Kingdom (UK, 10 regions, 1990–2011), and the United States of America (USA, 135 cities, 1985–2006). These data have been used in previous single- or multi-country studies (Gasparrini et al., 2015b, 2015a; Vicedo-Cabrera et al., 2016). A more detailed description of the data is provided in the appendix (Table S1). Daily mean temperature was considered as the main exposure variable in the present study.

2.2. Estimation of yearly heat- and cold-mortality associations

We adopted a two-stage time series design to assess the temporal patterns in heat and cold impacts in each country, throughout the study period available in each location between 1985 and 2012. Methods have been illustrated in detail in previous papers (Gasparrini et al., 2015b, 2015a).

2.2.1. First-stage time series analysis

We estimated the location-specific temperature-related mortality associations for each year of the series through quasi-Poisson regression and time-varying distributed lags non-linear models (DLNMs). This class of models can describe complex non-linear and lagged dependencies, through the combination of two functions into a cross-basis that define the conventional exposure-response association and the additional lag response association, respectively. We extended the methodology of the basic DLNMs, which assumes time-constant exposure-lag-response associations, to time-varying DLNMs by including a linear interaction between time and the cross-basis function defining the exposure-lag-response associations (Gasparrini et al., 2015a).

Specifically, the cross-basis function of daily mean temperature was composed of a natural cubic spline function for the temperature dimension with 3 internal knots in the 10th, 75th and 90th percentile of the location-specific temperature distributions, and a natural cubic spline with an intercept and 2 internal knots placed along equally-spaced values on the log scale, for the lag dimension. The lag period was extended to 21 days to capture the long-lagged associations and potential short-term harvesting. The chosen combination of nonlinear

functions and knots provided the lowest quasi-Akaike score (Q-AIC), compared to alternative models (see Methods S1). A natural cubic B-spline function with 8 df per year of series of the time variable was included to control for long-term trends and seasonality, together with an indicator term for day of the week. We included in the model the interaction terms obtained by multiplying cross-basis variables and time. The selection of the model specifications was based on previous work using a similar dataset (Gasparrini et al., 2015b).

We predicted the exposure-lag-response association for each of the years included in the study period, in each location by centering the time variable on the middle day (1st July) of the corresponding year (Gasparrini et al., 2015a). Bi-dimensional spline functions estimated for each year were reduced to uni-dimensional overall cumulative exposure-response. This step reduces the number of parameters to be pooled in the second-stage meta-analysis, and preserves the complexity of the estimated dependency. We additionally estimated the average temperature-mortality associations over the whole study period in each location from the basic DLNMs, using models that do not include the interaction term.

2.2.2. Second-stage meta-analysis

Year-specific and average cumulative exposure-response associations estimated for each location were pooled through separate multivariate meta-analytical models of the first-stage coefficients (Gasparrini and Armstrong, 2013). We included location-specific average and temperature range, and a categorical variable identifying each country as meta-predictors, to partially account for between-location differences in temperature-mortality associations. We derived the best linear unbiased prediction (BLUP) of the overall cumulative exposure-response association in each location and year which will be used to estimate attributable risk in subsequent steps (see the section below) (Gasparrini et al., 2015b; Gasparrini and Armstrong, 2013).

To explore temporal changes in the association, we reconstructed the country-specific exposure-response shapes for the first and last year of each series, as described in a previous study (Gasparrini et al., 2015b). Heat- and cold-mortality associations for the two selected years were summarized by computing the RR at the 99th and 1st percentile, respectively, of the year-specific temperature distribution, using the year-specific minimum mortality temperature (MMT) as a reference (minimum mortality percentile (MMP) between the 50th and the 99th of the year-specific temperature distribution). Additionally, we formally assessed the temporal variation using the multivariate Wald test on the pooled interaction terms resulting from the reduced location-specific coefficients (Gasparrini et al., 2015a). The null hypothesis of the test is that none of the coefficients are different from 0, thus no temporal changes in the whole exposure-response curve are observed.

2.3. Trends in heat- and cold-mortality impacts

Yearly-attributable fractions (AFs) were estimated using the year-specific BLUPs in each location and aggregated by country, as described elsewhere (Gasparrini and Leone, 2014). Components attributable to cold and heat were computed by summing the mortality attributable to heat and cold on days where temperatures were lower or higher than the estimated optimal temperature, and then dividing by the total number of deaths in each year. Optimal temperature was represented by the location- and year-specific MMT, estimated from the corresponding BLUPs, defined between the 50th and the 99th percentiles of the year-specific temperature distribution. Yearly AFs estimates were additionally aggregated into 5-year sub-periods (1985–1989, 1990–1994, 1995–1999, 2000–2004, 2005–2009).

As mentioned before, temporal variation in attributable risk is influenced by changes in the yearly temperature distribution (due to global warming), and by the temporal evolution of the temperature-mortality curves (due to changes in susceptibility to heat and cold). In order to disentangle the contribution of these two elements in defining

the temporal trends in temperature-mortality impacts, we predicted the yearly-AF in each country using the procedure described above but in two different counterfactual scenarios, defined in terms of exposure-response functions and temperature distributions:

- (1) *Temporal variation uniquely driven by changes in exposure-response association*: we predicted yearly-AFs in each location and aggregated by country assuming a constant mean temperature distribution throughout the study period. We applied the city- and year-specific BLUPs (obtained using time-varying DLNMs similar to the original approach), but over the whole-period mortality-temperature series in each location, instead of each year-specific series.
- (2) *Temporal variation uniquely driven by changes in temperature distribution*: we assumed a constant exposure-response association across the study period, while allowing time-varying temperature distributions. In this case, we applied the average exposure-response association (common to all years and represented by the corresponding location-specific average BLUPs derived from the DLNMs without the interaction term), over the temperature-mortality series of each year of each location and predicted the corresponding yearly-AF in each location and subsequently aggregated by country.

The comparison of the observed changes with those predicted in the two counterfactual scenarios above can help to determine the pace of potential changes in vulnerability to non-optimal temperatures, and help determine how much of these trends are explained by changes in temperature distribution. This can provide insights on the role of potential adaptive mechanisms in defining these trends, that is, either purely climate change adaptation or other attenuation mechanisms. For example, in the case of an absence of a changing climate (no changes in temperature exposure), a reduction in susceptibility would be entirely attributed to an attenuation of the effect due to non-climate driven mechanisms. Likewise, if the impact remains constant regardless of a shift towards warmer temperatures, this would suggest the presence of purely adaptation to a changing climate.

3. Results

Table 1 summarizes the mortality and temperature data from the 305 locations distributed in 10 countries included in the study (see also Table S2 in the Appendix). The data included nearly 75 million deaths, and countries contributed an average of 20.5 years to the time series data, ranging from 14 years (Brazil) to 27 years (Japan). In most countries, the temperature distribution progressively shifted towards warmer temperatures, consistent with observed global warming (Table 1 and Fig. S1). Only in Brazil and Australia did the temperature distribution remain fairly stable across the 5-year periods.

Table 2 summarizes the temporal changes in temperature-mortality associations reported in terms of RR for the first and the last year of the series in each country. Fig. S2 and S3 display the exposure-response curves and the effect modification of time on the overall cumulative exposure-response, respectively. Most of the countries show a reduction in heat-mortality associations, which is statistically significant (according to the Wald test) in Canada, Japan, Spain and USA, as shown in Fig. S3. We found less consistent temporal patterns in cold-mortality associations, with countries showing either an increase (South Korea), a decrease (Australia, Ireland, Spain, Switzerland, and the UK) or stable trends (Brazil, Canada, Japan and USA). Similar estimates were obtained using alternative combinations of cross-basis specifications (Table S3).

Table 3 shows country-specific cold- and heat-AFs in each 5-year period (with 95% confidence interval (CI)). Tables S4 and S5 show the corresponding yearly estimates, and these are reported graphically in Figs. S4–S5. Cold temperatures exhibit larger attributable mortality (above 5%) compared to heat (around or below 1%) in all countries.

Cold-mortality impacts persisted throughout the study periods in most of the countries, although following different temporal patterns (Fig. S4). Specifically, cold-AFs slightly decreased in Brazil (4.39% vs. 2.60%, 1st vs. last 5-year period), Japan (10.25% vs. 8.91%) and Spain (6.58% vs. 3.89%), whereas they increased in the USA (5.63% vs. 6.54%). AFs in Australia and Ireland display a steeper decrease, although notably these were countries with a lower number of study locations. Canada, Switzerland, South Korea and the UK show a more stable pattern, with cold-AFs ranging around 5%, 3%, 8% and 9%, respectively. Heat-AFs ranged from 1.66% in Switzerland (1995–1999) to 0.15% in Japan (2005–2009) (Table 3). Ireland was the only country showing a null impact of heat in the 5 sub-periods. Contrary to cold-related impacts, heat-related impacts decreased in most countries, but estimates show more unstable patterns in terms of yearly variations (Fig. S5). Canada, Japan, Spain, Switzerland, South Korea and the USA show a decreasing trend in heat-attributable AFs, from 0.45–1.66% in the first 5-year sub-period to 0.15–0.93% in the last 5-year sub-period. Heat impacts remained stable in UK and Brazil at around 0.2–0.4% and 0.6–0.7%, respectively, whereas it increased in Australia from 0.05% to 0.67%.

Figs. 1 and 2 compare the temporal trends in the observed yearly AFs for cold (blue) and heat (red) in each country with that predicted in the two modelled scenarios, specifically assuming either a constant temperature distribution (black line) or exposure-response relationship (grey line). The same plots with the corresponding 5-year average estimates are shown in Figs. S6 and S7. Overall, the long-term trend in the observed attributable mortality is mostly captured by the temporal variation due to changes in the exposure-response associations (black line), while year-to-year fluctuations seem largely explained by the changes in temperature distribution (grey line). Trends in heat-AFs defined only by variation in temperature distribution showed an irregular, but on average increasing, pattern across most of the countries, consistent with the shift towards warmer temperatures due to the global warming. All countries, except for Australia and Brazil, showed a decreasing trend in AFs when keeping the temperature distribution constant, consistent with the trends observed in the 5-year RRs (Table 3). These results suggest that the observed reduction in susceptibility to heat could have compensated for and eventually reversed the increase due to the progressive warming in climate, resulting in a net reduction in heat-mortality impacts. In contrast, cold-attributed AFs predicted in the two scenarios show heterogeneous trends, suggesting a more complex pattern and potentially the involvement of different mechanisms compared to heat.

4. Discussion

The assessment of temporal variations in temperature-mortality

associations in the past decades, and the contribution of adaptation to these observed trends, are crucial for the quantification of current and future climate change impacts. In the present study, we contribute to this topic by comprehensively exploring trends in heat and cold-mortality impacts across the last decades in 10 different countries. By applying a complex and flexible but easily reproducible methodology, we also disentangle the contribution of different components responsible for these changes. We found evidence of an attenuation of heat-mortality impacts in most of the countries well and beyond that simply expected from the pure adaptation to the changing climate. In contrast, cold-mortality impacts did not show a consistent pattern, with trends either stable or showing increasing or decreasing trends across countries. However, the extent of the reduction, where it happened, was weaker than for heat.

This is the first study in which temporal trends in both cold- and heat-mortality impacts are simultaneously assessed in a wide multi-country setting through a common study design and statistical framework. While most studies on temporal variations relied on simplifications of the exposure-response function (Åström et al., 2013; Barnett, 2007; Nordio et al., 2015), the more advanced time-varying DLNMs applied in the present study can characterize complex temperature–health dependencies and flexibly model their changes over time (Gasparrini et al., 2015a). Our method enables us to examine continuous patterns of change across the whole study period with the estimation of year-specific temperature-mortality associations. This avoids the splitting of the study period into arbitrary intervals of time which would compromise the statistical power (Carson et al., 2006; Davis et al., 2003). Moreover, temporal trends were expressed in terms of impact estimates, more specifically AFs, providing a comprehensive and tangible picture on how climate change affected population during the last decades.

Our findings - of an attenuation of heat-mortality risks in most of the countries studied - are consistent with evidence from previous studies (Carson et al., 2006; Coates, 2014; Donaldson et al., 2003; Gasparrini et al., 2015a; Heo et al., 2016; Nordio et al., 2015; Onozuka and Hagihara, 2015). We found similar but not identical results to Gasparrini et al. (2015a) using similar data. The difference in results could be due to the increased lag period of this analysis (accounting for more lagged and harvesting effects) and by our use of all-year data. Likewise, a recent study using historical data in Australia corroborates the unexpected positive slope found for this country, mostly during the first decade of the current century when several extreme heat events occurred (Coates, 2014).

In contrast to the decline in risk seen for heat, we found heterogeneous patterns in cold-related risks. For example, we found that total cold-related mortality slightly increased in the USA, contrary to the conclusions of previous studies (Barnett, 2007; Nordio et al., 2015).

Table 1
Descriptive statistics by country: number of locations, study period, total number of deaths and temperature distribution.

Country (N locations)	Period	^b N deaths	^a Daily average temperature (median [IQR])					
			Entire Series	1985–1989	1990–1994	1995–1999	2000–2004	2005–2009
Australia (3)	1988–2008	1,155,651	18.0 [14.6; 21.2]		17.7 [14.4; 21]	17.7 [14.5; 20.9]	18.1 [14.7; 21.3]	18.3 [14.8; 21.6]
Brazil (18)	1997–2011	3,401,136	24.7 [23.2; 26.1]			24.7 [23.1; 26.1]	24.7 [23.2; 25.9]	24.8 [23.3; 26.1]
Canada (25)	1986–2011	2,734,629	7.3 [– 0.9; 15.7]	7.2 [– 1.1; 15.6]	7.1 [– 0.8; 15.5]	7.2 [– 0.9; 15.8]	7.2 [– 1.0; 15.6]	7.5 [– 1.1; 15.9]
Ireland (6)	1985–2007	1,012,684	9.7 [6.5; 13.2]	9.3 [5.9; 12.7]	9.4 [6.4; 12.9]	10.0 [6.5; 13.5]	9.8 [6.7; 13.5]	10.2 [7.0; 13.8]
Japan (47)	1985–2012	26,893,197	15.7 [7.8; 22.4]	15.1 [7.4; 21.7]	15.5 [8.1; 22.1]	15.9 [7.7; 22.4]	16.0 [8.1; 22.6]	16.1 [8.1; 22.7]
South Korea (7)	1992–2010	1,726,938	14.8 [5.7; 21.8]		14.3 [5.1; 21.3]	14.8 [5.6; 21.8]	14.8 [6.0; 21.8]	15.1 [5.8; 21.8]
Spain (50)	1990–2010	3,470,088	14.9 [10.4; 20.6]		14.2 [10; 20.2]	15.3 [10.9; 20.4]	14.9 [10.6; 20.9]	15.4 [10.4; 20.9]
Switzerland (8)	1995–2012	231,606	10.8 [4.5; 16.5]			10.5 [4.2; 16.0]	10.8 [5.0; 16.6]	11.0 [4.3; 16.7]
UK (10)	1990–2011	11,748,764	10.2 [6.4; 14.4]		9.8 [6.2; 13.9]	10.2 [6.2; 14.4]	10.2 [6.6; 14.5]	10.6 [6.7; 14.7]
USA (131)	1985–2006	22,557,070	15.3 [8.2; 22.1]	15.2 [7.8; 22.0]	15.3 [8.3; 22.1]	15.1 [8.3; 22.1]	15.4 [8.1; 22.0]	

5-year estimates reported when each country contributed with at least 3 years to the corresponding sub-period.
^a Values correspond to the average value of the location-specific median [interquartile range (IQR)] in each country.
^b Number (N) of deaths due to all-causes or non-external causes (see Table S1 for details).

Table 2

Temporal changes in cold- and heat-mortality associations: relative risk (RR) and 95% confidence interval (CI) for cold and heat, temperature of minimum mortality (MMT) and minimum mortality percentile (MMP) for the first and last year of each country-specific series.

Country	Year	MMT [MMP]	RR cold [95%CI] ^a	RR heat [95%CI] ^b	p-value interaction ^c
Australia	First	27.4 [99]	1.807 [1.498;2.178]	1.000 [1.000;1.000]	< 0.001
	Last	22.8 [86]	1.069 [0.933;1.226]	1.261 [1.128;1.411]	
Brazil	First	25.2 [64]	1.269 [1.196;1.347]	1.095 [1.038;1.155]	0.471
	Last	24.8 [54]	1.222 [1.151;1.298]	1.065 [1.015;1.117]	
Canada	First	17.1 [83]	1.167 [1.076;1.265]	1.174 [1.102;1.249]	0.030
	Last	18.7 [85]	1.110 [1.032;1.193]	1.049 [0.998;1.103]	
Ireland	First	15.1 [93]	1.746 [1.563;1.950]	1.021 [0.933;1.117]	0.010
	Last	17.1 [99]	1.318 [1.162;1.494]	1.000 [1.000;1.000]	
Japan	First	24.4 [82]	1.364 [1.308;1.424]	1.190 [1.155;1.226]	< 0.001
	Last	29.7 [99]	1.371 [1.323;1.420]	1.000 [1.000;1.000]	
South Korea	First	24.1 [86]	0.953 [0.832;1.093]	1.101 [1.018;1.190]	< 0.001
	Last	25.6 [85]	1.409 [1.241;1.599]	1.049 [0.975;1.129]	
Spain	First	22.3 [80]	1.421 [1.346;1.501]	1.340 [1.271;1.412]	< 0.001
	Last	23.1 [83]	1.158 [1.093;1.227]	1.196 [1.144;1.250]	
Switzerland	First	10.7 [50]	1.351 [1.180;1.546]	1.320 [1.109;1.571]	0.176
	Last	19.6 [87]	1.174 [0.986;1.397]	1.068 [0.931;1.226]	
UK	First	17.2 [90]	1.407 [1.338;1.479]	1.110 [1.070;1.151]	0.005
	Last	16.3 [90]	1.365 [1.308;1.425]	1.087 [1.053;1.122]	
USA	First	23.4 [83]	1.216 [1.183;1.249]	1.109 [1.084;1.134]	0.009
	Last	24.6 [86]	1.229 [1.199;1.258]	1.061 [1.040;1.082]	

^a RR Cold: 1st vs. MMP.

^b RR heat: 99th vs. MMP.

^c Significance test on temporal variation, based on a multivariate Wald test of the pooled reduced coefficients of the interaction terms. The null hypothesis is that no change in time occurred. See Fig. S3.

Likewise, while we found that cold-related impact remained constant in UK, a study on historical data in England found a decrease in cold-mortality risk (Carson et al., 2006). However, results obtained in these investigations cannot be directly compared, given the relatively short overlap between study periods.

Our results suggest that the gradual reduction in heat-related impacts can be mostly attributed to the attenuation in the exposure-response curve, as discussed in previous studies (Barreca et al., 2016; Davis et al., 2003; Petkova et al., 2014). In fact, the reduction in heat-attributed mortality occurred despite the progressive shift of temperatures towards warmer temperature ranges observed during the last decades. The second scenario used in our study predicted that heat-related AFs would increase if only driven by changes in the temperature distribution (see methods), without a change in exposure response

function. Therefore our results indicate that the populations under study have potentially adapted to heat with a pace fast enough to anticipate and actually reverse the potential impact of the global warming experienced so far. Such a pattern suggests that non-climate-driven attenuation mechanisms, such as infrastructure changes and improved health care, have made a large contribution to the decrease in susceptibility to heat, compared to ‘pure adaptation’ to the warming climate.

However, we failed to find clear conclusions about the changes in cold-mortality impacts, which remained significant despite the temporal decline in risk in some countries. Predicted AFs in the two counterfactual scenarios displayed heterogeneous trends, which would explain the variable trends in the observed impacts. This would indicate the influence of other factors not directly related to cold temperatures

Table 3

Observed mortality fraction attributable to heat and cold by country estimated in each 5-year period.

Country	^a Temp. range	Attributable fraction per 5-year period (%) [95% CI]				
		1985–1989	1990–1994	1995–1999	2000–2004	2005–2009
Australia	Cold		15.43 [10.98; 19.51]	10.51 [7.94; 12.89]	5.94 [3.69; 8.17]	2.16 [− 1.2; 5.32]
	Heat		0.05 [− 0.11; 0.18]	0.26 [0.07; 0.43]	0.52 [0.32; 0.71]	0.67 [0.42; 0.90]
Brazil	Cold			4.39 [3.57; 5.13]	3.35 [2.90; 3.78]	2.60 [1.92; 3.22]
	Heat			0.78 [0.57; 0.97]	0.53 [0.41; 0.63]	0.68 [0.50; 0.85]
Canada	Cold	5.57 [3.99; 6.99]	5.62 [4.38; 6.73]	5.57 [4.80; 6.32]	5.42 [4.84; 5.94]	5.37 [4.67; 6.05]
	Heat	0.69 [0.55; 0.83]	0.42 [0.33; 0.51]	0.49 [0.38; 0.58]	0.43 [0.33; 0.53]	0.38 [0.20; 0.53]
Ireland	Cold	15.38 [12.31; 18.29]	12.28 [9.45; 14.99]	10.55 [8.07; 12.9]	9.34 [6.04; 12.42]	8.54 [4.37; 12.16]
	Heat	0.04 [− 0.03; 0.10]	0.02 [− 0.02; 0.06]	0.03 [− 0.06; 0.11]	0.00 [− 0.02; 0.01]	− 0.02 [− 0.06; 0.01]
Japan	Cold	10.25 [9.44; 10.96]	9.45 [8.82; 10.02]	9.52 [9.07; 9.93]	9.05 [8.84; 9.25]	8.91 [8.51; 9.26]
	Heat	0.45 [0.40; 0.49]	0.63 [0.57; 0.69]	0.45 [0.40; 0.49]	0.34 [0.30; 0.39]	0.15 [0.11; 0.18]
South Korea	Cold		8.37 [4.84; 11.59]	8.15 [5.87; 10.30]	8.06 [6.52; 9.50]	8.11 [5.94; 10.00]
	Heat		0.53 [0.28; 0.75]	0.33 [0.18; 0.48]	0.22 [0.11; 0.33]	0.17 [0.03; 0.29]
Spain	Cold		6.58 [5.76; 7.3]	5.06 [4.44; 5.67]	4.26 [3.79; 4.69]	3.89 [3.22; 4.51]
	Heat		1.39 [1.1; 1.65]	0.90 [0.81; 0.99]	1.12 [1.05; 1.19]	0.93 [0.84; 1.01]
Switzerland	Cold			2.94 [1.71; 4.11]	1.95 [0.88; 2.95]	3.05 [0.76; 5.14]
	Heat			1.66 [0.72; 2.56]	1.32 [0.67; 1.94]	0.54 [0.27; 0.78]
UK	Cold		9.01 [8.01; 9.93]	9.04 [8.50; 9.61]	8.85 [8.53; 9.16]	9.06 [8.56; 9.56]
	Heat		0.23 [0.18; 0.27]	0.42 [0.36; 0.48]	0.32 [0.27; 0.37]	0.28 [0.23; 0.32]
USA	Cold	5.63 [5.09; 6.06]	5.73 [5.35; 6.07]	6.25 [5.99; 6.49]	6.54 [6.36; 6.70]	
	Heat	0.45 [0.40; 0.49]	0.40 [0.36; 0.43]	0.36 [0.32; 0.40]	0.26 [0.22; 0.29]	

^a Cold: days with mean daily temperature < minimum mortality temperature; Heat: days with mean daily temperature > minimum mortality temperature.

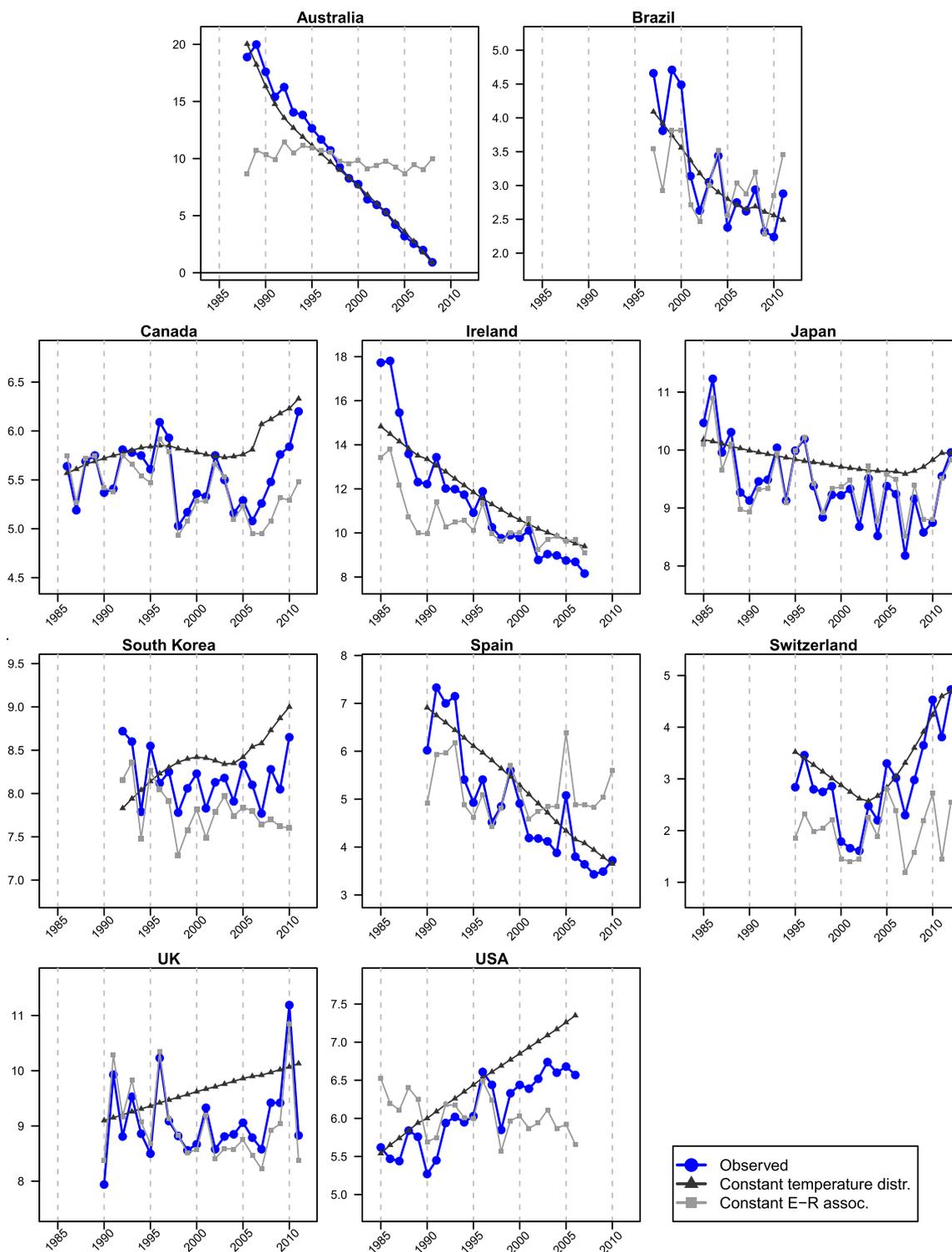


Fig. 1. Observed and predicted yearly cold-attributable fractions (%) (95% confidence interval) assuming a constant temperature distribution and a constant exposure-response relationship in each country (temperatures below the temperature of minimum mortality). The y-axis is scaled to the country-specific range. (For interpretation of the references to color, the reader is referred to the web version of this article.)

or more complex mechanisms involved in determining the temporal variation in impacts, as suggested in previous studies (Kalkstein and Greene, 1997; Kinney et al., 2015; von Klot et al., 2012), apart from purely adaptation to the changing climate and changes in temperature distribution itself. Indeed, mechanisms driving cold-related mortality still remain largely unknown (Ebi and Mills, 2013), as suggested by Ebi and Mills (2013).

To our knowledge, no previous study has directly attempted to

identify the contribution of changes in susceptibility and compared it with the changes due to the shift of the temperature distribution. Some studies aimed at quantitatively attributing changes in vulnerability to heat to specific adaptive measures, with contrasting conclusions (Bobb et al., 2014; Davis et al., 2003; Nordio et al., 2015), while others provided only qualitative explanations on adaptation for the observed attenuation in heat impact (Åström et al., 2013; Carson et al., 2006; Petkova et al., 2014). Adaptation to cold has not been specifically

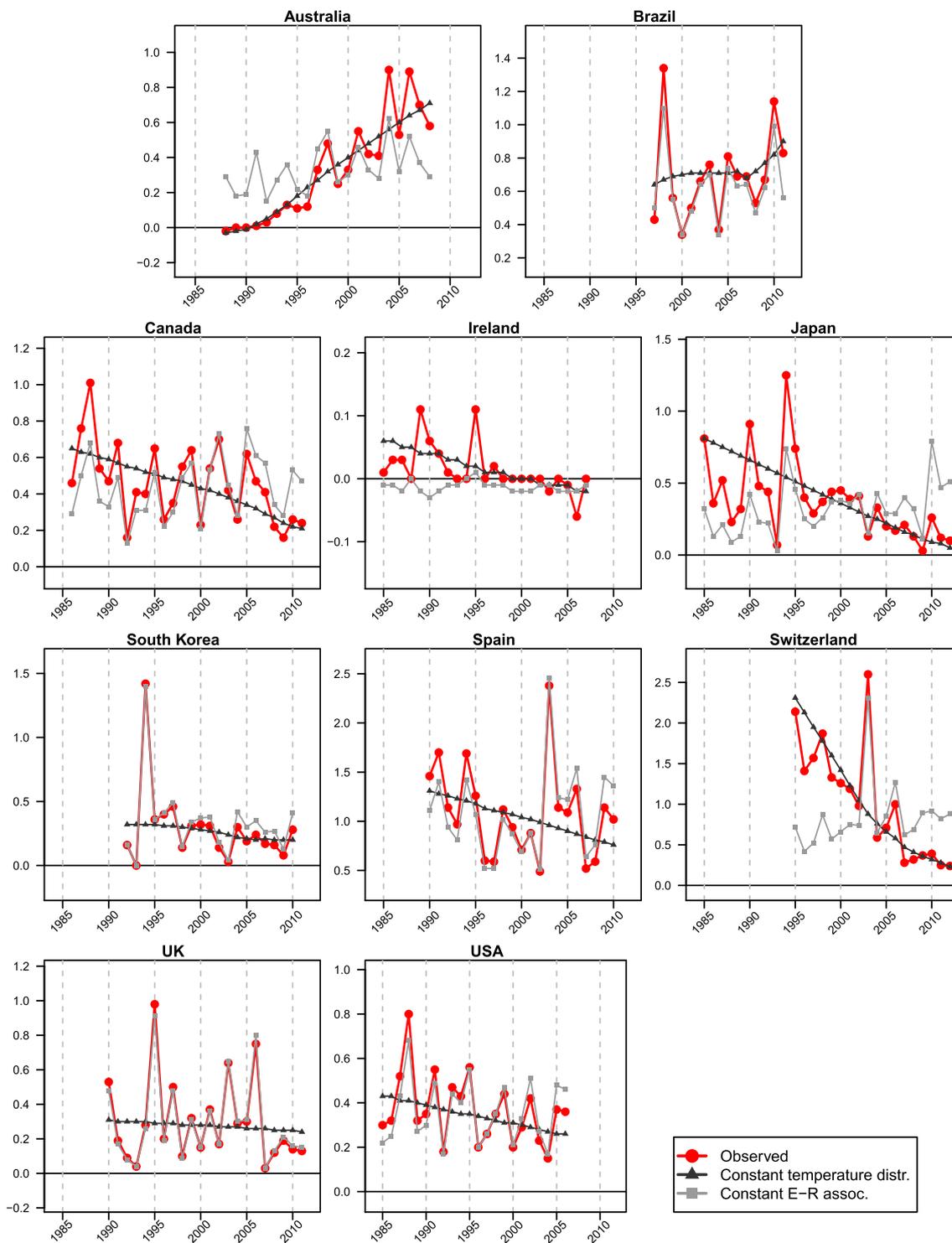


Fig. 2. Observed and predicted yearly heat-attributable fractions (%) (95% confidence interval) assuming a constant temperature distribution and a constant exposure-response relationship in each country (temperatures above the temperature of minimum mortality). The y-axis is scaled to the country-specific range. (For interpretation of the references to color, the reader is referred to the web version of this article.)

addressed in previous studies. Thus, further investigations are needed to clarify its role in the context of climate change.

Some limitations must be acknowledged. First, we could not rule out potential influence of changes in air pollution levels or influenza epidemics on the temporal evolution of temperature-mortality impacts due to the lack of data. However, the role of air pollution as confounding factor of the temperature mortality remains under discussion (Buckley et al., 2014) and the few studies that considered ambient air pollution

in the main model or in the sensitivity analysis showed no changes in the overall temperature-mortality trends (Bobb et al., 2014; Carson et al., 2006). Likewise, we did not disentangle the influence of specific non-climate driven factors changing overtime, such as urbanization, economic growth or demographic changes, which could potentially affect the trends in the exposure-response association. In addition, our results were reported as average trends per country by means of simplicity and better communication of the conclusions in the international

context of the study. These estimates might mask within-country trends defined according to different climate conditions, as other studies suggested (Bobb et al., 2014; Heo et al., 2016; Nordio et al., 2015). Finally, we argue that the progressive urbanization of the cities would have not altered the representativity of the meteorological stations given that the study period (up to 20 years) would not be long enough to cause noticeable changes in the degree of exposure misclassification.

In conclusion, despite the progressively warmer temperatures, our findings indicate a strong reduction in vulnerability to heat in the past decades in most of the countries included in the present study. This suggests that the pace of decrease in susceptibility to heat has been faster than the observed warming, which indicates scope for adaptation to further warming under climate change. In contrast, no clear conclusions were reached on either cold-mortality temporal variation or adaptation due to the potential mixture of factors influencing the trends. In addition, health burden attributed to ambient temperatures persisted at the end of the study period in most of the locations, with a considerably larger extent for cold. Thus, there exists potential for further gains in mitigating excess temperature-related mortality by, for example, properly identifying the underlying vulnerability factors, both at individual and community levels. Furthermore, this evidence can help to improve projections of future health risks under different climate change scenarios, and the design of better targeted public health measures towards population sub-groups with limited adaptability to global warming.

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.envint.2017.11.006>.

Conflicts of interest

None.

Funding sources

This work was primarily supported by the Medical Research Council-UK (Grant ID: MR/M022625/1). The following individual grants also supported this work: AT was supported by Ministry of Education (Spain) grant PRX17/00705. HK was supported by the Global Research Lab (K21004000001-10A0500-00710) through the National Research Foundation of Korea. YC was supported by the Senior Research grant (2016R1A2B1007082) from the National Research Foundation of Korea (NRF) funded by the Ministry of Science, ICT. YG was supported by the Career Development Fellowship of Australian National Health and Medical Research Council (#APP1107107).

References

- Arbuthnott, K., Hajat, S., Heaviside, C., Vardoulakis, S., 2016. Changes in population susceptibility to heat and cold over time: assessing adaptation to climate change. *Environ. Health* 15 (Suppl. 1), 33. <http://dx.doi.org/10.1186/s12940-016-0102-7>.
- Åström, D.O., Forsberg, B., Edvinsson, S., Rocklöv, J., 2013. Acute fatal effects of short-lasting extreme temperatures in Stockholm, Sweden: evidence across a century of change. *Epidemiology* 24, 820–829. <http://dx.doi.org/10.1097/01.ede.0000434530.62353.ob>.
- Barnett, A.G., 2007. Temperature and cardiovascular deaths in the US elderly: changes over time. *Epidemiology* 18, 369–372. <http://dx.doi.org/10.1097/01.ede.0000257515.34445.a0>.
- Barreca, A., Clay, K., Deschenes, O., Greenstone, M., Shapiro, J.S., 2016. Adapting to climate change: the remarkable decline in the US temperature-mortality relationship over the twentieth century. *J. Polit. Econ.* 124, 105–159. <http://dx.doi.org/10.1086/684582>.
- Bobb, J.F., Peng, R.D., Bell, M.L., Dominici, F., 2014. Heat-related mortality and adaptation to heat in the United States. *Environ. Health Perspect.* 122, 811–816. <http://dx.doi.org/10.1289/ehp.1307392>.
- Buckley, J.P., Samet, J.M., Richardson, D.B., 2014. Commentary: does air pollution confound studies of temperature? *Epidemiology* 25, 242–245. <http://dx.doi.org/10.1097/EDE.0000000000000051>.
- Carson, C., Hajat, S., Armstrong, B., Wilkinson, P., 2006. Declining vulnerability to temperature-related mortality in London over the 20th century. *Am. J. Epidemiol.* 164, 77–84. <http://dx.doi.org/10.1093/aje/kwj147>.
- Coates, L., 2014. Exploring 167 years of vulnerability: an examination of extreme heat events in Australia 1844–2010. *Environ. Sci. Pol.* 42, 33–44.
- Davis, R.E., Knappenberger, P.C., Michaels, P.J., Novicoff, W.M., 2003. Changing heat-related mortality in the United States. *Environ. Health Perspect.* 111, 1712–1718.
- Donaldson, G.C., Keatinge, W.R., Näyhä, S., 2003. Changes in summer temperature and heat-related mortality since 1971 in North Carolina, South Finland, and Southeast England. *Environ. Res.* 91, 1–7.
- Ebi, K.L., Mills, D., 2013. Winter mortality in a warming climate: a reassessment: winter mortality in a warming climate. *Wiley Interdiscip. Rev. Clim. Chang.* 4, 203–212. <http://dx.doi.org/10.1002/wcc.211>.
- Ekamper, P., van Poppel, F., van Duin, C., Garssen, J., 2009. 150 years of temperature-related excess mortality in the Netherlands. *Demogr. Res.* 21, 385–426. <http://dx.doi.org/10.4054/DemRes.2009.21.14>.
- Gasparrini, A., Armstrong, B., 2013. Reducing and meta-analysing estimates from distributed lag non-linear models. *BMC Med. Res. Methodol.* 13 (1). <http://dx.doi.org/10.1186/1471-2288-13-1>.
- Gasparrini, A., Leone, M., 2014. Attributable risk from distributed lag models. *BMC Med. Res. Methodol.* 14, 55. <http://dx.doi.org/10.1186/1471-2288-14-55>.
- Gasparrini, A., Guo, Y., Hashizume, M., Kinney, P.L., Petkova, E.P., Lavigne, E., Zanobetti, A., Schwartz, J.D., Tobias, A., Leone, M., Tong, S., Honda, Y., Kim, H., Armstrong, B.G., 2015a. Temporal variation in heat-mortality associations: a multicountry study. *Environ. Health Perspect.* 123, 1200–1207. <http://dx.doi.org/10.1289/ehp.1409070>.
- Gasparrini, A., Guo, Y., Hashizume, M., Lavigne, E., Zanobetti, A., Schwartz, J., Tobias, A., Tong, S., Rocklöv, J., Forsberg, B., Leone, M., De Sario, M., Bell, M.L., Guo, Y.-L.L., Wu, C., Kan, H., Yi, S.-M., de Sousa Zanotti Stagliorio Coelho, M., Saldiva, P.H.N., Honda, Y., Kim, H., Armstrong, B., 2015b. Mortality risk attributable to high and low ambient temperature: a multicountry observational study. *Lancet* 386, 369–375. [http://dx.doi.org/10.1016/S0140-6736\(14\)62114-0](http://dx.doi.org/10.1016/S0140-6736(14)62114-0).
- Guo, Y., Barnett, A.G., Tong, S., 2012. High temperatures-related elderly mortality varied greatly from year to year: important information for heat-warning systems. *Sci. Rep.* 2. <http://dx.doi.org/10.1038/srep00830>.
- Heo, S., Lee, E., Kwon, B.Y., Lee, S., Jo, K.H., Kim, J., 2016. Long-term changes in the heat-mortality relationship according to heterogeneous regional climate: a time-series study in South Korea. *BMJ Open* 6. <http://dx.doi.org/10.1136/bmjopen-2016-011786>.
- Hess, J.J., Eidson, M., Tlumak, J.E., Raab, K.K., Luber, G., 2014. An evidence-based public health approach to climate change adaptation. *Environ. Health Perspect.* 122, 1177–1186. <http://dx.doi.org/10.1289/ehp.1307396>.
- Kalkstein, L.S., Greene, J.S., 1997. An evaluation of climate/mortality relationships in large U.S. cities and the possible impacts of a climate change. *Environ. Health Perspect.* 105, 84–93.
- Kinney, P.L., Schwartz, J., Pascal, M., Petkova, E., Tertre, A.L., Medina, S., Vautard, R., 2015. Winter season mortality: will climate warming bring benefits? *Environ. Res. Lett.* 10, 064016. <http://dx.doi.org/10.1088/1748-9326/10/6/064016>.
- von Klot, S., Zanobetti, A., Schwartz, J., 2012. Influenza epidemics, seasonality, and the effects of cold weather on cardiac mortality. *Environ. Health* 11, 74. <http://dx.doi.org/10.1186/1476-069X-11-74>.
- Nordio, F., Zanobetti, A., Colicino, E., Kloog, I., Schwartz, J., 2015. Changing patterns of the temperature-mortality association by time and location in the US, and implications for climate change. *Environ. Int.* 81, 80–86. <http://dx.doi.org/10.1016/j.envint.2015.04.009>.
- Onozuka, D., Hagihara, A., 2015. Variation in vulnerability to extreme-temperature-related mortality in Japan: a 40-year time-series analysis. *Environ. Res.* 140, 177–184. <http://dx.doi.org/10.1016/j.envres.2015.03.031>.
- Petkova, E.P., Gasparrini, A., Kinney, P.L., 2014. Heat and mortality in New York City since the beginning of the 20th century. *Epidemiology* 25, 554–560. <http://dx.doi.org/10.1097/EDE.0000000000000123>.
- Vicedo-Cabrera, A.M., Forsberg, B., Tobias, A., Zanobetti, A., Schwartz, J., Armstrong, B., Gasparrini, A., 2016. Associations of inter- and intraday temperature change with mortality. *Am. J. Epidemiol.* 183, 286–293. <http://dx.doi.org/10.1093/aje/kwv205>.