Seasonal variation in mortality and the role of temperature: a multi-country multi-city study

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Abstract

Background: Although seasonal variations in mortality have been recognised for millennia, the role of temperature remains unclear. We aimed to assess seasonal variation in mortality and to examine the contribution of temperature.

Methods: We compiled daily data on all-cause, cardiovascular, and respiratory mortality, temperature, and indicators on location-specific characteristics from 719 locations in tropical, dry, temperate and continental climate zones. We fitted time-series regression models to estimate the amplitude of seasonal variation in mortality on a daily basis, defined as the peak-to-trough ratio (PTR) of maximum mortality estimates to minimum mortality estimates at day-of-year. Meta-analysis was used to summarise location-specific estimates for each climate zone. We estimated PTR with and without temperature adjustment, with the differences representing the seasonal effect attributable to temperature. We also evaluated the effect of location-specific characteristics on PTR across locations by using meta-regression models.

Results: Seasonality estimates and responses to temperature adjustment varied across locations. Unadjusted-PTR for all-cause mortality was 1.05 (95% confidence interval (CI): 1.00–1.11) in the tropical zone and 1.23 (95% CI: 1.20–1.25) in the temperate zone; adjusting for temperature reduced the estimates to 1.02 (95% CI: 0.95–1.09) and 1.10 (95% CI: 1.07–1.12), respectively. Furthermore, unadjusted-PTR was positively associated with average mean temperature.

Conclusions: This study suggests that seasonality of mortality is importantly driven by temperature, most evidently in temperate/continental climate zones, and that warmer locations show stronger seasonal variations in mortality, which is related to a stronger effect of temperature.

Key words: Seasonality, mortality, temperature

Key messages:

- To our knowledge, this is by far the largest study on seasonality of mortality by including 719 locations from 34 countries in tropical, dry, temperate and continental climate zones.
- Our study provides evidence that the generally higher mortality in cold seasons than in warm seasons is considerably explained by temperature, and this pattern is most evident in temperate and continental climate zones.
- Seasonality estimates and responses to temperature adjustment varied across locations, and locations characterised by warm climate experienced larger seasonal variations in mortality, which was related to stronger effect of temperature.
- Our investigation of this long-known complex phenomenon provides important evidence for understanding the epidemiology and ecology of seasonal variation in mortality and the role of temperature.
- Our findings also provide a basis for developing hypotheses about the potential impact of climate change on seasonality of mortality for future investigations.

Introduction

Seasonal variation in mortality as a broad phenomenon has been recognised since Hippocrates.[1] During certain times of the year, mortality increases substantially, which consequently increases demand for healthcare services and may exert intense pressure on healthcare systems.[2–10] The most plausible underlying mechanisms include seasonal fluctuations in environment, human behaviors, and infectious diseases.

Although consensus exists among researchers that ambient temperature is a key driver, the extent to which temperature is actually the proximal cause of seasonal variation in mortality is a matter of long-standing debate.[11,12] Few studies have attempted to address this topic.[6] More importantly, previous investigations focused on a small number of locations within a limited geographical scope, which makes it difficult to draw comprehensive conclusions across different climate zones. To better understand the epidemiology and ecology of seasonal variation in mortality and the role of temperature, a systematic and comprehensive investigation on highly diverse populations including multiple locations from multiple climate zones is crucial. Such investigation should further help us to develop hypothesis about the impact of warming climate on seasonal dynamics of mortality for future investigations.

Moreover, the magnitude of seasonal variation in mortality varies substantially among different locations, possibly due to the differences in location-specific characteristics, e.g., socio-economic development. To date, some studies have explored this issue but were limited in geographical locations and climate zones.[5,9,10,13–16] A comprehensive evaluation across multiple locations with various characteristics is warranted, as it will aid in identifying more vulnerable locations with a greater need for intervention.

In this research, we investigated seasonality of mortality, with particular focus on its magnitude, by analyzing daily time-series data of mortality and temperature from 719 locations (i.e., city/province/prefecture) in 34 countries from tropical, dry, temperate and continental climate zones. Our primary focus in this study was to estimate the magnitude of seasonal variation in mortality (i.e., seasonal amplitude) and to examine the extent to which temperature explains seasonality of mortality. We also evaluated the modifying effects of location-specific characteristics on seasonal variation of mortality. To our knowledge, this is by far the largest multi-country study on seasonality of mortality.

Methods

Data collection

We collected daily time-series of mortality and mean temperature from 719 locations in 34 countries in largely overlapping periods ranging from January 1969 to December 2016. The data were obtained through the Multi-country Multi-city (MCC) Collaborative Research Network (http://mccstudy.lshtm.ac.uk/).[17] Mortality was represented by daily counts of death from all causes or, where not available, non-external causes (International Classification of Diseases [ICD]-9 0-799, ICD-10 A00-R99) and cardiovascular (ICD-8 390-458, ICD-9 390-459, ICD-10 I00-I99) and respiratory diseases (ICD-8 and ICD-9 460-519, ICD-10 J00-J99). We also obtained information on Köppen–Geiger climate groups for each location, including tropical, dry, temperate, and continental climate zones.[18]

We collected data on the indicators of location-specific characteristics for each location, including environmental factors, demographics, and socioeconomic factors. For environmental indicators, we considered the multi-year average value of daily mean temperature, daily mean temperature range, daily mean relative humidity, and annual $PM_{2.5}$ levels. For demographic and socioeconomic factors, we collected from the Organisation for Economic Co-operation and Development Regional and Metropolitan Database, including the proportion of population aged over 65 years old, gross domestic product (GDP), gross value added (GVA, a measure of labour productivity), education level, unemployment rate, and Gini index (a measure of wealth inequality). The details for the indicators are included in supplementary material (Page 5, supplementary material).

Statistical analysis

Estimating location-specific seasonality

In the first step, we performed location-specific time-series analyses to assess seasonality of mortality using quasi-Poisson regression models[19] throughout the study period available in each location. Day-of-year was considered as the exposure indicator for seasonality. This is different from previous studies,[2–10] which used monthly aggregated data to compare winter mortality with other times of the year. In this study, we took values from 1 to 366 to represent day of year, corresponding to 1 January through 31 December for locations in the northern hemisphere and 1 July to 30 June of the following year for locations in the southern hemisphere. To model seasonality we used a cyclic spline with 4 degrees of freedom (*df*) for day of year. The days-of-year with maximum and minimum mortality predictions were identified as the peak and trough, respectively, of seasonality of mortality. We then took the ratio of mortality predicted at peak to mortality prediction at trough (peak-to-trough ratio, PTR) to summarise seasonality. A stratum defined by year, day of week and their interaction was used to control for long-term trends and effect of day of week.

We then added temperature to the model described above for each location, by using a distributed lag non-linear model (DLNM)[20] to estimate seasonality adjusting for temperature effect. We modelled the non-linear and non-linearly delayed effect of temperature on mortality using a cross-basis with natural cubic spline for temperature with three internal knots at the 25th, 50th, and 75th percentiles of temperature, and another natural cubic spline for lag with 3 *df*. The lag was extended up to 21 days.[17] From this model, we also calculated PTR to represent temperature-adjusted seasonality.

Pooling the location-specific seasonality by country and climate zone

In the second step, location-specific estimates of seasonal curve (i.e., coefficients of knot points) with and without temperature adjustment were pooled separately by climate zone through two-level (locations nested within country/region) random-effects multivariate meta-analysis techniques.[21] We also pooled the estimates by each of 34 countries/regions with location considered as the random effect factor. Using the pooled coefficients, the seasonal curve and corresponding PTR were estimated for each country and each climate zone.

Modification of seasonality by location-specific characteristics

In the final step, we first explored the between-location heterogeneity of the seasonal curve by including location-specific average temperature, temperature range, indicator for country, and indicator for Köppen–Geiger climate zone as meta-predictors in the random effects meta-regression.[22] The heterogeneity was tested for location-specific seasonality estimates before and after adjusting for temperature separately. Next, we evaluated the association of unadjusted and adjusted PTR with each indicator in separate meta-regression models including indicators for countries and climate zones. For each indicator, the original value was scaled by the country's average value to remove the between-countries effects from the correlation. Results were expressed as log (PTR) variation for a standard deviation increase of the indicator.

Sensitivity Analysis

We performed several sensitivity analyses. First, we evaluated how results changed with 5 and 6 df for the cyclic spline included in the location-specific time-series regression model. Second, we conducted seasonality assessment by using the subset of data since year 2000.

Finally, we investigated the sensitivity by changing the types of splines, lag days and df for the cross-basis function for temperature adjustment in the location-specific regression model.

We investigated seasonality of all-cause, cardiovascular, and respiratory mortality in separate analyses with R software, version 3.6.0 (R Development Core Team) using dlnm and mixmeta packages.

Results

The final analysis included 138 868 448 deaths from all or non-external causes in 719 locations in 34 countries, 39 777 149 deaths from cardiovascular diseases, and 12 805 050 deaths from respiratory mortality in 519 locations in 22 countries. The country-specific average mean temperature ranged from 4.7°C in Norway to 27.6°C in Thailand. These temperatures are illustrative of locations characterised by four Köppen–Geiger climate zones[18] (Figure 1), including 94 locations in the tropical climate zone (e.g., Ho Chi Minh City, Vietnam), 57 locations in the dry climate zone (e.g., Mashhad, Iran), 440 locations in the temperate climate zone (e.g., London, UK), and 128 locations in the continental climate zone (e.g., Hokkaido, Japan). Table 1 shows a summary of daily data for each climate zone. Supplementary Table S1 summarises mortality in each season for each country/region.

A descriptive summary of location-specific indicators is shown in Supplementary Table S2. Unemployment rate and $PM_{2.5}$ concentrations showed a large variation between locations. Socioeconomic indicators included in the analysis were correlated, and averaged mean temperature was correlated with the other indicators (Supplementary Figure S1).

Before adjustment for temperature, a seasonal pattern was observed in all climate zones with a high mortality in cold seasons and a low mortality in warm seasons (Figure 2). When temperature was adjusted, seasonality of mortality remained higher in cold seasons in most climate zones, except for seasonality of all-cause mortality in the tropical climate zone, where the adjusted seasonality became almost flat with a large confidence interval (Figure 2). The unadjusted PTR varied between climate zones, with the lowest estimate observed in the tropical zone (Table 2). The unadjusted PTRs for all-cause mortality were 1.05 (95% confidence interval (CI)1.00–1.11) in the tropical climate zone and 1.23 (95% CI: 1.20–1.25) in temperate climate zone, respectively (Table 2). Adjusting for temperature reduced the PTRs to different degrees, from a slight reduction observed in the tropical climate zone to a large reduction in the temperate climate zone: the pooled unadjusted PTR for all-cause mortality was reduced to 1.02 (95% CI: 0.95–1.09) in tropical climate zone, and 1.10 (95% CI: 1.07–1.12) in temperate climate, respectively (Table 2).

Our findings were generally similar for cause-specific mortalities (Figure 2 and Table 2). However, the change of seasonality estimates by temperature adjustment was more evident for cardiovascular mortality while less profound for respiratory mortality.

The location-specific seasonality estimates were presented in Figure 3 (Supplementary Table S3) and summarised for each country/region in Figure 4 (Supplementary Figure S2). Although the location- and country/region-specific results are generally consistent with our findings from the climate zone-specific assessment, PTR estimates varied between locations/countries/regions even for those within the same climate zone (Page 37, supplementary material).

Our meta-analysis showed substantial heterogeneity between locations for seasonality estimates both with and without temperature adjustment (Supplementary Table S4). Results from our multivariate meta-regression models suggest that the heterogeneity for seasonality estimates with/without temperature adjustment for all mortality types was reduced when country indicators were included (Supplementary Table S4). The other three predictors (i.e., the indicators for climate zones, location-specific average mean temperature and location-specific total temperature range) all significantly modify the effect of seasonality both in the single-predictor and the full models, and account for a small proportion of heterogeneity (Supplementary Table S4).

Figure 5 presents the association between each of location-specific characteristics and PTR. Average mean temperature was positively associated with unadjusted PTR for all-cause mortality, and adjusting for temperature in PTR moved the estimate towards the null. The other indicators showed no associations with PTRs for all-cause mortality. Our analysis of cause-specific mortality showed similar results, with a few additional findings: for cardiovascular mortality, total range of daily mean temperature was negatively associated with unadjusted PTR, which moved toward the null after adjustment for temperature in PTR; for respiratory mortality, averaged mean relative humidity was negatively associated with both unadjusted and adjusted PTR.

Results from sensitivity analyses (Supplementary Table S5) suggest that pooled seasonality curve and PTR in each climate zone of the main analysis were generally robust to different approaches (Supplementary Figure S3 & Figure S4). Country- and region-specific PTR estimates for those with most locations characterised by tropical climates seemed to be less sensitive to different modelling choices (Supplementary Table S6 and Table S7). Unadjusted PTR for most countries/regions was reduced in the subperiod analysis by using data since year 2000 (Supplementary Table S6). In addition, associations between indicators and PTR remained similar when using different approaches (Supplementary Figure S5).

Discussion

Our study systematically and comparatively investigated seasonality of mortality in 719 locations of 34 countries covering a wide range of environmental conditions, population dynamics and socioeconomic status. To our knowledge, this is the largest investigation on seasonality of mortality. Our study provides evidence that the generally higher mortality in cold seasons than in warm seasons is considerably explained by temperature, and this pattern is most evident in temperate and continental climate zones. Despite a similar pattern, the amplitudes of seasonality varied between locations. Locations characterised by warm climate experienced larger seasonal variations in mortality, which was related to stronger effect of temperature. Our investigation of this long-known complex phenomenon provides important evidence for understanding this phenomenon and informing the ongoing discussion on future impacts of warming climate.

Winter peaks and summer troughs in seasonality of mortality have been broadly defined and consistently described in previous studies,[2–10] and we observed a similar seasonal pattern for most of the locations in our study. Although previous studies measured the magnitude of seasonality in mortality, direct comparison with our findings (i.e., unadjusted PTR) is difficult due to the differences in modelling approaches. Where we applied time-series analysis to estimate mortality on each day of the year and then compared maximum mortality estimates with minimum mortality estimates on a daily basis to measure the strength of seasonality, previous studies used mortality data aggregated to each month or, to a lesser extent, for each week, and applied Fourier transforms to compare mortality estimates in peak months with those trough months. Stewart et al. reviewed 48 studies on seasonality of cardiovascular mortality mostly from temperate areas in Europe and North America and reported an estimate of 1.23-fold (95% CI: 1.16–1.31) for the relative difference of cardiovascular mortality in peak-versus-trough season,[2] which was lower than our estimate on seasonality of cardiovascular mortality in temperate zone (1.32 (95% CI: 1.27–1.36)).

One highlight of our investigation is the assessment of the extent to which the seasonal variation of temperature is associated with seasonal variation in mortality. Despite the extensive literature on the effects of cold and hot temperatures on health, debate remains regarding whether temperature is the main cause for seasonality of mortality.[11,12,23] Addressing this issue is essential for understanding the epidemiology and ecology of seasonal variation in mortality. Using multi-decade data from 36 cities in the US and three cities in France covering a wide range of winter temperatures from −5 to over 20°C, Kinney et al. observed no correlations between seasonal temperature differences (the difference in mean temperature between winter and summer) and winter excess mortality, and concluded that temperature was not a key driver of winter excess mortality.[12] However, this conclusion can be misleading, as their findings actually answered the question whether the spatial variation in the strengths of seasonal variation in mortality was related to the differences in seasonal temperature differences. In our study, we estimated temperature-adjusted seasonal variation in mortality and demonstrated that temperature is an important driver of seasonal variation in mortality, especially in temperate/continental climate zones. Our findings, on the other hand, provide a basis for developing hypotheses about the potential impact of climate change on seasonality of mortality, for example, whether an increasing temperature and shortening winter season will reduce winter mortality, increase summer mortality, and subsequently attenuate their variation between seasons. Future investigations are merited to investigate these hypotheses by taking into account the increasing extreme weathers (e.g., cold spells, snowfall or ice), other seasonal events (e.g., infectious disease outbreaks) and human adaptation, which is beyond the scope of the current study.

It should be noted that other unmeasured seasonally varying factors, e.g., sunlight, rainfalls, infectious disease incidence, and human behaviour, may also contribute to seasonality of mortality.[2] For example, the increase in infectious disease-related mortality during rainy season may explain seasonal variation in total mortality in the tropical climate zone,[13] and influenza infections may increase the risk of excess mortality in winter.[23–25] Furthermore, we found that seasonal variation in respiratory mortality seems to be less explained by temperature than are all-cause and cardiovascular mortality. This result may be explained by the fact that the increase in respiratory mortality during the winter season can be considerably attributed to seasonal respiratory infections (e.g., influenza and respiratory syncytial virus). Further research in seasonal pattern of mortality considering various kinds of seasonally varying factors would complement the evidence provided in this study.

Our results showed a significant spatial variation in the amplitude of seasonality across locations, and climate factors at location level contributed to this spatial variation but cannot fully characterise differences between locations. Before adjusting for temperature in seasonality assessment, we found a larger seasonal variation in locations characterised by warm climate; this modification became weak on the remaining seasonality after removing the short-term effect of temperature. Consistently, previous studies on the effects of cold temperature reported that cold-related mortality was higher in warm climates than in cold climates.[10,26,27] One explanation is that populations routinely exposed to warm climate are less adapted to or prepared for cold weather during the year (e.g., lack of proper insulation). In addition, our results in cause-specific mortality showed that populations from less humid areas may exhibit a large seasonal variation for respiratory mortality. This result may be related to the impact of humidity on respiratory tract infections and transmissions (e.g., fomites). Low humidity in cold weather may increase survival of influenza virus and increase its transmission,[24] and a decrease in temperature and humidity can precede the onset of infections.[28] Therefore, humidity can possibly modify seasonality of respiratory mortality. Elaborating on this phenomenon could be a topic for future studies.

Some limitations must be acknowledged. First, our seasonality assessment was based on the assumption that seasonal variation in mortality and the role of temperature have not changed over the study period. In our sensitivity analysis, we repeated the assessment by using the data since 2000: although the results showed a reduction in unadjusted PTR for most countries/regions, the main findings and conclusions did not change. However, future studies are warranted to investigate this complex research topic— whether or not and how seasonality of mortality has changed over the years. Second, we used PTR as a numeric measure of seasonality, which may be limited as it only quantifies the amplitude of seasonal variation in mortality. In other words, PTR is not able to reflect the shape of seasonal variation in mortality. Further investigations would be beneficial by improving seasonality assessment, e.g., quantifying the area under seasonal curve as attributable fraction. Third, coverage of tropical and dry climate zones and less developed locations was limited in our study, especially for cardiovascular and respiratory mortality, so the results for these areas should be interpreted with cautions. The country-level estimates for several countries (e.g., Sweden, China and Iran) may not be representative, as only a small number of locations from these countries were included in our analysis. Fourth, we did not explore modifying effect of indicators by using a multivariable model, because of a high correlation between indicators. Finally, the collection (e.g., case ascertainment, codification) and processing of mortality data may vary between countries.

Despite these limitations, out study is, to our knowledge, the largest investigation on seasonality of mortality. This multi-country study used the largest database of location-level daily time-series for mortality for 719 locations from 34 countries and identified a strong seasonal variation in mortality in temperate climate zones, which was attenuated substantially after adjusting for temperature, whereas a small seasonal variation was observed in tropical climate zone. Moreover, populations consistently exposed to warm climates seem to be more susceptible to seasonal variation in mortality. Based on this large and geographically versatile dataset and well-tested methods, our findings provide a better understanding of this long-known complex phenomenon and a basis for generating hypotheses about the future impact of climate change on seasonality of mortality, which ultimately could help with the development of health systems and infrastructure planning in the future.

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Ethics approval: Not required.

Data availability:

Data have been collected within the MCC (Multi-City Multi-Country) Collaborative Research Network (https://mccstudy.lshtm.ac.uk) under a data sharing agreement and cannot be made publicly available. The R code for the analysis is available from the first author.

Supplementary data:

Supplementary data are available at IJE online.

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Conflict of interest:

None declared.

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Figure legends:

Figure 1. Spatial distribution of location-specific averaged annual mean temperature of 719 locations in four Köppen–Geiger climate zones (A: Tropical, B: Dry, C: Temperate, and D: Continental)

Figure 2. Seasonality of mortality without (black) and with (red) temperature adjustment in four Köppen–Geiger climate zones (A: Tropical, B: Dry, C: Temperate, and D: Continental)

The seasonality is computed as the relative risk (RR) of mortality estimates at each day-of-year to daily minimum mortality estimates at the trough day with 95% confidence intervals (95% CIs) for four Köppen–Geiger climate zones:

$$Relative\ risk = \frac{Mortality\ estimate\ at\ day_i}{Minimum\ mortality\ estimate\ at\ the\ trough}$$

These estimates are obtained by pooling location-specific estimates for each climate zone. We took values from 1 to 366 to represent day of year, corresponding to January 1st through December 31st for locations in the northern hemisphere and July 1st to June 30th of the following year for locations in the southern hemisphere (for common years, values were taken from 61 to 366 from the 60th day to the 365th day).

Figure 3. Peak-to-trough ratio (PTR) with 95% confidence intervals (95%CI) without (left) and with (right) temperature adjustment for each location for all-cause/non-external (blue), cardiovascular (red), and respiratory (green) mortality

The size of the points corresponds to the precision of the PTR estimate (i.e., the inverse of the standard error of the PTR).

Figure 4. Peak-to-trough ratio (PTR) with 95% confidence intervals (95%CI) without (black) and with (red) temperature adjustment for each country/region (numbers of locations in each country/region for each Köppen Geiger climate zone§**)**

These estimates are obtained by pooling location-specific estimates for each country/region.

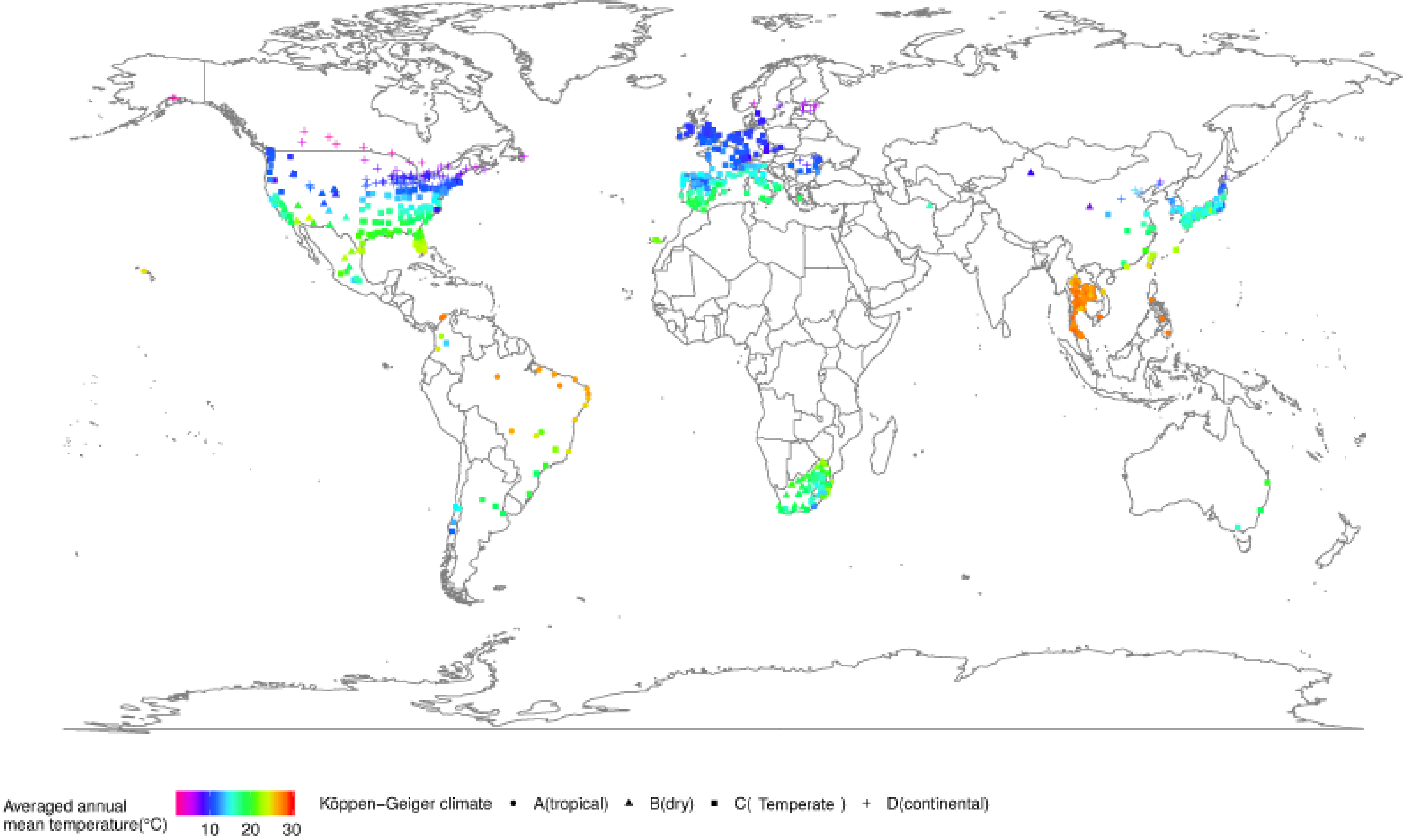
**Countries/regions which have data for all mortality causes.*

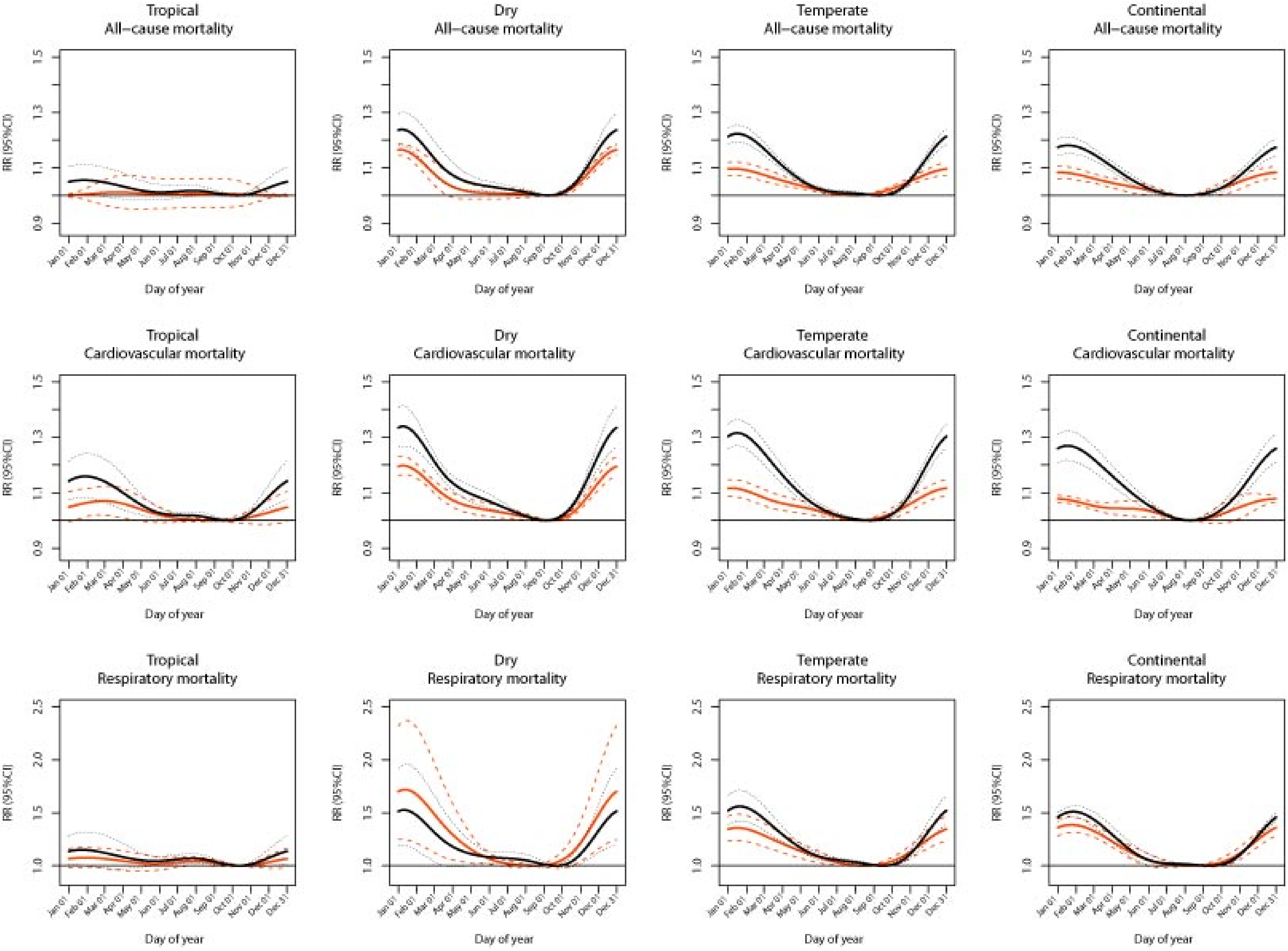
§ *Four Köppen Geiger climate zones (A: Tropical, B: Dry, C: Temperate, and D: Continental)*

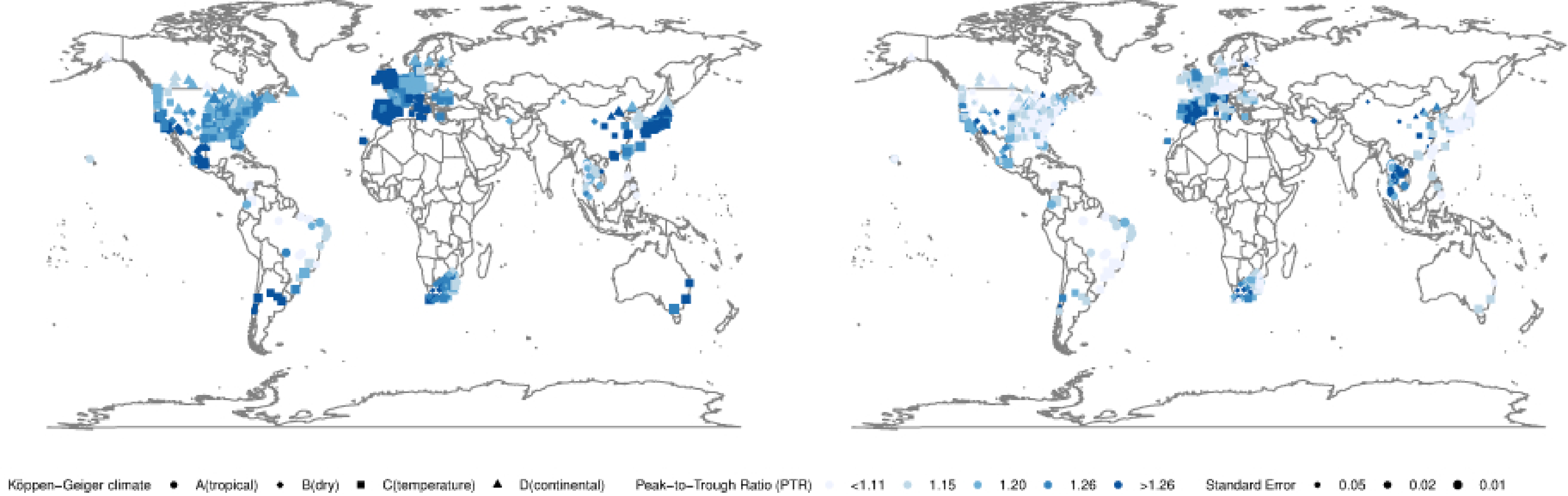
Different background colors were used to highlight the climate zone for each country (red: Tropical, yellow: Dry, green: Temperate, blue: Continental, and grey: multiple climate zones).

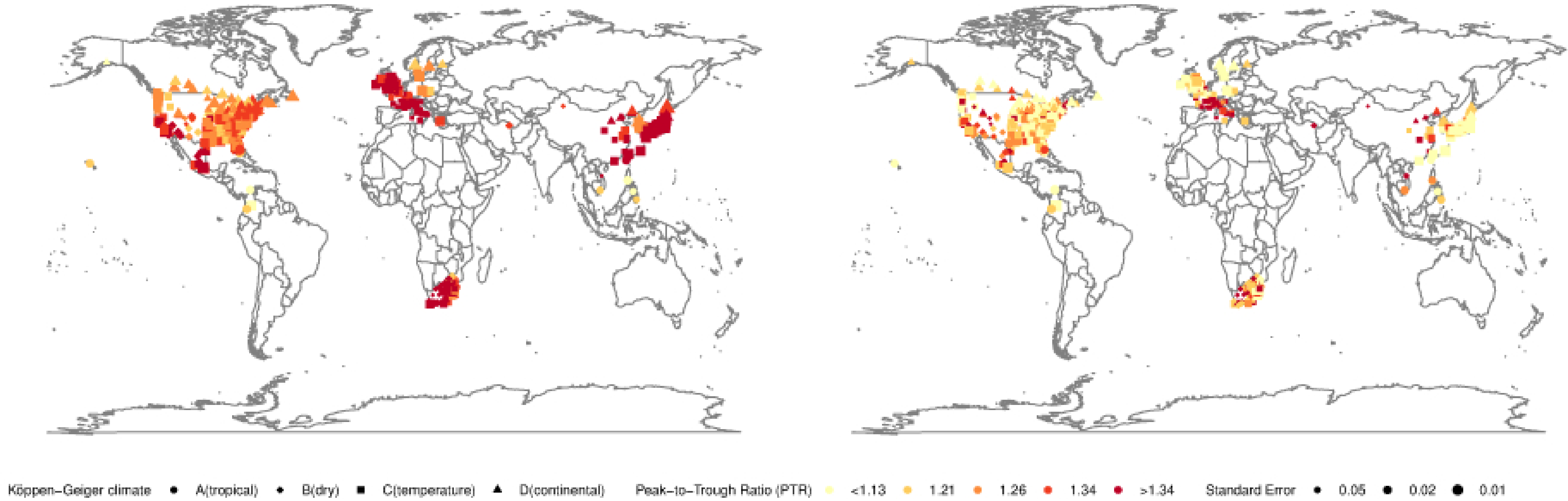
Figure 5. Associations between the indicators on location-specific characteristics and peak-to-trough ratio before (black) and after (red) temperature adjustment.

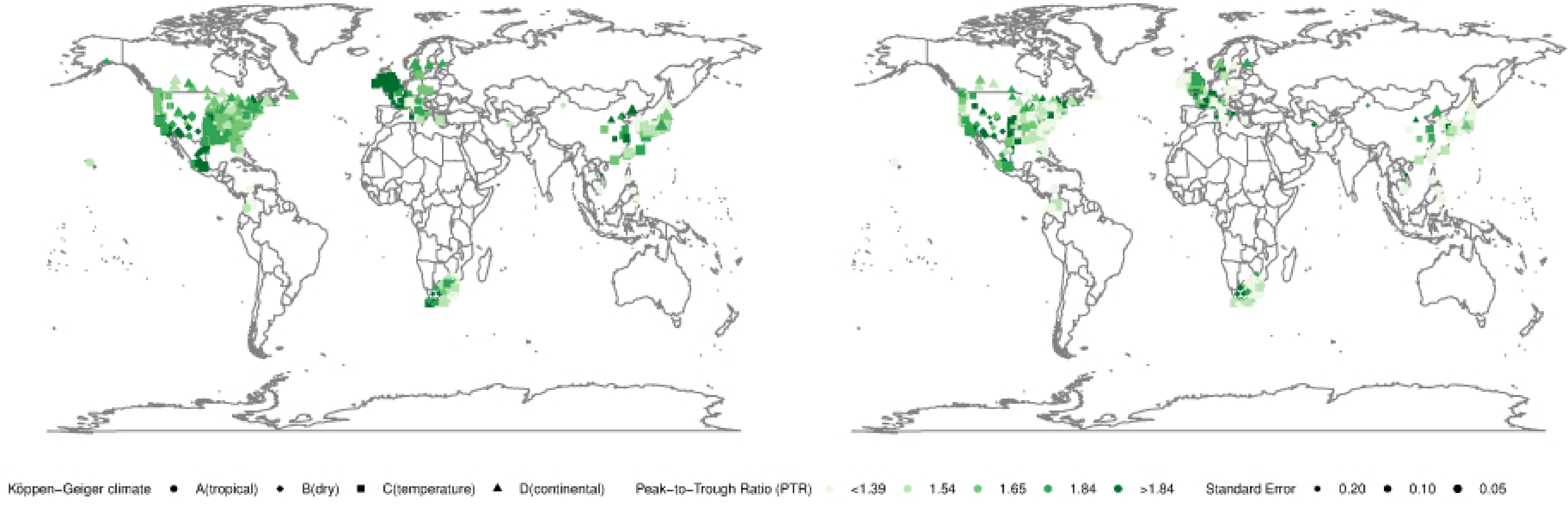
Coefficients with 95% confidence intervals (95% CIs) were obtained from a meta-regression model adjusted by indicators for country and climate zone. Results are expressed as the changes in log(PTR) for standard deviation increase in the indicators.

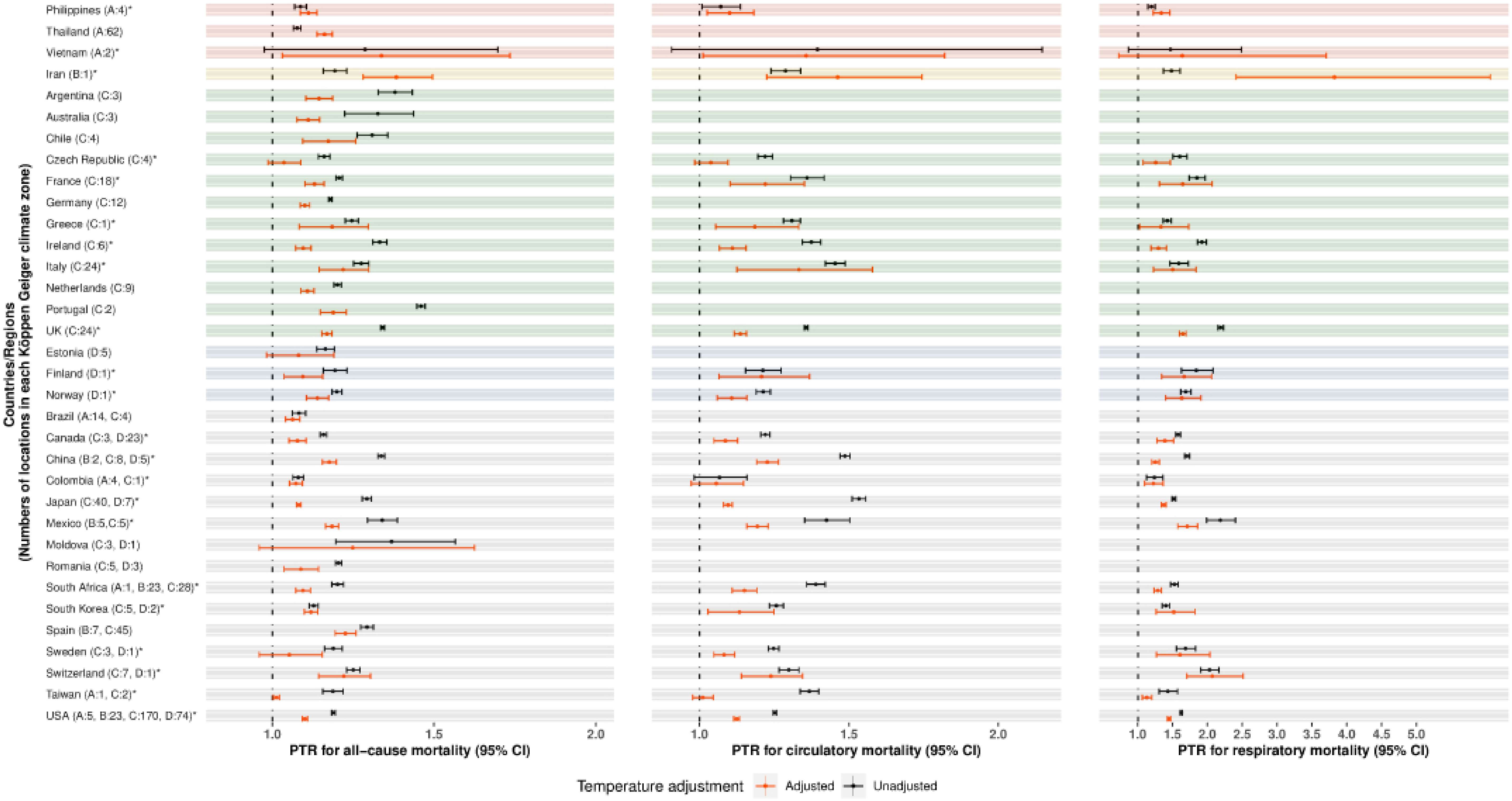

Averaged annual
mean temperature(°C)
10
20
30
Köppen−Geiger climate
A(tropical)
B(dry)
C(Temperate)
D(continental)


Tropical
All–cause mortality
Dry
All–cause mortality
Temperate
All–cause mortality
Continental
All–cause mortality
Tropical
Cardiovascular mortality
Dry
Cardiovascular mortality
Temperate
Cardiovascular mortality
Continental
Cardiovascular mortality
Tropical
Respiratory mortality
Dry
Respiratory mortality
Temperate
Respiratory mortality
Continental
Respiratory mortality
RR (95%CI)
0.9
1.1
1.3
1.5
1.0
1.5
2.0
2.5
Jan 01
Feb 01
Mar 01
Apr 01
May 01
Jun 01
Jul 01
Aug 01
Sep 01
Oct 01
Nov 01
Dec 01
Dec 31
Day of year


Köppen−Geiger climate
● A(tropical)
◆ B(dry)
■ C(temperature)
▲ D(continental)
Peak−to−Trough Ratio (PTR)
● <1.11
● 1.15
● 1.20
● 1.26
● >1.26
Standard Error
● 0.05
● 0.02
● 0.01


Köppen−Geiger climate
● A(tropical)
◆ B(dry)
■ C(temperature)
▲ D(continental)
Peak−to−Trough Ratio (PTR)
● <1.13
● 1.21
● 1.26
● 1.34
● >1.34
Standard Error
● 0.05
● 0.02
● 0.01


Köppen−Geiger climate
● A(tropical)
◆ B(dry)
■ C(temperature)
▲ D(continental)
Peak−to−Trough Ratio (PTR)
● <1.39
● 1.54
● 1.65
● 1.84
● >1.84
Standard Error
● 0.20
● 0.10
● 0.05


Countries/Regions
(Numbers of locations in each Köppen Geiger climate zone)
Philippines (A:4)*
Thailand (A:62)
Vietnam (A:2)*
Iran (B:1)*
Argentina (C:3)
Australia (C:3)
Chile (C:4)
Czech Republic (C:4)*
France (C:18)*
Germany (C:12)
Greece (C:1)*
Ireland (C:6)*
Italy (C:24)*
Netherlands (C:9)
Portugal (C:2)
UK (C:24)*
Estonia (D:5)
Finland (D:1)*
Norway (D:1)*
Brazil (A:14, C:4)
Canada (C:3, D:23)*
China (B:2, C:8, D:5)*
Colombia (A:4, C:1)*
Japan (C:40, D:7)*
Mexico (B:5,C:5)*
Moldova (C:3, D:1)
Romania (C:5, D:3)
South Africa (A:1, B:23, C:28)*
South Korea (C:5, D:2)*
Spain (B:7, C:45)
Sweden (C:3, D:1)*
Switzerland (C:7, D:1)*
Taiwan (A:1, C:2)*
USA (A:5, B:23, C:170, D:74)*
1.0
1.5
2.0
PTR for all-cause mortality (95% CI)
1.0
1.5
2.0
PTR for circulatory mortality (95% CI)
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
PTR for respiratory mortality (95% CI)
Temperature adjustment
Adjusted
Unadjusted

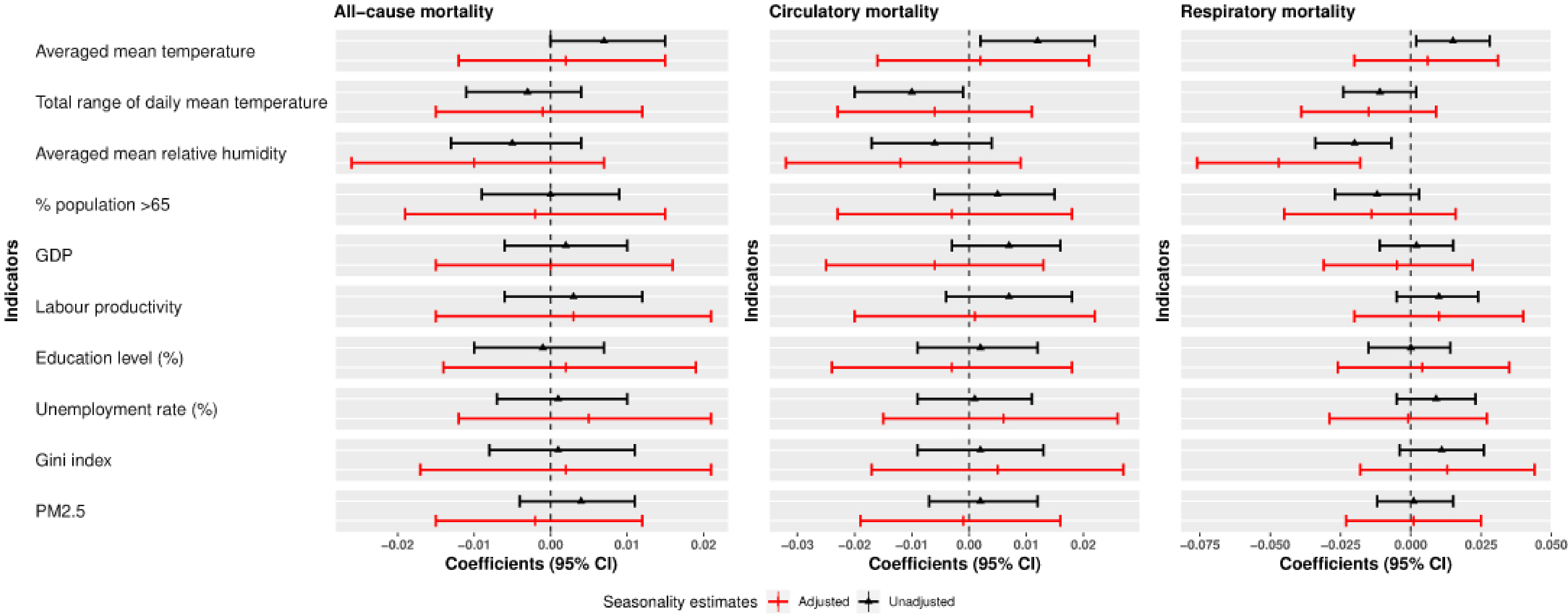

All−cause mortality
Circulatory mortality
Respiratory mortality
Indicators
Averaged mean temperature
Total range of daily mean temperature
Averaged mean relative humidity
% population >65
GDP
Labour productivity
Education level (%)
Unemployment rate (%)
Gini index
PM2.5
−0.02
−0.01
0.00
0.01
0.02
−0.03
−0.02
−0.01
0.00
0.01
0.02
−0.075
−0.050
−0.025
0.000
0.025
0.050
Coefficients (95% CI)
Seasonality estimates
Adjusted
Unadjusted

Table 1. Summary (mean± standard deviation) of daily mean temperature (°C) and daily mortalities (counts) by climate zones

Climate Zone	No. of locations[†]	Mean temperature	All-cause mortality[*]	Cardiovascular mortality	Respiratory mortality
Tropical	94/18	26.68±2.86	14.91±14.31	8.82±6.05	2.44±2.26
Dry	57/50	17.61±8.17	13.82±12.87	3.81±4.55	1.68±2.19
Temperate	440/350	14.51±8.43	23.82±36.96	8.44±15.19	2.58±5.34
Continental	128/118	8.85±10.87	11.58±17.86	4.24±6.41	0.96±1.37

[*] Data on non-external mortality was used when data on all-cause mortality is not available for some locations.

[†] No. of locations where all-cause/non-external mortality data are available/ No. of locations where cause-specific mortality data are available

Table 2. Pooled peak-to-rough ratio (95% confidence intervals) for each climate zone.

	Temperature	Tropical	Dry	Temperate	Continental
All-cause mortality	Unadjusted	1.05 (1.00, 1.11)	1.23 (1.18, 1.30)	1.23 (1.20, 1.25)	1.20 (1.17, 1.23)
	Adjusted*	1.02 (0.95, 1.09)	1.16 (1.14, 1.19)	1.10 (1.07, 1.12)	1.08 (1.06, 1.10)
Cardiovascular mortality	Unadjusted	1.16 (1.08,1.24)	1.34 (1.27,1.41)	1.32 (1.27,1.36)	1.27 (1.22,1.32)
	Adjusted*	1.07 (1.01, 1.13)	1.20 (1.16, 1.23)	1.11 (1.10, 1.13)	1.08 (1.07, 1.10)
Respiratory mortality	Unadjusted	1.19 (1.07, 1.33)	1.53 (1.19, 1.95)	1.61 (1.42, 1.73)	1.55 (1.46, 1.66)
	Adjusted*	1.08 (0.99, 1.17)	1.72 (1.25, 2.37)	1.36 (1.24, 1.49)	1.39 (1.31, 1.46)

* Temperature was adjusted for each location by using a distributed lag non-linear model (DLNM): the non-linear exposure-response association was modelled by a natural cubic spline function with three internal knots at 25th, 50th, and 75th percentiles of temperature, and the lag-response curve was fit by another natural cubic spline function with 3 df with extended lag up to 21 days.