Title: Mortality Burden of Diurnal Temperature Range and Its Temporal Changes: A Multi-Country Study

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ABSTRACT

Although diurnal temperature range (DTR) is a key index of climate change, far few studies have reported the health burden of DTR and its temporal changes at a multi-country scale. Therefore, we assessed the attributable risk fraction of DTR on mortality and its temporal variations in a multi-country data set. We collected time-series data covering mortality and weather variables from 308 cities in 10 countries from 1972 to 2013. The temporal change in DTR-related mortality was estimated for each city with a time-varying distributed lag model. Estimates of each city were pooled using a multivariate meta-analysis. The results showed that the attributable fraction of total mortality to DTR was 2.5% (95% eCI: 2.3-2.7%) over the entire study period. In overall countries, the attributable fraction has increased from 2.4% (2.1-2.7%) to 2.7% (2.4-2.9%) between the first and last study years. This study found that DTR has significantly attributed to mortality in overall countries, and this attributable fraction has significantly increased overtime in the USA, UK, Spain, and South Korea. Therefore, because the health burden of DTR is likely to increase in future, countermeasures are needed against the increase.

Keywords: Diurnal temperature range, Attributable mortality risk fraction, Time-varying Effect, Climate Change.

Abbreviations: Attributable risk fraction (ARF), Distributed Lag Non-linear Model (DLNM).

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1. Introduction

Diurnal temperature range (DTR, i.e., the intra-day temperature change) is a well-known risk factor of weather-related human health. Numerous studies have described a positive association between DTR and mortality (Cao et al. 2009; Lim et al. 2015; Tam et al. 2009; Vutcovici et al. 2014; Yang et al. 2013a), and have reported that people who are elderly, less educated, female or have cardiovascular or respiratory disease are more susceptible to DTR than others (Kan et al. 2007b; Lim et al. 2012a; Yang et al. 2013b). In addition, because the DTR has been reported as an important meteorological indicator closely related with global climate change (Braganza et al. 2004; Kan et al. 2007b; Yang et al. 2013b), an in-depth investigation of the DTR-mortality relationship becomes important as it helps to assess the future health impact of climate change more comprehensively.

Biological mechanisms through which a sudden change in absolute temperature might affect mortality have been described in previous medical and epidemiological studies (Garrett et al. 2009; Garrett et al. 2011; Greenberg et al. 1983; Keatinge et al. 1984a; Martinez-Nicolas et al. 2015; Qiu et al. 2013). Sudden changes in within-day temperature may cause physiological health problems (Garrett et al. 2009; Garrett et al. 2011); unstable weather or temperature changes can lead to the onset of cardiovascular events brought on by increased workload. This can affect the respiratory system by triggering inflammatory nasal responses (Ballester et al. 1997; Carder et al. 2005; Graudenz et al. 2006; Hashimoto et al. 2004; Imai et al. 1999; Luurila 1980). These mechanisms have been suggested as potential causes of increasing human mortality (Buguet 2007; Guo et al. 2016).

Based on this biological evidence, previous studies have tried to estimate the risk of DTR on mortality (Lim et al. 2015; Tam et al. 2009; Vutcovici et al. 2014). However, most previous studies assessed the risk of DTR using only terms of relative risk (RR), not attributable risk fraction which can quantify the mortality burden. Furthermore, because a majority of the previous studies were conducted in single cities or single countries and used statistically different methods (Kan et al. 2007b; Lim et al. 2012a; Yang et al. 2013b), results of these studies might have limited applicability to a multi-country scale.

Most previous studies estimated the risk of DTR on mortality using historical data (Kan et al. 2007b; Lim et al. 2012a) and the estimated impact of DTR was assumed to be consistent overtime. However, this assumption might not be suitable in predicting the health impacts of climate change because several factors, including intrinsic biological (e.g., disease/nutrition status) and extrinsic factors (e.g., forecast and infrastructure improvements, local environment, or social system conditions), can modify the population’s vulnerability to absolute temperature and rapid temperature change within a day (Gasparrini et al. 2015a; Linares et al. 2014; Wu et al. 2014). Therefore, it is important to assess temporal change in the DTR-related mortality relationship to examine whether people are adapted or mal-adapted to DTR.

In this study, we assess the percent increases in risks and the attributable risk fraction of DTR for 308 cities of 10 countries. We examine whether the excessive risks and attributable risk fractions have changed during the study period. We used a Multi-Country Multi-City (MCC) Collaborative Network to assess the impacts of weather on mortality using a multi-country data set as referenced in previous papers (Gasparrini et al. 2015a; Gasparrini et al. 2016; Guo et al. 2014; Guo et al. 2016).

2. Material and methods

2.1. Data

Time-series data covering mortality and weather variables were collected from 385 locations in 10 countries: Canada (26 cities, 1986-2011), United States (USA) (135 cities, 1985-2006), Brazil (18 cities, 1997-2011), Colombia (5 cities, 1998-2013), United Kingdom (UK) (10 regions, 1990-2012), Ireland (6 regions, 1984-2007), Spain (51 cities, 1990-2010), Japan (47 prefectures, 1972-2012), South Korea (7 cities, 1992-2010), and Australia (3 cities, 1988-2009). For convenience of interpretation, the location is described as "city" in this study. The daily mortality count is the daily count of death for all causes. If a daily count of all causes of death was not available for a city, then death for non-external causes (ICD-9: 0-799, ICD-10: A00-R99) was used instead. DTR was chosen as the exposure index, computed from monitoring stations as the difference between the daily maximum and daily minimum temperatures. Detailed information regarding data collection is provided in the Supplementary Material (Data details).

2.2. First-stage time series model

The first-stage time series model was divided into a two-step procedure. First, a time-series regression was applied, based on a generalized linear model using a quasi-Poisson distribution with parameters for: DTR, the day of week, seasonal long-term trend, inter-day temperature change (the change in mean temperature between two neighboring days), and absolute temperature. We modeled the DTR-response curve with a linear function and the lag-response curve with two internal knots placed at equally spaced values on a log scale using natural cubic

B-spline with 14 days of lag. Inter-day temperature change was adjusted in the same way as DTR. We also modeled the temperature-response relationship using a quadratic B-spline with three internal knots (placed at the 10th, 75th, and 90th percentiles of location-specific temperature distributions) and a lag-response (up to 21 days) curve with natural cubic B-spline with three internal knots placed at equally spaced values on the log scale. This model approach was used in a previous multi-country temperature-mortality study using a distributed lag non-linear model (DLNM) (Gasparrini et al. 2010; Gasparrini et al. 2015b). Seasonal trends were adjusted using a natural cubic B-spline of time with 8 degrees of freedom (df) per year, and day of week was included as an indicator variable. Results of the first stage estimate the association between DTR and mortality for each city.

2.3. Time varying distributed lag non-liner model

The DLNMs, described in the first-stage analysis, assumed that the exposure-lag-response associations between DTR and mortality in each location were constant across the whole study period. We also applied a time-varying DLNM with a linear interaction (Gasparrini et al. 2015a; Gasparrini et al. 2016) between DTR and year. Using the time-varying DLNM, we derived coefficients representing the exposure-lag-response association for the first and last year of the study periods for each city. The set of four coefficients (the entire period, the first and the last year for each location) were reduced to one coefficient that modeled the overall cumulative associations between DTR and mortality. The sets of four coefficients were used to determine the lag-response relationships at the 99th percentile of DTR reference at 0°C DTR.

2.4. Second stage meta-analysis

We pooled one parameter of the overall cumulative exposure-response relationship and the four parameters of the lag-response relation. Multivariate random-effect meta-regression was used to pool the parameters by country. We used indicators of country as predictors in the meta-regression to country-pooled estimates and city-specific predicted parameters (Best Linear Unbiased Prediction, BLUP). Overall pooled coefficient (only for calculating excessive relative risk of overall countries) was estimated by meta-analysis without predictors. All analyses were performed using R software (version 3.3.1) packages dlnm and mvmeta (Gasparrini 2011; Gasparrini et al. 2012; Gasparrini et al. 2010).

2.5. Attributable mortality risk faction

Overall cumulative relative risk estimated from BLUP for each city was used to compute the attributed number of deaths, and the fraction of deaths over the following 14 days at each location. The total number of deaths attributed to DTR was calculated as the sum of all days in the series when DTR contributed to death and its ratio with the total number of deaths; this provides the ‘total attributable fraction’ (Gasparrini and Leone 2014). We also computed the time-varying attributable risk of DTR based on BLUP for each city from the time-varying DLNM. Although time-dependent distributions of DTR and death could be used to estimate time-varying attributable risk, we used DTR and mortality distribution for the entire period because we did not find a clear difference between DTR distributions for the first and last three years of the series for each city (Table 1).

2.6. Sensitivity analysis

In order to test the sensitivity of our results to the modeling parameters and assumptions described above, we changed lag days for DTR (21 days), inter-day temperature changes (10 and 21 days), and the degrees of freedom (df) of lag knots for DTR (df=5), and analyzed the first results. We also assessed sensitivity to controlling for humidity (only for 6 countries which include relative humidity data), air pollution (Korea, O3 and PM10), flexibility of long-term trend (df=7 and 9) and absolute temperature using various knot percentiles and changing lag days (14 and 28 days).

3. Results

Descriptive statistics of mortality, absolute temperature, and the distribution of DTR are in Table 1. Fig. 1 displays the geographical distributions of the 308 cities within the 10 countries included in the analyses and the corresponding annual averaged DTR (□C). The data set included 85,912,372 deaths. A variability in DTR was observed among countries over the entire study period, with mean values ranging from 6.7□C (Ireland, 6 cities) to 10.9□C (USA, 135 cities). Table 1 also shows the DTRs and absolute temperature distributions during the first and second halves of the time periods for each country. As expected, the mean temperature increased slightly over time, although we did not detect a clear temporal pattern in the DTR values. City-specific descriptive statistics are reported in Supplementary Table S1.

The percent increases in risks and attributable mortality risk fraction of DTR estimated from the model with no interaction (i.e. the average throughout the study period) are reported in Table 2. Percent increases in risks of DTR (per 10□C) are highest in South Korea (6%, 95% CI: 3-9.1%), Spain (4.4%, 3–5.8%), and Brazil (4.2%, 1.7-6.7%). Colombia (-1.2%, -6.3–4.1%) and Ireland (0.3%, -3–3.8%) showed the lowest percent increases in risk of DTR, although both were not significant. Table 2 also displays the total percentage of deaths attributable to DTR (reference at minimum DTR of each city, 2.5% with 95% empirical confidence interval (95% eCI): 2.3–2.7%). Similar with percent increases in risk, most of the country-specific estimated attributable risks were statistically significant. The risk fraction was highest in Korea (4.5%, 3-5.9%) and Spain (4.2%, 3.5-4.9%). The fractions were lowest in Colombia (-1.5%, -5.1–2.1%) and in Ireland (0.2%, -1.2–1.4%).

Fig. 2 displays the country-pooled lag-response associations at the 99th percentile of DTR referenced at 0□C. The coldest (Canada, Ireland, and UK) and warmest (Brazil, Colombia) countries showed the highest RR at lag 0 and lasted to a lag from 4–7 days. Other countries, which had moderate temperatures, have the highest RR in approximately 1–3 lag days and were limited to a lag of 7–14 days. The corresponding city-specific lag-response is displayed in Supplementary Fig. S1.

Results from an analysis of the temporal variation in the percent increases in risk of DTR are illustrated in Fig. 3. Table 3 displays temporal variation of estimates per year and test results for linear interaction (null hypothesis is the pooled interaction term is 0; the null hypothesis is that no temporal change occurred). The percent increases in risk of DTR increased from 2.5% (95% CI: 1.8–3.3%) to 3.8% (95% CI: 3.1–4.5%) between the first and last periods. Except for Ireland and Japan, all countries showed patterns of increasing percent increases in DTR risk, with -2.9–5% in the first year and 1.5–13.8% in the last year of the series. The temporal increase of percent increases in DTR risk were significant (P-value<0.05) in USA, UK, Spain, and South Korea (Table 3). Country-pooled temporal changes in the lag-response relationship are displayed in Supplementary Fig. S2. A comparison between the curves suggests that a longer lag-association and smaller harvesting effect were observed in most countries.

Fig. 4 and Table 3 display the temporal variation in the attributable mortality risk fraction of DTR. In overall, the attributable risk fraction of deaths increased from 2.4% (95% eCI: 2.1-2.7%) to 2.7% (2.4-2.9%) between the first and last periods. The increase in the attributable risk fraction of death overtime was observed in all countries except Japan (0.07% decrease per a year) and Ireland (0.23% decrease per a year). Korea (0.56% per year) and Colombia (0.31% per year) showed the fastest increase of risk fraction, whereas Canada (0.03% per year), USA (0.09% per year) and UK (0.11% per year) showed the slowest increasing patterns. Corresponding city-specific estimates are reported in the Supplementary Material (Supplementary Table S2). And main conclusions were robust to sensitivity analysis (Supplementary Table S3).

4. Discussion

Our findings show that DTR is responsible for a higher mortality risk increase (3.1%, 95% CI: 2.7–3.5%) and fraction of deaths (2.5%, 95% eCI: 2.3–2.7%) in all the countries studied. South Korea and Spain showed the highest percent increase in risk (6% and 4.4%, respectively) and attributable risk fractions (4.5% and 4.2%, respectively). This study also provides evidence of the incremental health impact of DTR during the last few decades. With the exception of Japan and Ireland, an increasing pattern of percentile increases in risks (3.8% in the last year of the study periods, compared with 2.5% in the first year) was observed, and the attributable risk fraction showed the same temporal increasing pattern (2.7% in the last year of the study periods, compared with 2.4% in the first year).

This study is comparable to a recent temperature variability-mortality association study in the MCC Collaborative Network (Guo et al. 2016). Both studies were based on a similar multi-country data set and addressed the significant association between temperature variability and mortality, even after controlling for the main effect of absolute temperature. Guo et al. developed a new composite index of intra- and inter-day temperature variability using a standard deviation of minimum and maximum temperatures during the exposure days, and found the temperature variability-mortality relationship varied with exposure days (0–7 days), countries (twelve countries/regions with 372 communities), and season (cold, hot, and moderate). Meanwhile, our study only focused on the association between intra-day temperature variability and mortality, using a classical meteorology index (DTR) and flexible statistical method, which considers a flexible lag-response structure of DTR. In addition, our study included data from 308 cities in the 10 countries with more than 15 years of study data to estimate the temporal changes in the DTR-mortality association. It also described an overall increase in the health burden of DTR on mortality during recent decades.

Interestingly, our finding suggested that the DTR effects on mortality were higher in warm countries (Brazil, Australia, and Spain) compared to cold countries (Canada, Ireland, and UK), although Korea and Colombia were exceptions. These finding are consistent with previous studies, such as multi-country studies that reported that the effect of temperature variability with short exposure durations (0–1, and 0–2 days) on mortality is highest in hot area (>22.9˚C) than other areas (cold, moderate cold, and moderate hot areas) (Guo et al. 2016). U.S. studies also showed that higher DTR effect in southern areas (percent change of non-accidental mortality per one unit of DTR 0.24-0.31%) than other regions (0.22-0.27%) (Lim et al. 2014).

Studies in China also showed a similar trend of a relatively higher and more significant effect of DTR in warm cities (Guangzhou, and Shanghai) than cold cities (Anshan and Xi'an, although Tangshan is an exception). To specifically assess the association between the DTR effects and annual mean of absolute temperature, we fitted a weighted regression model (Supplementary Fig. S3); a city-specific BLUP of DTR coefficient (i.e. log of relative risk, estimated from the second stage analysis) was used as a response variable, annual mean temperature was used as an explanatory variable, and inversed city-specific variances of the DTR coefficient were used as weights. We observed a significantly positive linear association between the DTR effect and the annual mean temperature from the weighted regression model (P-value=0.01). This result can be interpreted as evidence to support the hypothesis that there may be an impact on mortality from the positive interactions between long-term temperature and DTR.

The synergism effect of the DTR and long-term temperature on mortality may be due to a number of factors. One mechanism may be aggravation. Hot temperature can disturb normal physiological thermoregulation, including changes in blood viscosity, plasma cholesterol level, and red blood cell count (Keatinge et al. 1986). Increasing DTR may also impact mortality through lowering the thermoregulatory system and negatively affecting the heart rate, heart rate variability, blood platelets, red blood cells, and blood viscosity (Keatinge et al. 1984b; Lim et al. 2012b). Because warm countries can be exposed to hot weather more often, the DTR effect of warm areas can be amplified by the increase in biological burden. Another hypothesis is that the effect of the DTR is higher in warm areas because people in warm and moderate areas are more likely to keep their windows open and spend more time outdoors, which may increase exposure to DTR, thus increasing the effect of DTR. However, our results only suggest the possible associations of the aggravation hypothesis; further research should be conducted to find the causal relationship between DTR and long-term temperature on mortality.

Additional questions should be raised as to why the effect of DTR on mortality changed across time. We speculate several plausible explanations. The first hypothesis is deterioration by climate change, suggested in the previous paragraph. We found the higher risk and sharper risk increase in hot cities. This finding suggests that climate change may increase the risk of DTR. Secondly, an aging population may also be an important factor, as numerous studies have revealed that elderly people are more susceptible to DTR (Kan et al. 2007a; Lim et al. 2012a; Yang et al. 2013a), and the populations of developed and developing countries included in our research are aging (Börsch-Supan 2008; Faunce 2008). However, we could not identify the exact reason of the temporal increase, hence additional research regarding this topic is needed in further studies.

Although not found in our study, prior studies have reported that climate change factors (greenhouse gases, urbanization, and aerosols) have led to global decline in the DTR during twenty century, because the nocturnal minimum temperatures have increased faster than maximum temperature (Braganza et al. 2004; Makowski et al. 2008). However, it is still unclear how this decline in the DTR will affect human health. Also, since the increasing nocturnal temperatures can affect mortality and distribution of DTR simultaneously, a confounding effect of the nocturnal temperatures needs to be considered to estimate the effect of DTR on death. Even if the effect of increasing nocturnal minimum temperature is partly considered in our study by controlling the daily averaged temperature, there is a limitation to control the effect of nocturnal temperature due to lack of data. Therefore, we expect more comprehensive studies to be carried out under various climate conditions with longer study periods and more detailed weather data.

As described earlier, although DTR and absolute temperature may affect human health in different ways, because both have a mechanism that negatively affects human health, the effects of absolute temperature and temperature variability on mortality have been an interesting topic of prior environmental research. In addition, comparing the health effects of two variables has important implications for understanding human health in a climate change context (which can increase both the average values and the variability of temperature)(Guo et al. 2016; Stocker 2014; Vicedo-Cabrera et al. 2016). Recent studies asserted that DTR has a lesser effect than absolute temperature on mortality (Lee et al. 2017; Vicedo-Cabrera et al. 2016). Our results also suggest a lesser effect of DTR on mortality when compared with the total attributable mortality fraction of absolute temperature from a previous study (Gasparrini et al. 2015b). The total fraction of DTR attributed to mortality (2.5%) was much smaller than the fraction for total absolute temperature (7.71%)(Gasparrini et al. 2015b). However, our results may differ from the conclusions of previous studies (Chen et al. 2007; Kan et al. 2007a; Lim et al. 2015; Tam et al. 2009; Yang et al. 2013a) that used modeling strategies that did not fully control the flexible lag structures of absolute temperature. Because the effect of absolute temperature delayed up to several weeks of exposure, the estimates of DTR on mortality could be overestimated unless the main effects of temperature are fully adjusted. Hence, we contend that our modelling approach provides more appropriate results in estimating the health effects of DTR, in comparison with prior studies.

In this study, more acute DTR–mortality relationships (highest RR at 0 lag days) were observed in warm and cold countries (Brazil, Colombia, Canada, Ireland, and UK). In contrast, more delayed DTR–mortality relationships (highest RR at 2–4 lag days) were observed in other moderate temperature countries. Although this study does not explain the difference, we speculate that the exact factors are related to the physiological, technological, and behavioral adaptations to the climate.

A key strength of our study is the use of a large multi-country, multi-city data set with different demographic distributions, climate conditions, and socio-economic characteristics. To the best of our knowledge, our study is the largest of its kind including 308 locations and more than 85 million deaths from 10 countries. Our study also is the first and the largest study of time-varying DTR-related mortality, and the use of a uniform statistical framework across all cities makes the results directly comparable. In addition, unlike previous studies that have quantified the association on terms of RR (Kan et al. 2007b; Vicedo-Cabrera et al. 2016; Yang et al. 2013b), our study provides the attributable mortality burden of DTR. Because the attributable fraction considers the distribution and risks of each variable, we contend that the attributable fraction is a suitable measure to estimate mortality burden of the exposure variable and to establish corresponding public health strategies.

However, our study has some limitations that must be acknowledged. First, because regions of Africa, and large countries in Europe and Asia (such as France, Russia, and India) were not included in this study, our findings are not globally representative. Second, the data did not include age- or gender-specific mortality rates, which could be explored in future research. Third, we could only identify the suggestive association between DTR and all-causes mortality, and not the causal effect of DTR on mortality. Future studies should strive to overcome these limitations by expanding the study populations and improving the study design.

5. Conclusions

In summary, this study finds that the significant DTR effect on mortality across all countries, and provides evidence that the effect of DTR was higher in warm regions. Although our estimated attributable mortality fraction of DTR is smaller than fractions of absolute temperature from a previous multi-country study (Gasparrini et al. 2015b), it is higher than fractions of extreme heat and cold temperature. In addition, although the risks and contributions of DTR on mortality varied for each country, it increased at the multi-country scale with significant increases estimated in USA, UK, Spain, and South Korea; and non-significant increments in Canada, Brazil, Colombia, and Australia. The estimates of DTR-related mortality increased throughout the study period in overall regions, which could be interpreted as maladaptation to DTR. Consequently, there is a possibility that the health burden of DTR will increase in the near future. Hence, we suggest that public-health policies and climate change research that have so far focused on the effects of extreme heat should be extended to account for the health burden of DTR and its temporal variation.

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Table 1. Descriptive statistics by country. Including distribution of diurnal temperature range in first 3 years (First) and last 3 years (Last) of country-specific study periods. USA: United States of America, UK: United Kingdom.

Country (# of city)	Time Period	Total Deaths	Study Period (year)	Absolute temperature (°C)	Diurnal temperature range (°C)					
				Mean	Mean	10%	25%	50%	75%	90%
Canada (26)	Whole	2,989,901	1986-2011	6.8	10	4.4	6.6	9.7	13	15.9
	First			7	10.1	4.5	6.7	9.8	13	16
	Last			6.9	9.9	4.4	6.4	9.4	12.9	16.1
USA (135)	Whole	22,896,409	1985-2006	14.8	10.9	5.6	7.8	10.6	13.9	16.7
	First			14.7	11	5.6	7.8	10.6	13.9	17.2
	Last			15.1	10.7	5.6	7.8	10.6	13.3	16.1
Brazil (18)	Whole	3,435,502	1997-2011	24.2	9	5.4	6.8	8.6	10.7	13.2
	First			24.1	8.8	5.1	6.6	8.4	10.6	13.1
	Last			24.3	9.1	5.5	7	8.6	10.7	13.4
Colombia (5)	Whole	956,539	1998-2013	23.4	9	5.8	7	8.8	10.8	12.4
	First			23.1	8.9	5.6	6.8	8.7	10.8	12.5
	Last			23.5	8.9	6.1	7.2	8.7	10.4	12.1
UK (10)	Whole	1,2075,786	1990-2012	10.3	7.3	3.8	5.2	6.9	9.1	11.3
	First			10.1	7.3	3.8	5.1	6.9	9.1	11.3
	Last			10.1	7.5	3.9	5.3	7	9.4	11.7
Ireland (6)	Whole	1,058,215	1984-2007	9.7	6.7	3.4	4.8	6.4	8.3	10.3
	First			8.9	6.8	3.6	4.9	6.5	8.4	10.4
	Last			10.3	6.9	3.6	4.9	6.6	8.5	10.5
Spain (51)	Whole	3,480,531	1990-2010	15.5	10.6	4.9	7	10	13.8	17
	First			15.1	10.7	5	7.2	10.2	13.8	17.2
	Last			15.5	10.4	4.8	6.8	9.8	13.6	17
Japan	Whole	3,6113,897	1972-2012	15.1	8.4	4.2	6	8.2	10.6	12.8

(47)	First			14.4	8.8	4.4	6.3	8.6	11	13.3
	Last			15.5	8.2	4.1	5.9	8	10.2	12.4
South Korea	Whole	1,727,642	1992-2010	13.7	8.2	4.1	5.9	8	10.2	12.7
(7)	First			13.5	8	3.8	5.6	7.7	10.1	12.5
	Last			13.8	8.3	4.3	5.9	8	10.3	12.7
Australia	Whole	1,177,950	1988-2009	18.1	8.2	4.4	5.9	7.8	10	12.4
(3)	First			18.1	7.8	4.1	5.6	7.3	9.5	11.9
	Last			18.7	8.1	4.5	5.8	7.6	10	12.6

Table 2. Percent increases in risk (per 10°C) and attributable risk fraction (%) of diurnal temperature range on mortality by country. USA: United States of America, UK: United Kingdom.

Country	Percent Increases in Risk (%, 95% CI)	Attributable Risk Fraction (%, 95% eCI)
Canada	2.6 % (0.9 , 4.2)	2.7 % (1.8 , 3.5)
USA	2.9 % (2.3 , 3.6)	3.2 % (2.9 , 3.5)
Brazil	4.2 % (1.7 , 6.7)	3.7 % (2.6 , 4.9)
Colombia	-1.2 % (-6.3 , 4.1)	-1.5 % (-5.1 , 2.1)
UK	2.9 % (1.5 , 4.4)	2.1 % (1.6 , 2.7)
Ireland	0.3 % (-3 , 3.8)	0.2 % (-1.2 , 1.4)
Spain	4.4 % (3 , 5.8)	4.2 % (3.5 , 4.9)
Japan	3.1 % (2.3 , 3.9)	2.7 % (2.4 , 3)
South Korea	6 % (3 , 9.1)	4.5 % (3 , 5.9)
Australia	4.2 % (0.7 , 7.9)	3.3 % (1.1 , 5.3)
Overall	3.1 % (2.7 , 3.5)	2.5 % (2.3 , 2.7)

eCI: empirical confidence interval.

Table 3. Variation of excessive relative risk (per 10°C) and attributable fraction (%) of diurnal temperature range on mortality per a year, and p-value of the test. USA: United States of America, UK: United Kingdom.

		Variation (per year)		
Country	**Study Period (Years)**	**Percent Increases in Risk**	**Attributable Risk Fraction**	**p-value***
Canada	26	0.06 %	0.03 %	0.4384
USA	22	0.09 %	0.09 %	0.0209
Brazil	15	0.25 %	0.23 %	0.2243
Colombia	16	0.29 %	0.31 %	0.6583
UK	23	0.17 %	0.11 %	0.0344
Ireland	24	-0.35 %	-0.23 %	0.0989
Spain	21	0.28 %	0.23 %	0.0025
Japan	41	-0.09 %	-0.07 %	<0.0001
South Korea	19	0.78 %	0.56 %	<0.0001
Australia	22	0.3 %	0.26 %	0.1543

* Significant test on temporal change by Wald type test of the pooled reduced coefficient of the year-interaction terms. The null hypothesis is that no change in year occurred.

Figure legends

Fig. 1. Geographical locations of study cities and their annual mean values of diurnal temperature range (DTR, °C).

Fig. 2. Lag-response relationship between diurnal temperature range (DTR) and mortality predicted for the overall study periods of 10 countries; RR: relative risk. USA: United States, UK: United Kingdom.

Fig. 3: Temporal changes in percent increases in risk (%) between the first (First) and the last (Last) year of country-specific study periods; USA: United States, UK: United Kingdom.

Fig. 4. Temporal changes in attributable risk fraction (%) between the first (First) and the last (Last) year of country-specific study periods; USA: United States, UK: United Kingdom.

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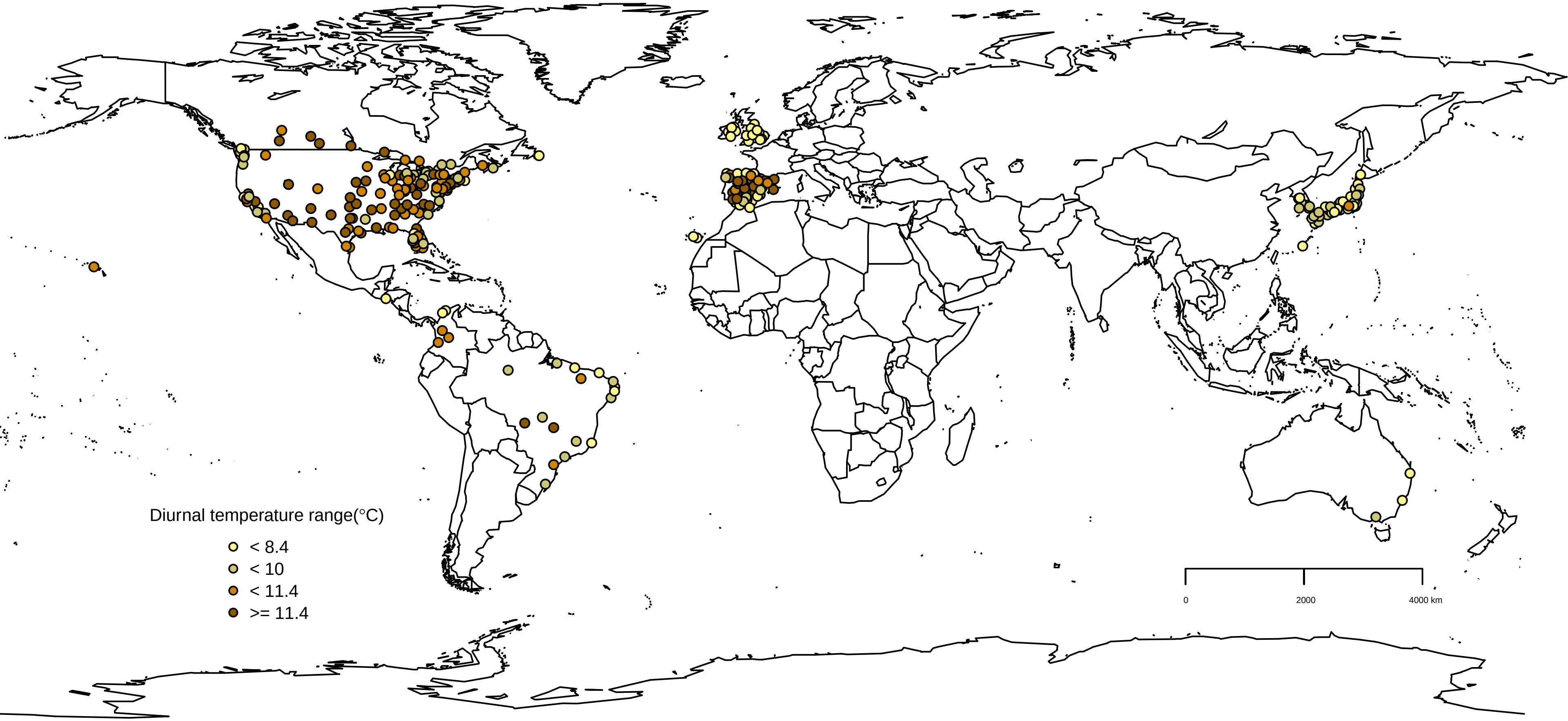
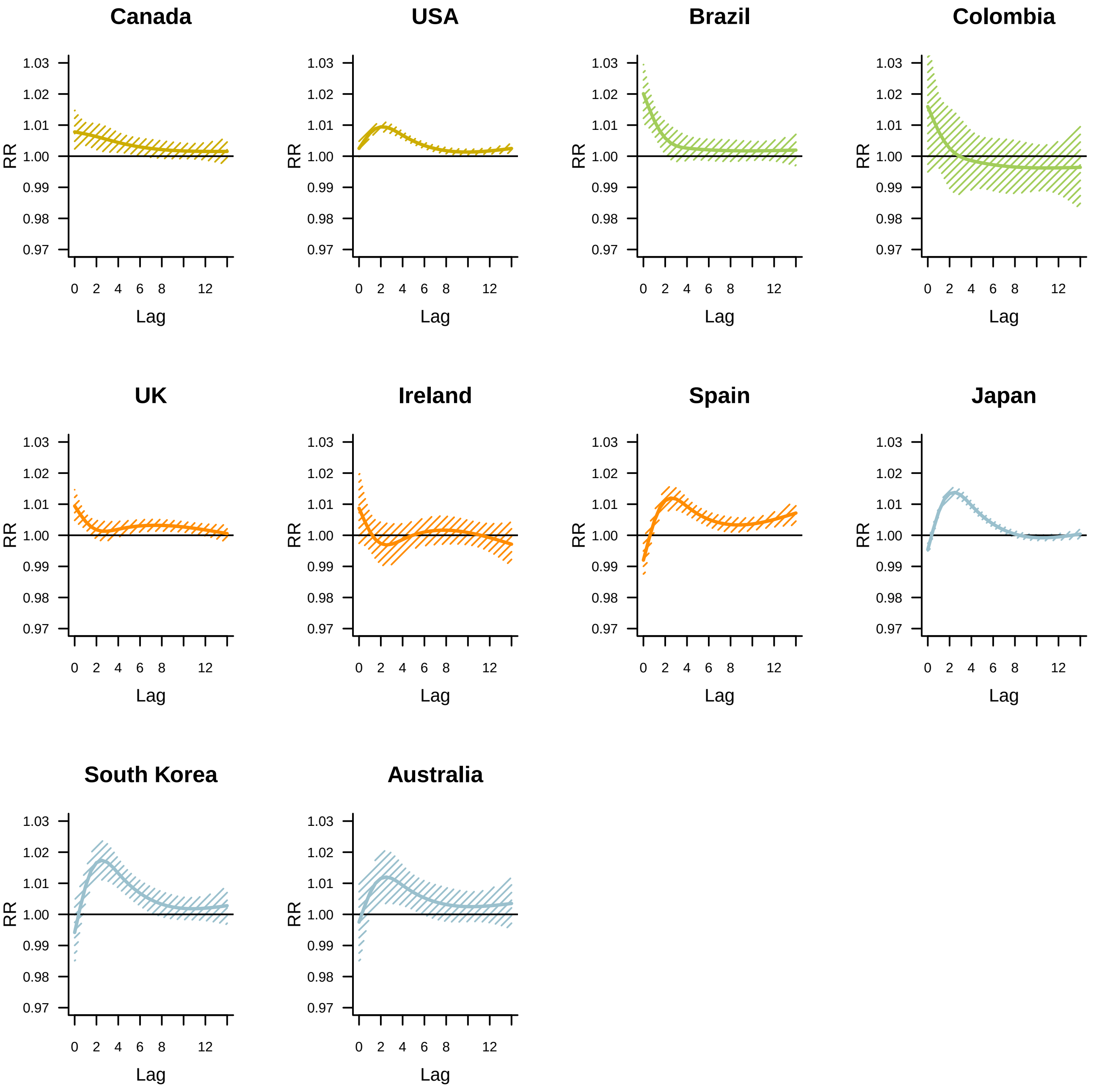
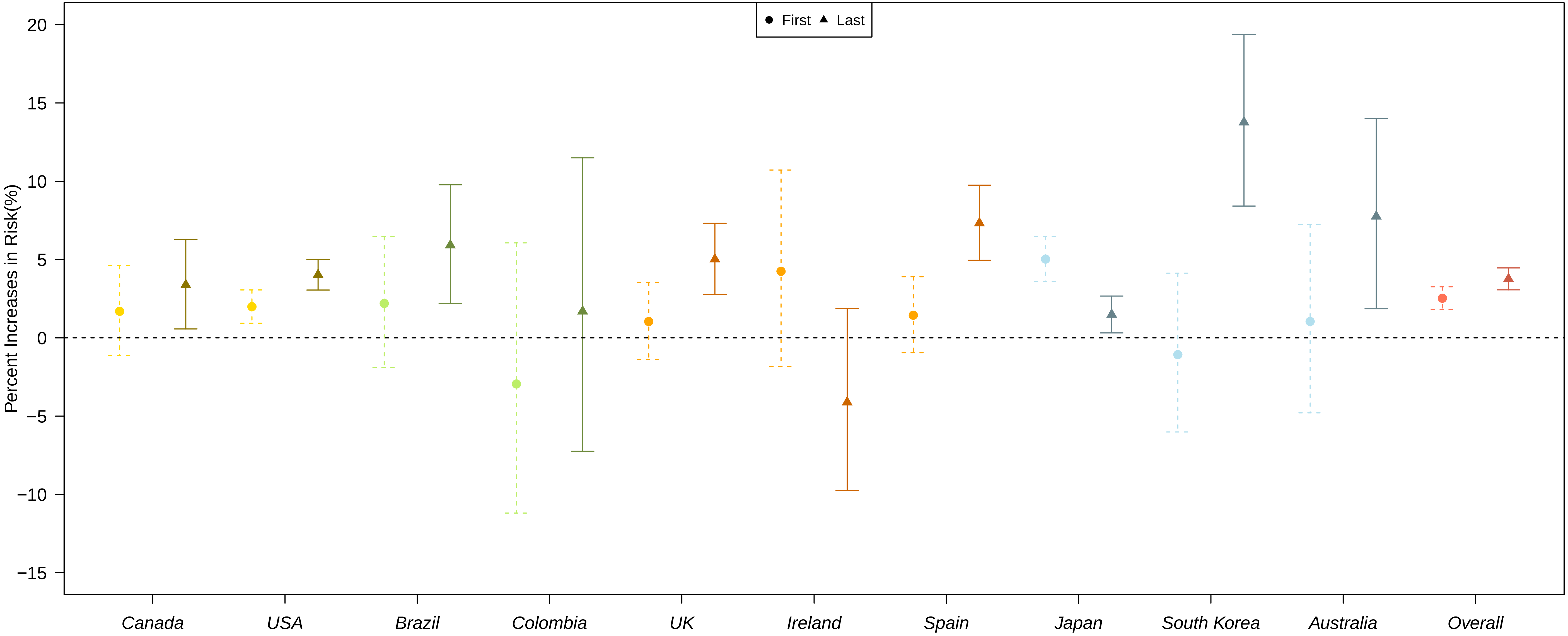
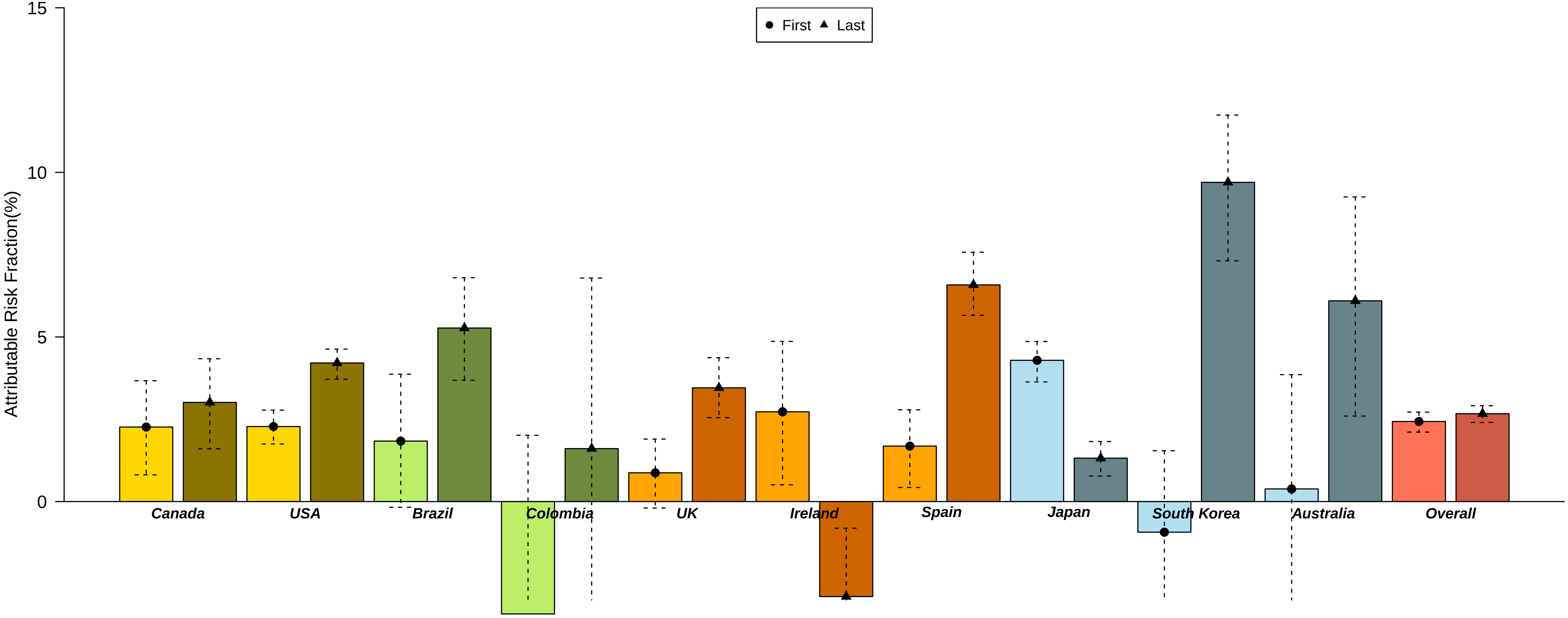

Diurnal temperature range(°C)
< 8.4
< 10
< 11.4
>= 11.4
0
2000
4000 km


Canada
USA
Brazil
Colombia
UK
Ireland
Spain
Japan
South Korea
Australia
RR
1.03
1.02
1.01
1.00
0.99
0.98
0.97
Lag
0
2
4
6
8
12


● First ▲ Last
Percent Increases in Risk(%)
20
15
10
5
0
−5
−10
−15
Canada
USA
Brazil
Colombia
UK
Ireland
Spain
Japan
South Korea
Australia
Overall



15
10
5
0
Attributable Risk Fraction(%)
● First ▲ Last
Canada
USA
Brazil
Colombia
UK
Ireland
Spain
Japan
South Korea
Australia
Overall