



# Association of diurnal temperature range with daily mortality in England and Wales: A nationwide time-series study



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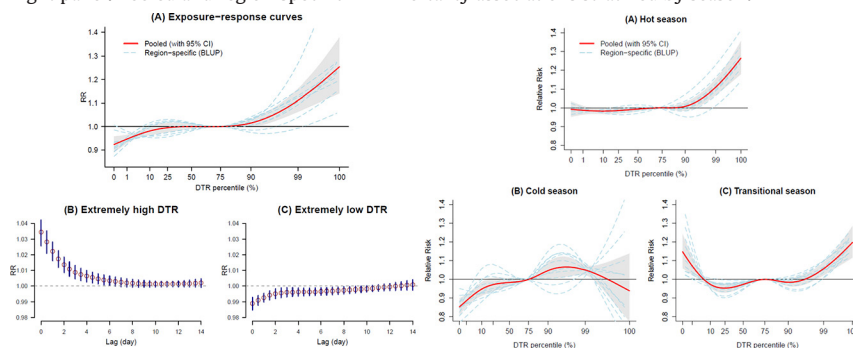
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## HIGHLIGHTS

- A nationwide investigation of fourteen-year time-series data
- A nonlinear DTR-mortality association was identified with distinct seasonal patterns.
- Extremely high DTR increased short-term mortality, whereas extremely low DTR exhibited entirely different seasonal effects.
- Mortality vulnerability to DTR extremes varied greatly by regional latitudes and climate conditions.
- Findings are important for public health decision-making in coping with climate change.

## GRAPHICAL ABSTRACT

Left panel: Pooled exposure-response relationship and lag patterns of extremely high and low DTR. Right panel: Pooled and region-specific DTR-mortality associations stratified by season.



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## ABSTRACT

**Background:** Diurnal temperature range (DTR) reflects within-day temperature variability and is closely associated with climate change. In comparison to temperature extremes, up-to-date DTR-health evidence at the regional and national scales has been still very limited worldwide, especially in Europe.

**Objectives:** This study aimed to provide nationwide estimates for DTR-associated effects on mortality, and explore whether season and regional-level characteristics modify DTR-mortality relation in United Kingdom.

**Methods:** Fourteen-year time-series data on weather and mortality were collected from 10 regions in England and Wales during 1993–2006, including 7,573,716 total deaths. A quasi-Poisson regression incorporated with distributed lag non-linear model was first applied to estimate region-specific DTR-mortality relationships. Then, a multivariate meta-analysis was employed to derive the pooled DTR effects at the national level. Also, the modifying effects of some regional characteristics (e.g., geographical and climatological) were examined by conducting multivariate meta-regression.

**Results:** A non-linear DTR-mortality relationship was identified in UK. At the national level, increasing DTR raised the mortality risk observably when DTR exposure was below 25th percentile or above 90th percentile of DTR distribution, with an intermediate risk plateau indicating no associations. Extremely high DTR exhibited greater adverse effect estimates in hot season compared with in cold and transitional season, whereas entirely different association patterns were observed for the season-specific effects of extremely low DTR. In addition to season, regional latitudes, average temperature and humidity were also found to significantly modify DTR-mortality relationship.

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**Conclusions:** Our study added strong evidence that extremely high DTR increased short-term mortality, whereas the effects of extremely low DTR exhibited entirely different seasonal patterns. Also, mortality vulnerability to DTR extremes varied greatly by regional latitudes and climate conditions.

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## 1. Introduction

Over the past decades, climate change has raised increasing research interests in weather-related health assessment. Temperature extremes, namely cold, heat or both, have been extensively linked with a wide variety of health consequences throughout our lives (Onozuka and Hagihara 2017; Song et al. 2017; Ye et al. 2012; Zhang et al. 2017c; Zhao et al. 2017). As shown in large bodies of epidemiologic studies, increased mortality burden arising from non-optimum temperature exposure remains a great public health threat across the globe (Gasparrini et al. 2015b; Hajat et al. 2010). The observed temperature-mortality relationships varied greatly by regions and climates, generally with U, V, or J-patterns (Gasparrini et al. 2015b; Guo et al. 2014; Ma et al. 2015a). Furthermore, heat effects tended to appear immediately and only persisted for several days, whereas cold effects were delayed and lasted for weeks (Guo et al. 2014; Zhang et al. 2017a).

In addition to heat and cold, unstable weather is an emerging environmental trigger for extra health risks. In some countries/regions, for instance, significant short-term associations of health with temperature changes during a certain period have been reported for cause-specific mortality (Lim et al. 2015; Zhan et al. 2017; Zhang et al. 2017b; Zhou et al. 2014) and hospital admissions (Liang et al. 2009; Lichtman et al. 2016; Lim et al. 2012a; Qiu et al. 2015; Teng et al. 2013). Also, two population-based cohort studies suggested the harmful effects on long-term survival in relation to within-season temperature variability (Shi et al. 2015; Zanobetti et al. 2012). These growing epidemiologic findings highlighted the significant role of unstable temperatures in influencing health, suggesting the great potential health benefit for the public to take some preventive and interventional actions in coping with large changes of regional climates.

Defined as the difference of maximum and minimum temperature within a day, diurnal temperature range (DTR) reflects daily temperature variability and is closely associated with climate change in regions such as European areas (Makowski et al. 2008; Yang et al. 2013). In recent years, the adverse impact of high DTR exposure has been identified in a growing number of time-series studies, while showing great differences in effect estimates and seasonal patterns (Cheng et al. 2014; Ding et al. 2015; Lim et al. 2012b; Luo et al. 2013). However, most available evidence was based on single-city investigations or limited within some developed metropolises, and relatively comprehensive understandings of DTR-health relation were thus very limited at the regional and national scales (Kim et al. 2016). Additionally, in comparison to temperature extremes, DTR-related health effects have been still less studied worldwide and worse understood in diverse climate zones, especially in Europe (Cheng et al. 2014).

In this study, we thus conducted a large-scale observational investigation covering all regions of England and Wales, aiming to provide nationwide estimates for DTR-associated effects on mortality, and explore whether season and regional-level characteristics modify DTR-mortality relation in UK.

## 2. Materials and methods

### 2.1. Weather and mortality data

We collected the 14-year time-series data on weather and mortality covering 10 UK regions from the open-access databases of a previous multi-country study (Gasparrini et al. 2015a). This dataset has been

also made publicly available by Dr. Antonio Gasparrini on his personal web page (<http://www.ag-myresearch.com/>). It consists of daily counts of all-cause deaths (i.e., natural and external) and weather conditions (e.g., daily minimum and maximum temperature, 24-hour average temperature and relative humidity) in 9 regions of England and in Wales from January 1, 1993 to December 31, 2006. Specifically, daily mortality counts were summed up based on date of death and divided by government region according to the postcode of residence at the time of death, while the meteorological data were population-weighted from an average of 29 monitoring stations (range: 7 in London to 44 in Wales). A detailed description of these data can be found elsewhere (Armstrong et al. 2011; Gasparrini et al. 2012b; Gasparrini et al. 2015b). Daily DTR was then calculated by subtracting minimum temperature from maximum temperature for each Government Office Region.

### 2.2. Statistical analysis

The DTR-mortality association was investigated with a two-stage analytic approach using the 14-year time-series data from the ten regions in England and Wales. In the first stage, we applied a time-series regression for each region to estimate region-specific DTR-mortality associations. A second-stage multivariable meta-analysis was then conducted to pool these estimated associations at the national level. This analytic strategy has been well documented in previous publications (Gasparrini and Armstrong 2013; Gasparrini et al. 2012a).

#### 2.2.1. First-stage time-series regression

A standard time-series generalized linear model (GLM) (Peng et al. 2006) assuming a quasi-Poisson distribution was first applied to assess region-specific DTR-mortality relationships. Distributed lag nonlinear model (DLNM) (Gasparrini 2011; Gasparrini et al. 2010) was incorporated into the GLM to model the lagged and nonlinear effects of DTR. Specifically, a flexible “cross-basis” function for DTR was defined by a combination of a natural cubic spline (NCS) with 3 internal knots (10th, 75th, and 90th) for DTR space and a NCS with 2 internal knots at equally spaced log-values for lag space. These modeling choices were motivated by previous large scale investigations (Gasparrini et al. 2015b; Guo et al. 2014). We extended the lag period to 14 days to capture the overall DTR effect since our preliminary analyses illustrated little effects after 14 days of lag.

To remove the long-term trends and seasonality of all-cause deaths, we used a NCS with 8 degrees of freedom (*df*) per year for calendar time (Gasparrini et al. 2015b). Day of the week (DOW) was included as an indicator variable to allow the short-term fluctuation (Zhang et al. 2016). Also, we controlled for the confounding effects of the current day's mean relative humidity (MeanRh), and the moving average of lag 0–14 days for mean temperature (MeanT<sub>0–14</sub>) using 3 *df* NCS at equally spaced quantiles (Chen et al. 2014; Zeng et al. 2017). Hence, the GLM model is given as follows:

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

$$\text{Log}(\mu_t) = \alpha + \beta \text{DTR}_{t,l} + \text{NCS}(\text{Time}_t, df = 14 \times 8) + \gamma \text{DOW}_t \\ + \text{NCS}(\text{MeanT}_{0-14t}, df = 3) + \text{NCS}(\text{MeanRh}_t, df = 3)$$

where *t* is the day of observation (*t* = 1, 2, 3, ..., 5113), and *Y<sub>t</sub>* is the observed daily death counts on day *t*; α is the intercept; DTR<sub>*t,l*</sub> is the cross-

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