



Environment, Green Space and Pollution

How urban characteristics affect vulnerability to heat and cold: a multi-country analysis

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Abstract

Background: The health burden associated with temperature is expected to increase due to a warming climate. Populations living in cities are likely to be particularly at risk, but the role of urban characteristics in modifying the direct effects of temperature on health is still unclear. In this contribution, we used a multi-country dataset to study effect modification of temperature–mortality relationships by a range of city-specific indicators.

Methods: We collected ambient temperature and mortality daily time-series data for 340 cities in 22 countries, in periods between 1985 and 2014. Standardized measures of demographic, socio-economic, infrastructural and environmental indicators were derived from the Organisation for Economic Co-operation and Development (OECD) Regional and Metropolitan Database. We used distributed lag non-linear and multivariate meta-regression models to estimate fractions of mortality attributable to heat and cold (AF%) in each city, and to evaluate the effect modification of each indicator across cities.

Results: Heat- and cold-related deaths amounted to 0.54% (95% confidence interval: 0.49 to 0.58%) and 6.05% (5.59 to 6.36%) of total deaths, respectively. Several city indicators modify the effect of heat, with a higher mortality impact associated with increases in population density, fine particles (PM_{2.5}), gross domestic product (GDP) and Gini index (a measure of income inequality), whereas higher levels of green spaces were linked with a decreased effect of heat.

Conclusions: This represents the largest study to date assessing the effect modification of temperature–mortality relationships. Evidence from this study can inform public-health interventions and urban planning under various climate-change and urban-development scenarios.

Key words: Temperature, heat, mortality, epidemiology, cities, climate

Key Messages

- Urban populations may experience higher risks due to exposure to non-optimal temperature, particularly in a changing climate, but the role of urban characteristics in modifying such direct health effects is still unclear.
- This represents the largest study to date assessing the effect modification of temperature–mortality relationships, performed by comparing different cities across the world and using standardized indicators.
- The effects of heat on mortality are higher in cities characterized by a higher level of inequalities, higher air-pollution exposure, fewer green spaces and lower availability of health services.
- Evidence from this study can inform public-health interventions and urban planning under various climate-change and urban-development scenarios.

Introduction

Several studies have evaluated the relationship between ambient temperature and mortality, consistently reporting increased risks at high and low temperatures.^{1–3} These risks are associated with a substantial health burden across populations living in different parts of the world, indicating that exposure to non-optimal temperature represents an important global contributor to excess mortality.^{1–3} The situation is not likely to improve in the context of climate change, as the health burden associated with non-optimal temperature is projected to increase in a warming planet.⁴ In addition, scenarios of socio-economic pathways suggest that future susceptibility is likely to increase with ageing populations, rapid urbanization and growing inequalities.⁵

Populations living in cities are particularly vulnerable to non-optimal temperature. The structure of urban areas could enhance temperature-related health risks through a combination of higher exposures (e.g. urban heat island effect) and higher vulnerability (e.g. population density and socio-economic differentials).^{6,7} Evidence of this excess health burden, particularly during extreme events as in Chicago in 1995, Paris in 2003 and Moscow in 2010, has motivated the development of public-health measures to reduce preventable mortality and morbidity (e.g. Heat Health Watch Warning System). Several heat health watch warning systems (also called ‘heat warning systems’ or ‘heat health warning systems’) have been implemented in several countries (e.g. the USA, Italy, Germany, France, Spain, Portugal, the UK, Australia, Canada, South Korea and China), some of which attempt to target potentially vulnerable groups in urban communities.^{8,9} In this context, identifying aspects that modify the susceptibility to the impacts of non-optimal temperatures can help improve health-protection programmes and contribute to the development of city-level mitigation and adaptation strategies, including urban planning and design.

A number of studies have contributed to this topic, investigating potential effect modifiers of temperature–mortality associations. In particular, some studies have adopted ecological study designs to assess community-level factors, such as urbanization, number of green areas or vegetative covering.^{10–19} However, most of the published studies included homogeneous populations; only a few compared regions with different geographic and climatic conditions, and populations with highly variable socio-economic and demographic characteristics.

In this study, we used data from the Multi-City Multi-Country (MCC) collaborative network (<http://mccstudy.lshtm.ac.uk/>) to evaluate the role of cities’ characteristics in modifying susceptibility to high and low temperatures.

The MCC database includes time-series data for hundreds of cities in 22 countries and provides a unique opportunity to compare health effects across highly heterogeneous populations. Specifically, we linked the MCC data with standardized measures of contextual factors at the city level and analysed their effect modification for mortality risks associated with both heat and cold.

Methods

MCC data

The analysis is restricted to 340 cities or metropolitan areas (from now on generally referred to as cities) available in the MCC dataset, distributed across 22 countries. For each location, the dataset comprises time series of daily mean temperature and mortality counts for all causes or non-external causes only (International Classification of Diseases—ICD-9: 0–799; ICD-10: A00–R99) in largely overlapping periods ranging from 1 January 1985 to 31 December 2014. The full list of cities, together with additional information, can be found in [Supplementary Material A](#) and [B](#), available as [Supplementary data](#) at *IJE* online.

Indicators

OECD Regional and Metropolitan Database

We collected data on several city-specific socio-economic indicators and urban development from the Organisation for Economic Co-operation and Development (OECD) Regional and Metropolitan Database.^{20,21} The OECD Regional Database provides a set of comparable statistics and indicators on about 2000 regions and 281 OECD metropolitan areas in 34 OECD member countries and other economies (<http://stats.oecd.org/Index.aspx>). They include yearly time series, from 2000 to 2014, for around 40 indicators of demography, economic, labour-market, social, environmental and innovation themes. Details on the regional and metropolitan OECD Database can be found in a specific OECD publication.²² OECD follows a strict Quality Framework for Statistical Activities.²³ The OECD quality framework defines two dimensions: the quality of national statistics that OECD receives and the quality of OECD internal processes for collection, processing, analysis and dissemination of data and metadata. OECD statistics have a high reputation for quality and integrity throughout the world and we are confident that the data we used have a high level of accuracy.

First, 136 cities in the MCC database were linked with the OECD Metropolitan Database at the metropolitan area (MA) level. In addition, all 340 MCC cities were

Table 1. OECD Regional and Metropolitan Database indicators included in the analysis: definition, years and geographical level of observation

| Indicator | Definition | Years | MA | SR | LR |
|--|---|------------------|-----|-----|-----|
| Demographic | | | | | |
| % population ≥65 years | % old population (65 years or more) | 2000 | 136 | 147 | 37 |
| Life expectancy (years) | Life expectancy at birth (years) | 2005–06; 2010–11 | | | 288 |
| Socio-economic | | | | | |
| GDP (US\$) | GDP per capita (US\$) (current prices, current PPP) | 2001; 2010 | 136 | 59 | 130 |
| Labour productivity (US\$) | Labour productivity (Gross Value Added (GVA) per worker) (current prices, current PPP) | 2005; 2009–10 | | | 280 |
| Educational level (%) | Share of labour force with at least secondary-level education | 2000 | | | 265 |
| Unemployment rate (%) | Unemployment rate (%) | 2001; 2010 | 136 | 130 | 41 |
| Gini index | Gini (disposable income, after taxes and transfers); high index means high inequality | 2009–14 | | | 280 |
| Poverty gap | Poverty rate after taxes and transfers; the poverty line reflects 60% of the national median income | 2009–14 | | | 280 |
| Health system | | | | | |
| Hospital-bed rates | Hospital-bed rates (hospital beds per 10 000 population) | 2008–10 | | | 279 |
| Urban characteristics | | | | | |
| Type of surrounding region (rural/urban) | The OECD regional typology is based on the following criteria: population density, degree of rurality and size of the urban centres located within a region: Predominantly urban = 1 Intermediate = 2 Predominantly rural = 3 Predominantly rural close to a city = 4 Predominantly rural remote = 5 | 2000 | | 272 | |
| Urbanized area share (%) | Urbanized area share (%): share of the urbanized area over total land of a metropolitan area | 2000–01; 2006 | 136 | | |
| Green area (square metres per million persons) | Land in the MA covered by vegetation, forest and parks in 2000 (source: MODIS MCD12Q1), divided by the population of the MA and then multiplied by 1 million | 2000 | 136 | | |
| Concentration of population in the core (%) | Share of population living in the core areas over the total metropolitan population | 2000 | 136 | | |
| Sprawl | The sprawl index measures the growth [over the periods 2000–06 and 2000–12, except Japan (1997–2006) and the USA (2001–06 and 2001–11)] in built-up areas adjusted for the growth in the city population | 2006 | 100 | | |

MA, city/metropolitan area; SR, small region; LR, large region.

linked with the OECD Regional Database both at small-region and large-region geographical levels. The former represents provinces or prefectures, the latter administrative regions or small states.²⁰ In total, a set of 14 indicators were selected from OECD Regional and Metropolitan Databases. These indicators encompass demographic, socio-economic, health-system and urban characteristics (Table 1). For each indicator, we used the data collected at the smallest geographical level available, using the value measured in a single year or averaged across multiple years in order to minimize the amount of missing data. The definition of each OECD indicator considered in this analysis is provided in Table 1.

The set of indicators related to urbanization (e.g. urbanized area, green area, concentration of population in the core, Sprawl index) is available for 136 MCC cities that are in the OECD MA Database. A subset of socio-economic indicators (e.g. Gini index, educational level) is available for OECD country members, but not for OECD country partners (e.g. China, Brazil, Colombia, Iran, Moldova, Philippines, Viet Nam). Other indicators (e.g. GDP, % population ≥65 years, unemployment rate) were available also among some OECD country partners (Brazil, China, Colombia). For each indicator, the list of countries with available information is reported in Supplementary Table 1, available as Supplementary data at *IJE* online.

Air-pollution indicators

To characterize long-term air-pollution exposures in each city, we used global estimates of annual fine particulate (PM_{2.5}) levels of the Data Integration Model for Air Quality available for the year 2014²⁴ and global annual mean ground-level nitrogen dioxide (NO₂) concentrations (3 years running mean for year 2001), developed by Geddes *et al.*²⁵ Both global estimates were calculated for grid cells with a spatial resolution of 0.1° for latitude and longitude.

We linked the 340 MCC cities with the databases containing the PM_{2.5} and the NO₂ global estimates. Specifically, for each city, we assigned the PM_{2.5} and NO₂ level of the grid cell [spatial resolution (0.1° × 0.1°), which is approximately 11 × 11 km at the equator] including the coordinates of the city as defined by the World Cities database (<https://simplemaps.com/data/world-cities>).²⁶

Population and density data

The World Cities database was used to retrieve population and density indicators for the year 2015. The former is an estimate of the city's population, whereas the latter is defined as population per square kilometre.

Weather variables

For each city, we calculated the average daily mean temperature and daily mean temperature range from the observed daily temperature distribution in the MCC dataset, in the city-specific observation period (between 1985 and 2014). These were used as basic indicators to avoid confounding by weather/climatological conditions.

Statistical methods

Description of the indicators

We summarize the distribution of indicators by country with the median, standard deviation and interquartile range (IQR). The relationships between indicators were examined first through the correlation matrix among all pairs of indicators. To remove the between-countries effects from the correlation, for all cities of a given country, the original indicator value was scaled by the country average indicator value. The country-adjusted correlation matrix was used as the input of a principal component analysis (PCA). The PCA is a statistical method that identifies factors (principal components) that best explain the covariability of the data. The principal components show groups of indicators that co-vary similarly in most cities, as can be illustrated in a score plot.

Association between the indicators and temperature–mortality impacts

We adopted a three-step approach to evaluate the association between the indicators and temperature–mortality impacts. Briefly, in the first stage, we calculated the city-specific temperature–mortality associations, followed by the estimation of the corresponding heat- and cold-attributable fractions and, in the last step, we fitted meta-regression models to evaluate the association between each indicator and heat and cold AF%. The three steps are described in more detail below.

First-stage time-series analysis

We estimated the city-specific temperature–mortality associations through quasi-Poisson regression²⁷ and distributed lags non-linear models (DLNMs).²⁸ We modelled the cross-basis function of daily mean temperature with a natural cubic spline function for the temperature dimension with three internal knots at the 10th, 75th and 90th percentiles of the city area-specific temperature distributions, and natural cubic spline with an intercept and two internal knots placed in equally spaced values in the log scale for the lag dimension. We extended the lag period to 21 days to capture the long delay in cold–mortality associations. We included a natural cubic B-spline function with 8 degrees of freedom (df) per year to control for long-term trends and seasonality, along with an indicator for day of the week. The model selection was based on previous work using a similar dataset.³ We tested these modelling choices in a sensitivity analysis.

Estimation of city-specific heat- and cold-attributable fraction

To estimate the city-specific temperature at which mortality was minimal (called minimum mortality temperature, MMT) with greater precision, we applied a shrinkage procedure that borrows information across cities in the same country with similar climate. Details of this method are given in previous work.³ We estimated attributable fractions (AF%, in percentage) using the first-stage (unshrunk) cumulative exposure–response associations, following a procedure described elsewhere.²⁹ In summary, we computed mortality attributable to cold and heat by summing the temperature-related deaths occurring in days with temperatures lower or higher than the MMT, and then dividing by the total number of deaths. We calculated empirical standard error using Monte Carlo simulations,²⁹ assuming a multivariate normal distribution of the first-stage reduced coefficients.

Table 2. MCC dataset: number of cities, deaths, period of observation and mean daily average temperature by country

| Country | Cities | Level of development ^a | Deaths | Period | Daily average temperature (degrees Celsius)—mean (range) |
|-------------|--------|-----------------------------------|------------|-----------|--|
| Australia | 3 | Advanced economy | 1 177 950 | 1988–2009 | 18.1 [5.6; 35] |
| Brazil | 18 | Developing economy | 3 401 136 | 1997–2011 | 24.6 [3.6; 33.5] |
| Canada | 26 | Advanced economy | 2 989 901 | 1986–2011 | 6.8 [–39.7; 32.1] |
| Chile | 4 | Developing economy | 325 462 | 2004–14 | 13.7 [–1.7; 27.5] |
| China | 15 | Developing economy | 950 130 | 1996–2008 | 15.1 [–23.7; 36.4] |
| Colombia | 5 | Developing economy | 956 539 | 1998–2013 | 23.4 [10.5; 31.1] |
| Finland | 1 | Advanced economy | 130 325 | 1994–2011 | 6.2 [–22.9; 25.5] |
| France | 18 | Advanced economy | 1 197 555 | 2000–10 | 12.6 [–11.6; 32.4] |
| Iran | 1 | Developing economy | 121 585 | 2004–13 | 16.0 [–14.7; 33.3] |
| Italy | 16 | Advanced economy | 645 420 | 2001–10 | 15.7 [–10.7; 39.5] |
| Japan | 7 | Advanced economy | 3 123 487 | 1985–2009 | 15.0 [–12.0; 33.1] |
| Mexico | 10 | Developing economy | 2 980 086 | 1998–2014 | 18.8 [0.4; 35.3] |
| Moldova | 4 | Developing economy | 59 906 | 2001–10 | 10.7 [–25.0; 32.6] |
| Philippines | 4 | Developing economy | 274 516 | 2006–10 | 28.2 [21.8; 33.3] |
| South Korea | 7 | Advanced economy | 1 726 938 | 1992–2010 | 13.7 [–15.7; 33.0] |
| Spain | 51 | Advanced economy | 3 479 881 | 1990–2010 | 15.5 [–10.9; 36.8] |
| Sweden | 1 | Advanced economy | 201 197 | 1990–2010 | 7.2 [–21.5; 26.8] |
| Switzerland | 8 | Advanced economy | 243 638 | 1995–2013 | 10.4 [–14.9; 29.0] |
| Taiwan | 3 | Advanced economy | 765 893 | 1994–2007 | 24.0 [8.1; 33.0] |
| UK | 1 | Advanced economy | 1 325 902 | 1990–2012 | 11.6 [–5.5; 29.1] |
| USA | 135 | Advanced economy | 22 953 896 | 1985–2006 | 14.9 [–31.4; 41.4] |
| Vietnam | 2 | Developing economy | 108 173 | 2009–13 | 27.1 [14.4; 33.9] |

^aInternational Monetary Fund Advanced and Developing Economies List. World Economic Outlook, April 2016, p. 148; World Economic Outlook, April 2015, pp. 150–53, retrieved 26 June 2015; World Economic Outlook, Database—WEO Groups and Aggregates Information, April 2015, retrieved 26 June 2015.

Association between the indicators and heat- and cold-attributable fraction

We estimated whether the city-specific estimated temperature–mortality associations differed by city characteristics. For each indicator, we used the set of cities with available information and two separate meta-regression models were used to evaluate the association between the indicator and heat and cold AF% including indicators for countries, and average and range of daily mean temperature as meta-predictors. We tested and reported residual heterogeneity using the Cochran Q test and I^2 statistic, respectively.³⁰

Results

Description of the sample

Descriptive statistics of mortality and temperature data are reported in Table 2. Almost 50 million deaths were observed in the study period. The 340 cities are located in 22 countries, 13 of which, according to the International Monetary Fund, are developed countries whereas 9 are developing countries (Table 2). Figure 1 shows the geographical distribution of the 340 cities and their average daily mean temperature, illustrating how this study covers various regions and climatic areas across the world.

Descriptive statistics of the 18 indicators considered in the analysis are shown in Table 3. Cities considered in this analysis show highly variable socio-economic, demographic, urban characteristics and air-pollution levels.

Weather variables, country and attributable mortality

Overall, we estimated that 0.54% (95% confidence interval: 0.49 to 0.58%) and 6.05% (5.59 to 6.36%) of mortality in the 340 MCC cities were attributable to heat and cold, respectively (Supplementary Table 2, available as Supplementary data at *IJE* online). Larger between-city heterogeneity was observed for heat AF% ($I^2 = 85.4%$) than for cold AF% (64.2%). Country explained 15.7 and 10.9% of heterogeneity for heat AF% and cold AF%, respectively. In total, weather variables explained a further 22% of cold AF% heterogeneity, whereas heat AF% heterogeneity decreased by only 2.3%.

Demographic, socio-economic, environmental and urban indicators and attributable mortality

Associations between the indicators and heat- and cold-related AF% are reported in Figure 2 and Supplementary Table 3, available as Supplementary data at *IJE* online. Results are expressed as AF% variation for a standard

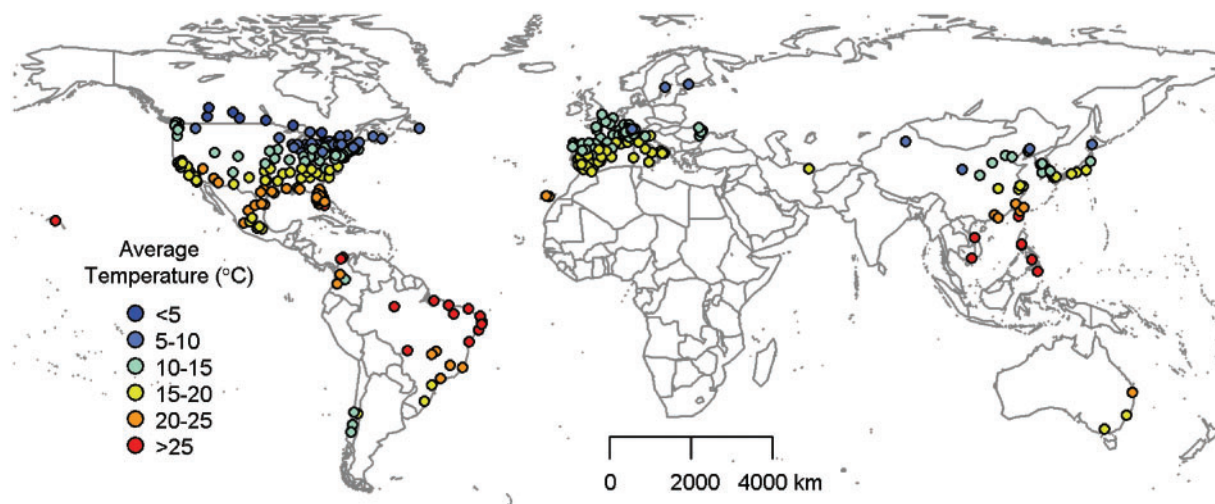


Figure 1. Average daily mean temperature in 340 MCC cities.

Table 3. Descriptive statistics of the 18 city-specific indicators considered in the analysis

| Indicator | Number of cities | Median | IQR range | Range | SD |
|---|------------------|--|----------------------|--------------------|-------------|
| Demographic | | | | | |
| Population | 340 | 418 800 | [174 184; 1 416 981] | [7678; 26 174 599] | 3 068 757.2 |
| Density (population/km ²) | 339 | 2771.0 | [1282.6; 5638.6] | [9.3; 49 045.1] | 7289.3 |
| % population ≥65 years | 320 | 12.8% | [10.4%; 15.1%] | [3.1%;27.2%] | 4.7% |
| Life expectancy (years) | 288 | 80.3 | [78.5; 81.6] | [70.6; 85.0] | 2.3 |
| Socio-economic | | | | | |
| GDP (US\$) | 325 | 37 660 | [27 096; 47 585] | [3168; 78 444] | 15 838.5 |
| Labour productivity (US\$) | 280 | 70 450 | [64 019; 79 388] | [14 647; 366 027] | 29 071.5 |
| Educational level (%) | 265 | 21.5% | [19.8%; 25.6%] | [9.0%; 39.3%] | 5.3% |
| Unemployment rate (%) | 307 | 6.5% | [4.4%; 9.4%] | [2.5%; 29.7%] | 5.2% |
| Gini index | 280 | 0.355 | [0.315; 0.398] | [0.253; 0.484] | 0.047 |
| Poverty gap | 280 | 22.1% | [18.2%; 26.3%] | [9.2%;40.0%] | 6.0% |
| Health system | | | | | |
| Hospital-bed rates | 279 | 29.0 | [23.8; 35.3] | [1.6; 192.0] | 23.0 |
| Urban characteristics | | | | | |
| Type of surrounding region (rural/urban) | 272 | Predominantly urban = 125 Intermediate = 84 Predominantly rural = 63 | | | |
| Urbanized area (%) | 136 | 13.8% | [8.9%; 24.1%] | [0.2%; 68.7%] | 13.4% |
| Green area (m ² per million persons) | 136 | 196.6 | [37.6; 824.6] | [0.01; 6660.6] | 1042.9 |
| Concentration of population in the core (%) | 136 | 83.5% | [72.8%; 93.4%] | [22.6%;100.0%] | 16.0% |
| Sprawl | 100 | -0.99 | [-2.71; 1.79] | [-12.13;10.97] | 4.0 |
| Air pollution | | | | | |
| PM _{2.5} (µg/m ³) | 340 | 9.6 | [8.2; 13.9] | [4.7; 103.1] | 13.2 |
| NO ₂ (ppb) | 339 | 2.37 | [1.08; 4.47] | [0.04; 23.3] | 3.16 |

deviation (SD) increase of the indicator (provided in Table 3). No indicator is associated with cold-related AF. For heat, among demographic indicators, high life expectancy and high population density predicted high AF. Regarding the socio-economic indicators, GDP and educational level were positively associated with heat-related AF%. An inverse association was observed between number of hospital

beds pro-capita and heat-related AF%. Cities with more inequalities (higher Gini index) had a larger mortality impact attributable to heat. Among the urban and environmental indicators considered, cities surrounded by a predominantly rural region and those with a larger green surface showed lower heat-related AF%, whereas PM_{2.5} was positively associated with heat AF%.

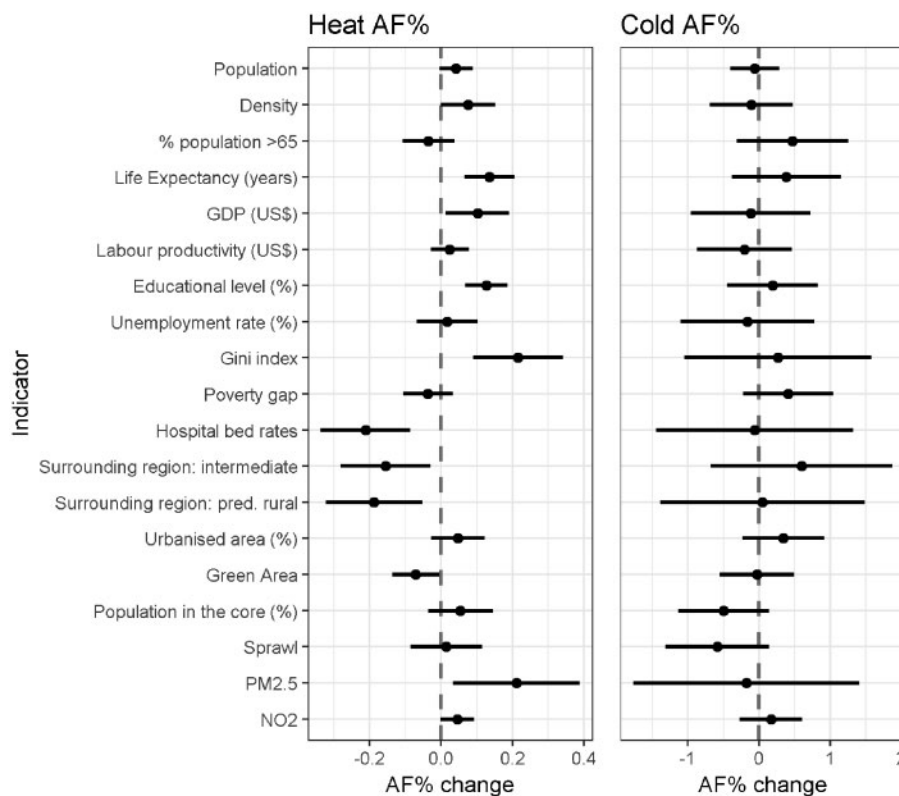


Figure 2. Associations between the indicators and heat and cold AF%. Coefficients and 95% confidence intervals calculated from a meta-regression model adjusted by country and weather variables. Results are expressed as AF% change for standard deviation increase in the indicators. The estimates of the coefficients and 95% confidence intervals are reported in [Supplementary Table 3](#), available as [Supplementary data](#) at *IJE* online.

To give some insight into the inter-relationship between indicators and their association with attributable mortality, we performed a PCA. [Supplementary Figures S1](#) and [S2](#), available as [Supplementary data](#) at *IJE* online, show the correlation matrix and the results of the analysis. The first two principal components explained 44.4% of the total inertia. The first component seems characterized by the economic development of the MCC cities: high positive loading scores (represented by arrows) were observed for GDP, educational level and life expectancy. All these three variables showed a positive association with heat-related AF%. The second component characterized cities with higher levels of air pollution (PM_{2.5} and NO₂), unemployment rates, inequalities (Gini index), poverty gaps, population and density. PM_{2.5}, Gini index and density were all positively associated with heat-related AF%.

Discussion

This study is based on the largest dataset ever collected to assess city-level modifiers of the temperature–health associations, which include more than 50 million deaths in 22 countries. The analysis allows investigating the heterogeneity of temperature-attributable mortality across 340 cities with a wide range of demographic, socio-economic and

urban characteristics. Strengths of the study are the use of a standardized set of indicators, as well as the application of flexible statistical methods. Our findings suggest that more developed cities are perhaps surprisingly characterized by higher mortality attributable to heat, as indicated by the significant association with GDP, life expectancy and educational level. Furthermore, a second pattern emerged, with higher impact of heat on mortality in cities characterized by high population density, inequalities, pollution levels and fewer green spaces.

Cities have been centres of innovation and growth and the engines of economic development, but they are particularly vulnerable to the effects of climate change.^{6,31,32} The nature of urban infrastructure creates microclimates that affect temperature; the urban heat island effect is an example, where cities are warmer than their surrounding hinterlands due to the thermal storage capacity of the built environment.³³ In our results, urban density is associated with an increased heat effect, which is also shown in other contextual studies.^{5,14,19}

We used the OECD regional typology to characterize the region surrounding the urban setting considered in the analysis. This indicator is based on population density, degree of rurality and size of the urban centres located within the region. This indicators allows the identification of 63

cities in predominately rural regions (mainly based in the USA and Spain) and 84 in intermediate (both rural and urban) regions more evenly distributed across countries. These cities show a lower heat effect—a result that could be explained by a lower urban heat island effect and that is consistent with the increased heat effect observed for urban density.

Additional factors contribute to the vulnerability of cities. Among those of particular relevance are demographic structure, low socio-economic status and social inequity. In our study, we found a positive association between the Gini index of the city's region (an indicator of inequality) and heat impact. This result is consistent with those observed in contextual^{10,11,19,34} and individual³⁵ studies showing a higher heat effect on communities or subjects with lower socio-economic status. Poorer housing conditions, lower prevalence of air conditioning, poorer health status and limited access to health care have been suggested as factors responsible for the increased heat effect in more deprived communities.^{10,11,19} The elderly are more sensitive to non-optimal temperatures due to their higher prevalence of debilitating diseases, such as heart conditions, Alzheimer's disease and dementia,³⁶ which are associated with an increased effect of temperature on mortality.¹⁹ In our study, we did not observe evidence of an association between the proportion of people aged more than 65 years and heat (or cold) attributable fraction. These results could be partially explained by the limited range of variation in age distributions across areas within the same country, as shown in our study, where the IQR range of the country-centred proportion aged more than 65 years was (−1.8%; 1.1%) on average within countries. Moreover, the proportion of elderly populations is higher in less urbanized and dense cities [+2.5% (+1.5%; +3.5%)]. The limited range of the exposure and possible confounding effect of urbanization could have limited in our study the power to detect the modifier role of age on the heat effect. We also note that our data are community-level and that future work with individual-level data is more suited to investigating these issues.

Urbanization is part of the development process and is generally associated with higher income, education and productivity level³³; this relationship is shown in our study with a positive correlation ($r=0.33$) between GDP and city density. At the individual level, higher income and education have been associated with lower heat-related mortality³⁵ due to the higher quality of housing and better access to information. In our study, however, heat-related impacts are higher in cities with a higher economic development characterized by a higher GDP, productivity, educational level and life expectancy. Using GDP as an indicator, Anderson and Bell¹⁰ observed a similar positive

contextual association in 107 US urban communities, whereas Hajat and Kosatky³⁷ found a negative association with GDP when meta-regressing heat coefficients across studies internationally. No association was observed at a contextual level in three other studies.^{13,34,38} The increased impacts of heat on cities with higher GDP, educational level and life expectancy are not necessarily due to those cities being more unequal, as the correlation of those indicators with Gini is low. One explanation might be an association between economic development with features of urbanization such as the urban heat island, but further studies, including individual-level socio-economic indicators, are needed to clarify this.

The vulnerability of cities to climate change has motivated the development of city-level adaptation measures,^{6,39} among which are urban planning and design including, for instance, cooling by greening and ventilation. Several studies have evaluated the modification effect of urban-landscape characteristics on the temperature–mortality association.^{40–49} They used different neighbour-level indicators related to urban land use and land cover (e.g. impervious surface, open space, vegetation abundance), with some evidence of a protective effect of vegetation to reduce the heat effect on mortality.^{41,44,49} These results are consistent with the negative association between green areas and heat AF% observed in our multi-city study.

Air pollution is also a well-known public-health risk factor. Particulate matters (PM₁₀, PM_{2.5}), ozone, nitrogen dioxide and sulphur dioxide have been linked to increases in morbidity and mortality.⁵⁰ There has been increasing interest in the synergist effect of temperature and pollution on morbidity and mortality.^{51,52} Suggested mechanisms under the synergy hypothesis are, among others, that episodes of air pollution can increase vulnerability to the effects of temperature (e.g. respiratory diseases) and that elderly populations with deficiency of thermoregulation might suffer from high pollution levels.⁵³ The synergistic effect of pollutants and temperature has been studied mostly using case-only or time-series studies, with some evidence of an increased effect of particulate matters at higher temperatures.^{51,52} In our study, we found a tendency for a higher AF% for heat in cities with higher levels of pollution as measured by PM_{2.5} and NO₂; Benmarhnia *et al.*¹¹ found a similar contextual association between NO₂ and heat effect in Paris. These results need to take into account possible ecological confounding, as, in our dataset, the chronic level of pollutant examined (PM_{2.5} and NO₂) is correlated with the city population and density, and shares with these urban-density indicators the tendency to increase the measured heat AF%.

Few studies have evaluated the role of healthcare access to reduce the temperature-related mortality.^{13,34,37} Our

finding of reduced heat AF in cities with more hospital beds provides some evidence that an increased level of health services is an important component of adaptive capacity in an urban context.

Few studies have evaluated the role of area-level indicators as modifiers of cold effects on mortality with inconsistent results.^{10,12–14,19,54} In our analysis, climate variables explain 22% of the heterogeneity, suggesting for cold-related effects a greater role of acclimatization. Moreover, more complex mechanisms for cold-related effects have been described⁵⁵ that may not be well captured by our set of indicators. Further research is needed in this area, possibly increasing the number of cities or the set of indicators, or with addition data such as individual-level data.

This study has several advantages. It represents the first investigation in which modifiers to both cold and heat effects at the city level were simultaneously assessed in a wide multi-country setting through a common study design and statistical framework. Previous multi-country studies^{34,35,37,38} relied on simplifications of the exposure–response function^{34,37,38} or qualitatively reviewed the evidence.³⁵ The statistical framework used in this analysis is based on a two-stage design that incorporates DLNMs and multivariate meta-regression to flexibly characterize complex temperature–health dependencies at a local level and to investigate their variations across cities.⁵⁶ We used the OECD Regional and Metropolitan Database as a source for defining socio-demographic indicators at the city level. This choice ensures a set of indicators collected using standardized criteria. We must also acknowledge some limitations. The observational periods and data-collection procedures are not uniform across all countries. Logistical constraints hinder perfectly consistent data streams across the globe, as different countries have various protocols for data acquisition and maintenance. However, our study design is not sensitive to potential biases arising from these differences and can appropriately pool information from data obtained from different sources. Specifically, our two-stage analytical framework includes indicators for countries as meta-predictors in the second-stage meta-regression. This means that, implicitly, the comparison is based on variations across locations within the same country, as any structural difference across countries is accounted for by the fixed-effects indicators. These differences include potential variations due to non-overlapping periods. The time frame of data collection varied for some variables and the reference period used for indicators varied between 2000 and 2014. Moreover, some of the indicators were measured after the actual city-specific time period of investigation. As a consequence, there could be some measurement errors in the level of the indicator associated with

each city for the observational period. Under the hypothesis of no systematic bias within a country, this measurement error should lower the association under study towards a conservative error. However, we found a high correlation between indices in different years (data not shown), consequently this conservative error should be minor. The dataset includes several regions around the world, including developed and developing countries, but entire areas of the world are not covered, and there is a lack of information from countries with a lower degree of socio-economic development. Results might therefore not be globally representative. In our analysis, we considered each indicator as an explanatory variable in a meta-regression model adjusted by country and weather variables. We did not attempt a multivariable model, as many indicators exhibited collinearity, as shown in the PCA. Although it is an interesting research area, we did not plan subgroup analyses by climate zones or geographical regions. Further work increasing the number of locations, hopefully including developing countries, is needed to address this research question.

Conclusion

This study identifies several city characteristics that modify the vulnerability of urban populations to heat. These results can be used for determining the health burden projected in the future under specific climate-change and socio-demographic scenarios, and for the implementation of urban-development plans to mitigate the risk.

Supplementary data

Supplementary data are available at *IJE* online

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