

Excess mortality attributed to heat and cold: a health impact assessment study in 854 cities in Europe



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Summary

Background Heat and cold are established environmental risk factors for human health. However, mapping the related health burden is a difficult task due to the complexity of the associations and the differences in vulnerability and demographic distributions. In this study, we did a comprehensive mortality impact assessment due to heat and cold in European urban areas, considering geographical differences and age-specific risks.

Methods We included urban areas across Europe between Jan 1, 2000, and Dec 12, 2019, using the Urban Audit dataset of Eurostat and adults aged 20 years and older living in these areas. Data were extracted from Eurostat, the Multi-country Multi-city Collaborative Research Network, Moderate Resolution Imaging Spectroradiometer, and Copernicus. We applied a three-stage method to estimate risks of temperature continuously across the age and space dimensions, identifying patterns of vulnerability on the basis of city-specific characteristics and demographic structures. These risks were used to derive minimum mortality temperatures and related percentiles and raw and standardised excess mortality rates for heat and cold aggregated at various geographical levels.

Findings Across the 854 urban areas in Europe, we estimated an annual excess of 203 620 (empirical 95% CI 180 882–224 613) deaths attributed to cold and 20 173 (17 261–22 934) attributed to heat. These corresponded to age-standardised rates of 129 (empirical 95% CI 114–142) and 13 (11–14) deaths per 100 000 person-years. Results differed across Europe and age groups, with the highest effects in eastern European cities for both cold and heat.

Interpretation Maps of mortality risks and excess deaths indicate geographical differences, such as a north–south gradient and increased vulnerability in eastern Europe, as well as local variations due to urban characteristics. The modelling framework and results are crucial for the design of national and local health and climate policies and for projecting the effects of cold and heat under future climatic and socioeconomic scenarios.

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Introduction

Heat and cold are now established health risk factors, with several studies reporting important mortality effects in populations around the world.^{1–3} The associated health burden is expected to increase with climate change, especially under the most extreme scenarios of global warming.^{4,5} However, robust estimates of excess mortality in the current and future periods are still challenging to obtain due to the numerous factors influencing vulnerability to heat and cold, including climatic, environmental, and socioeconomic conditions.⁶ These factors represent the main drivers of variation in mortality risks, which have been shown to differ geographically and across age groups.

Cities are particularly affected by environmental stressors and potential impacts of climate change.⁷ Around 40% of the EU population lives in cities of at least 50 000 inhabitants⁸ and the urban population experiences overall higher levels of temperature stress,

particularly heat.^{9,10} In addition, European cities vary in socioeconomic, environmental, and climatic conditions, and it is reasonable to expect that these differences lead to high variation in vulnerability to temperature-related risks. Better knowledge of the city-level mortality effects of climate change-related stressors is crucial for the design and implementation of adaptation policies.

Few European-wide assessments of the mortality burden related to temperature have been published. Martínez-Solanas and colleagues⁵ estimated the Europe-wide risk of both heat and cold at the regional level, whereas other studies have provided evidence at the local level, focusing on specific European countries^{11–14} or regions.¹⁵ Other assessments have included the European region in global evaluations.² Although some consistent results emerge from these analyses, such as an overall north–south gradient and increased risks of heat in more urbanised areas, there are also disparities in the reported estimates.

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See Online for appendix

Research in context

Evidence before this study

The mortality risks and effects related to non-optimal temperature are widely studied topics with evidence provided for many countries in Europe. We searched PubMed, Web of Science, and Google Scholar for mortality impact assessments in Europe, whether included in global studies or restricted to smaller parts of the continent, using the search terms “temperature” AND “mortality” AND “impact”, for articles published between Jan 1, 2010, and Dec 31, 2021, in English. Our search revealed that a handful of global studies included a small number of European cities in their assessment, had aggregated evidence at the national or regional level, or, for studies of a small-area level, were restricted to single countries. In particular, studies have focused almost exclusively on western European countries compared with Scandinavian or eastern locations. Finally, and more importantly, no study has accounted for demographic differences across Europe.

Added value of this study

This Europe-wide assessment provides risk estimates and mortality impact assessment related to both heat and cold

across a representative selection of urban areas, namely 854 European cities, including several regions with little previous evidence, such as Scandinavia and eastern Europe. Additionally, estimates of this study account for an extensive list of city-level socioeconomic, climatic, and environmental characteristics to represent differences in vulnerability across countries and regions. This study also fully integrates age as a risk modifier and provides age-standardised excess mortality estimates to account for demographic differences.

Implications of all the available evidence

The results and maps provided in this study offer a comprehensive picture of the mortality impact of non-optimal temperature across Europe, characterising geographical differences in vulnerability among urban populations across the continent. This evidence is valuable to policy makers to protect the most vulnerable populations and identify strategies to design effective adaptation policies. The proposed modelling framework provides a blueprint for the projection of non-optimal temperature-related mortality under various climate and socioeconomic scenarios.

Differences in risks and related burdens can be partly attributed to the geographical scale of the studies. Previous assessments have focused either on large-scale analyses that do not fully represent local vulnerabilities in urban populations or were based on data with higher resolution but with little geographical scope. Most of the evidence is also limited to western European countries, with Scandinavia and eastern Europe less represented.^{16,17} Another important limitation is the absence of consideration for demographic differences, whereby the differential risks across age groups reported in the literature can lead to variation in estimated mortality effects.³ In addition, previous analyses have not considered other characteristics that can modify the vulnerability to heat and cold, such as location-specific socioeconomic and environmental variables. These shortcomings pose important limits to the design and implementation of effective public health and climate adaptation strategies.

The objective of the present study is to provide a comprehensive and consistent assessment of the current mortality burden associated with non-optimal temperature across most European cities, characterising differences in risks due to local distributions of vulnerability factors and demographic distributions. We take advantage of a large dataset of daily time series of mortality and temperature to derive exposure-response relationships and excess mortality in 854 cities across Europe. The assessment is based on an advanced modelling framework that allows an in-depth exploration of geographical differences with the provision of age-specific risks and age-standardised effects to

facilitate the comparison across locations and countries. The model and results can be applied for projections in future climatic conditions, accounting for shifts in the age distribution and various socioeconomic scenarios, and eventually be used to design adaptation policies.

Methods

Selection of representative cities

We defined a comprehensive list of European cities using the Urban Audit dataset of Eurostat.¹⁸ This database includes data of 870 European urban areas exceeding 50 000 inhabitants, based on the degree of urbanisation methodology.¹⁹ From this list of cities, we excluded remote overseas locations with very different climates from France, Spain, Portugal, and Reykjavik (Iceland)—eg, Azores and Canary Islands. The final sample included 854 cities from 30 countries (27 countries in the EU and Norway, Switzerland, and the UK).

For a selection of 232 cities, we were able to retrieve observed daily counts of mortality for all causes or non-accidental causes (International Classification of Diseases [ICD]-9 codes 0–799 and ICD-10 codes A00-R99) in overlapping periods from the database of the Multi-country Multi-city (MCC) Collaborative Research Network.¹⁴ The available MCC cities cover the various regions and climates represented in the Urban Audit dataset. Daily mortality data were available as both all-age and age-specific series, with age groups differing between countries (appendix pp 3–6).

Additionally, we retrieved annual vital statistics for all 854 cities from the dataset of Eurostat.²⁰ These data were

available at various nested levels of the Nomenclature of Territorial Units for Statistics (NUTS). Specifically, we collected crude death rates and the demographic structure from the corresponding NUTS3 level, and life expectancy from the NUTS2 level, by 5-year age groups. This information was used to reconstruct predicted city-level daily mortality counts and the average age of death for selected age groups in the period 2000–20.

We extracted daily series of mean air temperature at 2 m from the ground for each of the 854 cities for the period 1990–2019 from the fifth generation of European Reanalysis (ERA5)-Land dataset.²¹ ERA5-Land represents one of the most advanced climate reanalysis products and offers land-surface data on a global grid with a resolution of approximately 9 km. The ERA5-Land database was found to provide a satisfactory proxy to station-based series.^{22,23} Temperature series were created by averaging the grid cells-specific series with centroids within the spatial boundaries of each city.

We also collected several city-specific variables to differentiate patterns of vulnerability across urban populations within Europe. These variables were gathered from multiple sources and represent various socioeconomic, environmental, topographical, and infrastructural characteristics. Similarly to mortality and population data, the variables were defined by averaging all available values in 2000–20. Specifically, we collected information on 22 characteristics (described in appendix pp 7–9). Total population, the proportion of population aged older than 65 years, population density, and the proportion of single-person households were extracted directly from the Urban Audit dataset. Other variables unavailable at the city level were gathered at higher administrative levels. Gross domestic product was assigned from the corresponding NUTS3. Other factors including life expectancy at birth, unemployment rate, education level, deprivation rate, and hospital bed rates were collected at NUTS2. In addition, we derived some variables from remote sensing satellite measurements and global reanalysis datasets, including the normalised difference vegetation index from the moderate resolution imaging spectroradiometer instrument onboard Terra and Aqua US National Aeronautics and Space Administration satellites,²⁴ and we derived variables for fine particulate matter (PM_{2.5}) and nitrogen dioxide (NO₂) concentrations from the Atmospheric Composition Analysis Group website.²⁵ Land cover characteristics were retrieved from the Copernicus Pan-European High Resolution Layers, including characteristics for imperviousness, tree cover density, grassland, water and wetness, and small woody features. Similarly to the temperature data, we extracted and averaged all pixels with centroids within the city boundaries. Finally, we derived mean and range annual temperature directly from the temperature series described in the previous section.

	Number of cities	Cities in Multi-country Collaborative Research Network	Population	Annual deaths	Mean temperature (IQR) in Celsius (°C)
Northern Europe					
Denmark	4	0	1 211 882	10 719	9.1 (3.9 to 14.3)
Estonia	3	3 (100%)	565 429	6 100	6.4 (−0.2 to 13.9)
Finland	9	1 (11%)	1 903 948	16 312	5.1 (−1.3 to 12.8)
Ireland	5	1 (20%)	1 489 041	9 162	10.2 (7.2 to 13.6)
Latvia	10	0	1 098 034	15 893	7.4 (0.9 to 14.6)
Lithuania	6	0	1 316 515	17 917	7.8 (1.1 to 15.0)
Norway	4	1 (25%)	1 098 188	7 542	5.5 (0.4 to 11.2)
Sweden	14	3 (21%)	3 726 071	30 938	7.4 (1.3 to 13.8)
UK	135	103 (76%)	35 643 424	301 742	9.9 (6.0 to 13.9)
Western Europe					
Austria	6	0	2 454 346	21 943	8.7 (1.8 to 15.2)
Belgium	15	0	3 251 039	31 110	10.7 (6.0 to 15.5)
France	72	18 (25%)	24 360 709	194 887	12.1 (7.2 to 16.8)
Germany	127	12 (9%)	28 937 024	310 577	10.0 (4.3 to 15.5)
Luxembourg	1	0	91 239	647	9.7 (4.3 to 14.9)
Netherlands	47	5 (11%)	7 387 464	63 222	10.7 (6.0 to 15.4)
Switzerland	12	8 (67%)	2 506 596	20 025	9.1 (2.9 to 14.8)
Eastern Europe					
Bulgaria	18	0	3 232 248	46 878	11.8 (4.5 to 19.0)
Czechia	18	3 (17%)	3 172 388	33 165	9.0 (2.4 to 15.4)
Hungary	19	0	3 499 014	45 490	11.5 (4.1 to 18.6)
Poland	68	0	12 999 552	144 574	9.1 (2.5 to 15.8)
Romania	35	8 (23%)	7 627 652	100 534	10.8 (3.0 to 18.3)
Slovakia	8	0	1 122 490	10 912	9.4 (2.0 to 16.3)
Southern Europe					
Croatia	7	0	1 390 152	16 410	13.0 (6.8 to 19.4)
Cyprus	3	3 (100%)	599 105	4 085	20.3 (13.9 to 26.4)
Greece	14	1 (7%)	4 296 023	45 581	15.7 (9.5 to 22.1)
Italy	87	16 (18%)	21 359 668	221 951	14.6 (8.8 to 20.4)
Malta	1	0	214 150	1 627	19.3 (14.8 to 23.8)
Portugal	14	2 (14%)	4 384 586	43 230	15.2 (11.4 to 19.1)
Slovenia	2	0	3 888 799	35 160	10.4 (3.6 to 16.8)
Spain	90	44 (49%)	23 684 538	211 589	15.3 (10.2 to 20.3)
Total	854	232 (27%)	205 011 394	1 988 278	10.8 (5.0 to 16.8)

Table 1: Descriptive statistics of selected cities by country

City and age-specific risk estimation

The mortality impact assessment was based on an advanced three-stage modelling framework. Full modelling and computational details are provided in the appendix (p 10). In the first stage, we estimated temperature-related risks in the subset of 232 cities with observed daily mortality data through a quasi-Poisson regression model. Exposure-response functions (ERFs) between temperature and mortality accounting for non-linearity and lagged effects were specified with a distributed lag non-linear model,²⁶ using a parameterisation previously applied in other multi-country analyses.¹ The model also included indicator terms for the day of the week and a natural spline

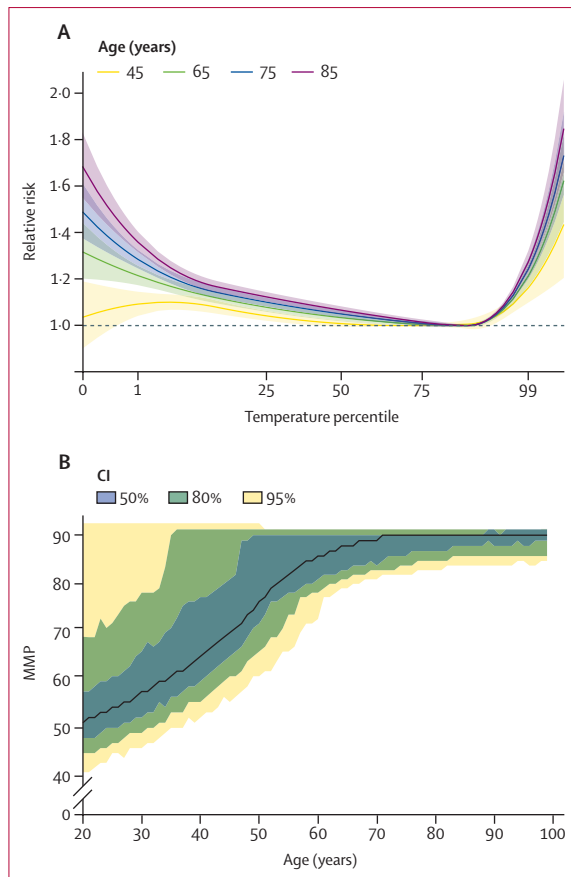


Figure 1: Overall age effect in the predicted risk
 (A) Pooled overall cumulative exposure–response relationship predicted at several ages. (B) MMP versus age. Filled ribbons represent several degrees of CIs. MMP=minimum mortality percentiles.

of time with 7 degrees of freedom per year to control for time-varying confounders. We excluded data for August, 2003, from the model because results were sensitive to the exceptional mortality effect related to the European heat wave in some locations.

In each city, the model is fitted on multiple age-specific series, when available, or otherwise on the single all-age mortality data. Age groups, varying across countries (see appendix p 5), were merged when needed to ensure a minimum total death count of 5000 to avoid convergence issues in the first-stage regression.²⁷ Therefore, we obtained 577 age-specific sets of estimates across the 232 cities. We then extracted the reduced coefficients representing the overall cumulative ERFs for each city and age group.²⁸

In the second stage, we first pooled all the 577 ERF coefficients in a repeated-measure multivariate meta-regression model, with city-level random effects assigned to multiple age-specific observations.²⁹ The model included smooth terms to represent age effects and composite vulnerability terms to capture geographical differences in temperature-related mortality risks, in

addition to indicators for the four cardinal regions in Europe.³⁰

To model age differences, we first attributed a specific value to each city-specific age group. This value corresponded to the average age of death computed using 5-year age-specific death rates. We created a continuous age variable, which was included as a linear term in the meta-regression model. The composite vulnerability terms were created through partial least-squares (PLS)³¹ reduction of the 22 city-specific characteristics. The PLS procedure allowed us to combine information from a high number of highly correlated variables to define a lower number of uncorrelated components that can easily be integrated within the meta-analysis framework to disentangle geographical differences in risk. We eventually included the first four PLS components following a selection based on minimising the Akaike information criterion of the meta-regression model. In addition, we captured spatial differences in ERFs not explained by city characteristics by interpolating residuals from the meta-regression using ordinary kriging.³² This procedure created a continuous spatial field of local differentials in vulnerability (appendix pp 20–23).

We used these models as predictive tools to extrapolate age and city-specific ERFs for the full set of 854 cities. The point estimates and associated variance or covariance matrix of the ERF coefficients were computed as the sum of the predictions from the meta-regression model, given specific age values and observed characteristics reduced to PLS components, plus deviations defined by the kriging field. From ERFs, we reported relative risks at the first and 99th percentiles as well as the minimum mortality percentile (MMP) and minimum mortality temperature (MMT). Uncertainty in MMT and MMP was assessed following a previously used method.³³

Mortality impact assessment

In this final stage, we used the framework described to predict ERFs for five age groups (20–44, 45–64, 65–74, 75–84, and ≥ 85 years) for each of the 854 cities. Data for people younger than 20 years were excluded from the impact assessment due to low availability and high uncertainty of data in the youngest age groups. We also predicted the city-specific average age of death within each age group, which was computed from crude death rates and life expectancy at 85 years for the oldest age group. For each city and age group, we then computed the excess number of deaths due to heat and cold separately using a standard method.³⁴ These numbers were then divided by the total population to compute the contribution of each age group to the excess deaths. To compare the impact across locations with potentially different demographic distributions, we then computed standardised death rates as follows: the excess number of deaths was first divided by the population to obtain

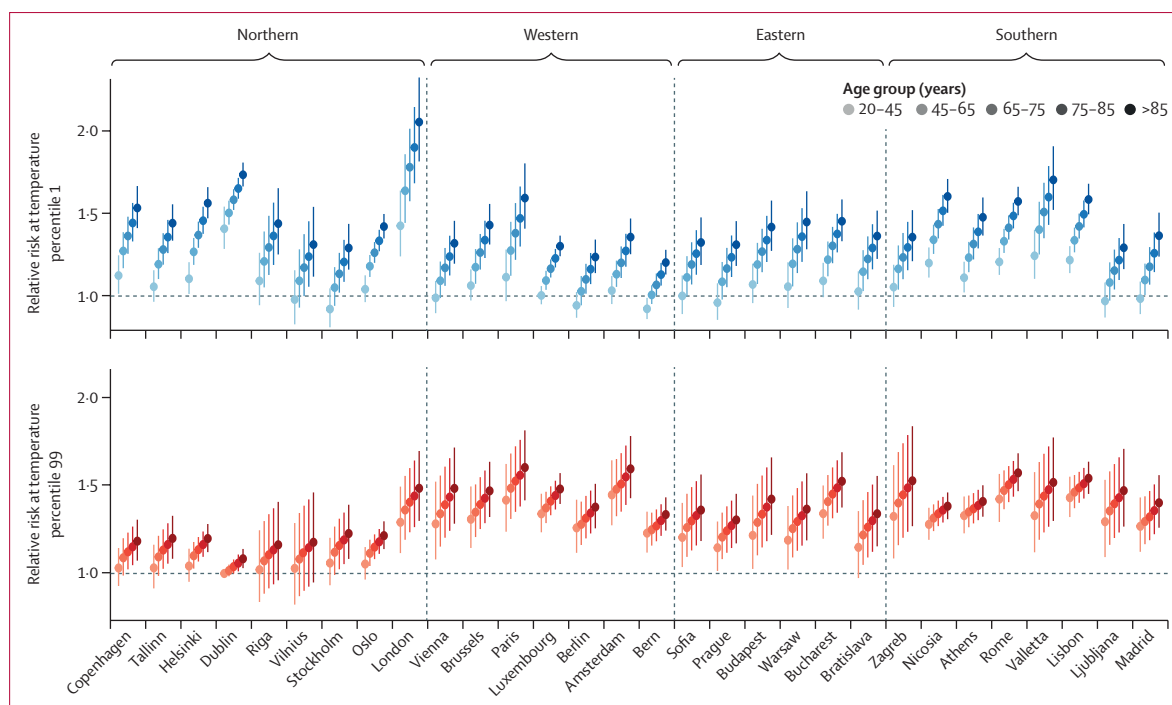


Figure 2: Cold (first percentile of temperature, in blue) and heat (99th percentile of temperature, in red) relative risks in capital cities for five age groups. Relative risks are predicted at the average age of death for each group. Separations correspond to the M49 region classification.

age-specific excess death rates, which were then combined in standardised death rates computed for each city (using the European standard population of 2013 as a reference).

Uncertainty in excess deaths and rates was quantified as empirical CIs using Monte Carlo simulations, adapting a previously proposed method to account for the dependencies related to the pooling of city-specific risks.³⁴ Specifically, we did 1000 Monte Carlo iterations by sampling directly from the estimated coefficients and associated variance and covariance matrix of the meta-regression model and then the residuals of the kriging procedure. Details are provided in the appendix (p 24).

Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

Descriptive statistics aggregated at the country level are shown in table 1, including the subset of 232 MCC cities with observed mortality series used to estimate the risk associations (appendix p 6). The assessment covered a population of over 200 million inhabitants of cities in the 30 countries. Luxembourg is the smallest country with a single city representing 91 239 people, whereas the UK had the largest representation with 135 cities and more than 35 million people. The mortality impact

assessment included almost 2 million deaths occurring annually across the 854 cities. The countries represent diverse climates within Europe, with mean temperatures ranging from 5.1°C (IQR −1.3 to 12.8) in Finland to 20.3°C (13.9 to 26.4) in Cyprus.

The pooled exposure–response associations for different ages, representing average temperature-related mortality relative risks (RR) across Europe and represented as temperature percentiles using the European average temperature distribution, are shown in Figure 1A. The curves show the common reversed-J shape, with a moderately high MMP and the mortality risk increasing for both colder and hotter temperatures. The shapes of the curves were very similar for ages 65 and older, with the curves becoming steeper as age increases. Specifically, the cold-related RRs estimated at the first percentile versus the MMP varied from 1.21 (95% CI 1.17–1.26) for people aged 65 years to 1.36 (1.31–1.40) for people aged 85 years. The heat-related RR at the 99th percentile raised from 1.21 (1.17–1.26) for people aged 65 years to 1.27 (1.23–1.32) for people aged 85 years. The curve predicted for people aged 45 years was much flatter than for those aged 65 years and older, with a lower MMP and a slight decrease of risk of exposure to extreme cold but still a risk associated with heat. The change of MMP with age is shown in figure 1b, which suggests an increasing trend in MMP until it reaches the 90th temperature percentile at age 70 years. The uncertainty in MMP at younger ages reflects the lower statistical power in these age bands.

	Excess deaths (cold)	Excess deaths (heat)	Attributable fraction (%; cold)	Attributable fraction (%; heat)	Excess death rates (per 100 000 person-years; cold)	Excess death rates (per 100 000 person-years; heat)	Standardised excess death rates (per 100 000 person-years; cold)	Standardised excess death rates (per 100 000 person-years; heat)
Northern Europe								
Denmark	1319 (1080 to 1537)	44 (24 to 61)	8.64 (7.08 to 10.08)	0.29 (0.16 to 0.40)	144 (118 to 168)	5 (3 to 7)	165 (134 to 193)	6 (3 to 8)
Estonia	727 (495 to 954)	29 (11 to 46)	8.49 (5.78 to 11.14)	0.34 (0.12 to 0.53)	165 (112 to 217)	7 (2 to 10)	177 (120 to 232)	7 (3 to 11)
Finland	2231 (1548 to 2821)	69 (26 to 108)	9.28 (6.44 to 11.74)	0.29 (0.11 to 0.45)	153 (106 to 193)	5 (2 to 7)	165 (115 to 209)	5 (2 to 8)
Ireland	1664 (1442 to 1866)	10 (1 to 18)	12.71 (11.00 to 14.24)	0.08 (0.01 to 0.14)	153 (132 to 171)	1 (0 to 2)	227 (196 to 255)	1 (0 to 3)
Latvia	2095 (1322 to 2855)	126 (-17 to 251)	9.72 (6.14 to 13.25)	0.59 (-0.08 to 1.16)	240 (151 to 327)	14 (-2 to 29)	243 (154 to 331)	15 (-2 to 29)
Lithuania	2301 (1431 to 3178)	141 (-33 to 289)	9.39 (5.84 to 12.96)	0.58 (-0.13 to 1.18)	223 (138 to 307)	14 (-3 to 28)	233 (145 to 322)	14 (-3 to 29)
Norway	1085 (794 to 1356)	28 (10 to 42)	9.89 (7.24 to 12.36)	0.25 (0.09 to 0.38)	131 (96 to 163)	3 (1 to 5)	167 (123 to 209)	4 (2 to 6)
Sweden	4168 (3297 to 4909)	134 (83 to 181)	8.92 (7.06 to 10.51)	0.29 (0.18 to 0.39)	148 (117 to 175)	5 (3 to 6)	153 (121 to 181)	5 (3 to 7)
United Kingdom	42 915 (37 396 to 47 920)	762 (530 to 975)	9.87 (8.60 to 11.03)	0.18 (0.12 to 0.22)	162 (141 to 181)	3 (2 to 4)	183 (159 to 204)	3 (2 to 4)
Total	58 505 (51 237 to 65 142)	1343 (880 to 1763)	9.76 (8.55 to 10.87)	0.22 (0.15 to 0.29)	163 (142 to 181)	4 (2 to 5)	183 (160 to 204)	4 (3 to 6)
Western Europe								
Austria	1586 (845 to 2228)	215 (158 to 273)	4.97 (2.65 to 6.98)	0.67 (0.49 to 0.86)	81 (43 to 114)	11 (8 to 14)	90 (48 to 127)	12 (9 to 15)
Belgium	2093 (1422 to 2763)	247 (196 to 298)	4.48 (3.04 to 5.92)	0.53 (0.42 to 0.64)	85 (58 to 113)	10 (8 to 12)	82 (56 to 108)	10 (8 to 12)
France	17 730 (12 790 to 21 886)	1388 (1107 to 1653)	5.96 (4.30 to 7.35)	0.47 (0.37 to 0.56)	99 (71 to 122)	8 (6 to 9)	89 (63 to 110)	7 (6 to 8)
Germany	19 728 (13 778 to 25 405)	2886 (2380 to 3410)	4.37 (3.05 to 5.63)	0.64 (0.53 to 0.76)	84 (59 to 109)	12 (10 to 15)	81 (57 to 105)	12 (10 to 14)
Luxembourg	46 (27 to 64)	6 (4 to 7)	4.76 (2.80 to 6.63)	0.59 (0.44 to 0.73)	66 (39 to 91)	8 (6 to 10)	84 (50 to 117)	10 (8 to 13)
Netherlands	3419 (1463 to 5258)	479 (346 to 601)	3.68 (1.58 to 5.67)	0.52 (0.37 to 0.65)	61 (26 to 93)	8 (6 to 11)	70 (30 to 108)	9 (7 to 12)
Switzerland	1538 (889 to 2108)	213 (172 to 250)	4.91 (2.84 to 6.73)	0.68 (0.55 to 0.80)	78 (45 to 107)	11 (9 to 13)	78 (45 to 107)	11 (9 to 13)
Total	46 141 (35 034 to 56 752)	5433 (4511 to 6329)	4.84 (3.68 to 5.96)	0.57 (0.47 to 0.66)	86 (66 to 106)	10 (8 to 12)	83 (63 to 102)	10 (8 to 12)
Eastern Europe								
Bulgaria	5745 (4458 to 7031)	522 (261 to 744)	9.25 (7.18 to 11.32)	0.84 (0.42 to 1.20)	221 (172 to 271)	20 (10 to 29)	266 (206 to 324)	24 (12 to 34)
Czechia	3716 (2391 to 4932)	235 (139 to 324)	8.00 (5.15 to 10.62)	0.51 (0.30 to 0.70)	147 (95 to 196)	9 (6 to 13)	180 (117 to 238)	11 (7 to 15)
Hungary	5295 (4036 to 6543)	402 (230 to 563)	8.78 (6.69 to 10.85)	0.67 (0.38 to 0.93)	189 (144 to 233)	14 (8 to 20)	211 (162 to 261)	16 (9 to 22)
Poland	16 510 (12 280 to 20 579)	1263 (754 to 1737)	8.44 (6.28 to 10.52)	0.65 (0.39 to 0.89)	159 (118 to 198)	12 (7 to 17)	182 (136 to 227)	14 (8 to 19)
Romania	12 939 (10 280 to 15 493)	1137 (633 to 1598)	10.01 (7.95 to 11.99)	0.88 (0.49 to 1.24)	215 (171 to 258)	19 (11 to 27)	262 (209 to 313)	23 (13 to 32)
Slovakia	1203 (890 to 1507)	99 (57 to 138)	8.51 (6.30 to 10.67)	0.70 (0.40 to 0.97)	137 (101 to 172)	11 (6 to 16)	202 (152 to 252)	16 (10 to 23)
Total	45 408 (34 920 to 55 579)	3659 (2203 to 4970)	8.94 (6.88 to 10.94)	0.72 (0.43 to 0.98)	180 (139 to 220)	15 (9 to 20)	213 (165 to 259)	17 (10 to 23)
Southern Europe								
Croatia	1714 (1177 to 2240)	412 (277 to 535)	7.52 (5.17 to 9.83)	1.81 (1.21 to 2.35)	156 (107 to 203)	37 (25 to 49)	178 (123 to 232)	42 (28 to 55)
Cyprus	507 (404 to 611)	74 (52 to 92)	8.29 (6.60 to 9.99)	1.20 (0.86 to 1.51)	111 (88 to 134)	16 (11 to 20)	166 (132 to 199)	23 (17 to 29)
Greece	4693 (3442 to 5899)	738 (459 to 994)	6.98 (5.12 to 8.78)	1.10 (0.68 to 1.48)	138 (101 to 173)	22 (14 to 29)	127 (93 to 160)	20 (13 to 27)
Italy	23 283 (17 955 to 28 269)	5034 (3942 to 6112)	6.75 (5.21 to 8.20)	1.46 (1.14 to 1.77)	135 (104 to 164)	29 (23 to 36)	112 (86 to 136)	25 (19 to 30)
Malta	178 (129 to 226)	35 (22 to 47)	7.73 (5.62 to 9.82)	1.51 (0.95 to 2.06)	104 (76 to 133)	20 (13 to 28)	138 (100 to 175)	27 (16 to 36)
Portugal	4573 (3539 to 5587)	529 (385 to 658)	6.96 (5.38 to 8.50)	0.80 (0.59 to 1.00)	132 (102 to 162)	15 (11 to 19)	129 (100 to 158)	15 (11 to 19)
Slovenia	278 (163 to 381)	70 (44 to 93)	5.41 (3.17 to 7.41)	1.37 (0.86 to 1.81)	90 (53 to 124)	23 (14 to 30)	98 (58 to 134)	25 (16 to 33)
Spain	18 342 (12 300 to 23 265)	2848 (2053 to 3589)	5.55 (3.72 to 7.04)	0.86 (0.62 to 1.09)	98 (66 to 124)	15 (11 to 19)	88 (59 to 111)	14 (10 to 18)
Total	53 566 (40 211 to 65 368)	9738 (7455 to 11 879)	6.34 (4.76 to 7.74)	1.15 (0.88 to 1.41)	120 (90 to 146)	22 (17 to 27)	106 (79 to 129)	19 (15 to 24)
Total	203 620 (180 882 to 224 613)	20 173 (17 261 to 22 934)	7.01 (6.23 to 7.73)	0.69 (0.59 to 0.79)	128 (113 to 141)	13 (11 to 14)	129 (114 to 142)	13 (11 to 14)

Table 2: Country-level annual excess number of deaths, attributable fractions, and raw and age-standardised rates for cold and heat for the population aged 20 years and older

A comparison of the age-specific risks associated with cold and heat in the capital city of each country is displayed in figure 2, which shows the RRs at the first and 99th percentile versus the MMT computed for five different age groups. The cold-related RR increases with age and is slightly higher in northern and southern

countries than in western and eastern countries. High risks for the age group 85 years and older were estimated in London (UK; RR of 2.05 [95% CI 1.82–2.32]), Dublin (Ireland; 1.73 [1.66–1.81]), and Valletta (Malta; 1.70 [1.52–1.91]). Heat-related RRs also showed an increasing trend by age and were generally lower in the northern

region. The city with the highest heat-related RRs across all ages was Paris (France), with a RR of 1.60 (1.42–1.81) for the age group 85 years and older.

The mortality impacts, quantified as the excess number of deaths and fractions, as well as standardised rates for 100 000 person-years, are reported in table 2. Across the 30 countries, we estimated an annual average excess of 203 620 (empirical 95% CI 180 882 to 224 613) deaths due to cold and 20 173 (17 261 to 22 934) due to heat, which amount to attributable fractions of 7.01% (6.23 to 7.73) and 0.69% (0.59 to 0.79), respectively. When reported as standardised excess rates, these figures correspond to 129 (114 to 142) and 13 (11 to 14) excess deaths per 100 000 person-years. Figure 3 shows the raw excess death rates broken down by age groups at the country level. For both cold and heat, the effect was noticeably larger for the oldest age group, with 82 (72 to 91) and seven (six to eight) excess deaths per 100 000 person-years. This excess represented around 60% of the total burden for both cold and heat. In contrast, there was around one death per 100 000 person-years in the youngest age group for cold, and less than one per 100 000 person-years for heat. The impact of cold is important everywhere, but is generally smaller in the western region and larger in the northern and eastern regions, with a maximum of 240 (151 to 327) raw excess deaths per 100 000 person-years due to cold in Latvia. There is wider heterogeneity in the effect of heat, which is low in the northern region, with the exception of Latvia and Lithuania, and much higher in the southern region, with a maximum of 37 (25 to 49) excess deaths per 100 000 person-years in Croatia.

The full geographical distribution of temperature effects across the 854 cities is shown in figure 4. The MMP and MMT display an overall north–south gradient but in opposite directions, with the MMP smoothly decreasing and the MMT increasing as temperature distributions get hotter, although with local exceptions. The MMP ranges from the 68th percentile in Ferrol and San Sebastian (Spain), with overall low values in Mediterranean Europe, to the 96th percentile in several cities within the UK and Ireland. The MMTs range from 14.5°C (empirical 95% CI 14.1–15.0) in Aberdeen (UK) to 27.2°C (27.0–27.8) in Nicosia (Cyprus).

Cold and heat-related standardised excess death rates are shown in figure 4 at the city level and in table 2 at the country level. These standardised risk summaries account for demographic differences and provide a fairer geographical comparison than raw excess death rates. Cold-related standardised excess rates are important in the eastern-most countries as well as the UK and Ireland, with a maximum of 353 (empirical 95% CI 272–429) deaths per 100 000 person-years in Vidin (Bulgaria). Regarding heat-related effects, there was a clear northwest–southeast gradient, with relatively small standardised excess rates in Ireland and the UK, but large standardised excess rates in the southeastern

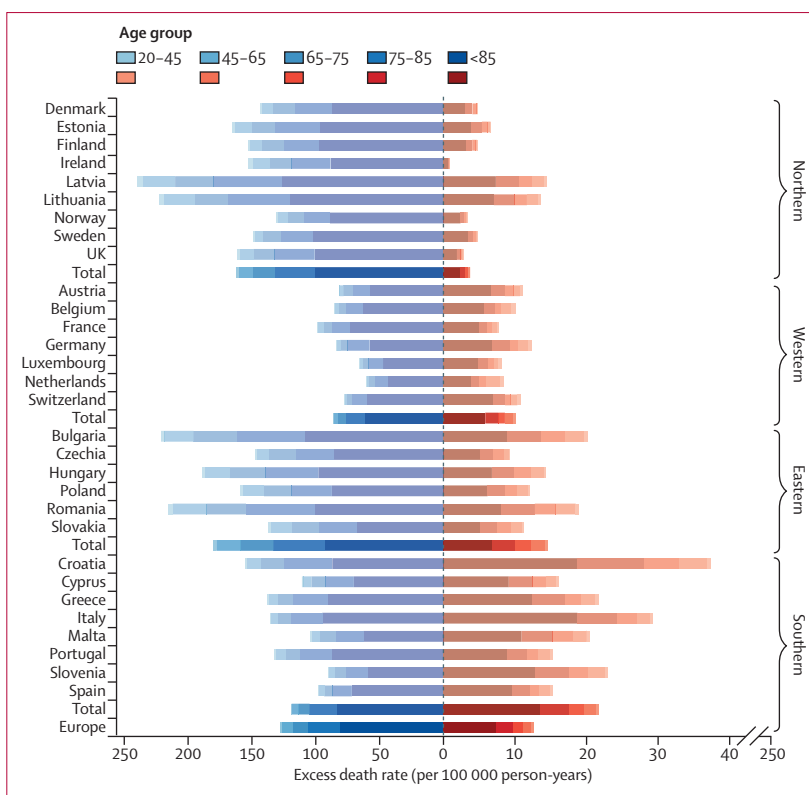


Figure 3: Country-level cold (in blue) and heat (in red) annual raw death rates broken down by age group

countries. The highest heat-related standardised excess death rate was 58 (37–76) per 100 000 person-years in Osijek (Croatia). Heat-related standardised rates were similar in the eastern region compared with the southern region (see table 2), whereas excess deaths in figure 3 were larger in southern countries (as the population was generally older). There was some suggestion of a slight coastal effects, with higher cold-related and lower heat-related effects in locations close to the sea compared with their inland neighbours. All these patterns reflect contributions of city-level characteristics, combined in composite indices of vulnerability included in the second-stage meta-regression model (appendix pp 16–19).

Discussion

This study provides a comprehensive mortality impact assessment related to non-optimal temperatures in the urban population of Europe by evaluating risks and impacts in 854 cities across the continent. Results indicated large vulnerability differences between ages and low vulnerability to cold for younger ages, indicated by lower MMPs and a flatter exposure–response function at lower percentiles. The vulnerability to heat also increased with age, although the difference was less steep than it was for cold, suggesting that the effect of heat affected all ages more homogeneously. Overall, the population aged older than 85 years contributed around 60% of the total mortality burden.

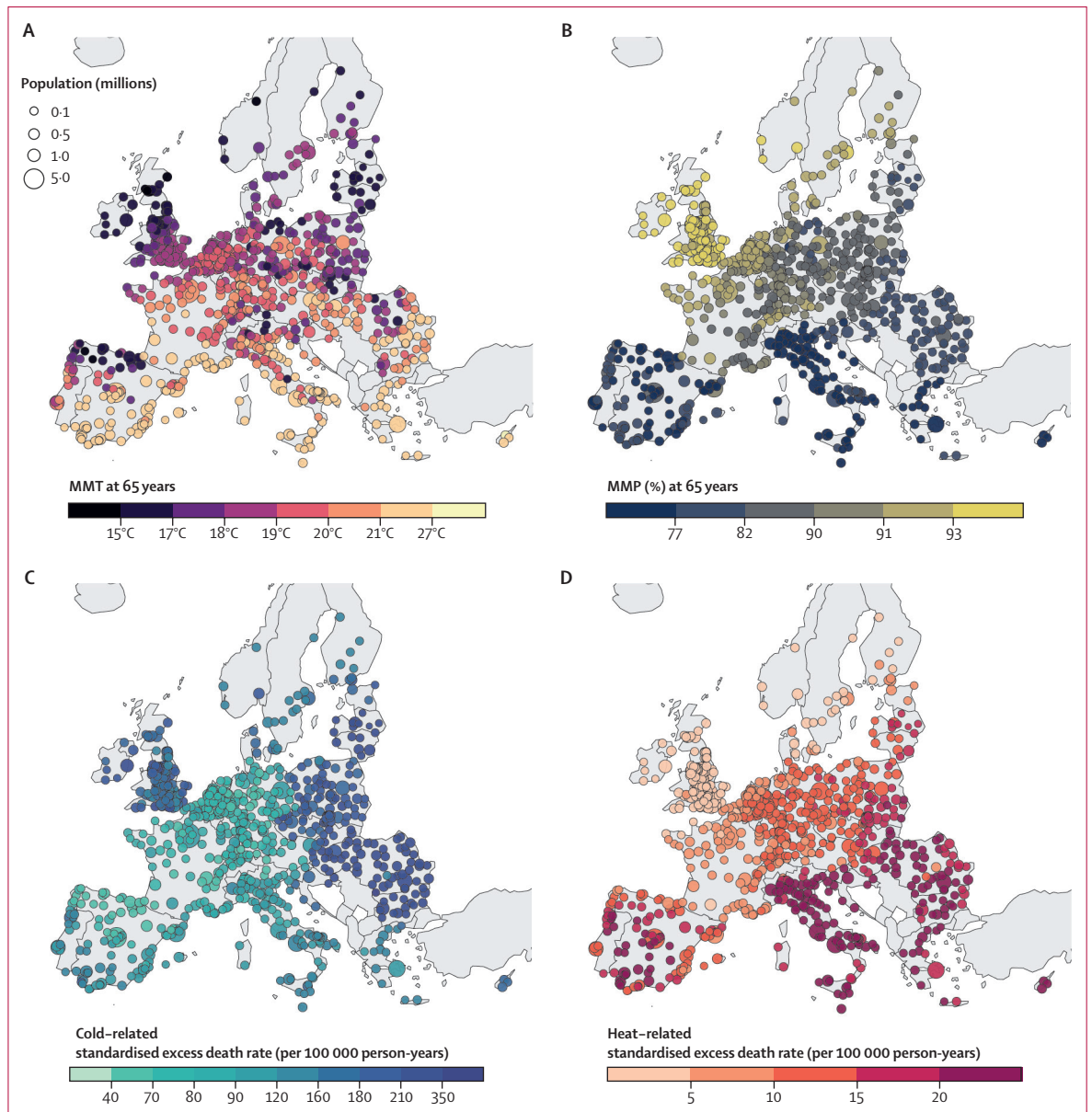


Figure 4: Maps of annual impacts of cold and heat on mortality across European cities

MMTs (A) and MMPs (B) predicted at age 65 years and standardised excess death rates for heat (C) and cold (D). MMP=minimum mortality percentiles. MMT=minimum mortality temperature.

Standardising for age differences, we found substantial vulnerability differences between regions. In particular, there were increased impacts of both cold and heat in eastern Europe, with countries such as Croatia, Bulgaria, and Romania showing higher vulnerability than countries in western Europe. Excess mortality was generally lower in western Europe than in the other regions, including northern and southern Europe, except for a few very large cities such as London (UK) and Paris (France). Northern countries showed the lowest risks for heat but also relatively low vulnerability to cold given the much higher

exposure to low temperatures, suggesting an adaptive capacity to rigid cold climates, especially when compared with countries in the eastern region. We also found impacts associated with heat in Mediterranean locations, although this impact was lower when age differentials were accounted for. Some within-country differences can also be noted, particularly in the MMT, linked to variations in the local climate and to urban heat island effects.

The disparities observed in vulnerability to heat and cold could be associated with a number of factors, including the local climate, urban heat island effects,

access to health care, or land cover (eg, the accessibility of water or trees). Previous studies have found associations between vulnerability to heat and green areas, PM_{2.5}, population density, or economic inequalities.^{6,35} The composite indices of vulnerability created in this study also suggest effect modification from the city size, proximity to water and green areas, and socioeconomic inequalities (appendix p 18). However, there is still little evidence on effect modifiers and this necessitates additional research.³ The highly complex interaction between various factors is not usually accounted for, and a method such as PLS does not allow drawing conclusions for individual factors.

An important strength of our study was the provision of detailed impact estimates with unprecedented city coverage. In contrast to past assessments focusing solely on extreme heat,^{36,37} our analysis quantified risks across the whole spectrum of non-optimal temperatures. We provided local estimates of excess mortality in a representative sample of more than 800 cities across Europe, compared with previous regional or country-level analyses,^{5,38} also extending the assessment to Scandinavia and eastern Europe. The characterisation of ERFs was based on the application of state-of-the-art statistical models to actual daily series of mortality and temperature, and not inferred from external data.³⁸

Compared with other published mortality impact assessments,^{1,2,5,37,38} one of the most important advantages of this study is the provision of multiple risk measures, including standardised excess mortality rates. The standardisation removes demographic differences across locations and countries, thus offering a homogeneous geographical comparison of mortality impacts. Indeed, the analysis confirms that age is an important risk factor, as shown by the comparison of age-specific pooled ERFs. Results show that the differences in population structures across locations noticeably alters the vulnerability picture. This finding was demonstrated, for instance, by the higher relative impact of heat found in eastern Europe once standardised excess rates were used as the risk measure.

More generally, this study benefited from other important methodological extensions of standard multi-location analyses. The statistical framework was based on flexible techniques to define and pool complex temperature–mortality ERFs,^{26,29} applied in previous analyses.^{1,2} These methods can depict fine aspects of the associations, such as non-linear and lagged effects of heat and cold, and identify optimal temperatures. However, the modelling framework is extended here to characterise vulnerability differences between cities through several socioeconomic, infrastructural, and environmental characteristics of urban areas. Previous studies presented simple pooled relationships,⁵ analysed effect modification by single characteristics,⁶ or included a small set of location-specific factors^{2,38} that can be insufficient to capture differences in vulnerability to cold

or heat. In contrast, we applied a novel methodology based on the PLS reduction of a long list of city-specific characteristics, allowing us to identify latent vulnerability patterns. Latent vulnerability patterns identified included the increased heat-related risk in large conurbations or differences in cold effects between Mediterranean and Atlantic coastal areas. Finally, we included an additional spatial component through a kriging procedure to capture residual spatial patterns that were not well represented by the composite vulnerability indicators.

Besides the quantification of current risks and impacts, this study provides a blueprint for the projection of future temperature-related health impacts under climate change scenarios. As climate change is expected to increase the burden of hot days and add unprecedented cold and heat events at high risks of causing deaths, these results allow for an accurate representation of the risks caused by changes in temperature.³⁹ The integration of age and vulnerability characteristics directly into the modelling framework allows the extrapolation of ERFs tailored to potentially complex scenarios. These can include a combination of climatic, demographic, and socioeconomic pathways, and their comparison can offer quantitative evidence of the potential benefits of alternative adaptation strategies.

A number of limitations of our study must be acknowledged. This assessment was based on the geographical extrapolation of ERFs across European cities. Although their characterisation is based on a large subset of cities with actual daily series of temperature and mortality, we cannot exclude biased predictions, especially in less covered areas such as eastern Europe. Results in these areas can be quite variable depending on some modelling choices, such as the number of PLS components. In addition, the residual spatial patterns identified by the kriging procedure, although small when compared with the range of differences captured by the PLS components in the second-stage meta-regression, suggest that the predictive model does not fully characterise the differences in vulnerability to heat and cold across the cities. Additional research is needed to assess the methodology used in this study, improve second-stage risk extrapolation, and disentangle effect modification by individual characteristics.

There are other limitations regarding the modelling approach. First-stage estimates can be inaccurate in the presence of overall low counts of deaths.²⁷ Therefore, we could not reliably estimate ERFs for people younger than 20 years and we needed to quantify the effects of temperature over large age bands for these groups. In addition, the modelling framework provides averaged estimates of temperature-related risks and effects over the study period, without accounting for temporal changes previously reported⁴⁰ or within-year seasonality in mortality. Finally, there are some limitations in the data. The information was collected from various sources with different geographical resolutions, and some

city-specific variables were derived from regional (NUTS2) databases, which usually encompass several cities. The temperature data were extracted from the ERA5-Land dataset and linked to city-specific mortality counts; however, we could not explore intra-city differences in exposure and vulnerability.

In conclusion, this study provides a detailed and comprehensive picture of cold and heat-related excess mortality in 854 cities across Europe, accounting for demographic and vulnerability differences. These results provide valuable information for policy makers to design national, regional, and local climate and public health policies, and represent a first important step towards accurate assessments of temperature-related health impacts under future climate scenarios and shared socioeconomic pathways for Europe.

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Contributors

PM, AG, and AM-VC developed the analysis, implemented by PM and AG. PM and AG wrote initial versions of the manuscript. PM and MM extracted data from Eurostat and MM extracted remote sensing data from Copernicus and Google Earth Engine. HO, AU, SB, VH, AS, ES, MS, FdD, SR, and the rest of the MCC Collaborative Research Network provided mortality data. All authors contributed to the interpretation of results through early circulation of the analysis results and tentative graphical output, as well as to the revision and approbation of the manuscript. PM, MM, and AG have accessed and verified the full

dataset. PM and AG were responsible for the decision to submit the manuscript after consultation with all listed authors. All authors have seen and approved the final publication.

Declaration of interests

We declare no competing interests.

Data sharing

The exposure-response functions derived in this analysis, full results, and intermediary data are publicly available in a Zenodo repository (<https://doi.org/10.5281/zenodo.7672108>). The associated R code to reproduce the analysis is available in the corresponding author's GitHub page (<https://github.com/pierremasslot>). The mortality data have been obtained through a restricted data use agreement with each national institute and are therefore not available for public dissemination.

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References

- Gasparrini A, Guo Y, Hashizume M, et al. Mortality risk attributable to high and low ambient temperature: a multicountry observational study. *Lancet* 2015; **386**: 369–75.
- Zhao Q, Guo Y, Ye T, et al. Global, regional, and national burden of mortality associated with non-optimal ambient temperatures from 2000 to 2019: a three-stage modelling study. *Lancet Planet Health* 2021; **5**: e415–25.
- Son J-Y, Liu JC, Bell ML. Temperature-related mortality: a systematic review and investigation of effect modifiers. *Environ Res Lett* 2019; **14**: 073004.
- Gasparrini A, Guo Y, Sera F, et al. Projections of temperature-related excess mortality under climate change scenarios. *Lancet Planet Health* 2017; **1**: e360–67.
- Martínez-Solanas È, Quijal-Zamorano M, Achebak H, et al. Projections of temperature-attributable mortality in Europe: a time series analysis of 147 contiguous regions in 16 countries. *Lancet Planet Health* 2021; **5**: e446–54.
- Sera F, Armstrong B, Tobias A, et al. How urban characteristics affect vulnerability to heat and cold: a multi-country analysis. *Int J Epidemiol* 2019; **48**: 1101–12.
- Nieuwenhuijsen MJ. Urban and transport planning, environmental exposures and health—new concepts, methods and tools to improve health in cities. *Environ Health* 2016; **15** (suppl 1): 38.
- Dijkstra L, Poelman H. Cities in Europe—the new OECD-EC definition. European Commission. January, 2012. <https://land.copernicus.eu/user-corner/technical-library/oecd-definition-of-functional-urban-area-fua> (accessed Feb 20, 2023).
- Oleson KW, Monaghan A, Wilhelm O, et al. Interactions between urbanization, heat stress, and climate change. *Clim Change* 2015; **129**: 525–41.
- Tong S, Prior J, McGregor G, Shi X, Kinney P. Urban heat: an increasing threat to global health. *BMJ* 2021; **375**: n2467.
- Bennett JE, Blangiardo M, Fecht D, Elliott P, Ezzati M. Vulnerability to the mortality effects of warm temperature in the districts of England and Wales. *Nat Clim Change* 2014; **4**: 269–73.
- Ragetli MS, Vicedo-Cabrera AM, Schindler C, Rössli M. Exploring the association between heat and mortality in Switzerland between 1995 and 2013. *Environ Res* 2017; **158**: 703–09.
- Martínez-Solanas È, Basagaña X. Temporal changes in temperature-related mortality in Spain and effect of the implementation of a heat health prevention plan. *Environ Res* 2019; **169**: 102–13.
- Huber V, Krummenauer L, Peña-Ortiz C, et al. Temperature-related excess mortality in German cities at 2°C and higher degrees of global warming. *Environ Res* 2020; **186**: 109447.
- Zafeiratou S, Analitis A, Founda D, et al. Spatial variability in the effect of high ambient temperature on mortality: an analysis at municipality level within the greater Athens area. *Int J Environ Res Public Health* 2019; **16**: 3689.

- 16 Orru H, Åström DO. Increases in external cause mortality due to high and low temperatures: evidence from northeastern Europe. *Int J Biometeorol* 2017; **61**: 963–66.
- 17 Oudin Åström D, Ebi KL, Vicedo-Cabrera AM, Gasparrini A. Investigating changes in mortality attributable to heat and cold in Stockholm, Sweden. *Int J Biometeorol* 2018; **62**: 1777–80.
- 18 Eurostat. Cities (Urban Audit). <https://ec.europa.eu/eurostat/web/cities/background> (accessed Dec 13, 2021).
- 19 Eurostat. Applying the degree of urbanisation—a methodological manual to define cities, towns and rural areas for international comparisons. 2021 edition. <https://ec.europa.eu/eurostat/web/products-manuals-and-guidelines/-/ks-02-20-499> (accessed Nov 11, 2022).
- 20 Eurostat. Regions. <https://ec.europa.eu/eurostat/web/regions/background> (accessed Dec 14, 2021).
- 21 Muñoz-Sabater J, Dutra E, Agustí-Panareda A, et al. ERA5-Land: a state-of-the-art global reanalysis dataset for land applications. *Earth Syst Sci Data* 2021; **13**: 4349–83.
- 22 Mistry MN, Schneider R, Masselot P, et al. Comparison of weather station and climate reanalysis data for modelling temperature-related mortality. *Sci Rep* 2022; **12**: 5178.
- 23 van Buuren S. Multiple imputation of discrete and continuous data by fully conditional specification. *Stat Methods Med Res* 2007; **16**: 219–42.
- 24 Didan K. MOD13Q1. MODIS/Terra vegetation indices 16-day L3 global 250m SIN grid V006. <https://lpdaac.usgs.gov/products/mod13q1v006/> (accessed Dec 16, 2021).
- 25 van Donkelaar A, Martin RV, Brauer M, et al. Global estimates of fine particulate matter using a combined geophysical-statistical method with information from satellites, models, and monitors. *Environ Sci Technol* 2016; **50**: 3762–72.
- 26 Gasparrini A, Armstrong B, Kenward MG. Distributed lag non-linear models. *Stat Med* 2010; **29**: 2224–34.
- 27 Armstrong BG, Gasparrini A, Tobias A, Sera F. Sample size issues in time series regressions of counts on environmental exposures. *BMC Med Res Methodol* 2020; **20**: 15.
- 28 Gasparrini A, Armstrong B. Reducing and meta-analysing estimates from distributed lag non-linear models. *BMC Med Res Methodol* 2013; **13**: 1.
- 29 Sera F, Armstrong B, Blangiardo M, Gasparrini A. An extended mixed-effects framework for meta-analysis. *Stat Med* 2019; **38**: 5429–44.
- 30 UN Statistical Commission. Standard country or area codes for statistical use (M49). <https://unstats.un.org/unsd/methodology/m49/#fn1> (accessed Nov 24, 2021).
- 31 Wold S, Sjöström M, Eriksson L. PLS-regression: a basic tool of chemometrics. *Chemom Intell Lab Syst* 2001; **58**: 109–30.
- 32 Cressie NAC. Spatial prediction and kriging. In: *Statistics for spatial data*. New York, NY: John Wiley & Sons, 1993: 105–209.
- 33 Tobias A, Hashizume M, Honda Y, et al. Geographical variations of the minimum mortality temperature at a global scale: a multicountry study. *Environ Epidemiol* 2021; **5**: e169.
- 34 Gasparrini A, Leone M. Attributable risk from distributed lag models. *BMC Med Res Methodol* 2014; **14**: 55.
- 35 Bakhtsiyarava M, Schinasi LH, Sánchez BN, et al. Modification of temperature-related human mortality by area-level socioeconomic and demographic characteristics in Latin American cities. *Soc Sci Med* 2023; **317**: 115526.
- 36 Gasparrini A, Masselot P, Scortichini M, et al. Small-area assessment of temperature-related mortality risks in England and Wales: a case time series analysis. *Lancet Planet Health* 2022; **6**: e557–64.
- 37 Forzieri G, Cescatti A, E Silva FB, Feyen L. Increasing risk over time of weather-related hazards to the European population: a data-driven prognostic study. *Lancet Planet Health* 2017; **1**: e200–08.
- 38 Burkart KG, Brauer M, Aravkin AY, et al. Estimating the cause-specific relative risks of non-optimal temperature on daily mortality: a two-part modelling approach applied to the Global Burden of Disease Study. *Lancet* 2021; **398**: 685–97.
- 39 Vicedo-Cabrera AM, Sera F, Gasparrini A. Hands-on tutorial on a modeling framework for projections of climate change impacts on health. *Epidemiology* 2019; **30**: 321–29.
- 40 Gasparrini A, Guo Y, Hashizume M, et al. Temporal variation in heat-mortality associations: a multicountry study. *Environ Health Perspect* 2015; **123**: 1200–07.