

Global, regional, and national burden of mortality associated with non-optimal ambient temperatures from 2000 to 2019: a three-stage modelling study



Qi Zhao, Yuming Guo, Tingting Ye, Antonio Gasparrini, Shilu Tong, Ala Overcenco, Aleš Urban, Alexandra Schneider, Alireza Entezari, Ana Maria Vicedo-Cabrera, Antonella Zanobetti, Antonis Analitis, Ariana Zeka, Aurelio Tobias, Baltazar Nunes, Barrak Alahmad, Ben Armstrong, Bertil Forsberg, Shih-Chun Pan, Carmen Íñiguez, Caroline Ameling, César De la Cruz Valencia, Christofer Åström, Danny Houthuijs, Do Van Dung, Dominic Royé, Ene Indermitte, Eric Lavigne, Fatemeh Mayvaneh, Fiorella Acquaotta, Francesca de' Donato, Francesco Di Ruscio, Francesco Sera, Gabriel Carrasco-Escobar, Haidong Kan, Hans Orru, Ho Kim, Iulian-Horia Holobaca, Jan Kyselý, Joana Madureira, Joel Schwartz, Jouni J K Jaakkola, Klea Katsouyanni, Magali Hurtado Diaz, Martina S Ragettli, Masahiro Hashizume, Mathilde Pascal, Micheline de Sousa Zanotti Stagliorio Coêlho, Nicolás Valdés Ortega, Niilo Rytö, Noah Scovronick, Paola Michelozzi, Patricia Matus Correa, Patrick Goodman, Paulo Hilario Nascimento Saldiva, Rosana Abrutzky, Samuel Osorio, Shilpa Rao, Simona Fratianni, Tran Ngoc Dang, Valentina Colistro, Veronika Huber, Whanhee Lee, Xerxes Seposo, Yasushi Honda, Yue Leon Guo, Michelle L Bell, Shanshan Li

Summary

Background Exposure to cold or hot temperatures is associated with premature deaths. We aimed to evaluate the global, regional, and national mortality burden associated with non-optimal ambient temperatures.

Methods In this modelling study, we collected time-series data on mortality and ambient temperatures from 750 locations in 43 countries and five meta-predictors at a grid size of $0.5^\circ \times 0.5^\circ$ across the globe. A three-stage analysis strategy was used. First, the temperature–mortality association was fitted for each location by use of a time-series regression. Second, a multivariate meta-regression model was built between location-specific estimates and meta-predictors. Finally, the grid-specific temperature–mortality association between 2000 and 2019 was predicted by use of the fitted meta-regression and the grid-specific meta-predictors. Excess deaths due to non-optimal temperatures, the ratio between annual excess deaths and all deaths of a year (the excess death ratio), and the death rate per 100 000 residents were then calculated for each grid across the world. Grids were divided according to regional groupings of the UN Statistics Division.

Findings Globally, 5 083 173 deaths (95% empirical CI [eCI] 4 087 967–5 965 520) were associated with non-optimal temperatures per year, accounting for 9.43% (95% eCI 7.58–11.07) of all deaths (8.52% [6.19–10.47] were cold-related and 0.91% [0.56–1.36] were heat-related). There were 74 temperature-related excess deaths per 100 000 residents (95% eCI 60–87). The mortality burden varied geographically. Of all excess deaths, 2 617 322 (51.49%) occurred in Asia. Eastern Europe had the highest heat-related excess death rate and Sub-Saharan Africa had the highest cold-related excess death rate. From 2000–03 to 2016–19, the global cold-related excess death ratio changed by -0.51 percentage points (95% eCI -0.61 to -0.42) and the global heat-related excess death ratio increased by 0.21 percentage points (0.13 – 0.31), leading to a net reduction in the overall ratio. The largest decline in overall excess death ratio occurred in South-eastern Asia, whereas excess death ratio fluctuated in Southern Asia and Europe.

Interpretation Non-optimal temperatures are associated with a substantial mortality burden, which varies spatiotemporally. Our findings will benefit international, national, and local communities in developing preparedness and prevention strategies to reduce weather-related impacts immediately and under climate change scenarios.

Funding Australian Research Council and the Australian National Health and Medical Research Council.

Copyright © 2021 The Author(s). Published by Elsevier Ltd. This is an Open Access article under the CC BY 4.0 license.

Introduction

Earth's average surface temperature has risen at a rate of 0.07°C per decade since 1880, a rate that has nearly tripled since the 1990s.¹ The acceleration of global warming has resulted in 19 of the 20 hottest years occurring after 2000 and an unprecedented frequency, intensity, and duration of extreme temperature events,

such as heatwaves, worldwide. Exposure to non-optimal temperatures has been associated with a range of adverse health outcomes (eg, excess mortality and morbidity from various causes).^{2–6} All populations over the world are under certain threats from non-optimal temperatures, regardless of their ethnicity, location, sex, age, and socioeconomic status. For example, in China, 14.3% of

Lancet Planet Health 2021;
5: e415–25

Department of Epidemiology, School of Public Health, Cheeloo College of Medicine, Shandong University, Jinan, China (Prof Q Zhao PhD); Department of Epidemiology and Preventive Medicine (Prof Q Zhao, Prof Y Guo PhD, T Ye MSc, S Li PhD) and Climate, Air Quality Research Unit (Prof Y Guo, T Ye, S Li), School of Public Health and Preventive Medicine, Monash University, Melbourne, VIC, Australia; Department of Public Health, Environments and Society (Prof A Gasparrini PhD, Prof B Armstrong PhD, F Sera MSc), Centre for Statistical Methodology (Prof A Gasparrini), and Centre on Climate Change and Planetary Health (Prof A Gasparrini), London School of Hygiene and Tropical Medicine, London, UK; Shanghai Children's Medical Centre, Shanghai Jiao Tong University, Shanghai, China (Prof S Tong PhD); School of Public Health, Institute of Environment and Population Health, Anhui Medical University, Hefei, China (Prof S Tong); Center for Global Health, Nanjing Medical University, Nanjing, China (Prof S Tong); School of Public Health and Social Work, Queensland University of Technology, Brisbane, QLD, Australia (Prof S Tong); Laboratory of Management in Science and Public Health, National Agency for Public Health of the Ministry of Health, Chisinau, Moldova

(A Overcenco PhD); **Institute of Atmospheric Physics, Czech Academy of Sciences, Prague, Czech Republic** (A Urban PhD, J Kyselý PhD); **Faculty of Environmental Sciences, Czech University of Life Sciences, Prague, Czech Republic** (A Urban, J Kyselý); **Institute of Epidemiology, Helmholtz Zentrum München—German Research Center for Environmental Health, Neuherberg, Germany** (A Schneider PhD); **Faculty of Geography and Environmental Sciences, Hakim Sabzevari University, Sabzevar, Iran** (A Entezari PhD); **F Mayvaneh PhD; Institute of Social and Preventive Medicine** (A M Vicedo-Cabrera PhD) and **Oeschger Center for Climate Change Research** (A M Vicedo-Cabrera), **University of Bern, Bern, Switzerland; Department of Environmental Health, Harvard T.H. Chan School of Public Health, Harvard University, Boston, MA, USA** (A Zanobetti PhD, B Alahmad MPH, Prof J Schwartz PhD); **Department of Hygiene, Epidemiology and Medical Statistics, National and Kapodistrian University of Athens, Athens, Greece** (A Analitis PhD, Prof K Katsouyanni PhD); **Institute of Environment, Health and Societies, Brunel University London, London, UK** (A Zeka PhD); **Institute of Environmental Assessment and Water Research, Spanish Council for Scientific Research, Barcelona, Spain** (A Tobias PhD); **Department of Epidemiology** (B Nunes PhD) and **Department of Environmental Health** (J Madureira PhD), **Instituto Nacional de Saúde Dr Ricardo Jorge, Porto, Portugal; Centro de Investigação em Saúde Pública, Escola Nacional de Saúde Pública, Universidade NOVA de Lisboa, Lisbon, Portugal** (B Nunes); **Department of Public Health and Clinical Medicine, Umeå University, Umeå, Sweden** (Prof B Forsberg PhD, C Åström PhD); **National Institute of Environmental Health Science, National Health Research Institutes, Zhunan, Taiwan** (S-C Pan PhD, Prof Y L Guo PhD); **Department of Statistics and**

Research in context

Evidence before this study

The association between non-optimal temperatures and premature deaths has been frequently reported, with the strength varying between different populations. However, the mortality burden attributable to non-optimal temperatures across countries and regions has not been well quantified at the global level. We searched PubMed, Scopus, Web of Science, and Google Scholar for studies published in English between database inception and Oct 20, 2020, that explore the temperature-related mortality burden. We used a combination of search terms, including “temperature”, “mortality”, “mortality burden”, “death”, “excess death”, and “attributable”. Most previous studies quantified the temperature-related mortality burden within a single country or small area (eg, several cities in Europe). One study explored this topic across 13 countries or territories. Another study estimated the global burden of temperature-related mortality on the basis of data of 12 causes of death from eight countries (five in Latin America and the Caribbean), and did not consider the spatiotemporal variation in the exposure–response relationship.

Added value of this study

To the best of our knowledge, this study is the first to provide a global overview of mortality burden attributable to non-optimal temperatures and the temporal change at a spatial resolution of 0.5° × 0.5° between 2000 and 2019—the hottest period since the pre-industrial age. We modelled the variation in the exposure–response relationship between temperature and mortality, reducing the uncertainties of the mortality burden, using data on more than 130 million deaths from 43 countries, which are located in five continents and

characterised by different climates, socioeconomics, demographics, and development levels of infrastructure and public health services. The large sample size and its representativeness improved the generalisability of our results. We found that 5 083 173 deaths were associated with non-optimal temperatures per year, accounting for 9.43% of all deaths and equating to 74 excess deaths per 100 000 residents. Most of these excess deaths were explainable by cold temperatures. The temperature-related mortality burden showed substantial geographical variation. Of all excess deaths, more than half occurred in Asia, particularly in Eastern and Southern Asia. Eastern Europe had the highest heat-related excess death rate and Sub-Saharan Africa had the highest cold-related excess death rate. The average daily mean temperature of the studied grids rose by 0.26°C per decade between 2000 and 2019, consistent with the large decrease in the cold-related excess death ratio and the moderate increase in the heat-related excess death ratio. Taken together, however, the global excess death ratio declined.

Implications of all the available evidence

Our findings can help in understanding the impact of temperature events on population health globally, and across and within countries or regions. At a global level, the results indicate that global warming might slightly reduce net temperature-related deaths in the short term, although, in the long run, climate change is expected to increase the mortality burden. The disparate geographical patterns of temperature-related mortality burden are important to consider in developing policies and strategies in climate change mitigation and adaptation, and health protection.

non-accidental mortality in 2013–15 might have been related to non-optimal temperatures, with 11.6% of deaths explainable by cold exposure and 2.7% explainable by heat exposure.⁷ In the USA, the risk of mortality increased by 5–12% due to cold exposure and 5–10% due to heat exposure between 2000 and 2006.⁸ An association between ambient temperature and mortality risk has also been reported in India, Australia, the EU, South Africa, and other countries and regions.^{9–11}

Despite increasing evidence of the temperature–mortality association, the relevant burden of mortality attributable to non-optimal temperatures has not been well quantified at the country and region level. The Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) 2019 showed that non-optimal temperatures were among the ten leading causes of death worldwide.¹² GBD 2019 represents progress in quantifying the global burden of mortality attributable to non-optimal temperatures. However, considering that the study only used mortality data for non-optimal temperatures from eight countries, extrapolating the findings on a global level is difficult. In addition, GBD 2019 only used 12 causes of mortality to calculate all-cause

mortality, and did not consider the spatiotemporal variation in exposure–response curves between temperature and mortality.

Analysis of big data is required to solve inter-study differences in modelling, parameterisation, and results interpretation. We developed the Multi-Country Multi-City (MCC) Collaborative Research Network in 2014 to systematically assess temperature-related mortality risk across countries and regions using unified methodology.¹³ MCC studies used a three-stage analysis to calculate the burden of mortality attributable to non-optimal temperatures and estimated that 7.71% of total deaths in 13 countries or territories were attributable to non-optimal temperatures between 1985 and 2012 in the context of the MCC network.^{3,14} The MCC network has expanded in recent years, with data on time-series mortality and weather conditions updated to 750 representative locations in 43 countries or territories. These countries and or territories account for 46.3% of the world’s population.

Because of the inevitability of climate change, it is urgently important to provide a global view of the relevant mortality burden and to push and develop

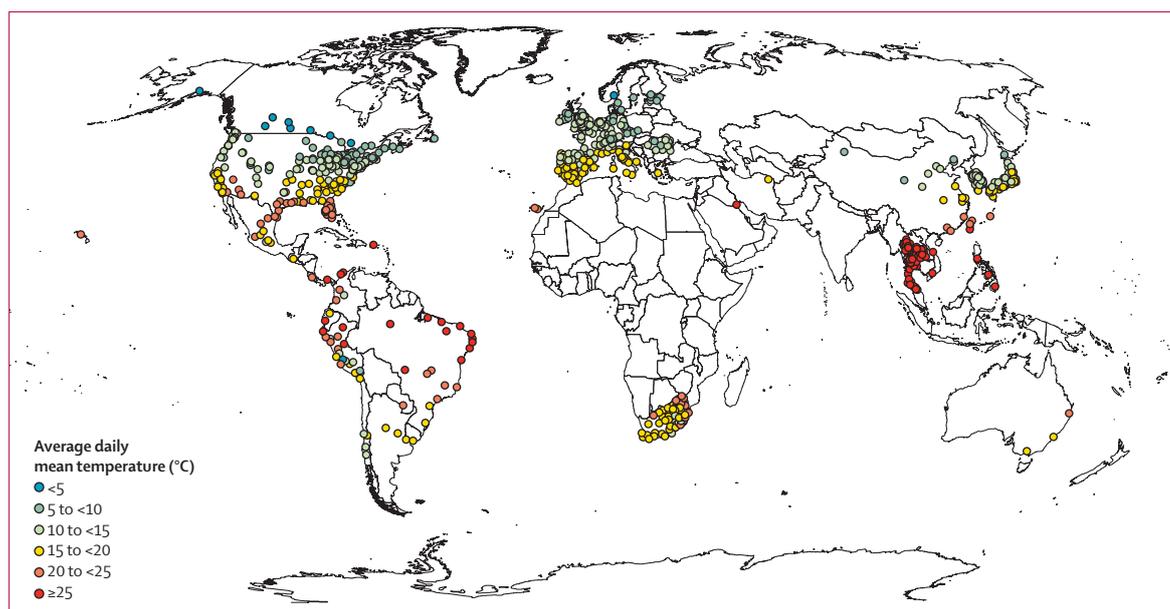


Figure 1: Average daily mean temperatures of the 750 locations from the 43 countries or territories included in the analysis

The colours represent the different ranges of average daily mean temperature during the data collection periods shown in the appendix (p 4).

intergovernmental strategies against the health impacts of temperature events. Therefore, we aimed to assess the global, regional, and national number of excess deaths associated with non-optimal ambient temperatures using the latest MCC data and a three-stage analysis strategy.

Methods

Data sources

The MCC network collects and updates daily time-series data on mortality and weather conditions from multiple countries. The details have been described in previous publications.^{3,14} The latest dataset covers 750 locations in 43 countries or territories (two countries in Northern America, 13 in Latin America and the Caribbean, 17 in Europe, nine in Asia, one in Africa, and one in Oceania; appendix p 4). Figure 1 shows the 750 locations with their average daily mean temperatures during the data collection periods. A detailed description of the data by continent and country is provided in the appendix (pp 2, 4). For each location, mortality was represented by daily counts of all-cause deaths. When such data were unavailable, mortality was represented by daily counts of deaths as a result of non-external causes (International Classification of Diseases-9 codes 0–799 or International Classification of Diseases-10 codes A00–R99). We developed our model using data on 130 217 521 deaths from the 43 included countries.

Daily minimum and maximum temperatures between Jan 1, 2000, and Dec 31, 2019, were collected from the Global Daily Temperature dataset (grid size 0.5°×0.5°) of the Climate Prediction Center. This dataset was developed, by use of a Shepard algorithm with observational data from 6000 to 7000 weather monitoring

stations worldwide,¹⁵ as a benchmark for a range of reanalysis products and climate change models. Daily mean temperature was calculated by averaging daily minimum and maximum temperatures. Annual data on gross domestic product (GDP; standardised to the 2005 rate) and population were provided by the Global Carbon Project at a spatial resolution of 0.5°×0.5° per 10 years between 1980 and 2010,¹⁶ which were used to calculate GDP per capita for each grid. In addition, GDP and population data at the central coordinate of each location were interpolated and extrapolated to the middle year of data collection to calculate the average location-specific GDP per capita during the period. Annual mortality rate in each country in 2010 was extracted from the World Bank.

Statistical analysis

Temperature-related mortality burden was estimated at a spatial resolution of 0.5°×0.5° by extending the three-stage meta-analytical approach that has been justified by our previous MCC studies.^{3,14,17} The key methodological innovation of this study is its prediction of the temperature–mortality association for areas without daily time-series data on mortality. An explanation of the methodology is provided in the appendix (p 2).

Briefly, in the first stage, the temperature–mortality association for each of the 750 locations was estimated by use of a quasi-Poisson regression with a distributed lag non-linear model,¹⁴

$$Y_{it} \sim \text{poisson}(\mu_{it})$$

$$\log(\mu_{it}) = \alpha + \text{cb}(\text{Temp}_{it}, \text{lag}=21) + \text{ns}(\text{Time}_{it}, \text{df}=8/\text{year}) + \beta \text{DOW}_{it}$$

Computational Research, Universitat de València, València, Spain (C Íñiguez PhD); CIBER of Epidemiology and Public Health, Madrid, Spain (C Íñiguez, D Royé PhD); Centre for Sustainability and Environmental Health, National Institute for Public Health and the Environment, Bilthoven, Netherlands (C Ameling BS, D Houthuijs MSc); Department of Environmental Health, National Institute of Public Health, Cuernavaca Morelos, Mexico (C De la Cruz Valencia MSc, Prof M Hurtado Diaz PhD); Department of Environmental Health, Faculty of Public Health, University of Medicine and Pharmacy at Ho Chi Minh City, Ho Chi Minh City, Vietnam (D V Dung PhD, T N Dang PhD); Department of Geography, University of Santiago de Compostela, Santiago de Compostela, Spain (D Royé); Institute of Family Medicine and Public Health, University of Tartu, Tartu, Estonia (E Indermitte PhD, H Orru PhD); School of Epidemiology and Public Health, Faculty of Medicine, University of Ottawa, Ottawa, ON, Canada (Prof E Lavigne PhD); Air Health Science Division, Health Canada, Ottawa, ON, Canada (Prof E Lavigne); Department of Earth Sciences, University of Turin, Turin, Italy (F Acquatoa PhD, S Fratianni PhD); Department of Epidemiology, Lazio Regional Health Service, Rome, Italy (F de' Donato PhD, P Michelozzi MSc); Norwegian Institute of Public Health, Oslo, Norway (F Di Ruscio PhD, S Rao PhD); Department of Statistics, Computer Science and Applications G. Parenti, University of Florence, Florence, Italy (F Sera); Health Innovation Lab, Institute of Tropical Medicine Alexander von Humboldt, Universidad Peruana Cayetano Heredia, Lima, Peru (G Carrasco-Escobar MSc); Division of Infectious Diseases, Department of Medicine, University of California, San Diego, CA, USA (G Carrasco-Escobar); Department of Environmental Health, School of Public Health, Fudan University, Shanghai,

China (Prof H Kan PhD); Graduate School of Public Health, Seoul National University, Seoul, South Korea (Prof H Kim PhD); Faculty of Geography, Babeş-Bolyai University, Cluj-Napoca, Romania (I-H Holobaca PhD); EPIUnit, Instituto de Saúde Pública, Universidade do Porto, Porto, Portugal (J Madureira); Center for Environmental and Respiratory Health Research and Biocenter Oulu, University of Oulu, Oulu, Finland (Prof J J K Jaakkola PhD, N Ryti PhD); Finnish Meteorological Institute, Helsinki, Finland (Prof J J K Jaakkola); School of Population Health and Environmental Sciences, King's College London, London, UK (Prof K Katsouyanni); Department of Epidemiology and Public Health, Swiss Tropical and Public Health Institute, Basel, Switzerland (M S Ragetti PhD); University of Basel, Basel, Switzerland (M S Ragetti); Department of Global Health Policy, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan (Prof M Hashizume PhD); Department of Environmental and Occupational Health, Santé Publique France, French National Public Health Agency, Saint Maurice, France (M Pascal PhD); Department of Pathology, Faculty of Medicine (M de Sousa Zanotti Stagliorio Coelho PhD, Prof P H Nascimento Saldiva PhD) and Department of Environmental Health (S Osorio MSc), University of São Paulo, São Paulo, Brazil; Department of Public Health, Universidad de los Andes, Santiago, Chile (N Valdés Ortega MSc, P Matus Correa MSc); Gangarosa Department of Environmental Health, Rollins School of Public Health, Emory University, Atlanta, GA, USA (N Scovronick PhD); School of Physics, Technological University Dublin, Dublin, Ireland (Prof P Goodman PhD); Instituto de Investigaciones Gino Germani, Facultad de Ciencias Sociales, Universidad de Buenos Aires, Buenos Aires, Argentina (R Abrutsky MSc); Department of Quantitative Methods, School of Medicine, University of the Republic, Montevideo, Uruguay

	Overall		Cold-related		Heat-related	
	Number of excess deaths (95% eCIs)	Regional proportion	Number of excess deaths (95% eCIs)	Regional proportion	Number of excess deaths (95% eCIs)	Regional proportion
Global	5 083 173 (4 087 967–5 965 520)	100.00%	4 594 098 (3 337 222–5 640 617)	100.00%	489 075 (304 216–732 518)	100.00%
Americas	391 469 (349 949–434 634)	7.70%	334 710 (294 660–385 116)	7.29%	56 759 (29 551–93 707)	11.61%
Northern America	191 414 (164 919–219 455)	3.77%	171 350 (148 863–196 266)	3.73%	20 064 (8 703–35 204)	4.10%
Latin America and the Caribbean	200 055 (181 608–227 270)	3.94%	163 360 (134 007–194 240)	3.56%	36 695 (20 064–59 526)	7.50%
Europe	835 897 (740 194–929 440)	16.44%	657 185 (585 782–723 962)	14.30%	178 712 (142 070–227 795)	36.54%
Northern Europe	85 878 (75 113–96 426)	1.69%	71 445 (63 009–78 495)	1.56%	14 433 (10 658–19 559)	2.95%
Southern Europe	166 485 (151 444–181 291)	3.28%	130 312 (118 584–140 789)	2.84%	36 173 (29 677–45 340)	7.40%
Western Europe	173 037 (153 969–191 754)	3.40%	140 271 (125 698–153 056)	3.05%	32 766 (25 376–42 719)	6.70%
Eastern Europe	410 497 (357 620–459 748)	8.08%	315 157 (274 617–352 139)	6.86%	95 340 (76 914–120 295)	19.49%
Africa	1 214 035 (140 886–2 213 802)	23.88%	1 188 486 (106 557–2 197 519)	25.87%	25 549 (15 385–38 113)	5.22%
Northern Africa	125 446 (27 007–206 661)	2.47%	118 265 (17 586–202 043)	2.57%	7 181 (4 774–10 237)	1.47%
Sub-Saharan Africa	1 088 589 (114 390–1 995 715)	21.42%	1 070 221 (88 971–1 984 511)	23.30%	18 368 (10 831–27 876)	3.76%
Asia	2 617 322 (2 345 204–2 857 273)	51.49%	2 393 300 (2 183 014–2 625 909)	52.10%	224 022 (112 925–366 535)	45.81%
Central Asia	40 461 (35 952–44 266)	0.80%	37 802 (34 426–41 543)	0.82%	2 659 (957–4961)	0.54%
Southern Asia	1 025 049 (901 671–1 137 823)	20.17%	913 436 (819 340–1 019 089)	19.88%	111 613 (61 937–173 188)	22.82%
Western Asia	126 815 (113 180–138 871)	2.49%	118 111 (107 252–130 991)	2.57%	8 704 (3 423–15 778)	1.78%
Eastern Asia	1 235 428 (1 137 659–1 318 445)	24.30%	1 155 656 (1 078 254–1 247 619)	25.16%	79 772 (35 814–139 634)	16.31%
South-eastern Asia	189 569 (158 500–216 544)	3.73%	168 295 (142 100–193 278)	3.66%	21 274 (9 498–36 426)	4.35%
Oceania	24 450 (15 401–35 023)	0.48%	20 417 (12 874–28 406)	0.44%	4 033 (1 029–8 423)	0.82%
Australia and New Zealand	19 324 (11 623–28 490)	0.38%	16 684 (10 751–23 579)	0.36%	2 640 (424–6 056)	0.54%
Other regions in Oceania*	5 126 (2 718–7 597)	0.10%	3 733 (1 945–5 566)	0.08%	1 393 (504–2 566)	0.28%

eCIs=empirical CIs. *Other regions in Oceania are defined as all areas outside of Australia and New Zealand in Oceania. All other regions in the table are defined according to the UN Statistics Division (M49) regional groupings.

Table 1: Annual average excess deaths due to non-optimal temperatures and regional proportions for 2000–19 by continent and region

where Y_{it} is the counts of deaths on day t in location i ; α is the intercept; cb is the cross-basis function of two natural cubic splines for temperature during 0–21 lag days, with three internal knots placed at the tenth, 75th, and 90th temperature percentiles and an intercept and three internal knots placed at equally spaced values in the log scale of lag days; ns is the natural cubic spline for time with eight df per year to control for long-term trends and seasonality; and DOW_{it} is a categorical variable for day of the week.

In the second stage, we collected location-specific predictors that could explain the majority of the

heterogeneity in the temperature–mortality associations across locations. A multivariate meta-regression model was built between the reduced cumulative association for each location and five location-specific meta-predictors (ie, the continents, indicators for Köppen–Geiger climate classification,¹⁸ GDP per capita, the yearly average of daily mean temperature, and the range of daily mean temperature). These predictors have been shown to explain the heterogeneity of location-specific associations.^{3,14,17}

In the extended third stage, the temperature–mortality association between 2000 and 2019 was predicted for

each grid individually by use of the fitted meta-regression from the second stage and the five meta-predictors at the grid level. The reference was set at the temperature value associated with the lowest risk of mortality (the minimum mortality temperature). The GDP per capita in 2010 was used to represent the grid-specific average between 2000 and 2019. Globally, there are numerous grids with very low or no population. To improve modelling stability, analyses were restricted to grids with a perceptible population size, which was defined as grids with at least one death annually. The annual deaths in each grid were calculated on the basis of the annual mortality rate of the country in which the grid was located and the population counts in the grid in 2010. This calculation assumed an identical mortality rate across all grids inside the country. Excluding grids with an imperceptible population size meant that 48 909 of 74 812 grids were included in the models, accounting for 99.995% of the world's population.

For each grid i on a specific day t , the excess deaths due to non-optimal temperatures (ED_{it}) were calculated as:^{19,20} $ED_{it} = (RR_{it} - 1) \times D_i$, where RR_{it} is the cumulative relative risk extracted from the grid-specific temperature–mortality association predicted in the third stage and D_i is the daily average of annual deaths in 2010 to capture the mortality burden purely derived by temperature change from 2000 to 2019. Daily counts were summed to get the annual excess deaths. The empirical CIs (eCIs) were calculated by use of Monte Carlo simulations (500 samples) to quantify the uncertainty in estimating excess deaths. In addition, the ratio between annual excess deaths and all deaths of a year (ie, the excess death ratio) and the annual excess death rate per 100 000 residents were also calculated. For a systematic assessment, the temperature-related mortality burden was described as due to all non-optimal cold temperatures and all non-optimal hot temperatures. The cold and hot temperatures were defined as temperatures either lower or higher than the minimum mortality temperature. In the interpretation of our results, grids were divided by region according to the regional groupings of the UN Statistics Division (M49) and by indicators of the Köppen–Geiger climate classification.²¹

The temporal change in temperature-related burden was explored as change per decade in excess death ratio and rate, and also as change in excess death ratio by region compared with the 2000–03 average. To compare our results with those of GBD 2019, the 43 countries from the MCC network were grouped into the seven countries included in GBD 2019 (except for New Zealand because of the paucity of data) and the remaining 36 countries. A classic two-stage time-series analysis was done by use of a relative temperature scale considering the various temperature ranges across locations. The pooled relative risk of mortality by temperature percentile was calculated for the two groups.

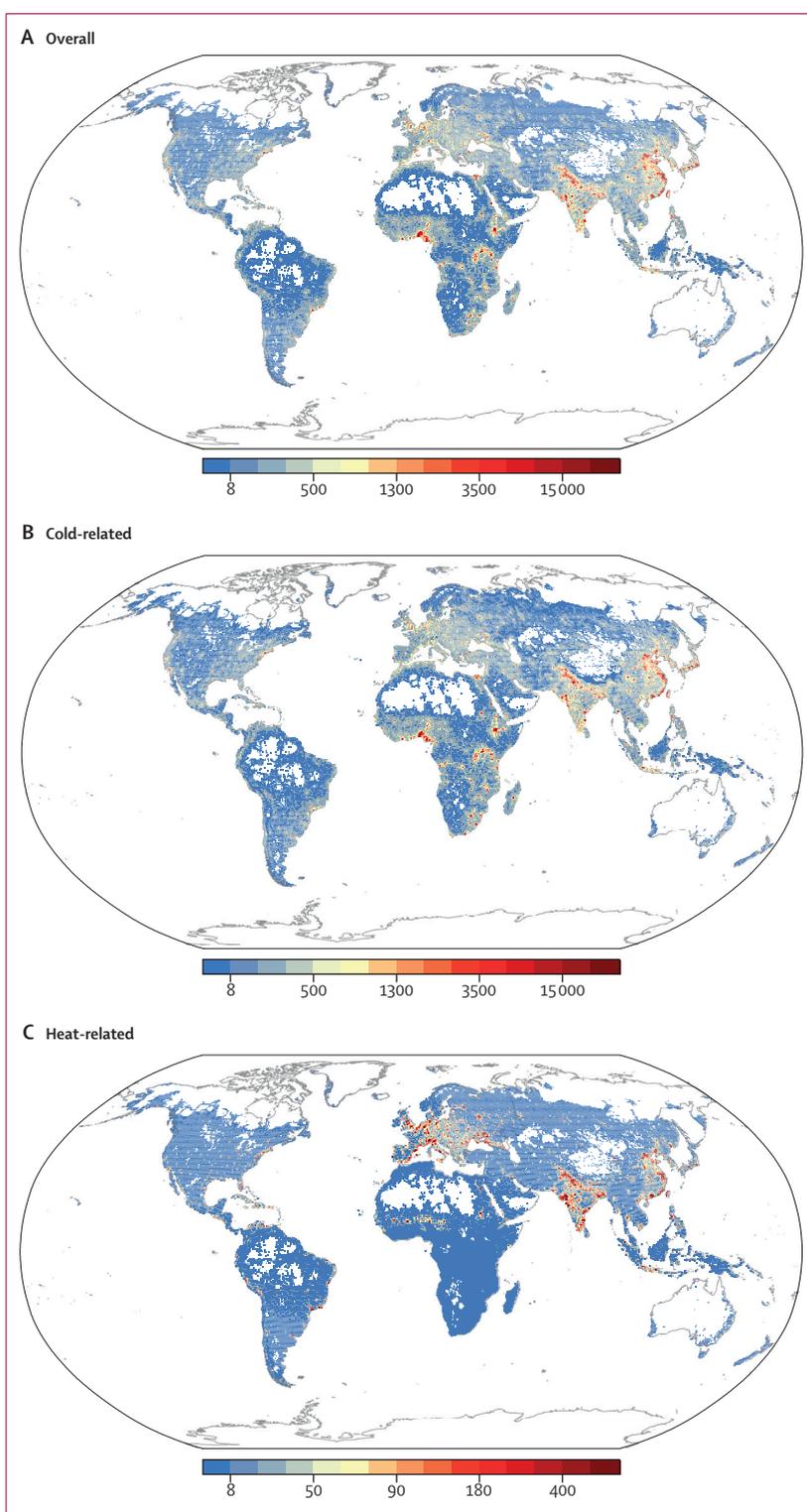


Figure 2: Average annual excess deaths due to non-optimal temperatures in 2000–19 at a spatial resolution of 0.5° x 0.5° (A) Overall annual excess deaths. (B) Cold-related annual excess deaths. (C) Heat-related annual excess deaths. Only grids with at least one annual death were included.

	Excess death ratio (95% eCIs)			Excess deaths per 100 000 residents (95% eCIs)		
	Overall	Cold-related	Heat-related	Overall	Cold-related	Heat-related
Global	9.43% (7.58–11.07)	8.52% (6.19–10.47)	0.91% (0.56–1.36)	74 (60–87)	67 (49–82)	7 (4–11)
Americas	6.33% (5.66–7.03)	5.41% (4.76–6.23)	0.92% (0.48–1.52)	42 (38–47)	36 (32–41)	6 (3–10)
Northern America	7.04% (6.07–8.07)	6.30% (5.48–7.22)	0.74% (0.32–1.30)	56 (48–64)	50 (43–57)	6 (3–10)
Latin America and the Caribbean	5.77% (5.24–6.56)	4.71% (3.87–5.60)	1.06% (0.58–1.72)	34 (31–39)	28 (23–33)	6 (3–10)
Europe	10.27% (9.09–11.41)	8.07% (7.19–8.89)	2.19% (1.74–2.80)	113 (100–126)	89 (79–98)	24 (19–31)
Northern Europe	9.42% (8.24–10.58)	7.84% (6.91–8.61)	1.58% (1.17–2.15)	87 (76–97)	72 (64–79)	15 (11–20)
Southern Europe	11.14% (10.14–12.14)	8.72% (7.94–9.42)	2.42% (1.99–3.04)	107 (98–117)	84 (76–91)	23 (19–29)
Western Europe	9.72% (8.65–10.77)	7.88% (7.06–8.60)	1.84% (1.43–2.40)	92 (82–102)	74 (67–81)	17 (13–23)
Eastern Europe	10.37% (9.04–11.62)	7.96% (6.94–8.90)	2.41% (1.94–3.04)	139 (121–156)	107 (93–119)	32 (26–41)
Africa	11.77% (1.37–21.45)	11.52% (1.03–21.30)	0.25% (0.15–0.37)	119 (14–217)	116 (10–215)	3 (2–4)
Northern Africa	9.73% (2.09–16.03)	9.17% (1.36–15.67)	0.56% (0.37–0.79)	60 (13–99)	57 (8–97)	3 (2–5)
Sub-Saharan Africa	12.06% (1.27–22.10)	11.85% (0.99–21.98)	0.20% (0.12–0.31)	134 (14–246)	132 (11–244)	2 (1–3)
Asia	9.02% (8.08–9.85)	8.25% (7.53–9.05)	0.77% (0.39–1.26)	63 (57–69)	58 (53–63)	5 (3–9)
Central Asia	10.40% (9.25–11.38)	9.72% (8.85–10.68)	0.68% (0.25–1.28)	67 (59–73)	62 (57–68)	4 (2–8)
Southern Asia	8.33% (7.33–9.25)	7.43% (6.66–8.29)	0.91% (0.50–1.41)	60 (53–67)	54 (48–60)	7 (4–10)
Western Asia	10.60% (9.46–11.61)	9.87% (8.96–10.95)	0.73% (0.29–1.32)	55 (49–60)	51 (46–56)	4 (1–7)
Eastern Asia	10.96% (10.09–11.70)	10.25% (9.57–11.07)	0.71% (0.32–1.24)	80 (73–85)	75 (70–80)	5 (2–9)
South-eastern Asia	4.92% (4.11–5.62)	4.37% (3.69–5.02)	0.55% (0.25–0.95)	32 (27–36)	28 (24–33)	4 (2–6)
Oceania	10.12% (6.38–14.50)	8.45% (5.33–11.76)	1.67% (0.43–3.49)	70 (44–100)	58 (37–81)	11 (3–24)
Australia and New Zealand	11.16% (6.71–16.45)	9.63% (6.21–13.61)	1.52% (0.24–3.50)	73 (44–107)	63 (40–89)	10 (2–23)
Other regions in Oceania*	7.51% (3.98–11.12)	5.47% (2.85–8.15)	2.04% (0.74–3.76)	60 (32–89)	44 (23–65)	16 (6–30)

eCIs=empirical CIs. *Other regions in Oceania are defined as all areas outside of Australia and New Zealand in Oceania. All other regions in the table are defined according to the UN Statistics Division (M49) regional groupings.

Table 2: Excess deaths ratio and deaths per 100 000 residents due to non-optimal temperatures in 2000–19 by continent and region

(V Colistro MSc); Potsdam Institute for Climate Impact Research, Potsdam, Germany (V Huber PhD); Department of Physical, Chemical and Natural Systems, Universidad Pablo de Olavide, Sevilla, Spain (V Huber); School of the Environment, Yale University, New Haven, CT, USA (W Lee PhD, Prof M L Bell PhD);

Although the parameterisations in the first two steps have been justified previously,³ we still tested the robustness of the main findings via a series of sensitivity analyses (eg, by changing the maximum lag from 21 days to 28 days and the positions or numbers of knots for the temperature or lag dimensions), a list of which can be found in the appendix (appendix p 10).

All data analyses were done by use of R software, version 3.4.3. The dlnm package was used to fit the

distributed lag non-linear model and the mvmeta package was used to fit the multivariate meta-regression.^{17,22}

Role of the funding source

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

Results

Between Jan 1, 2000, and Dec 31, 2019, the average daily mean temperature was 15.23°C (SD 10.40) across grids with a perceptible population size (appendix pp 5, 11). Eastern Europe had the coldest average daily mean temperature (2.36°C [SD 5.06]) and the warmest climates appeared in South-eastern Asia (26.35°C [2.19]) and regions in Oceania other than Australia and New Zealand (26.05°C [1.90]; appendix p 5). The global mean ambient daily temperature increased at an average rate of 0.26°C per decade (SD 0.44) between 2000 and 2019, varying from the highest rate of increase in other regions in Oceania (0.48°C per decade [0.23]) to the temperature decreasing at a rate of -0.16°C per decade (0.53) in Southern Asia (appendix p 5).

Globally, 5 083 173 deaths (95% eCI 4 087 967–5 965 520) were associated with non-optimal temperatures per year, consisting of 4 594 098 cold-related deaths (3 337 222–5 640 617) and 489 075 heat-related deaths (304 216–732 518; table 1). Of all excess deaths, 51.49% occurred in Asia, 23.88% occurred in Africa, 16.44% occurred in Europe, 7.70% occurred in the Americas, and 0.48% occurred in Oceania (table 1). Most grids with a high density of excess deaths were in large, low-lying, crowded coastal cities in Eastern and Southern Asia and cities in Eastern and Western Europe (figure 2).

Average excess deaths related to non-optimal temperatures accounted for 9.43% (95% eCI 7.58–11.07) of global deaths (74 deaths per 100 000 residents), with 8.52% of deaths explainable by cold temperatures (67 deaths per 100 000 residents) and 0.91% explainable by hot temperatures (seven deaths per 100 000 residents; table 2). The excess death ratio and rate per 100 000 residents showed regional differences. For example, compared with the global average, the excess death rates were nearly double in Eastern Europe and Sub-Saharan Africa and slightly less than half in Latin America and the Caribbean and South-eastern Asia (table 2). Specifically, Sub-Saharan Africa had the world’s highest cold-related excess death rate and the heat-related excess death rate in Eastern Europe was nearly five times higher than the global average (table 2). Europe was the only continent where both cold-related and heat-related excess death rates were higher than the global average. Maps on grid-specific excess death ratio and rate (0.5°×0.5°) provide a finer overview of temperature-related mortality burden across worldwide populations (figure 3; appendix p 12). For example, despite the low average excess death rates in Latin America and the Caribbean, the grid-specific values

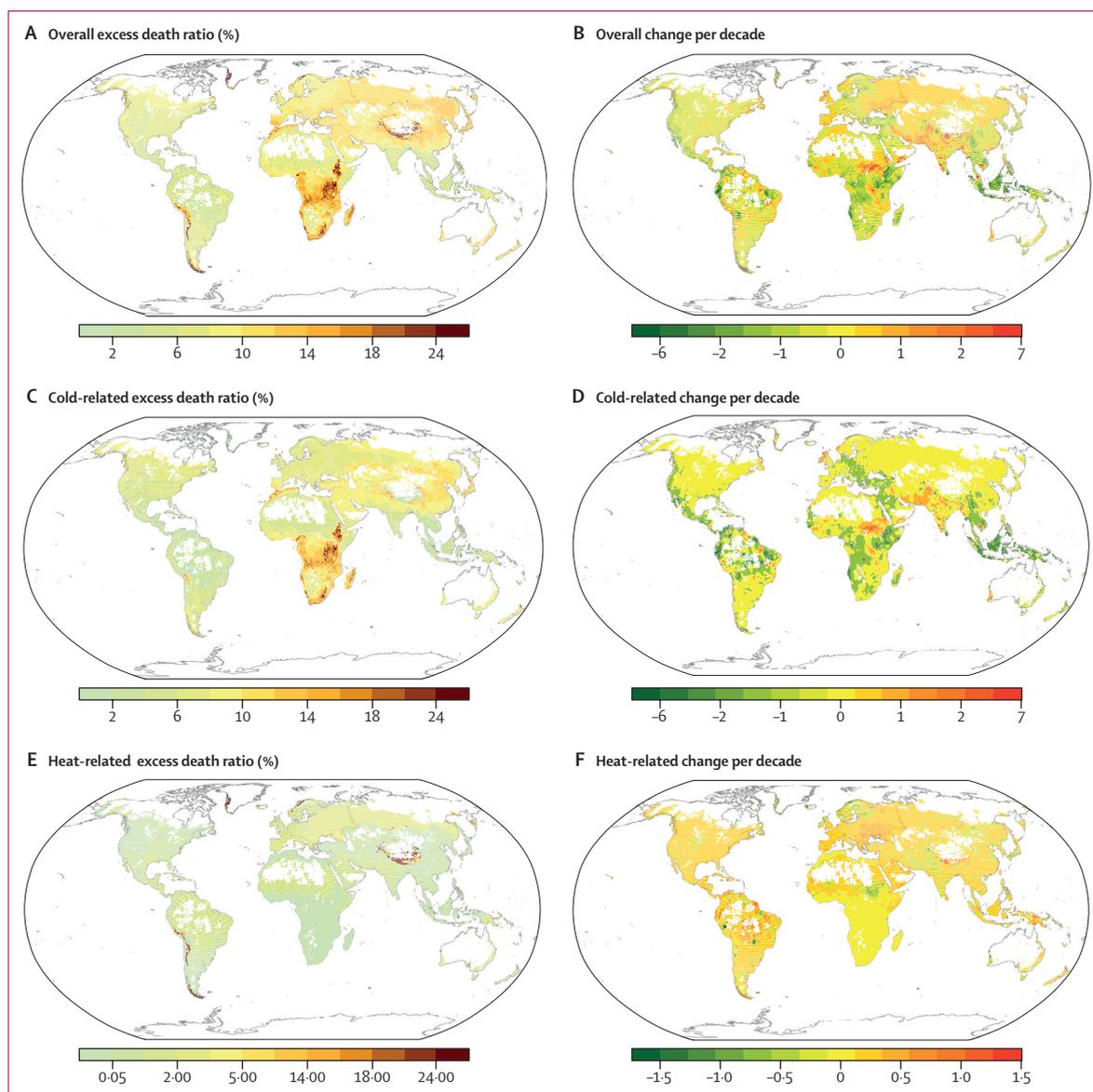


Figure 3: Average annual excess death ratio and change in average annual excess death ratio per decade due to non-optimal temperatures in 2000–19 at a spatial resolution of $0.5^{\circ} \times 0.5^{\circ}$

We present overall annual excess death ratio (A) and change per decade (B), cold-related excess death ratio (C) and change per decade (D), and heat-related excess death ratio (E) and change per decade (F). Only grids with at least one annual death were included.

were higher on its western coastline (appendix p 12). Excess death ratios and rates associated with non-optimal temperatures were higher in polar and alpine climates than in other climate zones (indicators of the Köppen–Geiger classification), with most cases associated with heat exposure (appendix p 6).

From 2000–03 to 2016–19, the global excess death ratio changed by -0.51 percentage points (95% eCI -0.61 to -0.42) for cold temperatures and increased by 0.21 percentage points (0.13 – 0.31) for hot temperatures, resulting in a net decline of -0.30 percentage points (-0.44 to -0.13 ; appendix pp 7–9). Figure 4 shows the

temporal change in excess death ratio by region, in comparison to the 2000–03 average. From 2000–03 to 2016–19, the cold-related excess death ratio declined in most regions, except for Northern Europe and Southern Asia (figure 4). The greatest decline in the cold-related excess death ratio occurred in South-eastern Asia and other regions in Oceania. The heat-related excess death ratio increased in most regions from 2000–03 to 2016–19, especially in Europe and Oceania (figure 4). However, the changing rates of cold-related and heat-related excess death ratios resulted in different net temperature-related burdens by 2016–19 in each region.

School of Tropical Medicine and Global Health, Nagasaki University, Nagasaki, Japan (X Seposo PhD, A Tobias); Faculty of Health and Sport Sciences, University of Tsukuba, Tsukuba, Japan (Prof Y Honda PhD); Environmental and Occupational Medicine, NTU College of Medicine and NTU Hospital (Prof Y L Guo) and Institute of Environmental and Occupational Health Sciences, NTU College of Public Health (Prof Y L Guo), National Taiwan University, Taipei, Taiwan

Correspondence to: Prof Yuming Guo, Climate, Air Quality Research Unit, School of Public Health and Preventive Medicine, Monash University, Melbourne, VIC 3004, Australia yuming.guo@monash.edu

or Dr Shanshan Li, Climate, Air Quality Research Unit, School of Public Health and Preventive Medicine, Monash University, Melbourne, VIC 3004, Australia shanshan.li@monash.edu

For more on extreme temperature events see <http://www.emdat.be>

See Online for appendix

For more on this dataset see <https://www.psl.noaa.gov/data/gridded/>

For more on the Global Carbon Project see <http://www.cgernies.go.jp/gcp/population-and-gdp.html>

For more on World Bank data see <https://data.worldbank.org/indicator>

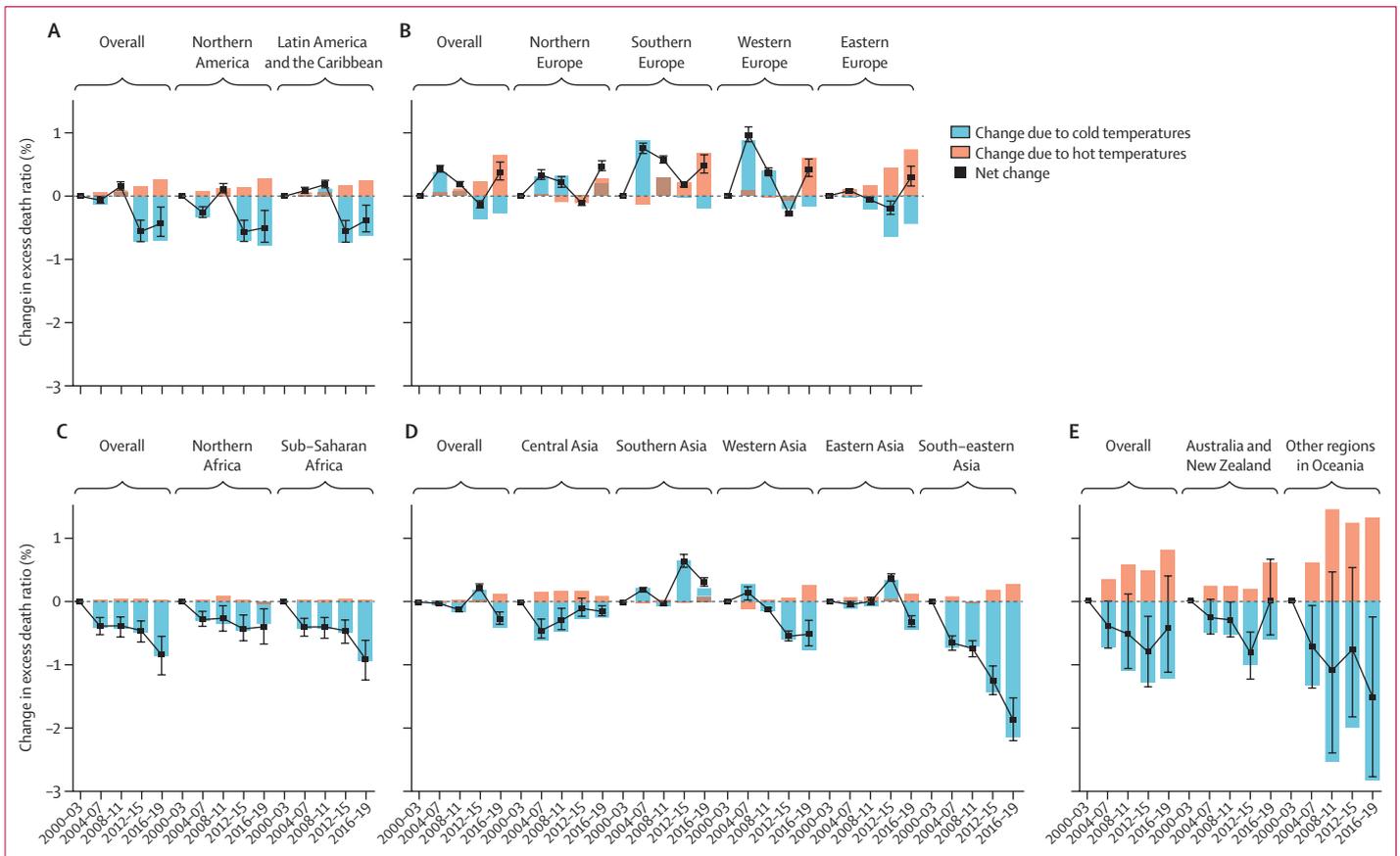


Figure 4: Regional change in annual excess death ratio between 2000 and 2019 compared with the 2000–03 average (A) The Americas. (B) Europe. (C) Africa. (D) Asia. (E) Oceania. Only grids with at least one annual death were included. The y-axis represents change in percentage points, not percentage change.

The net ratio declined substantially in Africa, Oceania, and South-eastern Asia, but increased in Southern Asia and Europe in a fluctuating pattern. Figure 3 and the appendix (p 12) show the changing nature per decade of the excess death ratio and rate at a spatial resolution of $0.5^{\circ} \times 0.5^{\circ}$. Finer geographical disparity could be observed within regions. For instance, northern areas of Latin America and the Caribbean had a more substantial decline in cold-related excess death ratio per decade than did other areas of this continent (figure 3).

Due to various limitations in the methodology of GBD 2019, the authors might have underestimated the global temperature-related mortality burden. Indeed, in our time-series analysis, the relative risk of mortality from both hot and cold temperatures was lower for the group of countries in GBD 2019 than for the remaining 36 countries in the MCC network (appendix p 13). Furthermore, the results of our sensitivity analyses indicate that our main findings are robust under a series of parameter changes during modelling (appendix p 10).

Discussion

This study estimated the global burden of mortality associated with non-optimal temperatures at a spatial

resolution of $0.5^{\circ} \times 0.5^{\circ}$, and explored the temporal change from 2000 to 2019. We found that there were 5 083 173 deaths per year associated with non-optimal temperatures, accounting for 9.43% of global deaths and equating to 74 temperature-related excess deaths per 100 000 residents. Most excess deaths were linked to cold temperatures (8.52%), whereas fewer were linked to hot temperatures (0.91%). Globally, from 2000–03 to 2016–19, the cold-related excess death ratio changed by -0.51 percentage points and the heat-related excess death ratio increased by 0.21 percentage points, leading to a net decline of -0.30 percentage points. The temperature-related mortality burden and its temporal changes showed disparate geographical variations.

Previous evidence shows that the strength of the temperature–mortality association can be modified by geographical, climatological, socioeconomic, and demographic factors at the population level.^{3,17,23} By October, 2020, only a few studies had quantified the variation of temperature-related mortality burden across countries and territories. Based on data of 74 million deaths from 13 countries or territories, a previous MCC study estimated that 7.71% of total deaths could be attributable to non-optimal temperatures, with the

burden varying geographically.³ For example, in Asia, the temperature-attributable fraction of mortality was much lower in Thailand (3·37%) than in China (11·00%). Another study that used similar variables estimated that the temperature-attributable fraction of mortality in India was 7·3%.⁹ Despite using different outcome indices, these results are largely consistent with our findings. By contrast, GBD 2019 reported a lower global temperature-related mortality burden (nearly 4%) than we do.¹² Further inconsistencies exist for regional estimations. For example, GBD 2019 estimated that the mortality burden for hot temperatures is higher than the mortality burden for cold temperatures in Southern Asia, which is opposite to the findings in our study and a previous report based on daily observational data of deaths.⁹ A possible explanation is that GBD 2019 estimated the global temperature-related burden on the basis of data from only eight countries, including five countries from Latin America and the Caribbean. This paucity of data might have introduced a representation issue. Furthermore, the calculation of temperature-related mortality burden only considered 12 causes of death. Moreover, a series of uncertainties were introduced during the fit of cause-specific exposure–response curves. For example, various numbers of knots were used for different causes of mortality, some cause-specific exposure–response curves were forced monotonically, and only significant parts of the exposure–response curves were considered, which might only account for less than a quarter of the whole curves. As a result, the global temperature-related mortality burden might have been underestimated, as supported by our analysis showing that the relative risk of mortality from both hot and cold temperatures was lower for the seven countries in GBD 2019 than for the remaining countries in the MCC network.

Our study found that more than half the excess deaths occurred in Asia, and especially in low-lying and crowded coastal cities in Eastern and Southern Asia. This result highlights how arduous the task will be for Asian countries to reduce the adverse effect of temperature on local population health and the substantial challenge to their health-care systems. The number of excess deaths is largely associated with population size. To systematically evaluate the geographical variation in temperature-related mortality burden, we introduced another two indices: excess death ratio and excess death rate (per 100 000 residents). Eastern Europe had the highest heat-related excess death rate and Sub-Saharan Africa had the highest cold-related excess death rate. Although Oceania only accounted for a small number of excess deaths, its excess death ratio and rate were still substantial compared with other regions. The lowest excess death ratio and rate occurred in Latin America and the Caribbean and South-eastern Asia. However, the results of a high-resolution analysis revealed a high heat-related mortality burden at the population level along the west coastline of Latin America.

This geographical variation suggests that the health threat of non-optimal temperatures is a global issue, requiring international collaboration to develop tailored health protective strategies for each region. Our previous MCC study found that most deaths attributable to hot and cold temperatures were brought forward by at least 1 year.²⁴ Combined with this finding, our new results strongly suggest that non-optimal temperatures are one leading cause of disease burden for population health.

Our study also explored the temporal change in temperature-related mortality burden from 2000 to 2019. The global daily mean temperature increased by 0·26°C per decade during this time, paralleled with a large decrease in cold-related deaths and a moderate increase in heat-related deaths. The results indicate that global warming might slightly reduce the net temperature-related deaths, although, in the long run, climate change is expected to increase mortality burden. However, regional disparities exist, with the ratio of cold-related excess deaths decreasing in South-eastern Asia. Southern Asia was the only region where the daily mean temperature per decade decreased, paralleling the increase in cold-related and overall excess deaths between 2000 and 2019. As a result, local countries should be aware of the effect of cold temperatures when developing health promotion strategies. In comparison, despite the substantial reduction in cold-related excess deaths in Oceania, the heat-related excess death ratio increased between 2000 and 2019 by more than most other regions. Europe was another continent where heat-related excess death ratio increased. Considering the inevitable warming trend in the next decades, the mortality burden associated with heat exposure is predicted to increase substantially in both continents.¹⁴

This study has some strengths. First, to the best of our knowledge, it is the largest investigation of the adverse impact of non-optimal temperatures on population health. Compared with previous studies confined to country-level or region-level estimations,^{3,7} the high-resolution (0·5°×0·5°) map provides an overview of mortality burden associated with non-optimal temperatures at the global level and within specific subregions. Our findings will help national and local governments and international communities to develop better cold weather plans and early warning systems, and more efficient health protection strategies against global warming. Second, the assessment of average temperature-related mortality burden and the temporal trend between 2000 and 2019 provides a better understanding of how global warming has affected different populations worldwide. Finally, we developed the model using data on more than 130 million deaths from 43 countries or territories, which are located in five continents and characterised by different climates, socioeconomics, demographics, and development levels of infrastructure and public health services. This large sample size and the representativeness of data helped to ensure the high quality of our findings at the global level.

Several assumptions and limitations should be acknowledged. In this study, we explored the temporal change in temperature-related mortality burden by fixing socioeconomic factors (ie, population, mortality, and GDP per capita) at the 2010 level. This assumption allows the results to reflect the excess death burden purely caused by temperature change. Another assumption is the identical mortality rate across grids within the same country, which was implemented because of the paucity of grid-specific mortality data. This assumption should not have substantially changed our findings at the country or large region levels; however, some overestimation or underestimation might exist at finer geographical scales, which can be improved in the future with available mortality data at the grid level. We built the multivariate meta-regression using five meta-predictors, which have been shown to explain the majority of heterogeneity in the temperature–mortality association across locations.¹⁴ However, we were unable to adjust for other potential effect modifiers (eg, age structure, sex, and deaths caused by influenza) because of a paucity of data. Sparse data from Southern Asia, the Arabian Peninsula, and Africa outside of South Africa could have reduced the modelling accuracy in these regions. This issue warrants further exploration and should be lessened in the future with an extended MCC network. We used modelled temperature data for grid-specific analyses because of the paucity of observational data for each grid. However, previous studies have found only very small differences in effect estimates between the two methods.^{25,26}

To conclude, a substantial burden of mortality is attributable to non-optimal temperatures, which exhibits complex geographical and temporal patterns worldwide. Our findings call for decisive and coordinated action to raise public awareness of temperature as a health risk. The variation in regional and local mortality burden associated with non-optimal temperature warrants in-depth exploration to design adaptive strategies against both excess heat and cold that protect health.

Contributors

YG, AG, MH, and BA set up the collaborative network. YG, SL, and QZ designed the study. YG, SL, QZ, and AG developed the statistical methods. YG, SL, and QZ took the lead in drafting the manuscript and interpreting the results. QZ, YG, TY, AG, ST, AO, AU, AS, AE, AMV-C, AZa, AA, AZe, AT, BN, BAL, BAf, BF, S-CP, CÍ, CAm, CDICV, CÂs, DH, DVD, DR, EI, EL, FM, FA, FdD, FDR, FS, GC-E, HKa, HO, HKi, I-HH, JK, JM, JS, JJKJ, KK, MHD, MSR, MH, MP, MdSZSC, NVO, NR, NS, PM, PMC, PG, PHNS, RA, SO, SR, SF, TND, VC, VH, WL, XS, YH, YLG, MLB, and SL provided the data, and contributed to the interpretation of the results and the submitted version of the manuscript. YG, SL, and QZ accessed and verified the data. All authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Declaration of interests

We declare no competing interests.

Data sharing

Data were collected within the MCC Collaborative Research Network under a data sharing agreement and cannot be made publicly available. Researchers can refer to MCC participants, who are listed as coauthors of this Article, for information on accessing the data for each country.

Acknowledgments

This study was supported by the Australian Research Council (DP210102076) and the Australian National Health and Medical Research Council (APP2000581). QZ was supported by the Program of Qilu Young Scholars of Shandong University, Jinan, China; SL by an Early Career Fellowship of the Australian National Health and Medical Research Council (number APP1109193); YG by career development fellowships of the Australian National Health and Medical Research Council (number APP 1163693); JK and AU by the Czech Science Foundation (project number 20–28560S); NS by the National Institute of Environmental Health Sciences-funded HERCULES Center (P30ES019776); S-CP and YLG by the Ministry of Science and Technology (Taiwan; MOST 109–2621-M-002–021); YH by the Environment Research and Technology Development Fund (JPMEEF15S11412) of the Environmental Restoration and Conservation Agency; MdSZSC and PHNS by the São Paulo Research Foundation (FAPESP); ST by the Science and Technology Commission of Shanghai Municipality (grant number 18411951600); HO and EI by the Estonian Ministry of Education and Research (IUT34–17); JM by a fellowship of Fundação para a Ciência e a Tecnologia (SFRH/BPD/115112/2016); AG and FS by the Medical Research Council UK (grant ID MR/R013349/1), the Natural Environment Research Council UK (grant ID NE/R009384/1), and the EU's Horizon 2020 project, Exhaustion (grant ID 820655); AS, SR, and FdD by the EU's Horizon 2020 project, Exhaustion (grant ID 820655); and VH by the Spanish Ministry of Economy, Industry and Competitiveness (grant ID PCIN-2017–046). This Article is published in memory of Simona Fratianni who helped to contribute the data for Romania.

Editorial note: the *Lancet* Group takes a neutral position with respect to territorial claims in published maps and institutional affiliations.

References

- National Centers for Environmental information. State of the climate. Global climate report—annual 2019. 2020. <https://www.ncdc.noaa.gov/sotc/global/201913> (accessed Oct 11, 2020).
- Zhao Q, Li S, Coelho MSZS, et al. Geographic, demographic, and temporal variations in the association between heat exposure and hospitalization in Brazil: a nationwide study between 2000 and 2015. *Environ Health Perspect* 2019; **127**: 17001.
- 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, Zhang Y, Zhang W, et al. Ambient temperature and emergency department visits: time-series analysis in 12 Chinese cities. *Environ Pollut* 2017; **224**: 310–16.
- Zhao Q, Li S, Coelho MSZS, et al. The association between heatwaves and risk of hospitalization in Brazil: a nationwide time series study between 2000 and 2015. *PLoS Med* 2019; **16**: e1002753.
- Lu P, Zhao Q, Xia G, et al. Temporal trends of the association between ambient temperature and cardiovascular mortality: a 17-year case-crossover study. *Environ Res Lett* 2021; **16**: 045004.
- Chen R, Yin P, Wang L, et al. Association between ambient temperature and mortality risk and burden: time series study in 272 main Chinese cities. *BMJ* 2018; **363**: k4306.
- Nordio F, Zanobetti A, Colicino E, Kloog I, Schwartz J. Changing patterns of the temperature-mortality association by time and location in the US, and implications for climate change. *Environ Int* 2015; **81**: 80–86.
- Fu SH, Gasparrini A, Rodriguez PS, Jha P. Mortality attributable to hot and cold ambient temperatures in India: a nationally representative case-crossover study. *PLoS Med* 2018; **15**: e1002619.
- Scovronick N, Sera F, Acquafatta F, et al. The association between ambient temperature and mortality in South Africa: a time-series analysis. *Environ Res* 2018; **161**: 229–35.
- Hajat S, Kovats RS, Lachowycz K. Heat-related and cold-related deaths in England and Wales: who is at risk? *Occup Environ Med* 2007; **64**: 93–100.
- GBD 2019 Risk Factors Collaborators. Global burden of 87 risk factors in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet* 2020; **396**: 1223–49.

- 13 Guo Y, Gasparrini A, Armstrong B, et al. Global variation in the effects of ambient temperature on mortality: a systematic evaluation. *Epidemiology* 2014; **25**: 781–89.
- 14 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.
- 15 Fan Y, Van den Dool H. A global monthly land surface air temperature analysis for 1948–present. *J Geophys Res Atmos* 2008; **113**: D011103.
- 16 Murakami D, Yamagata Y. Estimation of gridded population and GDP scenarios with spatially explicit statistical downscaling. *Sustainability* 2019; **11**: 2106.
- 17 Gasparrini A, Armstrong B, Kenward MG. Multivariate meta-analysis for non-linear and other multi-parameter associations. *Stat Med* 2012; **31**: 3821–39.
- 18 Kottke M, Grieser J, Beck C, Rudolf B, Rubel F. World map of the Köppen-Geiger climate classification updated. *Meteorol Z (Berl)* 2006; **15**: 259–63.
- 19 Zhao Q, Li S, Cao W, et al. Modeling the present and future incidence of pediatric hand, foot, and mouth disease associated with ambient temperature in mainland China. *Environ Health Perspect* 2018; **126**: 047010.
- 20 Guo Y, Gasparrini A, Li S, et al. Quantifying excess deaths related to heatwaves under climate change scenarios: a multicountry time series modelling study. *PLoS Med* 2018; **15**: e1002629.
- 21 UN Statistics Division. Methodology. Standard country or area codes for statistical use (M49). <https://unstats.un.org/unsd/methodology/m49/> (accessed Sept 21, 2020).
- 22 Gasparrini A, Armstrong B, Kenward MG. Distributed lag non-linear models. *Stat Med* 2010; **29**: 2224–34.
- 23 Son J-Y, Liu JC, Bell ML. Temperature-related mortality: a systematic review and investigation of effect modifiers. *Environ Res Lett* 2019; **14**: 073004.
- 24 Armstrong B, Bell ML, de Sousa Zanotti Stagliorio Coelho M, et al. Longer-term impact of high and low temperature on mortality: an international study to clarify length of mortality displacement. *Environ Health Perspect* 2017; **125**: 107009.
- 25 Royé D, Íñiguez C, Tobías A. Comparison of temperature-mortality associations using observed weather station and reanalysis data in 52 Spanish cities. *Environ Res* 2020; **183**: 109237.
- 26 Weinberger KR, Spangler KR, Zanobetti A, Schwartz JD, Wellenius GA. Comparison of temperature-mortality associations estimated with different exposure metrics. *Environ Epidemiol* 2019; **3**: e072.