Global, regional, and national burden of mortality associated with cold spells during 2000–19: a three-stage modelling study

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Summary

Background Exposure to cold spells is associated with mortality. However, little is known about the global mortality burden of cold spells.

Methods A three-stage meta-analytical method was used to estimate the global mortality burden associated with cold spells by means of a time series dataset of 1960 locations across 59 countries (or regions). First, we fitted the location-specific, cold spell-related mortality associations using a quasi-Poisson regression with a distributed lag non-linear model with a lag period of up to 21 days. Second, we built a multivariate meta-regression model between location-specific associations and seven predictors. Finally, we predicted the global grid-specific cold spell-related mortality associations during 2000–19 using the fitted meta-regression model and the yearly grid-specific meta-predictors. We calculated the annual excess deaths, excess death ratio (excess deaths per 1000 deaths), and excess death rate (excess deaths per 100 000 population) due to cold spells for each grid across the world.

Findings Globally, 205 932 (95% empirical CI [eCI] 162 692–250 337) excess deaths, representing 3·81 (95% eCI 2·93–4·71) excess deaths per 1000 deaths (excess death ratio), and 3·03 (2·33–3·75) excess deaths per 100 000 population (excess death rate) were associated with cold spells per year between 2000 and 2019. The annual average global excess death ratio in 2016–19 increased by 0·12 percentage points and the excess death rate in 2016–19 increased by 0·18 percentage points, compared with those in 2000–03. The mortality burden varied geographically. The excess death ratio and rate were highest in Europe, whereas these indicators were lowest in Africa. Temperate climates had higher excess death ratio and rate associated with cold spells than other climate zones.

Interpretation Cold spells are associated with substantial mortality burden around the world with geographically varying patterns. Although the number of cold spells has on average been decreasing since year 2000, the public health threat of cold spells remains substantial. The findings indicate an urgency of taking local and regional measures to protect the public from the mortality burdens of cold spells.

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Introduction

Despite global warming being the main manifestation of climate change,[1] climate change is also driving an increase in the frequency, intensity, and severity of cold spells in some regions.[2–4] For example, the average frequency of cold spells in Korea and Japan increased by 51·44% in the 2010s, compared with the 1990s.[3] In addition, the frequency of cold spells in mid-latitudes might not decrease in the future.[5] Existing evidence has observed higher mortality risks and burdens associated with low temperatures, compared with high temperatures.[6–8] For example, a global time-series study reported that 9·43% of all deaths annually, during 2000–19, were associated with non-optimal temperatures. The majority (8·52%) were associated with low temperatures and relatively fewer (0·91%) with high temperatures.[7] However, the global burden of cold spells was unknown.

A cold spell is an extreme weather event, manifested by extreme low temperatures over consecutive days.[9] Existing evidence indicates that cold spells are associated with a range of adverse health outcomes, such as injuries, mortality,[10–13] morbidity for respiratory and cardiovascular diseases,[14–16] preterm birth,[17] and birth defects.[18] The pathophysiological basis and the effects of ambient cold exposure in humans are relatively well understood, thanks to decades of experimental research.[19,20]

Although considerable evidence has emerged to explore the association between cold spells and mortality,[10–13,21–29] very few studies have assessed the global mortality burden due to cold spells. To the best of

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See **Online** for appendix

Research in context

Evidence before this study
Little is known about the mortality burden due to cold spells at the global scale. We searched PubMed, Web of Science, Scopus, and Google Scholar from the database inception to March 1, 2022 for studies published in English. We used a combination of search terms, including "cold spell", "cold wave", "cold surge", "mortality", "mortality burden", "death" and "excess death". Previous studies mostly quantified the association between cold spells and mortality within a single city or multiple cities within a single country; very few studies have assessed the global mortality burden due to cold spells. In addition, the estimated association is difficult to compare across studies owing to the high heterogeneity (eg, study period, study settings, cold spell definition, and modelling strategy).

Added value of this study
To the best of our knowledge, this is the first global study to comprehensively quantify the spatiotemporal mortality burden associated with cold spells at a high spatial resolution of 0·5° × 0·5° from 2000 to 2019. We found that the global cold spell days decreased at an average change of –0·20 days per year. Globally, 205 932 excess deaths, representing 3·81 excess deaths per 1000 deaths and 3·03 excess deaths per 100 000 population were associated with cold spells per year. Substantial geographical variations were observed. The excess death ratio and rate were the highest in Europe, whereas these indicators were the lowest in Africa.

Implications of all the available evidence
Our findings provide scientific evidence on the global mortality burden of cold spells. Our results suggested that cold spells were associated with a substantial mortality burden with geographical heterogeneity globally, even though a decreasing trend of exposure days was found in most regions. More targeted adaptation measures should be implemented in regions with higher cold spell-related mortality burdens.

our knowledge, the mortality burden attributable to cold spells at the global level has not been well demonstrated to date. In addition, high heterogeneities across different studies, such as cold spell definitions, lag periods and study periods, make it difficult to compare and generalise the results.[30] To help address these knowledge gaps, this study aimed to estimate the global, regional, and national mortality burdens associated with cold spells by means of a unified modelling strategy based on the global data from the Multi-Country Multi-City (MCC) Collaborative Research Network. A total of 1960 locations in 59 countries (or regions) were incorporated, covering 31·0% of the global population. Our findings will provide a better understanding of the global and regional mortality burdens due to cold spells, which is crucial for developing adaptation strategies for cold spells.[31]

Methods

Data sources
Daily all-cause mortality data were obtained from an integrated global dataset based on the MCC Collaborative Research Network database.[7,31] Detailed procedure on the collection and integration of the global dataset is provided in the appendix (pp 7–8). The latest database covers 1960 locations across 59 countries or regions (appendix pp 10–11).

Average daily mean temperatures at a spatial resolution of 0·5°×0·5° for the period 2000–19 were calculated by means of data from the Global Daily Temperature dataset, developed by the Climate Prediction Centre.[7] The dataset is interpolated by means of observation data from 6000–7000 temperature monitoring stations, using a Shepard algorithm.[32] Daily minimum and maximum temperature data were extracted for the period 2000–19 and were used to calculate daily mean temperature. Annual data on gross domestic product (GDP) standardised to the 2005 rate and population were obtained from the Global Carbon Project at a spatial resolution of 0·5°×0·5° per 10 years for the period 1980–2100. Additionally, GDP and population data were interpolated to the middle year of the study period.[7] The location-specific GDP and population data were then used to calculate the GDP per capita for each grid. The annual mortality rates for each country were extracted from the World Bank for the period 2000–19.

We used the most common cold spell definition,[30] which is based on statistically defined local temperature thresholds and prespecified durations.[11–13] Cold spells were defined by combining thresholds of the 5th percentiles of location-specific year-round daily mean temperatures and duration of at least 3 consecutive days.[13]

Statistical analysis
The analyses were restricted to cold seasons (the coldest 6 consecutive months for each location), which were identified by the monthly mean temperature during the study period. We estimated the global cold spell-related mortality burden at a spatial resolution of 0·5°×0·5° with an extending three-stage meta-analytical method. Details have been discussed in previous publications.[7,8,31,33,34] The innovation of this method is the prediction of the cold spell-related mortality burden for locations without daily mortality time-series.[7]

Briefly, in the first stage, location-specific associations between cold spells and mortality for 1960 locations were explored by means of a quasi-Poisson regression with a distributed lag non-linear model, with a lag period of up to 21 days.[7,35] The lag effects of cold spells on

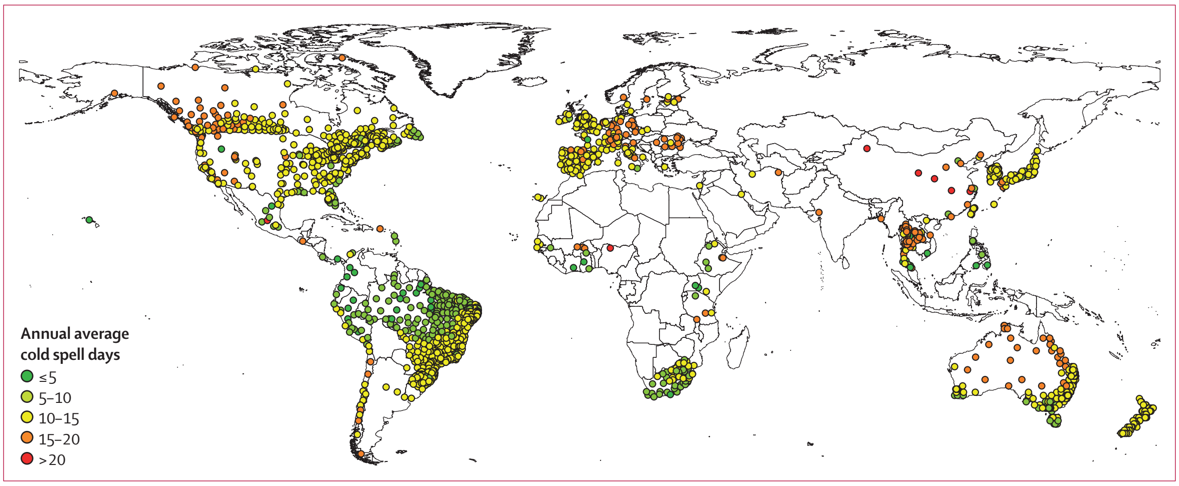

Figure 1: **Annual average cold spell days of the 1960 locations across 59 countries (or regions) included in the analysis**

mortality were modelled with a natural cubic spline with three degrees of freedom and two internal knots (plus an intercept) set at equally spaced log values of lag. The algebraic expression is as follows:

$$Y_{it} \sim \text{Poisson}(\mu_{it})$$
$$\log(\mu_{it}) = \alpha + \text{cb}(\text{CS}_{it}, \text{lag}=21) + \beta_i \text{Stratum}_{it} + \gamma_i \text{DOW}_{it},$$

in which Y_{it}, is the count of deaths on day t in location i; α is the intercept; CS_{it} is a binary variable representing cold spells (yes or no); $\text{cb}(\text{CS}_{it}, \text{lag}=21)$ is the cross-basis function to model the cumulative association on lag 0–21 days with a natural cubic spline with 3 degrees of freedoms; Stratum_{it} is a categorical variable of the year and calendar month (eg, 2010-Jan, 2010-Feb), to control for long-term trend and seasonal variation; DOW_{it} is a categorical variable of the day of the week; and β_i and γ_i are coefficients.

In the second stage, we constructed a multivariate meta-regression model with a random intercept of country (accounting for the dependence of the location-specific effects within the same country) using all location-specific effect estimates from the first stage and seven meta-predictors (continent, latitude and longitude, indicators for Köppen–Geiger climate classification, GDP per capita, yearly average temperature, and temperature range at the location level), which have been shown to explain the majority of the heterogeneity for location-specific effects.[7,8,33,34] Potential non-linear effects of latitude, longitude, average temperature, and temperature range were included in the model with a natural spline function of 3, 3, 5, and 5 degrees of freedom, respectively, which were chosen on the basis of the minimum Akaike information criterion. We quantified the residual heterogeneity of the meta-regression model for explaining variation in overall cold spell effects by the Cochran Q test and I^2 statistics. The I^2 of the final model was 25·1% (appendix p 12).

	Annual excess deaths	Annual excess death ratio (per 1000 deaths)	Annual excess death rate (per 100 000 population)
Global	205 932 (162 692 to 250 337)	3·81 (2·93 to 4·71)	3·03 (2·33 to 3·75)
Americas	24 865 (20 039 to 29 816)	3·96 (3·19 to 4·75)	2·69 (2·17 to 3·23)
Northern America	11 849 (9057 to 14 725)	4·22 (3·22 to 5·24)	3·44 (2·63 to 4·28)
Latin America and the Caribbean	13 016 (10 542 to 15 554)	3·76 (3·05 to 4·49)	2·25 (1·82 to 2·68)
Asia	122 661 (95 642 to 150 379)	4·28 (3·33 to 5·24)	2·99 (2·33 to 3·67)
Central Asia	1103 (567 to 1660)	2·81 (1·44 to 4·22)	1·84 (0·94 to 2·76)
Eastern Asia	52 336 (41 893 to 63 055)	4·78 (3·83 to 5·76)	3·40 (2·72 to 4·09)
Southern Asia	56 458 (42 629 to 70 656)	4·63 (3·49 to 5·79)	3·38 (2·55 to 4·23)
Western Asia	4898 (2938 to 6937)	4·12 (2·47 to 5·85)	2·16 (1·29 to 3·06)
Southeastern Asia	7867 (5151 to 10 664)	2·00 (1·31 to 2·71)	1·32 (0·87 to 1·79)
Europe	50 059 (40 919 to 59 475)	5·87 (4·80 to 6·97)	6·76 (5·52 to 8·03)
Southern Europe	8503 (7094 to 9947)	5·59 (4·66 to 6·54)	5·50 (4·59 to 6·44)
Eastern Europe	24 231 (18 085 to 30 623)	5·69 (4·25 to 7·19)	8·14 (6·07 to 10·28)
Northern Europe	5844 (4925 to 6788)	6·24 (5·26 to 7·24)	5·91 (4·98 to 6·86)
Western Europe	11 481 (9986 to 12 999)	6·36 (5·54 to 7·21)	6·06 (5·27 to 6·86)
Africa	8029 (1816 to 14 534)	0·77 (0·17 to 1·40)	0·82 (0·19 to 1·48)
Northern Africa	1806 (−171 to 3892)	1·45 (−0·13 to 3·12)	0·90 (−0·08 to 1·93)
Sub-Saharan Africa	6222 (1426 to 11 257)	0·68 (0·15 to 1·23)	0·80 (0·18 to 1·44)
Oceania	319 (158 to 486)	1·31 (0·65 to 2·00)	0·91 (0·45 to 1·39)
Australia and New Zealand	309 (150 to 475)	1·75 (0·85 to 2·69)	1·15 (0·56 to 1·78)
Other regions in Oceania	10 (−6 to 27)	0·15 (−0·09 to 0·41)	0·13 (−0·07 to 0·34)

Table 1: **Regional annual excess deaths, excess death ratio, and excess death rate with 95% empirical CI associated with cold spells in 2000–19**

In the extended third stage, we predicted the cold spell-mortality association for each grid individually between 2000 and 2019 using the fitted meta-regression from the second stage and the seven grid-level predictors of each year at the grid level.[7,36] We restricted the analyses to grids with at least one annual death to improve the modelling stability.[7,36] The annual deaths in each grid were calculated on the basis of the annual mortality rate of the country in

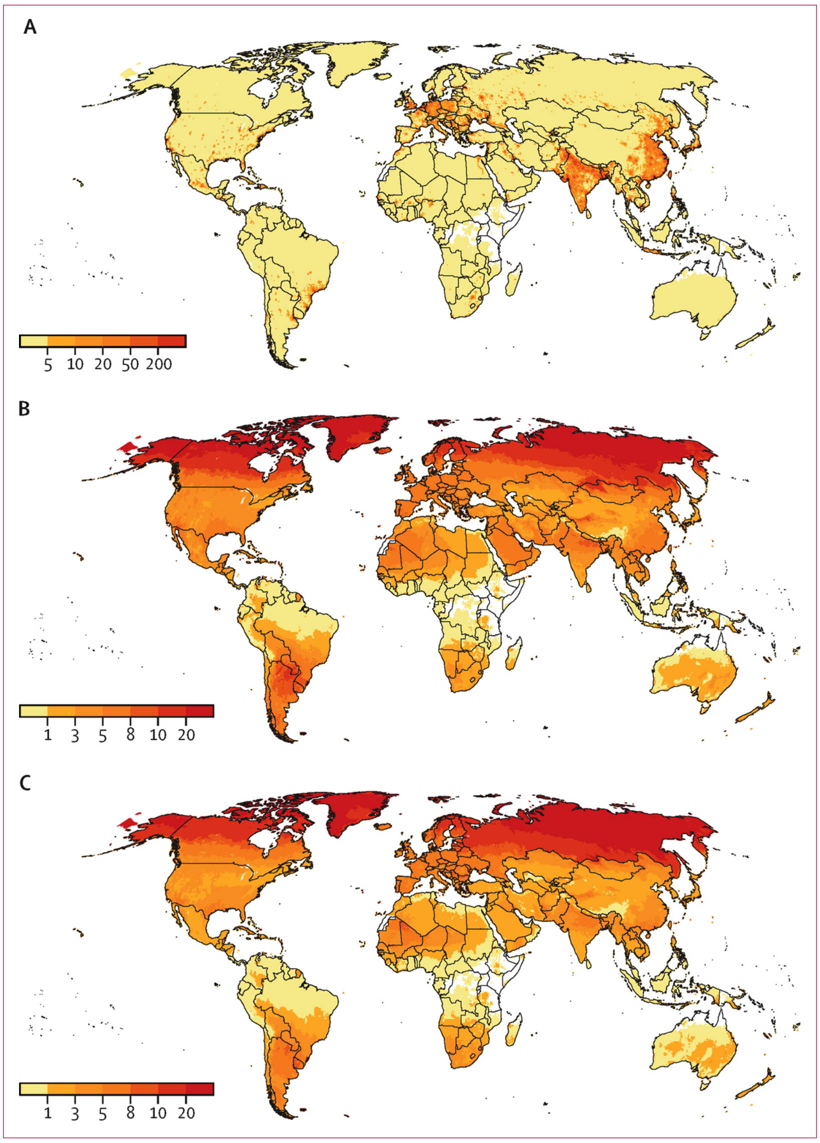

Figure 2: **Global annual excess deaths (A), excess death ratio (B), and excess death rate (C) associated with cold spells in 2000–19 at a spatial resolution of 0·5°×0·5°**

which the grid was located and the population in the grid of that year. This calculation assumed an identical mortality rate across all grids inside the country.[7,36]

For each grid on a specific year y, excess deaths due to cold spells CS_{iy} were calculated as: $CS_{iy}=(RR_{iy}-1)\times N_{iy}\times D_{iy}$, in which RR_{iy} is the cumulative relative risk derived from the grid-specific cold spell-mortality risk in year predicted in the third stage; N_{iy} and D_{iy} are the total number of cold spell exposure days and daily average deaths during the coldest 6 months in year y, respectively. Owing to lack of data on the grid-specific daily deaths during the 6 coldest months, we estimated D_{iy} by modelling the association of the ratio of deaths in the six coldest months to total deaths with the indicator of continents, Köppen–Geiger climate classification, GDP per capita, yearly average daily mean temperature and range of daily mean temperature with linear regression; estimating the ratio of deaths in the six coldest months to total deaths for each grid in year on the basis of the fitted model and the grid-specific predictors of year y; multiplying the estimated death ratio and the total deaths of grid i in year y.

To evaluate the uncertainty in excess deaths estimation, Monte Carlo simulations with 1000 samples were used to calculate the empirical CIs (eCIs). We also calculated the excess death ratio (excess deaths per 1000 deaths) and the excess death rate (excess deaths per 100 000 population). In interpreting our results, grids were divided by regions according to the regional groupings of the UN Statistics Division (M49) and the indicators of the Köppen–Geiger climate classification.[37]

We further applied Sen's Kendal slope estimator,[38] which is non-parametric and robust against outliers, to assess the annual trends in excess deaths, excess death ratio, and rate at the grid level (0·5°×0·5°) from 2000 to 2019. The temporal change of cold spell-related mortality burden was explored as the percentage changes by region compared with the 2000–03 average.

We did several sensitivity analyses to check the robustness of our results. First, we estimated the global annual excess deaths, excess death ratio, and excess death rate with 95% eCI in the following ways: changing the degrees of freedom for lag response relationship to 4 and 5; changing the lag days of the cold spell from 21 to 30 days; choosing alternative four and five coldest consecutive months to define the cold seasons. Second, we estimated the percentage change of cold spell-related mortality burdens by applying nine cold spell definitions with different temperature thresholds (2·5th, 5th, 7·5th) and duration days (≥2, ≥3, ≥4).

All the analyses were done in R software with the packages of "dlnm" for the first-stage analysis and "mixmeta" for the second-stage analysis. A two-sided $p<0·05$ was considered as significant.

Role of the funding source

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

Results

The summary statistics of the included countries (or regions) are presented in the appendix pp 10–11, including the number of locations, study period, total death counts and annual average number of cold spell days. In summary, a total of 43·2 million deaths from 1960 locations across 59 countries (or regions) were included. The geographical distribution and annual average cold spell days are presented in figure 1. The geographical distribution of cold spell days varied across the included 1960 locations, with an annual average number of 12 days. Higher number of cold spell days (>20 days) were mainly observed in China.

The annual average number and change of cold spell days are presented in the appendix p 13. Globally, between 2000–2019, the annual average number of cold spell days across grids with at least one annual death was 24 (range 0 to 51), whereas the annual average change of cold spell days was –0·20 (–2·40 to 2·50). The annual average number of cold spell days and the direction and magnitude in the average change of cold spell days between 2000 and 2019 varied across regions. For the annual average number of cold spell days, eastern Europe was the region with the highest (31, 18 to 48), whereas Micronesia (located in Oceania) was the region with the lowest (7, 2 to 11). For the annual average change of cold spell days, northern Europe was the region with the strongest decrease (–0·54, –0·86 to 1·00), whereas southern Asia was the region with the strongest increase (0·16, –1·33 to 2·50).

The excess deaths, excess death ratio, and the excess death rate associated with cold spells at the regional level are presented in table 1. Globally, from 2000 to 2019, 205 932 (95% eCI 162 692–250 337) excess deaths, representing 3·81 (2·93–4·71) excess deaths per 1000 deaths and 3·03 (2·33–3·75) excess deaths per 100 000 population were associated with cold spells per year. Of all excess deaths, 122 661 (59·56%) occurred in Asia, 50 059 (24·31%) occurred in Europe, 24 865 (12·07%) occurred in the Americas, 8029 (3·90%) occurred in Africa, and 319 (0·16%) occurred in Oceania. The excess death ratio and rate exhibited geographical heterogeneity. The excess death ratio and rate were the highest in Europe, whereas these indicators were the lowest in Africa. In detail, the highest excess death ratio occurred in Europe (5·87, 95% eCI 4·80–6·97), followed by Asia (4·28, 3·33–5·24), the Americas (3·96, 3·19–4·75), Oceania (1·31, 95% 0·65–2·00), and Africa (0·77, 0·17–1·40). For the excess death rate, the highest excess death rate occurred in Europe (6·76, 5·52–8·03), especially in eastern Europe (8·14, 6·07–10·28), followed by Asia (2·99, 2·33–3·67), the Americas (2·69, 2·17–3·23), Oceania (0·91, 0·45–1·39), and Africa (0·82, 0·19–1·48).

The global excess deaths, excess death ratio, and the excess death rate associated with cold spells at the grid level and their annual rate of change (estimated by Sen's Kendal slope estimator) are presented in figures 2 and 3 respectively. Grids with high excess deaths were mainly located in Europe and southern and eastern Asia (figure 2A), whereas grids with high excess death ratio and rate were mainly located in high latitudes of the northern hemisphere (eg, Russia, Canada, and Alaska; figure 2B, C). Grids with higher increased rates of excess deaths due to cold spells were observed mostly in southern Asia and eastern Asia (figure 3A), whereas grids with higher increased rates of excess death ratio and excess death rate due to cold spells were observed mostly in India (located in southern Asia), Canada (located in northern America), and Russia (located in eastern Europe; figure 3B, C).

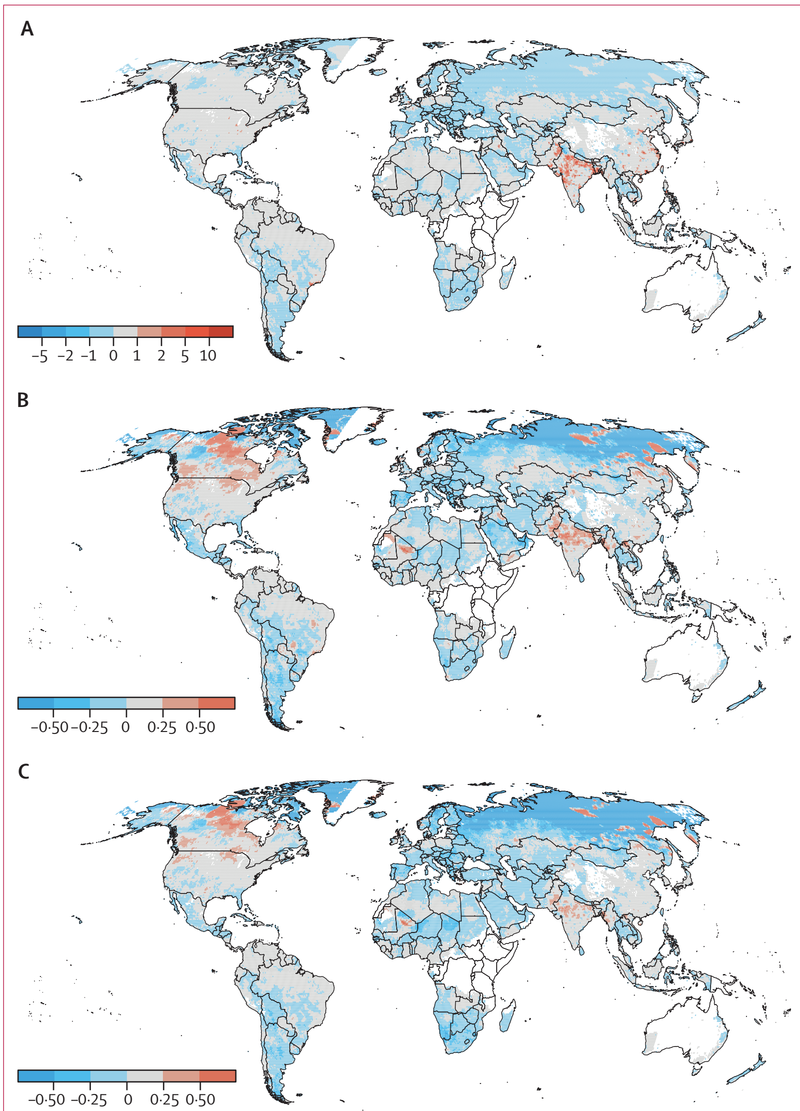

Figure 3: **Global annual rate of change (estimated by Sen's Kendal slope) in excess deaths (A), excess death ratio (B), and excess death rate (C) associated with cold spells in 2000–19 at a spatial resolution of 0·5° × 0·5°**

From 2000–03 to 2016–19, the global excess deaths, excess death ratio, and excess death rate increased in 2000–11 and then decreased in 2012–19, with the highest number in 2008–11 (appendix pp 14–16). From 2000–03 to 2016–19, the global excess death ratio increased by 0·12 percentage points from 2·38 (95% eCI 1·81–2·98) in 2000–03 to 2·50 (1·95–3·06) in 2016–19 (appendix p 15) and the global excess death rate increased by 0·18 percentage points from 2·38 (95% eCI 1·77–3·02) in 2000–03 to 2·56 (95% eCI 1·97–3·16) in 2016–19 (appendix p 16). Figure 4 shows the temporal change in overall excess deaths, excess death ratio, and excess death rate by region, compared with the 2000–03 average. From 2000–03 to 2016–19, the excess deaths, excess death ratio,

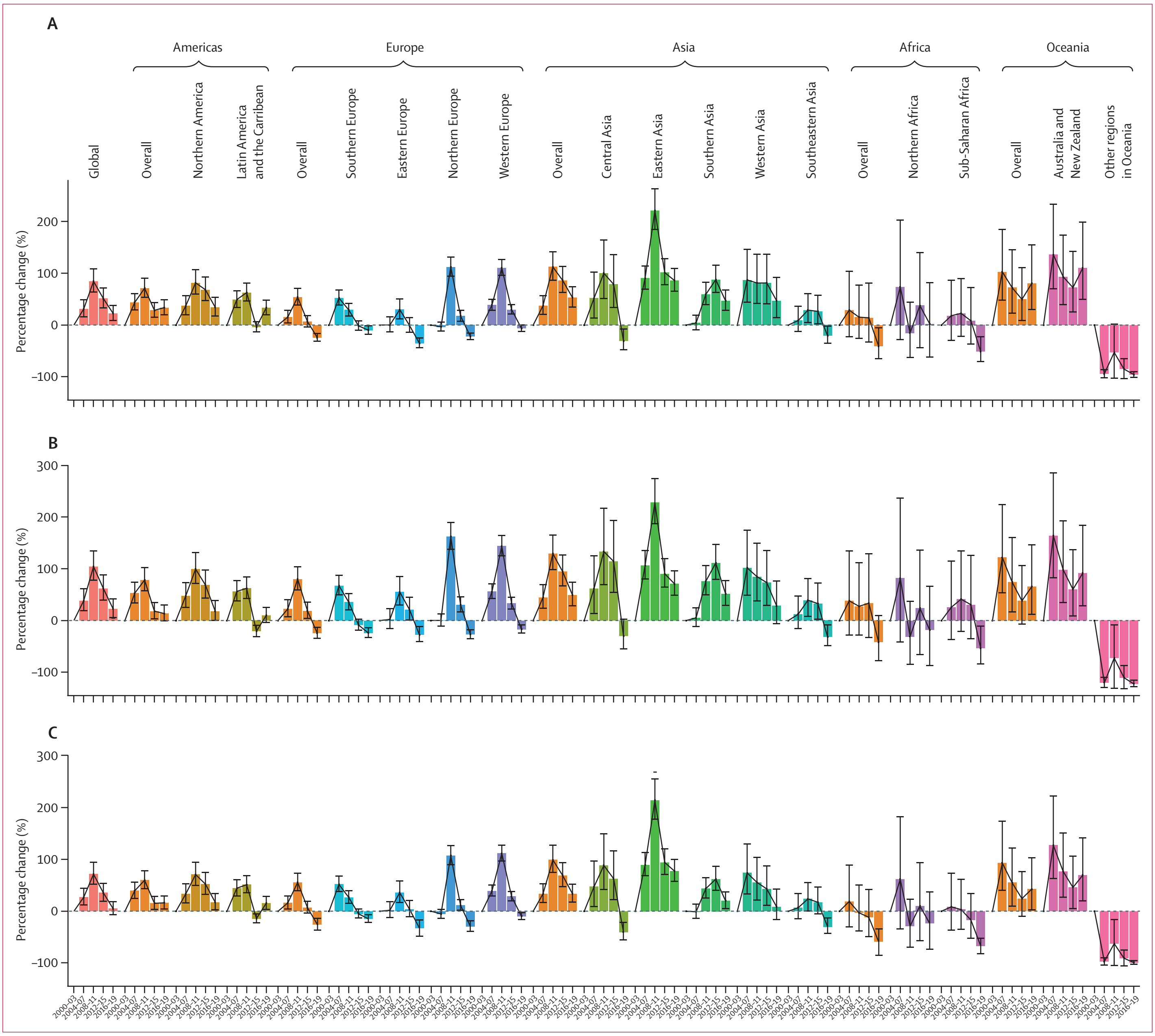

Figure 4: **Regional percentage change in annual excess deaths (A), excess death ratio (B), and excess death rate (C) associated with cold spells in 2000–19 compared with the 2000–03 average**

and excess death rate increased in most regions, except Europe, central and southeastern Asia, sub-Saharan Africa, and other regions in Oceania (figure 4). The greatest increase occurred in Australia and New Zealand. Temperate climates had higher excess death ratio and rate associated with cold spells than other climate zones (indicators of the Köppen–Geiger classification; appendix p 17).

The annual excess death rate for each decade and the entire period associated with cold spells in 2000–19 for the global top 20 countries are shown in table 2. The annual excess death rate from 2000 to 2019 associated with cold spells was the highest in Russia (located in eastern Europe; 9·82, 95% eCI 6·68–13·12), followed by Latvia (located in northern Europe; 9·75, 8·03–11·51). Globally, from 2000 to 2019, China (located in eastern Asia) had the highest excess deaths associated with cold spells (appendix p 18), whereas Iceland (located in northern Europe) had the highest excess death ratio associated with cold spells (appendix p 19).

The results of the sensitivity analyses indicated that our main findings were robust (appendix pp 20–21).

Discussion

This study estimated the global mortality burden associated with cold spells at a spatial resolution of $0 \cdot 5° \times 0 \cdot 5°$ from 2000 to 2019. To the best of our knowledge, this is the first global study to systematically explore the spatiotemporal mortality burdens associated with cold spells. We found that 205 932 excess deaths, representing 3·81 excess deaths per 1000 deaths and 3·03 excess deaths per 100 000 population globally, were associated with cold spells per year between 2000 and 2019. The mortality burden associated with cold spells showed temporal and geographical variations.

We observed a substantial mortality burden associated with cold spells globally. The biological model for these findings is reasonably well established.[19,20,39–41] Ambient cold exposure initiates reflex cutaneous vasoconstriction, which increases systemic vascular resistance, afterload, preload, and myocardial workload precipitating oxygen supply-demand mismatch.[41] Ambient cold exposure also increases central aortic blood pressure,[42] which in addition to the systemic effects of hypertension might work as a substrate for stroke and plaque rupture. Ambient cold exposure causes changes in fluid homeostasis, coagulation status, and inflammation,[43–46] whereas breathing cold air cools and dries the airway mucosa, and causes hyperosmolality and neural activation, airway damage and bronchoconstriction.[47,48] These are just a few examples of the known changes that occur within the timeframe relevant to our analysis. It is important to note, however, that although the health effects of cold exposure are well understood thanks to more than 50 years of experimental research, many previously described uncertainties in the causal chain from cold spells to individual-level health effects remain largely unsolved.[30] Understanding the places and types of most harmful individual exposures would help in creating evidence-based guidelines.

Our findings showed that most excess deaths associated with cold spells occurred in Asia, especially in densely populated locations in southern and eastern Asia, such as China and India. In addition, the highest annual increase of cold spell days, as well as higher increased rates of excess deaths, excess death ratio, and excess death rate due to cold spells, were observed mostly in southern Asia, which might be related to geographical variation in cold spells, as well as higher vulnerability and lower adaptability.[49] These results suggest that it is of vital importance for Asian countries to strengthen cooperation and implement effective strategies for cold spells, especially in southern and eastern Asia. We also observed that the excess death ratio and rate exhibited geographical heterogeneity. The highest cold spell-related excess death ratio and rate occurred in Europe, whereas the lowest excess death ratio and rate occurred in Africa. In addition, our results suggested that regions with temperate climates had the highest mortality burden associated with cold spells. The potential mechanism is that temperate climates might have higher cold spell frequency and intensity than other climate zones due to extreme weather variations.[50] These results suggest that more and deeper coordinated strategy work and public health action should be taken in regions with temperate climates to protect the public from the adverse effects of cold spells.

	2000–2009	2010–2019	2000–2019
Russia	9·64 (6·29–13·17)	10·00 (6·54–13·66)	9·82 (6·68–13·12)
Latvia	7·93 (6·36–9·53)	11·58 (9·41–13·82)	9·75 (8·03–11·51)
Lithuania	7·11 (5·76–8·50)	10·48 (8·56–12·46)	8·80 (7·29–10·34)
Estonia	7·85 (6·16–9·56)	9·27 (7·34–11·25)	8·56 (6·90–10·26)
Uruguay	8·84 (7·73–10·00)	7·44 (6·47–8·44)	8·14 (7·18–9·13)
Belarus	7·31 (5·75–8·93)	8·70 (6·85–10·59)	8·01 (6·43–9·62)
Finland	7·06 (5·56–8·64)	8·64 (6·76–10·63)	7·85 (6·29–9·49)
Portugal	8·89 (7·58–10·22)	6·82 (5·84–7·84)	7·85 (6·80–8·93)
Serbia	8·72 (6·77–10·73)	6·63 (5·26–8·06)	7·67 (6·14–9·26)
Hungary	8·63 (7·08–10·22)	6·02 (4·86–7·21)	7·33 (6·08–8·60)
Bulgaria	7·63 (5·47–9·86)	6·87 (5·10–8·69)	7·25 (5·44–9·11)
Germany	5·77 (4·90–6·65)	8·25 (7·08–9·43)	7·01 (6·07–7·96)
Norway	6·10 (4·86–7·39)	7·57 (5·94–9·25)	6·83 (5·52–8·20)
Sweden	5·68 (4·53–6·86)	7·79 (6·28–9·35)	6·73 (5·51–7·99)
Ukraine	6·68 (4·60–8·82)	6·59 (4·63–8·61)	6·64 (4·78–8·55)
Iceland	8·19 (6·19–10·33)	4·90 (3·64–6·27)	6·55 (5·04–8·15)
Belgium	5·69 (4·90–6·49)	7·37 (6·43–8·34)	6·53 (5·73–7·34)
Poland	5·00 (4·15–5·87)	7·64 (6·45–8·87)	6·32 (5·38–7·29)
Romania	6·29 (4·64–8·00)	6·30 (4·75–7·91)	6·30 (4·82–7·82)
Denmark	4·71 (3·77–5·67)	7·82 (6·47–9·23)	6·27 (5·21–7·36)

Table 2: **Temporal change in annual excess death rate (excess deaths per 100 000 population) with 95% empirical CI associated with cold spells for the leading 20 countries around the world in 2000–19**

Our study also investigated the temporal change in cold spell-related mortality burden in 2000–19. We found that the global annual average number of cold spell days decreased at an average change of –0·20 days per year and the global mortality burden of cold spells first increased and then decreased between 2000 and 2019. The results indicated that although the global average number of cold spell days was decreasing, the intensity of the adverse health effects from cold spells might not decrease.

The present study has several strengths. First, to the best of our knowledge, this is the first global estimation of mortality burden associated with cold spells that uses data involving over 40 million deaths from 1960 locations across 59 countries (or regions). This large sample size and the representativeness of data are essential to provide high-quality findings at the global level. Second, we explored the temporal and geographical change of cold spell-related mortality burden for different regions from 2000 to 2019, accounting for the covarying potential confounders (eg, GDP per capita). Our findings provide scientific information for regional and national governments and health authorities to develop better health interventions for cold spells, such as an early warning system, a cold spell response plan, and public health education. Third, an important strength of the study is that by using the Global Daily Temperature dataset to create a harmonised location-specific time-series of temperature over the study period 2000–19, we were able to ensure that the local cold spell definitions were in fact identical by concept.[30] It is more common in multi-city multi-country studies to use data from overlapping study periods in different locations, with a potential caveat that a percentile derived from a short time-series of daily temperatures might not necessarily reflect comparable intensity and rarity of the event threshold temperature than identical percentiles from a long time-series.

This study also has several limitations. First, though the included seven meta-predicators accounted for a large variation of cold spell effects across grids, residual confounding might still exist. Second, we assumed an identical mortality rate across different grids within the same country owing to the insufficiency of grid-specific mortality data. Although this assumption should not cause substantial change to our findings at the global, national, or regional levels, mis-estimation could exist at finer geographical levels. Third, although we adopted the most commonly used definition of cold spell in previous studies to enhance consistency and interpretability,[12,15,29,51-54] this definition did not completely account for the potential differences in cold spell characteristics across locations and might not fully capture the cold spells. However, this could bias our results to a modest degree as indicated by the robust results in sensitivity analysis by application of different cold spell definitions. Fourth, sparse data from Africa, India, Russia, and the Arabian Peninsula might reduce the accuracy of the model in these regions. Further studies are warranted to implement sophisticated analyses with more sufficient health data.

In summary, cold spells are associated with substantial mortality burden around the world with geographically varying patterns. This evidence corroborates previous findings and indicates an urgency for taking local and regional measures to protect the public from the adverse mortality effects of cold spells.

Contributors

YGu, AG, and BA set up the collaborative network. YGu, SL, YGa, and WH designed the study. YGu, SL, QZ, and AG developed the statistical methods. YGu, SL, YGa, and WH took the lead in manuscript drafting and results interpreting. All authors provided the data and contributed to interpretation of the results and revised the manuscript. YGu, SL, YGa, and WH 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

All used data were obtained from the Multi-Country Multi-City (MCC) Collaborative Research Network (https://mccstudy.lshtm.ac.uk/) under a data sharing agreement and cannot be made publicly available. Researchers can refer to MCC participants, who are listed as coauthors of our study, for information on accessing the data for each country.

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