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Temperature frequency and mortality: Assessing adaptation to local temperature

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ABSTRACT

Assessing the association between temperature frequency and mortality can provide insights into human adaptation to local ambient temperatures. We collected daily time-series data on mortality and temperature from 757 locations in 47 countries/regions during 1979–2020. We used a two-stage time series design to assess the association between temperature frequency and all-cause mortality. The results were pooled at the national, regional, and global levels. We observed a consistent decrease in the risk of mortality as the normalized frequency of temperature increases across the globe. The average increase in mortality risk comparing the 10th to 100th percentile of normalized frequency was 13.03% (95% CI: 12.17–13.91), with substantial regional differences (from 4.56% in Australia and New Zealand to 33.06% in South Europe). The highest increase in mortality was observed for high-income countries (13.58%, 95% CI: 12.56–14.61), followed by lower-middle-income countries (12.34%, 95% CI: 9.27–15.51). This study observed a declining risk of mortality associated with higher temperature frequency. Our findings suggest that populations can adapt to their local climate with frequent exposure, with the adapting ability varying geographically due to differences in climatic and socioeconomic characteristics.

1. Introduction

Non-optimum temperatures have been identified as one of the leading causes of mortality (GBD, 2020), with low and high temperatures ranked 6th and 26th in terms of the risk factors of global mortality burden (IHME, 2019). During the past 20 years, approximately 91.88 million deaths and 9.78 million deaths are associated with low and high temperatures across the globe, respectively (Zhao et al., 2021).

The relationship between non-optimum temperatures and mortality has been described as a J- or U-shaped curve, which suggests the existence of a minimum mortality temperature (MMT, temperature with the lowest mortality risk) (Gasparrini et al., 2015). The MMT has been found to vary both spatially and temporally worldwide (Astrom et al., 2016; Follos et al., 2020; Todd and Valleron, 2015), while the temperature percentile that corresponds to the MMT remains stable within a specific range of temperature distribution for most countries (Guo et al., 2014; Guo et al., 2018; Tobias et al., 2021). It has also been reported that the MMT is close to the most frequent temperature (MFT), indicating that, to some extent, people and societies can adapt to local temperatures after frequent exposure (Yin et al., 2019).

The increase in frequency and intensity of hot days, as a consequence of global warming, is anticipated to lead to a higher mortality rate (Gasparrini et al., 2015; Kephart et al., 2022). However, the projected rise or at least a steady impact of heat on mortality has not occurred as expected (IHME, 2019). A study of 10 countries reported a reduction in heat-related mortality (Vicedo-Cabrera et al., 2018). This unexpected decrease in heat mortality provides additional evidence suggesting that humans may have developed increased resilience to heat (Arbuthnott et al., 2016).

The frequency of specific temperatures, quantified as the number of

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days they occur within an exposure duration in a particular area, serves as a reliable indicator of the extent to which people have been exposed to those temperatures. Exploring the relationship between mortality and temperature frequency can provide valuable insights into human adaptation to local temperature. However, to our knowledge, no studies have investigated the relationship between mortality risk and temperature frequency, which highlights the need to investigate this relationship further. Obtaining this information will help explain the underlying mechanisms of MMT and its geographical and temporal variations.

Therefore, this study aimed to evaluate the association between temperature frequency and mortality risk using temperature and mortality data from 757 locations across 47 countries from Multi-Country Multi-City (MCC) Collaborative Research Network. Furthermore, we aimed to examine the variations in human adaptation to diverse temperatures.

2. Materials and methods

2.1. Data sources

2.1.1. Location-specific mortality data

The MCC Collaborative Research Network database (https://mccstudy.lshtm.ac.uk/) was used in this study. Mortality data were obtained from the local authorities of each country or region. The International Classification of Diseases, 9th and 10th revision (ICD-9 and ICD-10) codes were used to identify causes of death. We extracted the data series on non-external causes of death (ICD-9: 0–799; ICD-10: A00–R99) or, if not available, all-cause mortality. Two types of missing values in mortality data were observed: missing at random and missing not at random. In the case of missing at random, the missing values were observed only on random days during the study period. In contrast, for missing not at random, mortality data could be entirely missing for several months in a specific year in some locations. In these cases, we excluded the relevant years that contained non-random missing values from these locations. Finally, 757 locations across 47 countries/regions were included (Table S1). The overall missing rate of mortality data was 0.02 %.

2.1.2. Meteorological data

We collected hourly data of daily mean temperature from the European Centre for Medium-Range Weather Forecasts Reanalysis v5 (ERA-5) reanalysis data set, at a spatial resolution of $0.5^{\circ} \times 0.5^{\circ}$ (https://cds.climate.copernicus.eu/cdsapp#!/home) for the 757 locations included in this study. These data were transformed into daily observations by averaging all hourly observations for each day. The meteorological data were linked to the geographical centroid of each location based on its longitude and latitude.

2.2. Calculation of temperature frequency

We rounded the daily mean temperature (℃) to the nearest whole number and calculated the frequency, represented by the number of days, for each specific temperature value that occurred in each location during the study period. We then applied min–max normalization to allow for comparison across locations. This normalization transformed the frequency of temperature into a range of 0 to 1 by computing $\frac{Frequency_i - Minimum_{frequency}}{Maximum_{frequency} - Minimum_{frequency}}$, where a normalized frequency value of 1 denotes the frequency of the most frequent temperature in a specific location. Conversely, a normalized frequency of 0 indicates the frequency of the specific temperature value that occurred the least.

2.3. Statistical analysis

2.3.1. Estimating location-specific association between frequency and mortality

We utilized a standard two-stage time-series quasi-Poisson regression design. In the first stage, we applied a quasi-Poisson regression in each location to derive estimates of associations between mortality and normalized frequency of temperature,

$$Y_{it} \sim Poisson(\mu;\theta)$$

$$\mathrm{E}(Y_{it}) = \exp(\alpha_i + cb(Freq_{it}, lag = 21) + ns(Time_{it}, df = 7/year) + \gamma_i DOW_{it})$$

$$VAR(Y_{it}) = \theta\mu$$

where Y_{it} is the deaths count on day t in location i; α_i denotes the intercept; $cb()$ is a cross-basis function of frequency built by the distributed lag non-linear model (DLNM). We opted not to directly include absolute temperatures in the model for the following reasons: 1) absolute temperature and temperature frequency exhibit a one-to-many relationship. Including both in the model would introduce multicollinearity; 2) frequency inherently captures the effects of absolute temperature values. Considering that the effects of temperature are not independent of the frequency-mortality associations, temperature itself is not considered a confounder variable; 3) our initial ANOVA F-test did not reveal any significant enhancements in the model when incorporating the cross-basis function of mean temperature. Instead, we performed stratification analyses to explore the modification effects of mean temperature on the frequency-mortality association. We used parameters for frequency that align with empirical values of temperature. Specifically, the cross-basis function of frequency incorporated a natural cubic B-spline with one internal knot placed at the 50th percentiles of location-specific normalized frequency distributions and two boundary knots, to describe the exposure–response curve; and a natural cubic spline with an intercept and three internal knots placed at equally spaced values in the log scale to describe lagged associations of frequency over 21 days. $ns()$ is a natural cubic spline of time with 7 degrees of freedom (dfs) per year to control for seasonal and long-term trends; DOW_{it} is an indicator of the day of the week. $VAR(Y_{it})$ and μ denote the variance and expectation of Y_{it}, and θ is an overdispersion parameter. The relative risk (RR) was defined as the risk comparing the 10th percentile to the 100th percentile of normalized frequency, quantifying the difference in mortality risk between less frequent temperatures compared to the most frequent temperatures. Results are presented as percentage change of mortality comparing the 10th percentile to the 100th percentile of normalized frequency, which is derived as follows: (RR-1) × 100 %.

2.3.2. Pooling the location-specific estimates

In the second stage, we pooled the location-specific overall cumulative exposure–response associations obtained in the first stage at the national, regional, and global levels, using a multilevel *meta*-analytical model without predictors (Gasparrini et al., 2015; Meng et al., 2021; Sera et al., 2019). This model allowed us to account for variations in risk across two nested grouping levels, represented by cities within countries. Best linear unbiased predictions were used to obtain accurate location-specific estimates by borrowing information across units within the same hierarchical level.

2.3.3. Stratification analysis by temperature, climatic zone, and socioeconomic status

To investigate the modification effect of temperature on the frequency-mortality association, we separated temperatures into moderate and extreme components by defining extreme cold as temperatures lower than the 10th city-specific percentiles; moderate cold as the ranges fall between the 10th and 50th; moderate hot as the ranges fall

between the 50th and 90th; and extreme hot as temperatures higher than the 90th. An indicator for the temperature component was incorporated into the model, allowing us to extract exposure–response associations for each temperature component. We then repeated the second stage to pool the overall cumulative exposure–response associations for each temperature component.

The climatic zone and socioeconomic status have been proposed as crucial indicators of population adaptation to the local climate (Tobias et al., 2021; Xu et al., 2020). Therefore, we repeated our analyses using the Köppen-Geiger climate classification (A: tropical, B: arid, C: temperate, D: continental, and E: polar) and country income (Low-income economies, lower-middle-income economies, upper-middle-income economies, and high-income economies) as the pooling criteria to examine whether the frequency-mortality association would vary under different climatic zones and socio-economic levels.

2.3.4. Sensitivity analysis

We conducted several sensitivity analyses to check the robustness of our results. We used alternative maximum lag days of frequency (from 21 to 24 and 28 days) and alternative dfs for both the lag-response curve of frequency (from 3 to 4, 5, and 6) and long-term time trends (from 6 to 7 and 8). To explore temporal changes in the association, we reconstructed the pooled exposure–response curves for four distinct periods (1990–1995, 1995–2000, 2000–2005, and 2005–2010) using data from 206 locations covering the period 1990–2010. Normalization of frequency was done separately by period.

R software (version 3.6.2) was used to perform all analyses. A two-sided P-value < 0.05 was set as statistically significant.

3. Results

This study included 120,758,598 deaths across 757 locations from 47 countries/regions, as illustrated in Fig. 1. The study countries exhibited a wide range of local climates. Certain regions, such as Southeast Asia, the northeast Coast of Brazil, and the southern United States, tended to have a higher MFT. Across locations, the maximum annual average frequency of temperature ranged from 13 days in Regina, Canada to 204 days in Fortaleza, Brazil. On average, the MFT was 18.7 °C, with the highest value observed in Kuwait City, Kuwait (36 °C, annual average frequency: 26 days) and the lowest value observed in Nagano, Japan (−1 °C, annual average frequency: 16 days) (**Table S1**).

Fig. 2 shows the overall and region-specific exposure–response curves, illustrating the cumulative mortality risk over a 21-d lag period associated with normalized frequency of temperature. The curve shows a consistent decrease with no discernible thresholds, with a steeper slope at lower frequency temperatures. The pattern of the decreasing trend differs among regions. South Europe exhibited the greatest decrease with an increase in frequency, while the curves appeared flat for Middle-East Asia, sub-Saharan Africa, and Australia and New Zealand. Country-specific exposure–response curves are provided in **Figure S1**.

Fig. 3 shows the lag structures in the effects of the normalized frequency of temperature on mortality. The mortality risks were the strongest on the present day and attenuated drastically to lag day 21. As the exposure window increased, there was a greater reduction in mortality risks for the lower frequency (10th percentile), followed by the 50th percentile and 90th percentile.

Fig. 4 shows the percentage change of mortality comparing the 10th percentile to the 100th percentile of normalized frequency of temperature. A significant and positive association was observed, with an overall increase of 13.03 % (95 % CI 12.17, 13.91) in mortality risk comparing the 10th percentile of normalized frequency to the 100th percentile of normalized frequency. Across regions, South Europe exhibited the highest increase in mortality risk, with a percentage change of 33.06 % (95 % CI: 29.44, 36.79), followed by 21.61 % (95 % CI: 18.42, 24.89) in Central Europe, and 16.47 % (95 % CI: 14.30, 18.68) in North Europe. In contrast, the lowest increase in mortality risk was observed in Australia and New Zealand, with a corresponding change of 4.56 % (95 % CI: −3.76, 13.60).

When separating temperatures into moderate and extreme components, we observed distinct exposure–response curves in the relationship between frequency and mortality. As shown in Fig. 5, the various temperature components affected the frequency-mortality associations differently, resulting in an increase in mortality risk of 18.64 % (95 % CI: 16.38, 20.94) for extreme cold, 8.51 % (95 % CI: 7.25, 9.79) for extreme hot, 4.35 % (95 % CI: 3.56, 5.15) for moderate cold, and 2.38 % (95 % CI: 1.92, 2.85) for extreme cold, comparing the 10th percentile to the 100th percentile (MFT) of normalized frequency of each temperature component.

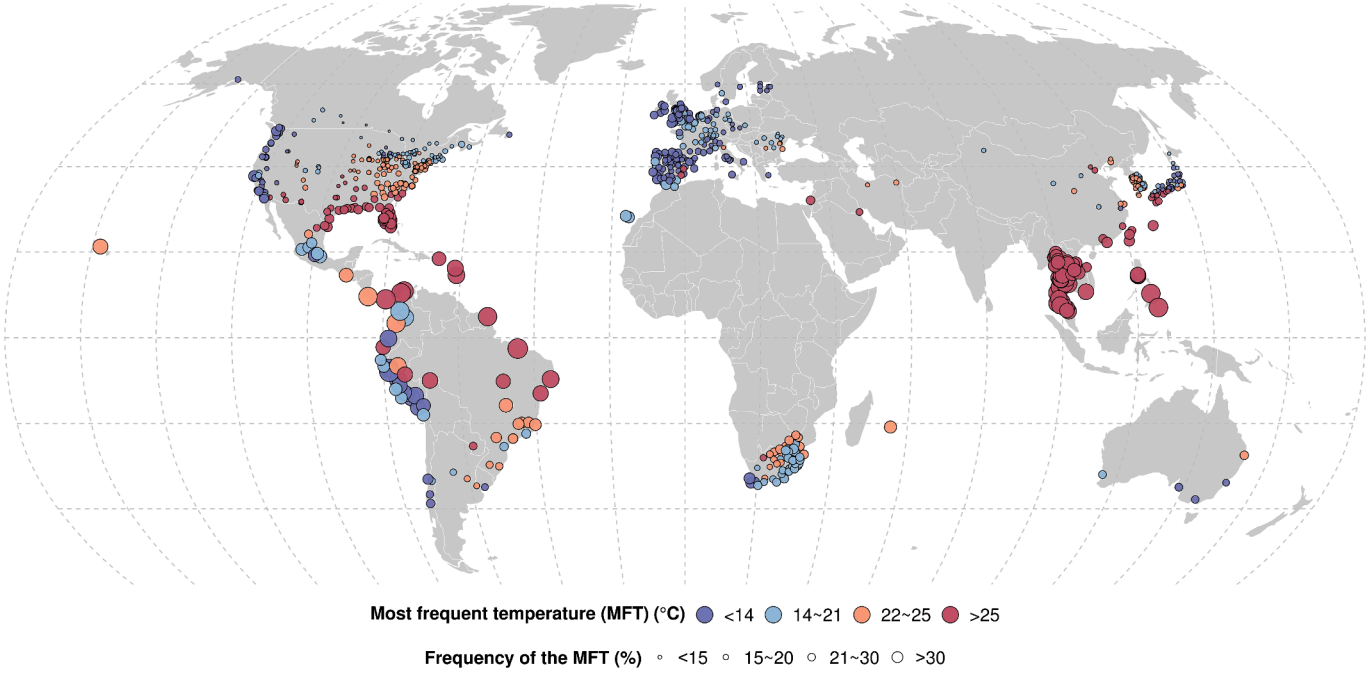


Fig. 1. World map of the 757 locations included in the analysis, the most frequent temperature (°C), and their relative frequency (%).

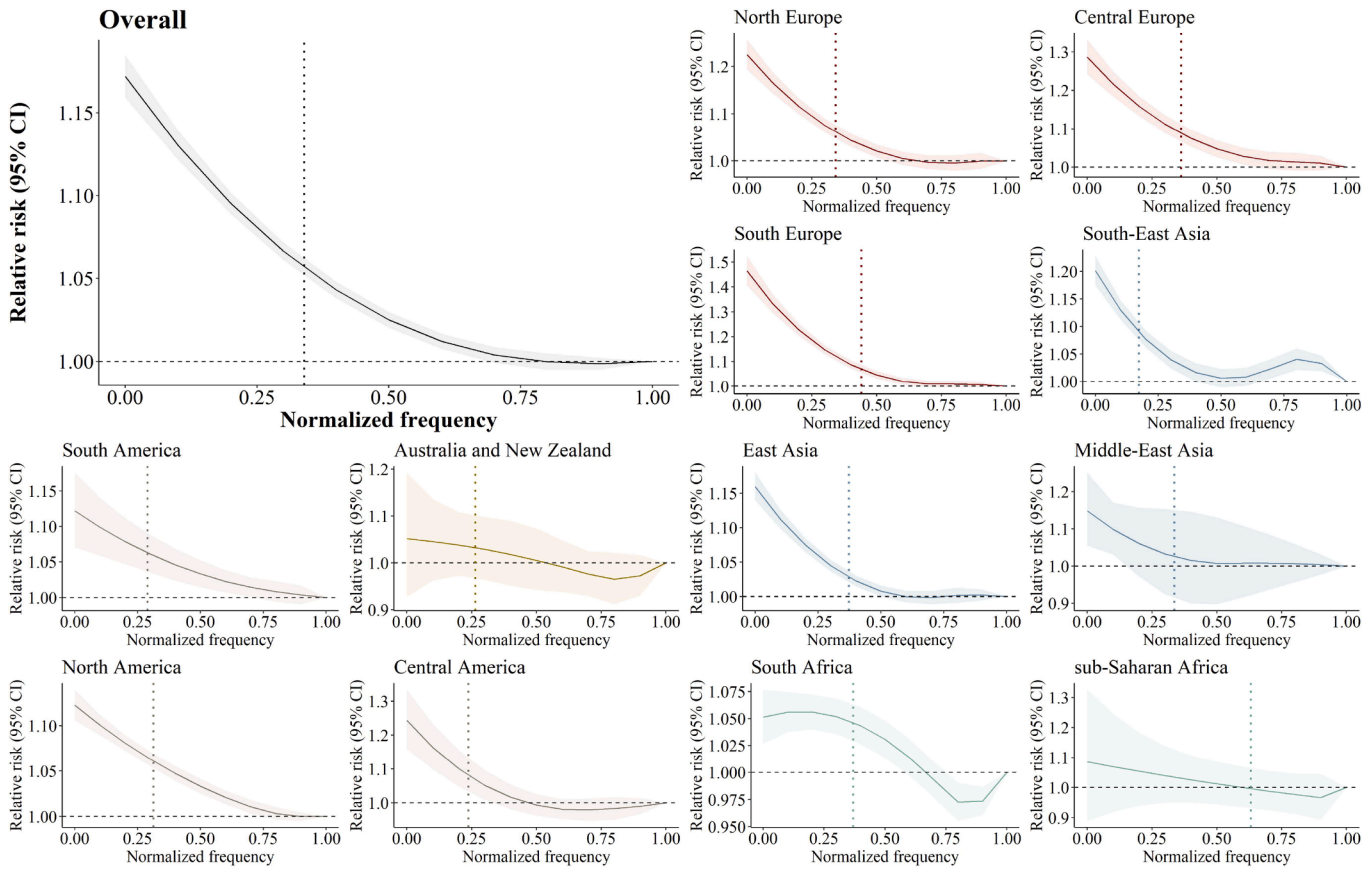


Fig. 2. Pooled cumulative associations between temperature frequency and all-cause mortality. The reference normalized frequency = 1 was used to calculate relative risks. The vertical line represents the 10th percentile of the normalized frequency of temperature. Based on the United Nations' M49 Standard for geographic regions, the French Reunion falls under the Eastern Africa region located within sub-Saharan Africa. For the region-specific analysis, the French Reunion is the only location included in sub-Saharan Africa.

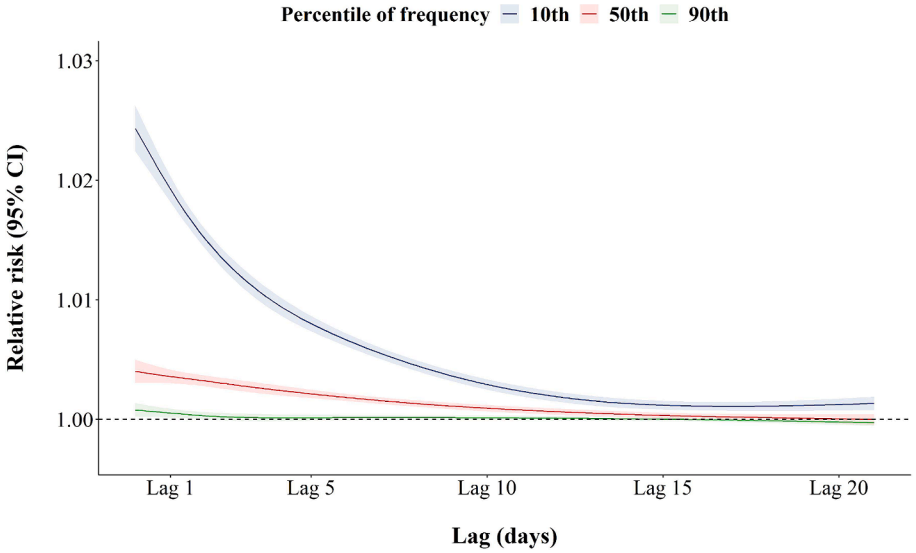


Fig. 3. Overall lag structure in effects of the normalized frequency of temperature on mortality. Effects were defined as the mortality risks at the 10th (A), 50th (B), and 90th (C) percentile of frequency distribution against the most temperature frequency (100th percentile of frequency distribution).

Table 1 shows the stratification results by climatic zones and socio-economic status. The temperate climates (C) exhibited the highest increase in mortality risk, with a percentage change of 14.79 (95 % CI: 13.61, 15.99); while the lowest increase in mortality was observed in the polar climates (E), with a corresponding change of −0.45 (95 % CI: −11.91, 12.50). Results for subgroups of each climate zone are shown in Table S2. After classifying countries by income level, the highest increase in mortality risk was observed for high-income countries, with a percentage change of 13.58 % (95 % CI: 12.56, 14.61).

The sensitivity analyses, which involved using alternative maximum

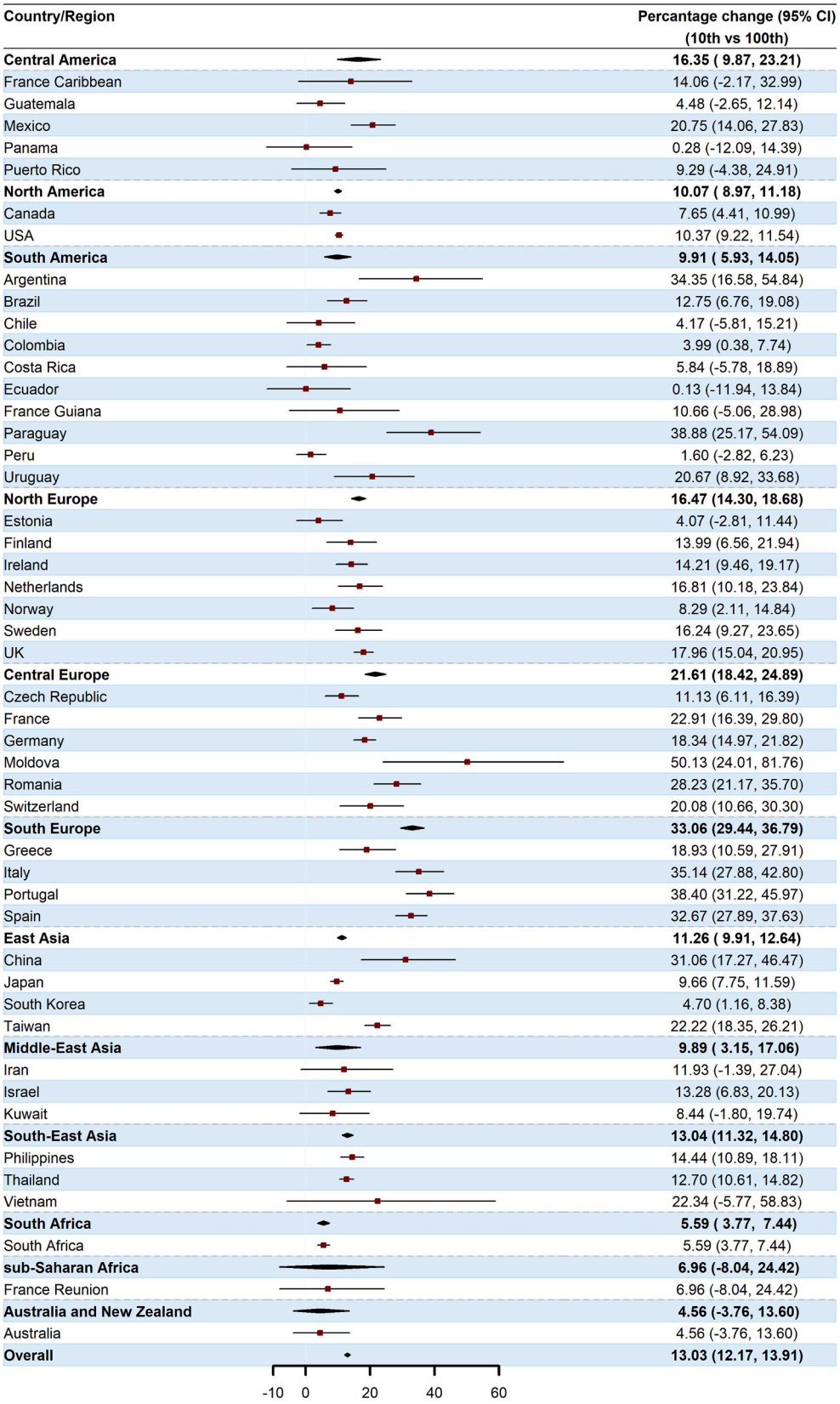


Fig. 4. Percentage change of mortality comparing the 10th percentile to the 100th percentile (the most frequent temperature) of normalized frequency of temperature.

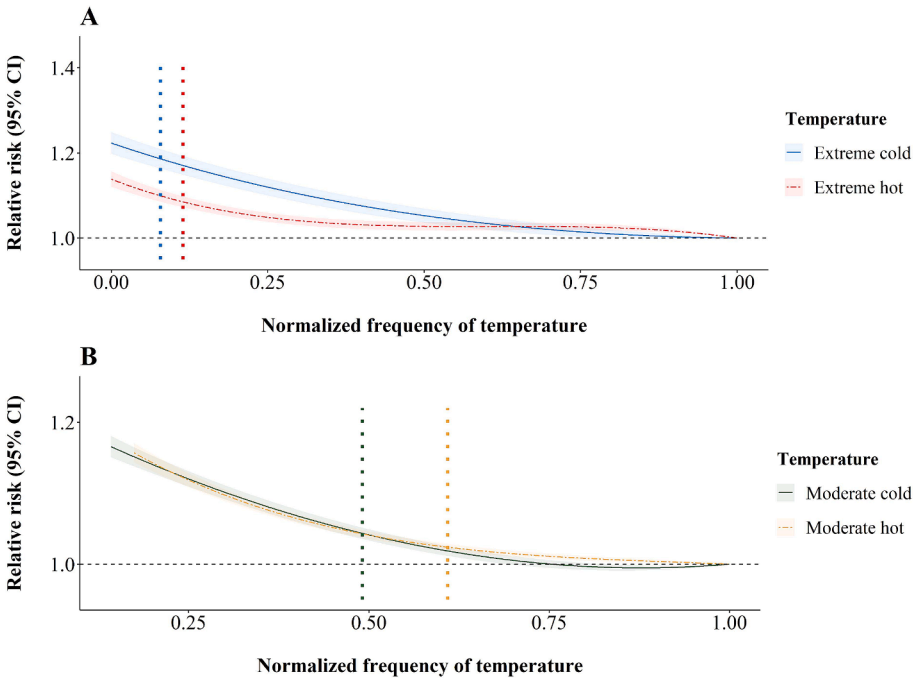


Fig. 5. Overall cumulative associations between temperature frequency and all-cause mortality, stratified by temperature group. Vertical lines represent the 10th percentile of the normalized frequency of each temperature component.

Table 1
Percentage change of mortality comparing the 10th percentile to the 100th percentile of normalized frequency of temperature by socio-economic status and climatic zones.

Groups	Number of locations	Percentage change (95 % CI) (10th vs 90th percentile)
Climate zones		
A (tropical)	103	11.50 (9.77, 13.25)
B (arid)	64	11.48 (8.31, 14.74)
C (temperate)	459	14.79 (13.61, 15.99)
D (continental)	127	9.82 (8.18, 11.48)
E (polar)	4	−0.45 (−11.91, 12.50)
Country income classification [*]		
Lower-middle	16	12.34 (9.27, 15.51)
Upper-middle	189	11.48 (9.71, 13.27)
High	552	13.58 (12.56, 14.61)

[*] No countries met the classification criteria for low-income economies. Abbreviations: CI, confidence interval.

lags and dfs of frequency and long-term time trends, yielded similar results. (Figure S2). The pooled exposure–response curves showed only slight changes across different periods (Figure S3).

4. Discussion

In this multi-country, population-based study, we found a consistent decrease in the risk of mortality as the frequency of temperature increases. The associations were consistent at the national, regional, and global levels. A higher increase in mortality risk was observed for the extreme cold component, followed by extreme hot, moderate cold, and moderate hot temperature components, comparing the 10th percentile of frequency to the 100th percentile of frequency of each temperature component. Socio-economic status and climate characteristics were potential modifiers of the frequency-related mortality risk.

This study introduces temperature frequency as a valuable concept for understanding temperature-mortality relationships. While studies on temperature-related mortality risk provide valuable insights, several key questions remain unanswered. These include: What biological mechanisms underlie the observed minimum mortality risk at a specific temperature? Why does the same absolute temperature have different mortality risks across various locations? Why does the MMT vary geographically? As reported in a study of 43 countries, MMT varies greatly across countries and regions, ranging from 14.2 to 31.1 °C (Tobias et al., 2021). Our findings suggest a linear relationship between temperature frequency and mortality risk, with the most frequent temperature having the minimum mortality risk. And this linear association holds consistently across distinct geographical locations. This might be explained by adaptation, elucidated by comparing the differences in mortality risks between low-frequency and high-frequency temperatures. Populations appear to develop better resilience to the temperatures they encounter most frequently in their environment. Additionally, our finding sheds light on the disparate mortality risks associated with the same temperature value in different locations, attributing such variations to the distinct frequency of a given temperature in each location.

The use of temperature frequency facilitates cross-location comparisons. Across the locations included in our study, MFTs ranged from −1 °C to 36 °C, indicating the inclusion of extreme values. Identical temperatures may exhibit varying frequencies across different locations. In one location, temperatures that occur infrequently may be commonplace in another location, leading to disparate adaptation patterns. This variability in temperature frequency influences the temperature-mortality relationship, which has been observed to follow a U-shaped pattern across different temperature ranges (Chen et al., 2018; Gasparrini et al., 2015). Consequently, the same temperature value has distinct effects across different locations. Therefore, pooling data across diverse locations would introduce bias. In contrast, temperature frequency offers an alternative approach by focusing on the most prevalent temperature within a location. By using temperature frequency, we avoid the comparison or aggregation of the effects of identical temperature values across different locations. Instead of assuming a universal minimum mortality risk associated with a specific temperature value, it is more appropriate to consider that the most frequent temperature

corresponds to the minimum mortality risk. Adopting this approach offers a novel strategy for directly comparing temperature frequency-mortality associations across locations. Through this method, we can identify common phenomena underlying temperature-mortality associations, shedding light on how populations adapt to local temperature conditions.

Our investigation highlighted that human adaptation to temperature varies depending on the specific temperature components. We observed a greater reduction in mortality risk associated with an increase in frequency for cold temperatures compared to hot temperatures. For example, a higher RR was observed for extreme cold than extreme hot temperatures, comparing the 10th percentile of frequency to the 100th percentile of frequency of each temperature component. This finding indicates that increasing the frequency of exposure to extreme cold temperatures leads to a greater reduction in mortality risk compared to increasing the frequency of exposure to extreme hot temperatures, implying that humans may be better adapted to extreme cold temperatures as extreme cold temperatures become more frequent. This might be counterintuitive, as previous studies have reported a higher extreme cold-related mortality risk than extreme hot-related mortality risk (Gasparrini et al., 2015). However, it is important to note adaptation often arises from prolonged and frequent exposure to temperatures. Should the occurrence of extreme temperatures be infrequent in specific locations, it would be inappropriate to attribute the mortality risks of extreme temperatures to long-term adaptation. The difference in the mortality risk between extreme hot and cold temperatures likely reflects the varying capacity of rapid thermoregulatory response of humans to extreme temperatures (Gasparrini et al., 2015).

In contrast, the underlying mechanisms behind adaptation refer to long-term adjustments of physiological acclimatization in response to repeated exposure to temperature (Hanna and Tait, 2015) and coping actions (extrinsic mechanisms) that individuals and societies can take action to modify the thermal environment, returning it to a comfortable state, for example, living in a climate-controlled environment, raising public awareness, utilization of warning system (Krummenauer et al., 2021; Krummenauer et al., 2019; Navas-Martin et al., 2022; Tipton et al., 2008; Woodruff, 2022). There are several forms of human adaptation to local climates, including developmental, acclamatory, and regulatory adjustments (Winiwarter., 2008). Developmental adjustments involve coping responses to extreme and continuing stress, leading to irreversible physiological change. Acclamatory adjustments, on the other hand, facilitate individual adaptation subsequent to developmental changes and are reversible. Regulatory adjustments, the most prevalent forms of adaptation, manifest through behavioral, social, and cultural means (Winiwarter., 2008). Behavioral responses involve actions such as modifying homes and landscapes to withstand heat and relocating or migrating from hazardous areas (Berrang-Ford et al., 2021). Individuals may transition to alternative economic and livelihood activities, transitioning from fishing to farming or altering food consumption practices to cope with extreme temperature events (Berrang-Ford et al., 2021). Institutional responses comprise the creation of policies, programs, regulations, and procedures, as well as the establishment of formal and informal organizations (e.g., social support groups, climate insurance services, capacity-building initiatives, and financial assistance programs) (Berrang-Ford et al., 2021). For example, adaptation to cold temperatures might begin with habituation of thermal sensations to cold, followed by genetic (e.g., change in gene expression), physiologic (e.g., circulatory adjustments, increase of fat layer), morphological (e.g., change in skin colour) or behavioural responses (e.g., use of hats, gloves, and scarves) (Makinen, 2010).

Socioeconomic factors may contribute to the heterogeneity in temperature frequency-related mortality risks. This study revealed a gradient in RR across income groups. High-income countries exhibited the highest RR comparing the 10th percentile (less frequent) versus the 100th percentile (most frequent) of the normalized temperature frequency. This finding indicates that for high-income countries, increasing the frequency of exposure to temperature leads to a greater reduction in mortality rates compared to increasing the frequency of exposure to temperature in middle-income countries. It implies that individuals in high-income countries may display enhanced adaptation to the local climate following frequent exposure. Similarly, a study conducted in Japan has reported a significant association between socioeconomic factors and mortality risks related to both heat and cold temperatures (Chung et al., 2018). It suggested that people with higher socioeconomic status are better equipped to cope with health risks by utilizing their resources, such as working in climate-controlled settings with air conditioners, having access to adequate sanitation conditions, good hygiene, and safe water (Chung et al., 2018; Xu et al., 2020). It is important to acknowledge that our findings do not allow us to draw conclusions suggesting that high-income countries are more susceptible to less frequent temperatures. For example, the RR at the 10th percentile signifies the ratio of mortality risk associated with the 10th percentile to that of the 100th percentile. Without knowledge of the mortality risks at the 100th percentile for both high-income and low-income countries, comparing mortality risks at the 10th percentile between them poses challenges.

Furthermore, in our study, the climate zone was also found to be an important determinant of frequency-related mortality risk. One possible explanation for this finding is the varying lifestyles across different climate zones. The Köppen climate classification is primarily based on patterns of seasonal precipitation and temperature. Seasonality can affect human behaviour (Guo et al., 2022), including dietary patterns (Ma et al., 2006), physical activity (Ma et al., 2006), sleep duration (Suzuki et al., 2019), and ultimately, human health (Chudasama et al., 2020).

Our study has important implications for understanding the relationship between temperature frequency and human health. The results imply that humans can adapt to a wide range of temperatures, which may be due to frequent exposure. These findings provide a new perspective on the mechanisms of optimal temperatures, and future research could further investigate the long-term shifts in MFT to better understand human health risks under a changing climate. Moreover, whereas increasing MMT shows that the population has adapted to warm temperatures, the heat-related mortality burden is expected to increase as a consequence of climate change (Yang et al., 2021). The fact that higher frequency did not reduce hot-related mortality as much as cold-related mortality highlights the need for more public health interventions to minimize the effects of hot temperatures.

We acknowledge some limitations of this study. Some limitations have been discussed by previous MCC studies (Wu et al., 2022), including being unable to characterize frequency-mortality association by age, sex, and cause of death. Demographic characteristics have been suggested to be an important determinant of thermoregulatory capacity (Chung et al., 2018), which could provide further insight into underlying adaptation mechanisms. Future research could complement our evidence by the collection of detailed data and assessment of frequency-mortality associations across age, sex, and cause of death. As quoted in previous time-series studies, we could not rule out the ecological fallacy and Berkson-type measurement error despite its minor impact on point estimates (Gasparrini and Armstrong, 2010). Due to limited data availability, only 3 locations were included for the Middle East and Southeast Asia regions. Similarly, only 1 location was available for South Africa and Australia/New Zealand. Consequently, the generalizability of our results in these regions is restricted, and interpretations should be made with caution. Finally, we are unable to investigate the associations between frequency and mortality in low-income countries. Additional research is necessary to validate our findings in these specific regions with lower income levels.

5. Conclusion

In conclusion, our results showed a decreasing mortality risk

associated with increased temperature frequency, suggesting that populations can adapt to their local climate through frequent exposure. This study provides a better understanding of the underlying mechanism responsible for the health consequences of temperature.

Ethical approval

This study did not require ethical approval or informed consent for secondary analysis of aggregate anonymized data from the MCC Collaborative Research Network.

CRediT authorship contribution statement

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

The authors do not have permission to share data.

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Appendix A. Supplementary data

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