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Minimum mortality temperature by cause of death and age group: A multi-country observational study (1990–2019)

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ABSTRACT

Minimum mortality temperature (MMT) is an important feature of temperature-mortality relationship, defined as the temperature at which mortality risk is lowest. Although numerous studies have estimated MMT for all-cause mortality, few have explored differences by age or cause of death. We analyzed daily mean temperature and mortality data from 667 communities across 39 countries. Mortality was classified by age and cause of death (cardiovascular, respiratory, or non-cardiorespiratory). A two-stage meta-analytic approach was applied to estimate the MMT and its corresponding percentile (MMTP) by age and cause of death. In the overall population, MMT was the highest for cardiovascular mortality (22.1 °C, 95% CI: 20.9–23.4 °C), whereas respiratory and non-cardiorespiratory causes were 0.87 °C and 0.66 °C lower, respectively, than that for cardiovascular causes. Similar patterns were observed for MMTP, which was highest for cardiovascular mortality (75%, 95% CI: 73–78%) and lower by 5% and 4% for respiratory and non-cardiorespiratory causes, respectively. MMT increased with age for cardiovascular (0.19 °C per 10 years, 95% CI: 0.14–0.23) and non-cardiorespiratory causes (0.13 °C per 10 years, 95% CI: 0.09–0.16). These patterns were generally consistent across geographical regions. Overall, both MMT and MMTP differed by cause of death and age, indicating that the optimal temperature varies across population subgroups.

1. Introduction

Numerous studies have reported that the temperature–mortality relationship typically follows a U- or J-shaped curve, indicating that both low and high temperatures are associated with increased mortality (Curriero et al., 2002; McMichael et al., 2006; Guo et al., 2014; Gasparrini et al., 2015; Song et al., 2017). One important feature of this association is the minimum mortality temperature (MMT), defined as the temperature at which the mortality risk is lowest. Alternatively, the minimum mortality temperature is also expressed as the minimum mortality temperature percentile (MMTP), which indicates its relative position within the temperature distribution. In many previous studies, MMT/MMTP has been used as the reference temperature (i.e., optimum temperature) to estimate the health burden attributable to non-optimum temperatures, including attributable number or fraction and relative risk (Ma et al., 2015; Chung et al., 2018; Vicedo-Cabrera et al., 2018; Alahmad et al., 2023; Achebak et al., 2024). In addition, variation in MMT/MMTP across populations or over time has also been discussed as potentially reflecting population adaptation to local temperature conditions (Todd and Valleron, 2015; Åström et al., 2016; Arbuthnott et al., 2016; Krummenauer et al., 2019; Folkerts et al., 2020; Navas-Martín et al., 2024; Tobías et al., 2021; Yang et al., 2024).

Earlier research primarily assessed MMT/MMTP at the level of individual cities or countries, particularly in regions, such as the Europe, China, and Japan, to better understand human adaptation to local climates (Ma et al., 2015; Todd and Valleron, 2015; Åström et al., 2016; Chung et al., 2018). With improved data availability and accessibility, recent studies have extended these analyses to the global scale (Tobías et al., 2021; Yang et al., 2024). These global investigations have identified patterns of temperature adaptation across diverse climates, regions, and time periods. However, most prior studies have focused on all-cause mortality in the overall population, despite substantial regional differences in age distribution and cause-of-death composition. Such aggregated estimates do not capture age- and cause-specific variation. In addition, the physiological mechanisms underlying temperature-related mortality differ by cause of death; however, evidence on corresponding differences in MMT/MMTP remains limited. This gap constrains the application of previous findings to climate adaptation policies and public health strategies targeting vulnerable subgroups.

Although one previous study reported age-related trends in the all-cause MMTP (Masselot et al., 2023), evidence jointly examining variation in MMT/MMTP by both age and cause of death remains scarce. Other studies have examined temperature–mortality relationships for

cardiovascular or respiratory diseases (Alahmadet al. 2023; Rai et al., 2023; Achebak et al., 2024) or explored age- and cause-specific associations (Scovronick et al., 2024), but without focusing specifically on MMT. These limitations underscore the need for a comprehensive global assessment of age- and cause-specific MMT/MMTP. Such evidence is essential for developing targeted public health interventions and policies to mitigate the adverse effects of temperature on susceptible populations.

In this study, we investigated differences in MMT and MMTP across causes of death (cardiovascular, respiratory, and non-cardiorespiratory) and age groups at the global scale. Using daily temperature and mortality data from 667 communities in 39 countries between 1990 and 2019, we examined how MMT/MMTP varied by cause and age in the overall population and across geographical regions.

2. Methods

2.1. Data description

Daily time-series data on mortality (classified by age group and cause of death) and mean ambient temperature were collected from 667 communities across 39 countries. The geographical distribution of the communities included in this study is shown in Fig. 1. Data collection was performed as described in previous studies, using a Multi-Country Multi-City Collaborative Research Network dataset (Gasparrini et al., 2015; Tobías et al., 2021; Yang et al., 2024). The data collection period varied by country, spanning 1969 to 2023 (Fig. S1). To maximize temporal overlap across countries, we restricted the analysis to 1990–2019 (Table S1).

In our study, we used mortality data that are categorized according to cause of death and age group. The availability of age- and cause-specific mortality data varied across countries. Among the 667 communities, 661 had mortality data categorized by cause of death, of which 533 had both age- and cause-specific mortality data. The causes of death were classified as cardiovascular, respiratory, or non-cardiorespiratory based on the International Classification of Diseases, 10th Revision (ICD-10; A00–R99). Age group classifications differed across countries. Ten countries used six age categories ($\leq$ 4, 5–14, 15–44, 45–64, 65–74, $\geq$ 75 years), while others applied different groupings. Detailed information on the availability of age- and cause-specific mortality data is provided in Table S1 and S2.

Indicators were created for each country, region, and climate zone (Fig. S2). The regional indicator classified each community into one of ten geographical regions (North America, Central America, South America, Northern Europe, Central Europe, Southern Europe, Southern Africa, Western Asia, Southeastern Asia, and Eastern Asia). The climate zone indicator assigned each community to one of four climatic zones according to Köppen's climate classification (Tropical, Dry, Temperate, and Continental).

2.2. Statistical analysis

We conducted a two-stage meta-analysis to estimate MMT/MMTP by age group and cause of death. In the first stage, community-specific MMT/MMTP was estimated for each age group and cause of death. In the second stage, these estimates were pooled for the overall population and by geographical region. All analyses were conducted in R (version 4.3.3) using the *dlnm* and *mixmeta* packages. Additional details are provided in the Supplementary Materials.

2.2.1. Estimating the community-specific MMT/MMTP by age group and cause of death

First-stage models were fitted separately for each community, each age group, and each cause of death. We applied quasi-Poisson regression model that included a natural cubic spline of time with eight degrees of freedom per year to control for long-term trends and seasonality, along with indicator variables for day of the week. To account for non-linear and delayed associations between temperature and mortality, we incorporated the distributed lag non-linear model (DLNM) (Gasparrini et al., 2010). The specifications of the DLNM cross-basis were based on previous studies (Gasparrini et al., 2015; Tobías et al., 2021; Yang et al., 2024). For the lag-response dimension, we employed a natural cubic spline with knots placed by dividing the lag period up to day 21 into three equal parts on a logarithmic scale. For the exposure-response dimension, we used a natural cubic spline with knots set at the 10th, 75th, and 90th percentiles of the community-specific temperature distribution.

After model fitting, the coefficients of the cross-basis term were

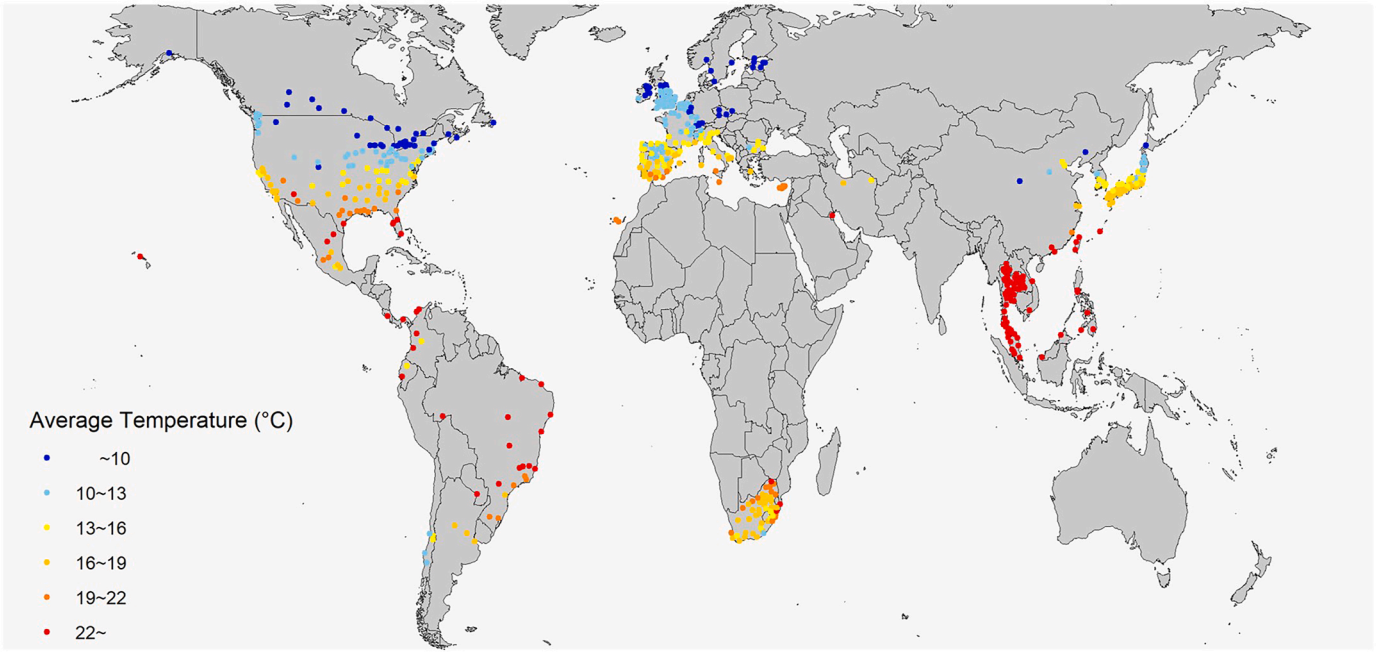

Fig. 1. Geographical distribution of the 667 communities included in this study and their average of daily mean temperatures.

transformed into reduced coefficients (Gasparrini and Armstrong, 2013). These reduced coefficients were used to represent the overall cumulative temperature-mortality curve, which captures the effect of temperature accumulated over all lags. Once the reduced coefficients were obtained for all communities by age group and cause of death, we calculated the MMT/MMTP as the temperature and corresponding percentiles that minimized the overall cumulative temperature–mortality curve. MMT represents an absolute temperature value, whereas MMTP provides a relative measure that facilitates comparisons across locations. To prevent MMT/MMTP from being estimated at the boundaries of the temperature range, the MMT/MMTP search was restricted to the 10th–95th percentile range. We selected this range as a compromise between stability and inclusiveness for estimation. The uncertainty of the MMT/MMTP was quantified using empirical confidence interval (CI) obtained through Monte Carlo simulations based on the asymptotic normality of the maximum likelihood estimates of the reduced coefficients (Lee et al., 2017).

2.2.2. Pooling the community-specific MMT/MMTPs

In the second-stage analysis, a series of mixed-effects meta-regression models (Sera et al., 2019) were fitted to address three main objectives: (1) compare MMT/MMTPs across causes of death, (2) examine age-related associations and their differences by cause of death, and (3) assess regional heterogeneity. These objectives were achieved by varying the fixed-effect specifications, while maintaining a consistent stratified random-effects structure that allowed information sharing within the same climatic zones of the same country.

First, for the entire population, we compared the pooled MMT/MMTPs across the causes of death using a model with the cause of death as a fixed-effect predictor. The all-cause MMT/MMTP were estimated using an intercept-only model for comparison.

Second, to investigate the associations of age with MMT/MMTP, and whether these associations differed by cause of death, we fitted another mixed-effects meta-regression model. The model included fixed effects for continuous age variable, cause of death, and their interaction. The continuous age variable was derived to represent each age group following the approach used in previous studies (Masselot et al., 2023). This variable was constructed using 5-year age-specific mortality estimates from the Global Burden of Disease (GBD) project (Institute for Health Metrics and Evaluation, 2025), as described in Supplementary Materials (see “Details of Statistical Methods”). To account for potential non-linear associations with age, we compared linear and natural cubic spline models with various knot configurations and selected the optimal form according to the Bayesian Information Criterion (BIC) (Fig. S4). For comparison, the global pooled association between age and all-cause mortality was estimated using a model that included only an intercept and a continuous age term as fixed effects. The likelihood ratio test (LRT) was applied to compare and select nested models.

Third, to assess regional heterogeneity, we refitted the same full model for each of the nine geographical regions (excluding Western Asia owing to limited data availability), with fixed effects for age (modeled linearly), cause of death, and their interactions.

The Wald test in univariate or multivariate form was applied to assess whether the fixed-effect coefficients associated with a specific cause were statistically significant. We evaluated whether MMT, MMTP, and age-related associations differed across causes.

2.2.3. Sensitivity analysis

To assess robustness of the findings, a series of sensitivity analyses were conducted by varying several modeling specifications. First, we modified (1) the locations of knots (25th, 50th, 75th/10th, 50th, 90th percentiles) and (2) lag period of the DLNM (7/14/28 days), and (3) the number of knots (6/10 per year) in the spline for long-term trend and seasonality control in the first stage model. Second, we examined the impact of the restriction applied to the MMT/MMTP search range (no restriction and 1st-99th/5th-95th percentiles). Third, to address potential heterogeneity in study periods across countries, we repeated the analysis in a subset of countries with relatively long observation periods (35 countries with ≥10 years, 17 countries with ≥20 years). Finally, MMT/MMTPs were pooled using stratified models in which each cause of death was analyzed separately. All of the results are presented in Table S5.

3. Results

A total of 9004 time-series data for cause- and age-specific mortality from 667 communities across 39 countries were analyzed. The geographical distribution of the communities and their daily mean temperatures are presented in Fig. 1.

Fig. 2 illustrates the pooled estimates for (A) MMT and (B) MMTP by cause of death for the overall population. MMT was the highest for cardiovascular causes as 22.1 °C (95% CI: 20.9–23.4). Compared with cardiovascular causes, the MMT was 0.87 °C lower (95% CI: 0.7–1.0) for respiratory causes and 0.66 °C lower (95% CI: 0.5–0.8) for non-cardiorespiratory causes. A similar pattern was observed for MMTP. The highest MMTP was observed for cardiovascular causes as 75th percentile (95% CI: 73–78), exceeding respiratory and non-cardiorespiratory causes by 5% (95% CI: 4–6) and 4% (95% CI: 3–5), respectively. Numerical results are presented in Table 1.

Fig. 3 presents the associations between age and (A) MMT and (B) MMTP by cause of death. Based on the BIC, linear association between age and MMT was the best-fitting option (Fig. S4). The LRT indicated that the model including the interaction between age and cause of death fit significantly better. MMT increased with age for cardiovascular (0.019 °C increase per year, 95% CI: 0.014–0.023) and non-cardiorespiratory causes (0.013 °C increase per year, 95% CI: 0.009–0.016). All pairwise joint Wald tests were statistically significant, indicating differences among the three causes. Numerical results are provided in Table 2. For the MMTP, using a natural cubic spline with knots at the 50th and 80th percentiles was the best-fitting option according to BIC (Fig. S4). MMTP exhibited nonlinear age-related patterns. For cardiovascular causes, MMTP increased up to approximately age 70 years, whereas for respiratory causes, the increase began after about age 70 years. All pairwise joint Wald tests were statistically significant, confirming differences in the age-related curves across causes.

Fig. 4 illustrates the association between age and (A) MMT and (B) MMTP by cause of death and region, presented as change in MMT or MMTP per 10-year increase in age. Consistent with the global pattern, positive increases in MMT or MMTP associated with age-increase were observed for most of causes across regions, though some of the increases were not significant as the 95% CI includes zero. Detailed regional estimates are provided in Table S3 and S4 in Supplementary Materials.

The results of the sensitivity analysis are presented in Table S5 in Supplementary Materials. Results were generally consistent for alternative model specifications in the first stage model; locations of knots in the exposure-response function, degrees of freedom for spline for long-term trend and seasonality control, and restrictions to the range of MMT/MMTP search. In addition, the findings remained consistent when alternative second-stage model was used and when restricting the analysis to countries with sufficiently long observation periods. However, some variation was observed depending on the lag period. Shorter lag periods resulted in larger differences in MMT/MMTP between causes, particularly for respiratory cause. The association between age and MMT/MMTP for cardiovascular causes was more evident at longer lags.

4. Discussion

In this study, we investigated the differences in MMT and MMTP across different causes of death (cardiovascular, respiratory, and non-cardiorespiratory) and age groups by analyzing daily time-series data for mortality and mean temperature collected from among 667 communities across 39 countries. MMT and MMTP varied by cause of death,

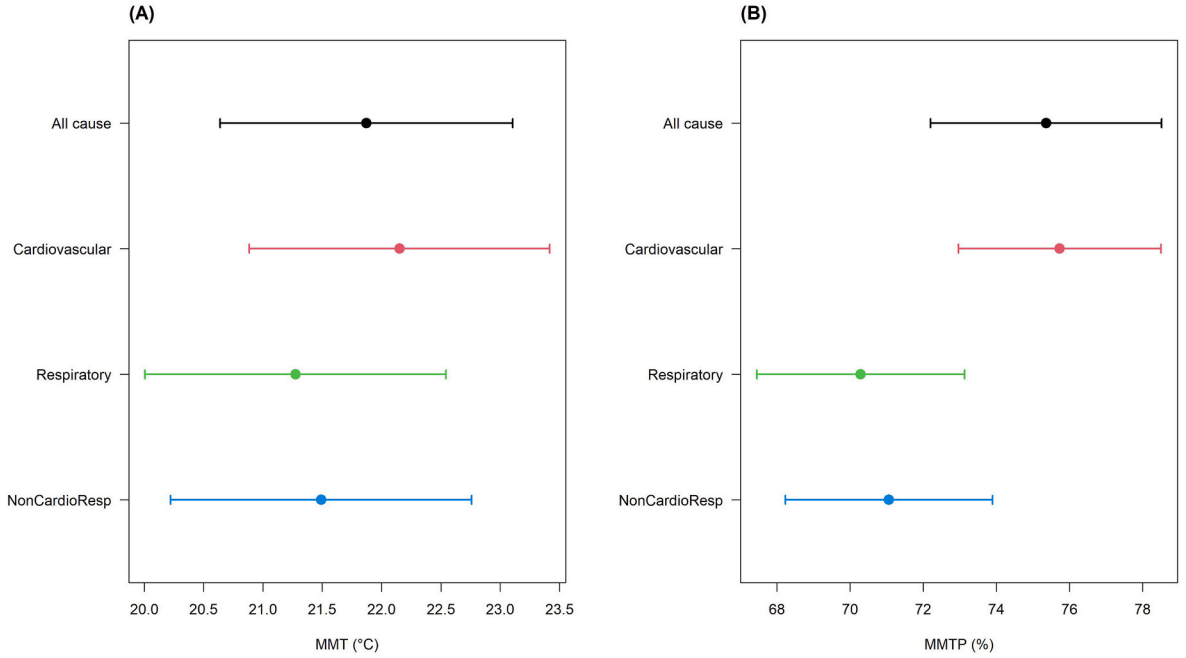

Fig. 2. Pooled estimates of (A) minimum mortality temperature (MMT, °C) and (B) minimum mortality temperature percentile (MMTP, %) by cause of death. Points and bars represent point estimates with 95% confidence intervals, respectively.

Table 1
Pooled estimates for minimum mortality temperature (MMT) and minimum mortality temperature percentile (MMTP) by cause of death.

	MMT (°C)		MMTP (%)	
	Estimate	95% CI	Estimate	95% CI
All cause	21.9	(20.6, 23.1)	75.3	(72.2, 78.5)
Cardiovascular	22.1	(20.9, 23.4)	75.5	(72.7, 78.2)
Respiratory	21.3	(20.0, 22.5)	70.3	(67.4, 73.1)
NonCardioResp	21.5	(20.2, 22.7)	71.3	(68.5, 74.1)
Pairwise Comparison[d]	**Estimated Difference**	**95% CI**	**Estimated Difference**	**95% CI**
Resp[a] vs Cardio[b]	−0.87	(-1.04, −0.70)	−5.2	(-6.3, −4.1)
NonCardioResp[c] vs Cardio	−0.66	(-0.82, −0.49)	−4.2	(-5.2, −3.1)
NonCardioResp vs Resp	0.21	(0.03, 0.40)	+1.0	(-0.3, 2.3)

[a] Respiratory.
[b] Cardiovascular.
[c] Non-Cardiorespiratory.
[d] Pairwise comparisons were derived from differences in cause-specific dummy coefficients relative to the baseline category. For example, in the comparison between respiratory and cardiovascular causes, the cardiovascular was the baseline category.

with the highest MMT observed for cardiovascular causes and the lowest for respiratory causes. Both MMT and MMTP generally increased with age, and the magnitude of this association differed by cause of death. These patterns were broadly consistent across geographic regions.

Although the observed differences were statistically significant, their practical relevance should be interpreted in light of their magnitude rather than statistical significance alone, particularly given the large size of the dataset. Moreover, while MMT provides a comparable summary on an absolute temperature scale, its interpretation is enhanced when considered alongside MMTP, which reflects the relative position within the local temperature distribution. In absolute terms, differences in MMT by cause of death were relatively small, generally remaining below 1 °C. However, the corresponding differences in MMTP were approximately 4–5%, suggesting a potentially meaningful shift in the relative position within the local temperature distribution. Similarly, although the estimated increase in MMT for 10-year increase in age was approximately 0.1-0.2 °C across different causes of death, the corresponding changes in MMTP were approximately 2-3%, indicating potentially meaning shifts in relative temperature positioning associated with increasing age.

A recent European study (Masselot et al., 2023) reported that all-cause MMTP increased with age, consistent with the present findings. The current analysis extends this evidence by demonstrating that age-related increases in MMT/MMTP may differ by cause of death and region. Another study (Scovronick et al., 2024) examining age- and cause-specific temperature–mortality associations found that cardiovascular MMTP was generally higher than that of other causes across most age groups, aligning with the present results. However, age-related increases in MMTP were observed only for non-cardiorespiratory causes in that study. This difference may reflect variations in data availability and analytic approach; in the previous study, MMTP was derived as the minimum of a pooled exposure–response function constructed from pooled reduced coefficients at the second-stage, without reflecting uncertainty in the MMTP. Meanwhile, in our study, we derived the MMT/MMTP from each location together with its uncertainty and pooled them in the second-stage modeling.

Differences in MMT by cause may partly reflect distinct physiological mechanisms and the temperature ranges at which these mechanisms are triggered. Cold exposure can induce vasoconstriction, elevate blood pressure, worsen hypertension, and precipitate cardiovascular events, such as myocardial infarction or heart failure (Alahmad et al., 2023; Achebak et al., 2024). Coldness may also cause vasoconstriction of the respiratory tract mucosa and suppress immune function, increasing susceptibility to infections (Mourtzoukou and Falagas, 2007) and exacerbating respiratory conditions, such as asthma and chronic obstructive pulmonary disease (COPD), particularly when exposure occurs abruptly without adaptation (D'Amato et al., 2018). These physiological mechanisms may operate at different temperature

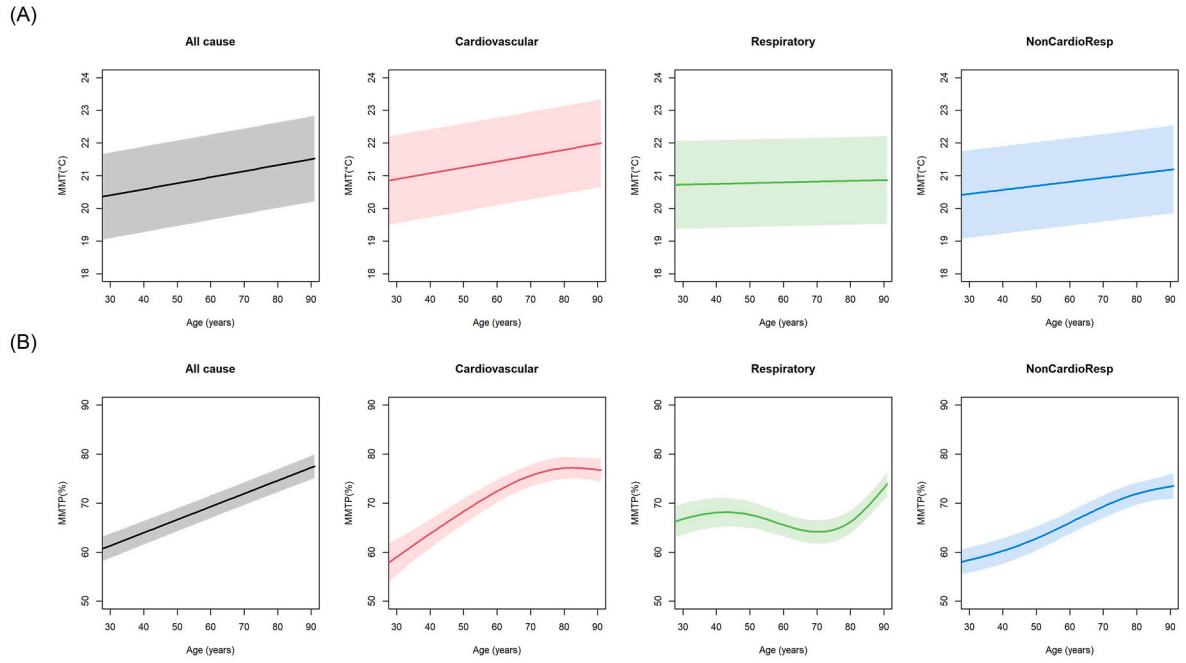

Fig. 3. Associations between age and (A) minimum mortality temperature (MMT, °C) and (B) minimum mortality temperature percentile (MMTP, %) by cause of death. Lines and shaded areas represent point estimates of regression line and 95% confidence intervals, respectively.

Table 2
Associations between age and MMT by cause of death.

	Coefficient for Age		Difference in Age Effect between Two Causes (Multivariate Wald test; p-value[d])	
	Estimated Slope	(95% CI)		
All cause	0.018	(0.015, 0.021)	-	
Cardiovascular	0.019	(0.014, 0.023)	Cardio[a] vs Resp[b]	<0.001
Respiratory	0.002	(-0.001, 0.006)	Cardio vs NonCardioResp[c]	<0.001
NonCardioResp	0.013	(0.009, 0.016)	Resp vs NonCardioResp	<0.001

[a] Cardiovascular.
[b] Respiratory.
[c] Non-Cardiorespiratory.
[d] The multivariate Wald test reports the p-value for assessing whether all cause-specific dummy coefficients, defined relative to the reference category, are jointly equal to zero.

thresholds depending on the underlying disease, and this variation in activation thresholds could explain the differences in MMT across causes. In this study, the MMT for respiratory diseases was lower than that for cardiovascular diseases, suggesting that cold-related effects may emerge at lower temperatures for respiratory diseases.

Our study showed that the minimum mortality temperature (MMT) increases with age. This age-related shift in MMT may reflect changes in physiological thermoregulation and differential vulnerability to heat and cold across the life course. Two complementary interpretations may help explain this pattern. First, the increase in MMT with age may suggest reduced cold tolerance among older adults. Older individuals generally have diminished physiological capacity to maintain core body temperature under cold exposure due to impaired vasoconstrictive responses, reduced metabolic heat production, lower muscle mass, and a blunted shivering response. Age-related cardiovascular and respiratory comorbidities may further increase susceptibility to cold-related stress, as cold exposure can elevate blood pressure, increase blood viscosity, and trigger adverse cardiovascular events. As a result, mortality risk in older populations may begin to rise at relatively milder cold temperatures compared with younger adults, shifting the temperature associated with minimum mortality toward warmer values.

In addition, although increases in MMT are typically interpreted as greater heat tolerance (Todd and Valleron, 2015; Åström et al., 2016; Arbuthnott et al., 2016; Folkerts et al., 2020), our results may not necessarily imply greater heat tolerance among older adults in an absolute sense, as substantial evidence indicates that older adults are highly vulnerable to heat-related mortality due to impaired sweating efficiency, reduced cardiovascular reserve, diminished thirst perception, and a higher prevalence of chronic disease and medication use that can compromise heat dissipation. Rather, the upward shift in MMT may reflect the relative balance between cold- and heat-related risks across age groups. If cold-related mortality risk increases more markedly with age than heat-related risk, the point of minimum overall mortality may move toward higher temperatures even if absolute heat vulnerability also increases. In other words, an increased MMT with age may be more indicative of disproportionately greater cold vulnerability than improved heat tolerance.

Regional heterogeneity in age-related MMT/MMTP change may reflect differences in climate and temperature exposure variability. Regions with greater seasonal fluctuations and wider temperature distributions, such as North America, Northern Europe, and Eastern Asia, may expose older populations to greater thermal stress, potentially leading to more pronounced age-related differences. In contrast, low-latitude regions, including Central America, Southeast Asia, and tropical South America, generally experience narrower annual temperature ranges, making age-related differences in MMT/MMTP less apparent.

MMT has been proposed in the literature as a potential indicator of population adaptation to local temperature conditions, as populations with greater adaptation may be expected to exhibit higher tolerance to heat or lower tolerance to cold. However, this interpretation is not straightforward, as MMT reflects the combined influence of multiple determinants beyond adaptation itself. These include physiological mechanisms underlying temperature-related mortality, the local temperature distribution, demographic composition, socioeconomic conditions, behavioral responses, and infrastructural factors such as housing quality, access to cooling, and healthcare availability. As a result, MMT

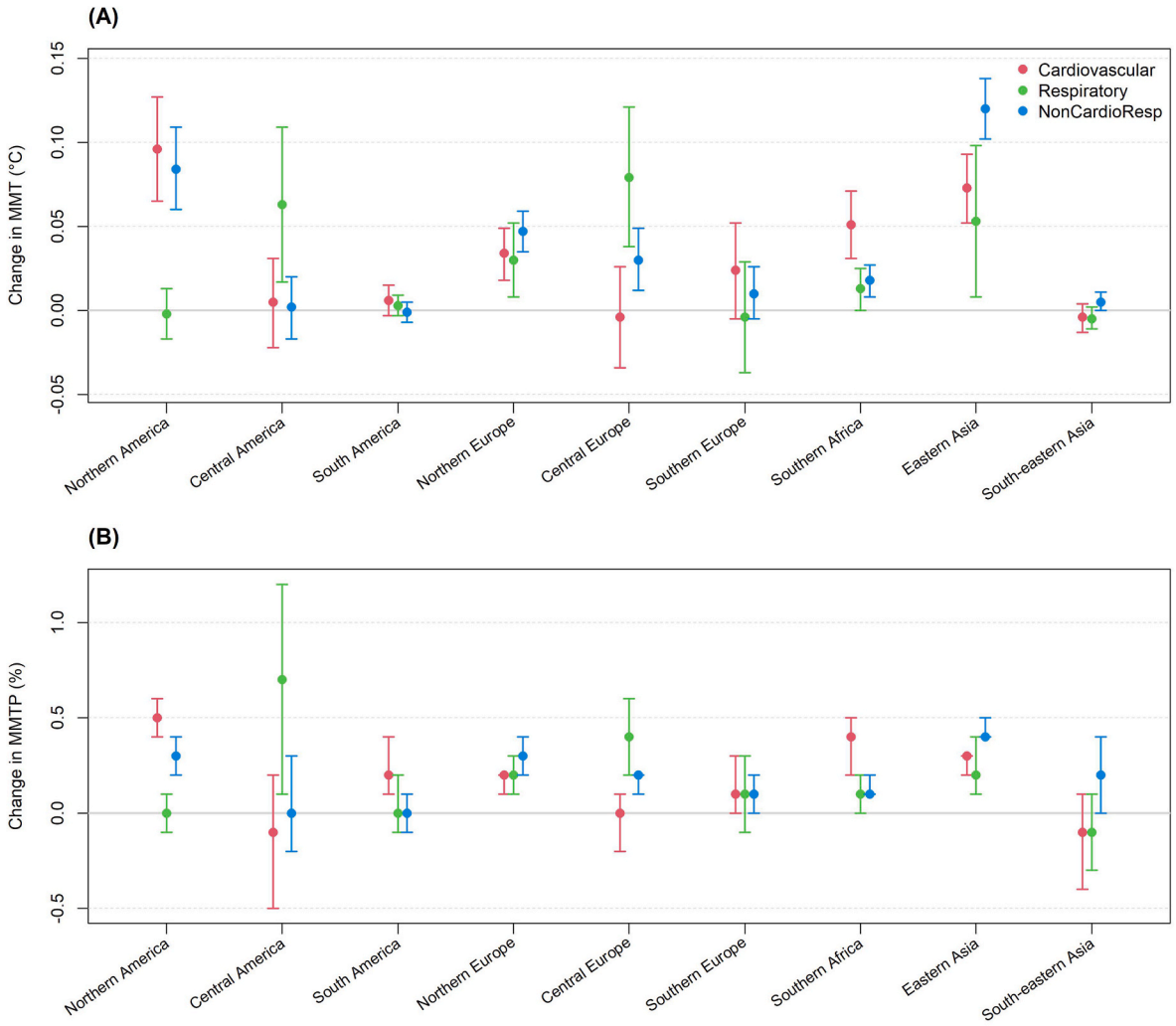

Fig. 4. Cause-specific associations between age and (A) minimum mortality temperature (MMT, °C) and (B) minimum mortality temperature percentile (MMTP, %) across regions. The y-axis represents the change in MMT or MMTP associated with 10-year increase in age. Points and bars represent point estimates with 95% confidence intervals, respectively.

should be interpreted as an indirect ecological indicator that may partly reflect adaptation, rather than a direct measure of population adaptive capacity. Accordingly, differences in MMT across populations should be interpreted cautiously, as they may arise from a complex interplay of structural and epidemiological factors rather than adaptation alone.

There are multiple sources of uncertainty in estimating age- and cause-specific MMT in our study. First of all, MMT estimates are inherently sensitive to model specification, including the choice of DLNM settings and the restrictions applied to the search range. To ensure the robustness of our findings, we conducted sensitivity analyses across various model specifications and confirmed that the overall conclusions remained unchanged. Nevertheless, one notable exception was observed when varying the lag structure, which was not unexpected. In temperature–mortality relationships, heat effects are typically acute, whereas cold effects tend to be delayed and accumulate over longer lag periods (Díaz et al., 2005; Anderson and Bell, 2009; Wang et al., 2016). Accordingly, shorter lag specifications may incompletely capture cold-related risks, potentially leading to a leftward shift in the estimated MMT. The magnitude of this shift may vary by cause of death, and such heterogeneity may amplify apparent differences between causes. As the lag period increases, the cumulative contribution of cold-related effects is more fully captured, resulting in estimates that are more consistent with those from the main analysis. A similar pattern was observed for age-related effects, with estimates based on longer lag periods showing greater consistency with the primary results.

In addition, heterogeneity in data availability and quality across countries represents an important source of uncertainty, particularly given differences in the number of communities included, observation periods, completeness of age- and cause-specific mortality data, and population coverage. Among the 39 countries included, 14 lacked age- and cause-specific mortality data, limiting the scope of subgroup analyses. Geographic coverage was also incomplete; regions such as Oceania and Central Asia were not represented, and South Africa was the only African country included. Coverage within some included countries was also limited, reducing representativeness even within sampled regions. Furthermore, differences in age group definitions and cause-of-death classifications across countries may have introduced further heterogeneity despite efforts to harmonize the data. Age-specific mortality data were also unevenly distributed, with limited cardiovascular and respiratory mortality data for individuals aged <30 years (Fig. S3), which may have reduced the precision of subgroup-specific estimates. Moreover, in certain areas, relatively short study periods increased uncertainty. As a result, some observed differences in age- and cause-specific MMT may partly reflect variations in data structure rather than solely underlying epidemiological patterns. To assess the robustness of our findings minimally, we conducted a subset analysis restricted to countries with longer data collection periods and confirmed that the overall conclusions remained unchanged.

Another source of uncertainty comes from converting heterogeneous age group categories into a continuous age variable. Using GBD 2019 mortality weights may have introduced additional uncertainty in estimating age-related MMT/MMTP, as applying 2019 weights to data spanning 1990–2019 may introduce temporal mismatch. Future research should consider more advanced methods for more precise estimation of the temperature–mortality relationship across age groups. Finally, although the meta-regression accounted for country and climatic zone, some residual heterogeneity may remain within these broad groupings, potentially reflecting unmeasured differences in local environmental conditions, socioeconomic characteristics, healthcare access, or other population-level factors across communities. Future research may consider incorporating additional variables into the modeling framework, where feasible, to better explain this residual heterogeneity.

One methodological issue in interpreting subgroup differences in MMT is that the lower-risk portion of the temperature–mortality curve is often relatively flat, such that the concept of a single minimum-risk temperature may oversimplify the underlying relationship. In practice, a range of temperatures may correspond to similarly low mortality risk, and the specific point identified as the MMT may be influenced by model specification, sampling variability, and uncertainty in estimating the exposure–response function near the minimum. Therefore, relatively small differences in estimated MMT between age groups or causes of death should be interpreted with caution and should not be overinterpreted as definitive evidence of biologically distinct temperature sensitivities. This concern is particularly important in subgroup analyses where data sparsity or heterogeneous exposure distributions may reduce precision. Accordingly, our findings are better interpreted as indicating broad differences in the location of the low-risk temperature region rather than precise shifts in a uniquely defined optimum temperature. Future studies may benefit from methodological approaches that explicitly estimate minimum-risk intervals rather than single-point MMT estimates.

Another technical issue is that the estimated MMT/MMTP may be sensitive to the search range used to identify the minimum risk point. We restricted the search to the 10th–95th percentile of the location-specific temperature distribution to balance the tradeoff between reducing unstable boundary estimates and avoiding overly restrictive bounds. Specifically, this choice was intended to reduce instability arising from sparse observations at extreme temperatures, while recognizing that excessively narrow bounds could potentially exclude the true minimum in some settings, particularly in warmer regions or locations with limited temperature variability. To evaluate the impact of this choice, we conducted sensitivity analyses using alternative search ranges. These analyses yielded similar overall patterns, suggesting that the main findings were robust to the selected search range. The percentile-based restriction also improves comparability across highly heterogeneous locations in this global analysis.

Although the interpretation of our findings warrants caution due to multiple sources of uncertainty, a major strength of this study is its global scope. To date, this represents the largest dataset used to examine cause- and age-specific MMT and MMTP across diverse regions. The inclusion of varied climates and populations allowed characterization of global patterns and regional heterogeneities. In addition, we employed a unified meta-analytic framework to jointly model cause- and age-specific estimates of optimal temperature. This approach enabled a rigorous assessment of heterogeneity and provided robust statistical comparisons across causes and age groups.

5. Conclusions

MMT and MMTP differed by cause of death and age, indicating heterogeneity in optimum temperature across population subgroups within the populations represented in this study. However, these findings should be interpreted with caution, given the multiple factors influencing MMT estimates and structural data limitations, including uneven geographic coverage, heterogeneity in data availability and quality, and differences in age and cause-of-death classifications across countries and regions. Within these constraints, our findings suggest that subgroup differences in temperature-related vulnerability may be relevant for public health planning and temperature adaptation strategies.

Declaration of generative AI use

None.

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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.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envres.2026.125043.

Data availability

Data will be made available on request.

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