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Global and Regional Cardiovascular Mortality Attributable to Nonoptimal Temperatures Over Time

Samuel Hundessa, PhD,[a] Wenzhong Huang, MSc,[a] Qi Zhao, PhD,[b] Yao Wu, MSc,[a] Bo Wen, MSc,[a] Barrak Alahmad, PhD,[c] Ben Armstrong, PhD,[d] Antonio Gasparrini, PhD,[e] Francesco Sera, MSc,[f] Shilu Tong, PhD,[g,h] Joana Madureira, PhD,[i,j,k] Jan Kyselý, PhD,[l,m] Joel Schwartz, PhD,[c] Ana Maria Vicedo-Cabrera, PhD,[d,n,o] Simon Hales, PhD,[p] Amanda Johnson, PhD,[a] Shanshan Li, PhD,[a] Yuming Guo, PhD,[a] the MCC Collaborators*

ABSTRACT

BACKGROUND The association between nonoptimal temperatures and cardiovascular mortality risk is recognized. However, a comprehensive global assessment of this burden is lacking.

OBJECTIVES The goal of this study was to assess global cardiovascular mortality burden attributable to nonoptimal temperatures and investigate spatiotemporal trends.

METHODS Using daily cardiovascular deaths and temperature data from 32 countries, a 3-stage analytical approach was applied. First, location-specific temperature-mortality associations were estimated, considering nonlinearity and delayed effects. Second, a multivariate meta-regression model was developed between location-specific effect estimates and 5 meta-predictors. Third, cardiovascular deaths associated with nonoptimal, cold, and hot temperatures for each global grid (55 km × 55 km resolution) were estimated, and temporal trends from 2000 to 2019 were explored.

RESULTS Globally, 1,801,513 (95% empirical CI: 1,526,632-2,202,831) annual cardiovascular deaths were associated with nonoptimal temperatures, constituting 8.86% (95% empirical CI: 7.51%-12.32%) of total cardiovascular mortality corresponding to 26 deaths per 100,000 population. Cold-related deaths accounted for 8.20% (95% empirical CI: 6.74%-11.57%), whereas heat-related deaths accounted for 0.66% (95% empirical CI: 0.49%-0.98%). The mortality burden varied significantly across regions, with the highest excess mortality rates observed in Central Asia and Eastern Europe. From 2000 to 2019, cold-related excess death ratios decreased, while heat-related ratios increased, resulting in an overall decline in temperature-related deaths. Southeastern Asia, Sub-Saharan Africa, and Oceania observed the greatest reduction, while Southern Asia experienced an increase. The Americas and several regions in Asia and Europe displayed fluctuating temporal patterns.

CONCLUSIONS Nonoptimal temperatures substantially contribute to cardiovascular mortality, with heterogeneous spatiotemporal patterns. Effective mitigation and adaptation strategies are crucial, especially given the increasing heat-related cardiovascular deaths amid climate change. (J Am Coll Cardiol 2024;83:2276–2287) © 2024 by the American College of Cardiology Foundation.

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From the [a]Climate, Air Quality Research Unit, School of Public Health and Preventive Medicine, Monash University, Melbourne, Victoria, Australia; [b]Department of Epidemiology, School of Public Health, Cheeloo College of Medicine, Shandong University, Jinan, China; [c]Department of Environmental Health, Harvard T.H. Chan School of Public Health, Harvard University, Boston, Massachusetts, USA; [d]Department of Public Health Environments and Society, London School of Hygiene & Tropical Medicine, London, United Kingdom; [e]Environment & Health Modelling (EHM) Lab, Department of Public Health Environments and Society, London School of Hygiene & Tropical Medicine, London, United Kingdom; [f]Department of Statistics, Computer Science and Applications "G. Parenti", University of Florence, Florence, Italy; [g]School of Public Health and Social Work, Queensland University of Technology, Brisbane, Australia; [h]National Institute of Environmental Health, Chinese Center for Disease Control and Prevention, Beijing, China; [i]Environmental Health Department, Instituto Nacional de Saúde Dr Ricardo Jorge, Porto, Portugal; [j]EPIUnit-Instituto de Saúde Pública, Universidade do Porto, Porto, Portugal; [k]Laboratório para a Investigação Integrativa e Translacional em Saúde Populacional (ITR), Porto, Portugal; [l]Institute of Atmospheric Physics, Czech Academy of Sciences, Prague, Czech Republic; [m]Faculty of Environmental Sciences, Czech University of Life Sciences, Prague, Czech Republic; [n]Institute of Social and Preventive Medicine, University of Bern, Bern, Switzerland; [o]Oeschger Center for Climate Change Research, University of Bern, Bern, Switzerland; and the [p]Department of Public Health, University of Otago, Wellington, New Zealand.

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Human activities, primarily the emissions of greenhouse gases, undeniably exert a significant influence on global warming. This influence becomes apparent when considering that the average global surface temperature rose to 1.1 °C above the preindustrial level from 2011 to 2020, largely due to these activities.[1] This temperature increase has led to heightened frequency and severity of extreme weather events,[1-3] exposing a growing number of individuals to temperature extremes.[4] Nonoptimal temperatures, defined as those falling above or below the minimum-risk exposure level, have consistently been associated with morbidity and mortality.[5,6] Studies indicate that both hot and cold temperatures are associated with an increased risk of death.[7-10] Although several studies have investigated the global association between nonoptimal temperatures and all-cause mortality,[9,11-13] there is limited evidence specifically addressing the cardiovascular mortality burden attributable to nonoptimal temperatures.

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Despite substantial public health advancements in cardiovascular disease (CVD) prevention since the mid-20th century, it remains the leading cause of death globally. In 2019, CVD was responsible for an estimated 17.9 million deaths, constituting 32% of global deaths that year.[14] According to the GBD (Global Burden of Disease) 2019 study, the number of cardiovascular deaths steadily increased from 12.1 million to 18.6 million between 1990 and 2019.[15] This trend is expected to escalate in the coming years due to ongoing global warming and greater susceptibility of individuals with multiple risk factors for CVD.[16,17]

Evidence indicates the association between nonoptimal temperatures and CVD and mortality.[18-21] However, previous studies have often been confined to single countries or regions, hindering global generalizability due to geographical heterogeneity in environmental conditions and population dynamics. The 2023 GBD study made progress in quantifying the global burden of CVD mortality attributed to nonoptimal temperatures.[16] However, its reliance on data from only 9 countries hinders extrapolation to a global scale. Moreover, the study overlooked spatiotemporal variations in temperature-mortality relationships, potentially underestimating temperature-attributable mortality. Addressing this issue, Alahmad et al[22] conducted a study, providing more inclusive analysis. However, estimating mortality burden at smaller scales allows for a more detailed understanding, thus enabling more effective and targeted intervention strategies.

Using 3-stage meta-analytical models in environmental epidemiology, the aim of the current study was to estimate the global and regional burden of cold and hot temperatures on cardiovascular mortality and investigate spatiotemporal trends in recent decades.

ABBREVIATIONS AND ACRONYMS

CVD = cardiovascular disease

eCI = empirical CI

GDP = gross domestic product

ICD = International Classification of Diseases

MCC = Multi-Country Multi-City

UN = United Nations

METHODS

DATA SOURCES. We obtained daily counts of cardiovascular deaths and corresponding daily temperature data from the latest version of the Multi-Country Multi-City (MCC) Collaborative Research Network data set, spanning January 1, 1969, to December 31, 2019. The MCC data set has been detailed in our previous studies.[9,22] In addition, we augmented the cardiovascular death data included in the MCC data set by obtaining more detailed cardiovascular mortality information for Australia, New Zealand, and Brazil. These additional data were aggregated according to date and location by using the pertinent administrative boundaries for each country or territory. The final data set encompassed global cardiovascular deaths (International Classification of Diseases [ICD]-9th Revision codes 390-459 and ICD-10th Revision codes I00-I99) for 1,847 locations across 32 countries or territories (Supplemental Table 1).

Daily mean temperature data were identical to those used in our previous global study.[13] In summary, daily temperature data (2000-2019) gridded at 55 km × 55 km resolution were obtained from the global daily temperature data set. These data were used to compute both the average and the range of annual mean temperatures for each grid cell. Country-level annual gross domestic product (GDP) and population data from the Global Carbon Project were used to calculate grid-specific GDP per capita. Climate zones were assigned to each grid cell by using the Köppen-Geiger climate classification.[23] Country-specific annual cardiovascular mortality rates were derived from the World Bank.

This study was approved by the Monash University Human Research Ethics Committee.

The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

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STATISTICAL ANALYSIS. A 3-stage analytical approach was applied to estimate the burden of cardiovascular mortality related to nonoptimal temperatures. A detailed description of this approach can be found in previous MCC studies.[9,13] First, we estimated the association between daily mean temperature and cardiovascular mortality for each study location. This involved the use of quasi-Poisson regression combined with a distributed lag nonlinear model.[24] The temperature variable was modeled with a natural cubic spline, featuring 3 internal knots placed at the 10th, 75th, and 90th percentiles of the city-specific temperature distribution. The lag effects of the temperature on cardiovascular mortality were modeled with an intercept and 3 internal knots, with evenly spaced values in the log scale as in previous studies.[9,13] A 21-day lag was used to fully capture the delayed effects of temperature and mortality displacement. A natural cubic spline for time with 8 degrees of freedom per year was used to control for long-term trends and seasonality. An indicator for the day of the week was also included to account for fine temporal patterns.[9,13] This analysis was conducted in 5-year intervals of the epidemiologic data period to account for potential change in the historical temperature-mortality relationship over time.

Second, we developed a multivariate meta-regression model linking the reduced cumulative association for each location with 5 location-specific meta-predictors. These predictors included the yearly average of mean temperature, temperature range, climate zones (Supplemental Figure 1),[23] an indicator of continents, and GDP per capita. These predictors were found to explain the heterogeneity in temperature-mortality relationships across locations.[9,25] The meta-regression model included random effect to account for differences between locations and time to adjust for the historic temperature-mortality relationship.[26]

Third, we estimated the temperature-cardiovascular mortality association for each grid per day, using the fitted meta-regression model and the grid-specific meta-predictors. These associations were then used to calculate the number of grid-specific daily excess deaths related to nonoptimal temperatures. Specifically, grid-specific daily excess deaths associated with nonoptimal temperatures were calculated by using the following formula:

$$Ed_{it} = (RR_{it} - 1) \times D_i$$

where Ed_{it} is grid-level daily excess cardiovascular deaths; RR_{it} is the cumulative relative risk predicted from the third stage of modeling, in grid i, on day t; and D_i is average daily death count in grid i, which was derived from the annual cardiovascular death rate of the country where the grid cell was situated, along with the population within that particular grid cell.[13] Similar to previous studies,[9,13,22] reference values were set to grid-specific minimum mortality temperatures, representing the temperature at which the mortality risk is at its lowest.[9] This value relates to human adaptability to local climate conditions, reflecting the temperature most conducive to human physiology.[27] The analyses were restricted to grids with a minimum of 1 cardiovascular death count per year to enhance the model stability.

We aggregated the daily excess cardiovascular deaths per grid cell, yielding annual global, continental, and regional values based on the regional classifications established by the United Nations (UN) Statistics Division (M49).[28] Considering demographic factors, the annual excess cardiovascular mortality ratio and rate per 100,000 population were calculated. Globally and across all regions, the temporal change in the temperature-related excess cardiovascular mortality ratio was calculated over five 4-year periods, using the earliest period (2000-2003) as a baseline. The presentation includes the excess cardiovascular mortality burden attributable to nonoptimal, cold, and hot temperatures, along with their 95% empirical CIs (eCIs), stratified according to global, continental, and UN regions. Furthermore, we provided mortality burden associated with extreme heat (≥97.5th percentile) and extreme cold (≤2.5th percentile) temperatures.[9] Monte Carlo simulations were used, with 500 iterations run to estimate uncertainty in mortality burden by drawing values from coefficients, variances, and covariances from the meta-regression model. To account for the spatial relationships between neighboring grids, ordinary kriging (using residual from the *mixmeta* model) was used, and a random component was integrated into the uncertainty measure, particularly in calculating the eCI.[29]

The strength of the results was measured by conducting sensitivity analyses by changing the parameters of the knots and lag days (Supplemental Table 2). Specifically, the exposure-response relationship were modeled with 4 knots at the 10th, 50th, 75th, and 90th percentiles and, alternatively, with 5 knots at the 5th, 25th, 50th, 75th, and 95th percentiles. In addition, the maximum lag periods were changed to 24 and 28 to examine the effect of temperature on mortality.

TABLE 1 Annual Average Excess Cardiovascular Mortality, Related to Nonoptimal Temperatures, 2000-2019, According to Continent and Region

	Excess Cardiovascular Mortality					
	All Nonoptimal (95% eCI)	Regional Percentage	Cold Related (95% eCI)	Regional Percentage	Heat Related (95% eCI)	Regional Percentage
Global	1,801,513 (1,526,632-2 202,831)	100.00	1,666,814 (1,369,292-2,351,730)	92.52	134,699 (100,165-199,769)	7.48
Americas	167,301 (106,270-278,173)	9.29	154,410 (88,752-267,046)	8.57	12,891 (4,884-24,677)	0.72
Northern America	89,503 (56,365-139,996)	4.97	83,298 (49,865-133,985)	4.62	6,205 (4,035-10,231)	0.34
Latin America and the Caribbean	77,798 (48,063-141,919)	4.32	71,112 (39,006-135,118)	3.95	6,686 (185-15,045)	0.37
Africa	215,632 (118,646-409,701)	11.97	196,411 (97,304-382,771)	10.90	19,221 (2,575-47,139)	1.07
Northern Africa	83,518 (49,461-138,730)	4.64	77,675 (44,809-132,153)	4.31	5,842 (2,405-11,387)	0.32
Sub-Saharan Africa	132,114 (70,721-272,059)	7.33	118,736 (53,870-252,766)	6.59	13,378 (4,633-36,075)	0.74
Asia	1,026,923 (967,420-1,285,784)	57.00	941,844 (867,846-1,191,959)	52.28	85,079 (75,590-109,946)	4.72
Central Asia	74,982 (64,703-96,600)	4.16	69,929 (59,409-91,058)	3.88	5,053 (4,371-6,954)	0.28
Eastern Asia	462,313 (428,245-563,170)	25.66	433,352 (396,558-529,594)	24.05	28,961 (25,993-38,868)	1.61
Southeastern Asia	53,639 (48,525-68,564)	2.98	46,036 (41,633-61,381)	2.56	7,603 (4,378-10,063)	0.42
Southern Asia	325,662 (303,476-418,001)	18.08	291,168 (267,589-381,038)	16.16	34,494 (28,975-45,780)	1.91
Western Asia	110,328 (69,348-180,118)	6.12	101,359 (59,486-169,486)	5.63	8,969 (5,341-15,042)	0.50
Europe	385,569 (266,084-593,821)	21.40	368,656 (242,478-575,876)	20.46	16,913 (12,318-28,004)	0.94
Eastern Europe	267,056 (190,621-408,500)	14.82	255,076 (176,607-393,021)	14.16	11,979 (8,906-20,190)	0.66
Northern Europe	27,752 (16,584-43,248)	1.54	26 976 (15,591-42,453)	1.50	776 (482-1,449)	0.04
Southern Europe	45,908 (27,625-73,413)	2.55	43,443 (24,540-70,769)	2.41	2,465 (1,664-4,200)	0.14
Western Europe	44,853 (27,276-70,274)	2.49	43,161 (25,051-68,579)	2.40	1,692 (1,089-2,973)	0.09
Oceania	6,088 (6,015-8,466)	0.34	5,493 (5,313-7,838)	0.30	595 (489-851)	0.03
Australia and New Zealand	4,414 (4,129-5,821)	0.25	4,243 (3,925-5,627)	0.24	172 (157-248)	0.01
Other regions in Oceania[a]	1,673 (1,528-3,048)	0.09	1,250 (992-2,660)	0.07	423 (295-634)	0.02

[a] Regions in Oceania except for Australia and New Zealand.

eCI = empirical CI.

All data organization and analyses were performed by using R software version 4.4.3 (R Foundation for Statistical Computing). The *dlnm* and *mixmeta* packages were used to fit the distributed lag nonlinear model and multivariate meta-regression, respectively.[24]

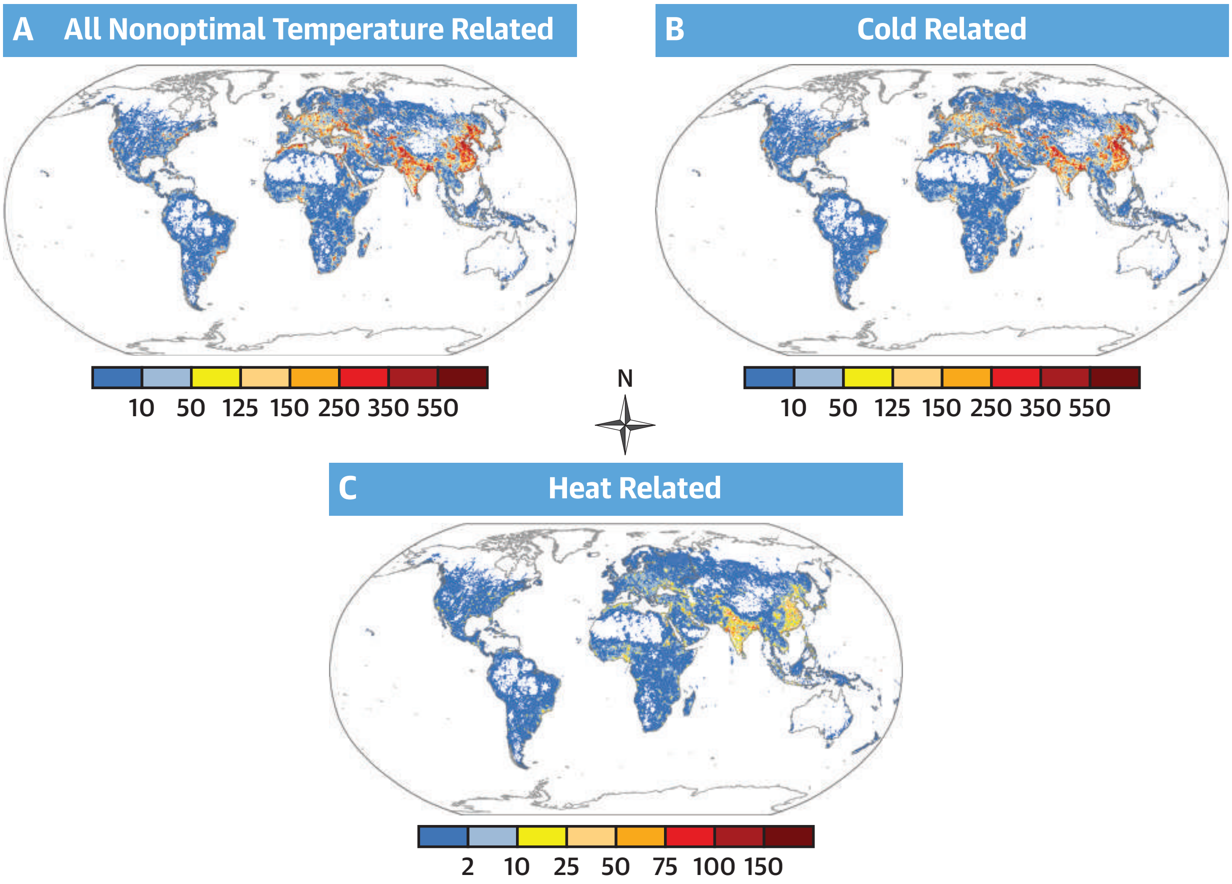
RESULTS

This study estimated the cardiovascular mortality burden related to nonoptimal temperatures from 2000 to 2019. The findings indicate that, globally, an estimated 1,801,513 cardiovascular deaths per year (95% eCI: 1,526,632-2,202,831 cardiovascular deaths per year) were associated with nonoptimal temperatures (**Table 1**). Of these, 1,666,814 deaths (95% eCI: 1,369,292-2,351,730 deaths) were linked to cold temperatures and 134,699 deaths (95% eCI: 100,165-199,769 deaths) to hot temperatures. More than one-half (57%) of all excess deaths occurred in Asia, followed by Europe (21%), Africa (11.97%), the Americas (9.29%), and Oceania (<1%). This distribution largely held true for cold-related deaths, with the highest proportions again concentrated in Asia and Europe, and the lowest in Oceania. However, a different pattern emerged for heat-related deaths. Asia still held the top position, but Africa saw a higher percentage compared with Europe. In summary, Asia experienced the highest proportion of excess cardiovascular deaths linked to both heat and cold, whereas Oceania had the fewest. A detailed overview of temperature-related excess deaths is presented in **Figure 1**.

The current analysis indicated that 8.86% (95% eCI: 7.51%-12.32%) of global cardiovascular deaths were associated with nonoptimal temperatures. Among these deaths, 8.20% (95% eCI: 6.74%-8.83%) were related to cold temperatures and 0.66% (95% eCI: 0.49%-0.98%) to hot temperatures. When calculating the global excess cardiovascular death rate, cold temperatures accounted for 24.17 (95% eCI: 19.86-34.10) and heat for 1.95 (95% eCI: 1.45-2.89) deaths per 100,000 population. Extreme temperature whether cold or heat accounted for only a small fraction: 1.53% (95% eCI: 1.45% to 1.79%) and 0.50% (95% eCI: 0.45% to 0.66%), respectively, and were observed on just a few days (Supplemental Tables 3 and 4).

Excess cardiovascular death ratios and rates varied considerably across regions (**Figures 2A to 2C**, **Table 2**). The highest regional excess cardiovascular death rate

FIGURE 1 **Average Annual Excess Cardiovascular Deaths**



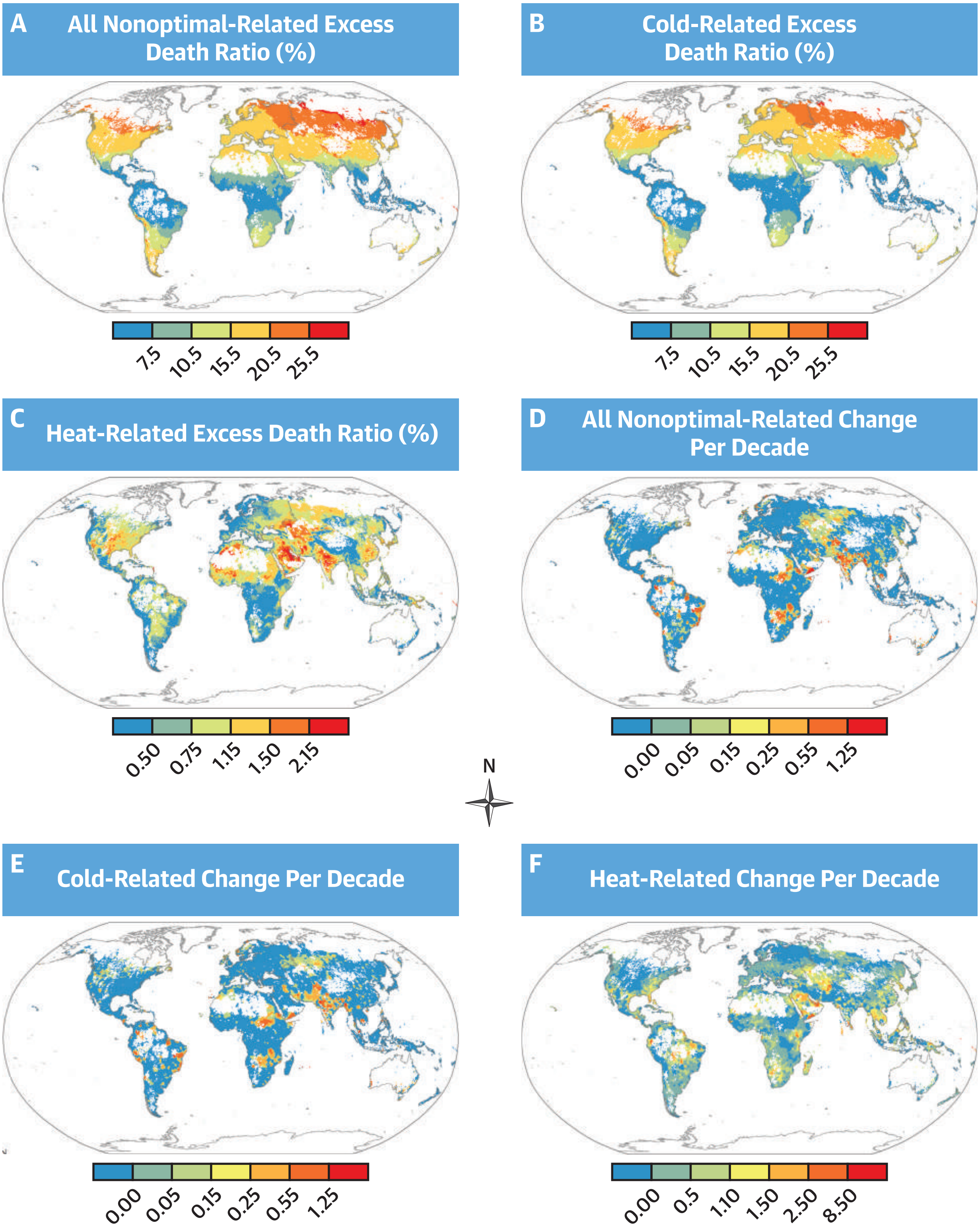
The excess deaths were calculated at a spatial resolution of 55 km × 55 km for the period spanning 2000 to 2019. All nonoptimal temperature related (A), cold related (B), and heat related (C).

was found in Central Asia, followed by Eastern Europe and Western Asia. Of note, the cold-related death rate observed in Central Asia was >4 times the global average. Eastern Europe and Western Asia also faced significant cold-related death burdens, exceeding the global average by >3 times in Eastern Europe. Interestingly, the pattern for heat-related deaths differed. Central Asia, Western Asia, and other regions in Oceania saw the highest rates. Notably, Central Asia had the highest excess cardiovascular death rates related to both cold and heat (**Table 2**). The grid-specific distribution of cardiovascular death ratio and rates are shown in Supplemental Figure 2.

Between 2000 and 2003 and 2016 and 2019, the cold-related global excess death ratio declined by 0.53 percentage point (95% eCI: −0.73 to −0.74 percentage point). Conversely, the hot-related excess death ratio increased by 0.20 percentage point (95% eCI: 0.15 to 0.28 percentage point). When the combined cold and hot nonoptimal temperature-related excess death ratio was assessed for the same periods, a net decline of 0.33 percentage point was observed (Supplemental Tables 5 to 7). Across regions, cold-related cardiovascular deaths declined, except in South Asia. The Americas, most regions of Asia, and Europe had fluctuating trends (**Central Illustration**, **Figure 3**). The biggest decline in total deaths was in Southeastern Asia, Sub-Saharan Africa, and Oceania.

Heat-related deaths increased considerably as a fraction of its initial low value in most regions, especially in Central Asia and North America. Europe and Asia exhibited unstable patterns. Net cardiovascular mortality ratio greatly declined in Sub-Saharan Africa, Oceania, Eastern Europe, and Southeast Asia but increased in Southern Asia. Americas, most regions of Asia, and Europe saw fluctuating

FIGURE 2 Average Annual Excess Cardiovascular Mortality Ratios and Change Per Decade



A All Nonoptimal-Related Excess Death Ratio (%)

B Cold-Related Excess Death Ratio (%)

C Heat-Related Excess Death Ratio (%)

D All Nonoptimal-Related Change Per Decade

E Cold-Related Change Per Decade

F Heat-Related Change Per Decade

The excess death ratios were calculated for each grid (cell size 55 km × 55 km). (A to C) Represents excess mortality ratios, and (D to F) depict changes in the mortality ratio per decade compared with the baseline (2000-2003) average.

TABLE 2 Cardiovascular Mortality Ratio and Rate Related to Nonoptimal Temperatures, 2000-2019, According to Continent and Region

	Excess Cardiovascular Death Ratio (%) (95% eCI)			Excess Cardiovascular Death Rate per 100,000 Population (95% eCI)		
	All Nonoptimal	Cold	Heat	All Nonoptimal	Cold	Heat
Global	8.86 (7.51-12.32)	8.20 (6.74-11.57)	0.66 (0.49-0.98)	26.12 (22.14-36.29)	24.17 (19.86-34.10)	1.95 (1.45-2.89)
Americas	10.16 (6.46-16.90)	9.38 (5.39-16.22)	0.78 (0.30-1.50)	17.87 (11.35-29.72)	16.50 (9.48-28.53)	1.38 (0.52-2.64)
Northern America	16.48 (10.38-25.77)	15.34 (9.18-24.67)	1.14 (0.74-1.88)	25.82 (16.26-40.38)	24.02 (14.38-38.65)	1.79 (1.16-2.95)
Latin America and the Caribbean	7.054 (4.35-12.87)	6.45 (3.53-12.25)	0.61 (0.02-1.36)	13.20 (8.16-24.08)	12.07 (6.62-22.93)	1.135 (0.03-2.55)
Africa	6.32 (3.48-12.01)	5.76 (2.85-11.22)	0.56 (0.07-1.38)	20.69 (11.39-39.32)	18.85 (9.34-36.73)	1.84 (0.25-4.52)
Northern Africa	8.233 (4.87-13.67)	7.657 (4.41-13.03)	0.58 (0.24-1.12)	39.42 (23.34-65.47)	36.66 (21.15-62.37)	2.757 (1.14-5.37)
Sub-Saharan Africa	5.513 (2.95-11.35)	4.95 (2.24-10.55)	0.56 (0.19-1.51)	15.91 (8.52-32.72)	14.30 (6.48-30.45)	1.612 (0.56-4.35)
Asia	7.86 (7.41-9.85)	7.21 (6.64-9.13)	0.65 (0.58-0.84)	24.79 (23.35-31.03)	22.73 (20.95-28.77)	2.05 (1.82-2.65)
Central Asia	14.25 (12.29-18.36)	13.29 (11.29-17.31)	0.96 (0.83-1.32)	122.51 (105.72-157.83)	114.25 (97.07-148.77)	8.256 (7.14-11.36)
Eastern Asia	9.81 (9.09-11.95)	9.1 (8.42-11.24)	0.62 (0.55-0.83)	29.75 (27.56-36.24)	27.89 (25.52-34.08)	1.864 (1.67-2.50)
Southeastern Asia	2.707 (2.44-3.46)	2.323 (2.10-3.09)	0.38 (0.22-0.51)	8.96 (8.11-11.45)	7.69 (6.954-10.25)	1.27 (0.73-1.681)
Southern Asia	6.597 (6.14-8.47)	5.898 (5.42-7.72)	0.69 (0.58-0.93)	19.23 (17.92-24.69)	17.19 (15.81-22.51)	2.037 (1.71-2.70)
Western Asia	12.216 (7.68-19.94)	11.22 (6.58-18.76)	0.99 (0.59-1.67)	46.69 (29.35-76.22)	42.89 (25.173-71.72)	3.796 (2.26-6.37)
Europe	18.09 (12.49-27.87)	17.3 (11.38-27.02)	0.79 (0.58-1.31)	52.19 (36.02-80.38)	49.9 (32.82-77.95)	2.29 (1.67-3.79)
Eastern Europe	18.787 (13.41-28.47)	17.94 (12.42-27.65)	0.84 (0.62-1.42)	90.81 (64.82-138.90)	86.73 (60.052-133.64)	4.073 (3.03-6.87)
Northern Europe	17.258 (10.31-26.89)	16.776 (9.69-26.40)	0.48 (0.3-0.90)	27.91 (16.68-43.49)	27.13 (15.67-42.69)	0.78 (0.48-1.46)
Southern Europe	16.13 (9.71-25.79)	15.264 (8.62-24.86)	0.87 (0.58-1.48)	29.50 (17.75-47.18)	27.92 (15.77-45.48)	1.584 (1.07-2.69)
Western Europe	16.99 (10.33-26.62)	16.35 (9.49-25.98)	0.64 (0.41-1.13)	23.65 (14.38-37.06)	22.76 (13.21-36.16)	0.892 (0.54-1.568)
Oceania	8.33 (8.23-11.58)	7.51 (7.27-10.72)	0.81 (0.67-1.16)	16.83 (16.63-23.41)	15.19 (14.69-21.67)	1.64 (1.35-2.35)
Australia and New Zealand	13.04 (12.19-17.19)	12.53 (11.59-16.62)	0.51 (0.46-0.73)	16.37 (15.31-21.58)	15.73 (14.55-20.86)	0.636 (0.58-0.92)
Other regions in Oceania[a]	4.263 (3.89-7.76)	3.184 (2.53-6.78)	1.08 (0.75-1.62)	18.19 (16.61-33.14)	13.59 (10.78-28.92)	4.602 (3.20-6.89)

[a] Regions in Oceania except for Australia and New Zealand.

eCI = empirical CI.

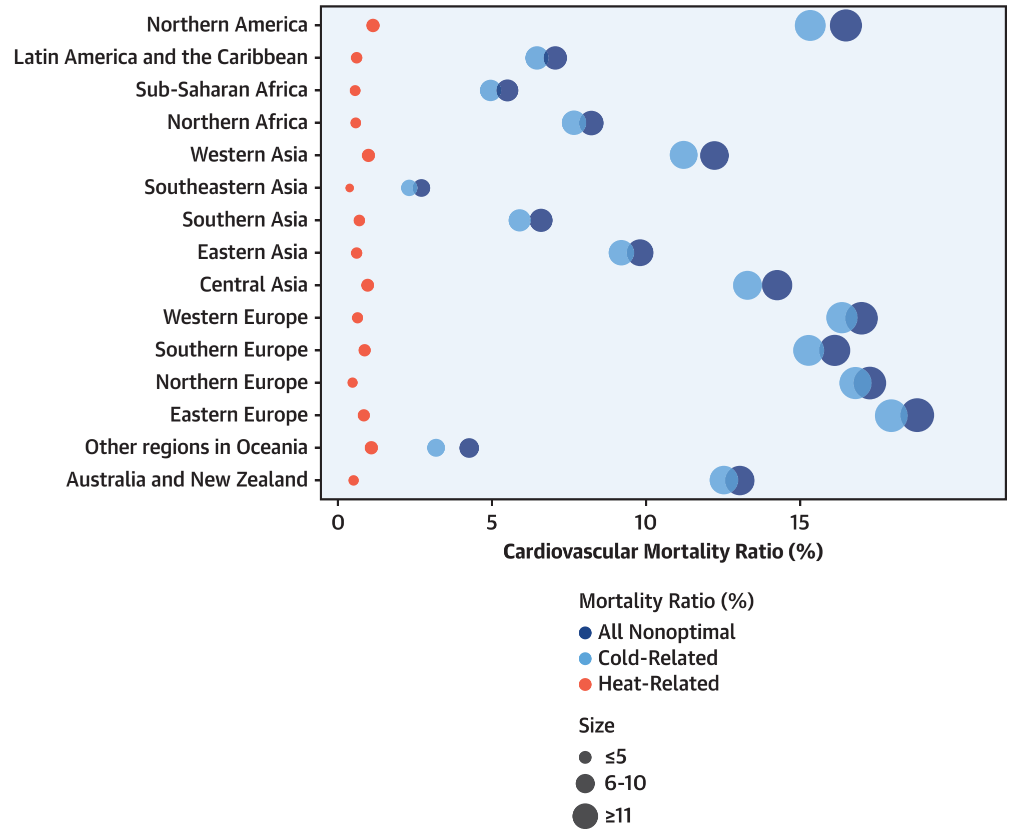
trends. Detailed spatial changes are shown in Figures 2D to 2F. Most grids observed declined cold-related deaths in North America, Europe, Eastern and Southeastern Asia, and Sub-Saharan Africa near the equator. Heat-related deaths slightly rose in tropical/subtropical zones. Supplemental Figure 2 shows the change in the mortality burden estimates in terms of rates for hot, cold, and nonoptimal temperature exposure at the grid level.

DISCUSSION

NONOPTIMAL TEMPERATURE–RELATED CVD MORTALITY BURDEN. This study estimated the global burden of cardiovascular mortality associated with nonoptimal temperatures at a spatial resolution of 55 km × 55 km and investigated temporal changes from 2000 to 2019. The findings indicate that, globally, 1,801,513 cardiovascular deaths yearly were linked to nonoptimal temperatures over the 2 decades, comprising 8.86% of total global cardiovascular deaths, or 26 excess cardiovascular deaths per 100,000 people. More excess deaths were associated with cold temperatures (8.20%) than hot ones (0.66%). Between 2000 and 2003 and 2016 and 2019, a global net excess death ratio declined by 0.33 percentage point. Notably, cold-related excess death fell by 0.53 percentage point, whereas hot-related death increased by 0.20 percentage point. Temporal and geographical variations were evident in the temperature-related cardiovascular mortality burden for both hot and cold temperatures.

Despite several studies having explored the associations between nonoptimal temperatures and cardiovascular mortality,[18-21] none has specifically quantified the cardiovascular mortality burden attributed to nonoptimal temperatures globally by using established statistical approaches. By using MCC data from 1,847 locations and a state-of-the-art 3-stage unified analytical strategy, this study revealed a cardiovascular mortality burden (8.86%) associated with nonoptimal temperatures, predominantly driven by cold temperatures (8.20%) compared with hot temperatures (0.66%). These findings align with prior research,[9,13,16] which consistently reported a higher burden of cold-related cardiovascular deaths compared with hot-related deaths, both nationally and globally. For example, a study conducted in China found that 11.62% of excess cardiovascular deaths were attributed to cold temperatures, whereas

CENTRAL ILLUSTRATION Cardiovascular Mortality Burden According to Region From 2000 to 2019



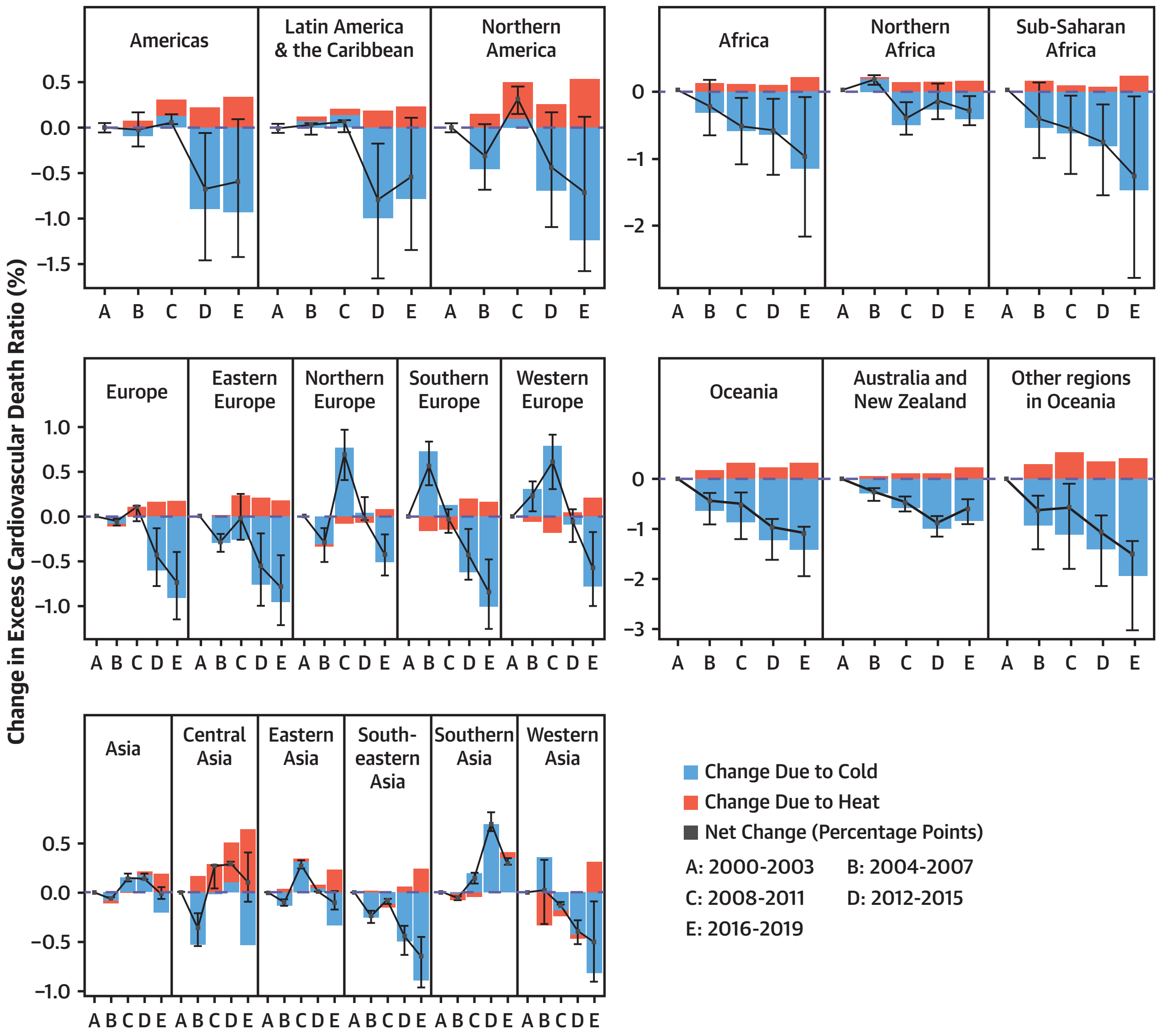
Hundessa S, et al. J Am Coll Cardiol. 2024;83(23):2276–2287.

The burden is represented by the average excess cardiovascular mortality ratio (%) per region from 2000 to 2019.

the ratio for hot-related deaths was 2.71%.[21] Similarly, a global study reported that 8.5% of all-cause excess mortality was linked to cold temperatures compared with 0.9% associated with heat.[13] Although the current study noted a slightly lower burden of heat-related cardiovascular mortality compared with previous findings, it exhibited a slight upward trend, which aligns with reports of increasing heat-related cardiovascular deaths.[16] These findings highlight the need for global communities and governments to address both cold- and heat-related mortality burdens when planning for climate change adaptation.

Several biologic mechanisms explain the link between nonoptimal temperatures and cardiovascular health. Heat exposure induces vasodilation (increased blood flow to the skin), triggers sweat production, and alters heart rate. Blood viscosity may also rise slightly. It disrupts body core temperature regulation and increases the risk of coronary events. It also increases metabolic activity and oxygen consumption.[30] Heat-induced fluid shifts can disrupt electrolyte balance, exacerbating arrhythmias.[31] These responses are rapid and consistent with the sharp risk increase above the optimum temperature (Supplemental Figures 3 and 4), which was associated with a comparatively low burden attributable to high temperature. Cold exposure raises blood viscosity, vasoconstriction, and muscle tone, elevating blood pressure and cardiac oxygen demand.[32,33] These responses can persist longer[32] and contribute to mortality risks with a pattern that is smooth and approximately linear, with most of the attributable deaths occurring on moderately cold days.

FIGURE 3 **Temporal Changes in Regional Cardiovascular Mortality Ratios**



The analysis depicts variation in the mortality ratios across consecutive 4-year periods compared with the baseline average of 2000 to 2003. The y-axis represents a change in percentage points. Other regions in Oceania refers to regions in Oceania, excluding Australia and New Zealand.

GEOGRAPHICAL VARIATIONS IN NONOPTIMAL TEMPERATURE-RELATED CVD MORTALITY. The current study found significant geographical disparities in nonoptimal temperature-related cardiovascular mortality. Central Asia and Eastern Europe had the highest rates for both cold and hot temperatures, aligning with a previous related study.[13] These disparities are likely due to differences in climate, environmental exposure, preexisting CVD prevalence, and baseline mortality rates. Eastern Europe's continental climate[23] with lower temperatures may explain its high burden of cold-related mortality. This aligns with the region's high cardiovascular mortality rate, as reported in the 2015 GBD study.[34] Notably, some countries such as Latvia and Romania have double the average of the European Union, further contributing to the trend. Our previous multicountry study also estimated that Eastern Europe has the highest regional heat-related mortality rates in Europe.[13] Despite these findings, there was no substantial increase in the net cardiovascular mortality burden in Eastern Europe during the study period. In Central Asia, the region's dry climate (60%) and significant recent temperature increases likely contributed to its observed heat-related burden.[35] The high cold-related burden aligns with previous findings linking cold temperatures to increased mortality in tropical regions. For example, a comparable study found a high cold-related mortality rate in Sub-Saharan Africa, known for its hot and dry tropical climates.[13] The association between cold temperatures and high mortality burdens in hot climatic regions may seem unexpected, given the generally warmer weather. However, the population's susceptibility to cold effects in hot climates suggests acclimatization to local conditions, where temperature deviations (whether cold or hot) can lead to health risks. In addition, factors beyond climate characteristics may contribute to the observed cold-related mortality burden in Central Asia. Studies highlight unusually high CVD prevalence and rate in Central Asia, ranking second in estimated age-standardized prevalence of ischemic heart disease in 2015 and having the highest cardiovascular mortality rate globally.[34]

CHANGE IN TEMPERATURE-RELATED CVD MORTALITY BURDEN. The current study also identified temporal variation in the nonoptimal temperature-related global cardiovascular mortality burden between 2000 and 2019. Over this period, there was a substantial decrease in the cold-related global excess deaths ratio and a slight increase in the heat-related excess death ratio, resulting in a net decline of 0.33 percentage point. This observation was consistent with our previous MCC study, which reported a net decline of 0.30 percentage point in all-cause temperature-related deaths.[13] These results imply that the overall temperature-related mortality burden might slightly decrease with climate change. However, the heat-related mortality burden is expected to rise in the long term under ongoing global warming. Nevertheless, there is a regional difference, with the ratio of cold-related deaths decreasing substantially or fluctuating in most UN regions, except in Southern Asia. Our previous global estimates of all-cause mortality indicated a similar trend in the mortality ratio in the region.[13] Thus, the local countries should consider the public health impact of low temperatures when developing climate mitigation and adaptation strategies. Conversely, the heat-related death ratio notably increased as a fraction of its initial low value in most regions, coinciding with change in annual mean temperature during the study period (Supplemental Figure 5). The highest regional increase in the heat-related excess death ratio occurred in Central Asia, Northern America, and other regions in Oceania, despite a considerable reduction in the ratio of cold-related cardiovascular deaths in the same period in the region. Furthermore, all regions experienced a substantial increase in heat-related mortality burden during the most recent 4 years of the study period (2016-2019), emphasizing the public health implications associated with rising global surface temperatures.[1] Ongoing warming is expected to increase mortality burden, especially in tropical and subtropical climate zones, including areas with high population densities, such as Southeast Asia.[36] Increased temperatures and associated mortality in these regions could potentially have substantial public health impacts.

STUDY STRENGTHS. To the best of our knowledge, this study is the largest to date quantifying the cardiovascular mortality burden attributable to nonoptimal temperatures and exploring spatiotemporal trends globally. The analysis used a high spatial resolution to enhance the ability to identify geographical variations and reduce the risk of exposure misclassification. The study assessed temperature-cardiovascular mortality associations by using a well-established statistical model based on the largest data set ever collected. Encompassing 1,847 locations spanning 32 countries across 5 continents, this study includes areas characterized by diverse climates, demographic characteristics, socioeconomics, and public health services, and it provides an estimate for global grids possessing approximately 6.9 billion individuals, representing 98.5% of the global population during the study period (2000-2019). This ensures global representativeness of our findings. Our study provides a robust evidence base for comprehending climate change's role in global cardiovascular mortality trends across regions. These findings aid regional and national governments in developing tailored policies to protect populations from temperature-related health risks.

STUDY LIMITATIONS. The grid-level temperature-related mortality burden was estimated by using country-level death rates due to the absence of mortality data for each grid cell. As a result, all grids within the same country were assumed to have identical mortality rates. The study incorporated 5 meta-predictors in the meta-regression model to help account for heterogeneity in temperature-mortality associations across locations.[9,36] However, there may be another factor contributing to geographic variation in the mortality burden not accounted for (eg, population age structure, underlying health conditions, air pollution, adaptation strategies). We were not able to consider this information because such data were not available for a sufficient number of locations. Although the grid system applied in the current study included the majority of the world's population, we were unable to estimate the temperature-related mortality burden in the least populated grids, which had insufficient numbers of cardiovascular deaths. We used standardized ICD codes, including cardiac arrest, but they may also include noncardiac conditions.

CONCLUSIONS

Nonoptimal temperatures substantially contribute to cardiovascular mortality burden, with notable increases in heat-related deaths over the past 2 decades. However, this burden varies spatially and temporally. Our findings provide an evidence base for developing and implementing effective strategies aimed at mitigating the public health consequences of nonoptimal temperatures, with a particular focus on the escalating impact of heat-related conditions in the context of global warming.

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ADDRESS FOR CORRESPONDENCE: Dr Yuming Guo OR Dr Shanshan Li, School of Public Health and Preventive Medicine, Monash University, 553 St Kilda Road, Melbourne, Victoria 3004, Australia. E-mail: yuming.guo@monash.edu OR shanshan.li@monash.edu.

PERSPECTIVES

COMPETENCY IN SYSTEMS-BASED PRACTICE: A substantial portion of cardiovascular mortality can be attributed to both cold and hot environmental temperatures, although there is considerable spatial and temporal variability.

TRANSLATIONAL OUTLOOK: Prospective studies are required to investigate the collective impact of population age distribution and environmental exposure on cardiovascular mortality.

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KEY WORDS cardiovascular death, death ratio, excess death, Global Burden of Disease, nonoptimal temperatures

APPENDIX For supplemental figures and tables, please see the online version of this paper.