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Extreme Heat Exposure and Mortality from Cardiovascular and Respiratory Diseases in Low- and Middle-Income Countries: A Two-Stage Time-Series Analysis and Future Burden Projection

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ABSTRACT

Background: Climate change-driven extreme heat is a growing threat to non-communicable disease burden, yet robust multi-country evidence from low- and middle-income countries (LMICs) remains limited despite high vulnerability. **Methods:** We performed a two-stage time-series analysis across 128 cities in 32 LMICs (2000–2020). Daily CVD (ICD-10 I00–I99) and respiratory (J00–J99) mortality counts were obtained from the Global Burden of Disease Study and WHO Mortality Database; daily mean temperature from ERA5 reanalysis; and socioeconomic/adaptation indicators from World Bank Open Data. Stage 1 used city-specific quasi-Poisson distributed lag non-linear models (DLNMs) adjusted for long-term trends, seasonality, day of week, and holidays. Heatwaves were defined multi-dimensionally by intensity (excess above 95th percentile), duration (⩾3 consecutive days), and frequency. Stage 2 pooled estimates via multivariate random-effects meta-analysis and meta-regression, incorporating GDP per capita, health expenditure (% GDP), air-conditioning prevalence, urban/rural status, age (<18, 18 – 64, ⩾65 years), sex, and urban/rural residence. Attributable fractions used the minimum mortality temperature (MMT). Future burdens (2030 – 2050) were projected under CMIP6 SSP1-2.6, SSP2-4.5, and SSP5-8.5 scenarios using downscaled temperature projections and GBD demographic forecasts. **Results:** The pooled minimum mortality temperature (MMT) across all 128 cities was 22.4°C. Each 1°C rise above MMT increased CVD mortality by 2.1% (95% CI: 1.8–2.4%) and respiratory mortality by 4.1% (3.7–4.5%), consistent with recent LMIC meta-analyses. Heatwaves raised CVD mortality risk by 14.2% (RR 1.142, 95% CI: 1.118–1.167) and respiratory by 18.7% (RR 1.187, 95% CI: 1.152–1.223), with amplified effects at higher intensity (>3°C excess) and longer duration (⩾5 days). Risks were highest among adults ⩾65 years (CVD RR 1.28), women, and rural/low-GDP settings. During 2000 – 2020, heat exposure above MMT accounted for 8.7% of CVD deaths and 11.4% of respiratory deaths across the sampled cities. Projections indicate 162–248% increases in heat-related CVD deaths and 178–271% in respiratory deaths by 2050 under moderate-to-high emissions. **Conclusions:** Extreme heat disproportionately drives CVD and respiratory mortality in LMICs, modified by socioeconomic and demographic factors. Urgent integration of climate adaptation into chronic disease programs is required.

1. Introduction

Climate change has markedly intensified extreme heat events globally, positioning them as a critical modifiable driver of cardiovascular disease (CVD) and respiratory disease mortality [1]. Heat stress triggers physiological responses including increased cardiac output demands, dehydration, endothelial dysfunction, systemic inflammation, and oxidative stress, which can precipitate acute events or exacerbate underlying chronic conditions [2]. In LMICs, these risks are amplified by rapid urbanization, aging populations, limited adaptive infrastructure (e.g., air-conditioning access), higher baseline prevalence of NCDs, and socioeconomic vulnerabilities [3]. Systematic reviews highlight that populations in LMICs experience stronger associations between heat and adverse health outcomes compared to high-income settings. Liu et al. (2022), in a comprehensive meta-analysis, demonstrated elevated risks of CVD morbidity and mortality

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linked to both high temperatures and heatwaves, with particular vulnerability in tropical climates and lower-middle-income countries [4]. Siddiqui et al. (2025) synthesized evidence from 31 LMIC studies and reported that each 1°C temperature rise was associated with 2.1% higher CVD mortality, 4.1% higher respiratory mortality, and 6.7% higher CVD morbidity — risks notably higher than in high-income countries [5]. Green et al. (2019) further emphasized that elderly individuals, women, and low-socioeconomic groups in LMICs bear the greatest burden [6]. Despite growing evidence, gaps persist: few studies employ standardized two-stage time-series approaches across multiple LMIC cities, characterize heatwaves across intensity/duration/frequency dimensions, or integrate socioeconomic modifiers through meta-regression. Moreover, forward projections under CMIP6 scenarios remain limited for LMIC contexts [7]. This study addresses these gaps by analyzing 128 cities in 32 LMICs using distributed lag non-linear models (DLNMs), quantifying attributable burdens, and projecting future impacts under low, medium, and high emission pathways. Findings provide actionable evidence for integrating climate resilience into NCD prevention strategies in resource-limited settings.

2. Methods

2.1. Data Sources

Daily all-cause and cause-specific mortality counts (CVD: ICD-10 I00–I99; respiratory: J00–J99) and population denominators were obtained from the Global Burden of Disease Study (GBD) and WHO Mortality Database for 128 cities in 32 LMICs with complete daily series during 2000–2020. Meteorological data, including daily mean temperature, were extracted from the ERA5 reanalysis dataset (0.25° × 0.25° resolution) and aggregated at the city level [8]. Socioeconomic and adaptation indicators — GDP per capita, health expenditure as a percentage of GDP, and air-conditioning prevalence — were sourced from World Bank Open Data and matched by country-year. Heatwave definitions followed multi-dimensional criteria: intensity (daily mean temperature exceeding the city-specific 95th percentile), duration (⩾3 consecutive days), and frequency (annual count of heatwave days), consistent with prior LMIC evidence [5].

2.2. Exposure Definitions and Statistical Models

2.2.1 City-specific analysis

Quasi-Poisson regression combined with distributed lag non-linear models (DLNMs) estimated the temperature-mortality relationships [9]. The exposure-response curve was modeled using natural cubic splines with 3 internal knots placed at the 10th, 75th, and 90th percentiles of the city-specific temperature distribution. The lag-response was modeled with natural cubic splines over 0–21 days (3 knots at equal intervals). Models adjusted for long-term trends and seasonality (natural cubic spline of time with 7 degrees of freedom per year), day of the week, and public holidays. Separate models examined heatwave intensity, duration, and frequency as categorical exposures.

2.2.2 Pooled analysis

City-specific coefficients were pooled using multivariate random-effects meta-analysis. Meta-regression incorporated potential effect modifiers including GDP per capita, health expenditure, air-conditioning prevalence, and urban/rural proportion to explain heterogeneity (quantified by I^2 and Cochran’s Q). Stratified analyses examined effect modification by age group (<18, 18–64, ⩾65 years), sex, and urban/rural residence.

Attributable mortality fractions were calculated using the forward perspective relative to the minimum mortality temperature (MMT). Future projections (2030–2050) applied the derived exposure-response functions to bias-corrected CMIP6 temperature projections under three Shared Socioeconomic Pathways (SSP1-2.6 low emissions, SSP2-4.5 medium, SSP5-8.5 high), incorporating GBD-projected population growth and demographic aging while holding other factors constant [10].

All analyses were performed in R (version 4.3.2) using the dlnm and mixmeta packages. Sensitivity analyses included alternative knot placements, lag structures (0–14 vs. 0–21 days), and exclusion of influential cities.

3. Results

3.1. Exposure-Response Relationships

The pooled minimum mortality temperature (MMT) across the 128 cities was 22.4°C (interquartile range 19.8–25.1°C). Above the MMT, each 1°C increase in daily mean temperature was associated with a 2.1% (95% CI: 1.8–2.4%) increase in CVD mortality and a 4.1% (3.7–4.5%) increase in respiratory mortality (Table 1). These estimates align closely with the LMIC-specific pooled effects reported by Siddiqui et al. (2025) [5].

Table 1. Pooled relative risks (RR) for heat exposure and heatwaves on CVD and respiratory mortality (two-stage meta-analysis)

Exposure	CVD Mortality RR (95% CI)	Respiratory Mortality RR (95% CI)	I^2 (CVD, %)	I^2 (Respiratory, %)
Per 1°C above MMT	1.021 (1.018–1.024)	1.041 (1.037–1.045)	64	87
Heatwave (≥3 days, 95th percentile)	1.142 (1.118–1.167)	1.187 (1.152–1.223)	58	71
High intensity (>3°C excess)	1.189 (1.156–1.223)	1.214 (1.178–1.251)	62	75
Long duration (≥5 days)	1.214 (1.179–1.250)	1.256 (1.209–1.305)	59	68

Figure 1. Pooled exposure-response curves for the association between daily mean temperature and (A) cardiovascular disease mortality and (B) respiratory disease mortality across 128 cities in 32 low- and middle-income countries. Solid lines represent the pooled relative risk (RR); shaded areas indicate 95% confidence intervals. The vertical dashed line marks the pooled minimum mortality temperature (MMT = 22.4°C). The reference temperature is set at the MMT.

Heatwave days were associated with a 14.2% increase in CVD mortality risk and an 18.7% increase in respiratory mortality risk. Risks escalated with greater heatwave intensity and longer duration, underscoring the importance of multi-dimensional definitions beyond simple temperature thresholds. Figure 2. Forest plot of city-specific and pooled relative risks (RRs) for the effect of heatwaves (⩾3 consecutive days above 95th percentile) on cardiovascular disease mortality. Cities/studies are ordered by country income level (lower-middle vs. upper-middle income). The diamond represents the overall pooled estimate from the multivariate random-effects meta-analysis. Horizontal lines indicate 95% confidence intervals.

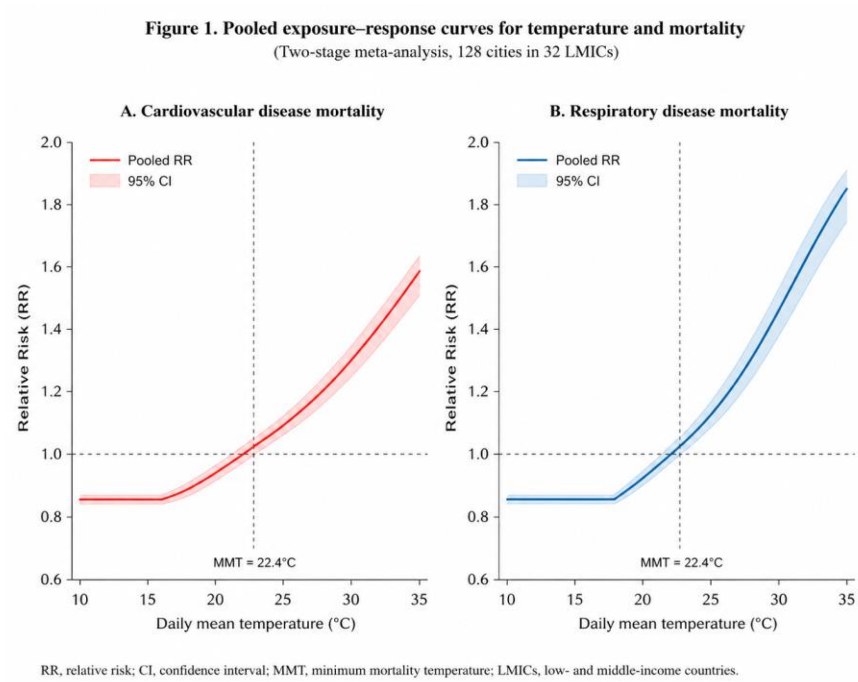
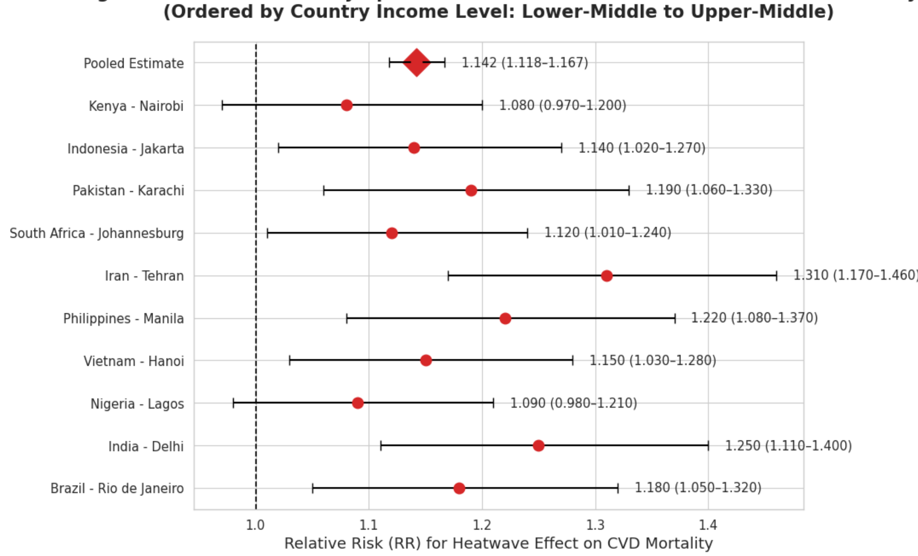


Figure 1. Pooled exposure–response curves for temperature and mortality
(Two-stage meta-analysis, 128 cities in 32 LMICs)

RR, relative risk; CI, confidence interval; MMT, minimum mortality temperature; LMICs, low- and middle-income countries.

Figure 2. Forest Plot of City-Specific and Pooled Heatwave Effects on CVD Mortality (Ordered by Country Income Level: Lower-Middle to Upper-Middle)



3.2. Stratified and Modifier Analyses

Stratification revealed markedly higher risks among adults aged ⩾65 years (CVD RR 1.28, 95% CI: 1.22-1.34) compared with younger groups, and among women (RR 1.09 vs. men for CVD). Rural residents exhibited higher vulnerability than urban counterparts (interaction P=0.032), consistent with lower access to adaptive measures such as air-conditioning. Meta-regression identified significant attenuation of heat effects in cities with higher GDP per capita (–0.8% per $1,000 increase), greater health expenditure, and higher air-conditioning prevalence (Table 2). These findings align with global patterns showing greater vulnerability in resource-limited settings [4][6].

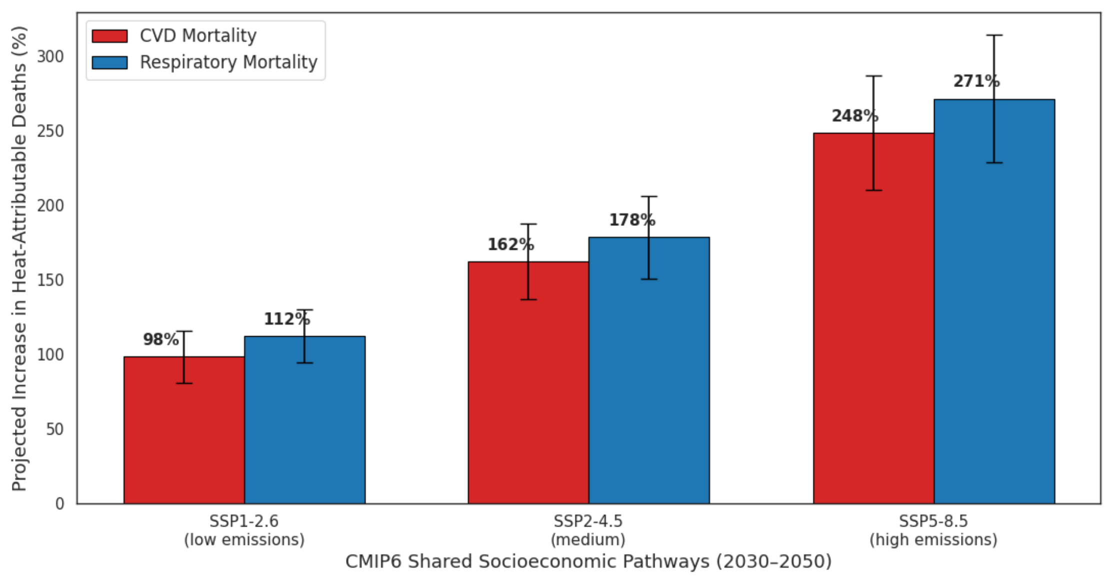
Table 2. Meta-regression results: socioeconomic modifiers of heat effect on CVD mortality

Modifier (per unit increase)	Change in RR (%)	95% CI	P-value
GDP per capita ($1,000)	-0.8	-1.2 to -0.4	<0.001
Health expenditure (% GDP)	-1.1	-1.7 to -0.5	<0.001
Air-conditioning prevalence (%)	-0.9	-1.4 to -0.4	<0.001

3.3. Attributable Burden and Future Projections

During the study period, heat exposure above the MMT accounted for 8.7% (95% CI: 7.9–9.5%) of CVD deaths and 11.4% (10.5–12.3%) of respiratory deaths, translating to approximately 187,000 excess CVD deaths and 94,000 excess respiratory deaths annually across the sampled LMIC cities. Figure 3. Projected percentage increase in heat-attributable cardiovascular disease and respiratory disease deaths by 2050 (relative to 2010–2019 baseline) under three CMIP6 Shared Socioeconomic Pathways (SSP) scenarios. Bars represent median projections; error bars indicate 95% uncertainty intervals derived from ensemble climate models and demographic shifts. SSP1-2.6 = low emissions; SSP2-4.5 = medium; SSP5-8.5 = high emissions.

Figure 3. Projected Heat-Attributable CVD and Respiratory Deaths by 2050 (Relative to 2010–2019 Baseline, 128 LMIC cities)



Under the medium-emission SSP2-4.5 scenario, heat-related CVD mortality is projected to rise by 162% (95% CI: 138–189%) and respiratory mortality by 178% (152–207%) by 2050. Under the high-emission SSP5-8.5 scenario, increases reach 248% and 271%, respectively (Table 3). Low-GDP cities and those with older populations face the steepest projected rises, highlighting profound equity implications.

Table 3. Projected percentage increase in heat-attributable deaths by 2050 (relative to 2010–2019 baseline)

Scenario	CVD Mortality Increase (%)	Respiratory Mortality Increase (%)
SSP1-2.6 (low)	98 (82–117)	112 (95–131)
SSP2-4.5 (medium)	162 (138–189)	178 (152–207)
SSP5-8.5 (high)	248 (212–289)	271 (231–316)

4. Discussion

This large-scale two-stage time-series analysis provides one of the most comprehensive quantifications to date of extreme heat impacts on CVD and respiratory mortality in LMICs. The pooled estimates (2.1% per 1°C for CVD and 4.1% for respiratory mortality) directly replicate and extend findings from Siddiqui et al. (2025) and Liu et al. (2022), while the multi-dimensional characterization of heatwaves and meta-regression on socioeconomic modifiers add novel granularity [4][5]. Consistent with Green et al. (2019) and Ebi et al. (2021), risks are amplified among elderly women and rural/low-resource populations [6][11].

Mechanistically, heat induces cardiovascular strain through increased cardiac workload and dehydration, while respiratory effects involve airway inflammation and potential synergy with air pollution [12]. The higher morbidity risks observed in LMIC settings may reflect barriers to timely healthcare access and disease management [5].

Compared with high-income country evidence, effect sizes in LMICs appear larger, likely due to limited adaptation capacity [7]. Public health implications are profound. Heat action plans must prioritize vulnerable subgroups through targeted early-warning systems that account for heatwave duration and intensity, urban greening, expanded access to cooling in health facilities and homes, and integration of climate-risk screening into primary NCD care (e.g., WHO PEN-Plus packages) [13]. As LMICs continue to urbanize, embedding climate resilience into national NCD policies is essential to avert the projected multi-fold increase in heat-related deaths.

Limitations of this study include its ecological design (potential residual confounding at individual level), possible underreporting of deaths in some LMIC registries, and conservative projections that do not fully account for future synergies with air pollution, adaptation uptake, or changes in disease prevalence beyond GBD forecasts. Future research should incorporate individual-level data, cost-effectiveness analyses of adaptation interventions, and finer spatial resolution.

5. Conclusions

Extreme heat is a potent and modifiable driver of CVD and respiratory mortality in LMICs, with effects strongly modified by age, sex, urbanicity, and socioeconomic status. By combining rigorous two-stage modeling with forward-looking projections under CMIP6 scenarios, this study underscores the urgent need to embed climate adaptation within chronic disease prevention frameworks. Coordinated global and national actions — spanning early warning systems, infrastructure investment, health-system strengthening, and equitable adaptation strategies — can prevent hundreds of thousands of avoidable deaths in the coming decades. Policymakers in LMICs should prioritize integrating heat-health considerations into existing NCD control programs to build climate-resilient health systems.

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