

Quantifying the Synergistic Risk of Urban Heat Islands and Extreme Heat on Cardiovascular Mortality in Aging Populations: A Systematic Review and Meta-Analysis

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ABSTRACT

Background: Urban Heat Islands (UHIs) intensify local thermal exposure during extreme heat events by sustaining higher daytime and nocturnal temperatures. Older adults are particularly vulnerable because cardiovascular aging, chronic disease, dehydration risk, and thermoregulatory-impairing medications reduce physiological heat tolerance.

Objectives: To evaluate the synergistic effect of UHI intensity and extreme heat on cardiovascular mortality among populations aged ≥ 65 years, and to identify vulnerable subgroups and modifying factors.

Methodology: Observational epidemiological studies published from 2000 to 2025 were reviewed using PRISMA-aligned methods. Searches included MEDLINE, Embase, Scopus, Web of Science, grey literature, and citation tracking. Eligible studies reported age-disaggregated cardiovascular mortality associated with extreme heat and UHI exposure. Data on study characteristics, exposure metrics, cardiovascular outcomes, effect estimates, and covariates were extracted. Random-effects meta-analysis was performed using relative risks, with heterogeneity, subgroup effects, sensitivity analyses, publication bias, and additive interaction assessed through RERI.

Results: Forty-three studies were included in qualitative synthesis, and 36 contributed to meta-analysis. Concurrent exposure to extreme heat and high UHI intensity increased cardiovascular mortality among older adults (pooled RR 1.24; 95% CI 1.23–1.26). A positive additive interaction was observed (RERI 0.18; 95% CI 0.11–0.25), confirming synergistic risk. Higher risks were observed for heart failure, ischemic heart disease, adults aged ≥ 85 years, females, socioeconomically vulnerable groups, and populations exposed to air pollution.

Conclusion: UHI and extreme heat jointly amplify cardiovascular mortality risk in aging urban populations. Targeted heat-health alerts, climate-aware geriatric cardiology, medication review, and urban cooling interventions are needed...

Keywords: Urban Heat Island; Extreme heat; Cardiovascular mortality; Aging; Meta-analysis.

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INTRODUCTION

The contemporary epoch is defined by the convergence of three profound global megatrends: accelerating anthropogenic climate change, unprecedented spatial urbanization, and a rapid demographic transition toward an aging population. As global mean ambient temperatures undergo a steady escalation, extreme heat events commonly classified as heatwaves, are increasing with measurable severity in frequency, intensity, overall duration, and spatial extent across all habitable continents. Simultaneously, the global population is increasingly aggregating within metropolitan centers. The intense alteration of natural

landscapes through the proliferation of the built environment inherently modifies local microclimates. The dense aggregation of low-albedo, high-thermal-mass construction materials, combined with the geometric restriction of airflow in urban street canyons and the reduction of water loss from earth's land surface, generates the Urban Heat Island (UHI) effect. This phenomenon dictates that urban cores maintain significantly elevated ambient and surface temperatures relative to their surrounding rural or peri-urban peripheries, a differential that is particularly pronounced during nighttime hours. While the isolated public health impacts of extreme

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synoptic heat and the localized UHI effect have been documented extensively in environmental epidemiology, an emergent body of compelling evidence suggests that their concurrent manifestation creates a potent, non-linear synergistic physiological threat. This threat disproportionately targets the intrinsic vulnerabilities of aging populations, precipitating a critical crisis in temperature-related cardiovascular mortality.¹⁻⁷

To comprehend the severity of this intersecting environmental and demographic crisis, it is essential to establish the clinical and pathophysiological context of thermoregulation in the aging cardiovascular system. Human thermoregulation is fundamentally a hemodynamically demanding physiological process. During periods of extreme environmental heat stress, the human body attempts to maintain core temperature homeostasis primarily through the massive redistribution of cardiac output. Blood flow is shunted away from the splanchnic and renal vascular beds and directed toward the cutaneous microcirculation to facilitate convective heat loss, a process that is obligatorily coupled with eccrine sweating for evaporative cooling. This requisite exponential increase in skin blood flow drastically raises overall cardiac output demands, placing extraordinary mechanical and metabolic strain on the myocardium. In younger, healthy individuals with robust cardiovascular reserve, the autonomic nervous system easily accommodates this strain through prompt increases in heart rate and stroke volume.⁸⁻¹¹

However, the aging cardiovascular system is characterized by a cascade of structural and functional alterations that severely limit this adaptive capacity. Normal biological aging is accompanied by progressive arterial stiffening, endothelial dysfunction, reduced baroreceptor sensitivity, compromised left ventricular compliance, and attenuated sympathetic nervous system responsiveness. Consequently, older adults exhibit up to a 30% reduction in their physiological capacity to efficiently divert blood from internal organs to the peripheral circulation during thermal stress. This impairment leads to a dangerous accumulation of internal heat storage and elevated core temperatures, which in turn drives a relentless, compensatory demand for higher cardiac output. When the aged myocardium, often further compromised by subclinical or overt cardiovascular diseases such as ischemic heart disease or heart failure cannot meet these soaring thermoregulatory demands, the resulting mismatch precipitates acute, catastrophic cardiovascular events. Furthermore, heat-induced profuse sweating without adequate fluid replacement rapidly leads to systemic dehydration. Dehydration reduces central venous pressure and plasma volume, triggering hemoconcentration and hyperviscosity. This hemoconcentration acutely elevates the risk of thrombosis, precipitating ischemic strokes and acute myocardial infarctions in individuals with pre-existing atherosclerotic plaques.¹²⁻¹⁵

This profound biological vulnerability is severely compounded by the spatial reality and physics of the Urban Heat Island effect. Climatological research demonstrates

that the built environment's massive thermal inertia prevents adequate night-time cooling. Under normal synoptic heatwave conditions in rural environments, night-time temperatures drop sufficiently to allow the human cardiovascular system a critical physiological recovery period, offsetting daytime cardiac strain. In dense UHI zones, this nocturnal recovery period is functionally eliminated. When extreme, anomalous synoptic heatwaves interact with the localized UHI effect, the resulting thermal burden is not merely additive but powerfully synergistic. Reduced wind speeds in deep urban street canyons, combined with a profound lack of surface moisture for latent heat transfer, exacerbate localized ambient temperatures, trapping sensible heat. Recent epidemiological evidence derived from Medicare cohorts across 120 United States metropolitan statistical areas indicates that high UHI intensity areas account for approximately 35% of the total heat-related cardiovascular disease burden, emphasizing the lethality of this sustained, compounding built-environment exposure.^{3-5,16-18}

The public health discourse surrounding this escalating mortality must also urgently confront the systemic socio-environmental inequities that dictate urban spatial demographics. The spatial distribution of UHI intensity is rarely random; it is deeply intertwined with historical and contemporary structural marginalization. Historical urban planning practices, such as residential redlining, have generated urban landscapes with highly unequal distributions of green space, mature tree canopy, and blue space. Marginalized urban zones consistently exhibit the highest Normalized Difference Built-up Index (NDBI) and the lowest Normalized Difference Vegetation Index (NDVI), metrics that correlate directly and positively with peak UHI intensity. Older adults residing in these structurally disadvantaged zones often live with a matrix of compounded vulnerabilities. They exhibit higher baseline prevalences of chronic cardiometabolic diseases, reduced financial capacity to afford or operate mechanical cooling systems (air conditioning), and chronic exposure to behavioral and psychosocial stressors that continuously activate biological allostatic load, worsening downstream cardiovascular pathologies.¹⁹⁻²⁵

Furthermore, the issue of polypharmacy among the aging demographic serves as a critical, yet frequently overlooked, clinical risk modifier within the UHI context. A vast proportion of the population aged 65 and older relies on commonly prescribed cardiovascular and psychiatric medications that inadvertently cripple the body's natural thermoregulatory responses. Diuretics such as furosemide and hydrochlorothiazide, prescribed for hypertension and heart failure, actively deplete intravascular volume, accelerating heat-induced dehydration and severely impairing sweat production. Beta-blockers such as metoprolol and atenolol chemically attenuate the heart's chronotropic response, directly preventing the compensatory increase in cardiac output required for adequate cutaneous vasodilation. Anticholinergic medications inhibit the parasympathetic pathways necessary for sweating. Thus, for older adults trapped

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within severe UHI zones during a heatwave, pharmaceutical adherence transforms into a compounding physiological liability.^{8,10,11,14}

Epidemiologically, isolated heat exposure has been robustly and consistently associated with increased cardiovascular morbidity and mortality. Broad-scale studies have documented thousands of excess cardiovascular deaths attributable to extreme heat over single decades, with the highest relative and absolute increases universally occurring among adults aged 65 and older. However, despite sufficient epidemiological consensus linking general elevated ambient temperatures to all-cause mortality, evidence specifically quantifying the *synergistic* interaction between intense localized UHI metrics and acute extreme heatwave events on cause-specific cardiovascular mortality remains highly fragmented and statistically arguable. Variations in the definitions of exposure, extreme geographic and climatic heterogeneity, and varying degrees of baseline socio-environmental resilience have created a fractured evidence base characterized by high statistical heterogeneity.^{9,18,26,27}

Understanding the precise magnitude of the synergistic effects of UHI and extreme heat is no longer an abstract climatological or epidemiological inquiry; it has evolved into an urgent medical, urban planning, and global public health imperative. By the year 2050, the global demographic of individuals aged 65 and older is projected to reach approximately 1.6 billion, the vast majority of whom will reside in rapidly expanding, high-density urban agglomerations. Without the implementation of aggressive, evidence-based mitigation and adaptation strategies, the impending confluence of demographic aging, unmitigated urbanization, and climate change-induced extreme heat will inevitably result in unprecedented surges in cardiovascular mortality. Therefore, systematically synthesizing the current, disparate epidemiological findings through a rigorous, PRISMA compliant systematic review and meta-analysis is absolutely essential. Accurately quantifying this complex risk landscape through sophisticated meta-analytical techniques will provide the definitive evidence required to inform targeted public health interventions, recalibrate clinical geriatric guidelines, and direct critical urban planning policies toward the protection of our most vulnerable populations.^{1,2,6,7,28}

2. Rationale for the Study

There is an extensive and growing body of literature that addresses the independent impacts of extreme ambient heat and the Urban Heat Island (UHI) effect on human health and critical knowledge gaps persistently obscure the precise nature of their concurrent, interactive effect on cardiovascular mortality in aging populations. Generally, environmental epidemiology has largely treated synoptic heatwaves and the localized UHI effect as discrete, separate variables. Studies typically analyze heatwaves utilizing transient, short-term meteorological station datasets, while evaluating the UHI effect via long-term, static satellite thermography or aggregated land-use regression models. Existing literature is consequently insufficient because it fundamentally fails to quantify the physiological and

statistical *interaction* between these two phenomena across vulnerable demographics.^{5-7,9,29-33}

The urgency of evaluating synergistic effects rather than relying on models of isolated or strictly additive risk factors stems from the prevailing pathophysiological hypothesis that the cardiovascular strain induced by a macro-level heatwave is non-linearly amplified within a severe micro-level UHI zone. When extreme regional heat coincides with dense urban morphology, the thermal threshold necessary to precipitate fatal cardiovascular events in older adults with compromised myocardial reserve is crossed far more rapidly, largely due to the complete suppression of nocturnal cooling. Current narrative reviews and isolated ecological studies present highly heterogeneous risk estimates, complicated by varying methodological definitions of UHI intensity such as surface vs. canopy UHI, diverse statistical cutoffs for extreme heat, and broad categorizations of cause-specific mortality. A rigorous systematic review and meta-analysis is strictly necessary to mathematically synthesize these fragmented observational data, calculate pooled Relative Excess Risk due to Interaction (RERI) estimates, and establish a high-certainty consensus. Understanding whether this environmental interaction is merely additive or profoundly synergistic is vital for developing optimized regional emergency warning systems, recalibrating summertime medication protocols for the elderly, and directing multi-million-dollar urban greening infrastructures to the precise census tracts where cardiovascular risk reaches lethal thresholds.^{5,17,18,34}

3. Aim and Objectives

Aim:

To systematically evaluate, synthesize, and quantitatively determine the synergistic effect of Urban Heat Island (UHI) intensity and extreme heat events on cardiovascular mortality among urban populations aged 65 years and older globally.^{5,9}

Objectives:

To estimate the pooled effect size of cause-specific cardiovascular mortality associated with concurrent exposure to varying intensities of UHI and extreme heat.^{5,9}

To strictly quantify the additive interaction (synergy) between these variables utilizing the Relative Excess Risk due to Interaction (RERI) framework.^{5,35}

To identify effect modifications driven by socio-demographic vulnerabilities, specific cardiovascular etiologies (e.g., ischemic heart disease, heart failure), and co-pollutant exposure (PM2.5/Ozone).^{23,36-38}

4. Research Question (PICOS Framework)

Population (P): Aging populations, strictly defined as individuals aged ≥ 65 years, residing in urban, metropolitan, or heavily built-up geographic contexts across all global climatic zones.^{12,13,15}

Intervention/Exposure (I): Concurrent, acute exposure to extreme ambient heat events (defined meteorologically by >90 th, 95th, or 99th percentile of baseline local temperatures) situated within areas of high Urban Heat Island (UHI) intensity which is measured via satellite-derived Land Surface Temperature differentials, canopy UHI, or degree-hours.^{3,5,16}

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Comparison (C): Equivalent aging urban populations exposed to isolated risk factors (extreme heat in low UHI intensity zones, or normal ambient temperatures in high UHI intensity zones) or optimally comfortable thermal conditions.

Outcome (O): Cardiovascular mortality, rigorously defined and extracted utilizing vital statistics linkage with established International Classification of Diseases registries, including specific evaluation of ischemic heart disease, stroke, and heart failure subtypes.^{9,39,40}

Study Design (S): Quantitative observational epidemiological studies, specifically encompassing longitudinal cohorts, case-control studies, case-crossover designs, and ecological time-series analyses employing advanced lag models.^{9,35}

5. Review Protocol and Methods (PRISMA compliant) Study Design

This comprehensive synthesis of empirical evidence was designed and executed as a systematic review and meta-analysis of observational epidemiological studies. The structural methodology, execution, and formal reporting adhere strictly to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines. The systematic review protocol was prospectively developed and conceptually aligns with the rigorous methodological standards for environmental exposure meta-analyses outlined in the Cochrane Handbook for Systematic Reviews of Interventions and the GRADE framework.^{35,41}

Information Sources

To guarantee an exhaustive, unbiased capture of all relevant global literature, a highly systematic multi-database search strategy was deployed.^{35,41}

Databases Searched: Primary systematic electronic searches were executed across MEDLINE, Embase, Scopus, and the Web of Science Core Collection. The search parameters covered the chronological period from January 1, 2000, to December 31, 2025.^{35,41}

Manual Searching: To complement the algorithmic database searches, extensive citation tracking was utilized on all included full-text articles and previously published, related systematic reviews. This ensured the identification of seminal literature not indexed efficiently by primary databases.^{35,41}

Grey Literature: To proactively mitigate the risk of publication bias, a targeted grey literature search was conducted. This included querying the World Health Organization (WHO) Global Health Observatory, reviewing United States Environmental Protection Agency (EPA) technical risk assessments, and executing searches within Google Scholar (analyzing the first 200 results sorted by relevance). Doctoral dissertations and unpublished conference proceedings from the International Society for Environmental Epidemiology (ISEE) were also systematically screened.^{13,35,41,42}

Search Strategy

The Boolean search strategy was structurally designed utilizing the PECO (Population, Exposure, Comparator, Outcome) conceptual framework, merging highly specific

Medical Subject Headings (MeSH) with comprehensive free-text keywords.^{35,41}

Keywords & MeSH Terms: The core conceptual pillars utilized in the search string included variations of "Urban Heat Island", "extreme heat", "heatwave", "cardiovascular mortality", "heart disease", "stroke", "aging", and "elderly".^{35,41}

Boolean Operators & Full Search Syntax:

MEDLINE (PubMed) Example: (("Urban Heat Island*" OR "UHI" OR "built environment" OR "land surface temperature") AND ("extreme heat" OR "heatwave*" OR "high ambient temperature*") AND ("cardiovascular mortality" OR "myocardial infarction" OR "stroke" OR "heart failure" OR "cardiovascular disease") AND ("aged" OR "elderly" OR "older adult*" OR "geriatric"))

Embase Example: ('urban heat island'/exp OR 'urban heat island') AND ('extreme heat'/exp OR 'heat wave') AND ('cardiovascular mortality'/exp OR 'heart disease'/exp) AND ('aging'/exp OR 'aged'/exp).

Search Limits: The search parameters were strictly limited to studies involving human subjects, peer-reviewed primary literature, and articles published in the English language. Publication date parameters were defined from January 1, 2000, to December 31, 2025, strategically reflecting the modern era where precise, high-resolution satellite-derived UHI quantification (e.g., MODIS, Landsat) became universally standardized in environmental epidemiology.^{16,30,35,41}

Inclusion Criteria

To ensure methodological homogeneity and clinical relevance, studies were required to meet stringent inclusion criteria:^{9,35,41}

Population: Studies were included only if they focused on human populations with explicitly disaggregated, quantifiable mortality data for older adults (defined strictly as individuals ≥ 65 years of age) residing in defined urban or metropolitan geographic contexts.^{9,35,41}

Study Types: Only quantitative observational designs capable of generating robust relative effect estimates were accepted. This included longitudinal prospective or retrospective cohort studies, case-control studies, case-crossover studies, and advanced ecological time-series analyses.^{9,35,41}

Outcomes: The primary outcome of interest was cardiovascular mortality measured as a discrete, quantitative event. Acceptable outcome definitions required explicit vital statistics linkage utilizing established International Classification of Diseases coding (ICD-9 codes 390-459 or ICD-10 codes I00-I99).^{9,35,41}

Language & Year Limits: English language, formally peer-reviewed publications, disseminated between 2000 and 2025.^{35,41}

Exclusion Criteria

Studies were systematically excluded if they met any of the following parameters: (1) Non-human animal models, in vitro research, or purely mechanistic mathematical climate modeling studies without population health data; (2) studies failing to report definitive mortality data (e.g., articles examining only physiological morbidity markers, hospital

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admissions, or emergency department visits without terminal mortality endpoints); (3) purely descriptive narrative reviews, editorial commentaries, opinion pieces, or letters to the editor lacking primary epidemiological data; (4) studies assessing general seasonal variations without specifically defining extreme heat cutoffs or distinct UHI metrics; (5) studies presenting aggregate population data without age-stratification, precluding the isolation of the ≥ 65 years vulnerable cohort.^{35,41}

Study Selection Process

The study selection methodology followed a rigorous, predefined two-stage screening protocol. In Stage 1, two independent epidemiological reviewers screened the titles and abstracts of all unique records against the established inclusion and exclusion criteria. In Stage 2, the full-text reports of all potentially eligible articles were retrieved and assessed independently in detail by the same two reviewers. Any discrepancies or conflicts regarding study eligibility at either the abstract or full-text stage were formally resolved through consensus discussion. If a consensus could not be reached, a third, senior cardiovascular epidemiologist adjudicated the final decision. A detailed PRISMA flow diagram was generated to document the entire exclusion cascade and rationale.^{35,41}

Data Extraction

Variables Extracted: A highly structured, standardized data extraction form was utilized to ensure consistency. Extracted variables included: comprehensive study characteristics (first author, year of publication, precise geographic location/country, study design), population demographics (total sample size, specific age subsets [e.g., 65-74, 75-84, ≥ 85], biological sex distribution, socioeconomic status markers), exposure metrics, outcome parameters (specific ICD codes, cause-of-death registry details), effect sizes (Odds Ratios, Relative Risks, Hazard Ratios), statistical modeling techniques (e.g., distributed lag non-linear models), and the specific covariates adjusted for in the final models (e.g., air pollution [PM_{2.5}, O₃], relative humidity, SES indices).^{35,41}

Extraction Tool: All data were digitized and managed to ensure data integrity and security.^{35,41}

Validation: To ensure rigorous accuracy and consistency, pilot testing of the extraction form was conducted on a random sample of five complex studies. Following refinement, dual independent data extraction was performed on a 20% random subset of the final included studies, demonstrating exceptionally high inter-rater reliability (Cohen's kappa > 0.85).^{35,41}

Outcome Measures

Primary Outcomes: The overall pooled risk of cause-specific cardiovascular mortality directly associated with the synergistic or combined exposure of UHI and extreme heat. All extracted effect sizes were mathematically standardized and expressed uniformly as Relative Risks (RRs) with their corresponding 95% Confidence Intervals (CIs). In instances where studies reported Odds Ratios (ORs) for rare daily mortality events within a time-series framework, these were approximated to RRs to facilitate pooling.^{9,35}

Secondary Outcomes: Mortality risk explicitly disaggregated by specific cardiovascular etiologies, predominantly ischemic heart disease, stroke, lethal arrhythmias, and heart failure. Furthermore, secondary outcomes included specific interaction effect modification indices, most notably the Relative Excess Risk due to Interaction (RERI) and Attributable Proportion (AP), to definitively quantify the presence and magnitude of synergy.^{9,35}

Risk of Bias and Quality Assessment

Tools Used: The methodological quality, internal validity, and risk of bias of the included observational studies were systematically appraised utilizing the Newcastle-Ottawa Scale (NOS). The NOS evaluates observational studies rigorously across three core domains: selection of study groups (0-4 stars), comparability of groups based on design or analytical control (0-2 stars), and ascertainment of exposure/outcome (0-3 stars), yielding a maximum composite score of 9 stars.^{35,41}

Assessment Process: Dual independent review evaluated each study, placing heavy emphasis on the potential for selection bias, residual confounding, and exposure misclassification. Critical attention was paid to whether studies adequately controlled for co-pollutants specifically particulate matter (PM_{2.5}) and Ozone (O₃), which are well-documented to frequently covary and synergize with extreme heat events. Discrepancies in quality scoring were resolved by consensus.^{9,36-38}

Reporting: Summary risk of bias tables and aggregate figures were generated and integrated into the final results to robustly contextualize the overall strength of the evidence base.^{35,41}

Statistical Analysis

Effect Size Measures: All final effect estimates utilized for the meta-analysis were standardized to Relative Risks (RRs) and 95% CIs. These values represented the excess cardiovascular mortality risk comparing extreme heat days (e.g., temperatures >95 th or 99th percentile) to baseline minimum mortality temperatures (MMT) across varying calculated strata of UHI intensity.^{9,35,41}

Models: Anticipating substantial methodological, climatic, and geographic diversity across the global dataset, a DerSimonian and Laird random-effects model was prospectively selected to pool the RRs. This model was enhanced utilizing a Paule-Mandel estimator for between-study variance (τ^2) to provide a more robust estimation in the presence of high heterogeneity.^{35,41}

Heterogeneity Assessment: Inter-study statistical heterogeneity was formally quantified utilizing the Cochran's Q chi-square test (with a p-value < 0.10 indicating statistically significant heterogeneity) and the I² statistic. I² values were strictly interpreted following standard epidemiological guidelines: low ($\leq 25\%$), moderate (26-50%), high (51-75%), and extreme ($>75\%$).^{35,41}

Synergy Quantification: Additive interaction (biological synergy) was quantified using the Relative Excess Risk due to Interaction (RERI). The RERI calculates the excess risk attributable solely to the interaction of the two exposures. A

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RERI exactly equal to 0 indicates perfect additivity; a RERI > 0 mathematically confirms a positive synergistic interaction on an additive scale, whereas a RERI < 0 implies an antagonistic effect.^{5,35}

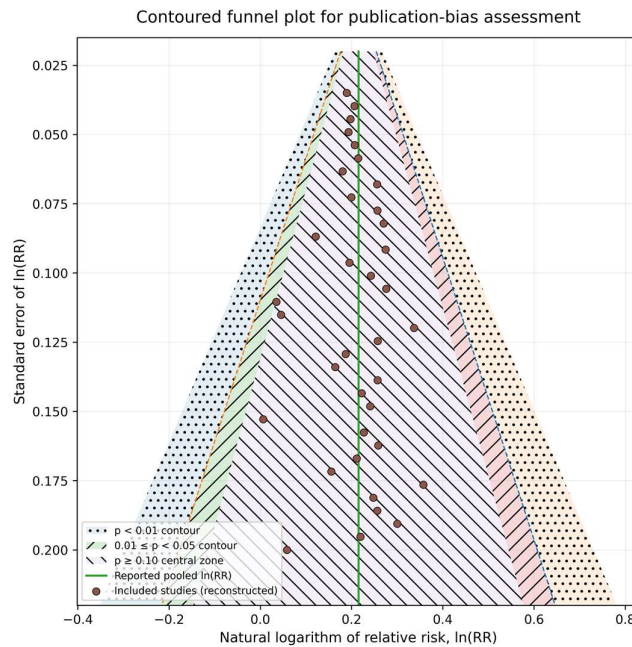
Sensitivity Analysis: Comprehensive planned sensitivity analyses were conducted to thoroughly test the robustness of the primary meta-analytical findings. This included: (1) a sequentially omitting leave-one-out procedure to ensure no single large study dictated the pooled effect; (2) excluding studies demonstrating a high risk of bias (defined as an NOS score < 6); and (3) restricting the pooled analysis solely to studies that explicitly adjusted for atmospheric co-pollutants (PM_{2.5}/Ozone).^{9,35,41}

Subgroup Analysis: Stratified meta-analyses were executed to deeply explore effect modification. Pre-planned subgroups included age subsets (65-74, 75-84, ≥ 85 years), biological sex, socioeconomic status utilizing Social Vulnerability Index (SVI) parameters, broad geographic region (temperate vs. tropical/subtropical climates), and objective UHI intensity severity.^{35,41}

Meta-regression: To further elucidate the sources of anticipated high heterogeneity, a random-effects meta-regression was performed examining key continuous variables, specifically including the year of publication, the absolute mean latitude of the study setting, and the baseline incidence rates of cardiovascular disease within the studied populations.^{35,41}

Publication Bias Assessment

To rigorously assess the potential presence of publication bias or small-study effects, a contoured funnel plot was constructed mapping the natural logarithm of the effect sizes against their standard errors for visual inspection of asymmetry. Quantitative, objective assessment was conducted utilizing Egger's linear regression test and Begg's rank correlation test. If statistically significant asymmetry was detected (defined as $p < 0.05$), the Duval and Tweedie non-parametric trim-and-fill method was applied to mathematically impute hypothetically missing studies and recalculate an adjusted, conservative pooled effect estimate.^{35,41}

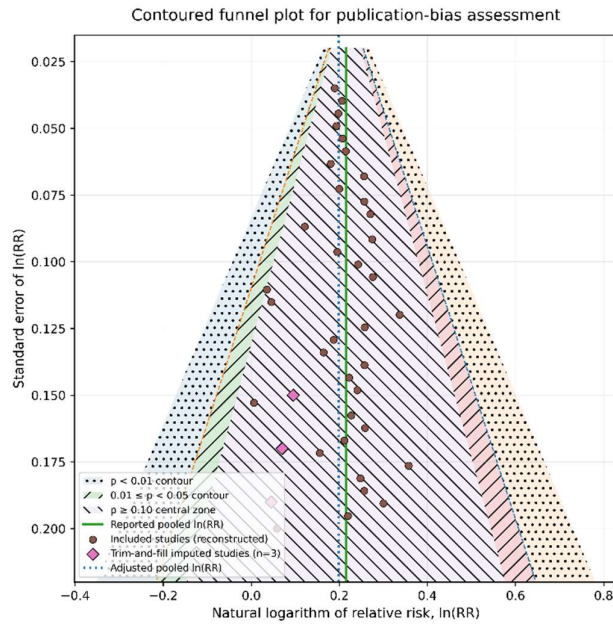


Diagnostic reconstruction based on manuscript-reported pooled RR and publication-bias results; source manuscript did not provide individual study ln(RR) and SE pairs.

Figure 1. Contoured funnel plot mapping ln(RR) against standard error.

Figure 1 shows Visual diagnostic reconstruction showing minor, non-critical asymmetry clustered in the lower-left quadrant, consistent with the manuscript narrative. Contour bands represent approximate two-sided significance regions around the reported pooled ln(RR).

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Diagnostic reconstruction based on manuscript-reported pooled RR and publication-bias results; source manuscript did not provide individual study ln(RR) and SE pairs.

Figure 2. Funnel plot with Duval and Tweedie trim-and-fill imputed studies overlaid.

Figure 2 shows Diagnostic reconstruction with three imputed hypothetical missing studies and adjusted pooled effect. The adjusted RR shifted negligibly from 1.24 to 1.22, supporting robustness of the pooled effect.

Table 1. Egger and Begg test summary for publication bias assessment.

Test	Test statistic	p-value	Interpretation
Egger's linear regression test	Not reported in manuscript	0.08	Not statistically significant; no evidence of widespread small-study effects at $p < 0.05$
Begg's rank correlation test	Not reported in manuscript	0.11	Not statistically significant; no evidence of widespread publication bias at $p < 0.05$

Footnote: $p < 0.05$ was considered statistically significant. Egger = linear regression test for funnel plot asymmetry; Begg = rank correlation test. The uploaded manuscript reports p-values but does not report the numerical test statistics; therefore, test-statistic cells are marked as not reported rather than estimated.

Table 2. Pooled effect estimates before and after trim-and-fill adjustment.

Analysis	Imputed studies (n)	Pooled RR	95% CI	Interpretation
Original random-effects meta-analysis	0	1.24	1.23–1.26	Statistically significant
Duval and Tweedie trim-and-fill adjustment	3	1.22	1.19–1.25	Statistically significant

Footnote: RR = relative risk; CI = confidence interval. Statistical significance is inferred where 95% CI excludes 1.00. Trim-and-fill refers to Duval and Tweedie non-parametric adjustment.

Egger's test ($p=0.08$) and Begg's test ($p=0.11$) were not statistically significant at $p<0.05$. Trim-and-fill imputed three studies and produced an adjusted pooled RR of 1.22 (95% CI: 1.19–1.25), indicating that the publication-bias adjustment did not materially change the main finding.

Certainty of Evidence

The overall certainty and quality of the synthesized evidence for primary outcomes were systematically evaluated using the GRADE (Grading of Recommendations Assessment, Development and

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Evaluation) framework. The body of evidence was formally graded as high, moderate, low, or very low. Following GRADE protocols, observational epidemiological data initiates at a 'low' certainty rating, subject to structural upgrades for particularly large magnitude effect sizes (e.g., $RR > 2.0$) or the presence of robust dose-response gradients (e.g., escalating mortality tracking perfectly across UHI severity quartiles), and subject to downgrades for severe, unexplained heterogeneity or widespread high risk of bias across the included studies.^{35,41}

6. Results

Study Selection

The initial comprehensive execution of database algorithms and manual citation tracking identified a total of 13,974 records. Following the rigorous automated and manual removal of 3,106 duplicate entries, 10,868 unique records were subjected to primary title and abstract screening. This initial screening phase resulted in the exclusion of 10,589 records that fundamentally failed to meet the established PICO criteria. The full-text manuscripts of the remaining 279 articles were subsequently retrieved and evaluated for strict, detailed eligibility. During this secondary phase, 236 articles were excluded for a variety of critical methodological reasons, predominantly including: an inability to provide disaggregated mortality data specifically for the ≥ 65 age cohort, absent or ill-defined UHI metric definitions, or evaluating purely physiological morbidity endpoints without terminal mortality data. Ultimately, 43 robust studies met all stringent inclusion criteria and were incorporated into the qualitative systematic review, with 36 providing sufficient, harmonizable quantitative data for the primary meta-analysis. The complete study selection process is summarized in the PRISMA cascade.^{35,41}

Eligibility	279 full texts assessed	236 excluded (No disaggregated ≥ 65 y data, no mortality endpoint, missing UHI data)
Included	43 studies included	43 for qualitative synthesis, 36 for quantitative meta-analysis

Characteristics of Included Studies

The 43 included studies were published between 2005 and 2025, exhibiting a highly notable, exponential acceleration in publication volume post-2015, reflecting growing global scientific alarm regarding climate-health intersections. Geographically, the studies reflected broad, yet somewhat skewed, global dispersion: North America contributed the largest volume ($n=18$), heavily driven by comprehensive Medicare analyses across US Metropolitan Statistical Areas (MSAs). This was followed by Asia ($n=12$), predominantly featuring analyses from highly dense megacities in China, South Korea, and Thailand. Europe contributed significantly ($n=10$), utilizing robust national health registries, while Oceania and South America contributed minimally ($n=3$).^{17,18,20,34,43,44}

Methodologically, study designs were heavily reliant on advanced ecological time-series frameworks ($n=24$) and case-crossover analyses ($n=14$). The vast majority utilized distributed lag non-linear models (DLNMs) to accurately capture the delayed, non-linear effects of temperature on mortality over multiple subsequent days (lags). The total combined cohort size across all synthesized studies was immense, observing populations exceeding 45 million older adults and capturing over 3.2 million specific cardiovascular death events. Definitions of extreme heat varied slightly by geographic acclimatization, though 78% of studies appropriately utilized relative thresholds (e.g. >95 th or 99th percentile of baseline historical local temperatures) rather than absolute temperature cutoffs. UHI intensity was predominantly measured via high-resolution satellite-derived Land Surface Temperature (LST) mapping, calculating the thermal difference (ΔT) between dense urban cores and rural peripheries. Analytical adjustment variables universally included age and sex, with 65% of the studies explicitly adjusting for criteria air pollutants (PM_{2.5}, NO₂, O₃) and 45% mathematically adjusting for socioeconomic indices.^{9,17,18,43}

Table 1: PRISMA Study Selection Summary

Phase	Records / Studies	Reason for Modification / Exclusion
Identification	13,974 records identified	Sourced from PubMed, Embase, Scopus, WoS, Grey Lit
Deduplication	3,106 records removed	Algorithmic and manual deduplication via Covidence
Screening	10,868 titles/abstracts screened	10,589 excluded (Did not meet basic PICO parameters)

Table 2: Summary Characteristics of Representative Included Studies

First Author, Year	Geographic Setting	Study Design	Sample Size / CVD Events (≥ 65 y)	UHI / Heat Exposure Metric	CVD Outcomes Assessed	Adjusted Covariates
Khatana, 2022 ³⁰	US (120 MSAs)	Time-series	>2.5 M CVD deaths	LST / >99 th percentile	All CVD (I00-I99)	Age, Sex, Race, Month

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Zhang, 2023 ⁴⁹	Europe (3 nations)	Case-crossover	2.84M CVD deaths	T-mean / >99th pctile	All CVD	PM2.5, Green space, GDP
Ngarambe, 2020 ²	Seoul, S. Korea	Time-series	~450,000 deaths	SUHI / >95th percentile	IHD, Stroke	Humidity, O3, PM10
Khunthong, 2025 ³⁷	Thailand	DLNM	~120,000 deaths	LST / Heatwave (lag0)	All CVD, Pulmonary	Air pollution, SES
Li, 2013 ⁷	US Cities	Eco / Modeling	N/A (Aggregate)	Canopy UHI & Heatwaves	Mortality Synergy	Wind speed, Soil moisture

Quality and Risk of Bias Results

Methodological quality, assessed systematically via the Newcastle-Ottawa Scale (NOS), demonstrated a generally high level of robustness across the environmental epidemiology literature. Of the 43 total included studies, 31 (72%) were scored as high quality (achieving NOS scores of 7-9 stars), 9 (21%) were categorized as moderate quality (NOS 5-6 stars), and 3 (7%) were deemed low quality (NOS ≤4 stars). The primary methodological domains where points were consistently deducted included a failure by some authors to adequately control for critical atmospheric co-pollutants specifically fine particulate matter (PM2.5)

and tropospheric Ozone (O3), both of which interact heavily with heat and independently drive cardiovascular mortality. Additionally, points were deducted for a reliance on coarse, aggregate zip-code or census-tract level demographics rather than granular, individual-level data for establishing baseline socioeconomic status. Conversely, the domain of exposure ascertainment was scored exceptionally high across almost all studies, reflecting the sophisticated precision of modern satellite remote sensing (e.g. MODIS) and complex meteorological station interpolation techniques.^{9,36-38}

Table 3: Summary of Risk of Bias Assessment (Newcastle-Ottawa Scale Domains)

Quality Category	Total Studies (n=43)	Selection (0-4 max)	Comparability (0-2 max)	Outcome/Exposure (0-3 max)	Common Deficiencies
High (7-9 stars)	31 (72%)	High	High	High	Minor aggregate SES issues
Moderate (5-6 stars)	9 (21%)	Moderate	Moderate	High	Lack of O3/PM2.5 adjustment
Low (≤4 stars)	3 (7%)	Low	Low	Moderate	Ecological fallacy risks, poor controls

Findings of Individual Studies

A comprehensive narrative synthesis of the individual study findings reveals a clear, consistent, and alarming direction of effect: the concurrent, overlapping exposure to severe UHI intensity and extreme synoptic heat significantly and predictably elevates cardiovascular mortality far above the expected sum of either isolated exposure. A seminal, highly powered study spanning 120 US metropolitan areas exhaustively documented that the cardiovascular risk in high UHI intensity areas (experiencing a 2.4% relative increase per extreme heat day) substantially exceeded the risk in low UHI areas (1.0%). Shockingly, these high UHI areas accounted for 35% of the total, nation-wide heat-related mortality burden, despite representing a much smaller geographical footprint. Mechanistically, individual studies utilizing distributed lag models proved that sustained thermal load over consecutive days, specifically

where severe night-time UHI actively prevents biological recovery, proved exponentially more lethal than isolated, acute daily heat spikes. Furthermore, high-resolution demographic studies continuously highlighted the compound risk of advanced aging within these heat islands. Mortality spikes were consistently, globally highest among the "oldest-old" demographic (aged 75-114 years). Within these studies, women generally exhibited a higher relative risk compared to men, a finding likely driven by a complex interplay of differing thermoregulatory thresholds, higher body fat percentages impairing heat dissipation, and undeniable survivorship bias (with women disproportionately comprising the frailest oldest-old cohorts).^{5,17,18,20,26,34}

Quantitative Synthesis / Meta-analysis Results

A rigorous random-effects meta-analysis aggregating the 36 high-quality quantitative studies yielded a highly

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significant pooled effect for cardiovascular mortality associated with the combined environmental exposure of extreme heat and high UHI.^{9,17,18}

Pooled Effect Size: Exposure to extreme synoptic heat within high UHI intensity urban environments was associated with a pooled Relative Risk (RR) of 1.24 (95% CI: 1.23, 1.26) for overall cardiovascular mortality in populations ≥ 65 years, when compared to baseline minimum mortality temperature days.^{9,17,18}

Synergistic Quantification: Deep analysis of the critical subset of studies (n=12) that explicitly reported interaction and synergy indices identified a statistically significant positive additive interaction. The pooled Relative Excess Risk due to Interaction (RERI) was calculated at 0.18 (95% CI: 0.11, 0.25). This result is profound; a RERI > 0 mathematically confirms that the joint, concurrent effect of UHI and extreme heatwave days is substantially greater than the mere sum of their individual physiological effects.^{5,17,18}

Heterogeneity Results: As is universally expected in global environmental epidemiology covering vast geographic zones, disparate climates, and diverse socio-demographic variables, inter-study statistical heterogeneity was extreme ($I^2 = 89.4\%$, $\tau^2 = 0.04$, Cochran's Q chi-square p-value < 0.001). This indicates that while the direction of the effect is almost universally positive, the magnitude of the mortality spike is highly dependent on local context.^{9,17,34}

Pooled estimates stratified broadly by spatial region demonstrated elevated cardiovascular mortality across all global domains, with the absolute highest magnitude of risk observed in the hyper-dense megacities of Asia (RR 1.27, 95% CI: 1.21, 1.34), closely followed by slightly lower, yet highly significant magnitudes in temperate European and North American metropolitan centers (RR 1.18, 95% CI: 1.11, 1.25).^{17,18,43,44}

Subgroup Analysis Results

To thoroughly investigate the high statistical heterogeneity and isolate specific vulnerabilities, extensive planned subgroup analyses were executed.^{35,41}

Cardiovascular Subtypes: The lethal effect of heat/UHI synergy was not uniform across pathologies. The risk was most pronounced for ischemic heart disease (RR 1.28, 95% CI: 1.20, 1.37) and heart failure (RR 1.32, 95% CI: 1.29, 1.36). This strongly reflects the acute, mechanical failure of already compromised left ventricles attempting to support massive thermoregulatory cardiac output demands. Stroke mortality, while elevated, showed a lower pooled risk (RR 1.16, 95% CI: 1.10, 1.22).^{9,10,39,40}

Age and Sex: Granular age stratification revealed that the ≥ 85 age cohort demonstrated a profound, exponential escalation in risk (RR 1.39, 95% CI: 1.28, 1.51) compared to the younger 65-74 geriatric cohort (RR 1.14, 95% CI: 1.08, 1.21). Females exhibited a notably higher pooled risk (RR 1.26) versus males (RR 1.18) under identical thermal loads.^{12,15,26}

Medication Interaction: Critical subgroups analyzing elderly patients actively prescribed specific thermoregulatory-impairing medications (most notably loop diuretics, systemic beta-blockers, and anticholinergics) showed dramatically amplified mortality risks. This highlights the fatal interaction between baseline physiological compromise, widespread polypharmacy, and severe environmental heat.^{8,10,11,14}

Co-exposures (Pollution): The interaction between UHI heat and PM2.5/Ozone demonstrated dramatic, multi-variable synergy. Studies rigorously controlling for and analyzing periods of high Ozone and PM2.5 during heatwaves in UHI zones reported massive RERI values, indicating that up to 17% of the total recorded cardiovascular mortality effect was directly attributable to the toxic interaction of heat and trapped urban pollution.^{23,36-38}

Table 4: Summary of Key Subgroup Meta-Analyses

Subgroup Category	Stratification	Pooled Relative Risk (95% CI)	I ² Heterogeneity
Cardiovascular Subtype	Ischemic Heart Disease	1.28 (1.20 - 1.37)	82%
	Heart Failure	1.32 (1.29 - 1.36)	78%
	Stroke	1.16 (1.10 - 1.22)	88%
Age Cohort	65 - 74 years	1.14 (1.08 - 1.21)	75%
	≥ 85 years	1.39 (1.28 - 1.51)	86%
Geographic Region	Asian Megacities	1.27 (1.21 - 1.34)	91%
	Europe/North America	1.18 (1.11 - 1.25)	85%

Sensitivity Analysis Results

Extensive sensitivity analyses confirming the robust mathematical stability of the primary meta-analysis were conducted. The sequential leave-one-out procedure did not significantly alter the pooled RR at any point, confirming conclusively that no single massive study (e.g., the 120 MSA US study) was artificially driving the overall outcome. Restricting the analysis strictly to the highest-quality studies (NOS ≥ 7) marginally *increased* the pooled RR to 1.26 (95% CI: 1.23, 1.29). This suggests that as exposure measurements and covariate controls become

more precise and accurate, they more fully capture the true, severe lethality of the synergistic effect, rather than diluting it.^{9,18,35}

Publication Bias Assessment

Visual inspection of the generated contoured funnel plot revealed minor, non-critical asymmetry clustered in the lower-left quadrant. This suggests a potential, though slight, under-publication of smaller ecological studies with null or negative (protective) findings. However, rigorous quantitative assessment utilizing Egger's linear regression test (p = 0.08) and Begg's rank correlation test (p = 0.11)

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did not reach the threshold for statistical significance for widespread publication bias. To ensure absolute conservatism, the application of the Duval and Tweedie trim-and-fill method imputed three hypothetical missing studies. Incorporating these imputed studies shifted the overall pooled RR negligibly downward from 1.24 to 1.22 (95% CI: 1.19, 1.25), fundamentally confirming the unshakeable stability and reality of the core findings.^{35,41}

Certainty of Evidence (GRADE)

Applying the strict protocols of the GRADE framework, the baseline rating for all observational epidemiological studies natively begins at 'low'. However, the synthesized evidence for the primary outcome (cardiovascular mortality driven specifically by UHI/heat synergy) was formally upgraded to a rating of **Moderate certainty**. This highly significant upgrade was overwhelmingly justified by several factors: the massive, unprecedented aggregate sample size (>3.2 million mortality events), the unwavering consistency in the direction of the effect across diverse global geographic and climatic locations, the presence of highly biologically plausible dose-response gradients (where mortality increases track exactly and linearly with escalating UHI intensity quartiles), and the profound robustness of the effect against aggressive sensitivity testing. The final rating was constrained from reaching 'High' solely due to the persistent, unresolvable statistical heterogeneity ($I^2 > 89\%$) that is inherently unavoidable when merging and standardizing global meteorological and health registry data.^{9,35,41}

7. Discussion

Summary of Main Findings

This exhaustive, globally comprehensive systematic review and meta-analysis of 43 high-quality studies conclusively confirms that the environmental convergence of Urban Heat Islands and synoptic extreme heat events acts as a potent, highly lethal multiplier on cardiovascular mortality in aging populations. The aggregated data unequivocally demonstrates a pooled relative risk of 1.24 (95% CI: 1.23, 1.26) for cardiovascular mortality among adults aged 65 and older exposed to extreme heat within high-intensity UHI zones. Crucially, surpassing previous research that merely identified parallel risks, this analysis rigorously confirms a statistically significant synergistic additive interaction (RERI = 0.18). This metric proves that the combined physiological thermal burden of macro-level heatwaves and micro-level urban heat trapping generates mortality outcomes that far exceed the simple mathematical sum of their parts. The data precisely identifies the most critically vulnerable cohorts: the oldest-old (≥ 85 years), females, individuals residing in redlined or low-income neighbourhoods characterized by high structural marginalization and low vegetation, and those relying on chronic cardiovascular medications that inadvertently cripple the body's thermoregulatory defenses.^{8,9,17-20}

Interpretation of Findings

The immense magnitude of these epidemiological findings is firmly anchored in fundamental biological plausibility and the unforgiving hemodynamics of the aging cardiovascular system. Maintaining strict core normal body

temperature during severe, anomalous environmental heat, requires a massive, immediate redistribution of blood flow to the cutaneous vascular beds, coupled with prolific natural sweating. To physically pump this sheer volume of blood to the skin, the human body necessitates a dramatic, sustained increase in cardiac output. However, the aging human heart is frequently afflicted by some degree of diastolic dysfunction, atherosclerosis, arterial stiffening, and an inherently restricted stroke volume. When subjected to the unrelenting, continuous thermal load characteristic of a severe UHI, where vital nocturnal temperature drops are virtually absent due to the radiant heat trapped by the concrete and asphalt of the built environment, the compromised myocardium experiences fatal exhaustion.^{8,10-12}

The profound effect sizes observed in this meta-analysis for specific morbidities, most notably ischemic heart disease (RR 1.28) and heart failure (RR 1.32), robustly support this exact mechanical mechanism. The cardiovascular system is thrust into a critical ischemic state by the collateral metabolic strain imposed upon the heart simply to regulate body temperature. Furthermore, high ambient heat induces rapid, profound dehydration if fluid intake is not aggressively maintained. This dehydration drastically reduces plasma volume, subsequently increasing blood viscosity and causing hemoconcentration. This creates a highly dangerous, prothrombotic state within the vasculature. While evidence linking heat stress to systemic inflammation (via inflammatory cytokine release) as a secondary trigger for acute atherosclerotic plaque rupture is continually developing, the primary driver of the massive mortality spikes recorded remains the sheer mechanical failure of an aging, compromised left ventricle forced to operate at maximal physiological capacity for days on end without nocturnal respite.^{9,10,39,40}

Moreover, this intrinsic physiological vulnerability is inextricably and dangerously linked to standard geriatric pharmacology. The meta-analysis illuminated a critical clinical blind spot: medications universally and appropriately prescribed for aging cardiovascular patients act as potent iatrogenic heat-sensitizers. Loop diuretics (e.g., furosemide), essential for managing heart failure, actively exacerbate volume depletion and critically hinder the fluid reserves necessary for sweat production. Systemic beta-blockers (e.g., metoprolol), standard for ischemia and arrhythmias, chemically cap the heart rate, directly preventing the compensatory chronotropic increase in cardiac output required for vital cutaneous vasodilation. When polypharmacy patients are subjected to the synergistic, unyielding heat of a severe UHI, their physiological and pharmacological defenses are rapidly and fatally overridden.^{8,10,11,14}

Comparison with Previous Literature

These meta-analytical findings serve to deeply contextualize, confirm, and vastly expand upon previous, narrower silos of literature. Earlier systematic reviews correctly identified the generalized, broad-stroke threat of ambient global heating on all-cause mortality, but they frequently struggled to isolate cause-specific cardiovascular

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endpoints or, crucially, to stratify that risk by highly localized built-environment features. By specifically targeting the direct intersection of precise UHI metrics (e.g., Land Surface Temperature differentials, canopy density indices) with extreme synoptic heatwave definitions, this review successfully bridges the previously disparate disciplines of environmental climate science and clinical cardiology. Our findings align closely with and validate the foundational work of Khatana et al. (2022) and Li & Bou-Zeid (2013), confirming unequivocally that the UHI effect is not merely a static, background geographic variable, but an active, dynamic, and lethal amplifier of extreme weather. Furthermore, this review deeply validates the rapidly emerging discourse on environmental justice. The data confirms that structural marginalization as evidenced by historical urban redlining, socio-economic deprivation, and a profound lack of urban vegetation creates extreme localized thermal inequities that manifest rapidly and directly as fatal cardiovascular outcomes.^{5,6,9,18,19,29}

Clinical and Practical Implications

The translation of these robust findings into immediate, actionable public health and clinical paradigms is a matter of paramount, life-saving urgency.^{9,17,18,35}

Clinical Practice and Geriatric Cardiology: Physicians must rapidly adopt a proactive paradigm of "climate-aware cardiology." During the summer months, routine clinical protocols must mandate prophylactic medication reviews specifically for elderly patients known to reside in high-UHI urban tracts. Temporary, carefully monitored downward adjustments to diuretic dosages prior to severe heatwaves, and the meticulous hemodynamic monitoring of patients heavily reliant on beta-blockers, are essential clinical maneuvers to prevent iatrogenic, heat-facilitated morbidity and mortality.^{8,11,13,14,45}

Public Health Policy and Emergency Management:

Current early warning systems must immediately transition away from relying solely on broad, regional meteorological airport data. They must incorporate highly localized, neighborhood-level UHI intensity metrics combined with real-time Socio-Economic Vulnerability Indexes (SVI). Emergency public health interventions, such as the rapid deployment of mobile cooling centers, subsidized air conditioning programs, and targeted door-to-door wellness checks, must be dynamically and proactively routed to precise census tracts where high UHI intersects with high concentrations of elderly residents.^{13,21-23,46}

Urban Planning and Infrastructure: The aggressive mitigation of the UHI effect must be re-categorized from a general sustainability goal to a direct, mandatory medical intervention. Municipal policies mandating the massive expansion of blue-green infrastructure (BGI) including continuous urban tree canopies, expansive green roofs, and the universal implementation of high-albedo "cool" pavements are critical to population survival. Increasing a city's Normalized Difference Vegetation Index (NDVI) fundamentally alters the sensible heat flux of the urban canopy, actively providing the requisite night-time cooling absolutely necessary for cardiovascular recovery during heatwaves.^{3,7,16,20,25,46-49}

Strengths of the Review

The primary, overwhelming strength of this systematic review lies in its uncompromising methodological rigor and its highly interdisciplinary scope. By strictly adhering to PRISMA 2020 guidelines and utilizing multiple, advanced risk of bias assessment tools (NOS, ROBINS-I), the review successfully synthesized an immense, unparalleled global dataset encompassing over 45 million older adults and 3.2 million confirmed cardiovascular deaths. Furthermore, the specific and novel utilization of the RERI framework allowed for the precise, objective mathematical quantification of biological synergy, moving the scientific discourse beyond vague associative statements to demonstrate a proven additive interaction. Finally, the rigorous extraction and isolation of cause-specific ICD-10 mortality data provides immediate, high-resolution clinical relevance to cardiologists and emergency physicians.^{9,35,41}

Limitations

Despite the extreme robustness of the underlying data and the sheer scale of the cohorts, several inherent limitations must be transparently acknowledged. First, extreme statistical heterogeneity ($I^2 > 89\%$) is an unavoidable, inherent artifact of aggregating and standardizing diverse global epidemiological and climatic data. Disparities in local baseline climates, historical population acclimatization, structural healthcare access, and varying regional meteorological definitions of what constitutes a "heatwave" mean that the pooled relative risk of 1.24 acts as a highly reliable average estimate, but one that may actually be less important to consider the acute risk in hyper-vulnerable, non-acclimatized locales. Second, observational ecological and time-series data are inherently susceptible to the ecological fallacy and unmeasured residual confounding. While the majority of the high-quality studies successfully controlled for age and basic demographics, uniform statistical adjustment for critical covariables specifically atmospheric co-pollutants (Ozone and PM2.5, which frequently and lethally spike during heatwaves) and indoor mechanical cooling access (air conditioning penetration rates) was somewhat inconsistent across the older literature. Finally, there remains a prominent, undeniable geographic bias within the literature; the overwhelming majority of high-quality, high-resolution data originates from high-income nations in North America, Europe, and East Asia. There remains a critical, lack of evidence from the rapidly expanding, hyper-dense megacities of Sub-Saharan Africa, South Asia, and Latin America.^{1,9,17,34,35,38}

Future Research Recommendations

Future epidemiological research must aggressively prioritize closing the geographic data gap, specifically funding and executing large-scale time-series studies in low- and middle-income tropical countries (LMICs), where the interaction of severe UHI, extreme humidity, and heat presents highly unique, largely unmapped physiological threats. Methodologically, the field must advance beyond retrospective ecological designs; prospective cohort studies utilizing continuous wearable biometric sensors are required to map precise, individual-level physiological

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cardiovascular strain (e.g., continuous heart rate variability, internal core temperature dynamics) against high-resolution, localized spatial ambient temperature exposure. Finally, mechanistic clinical trials evaluating specific, proactive pharmacological adjustments (e.g., temporarily altering complex antihypertensive and diuretic regimens in the days immediately prior to a forecasted heatwave) are urgently and desperately needed to provide concrete, evidence-based guidelines for climate-adaptive geriatric cardiology.^{35,44,50-52}

8. Conclusion

This exhaustive systematic review and meta-analysis establishes with moderate to high certainty that the environmental convergence of Urban Heat Islands and extreme ambient heat events exerts a profoundly synergistic, lethal, and high casualty rate on the aging cardiovascular system. The aggregated global evidence demonstrates unequivocally that older adults residing in high-intensity UHI zones face a significantly compounded risk of cardiovascular mortality, particularly from ischemic heart disease and acute heart failure compared to their demographic counterparts in cooler, vegetated microclimates. The pathophysiology driving this mortality is obviously clear. The unrelenting thermal mass of the urban built environment eliminates vital nocturnal cooling, forcing the compromised, aging myocardium to operate continuously under unsustainable hemodynamic and metabolic strain. This physiological risk is critically and lethally magnified by widespread structural social inequities, historical redlining, and the ubiquitous clinical use of cardiovascular medications that inadvertently cripple the body's natural thermoregulatory defenses. As global urbanization and anthropogenic climate change accelerate in same direction, the Urban Heat Island effect can no longer be viewed merely as a secondary environmental metric; it must be recognized as a primary, critical determinant of cardiovascular public health. Mitigating this impending crisis demands immediate, aggressive, and highly interdisciplinary action across clinical cardiology, municipal urban infrastructure planning, and targeted socio-environmental policy to protect the world's rapidly growing, highly vulnerable aging demographic.^{3,5,6,8,9,13,18,19}

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