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Review article

A systematic review and meta-analysis of the impact of environmental heat exposure on cardiovascular diseases, chronic respiratory diseases and diabetes mellitus in low- & middle-income countries

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ABSTRACT

Climate change has led to an increase in global temperatures and adversely impacted human health, for example, by exacerbating the burden of non-communicable diseases. This systematic review and meta-analyses aim to synthesize evidence on the effect of heat exposure on the morbidity and mortality associated with cardiovascular diseases, chronic respiratory diseases and diabetes mellitus in Low-and Middle-income countries (LMICs). Five databases (Medline, Embase, Web of science, Global health and Africa wide information) were initially searched using keywords related to heat, cardiovascular, respiratory disease, diabetes and LMICs to identify relevant peer-reviewed studies, published from inception to June 2024. An updated PubMed search on 29 April 2025 was done to identify additional eligible studies. Meta-analyses were conducted to quantify the pooled effects of the association between temperature and disease-related mortality/morbidity. The searches found 3884 studies, of which 31 were included in the review. A narrative synthesis was conducted for all the studies, and 18 studies were included in the meta-analyses. We found a positive association between heat exposure and mortality/morbidity related to the three diseases.

With each 1 °C rise in temperature, cardiovascular and respiratory mortality risk increased by 2.1 % and 4.1 % respectively. The risk of cardiovascular morbidity was higher, at 6.7 %. A higher heat-related mortality and morbidity was also observed in those aged 65-years plus, and in women. These findings show populations in LMICs are vulnerable to adverse effects of heat exposure. The higher risk of morbidity outcomes is a novel finding and may indicate differential access to care and disease management.

1. Introduction

Anthropogenic climate change has led to an increase in the intensity, frequency and duration of extreme heat events (White-Newsome et al., 2012), which can be defined as "sustained periods of abnormally and uncomfortably hot and unusually humid weather"(Meehl and Tebaldi, 2004). The ongoing societal impacts of extreme heat, including the impact on human health are disproportionately felt by vulnerable populations (Rocque et al., 2021). The impact of exposure to extreme heat on human health is well-documented (Liu et al., 2022; O'Neill et al., 2009). There is strong epidemiological evidence of heat-related adverse health impacts, for example, extreme heat exposure is associated with an increased risk of mortality and morbidity in people with existing non-communicable diseases (NCDs) (Watts et al., 2021; Khosla et al., 2021).

NCDs are the most common cause of mortality globally, and constitute a large group of diseases such as cardiovascular diseases, cancers, chronic respiratory diseases and diabetes mellitus (Bennett et al., 2018). Of these NCDs, cardiovascular and chronic respiratory diseases and diabetes, have a stronger and more consistent association with heat exposure as these are the conditions that are directly impacted through thermoregulation, physiological stress and heat-related

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dehydration (Keatinge et al., 1986; White, 2006; Hajat and Kosatky, 2010). As per the World Health Organization, these three diseases are attributed to a significant health burden, for example in 2003, they led to an estimated 24 million deaths globally (Organization, 2023a). Furthermore, the global burden of disease study estimated that 545 million people were living with chronic respiratory diseases in 2017, accounting for 7.4 % of the global population (Soriano et al., 2020). A study on in-patient mortality from chronic respiratory diseases found onset was strongly related to exposures to high-temperature and was therefore highest during the summer (Achebak et al., 2023). Similarly, several studies have found that people with diabetes mellitus have an increased number of emergency admissions, hospitalizations and deaths during periods of heat waves and under hot climatic conditions compared to those without DM (Vallianou et al., 2021; Gao et al., 2022b).

The epidemiological transition in many sub-Saharan African (SSA) countries shows a 67 % increase in all-age disability-adjusted-life years (DALYs) attributable to NCDs, and whilst this transition is likely linked to a combination of environmental, lifestyle and genetic risk factors, there is growing evidence that the disease burden is Moghadamnia et al. (2018) amplified by environmental change (Gouda et al., 2019; Friel et al., 2011). The 2023 Intergovernmental Panel for Climate Change (IPCC) report predicts that continued greenhouse gas emissions will further increase global warming, breaching the target for limiting warming below 1.5 °C, which will continue to increase the number of extreme heat related health events across the world (Lee et al., 2023).

The rise in environmental temperatures affects people unequally, with those in low- and middle-income countries (LMICs) experiencing more severe impacts (Watts et al., 2018). These challenges are expected to worsen as global temperatures continue to rise and as the prevalence of cardiovascular diseases, chronic respiratory diseases, and diabetes increase among the growing populations in LMICs (Roth et al., 2020).

Existing systematic reviews indicate that exposure to extreme heat is associated with increased morbidity and mortality related to cardiovascular diseases and respiratory diseases Kazi et al. (2024), Arsad et al. (2022), Xu et al. (2016); Bunker et al. (2016) reported 3.4 % (95 % CI: 3.10, 3.78) increase in cardiovascular disease mortality and 3.6 % (95 % CI: 3.18, 4.02) increase in chronic respiratory disease mortality in the elderly with each 1 °C temperature rise (Bunker et al., 2016).

Cheng et al. (2019) analyzed studies from 20 countries and found that heatwaves significantly increase cardiovascular mortality risk estimates by 15 % RE 1.15, (95 % CI: 1.09, 1.21) and respiratory mortality by 18 % RE 1.18, (95 % CI: 1.09, 1.28) compared to normal conditions (Cheng et al., 2019; Song et al., 2021 found those with diabetes and exposed to extreme heat had a 13 % increase in mortality (RR = 1.14, 95 % CI: 1.09, 1.19) and 1 % increase on morbidity (RR = 1.01, 95 % CI: 1.004, 1.02) (Song et al., 2021).

These systematic reviews and meta-analysis primarily focus on either mortality or morbidity related to one disease group (Liu et al., 2022; Phung et al., 2016c; Moghadamnia et al., 2017; Gao et al., 2022a) or at the most two disease group (Turner et al., 2012; Cheng et al., 2019). Moreover, these are primarily focused on high-income countries with low representation of LMICs (Stafoggia et al., 2023; Guo et al., 2017; Xu et al., 2016; Vicedo-Cabrera et al., 2021; Liu et al., 2022; Bunker et al., 2016; Basu, 2009; Ye et al., 2012; Perry et al., 2023). This leaves a significant gap in understanding how heat-related impacts manifest in LMICs, where vulnerabilities to heat exposure are often greater due to socioeconomic disparities, limited healthcare resources, and rapid urbanization. Given the unique challenges faced by LMICs and the rising burden of NCDs in these regions, our systematic review and meta-analysis aims to address this dearth of evidence by synthesizing the findings of the existing literature and provide insights critical for policy-making and development of climate-resilient health systems. Moreover, this systematic review synthesizes the evidence on both mortality and morbidity associated with three of the top four NCDs, cardiovascular disease, chronic respiratory disease and Diabetes Mellitus.

2. Materials and methods

This systematic review followed the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA-2020) guidelines (Page et al., 2021). The PRISMA abstract checklist and PRISMA 2020 checklist can be found in **Supplementary-1**.

2.1. Search strategy

Searches on 5 electronic bibliographic databases (Embase, Medline, Africa wide information, Global Health & Web of Science) were conducted between 30th May to 14th June 2024. Subsequently, an updated search was conducted in PubMed on 29th April 2025 to identify articles published after the previous search date of 30 May 2024. Databases, search dates and updated search strategy are provided in the,

Table-1
Inclusion and Exclusion criteria.

	Inclusion criteria	Exclusion criteria
Population	Human population, all age groups, living in LMICs as defined by the World Bank (McGregor et al., 2014), and being diagnosed with any of the following: cardiovascular disease (hypertension, coronary artery disease, heart failure), chronic respiratory disease (asthma, chronic obstructive pulmonary disease, emphysema) and diabetes mellitus (Type 1 and 2)	Studies with morbidity/ mortality outcomes other than Cardiovascular Diseases, Chronic Respiratory Disease and Diabetes Mellitus. Studies with animal subjects or any specific high-risk population other than general populations.
Exposure	Studies that measured increased heat-exposure such as daily mean temperature, minimum and maximum daily temperature, heat indices such as apparent temperature (AT). Heat events such as heat waves, temperature exceeding defined thresholds above the normal or optimal temperature.	Studies that did not derived quantifiable exposure-response functions from the population. Studies focused on physiological responses to heat as the outcome of interest e.g. heat strain, rising of core body temperature, change in heart rate, and heat stroke. Studies focusing on occupational heat-exposure
Comparator	Studies comparing the outcomes associated with days or time periods of exposure to higher temperatures with those at normal or optimal temperatures.	Studies without a clear comparison of different levels of exposure to heat.
Outcomes	Studies measuring changes in mortality/morbidity related to the three disease groups with the increase in heat-exposure as risk estimates such as relative risk (RR), hazard ratio (HR), odds ratio (OR), percentages or attributable fraction (AF).	Studies with outcomes other than mortality or morbidity related to the three identified disease groups e.g. economic impacts or modelling studies. Studies measuring impact of heat exposure on birth outcomes/neonatal outcomes.
Settings	Studies with populations living in LMICs as defined by the World Bank (McGregor et al., 2014).	Studies conducted on populations living in countries other than LMICs.
Study Designs	Studies with quantitative data on exposure-response relationships, and clear exposure-response metrics including randomized and non-randomized controlled trials, cohort studies, cross-sectional studies, case-control studies, time-series, and case-crossover designs, published in English language in peer-reviewed journals.	Qualitative studies, grey literature, commentaries reviews, unpublished manuscripts, conference abstracts. Studies published in languages other than English.

Supplementary -2, Table-1. The key terms included in the research questions were identified as heat exposure, cardiovascular diseases, chronic respiratory diseases, diabetes mellitus and low-and-middle-income countries. Boolean operators such as 'OR' were used for the exposure and outcome terms and 'AND' functions were used to combine the exposure and outcome search results. Both Medical Subject Headings (MeSH) and 'Free-text' terms were used for the key terms mentioned above. Detailed search strategies applied to 6 databases are placed at Supplementary -2.

2.2. Eligibility criteria

The Population, Exposure, Comparator, Outcome, and Study Design-(PECOS) framework was used to formalize the inclusion criteria, selecting keywords and performing the searches (Methley et al., 2014; Page et al., 2021). The inclusion & exclusion criteria for the studies have been tabulated in Table-1 below.

The primary outcomes of this study were mortality and morbidity associated with cardiovascular diseases (CVDs), chronic respiratory diseases (CRDs), and diabetes mellitus (DM), as classified under the International Classification of Diseases, 10th Revision (ICD-10) by the World Health Organization (2004). Cardiovascular diseases included conditions under codes I00–I99, encompassing ischemic heart diseases, cerebrovascular diseases, hypertensive disorders, heart failure, and peripheral vascular diseases, among others. Chronic respiratory diseases, coded under J40–J47, comprised chronic obstructive pulmonary disease (COPD), asthma, emphysema, and other chronic respiratory conditions. Diabetes mellitus, categorized under E10–E14, included type 1 and type 2 diabetes, malnutrition-related diabetes, and other specified or unspecified diabetes types.

Out of 31 studies included in this review, 28 studies defined the disease specific outcomes based on the ICD-10 and one study employed ICD-9 for outcome definition (Hashizume et al., 2009). The remaining two studies defined outcomes based on the hospital records wherein the diagnosis was approved by a committee/physician (Giang et al., 2014; Khajavi et al., 2019).

2.3. Selection of studies

The references were exported to Rayyan online screening tool. Deduplication was done by the program and manually. Two researchers screened the titles and abstracts for full-text review. Where there were discrepancies, an independent third reviewer decided on inclusion.

2.4. Data extraction and data items

The extraction and collation of relevant data from the articles selected through the full-text review were done on MS-Excel using a tool specifically developed for this review which was adapted from the Office of Health Assessment and Translation (OHAT) handbook for Systematic Reviews (Eick et al., 2020, (OHAT), 2015 (first publication)). All relevant data was extracted, and in the case of percentile-based relative risks (RR)s, the temperature points were recorded corresponding to the percentiles evaluated. Wherever available, information on RR estimates by age, sex and lag days was also extracted. Where lag specific RRs were provided, the lag giving the highest RR was selected, as done in a previous study (Luo et al., 2019).

2.5. Synthesis method

2.5.1. Narrative synthesis

The findings of the studies have been categorized according to the three disease groups cardiovascular, chronic respiratory diseases and diabetes mellitus. Heat related morbidity and mortality within each category are separately described as well as sex and age-stratified effects are described with a special focus on the elderly population. A narrative synthesis was conducted to summarise the findings of studies that did not contribute to the meta-analyses, this provided a comprehensive summary of the evidence.

2.5.2. Statistical analysis

The studies included in this review employed various types of statistical models, for example distributed lag model (DLM), distributed lag-non-linear model (DLNM), generalized additive model (GAM), generalized linear model (GLM) and lag-stratified models. We conducted meta-analyses on studies that utilized the DLNM due to adequate number of studies (i.e. more than three references) for a specific disease outcome.

Out of the 22 Time-series studies, there were only two studies with a GAM design. We were unable to include these two studies in the meta-analyses because of the way in which the outcomes were reported. The study by (Mohammadi et al., 2021) used multiple exposure indices (e.g. humidex, mean, min, max temperature) across various percentiles and lag days, but did not report a single pooled or summary estimate for heat-related cardiovascular morbidity. This made it challenging to extract a harmonized effect measure suitable for inclusion in a quantitative meta-analysis without introducing selective reporting bias. That is why it could not be included.

The other study with GAM design, by (Seposo et al., 2017) focused on Diabetes mortality. As there were only two studies that captured diabetes mortality, a meta-analysis could not be performed.

The meta-analyses were conducted in two stages.

Stage-I

The majority of studies with DLNM design reported the RR. However, five studies reported a percentage increase in mortality/hospitalization at a higher temperature. These measures were converted to RR, using the formulae; RR = 1+(Percentage Increase/100), as adopted in earlier studies (Luo et al., 2019; Lian et al., 2015; Liu et al., 2022). Eighteen studies reported RR of mortality/hospitalization at a higher percentile of daily mean temperature (DMT) compared to a lower percentile. Assuming a log-linear relationship, it was converted into RR per 1 °C change in temperature above a defined reference temperature, specific to the study. It was calculated as the log-RR divided by the temperature range between the two percentiles (Liu et al., 2022; Ma et al., 2014). Seventeen studies presented RR with respect to different lag-days (0,1,2,3, up to 30 days). Based on the practice adopted in earlier studies, the lag with the highest RR was selected for the meta-analyses (Liu et al., 2022; Luo et al., 2019).

Stage-II

After standardizing the RRs as described in stage-I, a random-effects inverse-variance model was used to analyse the pooled-effect of RRs reported in the time-series studies with DLNM designs (DerSimonian and Laird, 1986). To assess the heterogeneity among the studies, Cochran's Q test and I^2 statistic were estimated. The I^2 statistic represents the percentage variation across the studies arising out of heterogeneity rather than chance, a value above (≥75 %) was categorized as high, whereas (26–74 %) and (≤25 %) were considered moderate and low respectively (Liu et al., 2022; Higgins and Thompson, 2003). A Random-effects model was adopted in this review as it considers variability between the studies and provides a more generalizable estimate of pooled effect size (Phung et al., 2016c). Only the overall effect measures provided in the studies were included in the meta-analyses. All the analyses were conducted using Stata-18.0 SE-Standard Edition and Microsoft Excel software.

2.6. Study risk of bias assessment of studies

A risk of bias (RoB) assessment was carried out to evaluate whether

the findings of the included studies might be affected by errors or flaws in their design, execution, or analysis, which could lead to incorrect conclusions about the effect of temperature on the outcomes.

The OHAT tool for observational studies was used and comprises of the following evaluations (i) Selection bias, (ii) Confounding bias, (iii) Performance bias, (iv) Detection/measurement/information bias, (v) Missing data/Attrition/exclusion bias, (vi) Reporting bias, and (vii) other sources of biases arising out of conflict of interest, statistical analyses, funding sources etc. (Eick et al., 2020, (OHAT), 2015 (first publication)). We adapted the tool by excluding the performance bias criteria which was not relevant for this review.

The ratings were ascribed to each study in terms of four possibilities for RoB such as 'definitely low', 'probably low', 'probably high', and 'definitely High'. The overall ratings for each study were provided based on ratings of the individual criteria by classifying them into 3 tiers. Tier-1 includes studies having 'definitely low (++) or probably low ('+') in most of the key and other sources criteria, while Tier-3 study will have definitely high ('- -') or probably high ('-') in most of the key and other sources criteria. Tier-2 is the one which does not meet criteria for 'Low' or 'High'.

2.7. Ethics approval

Ethics was waived as this is a systematic review with no primary data. The study protocol was registered with the National Institute for Health Research (NIHR)'s International prospective register of systematic reviews, PROSPERO 2024 on 07 June 2024-(PROSPERO, 2024 CRD42024553532) (Siddiqui et al., 2024). Three more databases (Web of Science, Global Health and Pubmed) were searched in addition to the three mentioned in the registered protocol.

3. Results

3.1. Study selection

The PRISMA flow diagram (Figure-1) shows that 3755 titles were generated from the initial search conducted on 5 electronic databases. Subsequently, an updated search was conducted in PubMed on 29th April 2025, to identify articles published after the previous search date of 30th May 2024. With the updated search, the total number of articles generated from the 6 databases were 3884. After removal of 273 duplicates, 3611 articles were manually screened, of which 60 (54 from Initial search and 6 from updated search) studies were identified for full text review. Of these 60 studies, 29 were included in the review intially. Additional 2 studies were included after reference search of the selected studies, hence a total of 31 studies were included in the review.

3.2. Characteristics of the included studies

The characteristics of the included studies are presented in Table-2. The 31 studies were published between 2009 and 2023, with 9 conducted in Brazil, 7 in Iran, 6 in Vietnam, 3 in Philippines, 2 in Thailand, 1 each in Kazakhstan, India, Bangladesh and South Africa as depicted in Fig. 2. Studies used data from 1994 to 2018. There were several different methodologies used, with 22 time-series analysis, 8 time-stratified case-crossover studies (Xu et al., 2019, 2020; Silveira et al., 2021, 2023; Shrikhande et al., 2023; Mohammadi et al., 2018; Zhao et al., 2019; He et al., 2020) and 1 case-time series study (Requia et al., 2023b). Amongst the 22 time-series studies, 18 employed DLNM (Requia et al., 2023a; Sharafkhani et al., 2017; Seposo et al., 2015, 2017; Dang et al., 2016, 2019; Iranpour et al., 2020; Mascarenhas et al., 2022; Shrikhande et al., 2023; Khajavi et al., 2019; Giang et al., 2014; Phung et al., 2016a; Moghadamnia et al., 2018; Bühler et al., 2022; Jacobson et al., 2021; Pudpong and Hajat, 2011; Dadbakhsh et al., 2018; Grjibovski et al., 2012), 3 employed DLM (Zhao et al., 2019; Phung et al., 2016a; Xu et al., 2020), 4 studies had GLM (Hashizume et al., 2009; Silveira et al., 2019; Phung et al., 2016a, 2017) and 2 studies had GAM (Mohammadi et al., 2021; Seposo et al., 2017).

All the studies reported exposure at the population level, using meteorological data from the weather stations present in the same or neighbouring geographies. The meteorological data included daily maximum, minimum and mean temperature in degree Celsius (°C), precipitation (mm/day), dew point temperature, vapour pressure and relative humidity (%). The studies that utilized heat indices, calculated

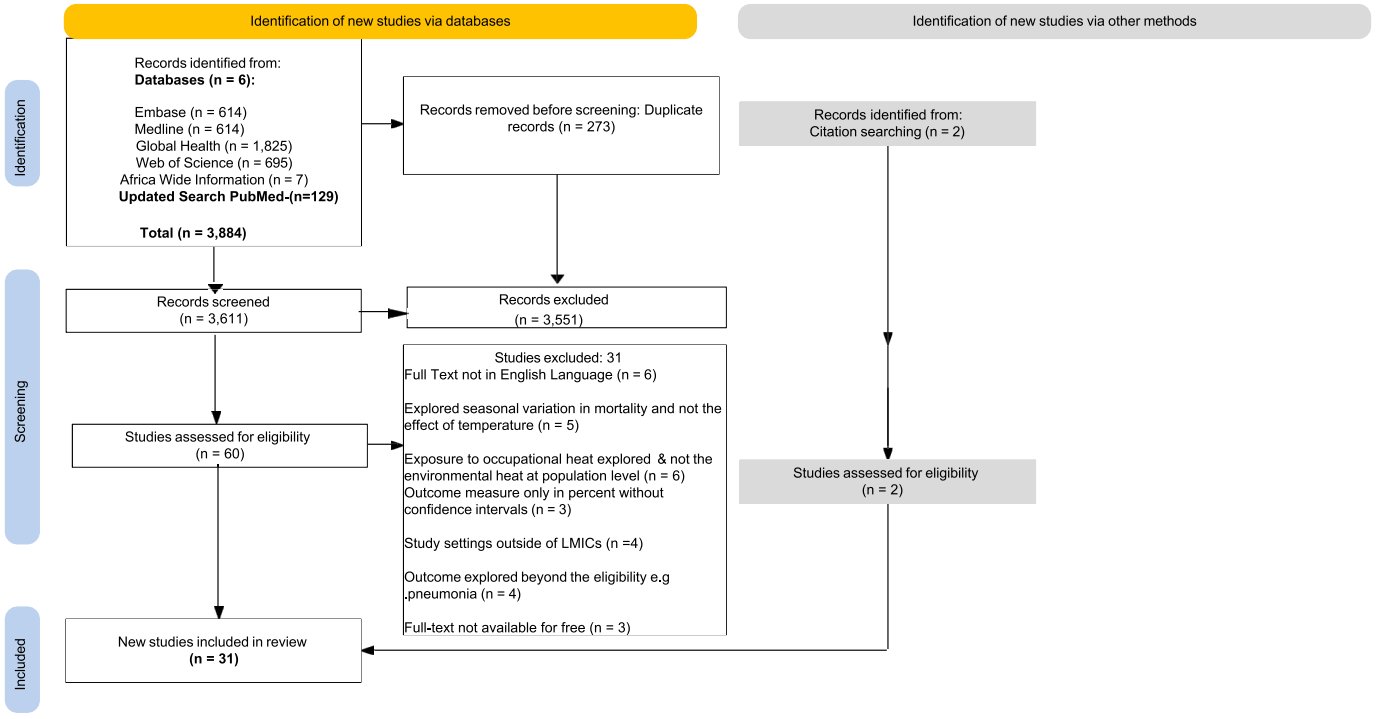

Fig. 1. Prisma Flow Diagram depicting the studies screening process.

Table 2
Study characteristics.

No. continued …	Author, Publication Year	Location	Study Period	Population Exposed	Study design & Model	Exposure	Effect Measure	Main Outcome	Result summary	Adjusted for Pollutants
1.	Xu R et al. (2020)	1814-cities (Brazil)	2000–2015	4,91,45,997	TSCC-DLM	DMT	RR of hospitalization with every 5 °C increase in DMT	CVD, CRD DM Morbidity	5 °C increases in DMT and hospitalization: CRD: RR = 1.030(1.022–1.037) P < 0.001 DM: RR not significant	Yes
2.	Pudpong and Hajat (2011)	Chiang-Mai (Thailand)	2002–2006	1,398,369 OPD visits 168,829 hospitalizations	Time-Series (TS)	DMT	% increase in hospitalization per 1 °C rise above 29 °C	CVD CRD, DM Morbidity	% increase in hospitalization per 1 °C above threshold (29 °C) for all ages CRD 2.8 % (0.6, 5.0) CVD -2.1 % (−13.3, 10.5) DM 4.2 % (−15.6, 22.9)	Yes
3.	Requia et al. (2023a)	Brazil	2003–2017	28,72,084	TS-DLNM	DMT	RRs of mortality with heat (99th P of DMT)	CRD & CVD mortality	Pooled national result: CVD mortality: 99th P: RR 1.11 (1.01; 1.21) CRD mortality: 99th P: RR 1.14 (0.99; 1.28)	Yes
4.	Sharafkhani et al., 2017	Urmia (Iran)	2005–2010	12,756	TS-DLNM	Diurnal Temperature Range Index	RRs comparing DMT 99th P and 97.5th P with DTR (14 °C)	CRD & CVD mortality	Mortality in low and high DTR values relative to DTR = 14 °C 1) CRD Mortality (RR): Hot Extreme DTR effect: 99th (22)- Lag0 RR1.20 (1.006, 1.44) 2) CVD Mortality (RR) Hot Extreme DTR effect: 99th (22)- Lag0-13 RR1.76 (1.06, 2.91)	Yes
5.	Seposo et al. (2015)	Manila (Philippines)	2006–2010	94,656	TS-DLNM	DMT	RRs mortality at 95th and 99th P of DMT with their respective MMTs.	CRD & CVD mortality	RR on heat Exposure with respect to Minimum Mortality Temperature (MMT): CVD (MMT 30 C) 99th P-RR 1.37 (1.07, 1.75) CRD (MMT 29 C): 99th P-RR 1.52 (1.23, 1.88)	No
6.	Dang et al. (2016)	Hue (Vietnam)	2009–2013	6214	TS-DLNM	DMT	RRs comparing 99th P (32.48C) to 50th P of DMT	CRD & CVD mortality	CRR comparing 99th P (32.4 °C) to 50th P (26.3 °C) at lag 0–2: CVD mortality: CRR = 1.6 (1.15, 2.22) CRD mortality CRR = 2.45 (0.91, 6.63)	No
7.	Silveira et al. (2023)	32-municipalities, (Brazil)	2000–2019	831084 deaths	TSCC	Heat Wave (HW) days	RRs for effect of heat waves on mortality at 90th, 95th & 99th P	CRD & CVD mortality	Effect of heat waves on mortality, lag 0–5 days: Risk ratio CVD 99th P-1.27 (1.13, 1.42) CRD 99th P-1.05 (0.73, 1.52)	No
8.	Iranpour et al. (2020)	Ahvaz (Iran)	2014–2018	6669	TS-DLNM	DMT	RRs comparing DMT 99th P to the 75th P	CRD & CVD mortality	Temperature Effect (99th P of DMT [41.2 °C] relative to 75th P [36.6 °C]) CVD mortality: Lag 0–3, RR 1.10 (0.92, 1.32)	Yes

(*continued on next page*)

Table 2 (*continued*)

No. continued …	Author, Publication Year	Location	Study Period	Population Exposed	Study design & Model	Exposure	Effect Measure	Main Outcome	Result summary	Adjusted for Pollutants
									CRD mortality: Lag-0, RR 0.96 (0.88, 1.04)	
9.	Dang et al. (2019)	Ho-Chi-Minh (Vietnam)	2010–2013	101,959 Deaths	TS-DLNM	Heat Wave (HW) days	RR of median of temp, distribution among heat wave days Vs MMT	CRD & CVD mortality & morbidity	CRD mortality: RR = 1.45, (1.25, 1.70) CRD morbidity: RR = 1.3 (1.19, 1.42)	No
10.	Phung et al., 2017	25 cities (Vietnam)	2002–2015	4217571 Hospitalizations	TS-GLM	Heat Index	RR comparing heatwave events (Heat Index (HI) Greater 90th) non heatwave condition (HI < 90th)	CRD & CVD morbidity	CVD admissions- 0.8 %(−1.6, 3.3) CRD admissions- 2.2 %, (−0.7, 5.2)	No
11.	Phung et al. (2016a)	Mekong-Delta (Vietnam)	2002–2014		TS-GLM & DLM	DMT	% increase in hospitalization at (lag-0) and 1 °C increase above 21 °C	CRD & CVD morbidity	% increase in risk of hospitalization with 1 °C rise above 21 °C CRD:1.1 % (0.5, 1.7) CVD: 0.2 % (0.002, 0.6)	No
12.	Requia et al. (2023b)	Brazil	2008–2018	2,37,91,093	Case-Time Series DLNM	DMT	RRs at (percentile 99th)	CRD & CVD morbidity	RR of hospitalization at 99th P of DMT: CRD: 1.29 (1.26, 1.32) CVD: 1.01 (0.99, 1.02)	Yes
13.	Mascarenhas et al., 2022	Brazil	1996–2017	531,733 deaths	TS-DLNM	DMT	Cumulative (RR) of mortality at predetermined temperature percentiles (P) relative to MMT	CVD mortality	RR for CVD mortality in 10 micro regions provided without a pooled national estimate.	No
14.	Silveira et al. (2019)	27 cities Brazil	2000–2015	NR	TS-GLM, DLNM	DMT	RRs at 99th P of DMT compared with (MMT)	CVD mortality	RR of CVD mortality (99th P vs. MMP) over lag 0–21 days: RR = 1.07 (1.01, 1.13)	No
15.	Hashizume et al. (2009)	Matlab (Bangladesh)	1994–2002	13270	TS-GLM	DMT	% increase in mortality Per 1 °C increase above the threshold	CVD mortality	% Increase in CVD mortality Per 1 °C above 30 °C: 62.9 % (23.2, 115.2)	No
16.	Silveira et al. (2021)	Rio-de-Janeiro (Brazil)	2001–2018	260874 deaths	TSCC-DLNM	DMT	RRs at 95th and 99th P compared to MMT and MMP	CVD mortality	CVD mortality: RR of CV Mortality at higher Percentile of DMT compared to MMT (26.5 °C), MMP-0.70 RR 99th P-1.34 (1.21, 1.49)	No
17.	Dadbakhsh et al. (2018)	Shiraz, (Iran)	2006–2012	17,167	TS	Tmin, Tmean, Tmax	% change in mortality Per 1 °C change in temperature using Pearson or Spearman correlation coefficient	CVD mortality	Crude and adjusted negative binomial regression analysis: Total Deaths: Temp Max: Crude IRR: 0.995(0.990–1.001); P = 144 Adjusted IRR:0.994(0.984–1.003); P = 0.236 Temp Mean: Crude IRR:0.995(0.989–1.001); P = 0.110 Adjusted IRR: 0.993 (0.983–1.003); P = 0.221	Yes
18.	Shrikhande et al., 2023	Puducherry (India)	2011–2020	3960 deaths	TSCC-DLNM	Tapp	Heat AF of CVD mortalities relative to the optimal temperature	CVD mortality	Heat AF of CVD mortality: 9.1 % (95 % CI: 0.9, 15.8 %)	No
19.	Grjibovski et al. (2012)	Astana (Kazakhstan)	2000–2001 and 2006–2010	2824171	TS	Tapp	% change in daily deaths with increase in temperature	CVD mortality	% Change in daily mortality per 1 °C increase: Cerebrovascular diseases 1.2 % (0.1, 2.4)	No

(*continued on next page*)

Table 2 (*continued*)

No. continued …	Author, Publication Year	Location	Study Period	Population Exposed	Study design & Model	Exposure	Effect Measure	Main Outcome	Result summary	Adjusted for Pollutants
									Hypertension: −2.2 % (0.03, 4.3) IHD No effect.	
20.	Khajavi et al. (2019)	Tehran (Iran)	1999–2014	9731	TS-DLNM	DMT	Relative Risks	CVD Mortality & Morbidity	Temperature had no significant effect on CVD	Yes
21.	Giang et al. (2014)	Thai-Nguyen (Vietnam)	2008–2012	18,975	TS-DLNM	Heat Index	RR of hospitalization with 1 °C increase above threshold	CVD Morbidity	RR of CVD hospitalization at 1 °C increase above 26 °C: RR = 1.17 (0.90,1.52)	No
22.	Phung et al. (2016b)	Ho-Chi-Minh (Vietnam)	2004–2013	129,014 Hospitalizations	TS-DLNM	DMT	RRs of CVD hospitalization associated with heat wave	CVD Morbidity	% increase in CVD hospitalization with HW event: 12.9 % (RR, 1.129; 95 %CI, 0.972–1.311)	No
23.	Mohammadi et al., 2018	Tehran (Iran)	2013–2016	15,835	TSCC-DLNM	DMT	RR at 95th P of DMT (33.3 °C) compared t0 75th P (28.4 °C)	CVD Morbidity	Hot effect: (*$p < 0.05$.) At Day Lags Lag 0–3 RR 1.15 (1.02, 1.30)*	Yes
24.	Moghadamnia et al. (2018)	Rasht (Iran)	2005–2014	continued …	TS-DLNM	Tapp	RR of CVD hospitalization at 99th P of Tapp (34.7 °C) compared to 75th P (26.9 °C)	CVD Morbidity	The cumulative effects of hot temperature on ACS with 99th P (34.7 °C) Vs 75th P (26.9 °C). ALL CASES: Lag0 : 1.09 (1.02, 1.19)	No
25.	Mohammadi et al. (2021)	Sabzevar city, Iran	2011–2017	5006 CVD Hospitalizations	TS-DLNM, GAM	Tmin, Tmean, Tmax, Humidex	RR for CVD hospitalization at 99th P of Mean, Min, Max, Tapp	CVD Morbidity	RR of CVD hospitalization: Tmean: RR at 99th P: Lag-0: 1.34 (1.10, 1.64) Tmax RR at 99th P: Lag-7: 1.18 (1.01, 1.37) Tmin: RR at 99th P: Lag-0: 1.34 (1.10, 1.64) Humidex: RR at 99th P: Lag-0: 1.45 (1.20, 1.74)	Yes
26.	Bühler et al., 2022	South Africa	2009–2016	3124 CVD admissions	TS-DLNM	Tapp	% increase in CVD Hospitalization above (26 °C) Heat AF of CVD hospitalization	CVD Morbidity	% increase in CVD hospitalization at 32 C compared to 26 C: 33 % (95 % CI: 0.75, 2.36) Heat AF of total CVD Hospitalization: 1.1 % (95 % CI: 1.4 %, 3.5 %)	No
27.	Zhao et al. (2019)	1642 cities (Brazi)l	2000–2015	523307	TSCC-DLM	DMT	Odds Ratio of hospitalization due to COPD for every 5 °C increase in DMT	CRD Morbidity	OR of hospitalization due to COPD for every 5 °C increase in DMT during hot seasons: 1.05 (95 % CI 1.04, 1.06)	No
28.	Jacobson et al. (2021)	27 cities (Brazil)	2000–2017	422,642 CRD deaths	TS-DLNM	DMT	RRs at local mean temperature compared to (MMT)	CRD Mortality	%Increase in risk of CVD hospitalization at 99th P compared to MMP in Elderly (60+) population: 27 % (95 % CI: 15, 39 %) (AF) of mortality (%) at 99th P Vs MMT-25.4 °C: 2.8 % (95 % CI: 1.45, 3.95 %)	No
29.	Seposo et al. (2017)	4 Cities Philippines	2006 to 2011	NR	TS-DLNM, GAM	DMT	RRs comparing DM mortality at (75th to 90th P) and (75th to 99th P)	DM Mortality	Cumulative RRs of diabetes mortality at high temperature Moderate-High (75th P Vs 90th P) Lag 0–7 1.33 (1.09, 1.62) Extreme-High (75th vis-à-vis 99th	No

(*continued on next page*)

Table 2 (*continued*)

No. continued …	Author, Publication Year	Location	Study Period	Population Exposed	Study design & Model	Exposure	Effect Measure	Main Outcome	Result summary	Adjusted for Pollutants
									P) Lag 0–7 1.62 (1.21–2.15)	
30.	Xu et al. (2019)	Brazil	2000–2015	5,53,351	TSCC	DMT	OR of diabetes hospitalization per 5 °C increase in DMT.	DM Morbidity	% increase in diabetes hospitalization with every 5 °C increase in DMT: OR = 1:06 (1.04, 1.07) Heat AF = 7.3 %(3.5, 10.9)	No
31.	Y. He et al., (2020)	Thailand	2000–2008	59,836 diabetes deaths	TSCC-DLNM	DMT	ORs of heat effects on DM mortality comparing 90th P with MMT	DM Mortality	Odds of Diabetes mortality at Pooled ORs of heat and extreme heat effects on DM mortality over different lag days Heat (90th P of DMT Vs MMT) OR lag 0: 1.10 (1.06, 1.15) Extreme heat (99th P of DMT Vs MMT) OR lag 0–1: 1.20 (1.10, 1.30)	No

CVD= Cardiovascular diseases, CRD= Chronic respiratory diseases, DM = Diabetes Mellitus, DMT = Daily mean temperature, P= Percentile, RR= Relative Risk, TS = time-series study, TSCC= Time Stratified Case-crossover, DLM = Distributed lag model, DLNM = Distributed lag non-linear model, GAM = Generalized Additive Model, GLM = Generalized linear model, DTR = Diurnal temperature range, AF= Attributable fraction, MMT = Minimum mortality temperature, MMP = Minimum mortality percentile, Tapp = Apparent Temperature.

them from the weather station data (Phung et al., 2017; Moghadamnia et al., 2018; Grjibovski et al., 2012; Mohammadi et al., 2021) and where there were missing meteorological variables they imputed it with chained equations followed by predictive mean matching (Bühler et al., 2022).

3.3. Exposure and outcome measures

There were a variety of ways in which the studies defined heat exposure. Most of the studies (N = 22) referred to daily mean temperature as the main exposure variable. While 7 studies used different heat stress indices, such as apparent temperature, diurnal temperature range index, humidex and heat index (Shrikhande et al., 2023; Grjibovski et al., 2012; Giang et al., 2014; Mohammadi et al., 2021; Moghadamnia et al., 2018; Bühler et al., 2022; Sharafkhani et al., 2017). These heat indices consider air temperature, dew point temperature, relative humidity and vapour pressure to arrive at the physiologically 'felt' exposure (Shrikhande et al., 2023). Two studies used heat wave days as a measure of exposure (Dang et al., 2019; Silveira et al., 2023).

Thirteen studies reported on cardiovascular disease mortality (Requia et al., 2023a; Sharafkhani et al., 2017; Seposo et al., 2015; Dang et al., 2016; Silveira et al., 2019, 2021, 2023; Iranpour et al., 2020; Mascarenhas et al., 2022; Hashizume et al., 2009; Dadbakhsh et al., 2018; Shrikhande et al., 2023; Grjibovski et al., 2012) and similarly another thirteen studies reported on cardiovascular disease morbidity (Xu et al., 2020; Pudpong and Hajat, 2011; Dang et al., 2019; Phung et al., 2016a, 2016b, 2017; Requia et al., 2023a; Khajavi et al., 2019; Giang et al., 2014; Mohammadi et al., 2018, 2021; Moghadamnia et al., 2018; Bühler et al., 2022). Seven studies reported mortality from chronic respiratory diseases (Requia et al., 2023a; Sharafkhani et al., 2017; Seposo et al., 2015; Dang et al., 2016; Silveira et al., 2023; Iranpour et al., 2020; Jacobson et al., 2021) and seven reported on morbidity (Xu et al., 2020; Pudpong and Hajat, 2011; Dang et al., 2019; Phung et al., 2016a, 2017; Requia et al., 2023a; Zhao et al., 2019). There were 2 studies related to diabetes mortality (Seposo et al., 2017; He et al., 2020) and 3 studies on diabetes morbidity (Pudpong and Hajat, 2011; Xu et al., 2019, 2020). There were seven studies that reported results after adjusting for air pollutants (Pudpong and Hajat, 2011; Requia et al., 2023a, 2023b; Sharafkhani et al., 2017; Iranpour et al., 2020; Dadbakhsh et al., 2018; Mohammadi et al., 2018, 2021). Age and sex stratified results were reported in all but 6 studies (Mascarenhas et al., 2022; Mohammadi et al., 2021; Bühler et al., 2022; Jacobson et al., 2021; Seposo et al., 2017; He et al., 2020).

3.4. Study findings

3.4.1. Meta-analysis and narrative synthesis

Meta-analyses of the pooled risks were conducted for the following 3 outcomes: cardiovascular mortality and morbidity and chronic respiratory diseases mortality. Other meta-analyses were not possible due to lack of studies. The section below reports the pooled estimates in more detail.

3.4.1.1. Cardiovascular diseases

3.4.1.1.1. Mortality. The meta-analysis from 6 studies on the risk of cardiovascular disease mortality, found a 2.1 % higher risk of death per 1 °C rise in temperature; RR = 1.02 (95 % CI: 1.01, 1.04), $p < 0.001$. There was moderate heterogeneity amongst the studies, $I^2 = 63.8$ %, $p = 0.017$, see Forest plot presented in Figure-3.

A total of thirteen studies reported findings related to cardiovascular disease mortality, of which seven were not included in the meta-analysis due to inability to combine outcomes. A regional variation in the reported risk was observed, for example, a time-series study from Bangladesh reported a risk of cardiovascular disease mortality per 1 °C increase above 30 °C temperature, RR = 1.63 (95 % CI:1.23, 2.15)

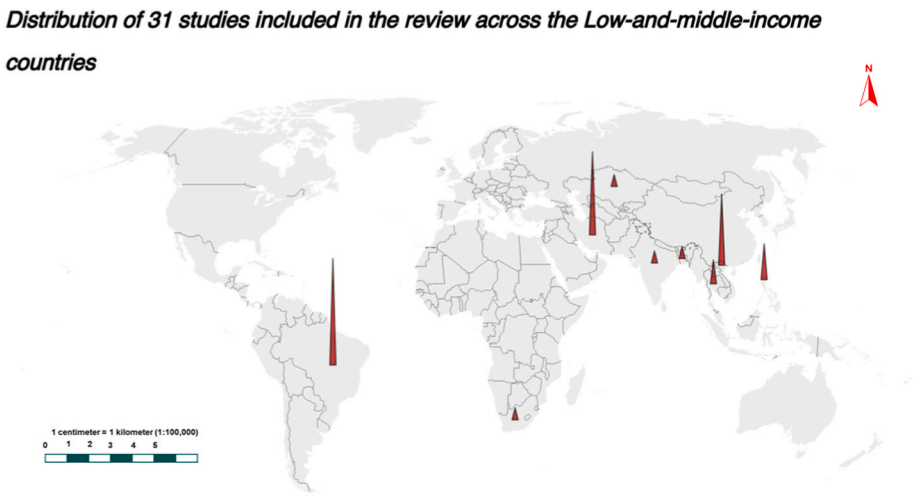

Fig. 2. Distribution of 31 studies included in the review across the Low-and-middle-income countries (Height of the bar is proportionate to the number of studies included from the respective countries) (Created on Datawrapper portal- (https://app.datawrapper.de/edit/wbEN4/publish#export-image).

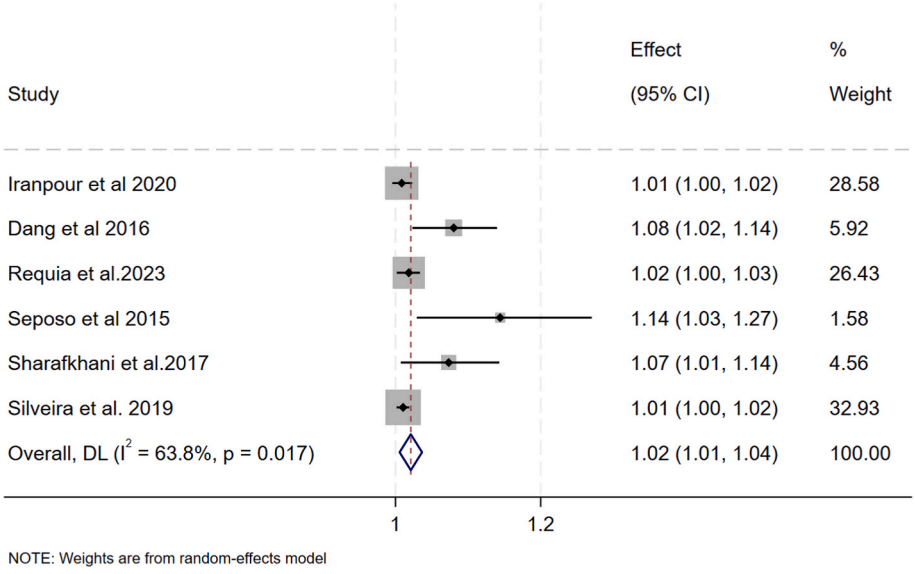

Fig. 3. Cardiovascular disease mortality estimates-meta-analysis.

(Hashizume et al., 2009), whereas a study from Manila city (Philippines) compared risk at 99th percentile (33 °C) with minimum mortality temperature (MMT) (30 °C) and reported 37 % higher risk of cardiovascular disease mortality, RR = 1.37 (95 % CI: 1.07, 1.75)(Seposo et al., 2015). A Brazilian study conducted in 32 cities of Amazonian region, assessed the impact of heatwaves (2 or more days) and found a 27 % risk of cardiovascular disease mortality at high intensity heat waves (99th percentile) compared to non-heat waves days; RR = 1.27 (95 % CI: 1.13, 1.42) (Silveira et al., 2023). A further study conducted in 27 Brazilian cities, reported a lower risk of cardiovascular disease mortality (7 %), comparing risk at 99th percentile (30.4 °C) to minimum mortality percentile (79th percentile; 27.7 °C), RR = 1.07 (95 % CI:1.01, 1.13) (Silveira et al., 2019).

The subgroup analyses of both the elderly (persons above 65 years of age), and women were both found to be at comparatively greater risk of cardiovascular disease mortality at higher temperatures. For example, a higher risk of cardiovascular disease mortality (40 %) was reported for persons above 65 years of age at 99th percentile compared to minimum mortality temperature (MMT) (26.5 °C), RR = 1.40 (95 %CI:1.24, 1.59) in a Brazilian study (Silveira et al., 2021). Women were found to be at 47 % greater risk of cardiovascular disease mortality at 99th percentile of daily mean temperature compared to MMT, RR = 1.47 (95 %CI:1.27, 1.70) in Brazil, whereas males were reported to be at 21 % risk, RR = 1.21 (95 %CI: 1.04, 1.41) (Silveira et al., 2021). Similarly,18 % higher risk was reported for women above 60 years of age in a study conducted in India, RR = 1.18 (95 % CI: 1.06, 1.29) at 95th percentile of Apparent Temperature (Shrikhande et al., 2023). A further study from Kazakhstan reported elderly women (60 years & above), were at 2 % higher risk of cardiovascular disease mortality with every 1 °C increase in Apparent Temperature (AT) compared to men in the same age group (Grjibovski et al., 2012).

3.4.1.2. Morbidity. The meta-analysis of 6 studies found a 6.7 % potential increased risk of hospitalization related to cardiovascular disease with each 1 °C rise, RR = 1.07 (95 % CI: 1.01, 1.13), $p < 0.001$. There was moderate heterogeneity amongst the studies, I2 = 57.3 %, p = 0.039 as shown in the Forest plot in Fig. 4.

A total of 13 studies reported on cardiovascular disease morbidity,

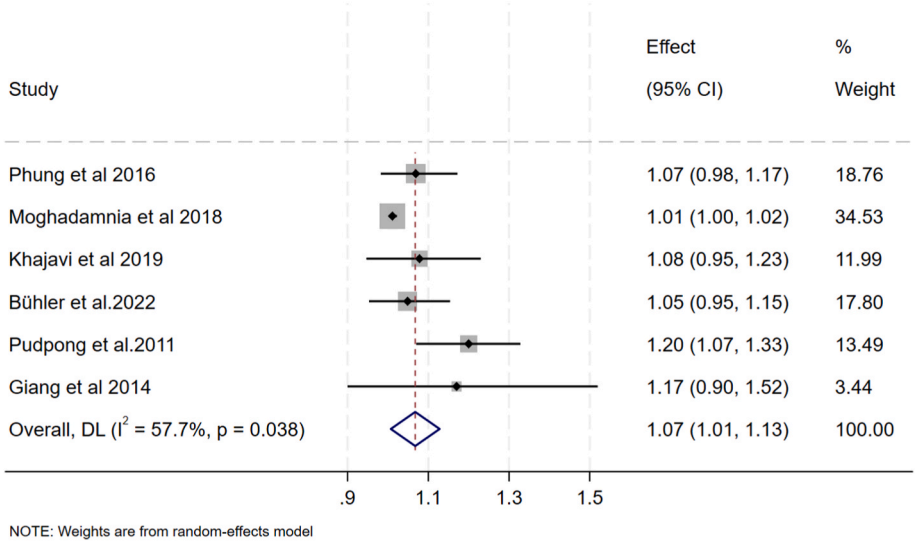

Fig. 4. Cardiovascular disease morbidity estimates-meta-analysis.

with 7 not included in the meta-analysis. One of these seven, a study from Sabzevar city, Iran, found a 34 % increased risk of hospitalization at 99th percentile (35.1 °C) of DMT compared to the median value of mean temperature (19.9 °C) RR = 1.34 (95 % CI: 1.10, 1.64) (Mohammadi et al., 2021). Whereas a time-stratified case-crossover study with DLNM design conducted in Tehran, Iran, reported a 15 % increased risk of cardiovascular disease related hospitalization at 95th percentiles of DMT (33.3 °C) compared to the 75th percentile (28.4 °C), RR = 1.15 (95 % CI:1.02, 1.30) (Mohammadi et al., 2018).

One of the Brazilian studies conducted in 1814 cities across 5 regions of the country used a time-stratified case-crossover design with DLM and found a relative risk of cardiovascular disease related hospitalization of RR = 0.989 (95 % CI: 0.982, 0.995) with every 5 °C increase in DMT (Xu et al., 2020). Another Brazilian study conducted in 5572 municipalities with a case-time series design reported RR = 1.01 (95 % CI: 0.99; 1.02) of hospitalization at 99th percentile of DMT compared to Minimum Risk Temperature (MRT) (Requia et al., 2023b). A time-series study conducted in Mekong Delta Region (MDR), Vietnam reported 0.2 % potential increased risk of cardiovascular disease related hospitalization, RR = 1.002 (95 % CI 1.00, 1.01) with each 1 °C increase in temperature above 21 °C (Phung et al., 2016a). Another time-series study conducted in 25 cities representing different ecological regions in Vietnam, reported RR = 1.008 (95 %CI: 0.984; 1.033) during heatwave (i.e. Heat Index above 90th percentile for 3 consecutive days) compared to non-heat wave days (Phung et al., 2017).

A mixed picture was observed on the risk of cardiovascular disease hospitalization related to age and sex. An Iranian study reported a higher risk (38–49 %) of cardiovascular disease hospitalization for those aged 65 years and older (RR = 1.49 (95 % CI:1.07, 2.07) compared to younger age groups (12 %–19 %), RR = 1.19 (95 % CI: 1.04, 1.37) (Mohammadi et al., 2018). Whereas, in the age stratified analysis, a nationwide Brazilian study reported the risk of cardiovascular disease hospitalization at 99th percentile of DMT, as 8 % higher in those aged 15–45 years, RR = 1.08 (95 %CI:1.04, 1.13) as opposed to 1 % risk of hospitalization for both 46–65 years and 65 years and above, RR = 1.01 (95 %CI: 1.005, 1.021), RR = 1.01 (95 %CI: 1.003, 1.024), respectively (Requia et al., 2023b). Age-stratified analyses of cardiovascular disease hospitalizations in the included studies (Pudpong and Hajat, 2011; Phung et al., 2016a, 2017) did not demonstrate clear evidence of differential effects across age groups.

In terms of sexes, there is also a mixed picture in the studies. Women were found to be at 30 % greater risk of hospitalization at 99th percentile of DMT compared to men, RR = 1.30 (95 %CI:1.26, 1.35) in a Brazilian study (Requia et al., 2023b), whereas in a study conducted in Iran, males were reported to be at a greater risk (29 %) of hospitalization, RR = 1.29 (95 %CI:1.06, 1.58) compared to women (Mohammadi et al., 2018).

3.4.1.3. Chronic respiratory disease

3.4.1.3.1. Mortality. A meta-analysis of 6 studies indicated a 4.1 % increased risk of death related to chronic respiratory diseases with each 1 °C rise in temperature, RR = 1.04 (95 % CI: 1.01, 1.07), $p < 0.001$, as shown in Figure-5. There was high heterogeneity amongst the studies, $I^2 = 86.9$ %, $p < 0.001$.

Of the eight studies that reported on chronic respiratory disease mortality, two were not included in the meta-analysis. A study done in Ho Chi Minh City, Vietnam reported a 45 % higher risk of chronic respiratory disease mortality during heat waves compared to non-heat wave days, RR = 1.45 (95 % CI: 1.25, 1.70). The study defined a heat wave as temperatures above the 97th percentile of DMT (30.9 °C) for two or more days (Dang et al., 2019). Another study with time-stratified case-crossover design conducted in 32 cities of Amazonian region in Brazil, assessed the impact of heatwaves (2 or more days unusually hot temperatures) and reported a 9 % potential increased risk of chronic respiratory disease mortality during heat waves (90th percentile) compared to non-heat wave days; RR = 1.09 (95 % CI: 0.98, 1.22) (Silveira et al., 2023).

Of all the studies reporting on chronic respiratory disease mortality, only one presented age-group related subgroup analysis. This study reported a 42 % higher risk of death from respiratory diseases in the age group of 65-years and above at 99th percentile of DMT compared to MMT, RR = 1.42 (95 %CI: 1.20, 1.64) compared to 4 % potential increased risk in 46–65 year and 13 % increased risk in 15–45 years age groups, RR = 1.04 (95 %CI: 0.98, 1.11), RR = 1.13 (95 %CI: 0.99, 1.26) respectively. Whereas, women exhibited a potential higher relative risk of chronic respiratory disease mortality at the 99th percentile of DMT compared to MMT RR = 1.18 (95 %CI: 0.93, 1.43) and no elevated risk of chronic respiratory disease mortality was observed among men, with a reported RR of 0.97 (95 % CI: 0.80, 1.14) (Requia et al., 2023a)

3.4.1.3.2. Morbidity. A total of 5 studies reported on chronic respiratory disease morbidity outcomes. Out of these, 2 were time-series analysis with DLNM, 2 were time-stratified case-crossover studies with DLM design and one was time-series with DLM & GLM design.

A time-series study with DLNM conducted in Ho Chi Minh City, Vietnam reported a 30 % higher risk of hospitalization during a heat wave (i.e. 97th percentile of DMT for 2 consecutive days) RR = 1.3 (95

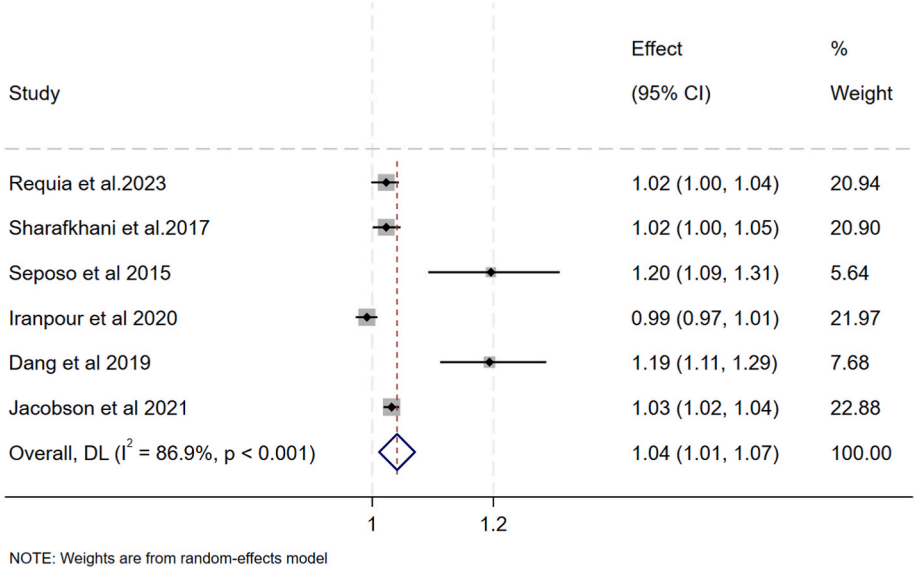

Fig. 5. Chronic respiratory disease mortality estimates-meta-analysis.

%CI 1.19, 1.42) as compared to non-heatwave days (Dang et al., 2019). Another time-series study conducted in Thailand, reported a 2.8 % higher risk of chronic respiratory disease hospitalization with each 1 °C rise above the threshold (29 °C), RR = 1.028 (95 % CI:1.006, 1.05) (Pudpong and Hajat, 2011). A nationwide time-stratified case-crossover study from Brazil reported 5 % higher odds of hospitalization per 5 °C increase in DMT during hot seasons, OR = 1.05 (95 % CI 1.04, 1.06) (Zhao et al., 2019). Another study done in 1814 cities in Brazil with a similar design reported a relative risk of 3 % per 5 °C increase above DMT, RR = 1.030 (95 % CI: 1.022–1.037) (Xu et al., 2020). In the Mekong Delta region of Vietnam, a time-series study employing DLM and GLM reported a 10 % potential increased risk of chronic respiratory disease-related hospitalizations per 1 °C rise above the 21 °C threshold (RR: 1.10; 95 % CI: 0.95–1.17) (Phung et al., 2016a).

Three studies from Brazil conducted in 1642 cities across four regions (North East, Central west, South East, South), Nationwide in five regions Midwest, (Midwest, North East, North, South East, South) and 27 cities of the country, all found higher risk of hospitalization in the elderly. The effect ranged from 13 % to 27 % increased risk, RR = 1.13 (96 % CI: 1.05, 1.21), RR = 1.23 (95 %CI: 1.13, 1.32), & RR = 1.27(95 % CI: 1.15 to 1.39) respectively (Zhao et al., 2019; Requia et al., 2023b; Jacobson et al., 2021).

Women were found to have a marginally higher risk of chronic respiratory disease hospitalization in three studies that disaggregated by sex. Requia et al., 2023 found a 30 % elevated risk of hospitalization at 99th percentile of DMT compared to MMT, RR = 1.30 (95 %CI:1.26, 1.35) in women versus 28 % in men in Brazil, RR = 1.28 (95 % CI:1.26–1.29) Requia et al. (2023b); Similarly, Zhao et al., 2019, observed that women were at an increased risk (9 %) of hospitalization at 99th percentile of DMT, RR = 1.09 (95 % CI:1.03, 1.15) versus 7 % in Men in 1642 Brazilian cities, RR = 1.07 (95 % CI: 1.01 to 1.12) (Zhao et al., 2019). In addition, Phung et al. (2016a), reported a slightly higher risk of hospitalization for women, RR = 1.016 (95 % CI: 1.015 to 1.052) versus men, RR = 1.012 (95 % CI: 1.004 to 1.027) with 1 °C increase in daily average temperature (Phung et al., 2016a).

3.4.1.4. *Diabetes mellitus*

3.4.1.4.1. Mortality. Two studies reported on mortality outcomes related to diabetes. One of them, a time-series study conducted in 4 Cities in Philippines observed 33 % higher risk of mortality at moderate-high temperature (75th compared to 90th percentile of DMT) and 62 % at extreme-high temperature (75th compared to 99th percentile of DMT), RR = 1.33 (95 % CI:1.09–1.62) and RR = 1.62 (95 % CI:1.21, 2.15) respectively (Seposo et al., 2017). While the other, a nationwide time-stratified case-crossover study with DLNM done in Thailand reported 21 % higher odds of death at 99th percentile compared to 90th percentile of DMT, OR = 1.21 (95 %CI 1.11, 1.32) (He et al., 2020).

3.4.1.4.2. Morbidity. Three studies reported on diabetes morbidity. A nationwide case-crossover study in Brazil reported 6 % higher odds of hospitalization with each 5 °C rise in DMT, OR = 1.06 (95 %CI 1.04,1.07) (Xu et al., 2019). Another study a time-stratified case-crossover, conducted in 1814 Brazilian cities, observed a 4.6 % higher risk of diabetes related hospitalization, with every 5 °C rise in temperature, RR = 1.046 (95 % CI: 1.027, 1.065) (Xu et al., 2020). The third study, a time-series analysis conducted in Chiang Mai, Thailand, reported a 4 % increase in risk of diabetes hospitalization with per 1 °C above the MMT (29 °C), though CI included null value, RR = 1.042 (95 % CI: 0.844, 1.229) (Pudpong and Hajat, 2011).

None of the studies presented age or sex stratified subgroup analysis focusing on diabetes mortality. However, one study presented a subgroup analysis on diabetes related hospitalization. The highest odds (18 %) of hospitalization related to diabetes was found in the older age group (80 years and above), OR = 1.18 (95 % CI: 1.13, 1.23) and women were found to have 6 % higher odds of hospitalization, OR = 1.06 (95 % CI: 1.04, 1.07) whereas men were found to have 5 % higher odds of hospitalization OR = 1.05 (95 %CI: 1.03, 1.07) (Xu et al., 2019).

3.4.2. *Risk of bias assessment*

The OHAT tool has been used to assess the risk of bias (RoB) in the included studies ((OHAT), 2015 (first publication)). The overall rating assigned to the studies and corresponding rationale are shown in **Supplementary-3, Risk of Bias analysis.** Out of 31 studies, 17 were classified as Tier-1 (Pudpong and Hajat, 2011; Silveira et al., 2019, 2021, 2023; Dang et al., 2019; Phung et al., 2016a, 2016b, 2017; Requia et al., 2023b; Iranpour et al., 2020; Khajavi et al., 2019; Mohammadi et al., 2018; Zhao et al., 2019; Seposo et al., 2017; Xu et al., 2019; He et al., 2020; Jacobson et al., 2021), 11 studies were classified as Tier-2 (Xu et al., 2020; Seposo et al., 2015; Dang et al., 2016; Mascarenhas et al., 2022; Hashizume et al., 2009; Giang et al., 2014; Bühler et al., 2022; Jacobson et al., 2021; Requia et al., 2023a; Grjibovski et al., 2012; Sharafkhani et al., 2017; Dadbakhsh et al., 2018; Moghadamnia et al., 2018) and 2 studies were classified as Tier-3 (Shrikhande et al., 2023; Mohammadi et al., 2021). Studies classified as Tier 3 were excluded from the meta-analyses due to their higher risk of bias, which could

compromise the reliability of risk estimates.

4. Discussion

This systematic review and meta-analyses show a consistent and positive association between heat exposure and risk of mortality and hospitalization related to cardiovascular diseases, chronic respiratory diseases and diabetes mellitus in the populations living in LMICs. The meta-analyses findings show that exposure to high temperatures is associated with an elevated risk of cardiovascular morbidity and mortality, with morbidity risks being slightly higher than mortality risks. We also found elevated mortality risk in those with chronic respiratory diseases. An increased risk of heat related mortality and morbidity was observed in elderly women with cardiovascular or chronic respiratory diseases or diabetes mellitus.

4.1. Cardiovascular diseases and heat-exposure

We found a 2.1 % higher risk of death from cardiovascular disease with each 1 °C increase in temperature above the reference level, which is in keeping with the existing literature (3 %–4.6 % higher risk of cardiovascular disease mortality per 1 °C rise) (Moghadamnia et al., 2017; Zafeiratou et al., 2021; Bunker et al., 2016; Perry et al., 2023; Liu et al., 2022). Therefore, we conclude that populations in LMICs are at a risk of cardiovascular disease mortality with the rising temperatures at a similar rate to those in high- or middle-income countries.

However, we found a 6.7 % potential higher risk of cardiovascular disease hospitalization per 1 °C increase above the reference level. This relative risk is higher than that reported in earlier reviews, e.g., Chen et al. (2017) observed a 2 % risk of cardiovascular disease hospitalization during a heatwave (2 or more days of maximum temperature above 98th percentile) compared to non-heatwave days, RR = 1.02 (95 % CI: 1.00, 1.05) (Chen et al., 2017). In a systematic review synthesizing evidence from high-income countries, Phung et al., 2016 reported a 2.2 % increased risk of cardiovascular disease hospitalization with heat wave exposure, RR = 1.022 (95 % CI: 1.006, 1.039)(Phung et al., 2016c).

We hypothesise that this additional risk in LMICs is due to differences in factors such as: exposure, in access to care and in disease management. For instance, limited access to cooling resources like fans or air conditioning, occupational exposure from a higher proportion of workers in manual and outdoor jobs, and inadequate urban planning to mitigate the heat island effect can all contribute to increased heat exposure for individuals (Singh et al., 2024). Air pollution and other environmental exposures could also be exacerbating the impact of extreme heat (Newell et al., 2018; Singh et al., 2013). Access to primary care and chronic disease management is often sporadic in LMICs, and as a consequence, there are higher rates of untreated or inadequately treated cardiovascular patients in LMICs which increases physiological vulnerability to heat exposure. (Lee et al., 2016; Ruan et al., 2018).

4.2. Chronic respiratory diseases and heat exposure

We found a 4.1 % higher risk of chronic respiratory disease mortality with each 1 °C rise in temperature, which is in keeping with the previous meta-analyses (3 %–6.3 % per 1 °C rise in temperature) (Song et al., 2017; Perry et al., 2023; Li et al., 2015; Zhao et al., 2021). The consistency across these studies strengthens the evidence of the adverse effect of heat exposure on chronic respiratory disease mortality. A recent detailed cardiopulmonary mortality study by Zhang et al. (2024), in Germany found higher risk of all-cause pulmonary related deaths than cardiovascular deaths with heat exposure as we have found in this study (Zhang et al., 2024). However the underlying physiological mechanisms have not been clearly defined (Ebi et al., 2021). A study reported relative risk of hospitalization in those with chronic respiratory disease was 30 % (RR = 1.3, 95 % CI: 1.19, 1.42) when exposed to a heat wave (defined as 97th percentile of the daily average temperature i.e. 30.9 °C for 2 consecutive days or more) compared to non-heatwave days (Dang et al., 2019). This is in contrast to earlier systematic reviews and meta-analyses where no association between heat exposure and respiratory morbidity was shown (Turner et al., 2012; Cheng et al., 2019; Ige-Elegbede et al., 2024; Kovats et al., 2004). We postulate that those diagnosed with chronic respiratory disease in LMICs are often already at the severe end of the disease spectrum due to lack of diagnostic capabilities such as spirometry. Therefore, those diagnosed with chronic respiratory disease are likely already close to their physiological limit and the additional burden of heat with the associated increase in respiratory rate could explain the increased mortality and morbidity risk.

4.3. Diabetes mellitus and heat exposure

Although we could not conduct a meta-analysis on studies that looked at diabetes, the highest mortality risk reported in a single study was 33 %–62 % which compared risk at 90th and 99th percentile to 75th percentile of daily mean temperature in those with diabetes (He et al., 2020). This is higher than previous evidence synthesized where a range of 14 %–18 % higher risk of diabetes related mortality with heat-exposure was found (Song et al., 2021; Moon, 2021; Gao et al., 2022b). This clearly warrants further studies to explore the association between heat exposure and mortality in those with diabetes especially considering the growing rates of diabetes mellitus in LMICs.

4.4. Age-groups & sexes

In the studies included in this review, the most vulnerable age group for cardiovascular and chronic respiratory disease mortality and chronic respiratory disease and diabetes morbidity was found to be 65-years old and above, in keeping with the existing literature. We found this older age group at increased risk of mortality in all disease groups. However, a mixed picture was observed on the risk of hospitalization related to cardiovascular disease. An Iranian study reported a higher risk of cardiovascular disease hospitalization for the age group above 65 years as compared to age group younger than 65 years. Whereas, a Brazilian study reported a higher risk of cardiovascular disease hospitalization at 99th percentile of DMT in the age group of 15–45 years, as compared to age groups of 46–65 years and 65 years and above (Requia et al., 2023b). However, we were unable to do a meta-analysis on this. This is a divergence from the findings of a previous systematic review by Liu et al. (2022), that reported cardiovascular disease hospitalization in 65 years and older age group increased as the heatwave intensity increased (low intensity RR = 0·975 (95 % CI: 0·920,1·030); middle intensity RR = 1·029, (95 % CI: 0·980–1·078); and high intensity RR = 1·126 (95 % CI: 0·997,1·255) (Liu et al., 2022). It is postulated that the higher risk in younger populations in LMICs is because during economically productive years there is a greater heat exposure (Zhang et al., Sun et al., 2021), and the growing burden of obesity and lifestyle changes increase the risk (Sun et al., 2023).

We found heat-related vulnerability of women was greater, as evidenced by consistently reported higher risk in most of the disease outcomes (Requia et al., 2023b; Zhao et al., 2019; Xu et al., 2019). It is likely that the higher heat vulnerability of women in LMICs is due to multiple factors related to both differential exposure, socio-economic status, care-seeking behaviour, access to care and treatment received. For example, cultural practices around dressing in some LMICs affect women's ability to thermoregulate through behavioural change and so increases the adverse effects of heat (Chan et al., 2016).

4.5. Policy implications

The results of this review highlight critical implications for public health policies in LMICs. The observed associations between rising environmental temperatures and an increased risk of morbidity and mortality from the three non-communicable disease groups indicate the

vulnerability of populations in these regions to climate change impacts. This underscores the need for governments and policymakers to recognize heat exposure as a significant determinant of health and to incorporate this evidence into national health strategies.

Moreover, this evidence can contribute meaningfully to the evolving scope of the World Health Organization (WHO) Global Air Quality Guidelines (AQGs), which, while traditionally focused on pollutants such as $PM_{2.5}$, NO_2, and O_3, acknowledge the interplay of environmental stressors like heat with air quality and health outcomes (Organization, 2021). Heat and air pollution often co-occur and may act synergistically to exacerbate disease outcomes, particularly among vulnerable populations (Willers et al., 2016). Recognizing this interlinkage can inform integrated environmental health policies that address both air quality and climate-related heat exposure. The review's findings also support the development of national heat–health action plans, improved urban planning to reduce heat islands, early warning systems, and tailored communication strategies for at-risk groups, in line with WHO recommendations on climate resilience and health (Organization, 2023b). Importantly, strengthening health system preparedness to respond to climate-sensitive diseases; including cardiovascular conditions, respiratory illnesses, and diabetes; is vital to reducing the projected burden in LMICs under climate change scenarios.

Finally, these results may influence the allocation of resources, prioritization of vulnerable populations, and the integration of climate adaptation measures into existing health programs. Additionally, the review provides a foundation for revising international and national health guidelines to account for environmental heat as a risk factor for NCD management.

4.6. Limitations

There are several limitations in this review. Meta-analyses were not possible for chronic respiratory disease morbidity and diabetes related mortality/morbidity due to limited studies. In addition, diversity in exposure definitions did not allow for a standardized calculation of effect estimates for all exposures. There were variations in the lag effects, temperature measurement (per 1 °C or percentile) thresholds, used in the included studies which brought about substantial heterogeneity in the pooled estimates. Moreover, the lack of control for confounders, especially air pollutants in meta-analyses, could alter the effect estimates of heat exposure and thereby reduce the accuracy of the risk estimates. Although this may not be a significant problem, as previous work has shown that the effects of air pollutants on the mortality/morbidity effect of heat may not be large (Bunker et al., 2016). Though a narrative synthesis has been done for age and sex stratified subgroups, their non-inclusion in stratified meta-analyses might mask the important differences in the pooled effects. Lack of evidence from Sub-Saharan Africa, and large parts of South America restricts the generalizability of the findings. Some of the included studies did not clearly distinguish between acute and chronic respiratory conditions. While we excluded studies focused on infections, a few reporting general respiratory morbidity were included based on contextual cues or ICD codes suggestive of chronic disease. This may have introduced minor misclassification, which should be considered when interpreting the findings. There was limited data on socioeconomic factors or information on adaptive capacities of communities in LMICs, which might have a bearing on exposure-outcome relationship. In addition, the heterogeneity in design and methodology of the included studies might introduce bias and affect the comparability of the results.

4.7. Future research

Future research should focus on exploring the research gaps through well-designed, multi-country studies, leveraging standardized methodologies to improve comparability. Investigating the effectiveness of climate adaptive interventions and policies in reducing the health impacts of heat on NCDs is essential to inform targeted public health responses in LMICs.

4.8. Conclusion

This systematic review and meta-analyses underscore the health risks associated with the increasing environmental temperatures in LMICs. The synthesized effect estimates indicate that populations in LMICs are vulnerable to adverse impact of heat exposure. The findings call for urgent public health and climate action to adapt and mitigate the adverse impacts of heat-exposure in these countries.

CRediT authorship contribution statement

Shahab Ali Siddiqui: Writing – review & editing, Writing – original draft, Visualization, Validation, Methodology, Formal analysis, Data curation, Conceptualization. **Sokhna Thiam:** Writing – review & editing. **Credo Houndodjade:** Writing – review & editing. **Peninah Murage:** Writing – review & editing, Validation, Supervision, Methodology, Funding acquisition. **Ana Bonell:** Writing – review & editing, Validation, Supervision, Methodology.

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Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Reports a relationship with that includes:. Has patent pending to. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envres.2025.121980.

Data availability

Data will be made available on request.

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