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Review article

Association between ambient temperature and heat waves with mortality in South Asia: Systematic review and *meta*-analysis

Asya Dimitrova [a,b,c,*], Vijendra Ingole [a,c], Xavier Basagaña [a,b,c], Otavio Ranzani [a,c], Carles Milà [a,c], Joan Ballester [a,c], Cathryn Tonne [a,b,c,*]

[a] *Barcelona Institute for Global Health (ISGlobal), Barcelona Biomedical Research Park (PRBB), Doctor Aiguader, 88, 08003 Barcelona, Spain*
[b] *Universitat Pompeu Fabra (UPF), Plaça de la Mercè, 10, 08002 Barcelona, Spain*
[c] *CIBER Epidemiología y Salud Pública, Avda. Monforte de Lemos 3-5, Madrid, Spain*

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ABSTRACT

Background: South Asia is highly vulnerable to climate change and is projected to experience some of the highest increases in average annual temperatures throughout the century. Although the adverse impacts of ambient temperature on human health have been extensively documented in the literature, only a limited number of studies have focused on populations in this region.

Objectives: Our aim was to systematically review the current state and quality of available evidence on the direct relationship between ambient temperature and heat waves and all-cause mortality in South Asia.

Methods: The databases Pubmed, Web of Science, Scopus and Embase were searched from 1990 to 2020 for relevant observational quantitative studies. We applied the Navigation Guide methodology to assess the strength of the evidence and performed a *meta*-analysis based on a novel approach that allows for combining nonlinear exposure–response associations without access to data from individual studies.

Results: From the 6,759 screened papers, 27 were included in the qualitative synthesis and five in a *meta*-analysis. Studies reported an association of all-cause mortality with heat wave episodes and both high and low daily temperatures. The *meta*-analysis showed a U-shaped pattern, with increasing mortality for both high and low temperatures, but a statistically significant association was found only at higher temperatures — above 31° C for lag 0–1 days and above 34° C for lag 0–13 days. Effects were found to vary with cause of death, age, sex, location (urban vs. rural), level of education and socio-economic status, but the profile of vulnerabilities was somewhat inconsistent and based on a limited number of studies. Overall, the strength of the evidence for ambient temperature as a risk factor for all-cause mortality was judged as *limited* and for heat wave episodes as *inadequate*.

Conclusions: The evidence base on temperature impacts on mortality in South Asia is limited due to the small number of studies, their skewed geographical distribution and methodological weaknesses. Understanding the main determinants of the temperature-mortality association as well as how these may evolve in the future in a dynamic region such as South Asia will be an important area for future research. Studies on viable adaptation options to high temperatures for a region that is a hotspot for climate vulnerability, urbanisation and population growth are also needed.

1. Introduction

Expected increases in temperature and the intensity and frequency of heat waves due to climate change have become a matter of growing public health concern (IPCC, 2014; Watts et al., 2017; Ebi et al., 2018; Maycock et al., 2018; Watts, 2019). Along with other climatic changes such as precipitation and atmospheric circulation patterns, temperature increases can affect human health and wellbeing through various pathways, including heat stress, increases in wildfires, spread of vector-borne and water-borne diseases, crop failure and its potential impact on food prices, nutrition, incomes, population displacement and conflict (Watts et al., 2017; Ebi, Campbell-Lendrum and Wyns, 2018). One of the most direct, and therefore, well-studied mechanisms through which changes in average weather impact human health is ambient temperature.

An extensive body of epidemiological literature has documented the

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* Corresponding authors at: ISGlobal, Barcelona Biomedical Research Park (PRBB), Doctor Aiguader, 88, 08003 Barcelona, Spain.
E-mail address: cathryn.tonne@isglobal.org (C. Tonne).

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adverse impacts of ambient high and low temperatures and isolated events such as heat waves and cold spells (normally defined as a prolonged period of abnormally high/low temperatures, with the exact number of days and temperature thresholds varying by study design) on human health in terms of increases in cardiovascular (Moghadamnia et al., 2017), respiratory, and all-cause mortality (Oudin Åström, Bertil and Joacim, 2011; Yu et al., 2012; Ryti, Guo and Jaakkola, 2016), as well as increases in emergency department visits and hospital admissions (Mastrangelo et al., 2007; Phung et al., 2016). Most of these studies have been conducted in countries with temperate climates in the Global North (mostly North America and Europe) and more recently China (Chen, 2018; Han et al., 2017; Zhang et al., 2014). Evidence on the relationship between temperature and health risks in low- and middle- income countries (LMICs) and hot climates, albeit growing, is still limited, even though the highest temperature increases and the global hotspots of population growth and urbanisation will occur there (IPCC, 2014; UNDESA, 2018; European Commission, Joint Research Centre, 2018).

Although two recent reviews have summarised the body of literature on temperature and mortality for LMICs and tropical countries (Burkart et al., 2014a; Green et al., 2019), a comprehensive review on one of the most vulnerable geographical regions in the world — South Asia — is still lacking (Mora et al., 2017; Byers et al., 2018; Muthukumara et al., 2018). South Asia is recognised as being at high risk of climate impacts due to the combination of its climate and geography (occupying areas with high year-round temperatures and humidity), large and growing population, rapid urbanisation, relatively low adaptive capacity in terms of high levels of poverty and inequality, poor health infrastructure, scarcity of resources and livelihood dependence on agriculture, which implies large occupational exposure to outdoor temperature. With a population of about 1.8 billion (World Bank, 2019b), South Asia, which comprises Afghanistan, Bangladesh, Bhutan, India, Maldives, Nepal, Pakistan, and Sri Lanka (World Bank definition), is the most densely populated and the second most populous region in the world (after East Asia&Pacific). The region accommodates the second highest number and proportion of people in extreme poverty (defined as living below $1 per day) (Islam, Newhouse, Yanez-Pagans, 2018) and 43% of its labour force works in agriculture (World Bank, 2019a).

South Asia has a diverse geography and climate, covering the glaciated and sparsely populated regions of the Himalayas, Karakoram, and Hindu Kush mountain, with annual average temperatures around 0 °C, as well as vast tropical and sub-tropical regions, with annual temperatures averaging between 25 °C and 30 °C (Mani et al., 2018). Given these characteristics, both high and low temperatures are likely to affect population health. Similar to other regions, South Asia has experienced a clear and considerable upward trend in annual average temperatures, albeit unevenly distributed geographically. Most pronounced increases over the period 1950–2010 have been observed in Western Afghanistan and southwestern Pakistan, ranging from 1.0 °C to 3.0 °C. Within the same decades, average annual temperatures have shifted upward by 1.0 °C to 1.5 °C in Southeastern India, western Sri Lanka, northern Pakistan, and eastern Nepal (Mani et al., 2018). These trends are projected to continue in the future. The Intergovernmental Panel on Climate Change (IPCC) indicates that, compared to the average in the 20th century, average annual temperatures in the region could rise by >2 °C over land by the mid-21st century, and exceed 3 °C over high latitudes, by the late 21st century under a high-emissions scenario (Carabine, 2014). Importantly, rising humidity, especially in regions with routinely warm and humid weather, can further amplify the health impacts of higher temperatures by compromising humańs’ ability to dissipate heat through sweating (Gosling et al., 2009; Im, Pal and Eltahir, 2017).

The threat of aggravating heat is also reflected in the increasing death toll reported from extreme temperatures in the region according to the Emergency Events Database (EM-DAT) (See Fig. 1). Some of the most notable historical episodes, which claimed thousands of human and livestock lives, include: the severe heat waves reported around Odisha (eastern India) in 1998, in Andhra Pradesh (2003), Ahmadabad (2010) and other parts of Gujarat (western India), the 2008 Afghanistan blizzard, and the more recent 2015 heat wave, which hit large parts of India and Pakistan, resulting in about 3500 deaths (Im, Pal and Eltahir, 2017). These figures are likely to be conservative and underestimate the total health burden of extreme heat, given the lack of official surveillance and misreporting. Furthermore, they do not capture the impact of moderate non-extreme temperatures, which are much more frequent, and therefore, contribute considerably to total heat and cold-related deaths (Gasparrini et al., 2015).

Although geographic location, climate, and latitude are of crucial importance, the literature has shown the pattern and magnitude of temperature-mortality effects are also highly dependent on local contexts and strongly influenced by the interaction of non-atmospheric factors such as demographic, socio-economic, and lifestyle characteristics, underlying disease burdens of the population, features of the built environment, and others (Uejio et al., 2011; Xu et al., 2013; Zanobetti et al., 2013). For instance, it has been demonstrated that exposure–response functions can differ even for populations within the same geographic or climatic area (Michelozzi, 2006; Anderson & Bell, 2009; Hajat & Kosatky, 2010).

It is also well known that populations are usually well adapted to the most frequent and/or moderate temperatures in their local climates, which explains higher thresholds for heat-related mortality in warmer climates and lower thresholds for cold-related mortality in colder climates (Gosling et al., 2009). Studies have also reported that exposure–response functions can change over time, highlighting the scope for adaptation and acclimatization (Hondula et al., 2015; Kinney, 2018a; Petkova et al., 2014). However, the speed at which adaptation is likely to take place and whether it can outpace future temperature changes are poorly understood. Furthermore, the scope of further acclimatization and adaptation for populations living in hot, and especially hot and humid climates, where heat adaptations and lifestyle modifications already exist, is likely to be more limited (Hanna and Tait, 2015). According to a climate simulation study, under the current business-as-usual trajectory of carbon emissions, by the end of the century some of the population in South Asia may experience hot and humid temperatures that exceed the “upper limit on human survivability “(Im, Pal and Eltahir, 2017). In this context, it has been argued that the population in the region might need to rely mainly on technological and behavioural adaptations in the future (Hanna and Tait, 2015).

In the context of climate change and the vulnerabilities in South Asia it is crucial to provide a comprehensive analysis on the region-specific

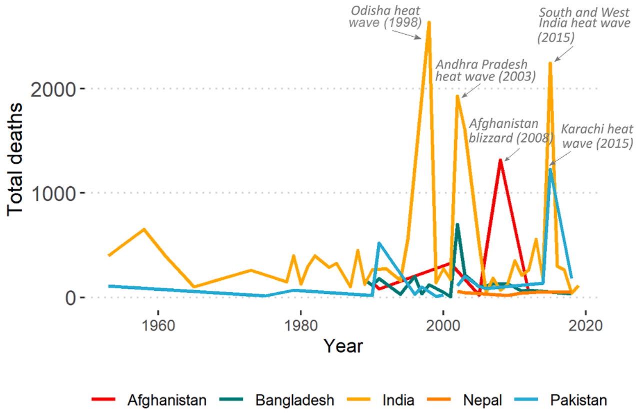

Fig. 1. Deaths from extreme temperature events in South Asia. Source: Own figure, EM-DAT database* (Centre for Research on the Epidemiology of Disasters CRED, 2019) *The data in the database are compiled from various sources, including UN agencies, non-governmental organizations, insurance companies, research institutes and press agencies. An extreme event is considered in the database only if >10 fatalities were reported. Annotations of major heat and cold events in the figure are added by the authors.

temperature-mortality effects in order to guide adaptation planning, inform targeted health interventions, and support sound and evidence-based health impact projections. To address this need and to establish the state of the available evidence, identify knowledge gaps, and highlight future research directions, we systematically reviewed the existing literature on temperature-related mortality in South Asia. Through a systematic review and a *meta*-analysis we investigated the following hypothesis: "Are ambient temperature (high and low), and heat wave events associated with increased all-cause mortality in the general population in South Asia?". We developed a "Population", "Exposure", "Comparator", and "Outcomes" and "study design" (PECOs) statement as follows:

- **Population:** the general population in South Asia (as defined by the World Bank in August 2018: Afghanistan, Bangladesh, Bhutan, India, Maldives, Nepal, Pakistan, Sri Lanka)
- **Exposure:** high and low ambient temperatures (defined as daily/weekly/monthly/annual mean/max/min temperatures or a composite index of temperature and other weather variable) and heat wave events.
- **Comparators:** A comparable population not exposed to the same temperature or heat wave event or the same population at a time when it was not exposed to the same ambient temperature or heat wave event.
- **Outcome:** all-cause or cause-specific mortality, Years of Life Lost (YLL), changes in life expectancy
- **Study design:** quantitative observational studies

We also perform more narrative review on the following exploratory research questions: i) "Are ambient temperatures (high and low), and heat wave events associated with increased cause-specific mortality in the general population in South Asia?", ii) Are certain population groups at higher risk of mortality from exposure to ambient temperature?", iii) At what time lags do temperature effects on mortality occur for the population in South Asia?"

We add to previous systematic reviews conducted for tropical regions (Burkart et al., 2014a), LMICs (Green et al., 2019) and India (Salve et al., 2018) by covering both effects from heat wave episodes and ambient temperature, assessing the strength and quality of the body of evidence, and including a *meta*-analysis of exposure–response functions based on a novel approach that allows combining nonlinear exposure–response associations without access to data from individual studies. We also identify key areas for future research.

2. Methods

2.1. Search strategy

We performed a systematic search of four electronic databases - Pubmed, Web of Science, Scopus, Embase – in order to identify epidemiological studies examining the direct relationship between ambient temperature and all-cause and cause-specific mortality in South Asia. We restricted the search to peer-reviewed articles published in English between January 1990 and August 2020. The search was initially run on 16 August 2018, and later updated on 13 August 2020. The systematic review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines and was based on a registered review protocol accessible online (PROSPERO CRD42018105730) (Dimitrova and Tonne, 2018). To ensure that all relevant articles were identified, we screened bibliographic reference lists of all included studies manually. Example of an exact electronic search strategy is provided in Supplementary Table S1.

2.2. Selection of studies

We considered peer-reviewed studies published since 1990 in English, which examined any of the eight countries in the region as defined by the World Bank in August 2018 (Afghanistan, Bangladesh, Bhutan, India, Maldives, Nepal, Pakistan, Sri Lanka), South Asia as a whole, or studies on a global level, which included at least one country of the region. We included only quantitative observational studies, which present results for the general population. Epidemiological studies based on medical records were also included when these stemmed from a representative number of hospitals in a country or from the leading hospitals in an urban area, that has a catchment area representative of the target population. In terms of outcome measures, we included studies using mortality counts as well as alternative population health metrics such as YLL or life expectancy. We excluded studies investigating morbidity effects only or those investigating indirect effects of temperature on mortality, for example through changes in crop yields, forest fires, droughts and water shortages, and others. We did not apply restrictions on the type or the timeframe of effects and exposure measures (e.g., year-round hot or cold temperatures, heat waves or cold spells).

We included studies based on daily, weekly, monthly or annual temperatures, and those combining measures of temperature and humidity (apparent temperature, Humidex, Heat Index, Wet Bulb Globe Temperature, etc.). Since there is no standard definition of heat waves with respect to human health in the literature, we included all studies referring to heat wave episodes. We excluded studies looking only at seasonal effects on mortality without explicitly considering temperatures. Regarding types of study design, we considered time series studies, case-crossover studies as well as single episode analyses. Since the focus was on studies examining the quantitative association between ambient temperature and mortality, we excluded discussion articles, case studies, and articles featuring descriptive analysis only (See Table S2).

After we combined the search results and removed duplicates, one of the reviewers (AD) screened all the titles and abstracts and assessed their relevance against the inclusion criteria (see Table S2). To validate these results a second reviewer (CT) screened a sample of 20% of all retrieved titles and abstracts. Independent judgment of the two reviewers differed for 0.3% of the titles and abstracts, but perfect agreement on which studies should be selected was reached through discussion. Two reviewers (AD and VI) separately assessed full texts for eligibility, based on the pre-defined inclusion and exclusion criteria. In the case of discrepancies, disagreements were resolved with the involvement of a third senior investigator (CT).

2.3. Data extraction

Both investigators independently retrieved the main characteristics and results of the included studies using a standardised data extraction form. The following information was retrieved from each article: location and study period, study design, statistical methods and sensitivity analysis, inclusion of lagged effects, control of confounding and modifying factors, exposure and outcome measure(s) and their data source(s), observed temperature and humidity ranges, minimum mortality temperature (MMT), reported effect estimates, subgroup analysis, mortality displacement, key findings, and modeled or suggested adaptation strategies. We pilot tested the data extraction form to ensure accuracy and consistency during the entire process. Data collected by both reviewers were compared and any discrepancies were resolved through discussion and consensus. In several instances, study authors were contacted to obtain additional data necessary for the analysis or to clarify ambiguous information.

2.4. Assessment of evidence

We assessed the quality and strength of the evidence separately for the association between ambient temperature and all-cause mortality and heat wave events and all-cause mortality following the Navigation

Guide framework (Johnson et al., 2014; Woodruff and Sutton, 2014). The Navigation Guide methodology has been specifically developed for the assessment of the quality and strength of the evidence of research in the environmental health field (Johnson et al., 2014). The assessment proceeded in three stages: i) rating the Risk of Bias (RoB) for each individual study, ii) rating the quality of the evidence across all studies, and iii) rating the strength, or certainty, of the evidence across all studies.

2.4.1. *Assessment of the risk of bias in individual studies*

We assessed the quality of individual studies using the Office of Health Assessment and Translation (OHAT) Risk of Bias Rating Tool for Human and Animal Studies. Since OHAT does not specifically consider time series environmental health study designs, in collaboration with subject-matter experts (CT, XB, OR, JB) we adapted some of its domains to better tailor it to our research question (See Table S3). We evaluated each study against the following six domains of Risk of Bias (RoB): selection, confounding, exposure assessment, outcome assessment, selective reporting and other bias (appropriateness of statistical methods). For each of these possible sources of bias we rated the RoB as *definitely low, probably low, probably high* and *definitely high*. The rating scale is based on a conservative approach, where insufficient information to judge the risk of bias for specific domain results in a rating of *probably high* risk of bias. The two reviewers (AD, VI) independently performed the risk of bias assessment and discussed results with the other co-authors in case consensus could not be reached. Following the Navigation Guide Methodology, we considered an individual study to have a *definitely low* or *probably low* RoB if all domains of assessment were rated as *definitely low* or *probably low*. Due to the very limited number of studies the results of the RoB assessment were not used to exclude studies from the quantitative synthesis.

2.4.2. *Assessment of the quality of the evidence across studies*

We rated the overall quality of the evidence for studies on ambient temperature and heat wave episodes separately. Rating categories included *high, moderate*, or *low*. Following the approach in the Navigation Guide, we initially rated the body of evidence as *moderate* and then "downgraded" or "upgraded" this rating based on eight factors. The downgrading factors included risk of bias across studies, indirectness, inconsistency, imprecision, publication bias, and the upgrading factors consisted of size of the effect, dose response pattern and possibility of confounding minimizing effects. We assessed the RoB across studies based on the RoB rating of individual studies, as outlined above. As recommended in the Navigation Guide, the RoB across studies was judged on the basis of each study, but with more weight placed on high quality studies.

2.4.3. *Assessment of the strength of the evidence across studies*

We also rated the strength of the body of evidence, separately for ambient temperature and heat wave episodes, based on the following four considerations outlined in the Navigation Guide: i) quality of the body of evidence (i.e., rating from previous assessment stage), ii) direction of effect, iii) confidence in the effect (likelihood that a new study would change our conclusions) and iv) any other attributes of the data that might affect certainty.

2.5. *Meta-analysis*

From the studies included in the review, we selected those that were sufficiently compatible in terms of study design, outcome and exposure measures, and lag structure, in order to conduct a *meta*-analysis of the association between temperature and mortality. After screening all studies, we identified that the most common choice of study design, outcome and exposure variables, and lag structure was the following: time series studies using daily all-cause mortality and daily mean temperature and reporting effects for lag 0–1 and lag 0–13 days. Hence, we limited our choice to studies with these characteristics (Burkart et al., 2011; Fu et al., 2018; Hashizume et al., 2009; Ingole et al., 2017; McMichael et al., 2008). For studies that included a plot of the temperature-mortality association, we extracted numerical representation of the exposure–response curves and their confidence intervals at every 0.5 increment of the temperature values using the web-based tool WebPlotDigitizer (Rohatgi, 2014). Authors of two studies that did not include such visualizations were contacted to acquire the necessary data. We also extracted the following data: i) average number of daily deaths, ii) number of days analysed in the study and iii) range of the distribution of exposure variables. The analysis was performed separately for the exposure response curves at lag 0–1 days and lag 0–13 days. Since the reference value used across studies differed (in most cases this was the MMT), recalculation of the curves and standard errors using a common reference value was necessary before combining the curves. We set the reference values for re-centering the curves to be equal to the average MMT across the included studies. This corresponded to 24.5 °C for the exposure response curves at lag 0–1 days and 26.5°C at lag 0–13 days. Even though the selected studies include locations within different climatic zones, they have comparable temperature distributions and all of them included the reference temperature values for the *meta*-analysis. Although the estimates across a single exposure–response curve are correlated because they share the same reference category, without available data on these correlations, it is not possible to compute the standard errors that would result from re-centering the curve to another reference value. To overcome this challenge and calculate the standard errors after re-centering the curves without access to the individual-level data, we applied the recently developed methodology by Basagaña (2019). Using the extracted data described above, the method allows to simulate individual datasets in order to change the reference category and approximate the confidence intervals (Basagaña, 2019). In brief, the approach consists in the generation of a dataset, which has an identical number of observations as the original one and upon analysis produces a good approximation of the exposure–response function and confidence interval reported by the study. A more detailed description of the methodology, including a reproducible example with R software code, is available in the publication Basagaña (2019). After calculating the standard errors and the exposure–response estimates at each temperature increment, we combined the non-linear exposure–response curves of the individual studies using a *meta*-smoothing approach (Schwartz and Zanobetti, 2000). The latter method consisted of conducting a random-effects point-wise *meta*-analysis for each exposure level (Schwartz and Zanobetti, 2000). The analysis was performed using the R (version 3.6.1) package '*metafor*' (Viechtbauer, 2010). The datasets and the R software code for conducting the analysis are available in the Supplementary Material of this publication.

3. Results

3.1. *Literature search*

We identified a total of 10, 713 references from the electronic databases' search and through other sources, after removal of duplicate entries. After screening these for relevance based on title and abstract, we selected 50 articles for in-depth review. A detailed evaluation of the content against the inclusion criteria resulted in 27 studies being included in the final analysis. The flow diagram in Fig. 2 illustrates in detail the literature search and the selection process.

3.2. *Characteristics of included studies*

Among the included studies, about half (n = 15; 56%) examined the effects of both heat and cold on mortality, five (19%) focused only on heat effects and one on cold effects, while nine studies (33%) assessed the association of heat waves with mortality and one addressed the

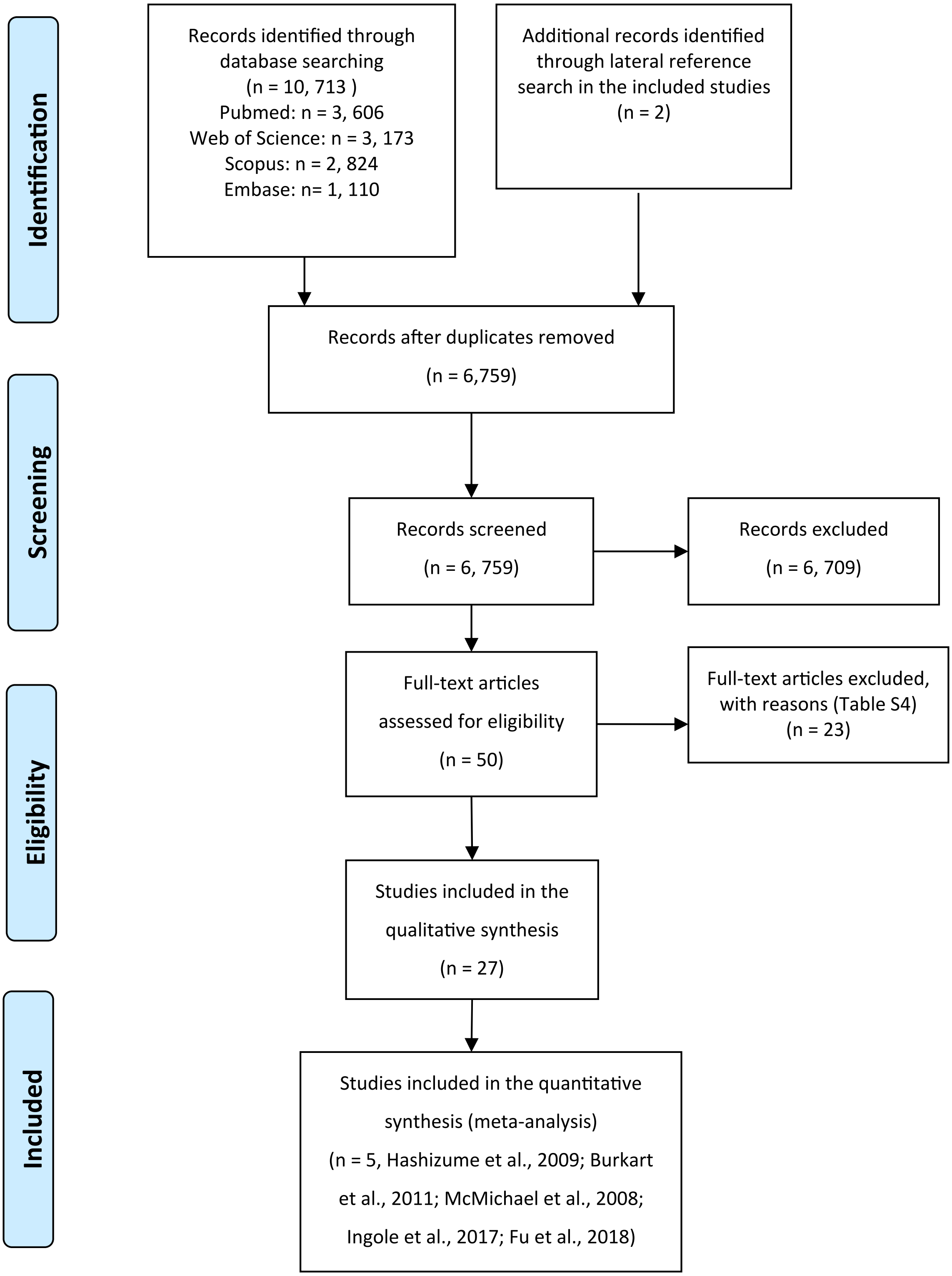

Fig. 2. Flow diagram of literature search and study selection process.

association between cold spells and mortality (See Table 1 for a more detailed description). The studies used diverse approaches for defining hot and cold temperature effects — based on the MMT, a specific percentile of the temperature distribution, an arbitrary temperature threshold, the season (summer/winter months), deviation of temperatures from their annual average, or simply based on the pattern of the temperature-mortality relationship. The definition of heat waves was not uniform across studies. Five used the conventional approach of considering both the duration and intensity of a heat wave (Mazdiyasni et al., 2017; Nissan et al., 2017; Nori-Sarma et al., 2019a; Singh et al., 2019; Nori-Sarma et al., 2019b), while the rest considered only its intensity. Four studies used the heat wave definition by the India Meteorological Department (IMD) based only on maximum temperature thresholds (Azhar et al., 2014; Murari et al., 2015; Nori-Sarma et al., 2019a; Nori-Sarma et al., 2019b) and one study did not provide a specific definition, but analysed maximum temperatures and heat-induced

Table 1
Characteristics of reviewed studies and main findings.

Reference	Methods						Exposure	Outcome	Main findings
	Study population and location	Category of effect	Study period	Study design and statistical method	Lag structure	Control variables (confounders and effect modifiers)	Measure and source	Measure and source	
Rural areas									
Alam et al. (2012)	General population Abhoynagar, Bangladesh	Heat and cold effects (continuous temperature)	1983–2009	Time series analysis, Poisson generalized additive model (GAM)	Lag 0–1 week, lag 0–2 week, lag 0–3 week	Time trend, seasonal pattern	Average weekly mean temperature Bangladesh Meteorological Department	All-cause mortality (n = 4,850) ICDRR, B́s Sample Vital Registration System (SVRS) in Abhoynagar subdistrict	Weekly mean temperatures (lag 0) below the 25th percentile and between the 25th (23 °C) and 75th percentiles (29.6 °C) were associated with increased mortality risk, particularly in females and adults aged 20–59 years by 2.3–2.4% (CI: 4.4, 0.1) for every 1 °C decrease. Temperature above the 75th percentile (29.6 °C) did not increase the risk.
Hashizume et al. (2009)	General population Matlab, Bangladesh	Heat and cold effects (continuous temperature)	1994–2002	Time series analysis, Poisson generalized linear model	Lag 0–1 days, lag 0–13 days (cumulative)	Year, season, day of the week, public holiday	Daily mean temperature Bangladesh Meteorological Department	All-cause mortality excluding external causes (n = 13, 270) and cause-specific mortality (cardiovascular, respiratory, perinatal, infectious and parasitic mortality and others) ICDRR, B́s Health and Demographic Surveillance System (HDSS) in Matlab	Every 1 °C decrease in mean temperature (lag 0–13) was associated with a 3.2% (95% CI 0.9, 5.5) increase in all-cause mortality. There was no clear heat effect on all-cause mortality for any of the lags examined. Heat effect was observed only for cardiovascular mortality (lag 0–1), mortality from infectious diseases (lag 0–13) and mortality in elderly people (lag 0–1).
Sewe et al. (2018)	General population 22 villages in Pune district, India	Heat and cold effects (continuous temperature)	2003–2012	Time series analysis, Quasi-Poisson distributed-lag non-linear models (DLNM)	Lag 0–14 (separate)	Trend, season, day of the week, indicator for “heaping days”	Daily max temperature National Oceanic and Atmospheric Administration (NOAA)	All-cause mortality (daily mean number of deaths: 0.9, n = 2,958) Vadu HDSS	Heat (lag 0–14) was associated with YLL (26.03 YLL; 95% CI: −0.36, 52.42 at the 95th percentile, 39 °C compared to 30 °C), but there was no evidence of an association with cold.
Ingole et al. (2017)	General population aged 15 and older 22 villages in Pune district, India	Heat and cold effects (summer and winter months)	2004 – 2013	Case-crossover study, Quasi-Poisson regression (1st stage analysis) and Conditional logistic regression model (2nd stage analysis)	Lag 0–1 days and lag 0–13 days (cumulative)	Season, time trend, education, occupation and ownership of agricultural land; potential temporal confounders and time-invariant confounders controlled for “by design”	Daily mean temperature National Oceanic and Atmospheric Administration NOAA and India Meteorological Department	All-cause mortality (n = 3,079) Vadu HDSS	Temperature above a threshold of 31 °C was associated with total mortality (OR 1.48, CI: 1.05, 2.09) per 1 °C increase in daily mean temperature. Odds ratios were higher among females, those with low education, those owing larger agricultural land, and farmers. In winter, per 1 °C decrease in mean temperature, OR for total mortality was 1.06 (CI = 1.00–1.12) in lag 0–13 days, with higher risk observed

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Table 1 (*continued*)

Reference	Methods Study population and location	Category of effect	Study period	Study design and statistical method	Lag structure	Control variables (confounders and effect modifiers)	Exposure Measure and source	Outcome Measure and source	Main findings
									among people occupied in housework.
Ingole et al. (2012)	General population 22 villages in Pune district, India	Heat and cold effects (continuous temperature)	Jan 2003 - May 2010	Time series analysis, Poission regression model	lag 0–1 days, lag 2–6 days, lag 7–13 days (cumulative)	Season, time trends	Daily mean temperature India Meteorological Department	All-cause mortality (n = 1 ,662) Vadu HDSS	Both high and low temperatures were associated with all-cause mortality over all age groups, with children aged 5 years or below being particularly affected. In the age group 20–59, 1 °C increase in temperature was associated with 9.4% increase in RR (95%CI: 3.6, 15.5) for lag 0–1 and 1 °C decrease in temperature with RR= − 9.5 (95%CI: −15.5, − 3.2) for lag 2–6.
Ingole et al. (2015)	General population aged 12+ 22 villages in Pune district, India	Heat and cold effects (continuous temperature)	Jan 2003 to Dec 2012	Time series analysis, Quasi-Poisson model and Logistic regression model	Lag 0–1 days, lag 0–4 days (cumulative)	Day of week, time trend	Daily maximum temperature India Meteorological Department	All-cause mortality (n = 2,302) and cause-specific mortality (infectious diseases, non-infectious diseases and mortality from external causes) Vadu HDSS	Heat was significantly associated with total mortality (RR = 1.33; 95% CI: 1.07, 1.60) and mortality from non-infectious diseases (RR = 1.57; CI: 1.18, 2.10) for lag 0–1. Men and people in the age group 12–59 showed elevated risk for total mortality. No association between total and cause-specific mortality was found for cold temperature.
Lindeboom et al. (2012)	General population Matlab, Bangladesh	Heat and cold effects (continuous temperature)	1983–2009	Time series analysis, Poisson generalized additive model (GAM)	Lag 0–21 days, (separate)	Time trend, season, public holiday, festivals, cyclones	Daily mean temperature, daily max temperature and daily min temperature Bangladesh Meteorological Department	All-cause mortality (n = 48,238) ICDRR, B́s (HDSS) in Matlab	1.4% (95 %CI: 0.7, 2.0) increase in mortality with every 1 °C decrease in mean temperature below 29.2 °C, and 0.2% (95% CI:0.1,0.3) increase in mortality with every 1 °C increase in mean temperature above 29.2 °C for lag 0. Elderly, aged 60 years and above, were most affected at lower temperatures, with a 5.4% (95% CI: −7.0, −3.5) increase in mortality with every 1 °C decrease in temperature below 23 °C (combined lag 0 and lag 1–5).
Babalola et al. (2018)	Infants and children under 5 years	Heat and cold effects (continuous temperature)	1982 – 2008	Time series analysis, OLS regression	Lag 0 months and lag 0–1 months	Month, age and gender	Monthly mean temperature, monthly max temperature Bangladesh	All-cause mortality (n = 49,426) ICDRR, B́s HDSS in Matlab	Each 1 °C increase in mean monthly temperature reduced monthly mortality by 3.7 (SE 1.5, p < 0.05)

(*continued on next page*)

Table 1 (*continued*)

Reference	Methods						Exposure	Outcome	Main findings
	Study population and location	Category of effect	Study period	Study design and statistical method	Lag structure	Control variables (confounders and effect modifiers)	Measure and source	Measure and source	
	Matlab, Bangladesh			with ARIMA errors			Meteorological Department		points. Effect sizes of mean monthly temperature were larger for neonates at 1.1 (SE 0.5, $p < 0.05$) than for post neonates at 0.9 (SE 0.3, $p < 0.05$) reductions in mortality per 1 °C.
Urban areas									
Hajat et al. (2005)	General population Delhi, India	Heat effects (continuous temperature)	1991–1994	Time series analysis, Poisson generalized linear model	Lag 0 days, lag 0–1 week, lag 0–4 weeks (cumulative)	Season, time trend, relative humidity, rainfall, particulate air pollution, day of the week, public holidays	Daily mean temperature India Meteorological Department	All-cause mortality, excluding violent deaths (mean daily number of deaths: 25, n ~ 36,500) and cause-specific mortality (cardiovascular, respiratory and other non-violent deaths) data from the New Delhi Municipal Committee (NDMC) provided by the World Bank	All-cause mortality increased by 3.2% (95%CI: 1.8, 4.5) per 1 °C increase in temperature above 20 °C (lag 0–7 days). Cardiovascular mortality increased by 4.3% (95%CI: 1.1, 7.6) per 1 °C increase in temperature above 20 °C and respiratory by 4.5% (95%CI: 0.0, 9.2) over the same lag. Heat effects were sustained up to 3–4 weeks for non-respiratory deaths. Children aged 0–14 years and elderly faced the highest risk, for children sustained up to 4 weeks.
McMichael (2008)	General population Delhi, India	Heat and cold effects (continuous temperature)	1991–1994	Time series analysis, Poisson generalized linear model	Lag 0–1 days, lag 0–13 days (cumulative)	Season, daily relative humidity, day of the week, public holidays, daily, particulate pollution concentration	Daily mean temperature India Meteorological Department	All-cause mortality, excluding external causes (mean daily number of deaths: 25, n ~ 36,500) and cause-specific mortality (cardio-respiratory and non-cardio-respiratory) data from the NDMC provided by the World Bank	All non-external causes of death increased by 3.9% (95%CI: 2.8, 5.1) for each 1 °C increase in temperature above 29 °C (95%CI: 8, 30) for lag 0–1 days and by 2.8% (95%CI: 0.7, 4.9) for each 1 °C decrease in temperature below 19 °C (95%CI:.–39) for lag 0–14 days. Cardiorespiratory mortality was found to increase by 203% (95%CI: 41.2, 553) for each 1 °C below a cold threshold of 12 °C (95%CI:. –13) and by 3.94% (95%CI: 2.38–5.53) above a heat threshold of 17 °C (95%CI: 12,19). Non-cardio-respiratory mortality increased by 2.7% (95%CI: 0.21, 5.16) for each 1 °C below 19 °C (.–30) and by 4.3% (95%CI: 2.89, 5.72) for each 1 °C above 30 °C (95% CI: 27, 31).

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Table 1 (*continued*)

Reference	Methods Study population and location	Category of effect	Study period	Study design and statistical method	Lag structure	Control variables (confounders and effect modifiers)	Exposure Measure and source	Outcome Measure and source	Main findings
Desai et al. (2015)	General population Surat, India	Heat effects (summer months)	2001–2012	Time series analysis, Studentś *t*-test, correlation analysis (lag 0, lag 1.)	Lag time correlation for one, two, three- and four-days lag	NA	Daily max T and heat index (HI) Tutiempo Network, S.L website, based on data exchanged under the World Meteorological Organization (WMO) World Weather Watch Program, local weather station	All-cause mortality (n = 36,167) Birth and Death Registration Department of Surat Municipal Corporation (SMC)	Daily mean number of deaths were 11% higher for days with maximum temperature above 40 °C compared to days with maximum temperature below 35 °C. Mean number of deaths were 9% higher during danger-level heat-risk days (HI = 41–54 °C) and 8% higher during high risk/ extreme danger heat days (HI = 41–54 °C), respectively, compared to mean number of deaths during less risky or caution days (HI = 27–31 °C).
Rathi et al. (2017)	General population Surat, India	Heat effects (summer months)	2014 – 2015 (March to May)	Time series analysis Analysis of variance, Student *t*-test, Turkeýs multiple comparison post hoc test, Pearson correlation analysis	Lag time correlation for one, two, three- and four-days lag	NA	Daily max temperature, heat index (HI) Tutiempo Network, S.L website, based on data exchanged under the WMO World Weather Watch Program, local weather station	all-cause mortality (n = 9,237) Health Department of SMC	The mean daily number of deaths for days with maximum temperature below 35 °C was 48.0 ± 7.7, which was 20% lower compared to the mean daily number of deaths for days with maximum temperature above or equal to 40 °C (57.3 ± 7.2).
Azhar (2014)	General population Ahmedabad India	Heat wave event	May 2010	Heat-episode analysis 7-day moving average; monthly rate ratio analysis; month-wise correlation	NA	NA	Daily max and monthly max temperature **Heat wave definition:** An excess of 5 °C over a normal daily historical maximum temperature (30-year average) of<40 °C; or an excess of 4 °C over a normal historical maximum temperature of>40 °C. If the actual maximum temperature is above 45 °C,a heatwave is declared irrespective of the normal historical maximum Temperature. Indian Meteorology Department's Meteorological Aerodrome Report, station at Ahmedabad airport	all-cause mortality (n = 4,462) Death records of Ahmedabad Municipal Corporation (AMC) Office of the Registrar of Births and Deaths	Excess mortality in May 2010 was estimated to be 1,344 deaths, or 43.1% above the reference period (May 2009 and May 2011). Mortality rate ratios for heatwave days (May 19–25, 2010) in 2010 were 1.76 (95% CI: 1.67, 1.83) compared to reference period 1 (May 12–18, 2010) and 2.12 (95% CI: 2.03, 2.21) compared to reference period 2 (May 19–25 from 2009 and 2011). The gender distribution highlights significantly more female deaths in the summer months and in the heatwave period.
Ghumman and Horney (2016)	General population Karachi, Pakistan	Heat wave event	June 2015	Heat-episode analysis Risk difference	NA	NA	Daily max temperature AccuWeather, State College, Pennsylvania USA	Deaths attributable to heat wave (n = 1,220) Official death certificates	Residents of Karachi were approximately 17 times as likely to die of a heat-related cause of death during June

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Table 1 (*continued*)

Reference	Methods Study population and location	Category of effect	Study period	Study design and statistical method	Lag structure	Control variables (confounders and effect modifiers)	Exposure Measure and source	Outcome Measure and source	Main findings
				and rate ratio calculation				from public and private hospitals	2015 (RR = 17.68; 95% CI: 13.8, 22.53) when compared with the reference period of June 2014. An excess risk of mortality from heat-related illness was found among the poor and those with lower levels of education during the 2015 heatwave period when compared with the reference period.
Hess et al. (2018)	General population Ahmedabad (Gujarat), India	Heat wave events	1 April to 30 June for 2007–2010 and 2014–15	Heat-episode analysis Distributed Lag Nonlinear Model	Up to 5 days lag	NA	Daily max temperature Meteorological Aviation Report (METAR) system	All-cause mortality Registrar of Births and Deaths office of AMC	Before the Heat Action Plan (HAP), the RR of mortality increased monotonically over 40 °C with maximum effect (RR of 2.34; 95% CI 1.98, 2.76) at 47 °C, lag 0. After the HAP, the RR also increased monotonically over 40 °C, but with a substantially lower maximum effect (RR of 1.25; 1.02, 1.53) estimated at 47 °C.
Nori-Sarma et al. (2019a)	General population (Mumbai $\geq$ 35 years old) Five cities in Northwest India: Jaipur, Churu, Idar, Himmatnag-ar, Mumbai	Heat wave episodes and continuous temperature	2000–2012	Time series analysis Generalized linear model for heat wave analysis and over-dispersed Poisson regression for continuous temperature analysis	NA	Day of the week, time trend, daily max temperature for a community at a specific lag (same day or previous day), adjusted dewpoint temperature, population offset	Daily max temperature, dewpoint temperature **Heat wave definitions:** 1) $\geq$ 2 consecutive days with daily maximum temperature (Tmax) higher than the community's 97th percentile Tmax. 2) Modified IMD definition: hill stations - Tmax of 5–6 °C or more above "normal" baseline temperature (over entire temperature record); plains stations - Tmax of 4–5 °C or more above "normal" baseline temperature (over entire temperature record) India Meteorological Department, NOAA's Global Summary of the Day (GSOD)	All-cause mortality (n = 389,665) Local municipal governments	Overall, across the four communities, mortality risk is estimated at 18.11% higher [95% interval – 5.31%, 47.33%] on 97PoT heatwave days compared to non-heatwave days. Using the IMD heatwave definition, estimated risk of mortality is 15.46% [−0.929%, 34.556%] comparing heatwave days to non-heatwave days. Limited evidence of effect modification by heatwave characteristics (intensity, duration, and timing in season) was found, but central estimates suggest more harmful heatwaves later in the warm season.
Nori-Sarma et al. (2019b)	General population (Mumbai $\geq$ 35 years old) Five cities in	Heat wave episodes	Jaipur (2005–2012); Churu (2003–2012); Idar and Himmatnagar	Time series analysis Propensity Score Matching, Quasi-	lag 0–14	time trend; seasonal and cyclical variation; days of the week; adjusted dew point temperature	Daily max temperature **Heat wave definitions:** 1) IMD heat wave definition; 2) > 2 days exceeding the 90th T	All-cause mortality (n = 389,665) Local municipal governments	There is a wide variation in the RR associated with heat waves depending on the criteria used for defining heat waves. RR of mortality

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Table 1 (*continued*)

Reference	Methods						Exposure	Outcome	Main findings
	Study population and location	Category of effect	Study period	Study design and statistical method	Lag structure	Control variables (confounders and effect modifiers)	Measure and source	Measure and source	
	Northwest India: Jaipur, Churu, Idar, Himmatnag-ar, Mumbai		(2006–2012); Mumbai (2000–2012)	Poisson regression model			percentile; 3) > 3 days exceeding the 90th T percentile; 4) > 4 days exceeding the 90th T percentile; 5) > 2 days exceeding the 92.5th T percentile; 6) > 3 days exceeding the 92.5th T percentile; 7) > 4 days exceeding the 92.5th T percentile; 8) > 2 days exceeding the 95th T percentile; 9) > 3 days exceeding the 95th T percentile; 10) > 4 days exceeding the 95th T percentile; 11) > 2 days exceeding the 97.5th T percentile; 12) > 3 days exceeding the 97.5th T percentile; 13) > 4 days exceeding the 97.5th T percentile; India Meteorological Department, NOAA's GSOD		ranged from 1.28 [95% CI:1.11, 1.46] in Churu under the 95%_2d heat wave definition to 1.03 [95% CI: 0.87, 1.23] in Idar and Himmatnagar under the 95%_4d definition. Some heat wave definitions were associated with a high RR; but lower attributable mortality because few days on record match those criteria. Heat waves that occur later in the season have a higher impact on health (higher RR) than those that occur earlier in the season.
Singh et al. (2019)	General population Varanasi, India	Continuous temperature (summer, winter, other months), heat wave episodes and cold spells	2009–2016	Time series analysis Semipara-metric quasi-Poisson regression model	A restricted distributed lag model up to 7 days' lag with polynomial of degree two and single lag model up to 7 days lag	Time trend, relative humidity, ambient air pollution and days of the week.	Daily min, max and mean temperature, diurnal temperature variations (DTV) **Heat wave definition:** an event during summer with daily mean temperature remaining equal to or above the 95th percentile of annual mean temperature (≥34.5 °C) for at least 3 consecutive days **Cold spell definition:** an event during winter with daily mean temperatures equal to or below the 5th percentile of annual mean temperature (≤14.7 °C) for at least 3 consecutive days [moving average lag (0–2)]. India Meteorological Department	All-cause mortality (n = 64,712) Municipal Corporation of Varanasi	During summer, a unit increase in daily temperature was associated with 5.6% increase in all-cause mortality (95% CI: 4.69, 6.53%). During winter, a unit decrease in daily temperature was associated with 1.5% increase in all-cause mortality (95% CI: 0.88, 2.18%). Increase in all-cause mortality was highest for people ≥ 65 years of age (−2.71% in winter to 6.83% in summer) and gradually reduced with the decrease in age, except for 0–4 years age group. Higher mortality found for non-institutional deaths (those dying outside the hospital) compared to institutional deaths (those dying within the hospital). RR of 1.13 (95% CI: 1.04, 1.22) for heat wave days vs. non-heat wave days and RR of 1.06 (95% CI: 0.98, 1.14)

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Table 1 (*continued*)

Reference	Methods Study population and location	Category of effect	Study period	Study design and statistical method	Lag structure	Control variables (confounders and effect modifiers)	Exposure Measure and source	Outcome Measure and source	Main findings
									for cold spell days vs. non-cold spell days. Higher RR for heat waves for females (RR 1.22, 95% CI: 1.09–1.37) compared to males (RR 1.09, 95% CI: 0.99–1.20), no significant difference for cold spells. Highest RR for heat waves for age group <4 years (RR 1.39, 95% CI: 1.16–1.69), and for cold spells – 45–64 years age group (RR 1.17, 95% CI: 1.03–1.33). The DTV showed a negative association with all-cause mortality.
Dutta et al. (2020)	General population Bhubaneswar city (Odisha), India	Continuous temperature (summer months)	March to July (2007 – 2014)	Time series analysis Generalized Additive Model with quasi-Poisson distribution, DLNM	Lag 0 and lag 0–1 days	lLLong-term trend, seasonality, day of the year, day of the week, relative humidity	Daily max and daily min temperature Bhubaneswar Meteorological Centre of the Indian Meteorological Department	All-cause mortality (n = 16,033) Bhubaneswar Municipal Corporation	Two ‘thresholds’ of max temperatures were identified, beyond which mortality increases – lower at 36.2 °C and upper at 40.5 °C. Every degree rise of T-max above 36.2 °C increased the mortality risk by 2% (RR: 1.02; 95% CI 1.01, 1.03) and each degree rise of T-max above 40.5 °C increased it by 6% (RR: 1.0616, 95% CI: 1.03, 1.09). Daily T-max had significantly more effect on daily all-cause mortality rates when the minimum T-min was above its median value (25.6 °C) as compared to when it was below the median.
Urban and rural areas									
Burkart et al. (2014b)	General population Bangladesh	Heat and cold effects (continuous temperature)	2003–2007	Time series analysis, Semi-parametric Poisson DLNM	Lag 0–1 days, lag 0–4 days for children and youths (cumulative)	Time trend, season, and day of the week	Daily mean values of the universal thermal climate index (UTCI) Bangladesh Meteorological Department	All-cause mortality, excluding accidental and maternity-related deaths and deaths of infants younger than 1 year of age (n = 22,840) and cause-specific mortality (cardiovascular and infectious diseases) ICDRR, B́s SVRS in Bangladesh	All-cause mortality and mortality from cardiovascular and infectious diseases were positively associated with UTCI below and above a threshold, ranging between 34 and 35 °C UTCI. All-cause mortality increased by 31.3% (95%CI: 24.5 – 44.3) per 1 °C increase in UTCI above breakpoint (lag 0–1). Heat effects were strongly

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Table 1 (*continued*)

Reference	Methods						Exposure	Outcome	Main findings
	Study population and location	Category of effect	Study period	Study design and statistical method	Lag structure	Control variables (confounders and effect modifiers)	Measure and source	Measure and source	
									pronounced for the elderly, for males, and for those living in urban and high socio-economic status areas.
Burkart et al. (2011)	General population Bangladesh	Heat and cold effects (continuous temperature)	2003–2007	Time series analysis, Poisson generalized additive model	Lag 0–1 days, lag 0–6 days and lag 0–13 days (cumulative)	Time trend, season, day of the month	Heat Index (HI), physiological equivalent temperature (PET), universal thermal climate index (UTCI) Bangladesh Meteorological Department	All-cause mortality, excluding accidental, maternity related and infant mortality (n = 21, 655) and cause-specific mortality (cardiovascular mortality) ICDRR,B́s SVRS in Bangladesh	Mortality increased by 4.4% (95%CI: +/-5.4) per 1 °C increase in temperature above a specific threshold in rural areas and 13.7% (95% CI: +/-10.9) in urban areas (lag 0–1). Mortality increased by 2.6 (95%CI: +/-0.6) per 1 °C decrease in temperature below threshold in rural areas and by 3.3% (95%CI: +/-1.8) in urban areas (lag 0–13), respectively. A heat effect on cardiovascular mortality was only observed in urban areas.
Fu et al. (2018)	General population India	Heat and cold effects (continuous temperature)	2001–2013	Case-crossover study, DLNM	Lag 0–21 days (cumulative)	Potential temporal confounders and time-invariant confounders controlled for "by design"	Daily mean temperature India Meteorological Department	All-cause mortality at all ages, excluding injury and ill-defined medical causes (n = 411,613) and cause-specific mortality (ischemic heart disease, respiratory diseases, malaria and cancer among adults aged 30–69) India's Million Death Study, Sample Registration System, Registrar General of India	For all medical causes and ages, moderately cold temperature was associated with a higher attributable risk (OR) (6.3%, 95% CI: 1.1, 11.1) than extremely cold, moderately hot, and extremely hot temperatures, each of which were<0.6%. The risk related to moderately cold temperature was most pronounced for the population aged 30–69 years and 70 + . For cause-specific deaths at ages 30–69 years, moderately cold temperature was associated with attributable risks of 27.2% (95% CI: 11.4, 40.2) for stroke, 9.7% (95% CI: 3.7 to 15.3) for IHD, and 6.5% (95% CI: 3.5, 9.2) for respiratory diseases.
Burkart and Kinney (2017)	General population Bangladesh	Cold effects (continuous temperature and seasonal temperature)	2003–2007	Time series analysis, Poisson GAM and Poisson DLNM	Lag 0–1 days, lag 0–2 days, lag 0–4 days, lag 0–7 days, lag 0–14 days and lag 0–21 days (cumulative)	Time trend, season, day of the month	Daily mean temperature, daily max temperature, daily min temperature, diurnal temperature range (DTR) Bangladesh Meteorological Department	All-cause mortality, excluding external causes and maternity-related deaths (n = 25, 226) ICDRR, B́s SVRS in Bangladesh	During the winter season, mortality increased with 1.7% (95% CI = 0.86–2.54%) per 1 °C decrease in temperature (lag 0–1 days). Heat effects observed during the summer

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Table 1 (*continued*)

Reference	Methods Study population and location	Category of effect	Study period	Study design and statistical method	Lag structure	Control variables (confounders and effect modifiers)	Exposure Measure and source	Outcome Measure and source	Main findings
									season were stronger than over the entire year.
Shrestha et al. (2017)	General population Nepal	Heat and cold effects (continuous variable)	2009–2014	Time series analysis Generalized linear model (GLM) with log link function (Poisson model)	3-day prior moving average for all-cause mortality; 7-day geometrical decay effect for water- and vector- borne mortality	Seasonal dummy variables, day of week (Saturday) and secular trend, humidity, wind [for all-cause mortality]; wind, time trend [for water- and vector-borne mortality]	Daily average temperature weekly data of the number of days of occurrence of extreme events Department of Hydrology and Meteorology (DHM), Kathmandu, 16 meteorological stations in the country	All-cause mortality (n = 10,000) and cause-specific mortality (vector-bore and water-borne diseases) inpatient records from 22 hospitals in Nepal	All-cause mortality increased by 1.4% per 1 °C increase in the absolute difference of average temperature with its overall average (20 °C) (3-day prior moving average) (parameter estimate: 0.014, 95% CI: 0.002, 0.026). All-cause mortality also increased with decreasing temperature relative to overall average condition (20 °C). Mortality from water-borne and vector-borne diseases increased by 3.7% per 1 °C rise in daily average temperature (7-day geometrical decay effect). Association between mortality from water-borne and vector-borne diseases and extremely cold days (<4.6 °C) was also reported, as well as between mortality from water borne and renal diseases and extremely hot days (above 95 percentile of maximum temperature).
Mazdiyasni et al. (2017)	General population India	Heat wave episodes	1960–2009	Annual time series analysis Correlation analysis, Kolmogorov-Smirnov test; Man-Kendall Test and Conditional probabilistic model	NA	NA	Daily mean and max temperature (summer months) **Heat wave definition:** Three or more consecutive days of temperatures above the 85th percentile of the hottest month for each specific location. Four different heatwave properties are assessed: (i) accumulated heatwave intensity, (ii) annual heatwave count, (iii) mean heatwave duration, and (iv) heatwave days. India Meteorological Department	heat-related mortality (n = 10, 619) India Meteorological Department, annual reports	The increase in summer mean temperature in India over 1960–2009 corresponds to a 146% increase in the probability of heat-related mortality events of >100 people.
Murari et al. (2014)	General population Four states in India: Delhi, Rajasthan,	Heat wave episodes	1997–2009	Annual Time series analysis OLS regression	NA	NA	Annual number of severe heat wave days (HWD) **Heat wave definition:** If the maximum	Heat wave-induced mortality (number of deaths not reported) Mortality records,	Positive significant association (90% CI) between annual mortality rates and annual number of

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Table 1 (*continued*)

Reference	Methods						Exposure	Outcome	Main findings
	Study population and location	Category of effect	Study period	Study design and statistical method	Lag structure	Control variables (confounders and effect modifiers)	Measure and source	Measure and source	
	Maharashtra and Orissa						temperature of a day exceeds 45° C, irrespective of the normal maximum temperature of a region, that day is defined as a severe HWD. In case a day's maximum temperature is<45° C, that day is defined as a severe HWD when (1) the day's maximum temperature is at least 7° C greater than the normal temperature, and (2) the maximum temperature of that day is above 40° C. Three different heat wave properties are characterised: (i) severe heat wave intensity, (ii) duration and (iii) frequency India Meteorological Department	obtained from the Ministry of Home Affairs (Government of India)	severe HWDs is found for Delhi (3.1, SE: +/-1.45), Rajasthan (5.6, SE:+/-1.46), and Maharashtra (2.3, SE:+/-1.46).
Nissan et al. (2017)	General population Bangladesh	Heat wave episodes	1989–2011	Time series analysis Generalized additive regression models	NA	NA	Daily max temperature, max and min day-and-night temperature, daily max heat index, daily max and min heat index, daily average temperature, average heat index **Heat wave definition:** Definitions of six heat wave indices are proposed and assessed, incorporating a range of conditions known to be important for heat stress: day- and nighttimes temperatures, humidity, and duration. According to all indices, a heat-wave day is declared on the third consecutive day on which one (or two) variables exceed the 95th percentile of daily values. [Calculated according to the formulation used by the U.S. National Weather Service] Bangladesh Meteorological Department	All-cause mortality, excluding maternal and accidental deaths (n = 25,223) ICDRR, B́s Sample Vital Registration System (SVRS) in Bangladesh	All proposed indices are a statistically significant predictor of mortality in Bangladesh, with effect estimates ranging between 10.4% and 24.0% increase in mortality during heat wave vs. non-heat wave days. The study findings recommend using the day-and-night index, which defines a heat wave as elevated day- and night-time temperatures above the 95th percentile for 3 consecutive days (22.3% increase in mortality, CI: 8.2, 38.2). The proposed definition is deemed appropriate for preparedness measures in a heat early warning system (HEWS) because it is both related to human health outcomes and forecastable.

mortality (Ghumman and Horney, 2016).

In terms of geographical coverage, 63% (n = 17) of the selected studies focused on India, eight on Bangladesh and one on Pakistan and Nepal, respectively. It is important to note that no epidemiological studies on the association between ambient temperature and mortality were identified for half of the countries in the region, namely Afghanistan, Bhutan, Maldives, and Sri Lanka. Eight of the studies included in this review (30%) focused solely on rural populations and eleven (40.7%) on urban, while eight studies (30%) evaluated the association between ambient temperature or heat waves and mortality for the general population in a country (including urban and rural areas). All the included studies on ambient temperature and heat waves are summarised in Table 1.

In total, the included studies analysed >1.5 million deaths. However, eleven (41%) of the selected articles were based on identical populations, analysed over the same or an overlapping period. The most extensive datasets were provided by the Matlabs Health and Demographic Surveillance System (HDSS) (around 49 thousand deaths), which is the oldest field site in the region dating back to 1966 and maintained by the International Centre for Diarrheal Disease Research, Bangladesh (ICDRR,B), and India's Million Death Study (around 412 thousand deaths), which is based on one of the largest Sample Vital Registration Systems (SVRS) in the world. Other data sources included several smaller HDSSs, ICDRR,Bs SVRS in Bangladesh, inpatient hospital records, death records from municipal registrars and heat-related mortality statistics compiled by the IMD. Apart from all-cause mortality, eight studies reported effects of temperature on cause-specific mortality, with the most commonly examined causes being cardiovascular, respiratory, and infectious disease mortality. Outcomes related to perinatal mortality, ischemic heart disease, cancer, malaria, parasitic, vector-borne and water-borne diseases, and external causes were also assessed. Some studies on heat waves analysed specifically heat-attributable deaths (Murari et al., 2015; Ghumman and Horney, 2016; Mazdiyasni et al., 2017)

Most selected articles (n = 24; 89%) examined the effects of short-term variations of temperature on mortality, thus measuring heat and/or cold exposure as daily temperature. However, several studies applied a different timeframe for assessing temperature-mortality effects: Alam et al. (2012) analysed effects based on weekly mean temperature "to minimise fluctuations due to small number" of observations, Babalola et al. (2018) used monthly mean and maximum temperature as a unit of analysis to investigate effects on infant and child mortality, while Murari et al. (2015) and Mazdiyasni et al. (2017) analysed annual (summer) mortality and occurrences of heat waves and heat wave days. The majority of articles considering continuous temperature effects (n = 11; 55%) used mean temperature as it was demonstrated to be a better predictor of the temperature-mortality relationship compared to maximum and minimum temperatures, or because it permitted better comparability with other studies. Several studies (n = 9; 45%) used maximum and minimum daily temperature, in some cases as a sensitivity analysis. Five articles evaluated the combined effect of other meteorological parameters such as humidity, wind speed, and mean radiant temperature with temperature by using an index (Heat Index, Universal Thermal Climate Index, Physiological Equivalent Temperature). Two studies also investigated the impact of temperature variability, i.e., the difference between daily maximum and minimum temperatures, or diurnal range. Excluding studies on heat waves, three of the selected articles limited their analysis to summer months and two to summer and winter months to isolate heat and cold effects. Also, the indices adopted by Nissan et al. (2017) incorporated relative humidity and day-time as well as night-time conditions.

About 80% of the studies used data from local stations obtained from a national meteorological department. Two studies relied on climatic records from weather websites provided from the World Meteorological Organization (WMO) under the World Weather Watch Program, one from a weather website, whose exact source we could not trace, and four on data from the National Oceanic and Atmospheric Administration (NOAA), which are collected from local airports. The period analysed in the time series studies ranged from several months to 49 years (Mazdiyasni et al. 2017).

Different approaches were used to determine a threshold for hot and cold effects and to quantify the temperature-mortality association. In general, threshold values were determined based on a specific percentile of the temperature data, through visual inspection of the temperature-mortality plots, or using statistical procedures such as maximum likelihood estimation. Four of the studies on heat waves selected thresholds based on an existing national heat wave definition and four based on a specific percentile of the data. MMTs in the included studies were highly dependent on the temperature and mortality measures, the health outcome of interest, the statistical analysis (non-linear, semi-linear or linear models) and the considered lag structure. Therefore, it is difficult to draw comparisons of the threshold values across studies directly. For articles using mean daily temperature and all-cause daily death counts the temperature threshold values below which mortality started to rise ranged from 19 °C to 30 °C for lags 0–13 and lag 0–14 (cold effects). The threshold above which deaths started to increase ranged from 20 °C to 31 °C for lag 0–1 days (heat effects). Outcomes were reported using a variety of metrics such as relative risk (RR), odds ratio (OR), percentage change in mortality, regression coefficients, and probability of a certain number of deaths.

As expected, there were wide variations in observed temperature ranges across studies and locations. For the articles reporting these, daily maximum temperatures varied between 37.8 °C and 46.2 °C (n = 9), daily minimum temperatures between 8.6 °C and 28.5 °C (n = 6) and daily mean temperatures were in the range of 13.2 °C and 35.6 °C (n = 10). These temperature ranges corresponded to the diverse climatic conditions in the region. Study locations covered eight main climatic zones based on the Koeppen-Geiger climate classification and were dominated by four main climatic zones: tropical wet and dry, humid subtropical, warm semi-arid and warm desert (see Fig. 3). Areas in the tropical zone, found along the southern parts of India and in Bangladesh, experience mostly hot summers and receive heavy rainfall during the monsoon periods. The humid subtropical zone, which spans the Indo-Gangetic plains, is also characterized by hot summers, but cooler winters. The warm semi-arid climate, found in some parts of India, tends to have hot summers and warm to cool winters, with very little precipitation. Finally, the warm desert climatic zone, found in the northern edge of India and most of Pakistan, is characterized by extreme temperature variations, with hot summers and cool or cold winters, and minimal precipitation.

Concerning study design, articles evaluating the impact of heat and/or cold on mortality were based either on time series or case-crossover design. As previously noted by Basu (2009) and demonstrated in several studies on temperature and mortality, study results should be similar irrespective of whether they are based on time series or case-crossover design. Studies investigating heat wave effects were based either on episode analysis, comparing deaths in a heat wave vs. matched non-heat wave period/days, or on time series analysis, regressing daily or annual mortality with heat wave/non-heat wave days or an annual number of heat waves.

Most time series studies included season and time trend as confounding variables in their models, using smoothing functions with specified degrees of freedom, while several studies considered additional confounders such as day of the week, public holidays, humidity, rainfall, and particulate air pollution. Control for most of these confounders was not necessary for case-control/case crossover studies since they controlled for potential temporal confounders "by design", i.e., by matching control days by day of the week and month across years. Also, in the case of case-crossover studies as well as time series controlling for trend, biases due to individual characteristics such as genetics, behaviours and physiological differences are also inherently accounted for by study design.

The majority of included time series studies also examined harvesting and delayed effects of non-optimum temperature exposure and reported cumulative impacts over periods prior to the mortality event, with the considered lag structure ranging from a single day for high temperatures to 28 days for low temperatures. Harvesting or mortality displacement effects are characterised as excess mortality over the first few days of relatively high temperature being offset by reduced mortality in the following days of lower temperatures. Analysing harvesting is essential for determining the full magnitude of the public health issue, since its presence indicates that frail individuals were the only major population subgroup affected by the exposure and that their deaths were brought forward by a certain number of days (Gasparrini, Armstrong and Kenward, 2010; Hajat and Kosatky, 2010).

3.3. *Assessment of the risk of bias in individual studies*

We found substantial variation in the quality of the included articles as shown in the summary table for all studies (Table 2) and in the summary tables for individual assessments (Supplementary Table S5-S31). We identified measurement of exposure, measurement of outcome, and appropriateness of statistical method as the most common weakness in the quality of the body of evidence. In particular, twelve studies were judged to have *definitely high* or *probably high risk* of exposure measurement bias. These low ratings were related to the use of weekly or monthly temperature observations as opposed to daily time series, which might attenuate the true temperature effect or capture seasonal effects rather than true temperature effects, as well as large spatial aggregation of exposure data, which might conceal local temperature effects on mortality, and lack of sufficient information on data source and quality control of the data. Fourteen studies were rated as having a *definitely high* or *probably high risk* of measurement bias due to the use of data from unofficial sources with low reliability (e.g. newspapers, unofficial reports) or the use of municipal and vital registry data, which is considered as incomplete and under-representative for the countries in the region as large number of people die outside hospitals and without being registered (Setel et al., 2007; Jha, 2014; Mikkelsen et al., 2015). Seven of the studies were judged to have *definitely high* or *probably high risk* of bias for using an inappropriate statistical method. In most cases this was related to the use of statistical methods not appropriate for count data (e.g. OLS regression, Pearson correlation coefficient, ANOVA analysis, *t*-test, etc.) or inference of a causal association based on inappropriate study design or method.

Four of the included studies were identified as being at *probably high risk* of selection bias. Eight of the studies did not control for some of the primary confounders (seasonality or time trend) or any confounders at all and were, therefore, rated as being at *definitely high* or *probably high risk* of confounding bias based on our assessment criteria. One study was evaluated as being at *definitely high* risk of bias due to inconsistencies in reporting.

Seven of the overall 20 studies that examined risk of mortality with continuous exposure to ambient temperature, were judged to have *definitely low* or *probably low risk* of bias across all the risk of bias domains. In contrast, all the nine studies focusing on the mortality risk of heat wave episodes received *probably high* or *definitely high risk* of bias rating for one or more of the domains.

3.4. *Synthesis of findings on primary research question*

3.4.1. *Synthesis of findings on temperature and all-cause mortality*

Included studies suggest that both hot and cold temperatures are associated with mortality in the South Asian population. However, results across studies were not homogenous in terms of the direction (increasing mortality with decreasing or increasing temperatures beyond cold and heat thresholds) and magnitude of effects. Furthermore, estimates from the *meta*-analysis confirm evidence of impacts for high temperatures only.

From the eight studies, which analysed the susceptibility of rural populations to non-optimum temperature, six found an association between cold temperature and mortality, while five found a heat effect. All studies on urban areas apart from two focused solely on heat effects and showed evidence for heat-related mortality, while two documented both heat and cold-related mortality (McMichael et al., 2008; Singh et al., 2019). Burkart et al. (2011) specifically examined and contrasted the temperature effects for urban and rural areas in Bangladesh. Although they observed an increase in mortality at high and low temperatures for both rural and urban areas, urban areas were found to exhibit generally stronger and longer lasting heat effects. The other four studies (Burkart et al., 2014b; Burkart and Kinney, 2017; Fu et al., 2018; Shrestha et al., 2017), which examined the relationship between temperature and excess mortality at a national scale, also ascertained both heat and cold effects. Overall, studies in India found that substantial health impacts occur even at temperatures lower than those specified in the national heat wave definition.

Results across studies also varied considerably in terms of the magnitude of the observed heat and cold effects. The heterogeneity of studies in terms of outcome and exposure metrics, temperature thresholds and lags examined did not permit direct comparison of effect estimates across studies. The mortality increases due to elevated daily mean temperatures in the included studies using linear approximation ranged from 0.2% to 3.2% per 1° C increase in temperature above a MMT threshold (n = 5), while for cold effects excess mortality was in the range of 1.4% – 3.2% per 1° C decrease in temperature below a MMT threshold (n = 4). While Burkart et al. (2011); Ingole et al. (2017); McMichael et al. (2008) found heat effects to outweigh cold effects in Vadu, Bangladesh, and Delhi, and Ingole et al. (2012) observed comparable effects of heat and cold in Vadu, Lindeboom et al. (2012) and Fu et al. (2018) found stronger effects for cold and moderately cold temperatures compared to hot temperatures in Matlab and India, respectively. Some inconsistencies in the reported results across studies may be partly attributed to differences in methodology and model specification (e.g., statistical method, adjustment for confounders, lag structure and thresholds used), but also specific characteristics of the locations or the populations that might determine vulnerability. Four of the twenty studies on ambient temperature and all-cause mortality were judged to have probably high or definitely high risk of bias by at least two of the assessment criteria.

Only five of the studies on all-cause mortality and ambient temperature were judged as homogenous enough to be combined in one *meta*-analysis. Only two of these were judged to have probably high or definitely high risk of bias based on one of the assessment criteria. Fig. 4 shows the pooled estimates of the association at every 0.5° C increment of temperature with reference to a common threshold of 24.5° C (lag 0–1) and 26.5° C (lag 0–13). Since not all studies cover the same temperature range, the colour shades and the legend underneath indicate how many and which studies specifically contribute to the pooled effect estimates at different temperature increments. The pooled RR estimates at different temperatures represent the *meta*-analysed RR estimates of individual curves at these points. The *meta*-analysis shows a U-shaped temperature-mortality relationship, with a temperature band of minimum mortality of 22° C – 25° C for lag 0–1 days and 25° C – 28° C for lag 0–13 days, respectively. However, a statistically significant association was found only at temperatures above the upper limits of these bands, i.e. indicating heat effects. In particular, a significant positive association can be observed at temperatures above 31° C for lag 0–1 days and above 34° C for lag 0–13 days. For lag 0–1 days, 10° C increase in temperature above 25° C was associated with a 22% (RR = 1.22, 95% CI: 1.10–1.36) increase in the risk of mortality, with the RR increasing steeply at higher temperatures. For lag 0–13 days, 5.5° C increase in temperature above 26.5° C was associated with a 23% (RR = 1.23, 95% CI: 1.11–1.37) increase in the risk of mortality, with the effect increasing even more steeply at the higher range of the exposure, but the precision of estimates decreasing due to the small number of studies reporting effects at these ranges.

3.4.2. *Synthesis of findings on heat wave events and all-cause mortality*

All nine studies, which examined the effect of heat waves on all-cause mortality find a positive association. Six of these studies refer directly to all-cause mortality, while three studies refer to all-cause mortality indirectly, by considering heat wave-induced, heat-related or heat-attributable mortality. Since none of the studies provides specific information on which causes of death were classified as "heat-related", we consider them as a proxy of all-cause mortality, but note that the selection criteria in these studies are likely to be arbitrary and to exclude unreported deaths or indirect causes of death. The reported RR of all-cause mortality during a heat wave vs. non-heat wave period/days in studies ranges between 1.03 and 2.34 (Hess et al., 2018; Nori-Sarma et al., 2019a; Singh et al., 2019). Nori-Sarma et al. (2019a) demonstrates that the estimated RR from heat waves depends considerably on the exact definition of heat waves, which highlights the difficulty of comparing results across studies with very heterogenous definitions.

Several studies report results using alternative effect estimates to risk ratios. For example, Azhar et al. (2014) report a 43.1% increase in all-cause deaths during the 2010 Ahmedabad heat wave compared to the reference period. Mazdiyasni et al. (2017) find that the increase in summer mean temperature in India over 1960–2009 corresponded to a 146% increase in the probability of heat-related mortality events of >100 people. Ghumman and Horney (2016) find that residents of Karachi were approximately 17 times as likely to die of a heat-related cause of death during the June 2015 heatwave when compared to a reference period of June 2014. Although all studies find a positive association between mortality and heat wave episodes, the different methodological approaches, study designs, definitions of heat waves and heat wave-related mortality do not allow for a direct comparison of effect estimates across studies. Five of the nine studies on heat waves were judged to have probably high or definitely high risk of bias by at least two of the assessment criteria, with three of them by five of the assessment criteria.

3.5. *Additional analyses*

3.5.1. *Temperature and cause-specific mortality*

Five studies reported a pronounced heat effect on cardiovascular disease (CVD) mortality, with effects ranging from 1.9% increase in mortality with every 1 °C increase in temperature above specific threshold in Delhi (Hajat et al., 2005) to 62.9% in Bangladesh (Hashizume et al., 2009). Burkart et al. (2011, 2014b) found severe heat effects on CVD mortality particularly in urban areas as opposed to rural areas. The analysis of Burkart et al. (2014b) also revealed a higher risk of heat-related CVD mortality among males than females. In comparison, only two studies reported cold effects on CVD mortality, but these were much weaker, 1% and 9.9%, respectively (Burkart et al., 2011; Hashizume, 2009). Fu et al. (2018) also documented both a cold and heat association of temperature with Ischemic Heart Disease (IHD)-related mortality.

Temperature effects on respiratory mortality were also mixed. Hashizume et al. (2009) reported strong cold effects (17.5% increase in mortality for each 1 °C decrease in temperature below a threshold), but no heat effects, while Hajat et al. (2005b) and Fu et al. (2018) demonstrated both heat and cold effects.

Regarding mortality from infectious diseases, both Burkart et al. (2014) and Hashizume et al. (2009) showed marked heat effects, with 83.4% (lag 0–13 days) and 10.4% increase in mortality above a

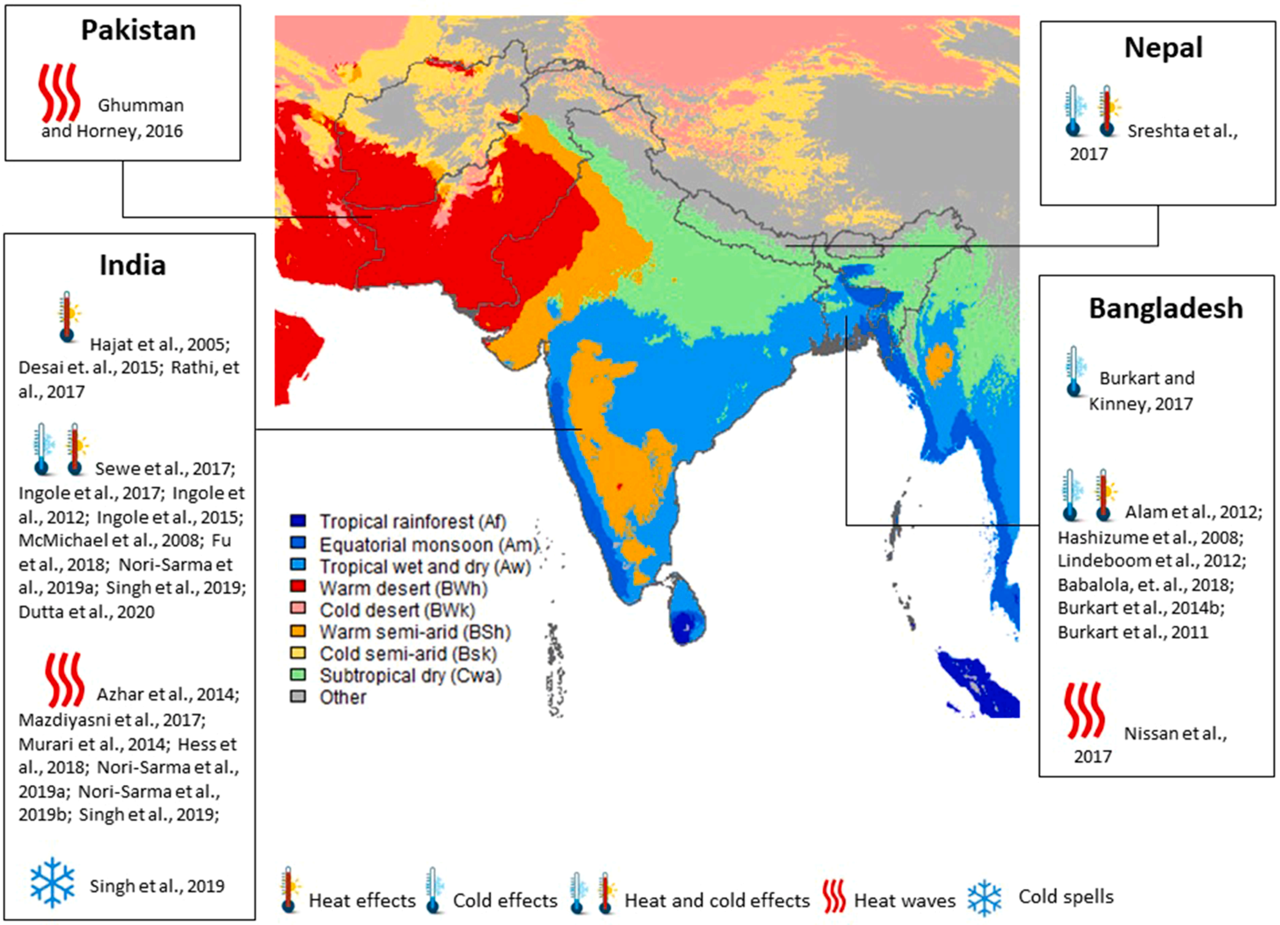

Fig. 3. Map of the climatic zones and the number of studies conducted in each country by category of effect. Source: Own figure, climatic zones based on Köppen-Geiger climate classification maps (Beck et al., 2018).

Table 2
Summary of the results of the risk of bias assessment in individual studies.

Study	Selection bias	Confounding	Exposure assessment	Outcome assessment	Selective reporting	Other bias
Studies on ambient temperatures (n = 20)						
Alam et al. (2012)	PL	PL	DH	PL	PL	PL
Hashizume et al. (2008)	PL	DL	PL	PL	PL	DL
Sewe et al. (2017)	DL	DL	PL	DL	PL	DL
McMichael et al. (2008)	PL	DL	PL	DH	PL	DL
Burkart et al. (2014b)	PL	DL	PH	PL	PL	DL
Burkart et al. (2011)	DL	DL	PH	DL	PL	DL
Ingole et al. (2017)	PL	DL	PL	PL	PL	DL
Ingole et al. (2012)	DL	PL	PL	DL	PL	DL
Ingole et al. (2015)	PL	DL	PL	PL	PL	DL
Hajat et al. (2005)	PL	DL	PL	PH	PL	DL
Fu et al. (2018)	PL	DL	PL	PL	PL	DL
Lindeboom et al. (2012)	PL	DL	PL	PL	PL	DL
Desai et al. (2015)	PH	DH	PH	PH	DH	DH
Burkart and Kinney (2017)	DL	DL	PH	DL	PL	DL
Babalola et al. (2018)	DL	PH	DH	DL	PL	PH
Rathi et al. (2017)	PL	PH	PH	PH	PL	DH
Sreshta et al. (2017)	PL	DL	PH	PH	PL	DL
Dutta et al. (2019)	PL	DL	PL	PH	PL	PL
Nori-Sarma et al. (2019a)*	PL	DL	DL	PH	PL	DL
Singh et al. (2019)*	DL	DL	PL	PH	PL	DL
Studies on heatwave episodes (n = 9)						
Azhar et al. (2014)	DL	PH	PL	PH	PL	DH
Ghumman and Horney (2016)	PH	PH	PH	PH	PL	DH
Mazdiyasni et al. (2017)	PH	PH	DH	DH	PL	DH
Murari et. al (2014)	PH	PH	PH	DH	PL	DH
Nissan et. al (2017)	PL	DL	PH	PL	PL	DL
Hess et al. (2018)	PL	PH	PL	PH	PL	PL
Nori-Sarma et al. (2019a)	PL	DL	DL	PH	PL	DL
Nori-Sarma et al. (2019b) *	PL	DL	PL	PH	PL	DL
Singh et al. (2019) *	DL	DL	PL	PH	PL	DL

DL = Definitely Low RoB; PL = Probably Low RoB; PH = Probably High RoB; DH = Definitely High RoB;
*The study examined both effects of heat wave episodes and continues temperature, therefore they have been included twice in the table.
The underlined studies are those included in the *meta*-analysis.

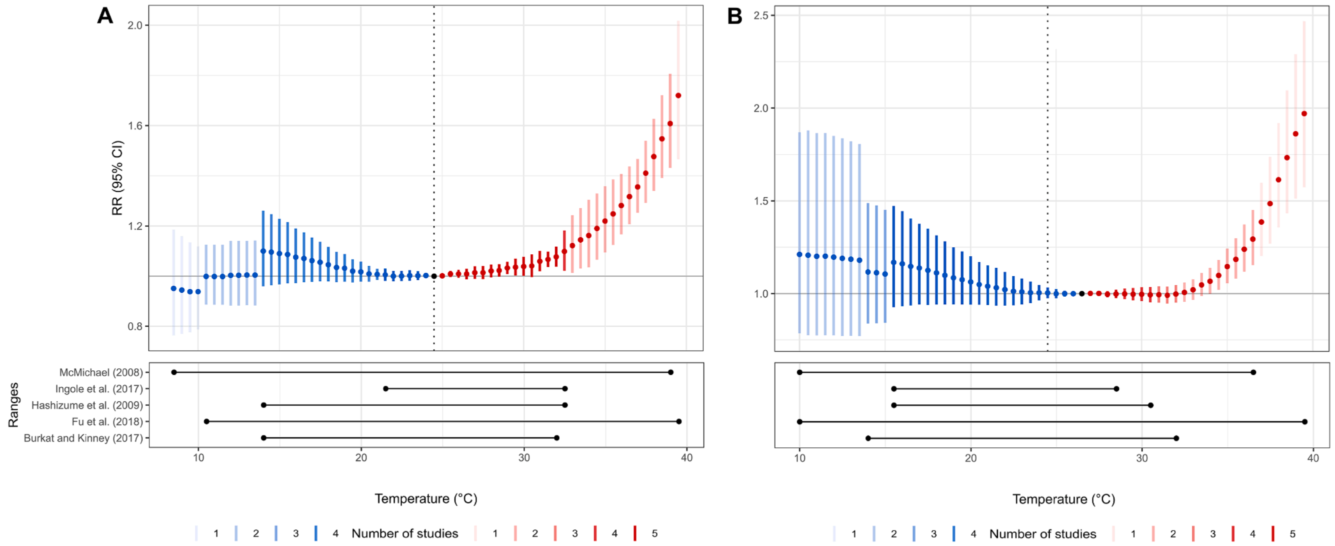

Fig. 4. Pooled estimates of the temperature-all-cause mortality association at (A) lag 0–1 days and (B) lag 0–13 days. Studies included in the *meta*-analysis: Burkart and Kinney (2017), Fu et al. (2018), Hashizume et al. (2009), Ingole et al. (2017), McMichael et al. (2008).

threshold per 1 °C in (equivalent) temperature, respectively. As opposed to the higher risk of heat-related all-cause and cardiovascular mortality observed in urban areas, Burkart et al. (2014) found a significant increase in infectious disease mortality only for rural areas. Ingole et al. (2015) did not find any association of deaths from infectious causes with heat or cold, considering delayed effects of up to 4 days.

With respect to the other examined causes of death, strong cold effects were found for perinatal mortality (Hashizume et al., 2009). Modest increases in risk of malaria deaths were observed at 14 °C – 20 °C (Fu et al., 2018). Statistically significant positive associations were shown for temperature and water- and vector-borne disease mortality (Shrestha et al., 2017) and no association was found for temperature with external causes of death (Ingole et al., 2015) and cancer (Fu et al., 2018).

3.5.2. *Lagged effects and mortality displacement*

Most of the studies also investigated the lag structure and some also the temporal displacement of heat and cold effects. In most studies hot temperatures were shown to have a more immediate effect, lasting from 1 to 6 days, but several studies (n = 4) showed heat effects over a sustained period of time (up to 21 days). Studies reported sustained impacts of cold temperatures over 4 to 14 days after exposure. The duration of temperature effects seemed to differ considerably across causes of death, age and sex. For instance, Burkart et al. (2014) reported more delayed heat effects in children and younger adults, and Hajat et al. (2005b) demonstrated more sustained risks for children and non-respiratory diseases. Babalola et al. (2018), who considered monthly infant mortality, found evidence for cold effects for lag 0 months. None of the five studies, which focused on mortality related to heat waves, formally modeled delayed effects of exposure. Azhar et al. (2014) assessed possible delayed effects graphically but did not find any evidence for these. Considering this methodological shortcoming, one cannot exclude that the reported excess mortality in the included heat wave studies represents, at least to a certain extent, a harvesting effect rather than a substantial increase in mortality. However, it has been shown that the more extreme weather events are, the smaller the harvesting effect is (Saha, Davis and Hondula, 2014).

3.5.3. *Vulnerable populations*

The identification of specific segments of the population most vulnerable to non-optimum temperatures has been of specific interest in most of the included studies as in climate-related research in general. However, results across studies do not provide a homogenous picture regarding vulnerabilities, and this is true even for studies based on the same population, but using different study design and/or statistical method. Most of the reviewed studies explored only vulnerabilities based on age and sex and cause of death, possibly due to the lack of sufficient data on socio-economic and other characteristics. Only Burkart et al. (2014) and Ingole et al. (2017) also analysed differences due to other individual or intra-population characteristics such as socio-economic status, education, occupation, housing, or level of urbanisation. Cold effects have been shown to be most pronounced among infants and children younger than 5 years (Ingole et al., 2012; Babalola et al., 2018) or <15 years (Hashizume, 2009), the elderly (Lindeboom et al., 2012; Ingole et al., 2017; Fu et al., 2018), adults aged 20–69 (Alam et al., 2012; Fu et al., 2018), and those employed in housework (Ingole et al., 2017). Alam et al. (2012) found cold to exert a stronger effect on females, while Ingole et al. (2017, 2012) and Singh et al. (2019) did not find any gender differences. Stronger heat effects were demonstrated for children aged 0–14 (Hajat et al., 2005; Sewe et al., 2018; Singh et al., 2019), adults aged 20–59 (Ingole et al., 2012) and the elderly (Burkart et al., 2014b; Singh et al., 2019). However, no such association was found by Ingole et al. (2015) for the elderly (60 and older) in Vadu HDSS. Burkart et al. (2014) and Ingole et al. (2015) showed that males in Bangladesh, particularly the elderly, and males in Vadu HDSS appear to face increased mortality risk on hot days. However, Ingole et al. (2017) demonstrated the opposite for women in Vadu (results were not statistically significant), and Ingole et al. (2012) did not find any significant association by gender. In terms of socio-economic factors, findings from Burkart et al. (2014) suggest a more pronounced risk of heat-related all-cause mortality for people living in urban and in high socio-economic status areas, especially among the elderly, as compared to rural and low socio-economic status areas. The higher heat-related risks for urban areas in Bangladesh were also demonstrated in a previous study by Burkart et al. (2011). Singh et al. (2019) report higher mortality for non-institutional deaths (those dying outside a hospital) compared to institutional deaths (those dying within a hospital), which the authors broadly attribute to lower socio-economic status. In a study conducted at the individual level in a rural setting in western India, stronger heat effects were observed among farmers, those with low educational attainment as well as those owing more agricultural land (Ingole et al., 2012).

Only a few studies on heat wave episodes investigated the role of non-atmospheric factors on the temperature-mortality relationship. Both Azhar et al. (2014) and Singh et al. (2019) report a higher RR of mortality from heat waves for females compared to males. Analysis of the deadly heat wave in Karachi, Pakistan during 2015, revealed excess risk of heat-related mortality among the poor and those with lower levels of education, but no effect of fasting during Ramadan was found as initially hypothesised.

3.6. *Quality of the evidence*

Table 3 summarizes the overall quality of the evidence on the association between ambient temperature and heat wave episodes and all-cause mortality for the general population in the countries in South Asia. We downgraded the overall quality of the evidence for studies on ambient temperature by the criterion on imprecision as several studies had large confidence intervals and two did not report any confidence intervals. We downgraded the overall quality of the evidence for studies on heat wave episodes for three of the criteria: risk of bias – due to the substantial risk of bias across studies, indirectness – due to ambiguity of outcome definition and imprecision – due to several studies having large confidence intervals and one not reporting any confidence intervals. We upgraded the quality of the evidence on ambient temperature since most studies reported a broadly consistent dose–response pattern, with risk of mortality increasing with increases and decreases of ambient temperatures beyond a certain threshold. The resulting overall quality of the evidence was judged as *moderate* for studies on ambient temperature and *low* for studies on heat wave episodes.

3.7. *Strength of the evidence*

Table 3 also summarizes the rating of the strength of the body of evidence. Our judgements were based on the following considerations:

- Quality of the body of evidence: *moderate* for studies on ambient temperature and *low* for studies on heat waves (as explained above).
- Direction of effect estimates was largely as expected – risk of mortality increasing with higher and lower ambient temperature beyond a threshold and with more frequent or intense heat wave episodes.
- Confidence in effect estimate: unlikely that a new study on ambient temperature and all-cause mortality would have an effect estimate that would make the results null or statistically insignificant. For heat wave exposure, due to the methodological deficiencies of the studies it cannot be ruled out that new studies might show different effects.
- Other compelling attributes of the data that may influence certainty: for ambient temperature studies, differences in exposure measurement, statistical methods, and contextual factors (completeness in mortality counts, population exposure level, vulnerability and physical and physiological adaptation) make interpretation and comparison difficult. Similarly, the included heat wave episode studies are very heterogenous in terms of heat wave definitions, consideration of lagged effects and mortality displacement, study design and contextual factors (completeness in mortality counts, population exposure level and vulnerability, physical and physiological adaptation), which makes interpretation less certain and clear. For both ambient temperature and heat wave exposure, evidence is based only on a few countries in the regions, with the vast majority of countries not being represented.

We compared these considerations to the strength of evidence definitions specified in the Navigation Guide (Table S32) and concluded that for high and low ambient temperatures there was *sufficient* human evidence that exposure affects all-cause mortality in South Asia and for heat waves – *limited* evidence.

4. Discussion

4.1. *Summary of evidence*

Our systematic review and *meta*-analysis resulted in five main findings. First, we found only a limited number of studies (n = 27), which have attempted to quantify the mortality effects of temperature and heat waves in South Asia. Studies were limited geographically, with half of the countries in the region not represented and two countries covered by only one study. Seven populations were analyzed more than once (e.g. four separate analyses based on the Vadu population, three based on the Matlab population, three on the total population of Bangladesh and two on Delhi, Surat, Ahmedabad and five Indian cities). Second, as summarised in Table 4 below, the strength of the evidence on ambient temperature as a risk factor for all-cause mortality was *sufficient* and on heat wave episodes — *limited*. The latter rating is not to suggest that heat waves are not a risk a factor for all-cause mortality in South Asia, but rather reflects the lack of a sufficient number of robust studies in a region with very heterogenous contexts and a challenging environment for health data collection. Third, individual studies reported an association of all-cause mortality with both high and low temperatures and heat waves for the population in South Asia. However, our *meta*-analysis, indicated evidence of an association for high temperatures only, both at shorter and longer lags, possibly due to the very small number (n = 5) and skewed geographical representation of the included studies. In particular, steep supra-linear increase in risk was observed at temperatures above 31° C for lag 0–1 days and above 34° C for lag 0–13 days, with the risk being higher for longer lags. Fourth, in terms of cause-specific mortality, studies found evidence for both heat and cold effects on CVD, IHD and respiratory mortality. Heat effects were also identified for mortality related to infectious diseases and water- and vector-borne diseases, while cold effects were also found for perinatal mortality. Lastly, the profile of vulnerabilities identified in the reviewed studies is fragmented and sometimes conflicting, possibly due to differences in contexts, heterogeneity in study designs and limitations in data collection.

4.2. *Comparison with other systematic reviews*

Results from the *meta*-analysis are in contrast to findings from other systematic reviews on LMICs (Burkart et al., 2014a; Amegah, Rezza and Jaakkola, 2016), and evidence from higher income low-latitude countries in Europe and North America (The Eurowinter Group, 1997; Gasparrini et al., 2015), which found mortality effects for both hot and cold temperatures. The presence of cold effects in South Asia is plausible and, similar to populations in moderate climates, might be related to poor physiological and physical adaptation to cold weather, for instance, concerning thermal efficiency of housing and clothing (The Eurowinter Group, 1997; Healy, 2003; Burkart and Kinney, 2017) and relative perceptions of risk and vulnerability (Sperber and Weitzman, 1997). Other mechanisms have also been suggested to explain the somewhat counterintuitive cold effects on mortality in tropical and sub-tropical climates: the higher proportion of moderately cold than extremely cold or hot days (Fu et al., 2018), the importance of relative rather than absolute drop in temperatures (Burkart et al., 2014a; Guo et al., 2016), and insufficient control for seasonal confounding (Kinney et al., 2015). For instance, influenza outbreaks (Burkart et al., 2014a; Yang et al., 2009) and household air pollution due to biomass use for cooking and heating, could affect cold-related mortality due to their potential seasonal variations (Egondi et al., 2012; Ingole et al., 2017), but these have been poorly investigated in the included studies and in LMICs in general, possibly due to lack of routine data. Possible explanations for why we did not observe cold-related increase in mortality risk despite observations from individual studies in this review and evidence from the literature include the small number and limited geographical coverage of studies included in the *meta*-analysis as well as their large within-study standard errors at the

Table 3

Summary of the assessment of the quality and strength of the evidence on ambient temperature and heat wave events as a risk factor for all-cause mortality.

Reference	Ambient temperature (n = 20)		Heat wave events (n = 9)	
	Rating	Basis	Rating	Basis
Quality of evidence assessment				
i. Downgrade considerations				
Risk of bias across studies	0	Among all, one study with large sample size judged to have low risk of bias.	−1	There is a substantial risk of bias across most studies.
Indirectness	0	All-cause mortality was appropriate outcome, studies conducted in the population of interest, mostly direct measures of exposure.	−1	Three of the studies used “heat-related mortality”/” heat-induced mortality”/” heat-attributable mortality”, which was not well defined and is not directly comparable to the outcome of interest.
Inconsistency	0	The magnitude of effect estimates likely to differ because of differences in study methods (study design, statistical methods, lag structure considered, method for determining MMT) and not be driven by unexpected heterogeneity.	0	Effect estimates likely to differ because of differences in study methods (study design, statistical methods, study definition of heat waves) and not be driven by unexpected heterogeneity.
Imprecision	−1	Three studies had wide confidence intervals and two did not provide any confidence interval estimates.	−1	Two studies had wide confidence intervals and one did not provide any confidence interval estimates.
Publication bias	0	No evidence for publication bias for studies that would meet our inclusion criteria.	0	No evidence for publication bias for studies that would meet our inclusion criteria.
ii. Upgrade considerations				
Size of the effect	0	Effect sizes are small in most studies.	0	Confounding alone cannot be ruled out as an explanation for large effect estimates.
Dose response pattern	1	Most studies report broadly similar dose–response pattern, with risk of mortality increasing with increases and decreases of ambient temperatures beyond a certain threshold.	0	Dose response relationship is difficult to compare across studies due to differences in contexts, study designs and methods used.
Confounding minimises effect	0	No evidence found to suggest that possible residual confounders would reduce effect estimates.	0	No evidence found to suggest that possible residual confounders would reduce effect estimate.
iii. Summary of the quality assessment				
Overall quality of evidence starts: *Moderate*	*Moderate*	Moderate + (1) +(-1) = Moderate. Downgrading/upgrading resulted in moderate rating for the quality of evidence.	*Low*	Moderate + (-1) + (-1) + (-1) = Low. Downgrading changed the quality from moderate to low.
Summary of findings	n/a	Overall moderate quality of the evidence of higher risk of all-cause mortality for high and low ambient temperature exposure.	n/a	Overall low quality of the evidence of higher risk of all-cause mortality during heat wave episodes.
Strength of evidence assessment				
Quality of evidence	*Moderate*		*Low*	
Direction of effect estimates	n/a	Direction largely as expected: higher risk of mortality at high and low ambient temperatures.	n/a	Direction largely as expected: higher risk of mortality during heat wave episodes.
Confidence in effect estimate	n/a	Studies on ambient temperature measure directly the outcome of interest, direction of effect is largely consistent, majority score low on risk of bias, in particular one study with a large sample size, but several studies have large confidence intervals or do not report confidence intervals at all. It is unlikely that a new study on ambient temperature and all-cause mortality would have an effect estimate that would make the results null or statistically insignificant.	n/a	Most studies have high RoB, do not measure directly the outcome of interest and not all potential confounders are controlled for. Due to these methodological deficiencies it cannot be ruled out that new studies might show different effect estimates.
Other aspects	n/a	Differences in exposure measurement, statistical methods, and contextual factors, including completeness in mortality counts, population exposure level and vulnerability, differences in physical and physiological adaptation across study populations make interpretation and comparison difficult.	n/a	Differences in heat wave definitions, consideration of lagged effects and mortality displacement, study design, contextual factors, including completeness in mortality counts, population exposure level and vulnerability, physical and physiological adaptation across study populations make interpretation and comparison difficult.
Overall strength of evidence	*Sufficient*	We found sufficient evidence that ambient low and high temperatures are positively associated with all-cause mortality for the population in South Asia, where chance, bias, and confounding can be ruled out with reasonable confidence. The available evidence includes results from one or more well-designed, well conducted studies, and the conclusion is unlikely to be strongly affected by the results of future studies. Due to lack of comparability across studies quantitative estimates can only be interpreted in broad terms.	*Limited*	We found limited evidence that heat wave exposure is associated with all-cause mortality for the population in South Asia. A positive association is observed between exposure and outcome; however, chance, bias, and confounding cannot be ruled out with reasonable confidence. Confidence in the association is constrained by the limited number and size of studies and the low quality of individual studies. Further studies, particularly with more rigorous control for confounding, high quality outcome data and consideration of temporal aspects of the association may allow an assessment of effects.

lower temperature range. Further studies with large sample sizes and using comparable and advanced methodologies are necessary in order to understand better the direction and magnitude of temperature effects on mortality in the region, particularly for the six countries with limited or no epidemiological studies, namely Pakistan, Nepal, Afghanistan, Bhutan, Maldives, and Sri Lanka.

Interestingly, two of the included studies found only cold but no heat effects on mortality (Alam et al., 2012; Hashizume et al., 2009). Since both of them were conducted in rural areas (humid sub-tropical areas of Bangladesh), these results might be partly explained by the lower density, higher vegetation cover, and associated lack of urban heat island (UHI) in the study areas. However, other factors such as the population-specific acclimatization and adaptation to hot and cold weather, the demographic and health profile of the study populations as well as insufficient control for confounding cannot be excluded as possible explanations.

Our findings on cause-specific mortality are in line with systematic reviews on other tropical and sub-tropical regions and LMICs (Burkart et al., 2014a; Amegah, Rezza and Jaakkola, 2016; Green et al., 2019). Impacts of temperature on cardiovascular and respiratory mortality are some of the most well documented in the epidemiological literature. Cardiovascular impacts have been related to a range of physiological

Table 4
Summary of findings.

Summary of finding	Studies contributing to the findings	Certainty in the evidence (Navigation Guide)	Brief rationale of the rating around the certainty of the evidence
Ambient temperature: Positive association of all-cause mortality with temperatures below and above a MMT threshold.	Alam et al. (2012); Hashizume et al. (2009); Sewe et al. (2018); McMichael (2008);Burkart et al. (2014b); Burkart et al. (2011); Ingole et al. (2017, 2012, 2015); Hajat et al. (2005); Fu et al. (2018); Lindeboom et al. (2012); Desai et al. (2015); Burkart and Kinney (2017); Babalola et al. (2018); Rathi et al. (2017); Shrestha et al. (2017); Dutta et al. (2020); Nori-Sarma et al. (2019a); Singh et al. (2019)	**Sufficient**	Findings based on studies of large sample size and mostly of good quality. Overall, direction of effect was consistent across studies, but there was a lack of estimate comparability due to methodological differences. Evidence of an exposure–response pattern was found. Studies were very skewed geographically.
Heat wave episodes: Heat waves are associated with increases n all-cause mortality	Azhar (2014); Ghumman and Horney (2016); Mazdiyasni et al. (2017); Murari et al. (2014);Nissan et al. (2017); Hess et al. (2018); Nori-Sarma et al. (2019a); Singh et al. (2019); Nori-Sarma et al. (2019b)	**Limited**	Findings are consistent, but based on a small number of studies, many of which score high on risk of bias and have methodological weaknesses, thus chance cannot be ruled out. Studies were very skewed geographically and effect estimates were not comparable due to differences in study design and methods.

changes in the human body such as increased plasma viscosity, blood pressure, and elevated cholesterol levels (Basu, 2009; Moghadamnia et al., 2017; Zhang et al., 2014; Zhang et al., 2014). Cold has been associated with an increased risk of respiratory infections through bronchoconstriction and changes in immunological reactions (Gasparrini et al., 2015), while physiological stress of heat on the respiratory systems is less well understood (Seltenrich, 2015). Several causes of death, which have been associated with temperature in other epidemiological studies, namely deaths from cerebrovascular diseases (Stafoggia et al., 2006), diabetes (Seposo, Dang and Honda, 2017), pre-existing psychiatric disorders (Stafoggia et al., 2006) and adverse birth outcomes (Son et al., 2019), were not investigated in any of the included studies.

4.3. *Vulnerabilities and modifying factors*

The studies included in this review identified infants, children, the elderly, adults and people occupied in housework as more vulnerable to the impacts of low temperatures and children, adults, farmers, people with low educational attainment, and those owning agricultural land or living in urban areas as more susceptible to the impacts of high temperatures. Overall, women and people with lower socio-economic status were reported as more susceptible to the impacts of heat waves. However, evidence on certain vulnerabilities is often based on single studies and findings for some sub-groups (especially gender and age groups) are inconsistent, which warrants further investigation. Furthermore, some of the underlying factors shaping vulnerabilities are poorly understood and many questions are still to be elucidated — for instance, are people in urban areas more affected by heat because of higher exposure (e.g., UHI effect) or because of differences in age and disease patterns (Burkart et al., 2014b)? Are adults at higher risk because they are more involved in outdoor occupational activities? Are gender differences in vulnerability due to physiological predispositions, occupational differences or differences in treatment seeking behaviour? Are less educated people at higher risk because of occupation, their health status, access to resources (water, housing, information, health care, etc.), or heat-health awareness? How does personal perception of risk shape vulnerabilities? Answering these questions would require better understanding of contextual factors that moderate vulnerabilities.

Besides population characteristics, the built environment, in particular, building features, urban form, and density of green spaces, has also been shown to be an important determinant of temperature-related health risks (Scovronick & Armstrong, 2012; Dang et al., 2017; Lu et al., 2018; Horrison & Amirtham, 2016), but its modifying effect in the included studies and in LMICs in general has not been well investigated (Pramanik and Punia, 2019). One of the studies in this review (Alam, et al. 2012) hypothesised that differences in thermal efficiency of housing might be a possible explanation of the more marked effects of low temperatures on mortality in Matlab as opposed to Abhoyangar. However, Ingole et al. (2017) did not find mortality outcomes in the summer months in Vadu HDSS to be related to housing characteristics.

In terms of vulnerabilities, another important knowledge gap to be addressed are the temperature effects for the population living in substandard housing conditions in the region. 30.4% of the urban population in South Asia lives in informal settlements, with this share being particularly high in some countries such as Afghanistan (62.7%), Bangladesh (55.1%), Nepal (54.3%) and Pakistan (45.5%) (World Bank, 2014). Populations living in informal housing might be particularly vulnerable to non-optimum temperatures due to overcrowding, the poor quality and limited insulation of the housing, but also as a result of other interrelated factors such as poverty, lack of access to health care, sanitation and information on heat wave risks, limited access to clean drinking water and electricity, and restricted household ventilation. Two studies investigating how heat varies within the cities of Nairobi, Kenya and Ahmadabad, India, respectively, demonstrated higher local temperature exposure in informal settlements compared to other city areas, with average difference between 5 to almost 10 °F in the case of Nairobi (Scott et al., 2017; Wang et al., 2019). We found only one study globally, which has investigated the temperature effects on mortality in informal settlements, but this was based in Nairobi (Egondi et al. 2012). Clearly, the lack of routinely collected health data for populations in informal settlements hinders scientific studies. To overcome this, Scovronick et al. (2015) provide an overview of available data sources and epidemiological designs with modest data requirements, which could potentially be deployed for investigating the association between weather and health in these understudied populations.

Comprehensive analysis of vulnerabilities and their determinants could help identify more targeted and cost-effective adaptation strategies, which is particularly important for low income settings. Research in this direction can benefit from different study designs (e.g. case studies, mixed methods, personal temperature measures, etc.) as well as insights from other disciplines than public health such as exposure science, sociology, behaviour studies, economics, architecture, urban design, etc. (Maller and Strengers, 2011; Milà et al., 2020).

4.4. *Adaptation and policy implications*

The role of adaptation for minimising health impacts of non-optimum temperatures is poorly investigated in the reviewed articles. Nevertheless, the included studies propose a range of interventions based on their findings. Most of these are related to increasing public awareness of the problem through public messaging or health education campaigns; encouraging preventative measures (e.g. wearing light, bright-coloured and sun-protective clothing, avoiding physical activity or outdoor work during the hottest hours, staying hydrated), especially among the elderly, outdoor workers and those with existing cardiovascular, respiratory and other chronic diseases; enhancing response capacity and coordination of public health centers; distribution of electric fans; setting-up of cooling centers — air conditioned sites designated as shelters during extreme heat (Widerynski et al., 2016), and introducing early warning systems.

We note that some of the proposed technological cooling interventions are to be viewed with caution due to their limited scope and undesirable consequences. Although studies have shown the protective effect of the use of air conditioning units during heat waves (Barreca et al., 2016) and air conditioning is growing rapidly in South Asia, this solution still remains out of reach for the majority of the population due to its high operational costs (Mastrucci et al., 2019). Increased use of air conditioning units in urban areas is also shown to contribute to increase in outdoor temperatures by one degree or more (Lundgren and Kjellstrom, 2013), it leads to increased risk of power outages as a result of higher pressure on energy grids and, most importantly, it further contributes to climate change through upsurge in electricity consumption (Gupta et al., 2012). Use of electric fans has often been proposed as a more affordable alternative to air conditioning in low resource settings. However, a 2012 Cochrane systematic review showed that the benefits of using electric fans during heat waves are uncertain and may actually increase mortality risk, especially if ambient temperature is above body temperature (35° C), by contributing to an increased rate of dehydration and increased convective heat gain (Gupta et al., 2012).

A few formal evaluations of heat-health warning systems have been conducted so far, and they appear to show a notable reduction in excess mortality following a heat wave (Ebi et al., 2004; Martínez-Solanas and Basagaña, 2019). The first Heat Action Plan, including an early heat warning system, in South Asia was implemented in the city of Ahmedabad, in India's western province of Gujarat, following the deadly heat wave of May 2010. According to a pilot formal evaluation of the plan, it has been effective in averting 1190 (95%CI 162–2218) average annualized deaths two years after its implementation (Hess et al., 2018). Following the experience of Ahmedabad, the government is currently working with over 100 cities and districts within 23 states towards scaling up heat action plans and early warning systems across India (Pradesh et al., 2019). In light of the findings in this review, which demonstrated that temperature thresholds can differ substantially between regions in the same country and that health effects may occur at a temperature below those specified in national heat wave definitions, there is a need for more local epidemiological studies to establish appropriate temperature thresholds, which can inform such early warning systems.

Beyond the more immediate and upfront interventions mentioned above, long-term strategies for reducing temperature vulnerabilities are rarely discussed in the included studies. Evidence from other studies shows that improvement of public infrastructure, expansion of public transport, and reduction of the UHI effects through increase in tree canopy, deployment of heat-reflective surfaces on roofs and roads have the potential to decrease heat stress, especially in densely built urban and *peri*-urban areas (Rizwan, Dennis and Liu, 2008; Garg et al., 2016; Deilami, Kamruzzaman and Liu, 2018). Previous research has suggested that addressing broader development challenges such as economic diversification and shifting of labour away from the agricultural sector (Green et al., 2019), improvement in educational attainment (Lutz, Muttarak and Striessnig, 2014), expansion of essential healthcare, set-up of other social protection programmes and provision of access to electricity (Mastrucci et al., 2019) could be important for decreasing the human cost of climate-related threats.

4.5. Potential interactive effects of temperature and particulate or ozone air pollution

Another important avenue for future research is to explore the potential interactions between temperature or heat waves and particulate or ozone air pollution on mortality. Ambient air pollution is a major public health concern in the region: the 2015 iteration of the Global Burden of Disease project estimated that almost 60% of deaths attributable to $PM_{2.5}$ globally happened in South Asia (Cohen et al., 2017). McMichael et al. (2008) included particulate air pollution in their model for Delhi but found a minimal impact on the temperature effect estimate, while Singh et al. (2019) observed that the associations between mortality and extreme temperature in Varanasi, India are substantially confounded by different air pollutants, in particular PM_{10}. There is emerging evidence that the adverse effects of hot temperature or heat waves on human health can be amplified by high air pollution levels, and vice versa – the harmful effects of air pollution are enhanced by high temperature (Analitis et al., 2018; Burkart et al., 2014b; Kinney, 2018b). Various mechanisms have been identified as a possible explanation of these synergistic effects. Hot days might be associated with higher emissions of certain pollutants since ozone and secondary particles are generated faster in the atmosphere in the presence of sunlight and higher temperatures (Ebi and McGregor, 2008; Kinney, 2018b). Behavioural responses to hot temperatures, e.g., increased use of (air-conditioned) cars, can also increase emissions of air pollutants. Physiological stress in the body due to extreme heat may also make individuals more sensitive to air pollution exposure and allergens, or vice versa (Gordon, 2003; Ren et al., 2011). However, not all studies have identified synergistic effects of temperature and air pollution (Basu, Feng and Ostro, 2008; Zanobetti and Schwartz, 2008) and further research is warranted, particularly in South Asia.

4.6. Need for improved environmental and health monitoring

We identified the lack of reliable and regularly collected data on mortality and temperature as a major obstacle for conducting analysis in the region. Comprehensive analysis of temperature-related mortality requires daily all-cause or cause-specific mortality data, which are not readily available for most countries in South Asia. Similar to most LMICs, majority of deaths in countries of the region occur at home and remain undocumented or without a medically certified cause of death, hence the reliance on HDSSs and SVRSs for studying premature mortality (Jha et al., 2006). All countries in the region have some form of a vital registration system (UN DESA, 2010), but these have been rated as poorly functioning with the exception of the Maldives and Sri Lanka (Mikkelsen et al., 2015). Continued efforts to strengthen vital registration systems are important not only for mapping vulnerabilities due to temperatures but also to other climate-related health impacts.

4.7. Strengths and limitations

This review covered a region highly vulnerable to climate change but relatively understudied. Our review synthesises evidence from studies on ambient temperature, heat waves, and studies with different methodological approaches: a more inclusive approach than previous reviews (Green et al., 2019). We assessed the overall quality and strength of the evidence following the Navigation Guide, specifically developed for environmental health research. Finally, we used a new, flexible statistical approach, which allowed us to pool estimates of non-linear exposure response functions and calculate MMT across studies without having access to individual study data. In contrast, previous *meta*-analyses based on summary results from the literature relied on more simplified methods that did not account for non-linear and delayed effects.

Our study also has some limitations. The considerable heterogeneity of the included studies in terms of study design, lagged effects, outcome and exposure metrics, and the overlap of populations across publications limited the number of studies that could be included in the *meta*-analysis. Furthermore, although we tried to select studies with comparable designs, differences across studies remained: one study in the *meta*-analysis reported effects stratified by season as opposed to year-round effects (Ingole et al., 2017) and one reported cold effects for lag 0–14 instead of lag 0–13 days (Burkart and Kinney, 2017). A *meta*-regression could have elucidated differences due to methods, exposure measures, latitude, temperature thresholds, and others, but was not possible given the small number of eligible studies. Half of the studies included in the review and three in the *meta*-analysis were conducted in India. Therefore, generalizability of our findings might be somewhat limited since the countries in the region differ in terms of their climate, geography and topology, as well as culture, demography, economic development, and other population characteristics. This review has focused on excess mortality associated with temperature variability and extreme temperatures, not accounting for other potential health effects related to non-fatal conditions and psychological stress (Carleton, 2017; Pailler and Tsaneva, 2018).

Finally, we may have missed some relevant publications since the review did not cover research published in other languages than English. Also, given the policy relevance of this topic and the scientific practices in the region, it is likely that relevant publications in the grey literature have been excluded (e.g. reports from government or non-profit or international organisations). However, it is highly unlikely that their inclusion would appreciably change the conclusions in this review since high quality quantitative epidemiological studies are mainly published in peer-reviewed journals.

4.8. Conclusions

We found a limited number of studies, which have attempted to quantify the mortality effects of temperature in South Asia. The existing body of evidence, focused mainly on India and Bangladesh, points to excess mortality associated with hot and cold temperatures as well as heat waves, but our *meta*-analysis based on five of the included time series studies confirmed evidence for high temperatures only. More evidence is needed to reduce uncertainty in the shape and size of the temperature-mortality association in a region that is a hotspot for climate vulnerability and experiencing rapid population growth and urbanisation. In particular, a better understanding of the modifying factors of the temperature-mortality relationship is necessary to inform targeted interventions in the region. In light of slow progress in achieving greenhouse gas emission reduction targets, more evidence on viable adaptation options for the population in South Asia is particularly important. More robust exposure–response functions are also essential for health impact assessments of temperature-related mortality and morbidity burdens under different climate change mitigation or adaptation scenarios to inform decision making.

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Declaration of Competing Interest

The authors declared that there is no conflict of interest.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envint.2020.106170.

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