Environment International 91 (2016) 133–149

Contents lists available at ScienceDirect

Environment International

journal homepage: www.elsevier.com/locate/envint

Review article

Temperature-related morbidity and mortality in Sub-Saharan Africa: A systematic review of the empirical evidence

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ARTICLE INFO

Article history:
Received 12 November 2015
Received in revised form 22 February 2016
Accepted 24 February 2016
Available online 4 March 2016

Keywords:
Climate change
Morbidity
Mortality
Sub-Saharan Africa
Systematic review
Temperature variability

ABSTRACT

Background: Sub-Saharan Africa (SSA) contributes very little to overall climate change and yet it is estimated to bear the highest burden of climate change, with 34% of the global DALYs attributable to the effects of climate change found in SSA. With the exception of vector-borne diseases, particularly malaria, there is very limited research on human health effects of climate change in SSA, in spite of growing awareness of the region's vulnerability to climate change.
Objectives: Our objective is to systematically review all studies investigating temperature variability and non-vector borne morbidity and mortality in SSA to establish the state and quality of available evidence, identify gaps in knowledge, and propose future research priorities.
Methods: PubMed, Ovid Medline and Scopus were searched from their inception to the end of December 2014. We modified the GRADE guidelines to rate the quality of the body of evidence.
Results: Of 6745 studies screened, 23 studies satisfied the inclusion criteria. Moderate evidence exists to associate temperature variability with cholera outbreaks, cardiovascular disease hospitalization and deaths, and all-cause deaths in the region. The quality of evidence on child undernutrition is low, and for diarrhea occurrence, meningitis, Ebola, asthma and respiratory diseases, and skin diseases, very low.
Conclusions: The evidence base is somehow weakened by the limited number of studies uncovered, methodological limitations of the studies, and notable inconsistencies in the study findings. Further research with robust study designs and standardized analytical methods is thus needed to produce more credible evidence base to inform climate change preparedness plans and public health policies for improved adaptive capacity in SSA. Investment in meteorological services, and strengthening of health information systems is also required to guarantee timely, up-to-date and reliable data.

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http://dx.doi.org/10.1016/j.envint.2016.02.027
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1. Introduction

Anthropogenic climate change, manifesting mainly as intensification of extremes of ambient temperature and increases in the mean (McMichael and Lindgren, 2011) is now incontrovertible (Watts et al., 2015). Several epidemiological studies conducted mostly in high income countries, Europe and North America in particular, have found extreme temperatures to be associated with increased risk of illness and death (Basu and Samet, 2002; Basu, 2009; Kovats and Hajat, 2008; O'Neill and Ebi, 2009; Ye et al., 2012). A recent multi- country study has however shown the whole temperature range and not just the extremes to be important in understanding temperature-mortality dependencies (Gasparrini et al., 2015).

Climate change has been estimated to be responsible for the loss of over 150,000 lives and 5,500,000 disability adjusted life years (DALYs) globally in 2000 (Campbell-Lendrum et al., 2003; McMichael et al., 2004; Costello et al., 2009). Although Sub-Saharan Africa (SSA) contributes very little to overall climate change (Kula et al., 2013), the region is estimated to bear the highest burden of climate change, with 34% of the global DALYs attributable to the effects of climate change found in SSA (Costello et al., 2009; WHO, 2008). According to Byass (2009), with the population of SSA representing only 11% of the global population, the proposed estimate reflects a three-fold population-based risk for adverse effects of climate change among Africans compared with the global population. The recent Intergovernmental Panel on Climate Change (IPCC) assessment report made similar observations when it pointed out that Africa is one of the most vulnerable continents to climate change due to its high exposure and low adaptive capacity (Niang et al., 2014).

With the exception of vector-borne diseases, particularly malaria, there is very limited research on the human health effects of climate change in SSA, in spite of growing awareness of the region's vulnerability to climate change. Byass (2009), asserted that, in Africa, given the predominance of research on the effects of climate change on malaria transmission, it might be construed as the major climate change-related health problem in the region, when other relatively underdocumented effects are likely to have a numerically greater impact. Byass (2009), further stated that, on the African continent, where a large number of people are regularly exposed to extremes of high temperature, physiological effects of heat might equally be an important public health concern and worth investigating.

We therefore conducted a systematic review of all studies examining the relation between temperature variability and non-vector borne morbidity and mortality in SSA to establish the state and quality of available evidence, identify gaps in knowledge, and propose future research priorities. Documenting the effects of temperature variability is important for predicting the impact on health of climate change. According to Wilkinson et al. (2003), meteorological variables such as temperature are perhaps the most important exposure indicators for assessing the effects of climate on human health.

2. Methods

We searched Ovid Medline, PubMed, and Scopus databases, from their inception to the end of December 2014, with no language restrictions imposed for relevant studies. The search statement applied in the databases was {climate OR climatic OR weather OR temperature} AND {mortality OR death* OR morbidity OR illness* OR disease* OR sickness* OR infection* OR malnutrition OR undernutrition OR diarrhea OR cholera} AND africa.

We initially screened the articles for eligibility, based on the title and abstract with studies considered for inclusion in the review, if they were (a) original studies, (b) conducted in a human population in any Sub-Saharan African country and (c) investigated any health outcome with the exception of vector-borne diseases. Climate change impact on vector-borne diseases, especially malaria, has been widely investigated in Sub-Saharan Africa with several studies also reviewing the available evidence, hence the decision to exclude these outcomes from our study. Selected articles were retrieved in full and further assessed for eligibility. We also reviewed the reference list of all included studies to identify additional eligible studies.

The following information was extracted from eligible studies: location and study period, study design and statistical analysis, study population and size, temperature variable(s) and health outcome(s) and their data sources, control of confounding, and study findings.

We modified the GRADE (Grading of Recommendations Assessment, Development and Evaluation) guidelines (Balshem et al., 2011) to rate the quality of the body of evidence. GRADE assesses the quality of a body of evidence based on five criteria - study limitations (risk of bias), publication bias, imprecision of effect estimates, inconsistency of results and indirectness of evidence, and specifies four categories; high and moderate for evidence from randomized controlled trials, and low and very low for evidence from observational studies. Because of the difficulty in assessing publication bias qualitatively, we decided to exclude the publication bias criteria from our modified checklist. In the area of temperature variability/climate change and health research, observational designs are the only approach for generating evidence to inform policy decisions. Durrheim and Reingold (2010), suggested the evaluation of additional epidemiological domains and provision of a set of ratings to ensure that the GRADE framework which according to them addresses one evidence domain, remains relevant for the use of comprehensive public health evidence in informing policy making. Our modified GRADE guideline thus also specifies four categories - high, moderate, low and very low in spite of the evidence generating from observational designs. With the exception of study limitations, each of the other three criteria were assessed by assigning a score of 0 to "no" and a score of −1 to "yes". For study limitations, "no" attracted a score of 0, with "yes, serious" attracting a score of −1 and "yes, very serious" getting a score of −2. The scores were then summed up with summary scores of ≥−1 deemed as high quality, −2 as moderate quality, −3 as low quality, and ≤−4 as very low quality. We developed a checklist which was applied in rating the body of evidence for each study outcome (Appendix A).

3. Results

A flowchart of the study selection process is reported in Fig. 1. A total of 23 studies were included in the review.

3.1. Characteristics of included studies

The characteristics of included studies are presented in Table 1. Six studies were conducted in West Africa, five in East Africa, six in Southern Africa, two in Central Africa, and four in multiple countries. Four of the included studies (Jankowska et al., 2012; Grace et al., 2012; Alexander et al., 2013; Trærup et al., 2011) were conducted nationwide in their respective countries of origin.

Seventeen of the included studies were time series studies, of which ten studies applied Poisson regression (Azongo et al., 2012; Mrema et al., 2012; Egondi et al., 2012; Diboulo et al., 2012; Dukić et al., 2012; Fernández et al., 2009; Paz, 2009; Kynast-Wolf et al., 2010; Kovats

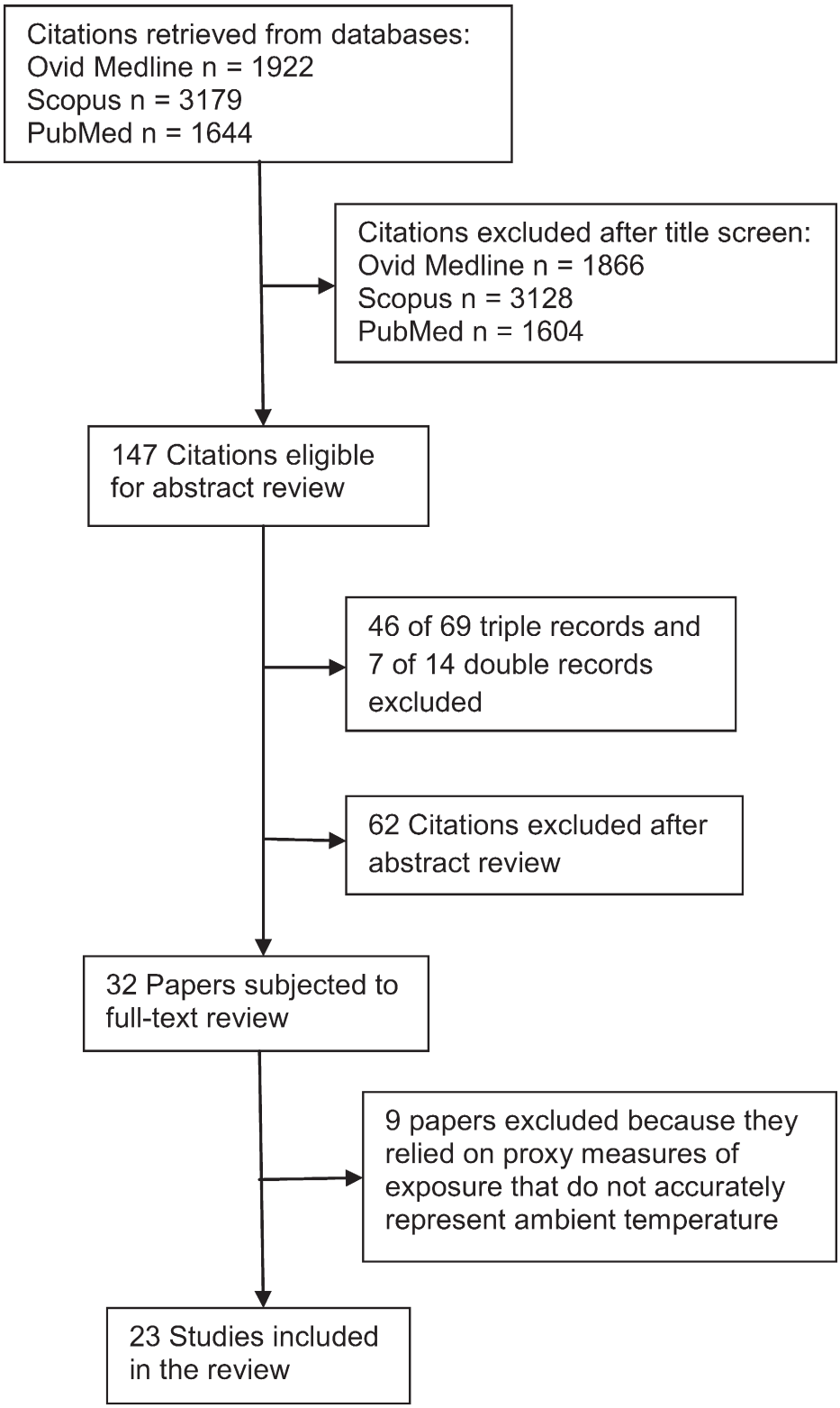

Fig. 1. Flowchart of study selection process.

Table 1
Characteristics of included studies.

Source	Location and period	Design and statistical analysis	Study population and sample	Temperature variable(s) and data source(s)	Outcome(s) and data source(s)	Confounding control	Main results
Thompson et al. (2012)	5 municipalities (Musina, Makhado, Polokwane, Tzaneen, Bela-Bela) in Limpopo province, South Africa. 1990–2010	Correlational study Pearson correlation, multiple linear regression	Children aged 0 to 13 years 7869 cases	Annual T_{mean}, T_{min} and T_{max} South Africa Weather Services meteorological data	Diarrhea, respiratory infection, asthma Hospital records 1999–2010		T_{max} showed an increase during the 21 year period for 4 municipalities with available data (r coefficients of 0.50, 0.56, 0.48, 0.02 for Bela-Bela, Tzaneen, Musina and Polokwane respectively) T_{min} showed a decrease over the period (r of 0.004, −0.383, −0.004 and 0.135 respectively) Increasing incidence in the diseases studied during the period 1999 to 2010 (r of 0.928, 0.930 and 0.813 for diarrhea, respiratory infection and asthma respectively) 37.9% of the disease incidence (incl. malaria and meningitis) may be attributable to climatic parameters (incl. rainfall, $R^2 = 0.379$) Unit increase in temperature will lead to a 1.329 fold increase in disease incidence ($\beta = 1.329$)
Jankowska et al. (2012)	Nationwide, Mali 1960–2009	Cluster analysis Multivariate linear regression	407 DHS clusters with 14,238 children	Seasonal air, land surface and infrared brightness temperature Global Historical Climatology Network archive NASA Thermal infrared data NOAA/CPC Geostationary Meteosat weather satellites	Child undernutrition - anemia, stunting and underweight 2006 DHS data	Age of household head, children ever born to mother, household wealth index, household use of unprotected well, child's age (months)	Temperature increase of >1.0 °C for the Sudan-Niger-Mali arc during the period and is equal to or greater than the inter-annual standard deviation of 0.65 °C Combined temperature and precipitation (PPET) index <−100 zone was associated with stunting ($\beta = -0.165$, $p < 0.001$), underweight ($\beta = -0.159$, $p < 0.001$) and anemia ($\beta = -0.149$, $p < 0.01$) for all clusters.
Grace et al. (2012)	Nationwide, Kenya 1998–2008	Cluster analysis Multi-level linear regression	320 clusters consisting of 2255 children aged 1–5 years	Average growing season temperature Meteorological stations Remotely sensed data	Child stunting 2008 DHS data	Age and sex of child, twin or singleton, breastfeeding duration, maternal report of child size at birth, mother's age, educational level and height, household water source and floor material, livelihood zones/strategy	Temperature appears to have no impact on stunting variation ($\beta = -0.0385$, $p > 0.1$ for mean temperature, and $\beta = 0.0878$, $p > 0.1$ for temperature variability)
Bandyopadhyay et al. (2012)	159 regions in 14 Sub-Saharan African countries	Time series Ordinary least squares regression Lag term of one month	Children under age of 3 years No. of children not reported	Average monthly T_{min} and T_{max} Africa Rainfall and Temperature Evaluation System (ARTES) database 1980–2000	Diarrhea prevalence DHS data from the dry seasons 1992–2001	Climatic zone, access to safe water, household toilet facility, education level of adult female, vaccination status, wealth index, nutritional status, survey year	Average diarrhea prevalence was 22.9% with moderate variation across climatic zones. Less variation in temperature during the period across the climatic zones and in the overall sample

Table 1 (*continued*)

Source	Location and period	Design and statistical analysis	Study population and sample	Temperature variable(s) and data source(s)	Outcome(s) and data source(s)	Confounding control	Main results
							Temperature was statistically associated with diarrhea prevalence; increase in T_{max} increased prevalence ($\beta = 1.039$, $p < 0.01$), while increase in T_{min} lowered prevalence ($\beta = -0.460$, $p < 0.05$).
Alexander et al. (2013)	Nationwide, Botswana 1974–2003	Time series Autoregressive analysis of covariance (ANCOVA) Lag term of one month 315 months of data	Diarrheal patients presenting to Government health facilities No. of cases not reported	Monthly T_{mean}, T_{min}, T_{max}, and DTR Climate Research Unit TS (time-series) 3.10 dataset	Diarrhea incidence Central Statistics Office Annual health reports		Elevated T_{min} was positively associated with increased diarrhea incidence in the dry season (proportion deviation from yearly seasonal mean [Pmy] = 0.074) but negatively associated with diarrhea in the wet season (Pmy = −0.0071) Increases in T_{max} not related to increased diarrhea prevalence
Azongo et al. (2012)	Kassena-Nankana District, Ghana 1995–2010	Time series Poisson regression through Generalized Additive Models (GAM) Sensitivity and stratified analysis Lag terms of 0–1, 2–6 and 7–13 days of mean daily temperature	31,144 deaths	Daily T_{mean}, T_{min} and T_{max} Navrongo Meteorology station	All-cause mortality Navrongo HDSS	Time trends, seasonality	U-shaped relationship between daily T_{mean} and mortality observed (temperature threshold = 30 °C) 1 °C decrease in daily T_{mean} below the 25th percentile (threshold = 27.4 °C) at lag days 0–1 associated with 0.19% (95% CI: 0.05, 0.21) increased risk of mortality. 1 °C increase in daily T_{mean} above the 75th percentile (threshold = 30.6 °C) increased risk at lag days 0–1, 2–6 and 7–13 days by 1.14% (95% CI: 0.12, 1.54), 0.32% (95% CI: 0.16, 0.25) and 0.31% (95% CI: 0.14, 0.26) respectively. Statistically significant increased risk was also noted among under 5 children with daily T_{mean} above the 75th percentile at lag days 2–6 and 7–13, and among the elderly (60 + years) with daily T_{mean} below the 25th and above the 75th percentile at lag days 0–1.
Mrema et al. (2012)	Rufiji District, Tanzania 1999–2010	Time series Poisson regression through GAM Stratified analysis Accounted for auto-correlation Lag terms of 0, 1, 2, 3 and 4 months	10,116 deaths	Monthly T_{mean}, T_{min} and T_{max} Tanzania Meteoro-logical Authority	All-cause mortality Rufiji HDSS	Lag effects	Threshold temperature was 26–27 °C for all age groups Monthly T_{mean} was significantly associated with mortality in all age groups. RRs of 0.934 (95% CI: 0.894, 0.974), 0.956 (95% CI: 0.928,

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Table 1 (*continued*)

Source	Location and period	Design and statistical analysis	Study population and sample	Temperature variable(s) and data source(s)	Outcome(s) and data source(s)	Confounding control	Main results
		of monthly average temperature					0.985) and 0.946 (95% CI: 0.912, 0.979) for 0–4, 5–59 and 60+ years respectively. Monthly T_{mean} was significantly associated with mortality at lag 2 days in age group 5–59 years (RR = 0.897 [95% CI: 0.801, 0.993])
Egondi et al. (2012)	Korogocho & Viwandani, Nairobi, Kenya 2003–2008	Time series Poisson regression through GAM Accounted for over-dispersion Sensitivity and stratified analysis Lag terms of 0–1, 2–6 and 7–13 days	60,146 individuals from 24,875 households 2512 non-accidental deaths	Daily T_{mean}, T_{min} and T_{max} Meteorological Department of Kenya (Moi Airbase weather station)	All-cause mortality Nairobi Urban HDSS	Rainfall, season, trend Lag effects	Threshold temperature was 18–20 °C Association between temperature and mortality was J-shape for all ages and U-shape for U5s. 1 °C increase in temperature above the 75th percentile (threshold = 20 °C) was significantly associated with U5 and non-communicable disease mortality (% change = 1 [95% CI: 0, 2] and 1 [95% CI: 0, 3] respectively) 1 °C decrease in temperature below the 25th percentile (threshold = 17.9 °C) was associated with 3%, 9% and 13% increase in all-cause, 50+ years and acute infections deaths respectively, albeit statistically not significant. All associations observed at lag 0–1 days
Diboulo et al. (2012)	Nouna, Burkina Faso 1999–2009	Time series Poisson regression through GAM Sensitivity and stratified analysis Lag terms of 0–1, 2–6 and 7–13 days	7402 deaths	Daily T_{mean}, T_{min} and T_{max} Nouna Health center meteorological stations (2004–2009) and nearest World Meteorological Organization associated monitoring station (1999–2009)	All-cause mortality Nouna HDSS	Time trends, seasonality	Statistically significant linear increase in mortality for all ages with increasing temperature at lag 0–1 was noted. A 1 °C increase in temperature at lag 0–1 was associated with a 2.6% (95% CI: 0.1, 5.2) increased risk in mortality. Among U5s, the increased risk was 3.7% (95% CI: 0.3, 7.3). For lags 2–6 and 7–13, a statistically not significant slightly decreasing trend was observed. The elderly (60+ years) were susceptible to both extreme low and high temperature in lag strata 0–1 (U-shape relationship), the associations were however not statistically significant.
Dukić et al.	Navrongo, Ghana	Time series	Meningitis Cases	Monthly T_{min} and	Meningitis	Air quality (dust, CO),	Higher levels of current

Table 1 (*continued*)

Source	Location and period	Design and statistical analysis	Study population and sample	Temperature variable(s) and data source(s)	Outcome(s) and data source(s)	Confounding control	Main results
(2012)	1998–2008	Poisson regression through GAM Lag terms of previous month and two months	No. of cases not reported	T_{max} Navrongo weather station	Laboratory confirmed cases at the Navrongo Health Research Center	social and behavioral processes (e.g. vaccination uptake, migration), health patterns (respiratory illness, influenza, immunity)	month T_{max} associated with higher meningitis incidence (8df and 4df GAM coefficient of 0.181 and 0.337 respectively). Higher levels of previous month's T_{min} associated with lower levels of meningitis incidence (GAM coefficients of −0.087 and −0.052 respectively)
Reyburn et al. (2011)	Unguja, Zanzibar 2002–2008	Time series Cross-correlation analysis Multivariate seasonal autoregressive integrated moving averages (ARIMA) model Accounted for auto-correlation Lag terms of 0, 1, 2, 3, 4 and 5 months	3245 cholera cases	Monthly T_{min} and T_{max} Zanzibar Government Meteorological Department (Unguja airport weather station)	Cholera Ministry of Health and Social Welfare cholera surveillance records	Season, trends, rainfall, humidity, ocean environmental variables	Cholera outbreaks was positively associated with T_{min} at lags 2 and 4 months (cross-correlation coefficient of 0.25, $p < 0.05$ and 0.23, $p < 0.05$ respectively), and negatively associated with T_{max} at lag 2 months (cross-correlation coefficient = −0.19, $p < 0.1$) With the 4-month lag term, a 1 °C increase in T_{min} resulted in a two fold increase in cholera cases (ARIMA $\beta = 2.208$, $p = 0.034$)
Fernandez et al. (2009)	Lusaka, Zambia 2003–2006	Time series Poisson regression through GAM Accounted for over-dispersion and auto-correlation Lag term of up to 8 weeks	Cholera patients in isolation centers (n = 13,069)	Weekly T_{max} Meteorological station of the Lusaka International Airport	Cholera Medical registers at cholera isolation centers of the Medecins Sans Frontieres	Seasonality	A 1 °C increase in temperature 6 weeks before the onset of the outbreak explained 5.2% of the increase in cholera cases (RR = 1.05, 95% CI: 1.04, 1.06) The attributable risk was 4.7%
Paz (2009)	Southeastern Africa - Uganda, Kenya, Rwanda, Burundi, Tanzania, Malawi, Zambia, Mozambique 1971–2006	Time series Poisson regression Accounted for auto-correlation Lag terms of current and previous year		Annual air temperature for southeastern Africa NOAA NCEP-NCAR	Cholera cases WHO Global Health Atlas		There is an association between annual air temperature increase and increase in cholera incidence. A 0.1 °C increase in the annual T_{mean} multiplies the annual number of cholera cases by 1.87 ($\beta = 0.63$, $p = 0.18$) for current year and 2.78 ($\beta = 1.02$, $p = 0.03$) for the previous year
Ng and Cowlin (2014)	Guinea, Gabon, DRC, South Sudan, Uganda 1976–2014	Time series Orthogonal polynomials in binomial regression models. Lag terms of 1, 2 and 3 months	28 reported Ebola virus disease (EVD) outbreaks	Monthly temperature Climate Research Unit, Uni of Anglia, UK 2013 and 2014 data imputed from data during the previous 3 years Data period ranged from 1 to 5 years in the study locations	EVD US CDC database	Absolute humidity Lag effects	Consistent patterns in annual variation of temperature was observed across the five countries Lower temperature was found to be log-linearly associated with increased risk of EVD outbreak onset during each month in the lag periods Cumulative ORs of EVD outbreaks associated

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Table 1 (*continued*)

Source	Location and period	Design and statistical analysis	Study population and sample	Temperature variable(s) and data source(s)	Outcome(s) and data source(s)	Confounding control	Main results
							with deviations (−1, −2 and −3 °C) from the mean monthly temperature were all statistically significant with a consistent dose-response relation across the entire lag period ranging from 1.20 to 1.71, 1.43 to 2.93, and 1.71 to 5.00 for the same, first and second month respectively.
Oloukoi et al. (2014)	Iseyin, Okeho and Shaki, Oke-Ogun Region, Nigeria Survey period: 12/2008–2/2009	Correlational study Household survey Focus group discussion (FGD) Key informant interviews (KII)	397 households FGD, n = 49 people KII, n = 6	Monthly T_{mean} 2006–2008 Ibadan Meteorology Zonal office Data available for Iseyin and Shaki	Skin diseases Monthly cases of diseases for Shaki and Iseyin Diseases Surveillance Unit of the Oyo State Ministry of Health 2006–2008		Community perceptions on seasonal climate variation suggested that in the last few years extreme heat has been observed. From the survey and the FGDs analysis, severe heat (increased temperature) during the dry season was linked to prevalence of skin diseases, malaria and fever. Household survey and correlation trends showed that cases of most modifiable diseases in the region increases during the dry season (Trend charts and correlation coefficients not provided)
Trærup et al. (2011)	Nationwide, Tanzania 1998–2004	Time series Negative binomial regression Correlation analysis	No. of cholera cases and deaths not reported	Monthly T_{mean}, T_{min} and T_{max} Tanzania Meteorological Agency	Cholera: nationwide monthly cases 1998–2004, nationwide yearly cases and deaths 1977–2004, regional (21 regions) yearly cases 1998–2004 Ministry of Health	Drought, time-trend (captures socioeconomic effects)	Cholera cases were positively correlated with T_{min} and T_{max} and their one-month lags. Using the monthly and regional annual data, a 1 °C increase in T_{max} increases the relative risk for cholera cases by 29% ($\beta = 0.256$, $p = 0.021$; IRR = 1.29) and 15% ($\beta = 0.141$, $p = 0027$; IRR = 1.15) respectively. Regarding the nationwide annual data, no statistically significant association was found.
Chang et al. (2004)	Kenya, Zambia and Zimbabwe 2/1989–1/1995 48, 12 and 48 study months respectively	Time series Negative binomial regression analysis Sensitivity analysis Lag effects of 1–3 months	Women aged 15–49 years experiencing cardiovascular events 153, 199 and 4 cases of venous thrombo-embolism (VTE), arterial stroke and acute myocardial infarction (AMI) respectively	Monthly T_{mean} Weather Websites and World Meteorological organization	Incident cases of AMI, arterial stroke and VTE Patients admitted to collaborating hospitals of the WHO Collaborative Study of CVD and Steroid Hormone Contraception	No effect modification by age and high blood pressure	IRRs for 5 °C change in T_{mean} Kenya: VTE, 0.43 (95% CI: 0.14, 1.27); stroke, 0.65 (95% CI: 0.11, 3.89) Zambia: VTE, 1.16 (95% CI: 0.21, 6.47); stroke, 0.89 (95% CI: 0.45, 1.75) Zimbabwe: VTE, 0.70 (95% CI: 0.49, 1.01); stroke, 0.91 (95% CI: 0.62, 1.34) Estimates not available for AMI due to few cases Summary estimate:

Table 1 (*continued*)

Source	Location and period	Design and statistical analysis	Study population and sample	Temperature variable(s) and data source(s)	Outcome(s) and data source(s)	Confounding control	Main results
							VTE, 0.69 (95% CI: 0.49, 0.96); stroke, 0.89 (95% CI: 0.64, 1.24); AMI, 0.96 (95% CI: 0.04, 21.2)
Longo-Mbenza et al. (1999)	Kinshasa, DRC Survey period: 1/1987–12/1991	Prospective study Correlational analysis Logistic regression	1032 stroke patients (deaths, n = 600)	T_{mean} and T_{max} Meteorology Institute at Kinshasa Binza All daily measurements during the month preceding stroke onset obtained and averaged.	Hematocrit, stroke Patients admitted to the Ngaliema Clinic, Lomo Medical Center and Kinshasa University Clinics		T_{mean} and T_{max} was positively and significantly correlated with hematocrit ($r = 0.124$, $p < 0.001$ and $r = 0.1$, $p < 0.01$ respectively) $T_{mean} > 28$ °C multiplied risk of stroke mortality by 21 (OR = 21; 95% CI: 15, 29)
Kynast-Wolf et al. (2010)	Kossi province, Burkina Faso 1999–2003	Time series Poisson regression	11,174 adults aged 40+	Monthly T_{mean} Dedougou temperature measurements (TuTiempo.net 2010).	All cause (n = 1238) and CVD (n = 98) mortality Nouna HDSS Cause of death ascertained by verbal autopsy		For all-cause mortality, T_{mean} for 65+ age group was highly significant ($\beta = 0.069$, $p < 0.0001$). An effect was also established for the 40–64 age group ($\beta = 0.030$, $p = 0.09$) For CVD mortality, the effects were not statistically significant ($\beta = 0.0060$, $p = 0.3$ and $\beta = 0.056$, $p = 0.2$ for 40–64 and 65+ age group respectively)
Tchidjou et al. (2010)	Yaounde, Cameroun 2006–2007	Time series Negative binomial regression	1306 children aged 0 to 18 years admitted to the Chantal Biya Foundation pediatric hospital	Monthly T_{min} and T_{max} National Meteorological Institute of Cameroun	Acute Respiratory Infections	Seasonality and trend Exclusion of malaria cases	T_{max} was associated with increased risk (IRR = 1.94, 95% CI: 1.34, 2.81) whereas T_{min} was associated with decreased risk (IRR = 0.72, 95% CI: 0.59, 0.87) Exclusion of malaria cases: T_{max} IRR = 1.43 (95% CI: 1.12, 1.84), T_{min} IRR = 0.84 (95% CI: 0.74, 0.95)
Kovats et al. (2005)	Cape Town, South Africa 1996–1999	Time series Poisson regression Stratified analysis	Approximately 76,000 deaths	Daily T_{mean} South African Meteorological Services	Cause-specific and all-cause mortality (Cardiovascular, respiratory, infectious, external, other)	Season, trend flu epidemics, day of week, holidays, air pollution (O_3, PM_{10})	Low temperature had an effect on all-cause mortality. The threshold was however not precisely defined Assuming a threshold of 15 °C, a 1 °C decrease in temperature resulted in a 3.14% (95% CI: 1.86, 4.43) and 1.77% (95% CI: 0.5, 3.3) increase in deaths among the elderly and children respectively. For cause-specific deaths, the greatest effects of low temperature was seen for infectious and cardiovascular diseases which increased by 4.42% (95% CI: 3.13, 5.73) and 2.53% (95% CI: 1.25, 3.83) respectively per 1 °C decrease
Heunis et al. (1995)	Cape Town, South Africa 1978–1985	Cross-sectional *t*-test Lag terms of 1, 2,	Elderly (60+ years) Restricted to white and coloured	Daily winter T_{min}, T_{max} and DTR South African	Cardiovascular disease mortality Central		Average deaths per day following extremely cold day were 9.41 (SD:

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Table 1 (*continued*)

Source	Location and period	Design and statistical analysis	Study population and sample	Temperature variable(s) and data source(s)	Outcome(s) and data source(s)	Confounding control	Main results
		3 and 4 days.	populations No. of participants not reported	Weather Bureau (Pretoria) for Cape Town International Airport July T_{min} of <4 °C and all winter months (May–September) T_{max} of >25 °C was considered as extreme cold and hot ("berg wind") conditions respectively 1960–1988	Statistical Services		3.10), 9.06 (3.42), 10.0 (3.12), 9.12 (3.22) and 8.65 (2.50) for lag days 0, 1, 2, 3 and 4 respectively. Average deaths per day following extremely hot day were 8.27 (2.66), 8.97 (2.54), 10.3 (3.13), 8.7 (2.72) and 8.67 (3.10) for lag days 0, 1, 2, 3 and 4 respectively. 2-day lag between occurrence of extremely cold and hot temperatures, and CVD mortality was statistically significant ($p < 0.1$ and 0.005 respectively) The highest mean daily CVD mortality was recorded on days with the largest July temperature range.
McMichael et al. (2008)	Cape Town, South Africa 1996–1999	Time series Poisson regression through Generalized linear models Adjusted for autocorrelation Sensitivity analysis that adjusted for ozone	No. of deaths not reported	Daily T_{max} and T_{min} Local meteorological station	All-cause mortality Daily counts of deaths for the period obtained from mortality register	Season, relative humidity, day of week, public holidays and particulate pollution	Temperature threshold for cold-and heat-related mortality was 17 °C (95% CI: 15, 22). Percentage increase in mortality for each 1 °C decrease in temperature below the temperature threshold was 3.82 (95% CI: 2.08, 5.60) Percentage increase in mortality for each 1 °C increase in temperature above the temperature threshold was 0.47 (95% CI: −0.31 to 1.24) Cold-related CVD deaths noted Respiratory disease mortality increased with heat

Abbreviations: DRC, Democratic Republic of Congo; T_{max}, maximum temperature; T_{min}, minimum temperature; T_{mean}, mean temperature; DTR, diurnal temperature range; HDSS, Health and Demographic Surveillance System; DHS, Demographic and Health Survey; CVD, cardiovascular disease; OR, odds ratio; IRR, incidence rate ratio; RR, relative risk; CI, confidence interval.

et al., 2005; McMichael et al., 2008), three studies applied negative binomial regression (Trærup et al., 2011; Chang et al., 2004; Tchidjou et al., 2010), one study applied ordinary least square regression (Bandyopadhyay et al., 2012), with the remaining three studies respectively applying autoregressive analysis of covariance (Alexander et al., 2013), cross-correlation analysis, and autoregressive integrated moving averages (Reyburn et al., 2011), and orthogonal polynomial regression (Ng and Cowling, 2014). All the time series studies except three (Trærup et al., 2011; Kynast-Wolf et al., 2010; Tchidjou et al., 2010) ascertained delayed (lagged) effects of the temperature variables, with terms ranging from days up to one year. Two studies (Thompson et al., 2012; Oloukoi et al., 2014) were correlation studies, with one study (Oloukoi et al., 2014) conducting focus group discussions and key informant interviews as part of the survey process. Two studies (Jankowska et al., 2012; Grace et al., 2012) were cluster analysis, with both applying multivariate linear regression. Of the two remaining studies, one study (Longo-Mbenza et al., 1999) was prospective in design, with the application of correlation analysis and logistic regression, and the other (Heunis et al., 1995), a cross-sectional study with the application of *t*-test.

With regards to study participants, five studies were conducted among children (Thompson et al., 2012; Jankowska et al., 2012; Grace et al., 2012; Bandyopadhyay et al., 2012; Tchidjou et al., 2010), one among women (Chang et al., 2004), and one among the elderly (Heunis et al., 1995). The remaining studies were not restricted to any specific population group.

3.2. Ascertainment of outcomes

Two studies (Jankowska et al., 2012; Grace et al., 2012) investigated child undernutrition, with the indicators studied being anemia, stunting, and underweight. Four studies investigated cholera incidence (Reyburn et al., 2011; Fernández et al., 2009; Paz, 2009; Trærup et al., 2011), whereas diarrhea occurrence was investigated in three studies (Thompson et al., 2012; Bandyopadhyay et al., 2012; Alexander et al., 2013). Thompson et al. (2012) also investigated respiratory infection

and asthma, in addition to diarrhea. One study (Tchidjou et al., 2010) investigated acute respiratory infections (ARI). One study each investigated meningitis (Dukić et al., 2012) and Ebola virus disease (Ng and Cowling, 2014). Cause-specific and all-cause mortality was investigated by nine studies (Azongo et al., 2012; Mrema et al., 2012; Egondi et al., 2012; Diboulo et al., 2012; Kynast-Wolf et al., 2010; McMichael et al., 2008; Kovats et al., 2005; Longo-Mbenza et al., 1999; Heunis et al., 1995). Longo-Mbenza et al. (1999) further investigated hematocrit levels. One study (Chang et al., 2004) focused on hospitalization from cardiovascular disease (CVD). One study investigated notable diseases in the study area including skin diseases (Oloukoi et al., 2014).

The studies investigating child undernutrition and one study investigating diarrhea (Bandyopadhyay et al., 2012) relied on Demographic and Health Survey (DHS) data for the outcomes. All but four studies (McMichael et al., 2008; Kovats et al., 2005; Longo-Mbenza et al., 1999; Heunis et al., 1995) investigating cause-specific and all-cause mortality relied on Health and Demographic Surveillance System (HDSS) for the mortality data. Hospital records, disease surveillance records and annual health reports of Ministries of Health and National Statistics Offices, and WHO and US CDC databases served as data sources for the cholera and other diarrhea studies. The study investigating ARIs was hospital-based, with the study outcomes being children hospitalized for ARI at a pediatric hospital. The outcome data for the study investigating meningitis (Dukić et al., 2012) were laboratory confirmed cases at a health research center.

Table 2
Summary of the temperature data measures and time period of the included studies.

Temperature measures	Time period
Daily (Azongo et al., 2012; Egondi et al., 2012; Diboulo et al., 2012; Longo-Mbenza et al., 1999; Kovats et al., 2005; McMichael et al., 2008; Heunis et al., 1995)	<1 year (Longo-Mbenza et al., 1999)
Weekly (Fernández et al., 2009)	1 to 5 years (Fernández et al., 2009; Kynast-Wolf et al., 2010; Kovats et al., 2005; McMichael et al., 2008; Chang et al., 2004; Ng and Cowling, 2014; Tchidjou et al., 2010; Oloukoi et al., 2014)
Monthly (Bandyopadhyay et al., 2012; Alexander et al., 2013; Mrema et al., 2012; Dukić et al., 2012; Reyburn et al., 2011; Ng and Cowling, 2014; Oloukoi et al., 2014; Trærup et al., 2011; Chang et al., 2004; Kynast-Wolf et al., 2010; Tchidjou et al., 2010)	6 to 10 years (Reyburn et al., 2011; Egondi et al., 2012; Trærup et al., 2011)
Yearly (Thompson et al., 2012; Paz, 2009)	11 to 20 years (Grace et al., 2012; Azongo et al., 2012; Mrema et al., 2012; Diboulo et al., 2012; Dukić et al., 2012)
Seasonal (Jankowska et al., 2012; Grace et al., 2012)	21 to 30 years (Alexander et al., 2013; Bandyopadhyay et al., 2012; Thompson et al., 2012; Heunis et al., 1995)
Diurnal temperature range (Alexander et al., 2013; Heunis et al., 1995)	>30 years (Jankowska et al., 2012; Paz, 2009)

3.3. Temperature indicators

Eleven studies relied on monthly temperature measurements (Bandyopadhyay et al., 2012; Alexander et al., 2013; Mrema et al., 2012; Dukić et al., 2012; Reyburn et al., 2011; Ng and Cowling, 2014; Oloukoi et al., 2014; Trærup et al., 2011; Chang et al., 2004; Kynast-Wolf et al., 2010; Tchidjou et al., 2010), seven studies on daily temperature measurements (Azongo et al., 2012; Egondi et al., 2012; Diboulo et al., 2012; Longo-Mbenza et al., 1999; Kovats et al., 2005; McMichael et al., 2008; Heunis et al., 1995), with two studies each relying on yearly (Thompson et al., 2012; Paz, 2009) and seasonal temperature measurements (Jankowska et al., 2012; Grace et al., 2012). One study used weekly temperature measurements (Fernández et al., 2009). Two studies (Alexander et al., 2013; Heunis et al., 1995) further relied on the diurnal temperature range.

The included studies obtained data from local weather stations and meteorological services departments, global climatology archives, Africa Rainfall and Temperature Evaluation System and World Meteorological Services databases, and weather websites. Mean, minimum and maximum measurements of these temperature indicators were explored by the included studies.

Temperature data collected spanned a period of <1 year in one study (Longo-Mbenza et al., 1999), 1 to 5 years in eight studies (Fernández et al., 2009; Kynast-Wolf et al., 2010; Kovats et al., 2005; McMichael et al., 2008; Chang et al., 2004; Ng and Cowling, 2014; Tchidjou et al., 2010; Oloukoi et al., 2014), 6 to 10 years in three studies (Reyburn et al., 2011; Egondi et al., 2012; Trærup et al., 2011), 11 to 20 years in five studies (Grace et al., 2012; Azongo et al., 2012; Mrema et al., 2012; Diboulo et al., 2012; Dukić et al., 2012), 21 to 30 years in four studies (Alexander et al., 2013; Bandyopadhyay et al., 2012; Thompson et al., 2012; Heunis et al., 1995) and >30 years in two studies (Jankowska et al., 2012; Paz, 2009). Table 2 summarizes the temperature data measures and time period of the included studies.

3.4. Methodological quality of included studies

There was a high possibility of selection bias in five studies that sampled patients admitted to a hospital (Chang et al., 2004; Longo-Mbenza et al., 1999; Tchidjou et al., 2010), and cases from an isolation center (Fernández et al., 2009) and a laboratory (Dukić et al., 2012), with implications for generalizability of the study findings. For all the included studies, the temperature data were ecologic measures that may not represent personal exposure experiences of study participants especially in studies covering larger geographical areas. Exposure measurement error leading to random or systematic errors of the effect estimates is thus possible in the included studies. Outcome measurement bias was minimized in the included studies as the studied outcomes were hospital/laboratory confirmed cases or ascertained through surveillance systems or from reliable reports, records and databases. None of the studies investigating cause-specific and all-cause mortality addressed the issue of harvesting (mortality displacement).

Of the time series studies, only four studies (Egondi et al., 2012; Fernández et al., 2009; Trærup et al., 2011; Chang et al., 2004) checked for overdispersion in the data with two of the studies (Egondi et al., 2012; Fernández et al., 2009) accounting for the problem in the analysis. Trærup et al. (2011) and Chang et al. (2004) on the other hand addressed the issue of overdispersion by applying negative binomial regression. Tchidjou et al. (2010) also applied negative binomial regression but did not mention in their report the basis for preferring this type of modeling. Five studies (Mrema et al., 2012; Reyburn et al., 2011; Fernandez et al., 2009; Paz, 2009; McMichael et al., 2008) mentioned checking and correcting for autocorrelation. Five studies (Diboulo et al., 2012; Azongo et al., 2012; Egondi et al., 2012; Chang et al., 2004; McMichael et al., 2008) conducted sensitivity analysis to ascertain the robustness of the study conclusions. Stratified analysis was undertaken by five studies (Diboulo et al., 2012; Azongo et al., 2012; Egondi et al., 2012; Mrema et al., 2012; Kovats et al., 2005) to assess population susceptibility.

Three studies specified lag terms of up to 4 and 5 months (Mrema et al., 2012; Reyburn et al., 2011) and 1 year (Paz, 2009) with implications for validity of their results as longer timescales tend to model seasonal patterns rather than short-term variation. Time series regression analysis is the preferred approach for investigating temperature-health relationships and was adopted by 17 of the included studies. Use of alternative analytical designs in exploring temperature-health relationships is justified but the basis for departure from the conventional approach and limitations of the approach adopted in investigating the relationship must be clearly specified. Of the six studies (Thompson et al., 2012; Oloukoi et al., 2014; Jankowska et al., 2012;

Grace et al., 2012; Longo-Mbenza et al., 1999; Heunis et al., 1995) that used alternative approaches, three studies (Jankowska et al., 2012; Grace et al., 2012; Oloukoi et al., 2014) partially adhered to this requirement by indicating the grounds but not the limitations of their approach. The remaining three studies did not justify their analytical approach in the reports. Regarding the study by Heunis et al. (1995), the use of *t*-test even after indicating that the temperature data was not normally distributed but showed a distinct bimodality is not statistically appropriate.

Two studies (Bandyopadhyay et al., 2012; Tchidjou et al., 2010) fitted minimum and maximum temperature in the same model and given these two temperature measures are strongly correlated, collinearity is a possibility leading to unstable parameter estimates and with implications for validity of the results reported. Two other studies that also fitted minimum and maximum temperature in the same model did however check for collinearity and either retained both measures in the model (Dukić et al., 2012) or fitted the measures in separate models (Reyburn et al., 2011).

On the issue of confounding control, eight studies (Thompson et al., 2012; Alexander et al., 2013; Paz, 2009; Oloukoi et al., 2014; Kynast-Wolf et al., 2010; Longo-Mbenza et al., 1999; Chang et al., 2004; Heunis et al., 1995) did not adjust for potential confounders. Chang et al. (2004) did however investigate the modifying effect of age and high blood pressure on the association. Of the fifteen studies that adjusted for potential confounders, seven studies controlled for time trend and seasonality solely (Azongo et al., 2012; Diboulo et al., 2012; Tchidjou et al., 2010) or in addition to other covariates (Egondi et al., 2012; Reyburn et al., 2011; Kovats et al., 2005; McMichael et al., 2008). Fernández et al. (2009) controlled only for seasonality with Trærup et al. (2011) controlling for time trend together with drought. Egondi et al. (2012) and two other studies (Mrema et al., 2012; Ng and Cowling, 2014) adjusted for the lag effects. Ng and Cowling (2014) and McMichael et al. (2008) further adjusted for absolute and relative humidity respectively. McMichael et al. (2008) also controlled for public holidays and clearly justified their decision to control for this variable. The studies which adjusted for lag effects did not however indicate whether the distributed lag model was unconstrained or constrained, an important element for making decisions about the precision of the estimates. Four studies (Jankowska et al., 2012; Grace et al., 2012; Bandyopadhyay et al., 2012; Dukić et al., 2012) adjusted for a range of potential confounders including demographic, household and socioeconomic factors, and nutritional, health and behavioral factors. Three studies (Dukić et al., 2012; Kovats et al., 2005; McMichael et al., 2008) adjusted for air quality with only McMichael et al. (2008) justifying their decision to adjust for particulate air pollution. McMichael et al. (2008) further indicated that even though they had available data on ambient ozone levels for a subset of cities, they did not control for it in the analysis because of their dependence on temperature and sunlight.

Overall, applying the modified GRADE guidelines, we rated the quality of the body of evidence for skin diseases, diarrhea, asthma and respiratory diseases, meningitis, and Ebola virus disease as very low. For child undernutrition, and respiratory and infectious disease hospitalization and deaths, we rated the body of evidence as low whereas for cholera, all-cause mortality, and CVD hospitalization and deaths, the body of evidence was rated as moderate. The summary scores for the respective outcomes and interpretation of the quality ratings is presented in Table 3.

3.5. Findings of included studies

3.5.1. Child undernutrition

In the study conducted in Mali (Jankowska et al., 2012), for all clusters, location within a zone with combined temperature and precipitation index <−100 resulted in a highly statistically significant reductions in height-for-age z-scores ($\beta = -0.165$, $p < 0.001$), weight-for-age z-scores ($\beta = -0.159$, $p < 0.001$), and hemoglobin levels ($\beta = -0.149$, $p < 0.01$). Grace et al. (2012) on the other hand, found temperature to have no impact on variation of height-for-age z-scores ($\beta = -0.0385$, $p > 0.1$ for mean temperature, and $\beta = 0.0878$, $p > 0.1$ for temperature variability).

3.5.2. Cholera incidence

A 1 °C increase in temperature resulted in a two fold increase in cholera cases (ARIMA $\beta = 2.208$, $p = 0.034$) with a lag term of 4 months in the Zanzibar study (Reyburn et al., 2011), and explained 5.2% increase in cholera cases (relative risk [RR] = 1.05, 95% CI: 1.04, 1.06) with a lag term of 6 weeks in a Zambian Study (Fernández et al., 2009). A 1 °C increase in temperature also increased the relative risk for cholera cases by 15% ($\beta = 0.141$, $p = 0027$; Incidence rate ratio [IRR] = 1.15) to 29% ($\beta = 0.256$, $p = 0.021$; IRR = 1.29) in a Tanzanian study (Trærup et al., 2011). A multi-country study conducted in southeastern Africa (Paz, 2009) also reported a 0.1 °C increase in annual mean temperature to multiply cholera cases by 2.78 ($\beta = 1.02$, $p = 0.03$) with a lag effect of one year.

Table 3
Summary of the quality of the body of evidence.

Outcome	Quality score	Quality rating	Interpretation of quality rating[a]
All-cause mortality (Azongo et al., 2012; Mrema et al., 2012; Egondi et al., 2012; Diboulo et al., 2012; Kynast-Wolf et al., 2010; McMichael et al., 2008; Kovats et al., 2005)	−2	Moderate	We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Cardiovascular disease hospitalization and mortality (Kynast-Wolf et al., 2010; McMichael et al., 2008; Kovats et al., 2005; Chang et al., 2004; Longo-Mbenza et al., 1999; Heunis et al., 1995)	−2	Moderate	
Cholera (Reyburn et al., 2011; Fernández et al., 2009; Paz, 2009; Trærup et al., 2011)	−2	Moderate	
Child undernutrition (Jankowska et al., 2012; Grace et al., 2012)	−3	Low	Our confidence in the effect estimate is limited. The true effect may be substantially different from the estimate of the effect.
Respiratory and infectious disease hospitalization and mortality (Egondi et al., 2012; Kovats et al., 2005; McMichael et al., 2008)	−3	Low	
Skin diseases (Oloukoi et al., 2014)	−5	Very low	We have very little confidence in the effect estimate. The true effect is likely to be substantially different from the estimate of effect.
Diarrhea (Thompson et al., 2012; Bandyopadhyay et al., 2012; Alexander et al., 2013)	−4	Very low	
Asthma and respiratory diseases (Tchidjou et al., 2010; Thompson et al., 2012)	−4	Very low	
Meningitis (Dukić et al., 2012)	−4	Very low	
Ebola virus disease (Ng and Cowling, 2014)	−4	Very low	

[a] As defined by the GRADE guidelines.

3.5.3. Diarrhea occurrence

Diarrhea occurrence increased with elevated maximum temperature in the multi-country study (Bandyopadhyay et al., 2012) ($\beta = 1.039$, $p < 0.01$) and the South African study (Thompson et al., 2012) ($r = 0.928$). In the study conducted in Botswana (Alexander et al., 2013), elevated maximum temperature was not associated with increased diarrhea prevalence. Alexander et al. (2013), during wet season, and Bandyopadhyay et al. (2012), found diarrhea occurrence to decrease with elevated minimum temperature ($\beta = -0.460$, $p < 0.05$ and Proportion deviation from yearly seasonal mean [Pmy] $= -0.0071$, respectively). Alexander et al. (2013) did however associated elevated minimum temperature with increased diarrhea incidence during the dry season (Pmy = 0.074). Thompson et al. (2012) further reported decreased minimum temperature to be associated with increased diarrhea incidence ($r = 0.928$). Overall, Thompson et al. (2012) observed a one unit increase in temperature to increase disease (including diarrhea) incidence by 1.329 fold ($\beta = 1.329$).

3.5.4. All-cause mortality

An increased risk of mortality with temperature extremes was noted by seven studies and was largely observed at shorter lag, albeit some of the associations were not statistically significant. A U-shaped relationship was observed among all age groups in a study conducted in Ghana (Azongo et al., 2012), among children under 5 years of age in Kenya (Egondi et al., 2012), and among the elderly (≥60 years of age) in a study conducted in Burkina Faso (Diboulo et al., 2012). Egondi et al. (2012) observed a J-shape relationship for all ages. The temperature threshold did however vary in the different study locations. In the Ghana study (Azongo et al., 2012), the 25th and 75th percentile temperature thresholds were 27.4 °C and 30.6 °C respectively, with mean daily temperature below the 25th percentile and above the 75th percentile at lag 0–1 days associated with 0.19% and 1.14% increased mortality risk, respectively. In the Kenya study (Egondi et al., 2012), the 25th and 75th percentile temperature threshold was 17.9 °C and 20 °C respectively, with mean daily temperature below the 25th percentile at lag 0–1 days associated with 3% increased risk of mortality. The threshold temperature in the study conducted in Tanzania (Mrema et al., 2012) was 26–27 °C, with monthly average temperature significantly associated with mortality in all age groups. According to the authors, a decrease in temperature below the threshold up to 24 °C would increase mortality by 80.7%, 65.7% and 74% in age groups 0–4, 5–59 and ≥60 years, respectively. When the delayed effects of temperature were examined, monthly average temperature was significantly associated with mortality at lag 2 days in age group 5–59 years (RR = 0.897; 95% CI: 0.801, 0.993). The study conducted in Burkina Faso (Diboulo et al., 2012) found a statistically significant linear increase in mortality for all ages with increasing temperature at lag 0–1 days. This finding according to the authors corresponds to approximately 50% increase in mortality over the range of temperature. The authors also found a 1 °C increase in temperature to be associated with a 2.6% increased risk of mortality. Subgroup analysis across the studies revealed the increased risk of mortality associated with temperature variability to be more pronounced among children under five years of age and adults aged 60 years or more. The two studies conducted in South Africa (Kovats et al., 2005; McMichael et al., 2008) also found low and high temperature to be associated with all-cause mortality. Kovats et al. (2005) was however unable to define precisely the threshold temperature but did report that when a threshold of 15 °C was assumed, a 1 °C decrease in temperature resulted in a 3.14% and 1.77% increase in deaths among the elderly and children, respectively. In the McMichael et al. study (McMichael et al., 2008), the temperature threshold was 17 °C with 1 °C decrease in temperature below the threshold and 1 °C increase in temperature above the threshold resulting in 3.82% (95% CI: 2.08, 5.60) and 0.47% (95% CI: −0.31 to 1.24) increased risk of mortality.

3.5.5. Cause-specific mortality and hospitalization

Regarding cause-specific mortality, Egondi et al. (2012) found a 1 °C increase in temperature above the 75th percentile to be significantly associated with a 1% increased risk of NCD mortality. Longo-Mbenza et al. (1999) also found mean temperature above 28 °C to increase the risk of stroke mortality by 21 in their study conducted in the Democratic Republic of Congo. Kovats et al. (2005) found low temperature to be associated with increased risk of infectious and cardiovascular diseases, with McMichael et al. (2008) associating low and high temperatures with CVD and respiratory disease deaths, respectively. Heunis et al. (1995) also associated the occurrence of extremely cold and hot temperatures with CVD mortality. Kynast-Wolf et al. (2010), in their study conducted in Burkina Faso, however, found no association between mean monthly temperature and CVD mortality. Egondi et al. (2012) further reported a 13% increase in deaths from acute infections for a 1 °C decrease in temperature below the 25th percentile, albeit the association was not statistically significant. The multi-country study that focused on hospitalization from CVD (Chang et al., 2004) found 5 °C change in the monthly mean temperature to be associated with decreased risk of hospitalization for venous thromboembolism (summary IRR = 0.69; 95% CI: 0.49, 0.96), stroke (summary IRR = 0.89; 95% CI: 0.64, 1.24), and acute myocardial infarction (summary IRR = 0.96; 95% CI: 0.04, 21.2). The association reported for acute myocardial infarction was however very weak and imprecise. Longo-Mbenza et al. (1999) found maximum and mean temperature to be positively correlated with hematocrit.

3.5.6. Meningitis, Ebola and respiratory diseases

In a study conducted in Ghana (Dukić et al., 2012), whereas increased maximum temperature was associated with increased meningitis incidence, increased minimum temperature was associated with decreased meningitis incidence. Lower temperature was also found to be associated with increased risk of EVD outbreak onset in the five study countries during the period 1976 to 2014 (Ng and Cowling, 2014). Thompson et al. (2012), also investigated respiratory infection and asthma in their study in South Africa and found incidence of these diseases to increase with increasing maximum temperature and decreasing minimum temperature during the period 1999 to 2010 ($r = 0.930$ and 0.813, respectively). In a study conducted in Cameroun (Tchidjou et al., 2010), maximum temperature was found to be associated with increased risk of acute respiratory infections, whereas minimum temperature was associated with decreased risk.

3.5.7. Skin and other diseases

The mixed methods study conducted in Nigeria (Oloukoi et al., 2014) found study participants suggesting extreme heat waves in the few years preceding the study period and linking severe heat (increased temperature) during the dry season to higher prevalence of skin diseases in the study area. The survey and correlation trends showed also that cases of most modifiable diseases in the region increased during the dry season.

4. Discussion

4.1. Summary of findings

We systematically reviewed 23 studies that investigated the association of ambient temperature variability with non-vector borne morbidity and mortality in Sub-Saharan Africa with the evidence gathered covering all the regional blocks. The quality of the body of evidence associating temperature variability with cholera outbreaks, cardiovascular disease hospitalization and deaths, and all-cause deaths in SSA is considered moderate. The quality of evidence on child undernutrition is low, and for diarrhea occurrence, meningitis, Ebola virus disease, asthma and respiratory diseases, and skin diseases, very low. The temperature threshold does however appear to differ from country to

country. With regards to population susceptibility, the evidence was not sufficient to draw definite conclusions.

4.2. Validity issues

We performed a comprehensive search of three electronic databases using a well-defined search strategy that involved the use of both controlled vocabulary and text words, and with no language restrictions. We also screened the reference list of all included studies and previous related reviews of the topic. Thus, all the studies relevant to answering the research question posed are likely to have been uncovered. We also considered all study designs, both short- and long-term exposure studies, so as to take care of both acute and chronic health endpoints of exposure. Although there were similarities in study designs and statistical methods applied, it was still extremely difficult to compare estimates between the included studies, mainly due to the different temperature thresholds and the use of varying lag structures. This issue and the small number of studies for most outcomes also made it practically impossible to undertake a meta-analysis. With all the included studies overlooking the effect modifying potential of socioeconomic circumstances, uncertainty surrounds the precision of the effect estimates and interpretation of the associations. We modified the GRADE guidelines with the development of a very detailed checklist to systematically evaluate the quality of the body of evidence available and does lend credence to the conclusions of our review.

4.3. Synthesis of findings with previous knowledge

Warming and unstable climate is playing an ever-increasing role in driving the global emergence, resurgence, and redistribution of infectious diseases (Leaf, 1989; McMichael et al., 1996). Lipp et al. (2002), have stated that increasing temperatures would be expected to expand the range and increase the prevalence of *Vibrio cholerae* and cholera incidence both geographically and temporally. The association of increased temperature with cholera outbreaks observed by the studies reviewed supports Lipp et al. (2002) postulation and possibly implicates regional and local climate change in the amplification of cholera epidemics in Sub-Saharan Africa. Even though the quality of the body of evidence was rated moderate, our findings should be interpreted with caution due to the small number of studies contributing to the body of evidence.

The mechanism linking climate change including temperature variability with cholera outbreaks is based on the established fact that copepods, a zooplankton, play an important role in the survival, multiplication and transmission of *V. cholerae* and other *Vibrio* spp. in the natural aquatic environment as was first postulated by Kaneko and Colwell (1973), and Huq et al. (1983). According to Borroto (1998), the most important climatic factor related to cholera outbreaks is temperature, especially of the water bodies and the aquatic environment. This factor according to Colwell (1996) governs the survival and growth of *V. cholerae* because of its direct influence on its abundance in the environment or through its indirect influence on the planktons to which the pathogen attaches itself. Temperature shifts will alter the latitudinal distribution of plankton species and should sea level rise as anticipated with higher temperatures, inland areas would experience greater saltwater intrusion and increased levels of marine and estuarine bacteria including *V. cholerae* (Lipp et al., 2002). We must underline that some of the evidence on the temperature-cholera relationship emanated from landlocked countries; Zambia (Fernández et al., 2009) and five of the eight countries in the multi-country study (Paz, 2009), and with cholera outbreaks well documented to primarily originate in coastal regions, the authors should have indicated this limitation of their study in the report and further provide alternative explanation for their findings.

Diarrhea, which is one of the leading causes of morbidity and mortality in Africa and in other developing regions of the world (Walker and Black, 2010; Lamberti et al., 2012) has been predicted to increase with climate change (Rosenthal, 2009; Kolstad and Johansson, 2011). There were some inconsistencies in the studies reviewed as to (a) which temperature variable(s) is the most important risk factor and (b) which direction of the temperature measures has the most pronounced effect on diarrhea incidence. Guo et al. (2014) have however suggested that daily mean temperature, an average of the multiple observations throughout the day, is believed to be a good estimate of exposure and less affected by measurement errors compared to other temperature measures. The most obvious mechanism that could explain increased diarrhea occurrence with elevated temperature as noted by some of the studies reviewed is food poisoning due to accelerated bacterial growth in food. Elevated temperatures are known to favor growth of food spoilage microorganisms and in settings where there is lack of or poor refrigeration as pertains in many areas of SSA countries, diarrhea incidence is most likely to increase. Our hypothesis is strengthened by studies conducted in multiple populations that have associated increased temperature with bacterial enteric (*Salmonella*, *Campylobacter* and *Escherichia coli*) infection (D'Souza et al., 2004; Kovats et al., 2004; Fleury et al., 2006; Naumova et al., 2007). If this is however the case, then diarrhea incidence should have a socioeconomic status (SES) gradient, declining as SES improves irrespective of climatic conditions and should have been explored by the studies reviewed.

The highest prevalence of child undernutrition is found in South Asia and Sub-Saharan Africa, where 40% of all children under five are stunted (Smith and Haddad, 2015). Climate variability and extreme weather events will affect the quantity, quality and stability of crop yields (Porter and Semenov, 2005; Phalkey et al., 2015). Elevated temperatures above a threshold of 29–32 °C decreases crop yield (Schlenker and Roberts, 2009). Higher temperatures can reduce or even halt photosynthesis, prevent pollination, and lead to crop dehydration (Wali et al., 1999; Brown, 2008). It is a well-documented fact that, in areas where the quantity and quality of food crops is compromised, levels of child undernutrition tend to increase. Even though the two studies that reviewed the relation of temperature with child undernutrition reported contradictory results, the causal mechanism enumerated suggest increasing temperature in SSA is a serious threat to child nutrition and survival.

The body of evidence linking temperature variability with meningitis and EVD outbreak, asthma and other respiratory diseases, and skin diseases in SSA was very low but should not be discounted due to the persistence of the association in different models (in the case of meningitis outbreak) and known biological mechanisms. Climate change and increased temperature compromise air quality through several pathways, including production and allergenicity of aeroallergens such as pollen and mold spores, and increases in ambient concentrations of ozone, fine particles and dust (Rogers et al., 2006; Shea et al., 2008; Vose et al., 2004; Wan et al., 2002; Houghton et al., 2001; Portier et al., 2010). Exposure to these pollutants has been well documented to cause or exacerbate asthma and several other respiratory diseases. The spread and transmission of pathogenic diseases including Ebola and meningitis depends on the ability of the pathogen to mature and replicate. Temperature and moisture availability has been identified as the most important meteorological factors affecting pathogen proliferation, with temperature especially having a strong effect on the rate of pathogen maturation and replication (WHO, 2004; UNECA-ACPC, 2011). According to Costello et al. (2009), the likelihood of infection increases as a result, with populations having little or no immunity to new infections being at increased risk. The skin is the most exposed organ to the environment, therefore cutaneous diseases are inclined to have a high sensitivity to climate (Balato et al., 2013).

The evidence of increased risk of CVD hospitalization and death with temperature variability that was uncovered should also be interpreted with caution in spite of its moderate rating, again due to the small number of studies that contributed to the body of evidence. Previous reviews (Basu and Samet, 2002; Basu, 2009; Ye et al., 2012) provide evidence of

increased risk of CVD morbidity and mortality with elevated ambient temperature exposure. Campbell-Lendrum et al. (2003), stated that CVD has the best characterized temperature-mortality relationship followed by respiratory disease. The association is supported by strong evidence for direct links between high or low temperatures and increased blood pressure, blood viscosity, plasma cholesterol and heart rate (Keatinge et al., 1984, 1986; Pan et al., 1995). According to Portier et al. (2010), there is also evidence that heat amplifies the adverse impact of ozone and particulates on CVD. Ozone, whose formation increases with temperature, increases cardiac effort and impairs pulmonary gas exchange (Gong et al., 1998).

We also observed evidence of increased risk of all-cause mortality with exposure to temperature extremes. Two reviews (Basu and Samet, 2002; Basu, 2009) summarizing the evidence on the temperature-mortality relationship reported elevated temperature to be associated with increased mortality. The evidence summarized by these authors, however emanated largely from high income countries, predominantly Europe and North America, with only two studies from Sub-Saharan Africa (both from South Africa), one of which (McMichael et al., 2008) met the inclusion criteria for our review. McMichael and colleagues study (McMichael et al., 2008) was however a multi-country study conducted in twelve countries and attempted for the first time to characterize and compare temperature-mortality relationships in low- and middle- income cities, in both tropical and temperate regions. The authors found evidence of increasing mortality at low temperatures in all cities except Ljubljana, Salvador, and Delhi, and also at high temperatures in all cities except Chiang Mai and Cape Town.

5. Conclusions

Our systematic review suggests that ambient temperature exposure may contribute to disease and mortality burden in Sub-Saharan Africa. Overall, the evidence base is somehow weakened by the limited number of studies uncovered, methodological limitations of the studies, and notable inconsistencies in the study findings. This situation calls for further research with robust study designs and standardized analytical methods to produce more credible evidence base to inform climate change preparedness plans and public health policies for improved adaptive capacity in the region. It must however be underlined that for most studies, the temperature trend analysis spanned a relatively short time period and does not constitute solid evidence of climate change in the region. Nevertheless, evidence on the health effects of temperature variability is important for understanding and projecting health impacts under climate change scenarios.

Limited meteorological stations, and poor health surveillance systems and records keeping across Sub-Saharan Africa, represent major obstacles to climate-health research in the region, and calls for investment in meteorological services, and strengthening of health information systems to guarantee timely, up-to-date and reliable data. SSA governments should also take urgent steps to remove the bottlenecks to accessing institutional data for research.

Characterizing vulnerable subgroups in the population is very important for developing plans to strengthen resilience in these subpopulations and should be a focus area of future studies. Profiling socioeconomic differentials in the temperature-health relationships in SSA should be another focus area of future studies owing to the widespread regional- and community-level socioeconomic inequalities in many SSA countries in order to provide the context for better interpretation of the associations for preventive actions.

Global and regional climate change has the potential to exacerbate the existing health inequities in SSA and erode the gains made in improving public health, hence the need for governments to invest in health research on temperature variability and other climate change phenomena. Future research should not only focus on clarifying the temperature-health relations but should also elaborate whether climate change phenomena are widening the health equity gap and derailing efforts at improving population health in the region in order to convince SSA governments that adaptation, mitigation, and preparedness programs are a necessary and appropriate investment.

Conflict of interest

The authors declare that no conflicts of interests exist.

Appendix A. Checklist for rating the quality of the body of evidence

1. Study limitations (risk of bias)
   - Possibility of selection bias Yes [ ] No [ ]
   - Poor/inaccurate exposure measurement Yes [ ] No [ ]
   - Poor/inaccurate outcome measurement Yes [ ] No [ ]
   - Harvesting (mortality displacement) was not accounted Yes [ ] No [ ]
   - Overdispersion in data was not checked and accounted Yes [ ] No [ ]
   - Autocorrelation was not corrected Yes [ ] No [ ]
   - Sensitivity/stratified analysis was not conducted Yes [ ] No [ ]
   - No/inadequate control of confounding Yes [ ] No [ ]
2. Imprecision of effect estimates
   - No mention of whether distributed lag model was unconstrained or constrained Yes [ ] No [ ]
   - 95% confidence intervals are very wide Yes [ ] No [ ]
   - Sample sizes are very small Yes [ ] No [ ]
3. Inconsistency of results
   - Point estimates vary widely across studies Yes [ ] No [ ]
   - Confidence intervals show minimal or no overlap Yes [ ] No [ ]
   - Conflicting findings Yes [ ] No [ ]
4. Indirectness of results
   - Study populations differ from those of interest Yes [ ] No [ ]
   - Exposures measured differ from those of interest (surrogate exposures) Yes [ ] No [ ]
   - Outcomes ascertained differ from those of interest (surrogate outcomes) Yes [ ] No [ ]
   - No or wrong comparisons Yes [ ] No [ ]

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