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S Gyaase; S Nyame; Kerstin Klipstein-Grobusch; K. P Asante; G. S Downward

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GLOBAL HEART

Climate, Air Quality and Their Contribution to Cardiovascular Disease Morbidity and Mortality in Low- and Middle-Income Countries: A Systematic Review and Meta-Analysis

ORIGINAL RESEARCH

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STEPHANEY GYAASE
KWAKU POKU ASANTE
SOLOMON NYAME
GEORGE S. DOWNWARD
KERSTIN KLIPSTEIN-GROBUSCH

*Author affiliations can be found in the back matter of this article

ABSTRACT

Background: Increasing exposure to climatic features is strongly linked to various adverse health outcomes and mortality. While the link between these features and cardiovascular outcomes is well established, most studies are from high-income countries.

Objectives: This review synthesizes evidence as well as research gaps on the relationship between climate indicators, household/ambient air pollution, and all-cause cardiovascular disease (CVD) morbidity and mortality in low- and middle-income countries (LMICs).

Methods: Seven electronic databases were searched up to June 15, 2024. Articles were included if they focused on LMICs, addressed all-cause CVD morbidity and/or mortality, and studied climate or environmental exposures. Studies were selected using ASReview LAB, extracted and analyzed with random effect meta-analysis performed if sufficient articles were identified.

Results & Conclusion: Out of 7,306 articles, 58 met the inclusion criteria: 26 on morbidity, 29 on mortality, and 3 on both. Exposures included PM_{10}, $PM_{2.5}$, NO_2, SO_2, BC, O_3, CO, solid fuel usage, and temperature variation. Short-term exposure to $PM_{2.5}$ was significantly associated with CVD morbidity (RR per 10 μg/m^3 increase:1.006, 95% CI 1.003–1.009) and mortality (RR:1.007, 95% CI 1.002–1.012). Short-term exposure to NO_2 and O_3 also increased CVD mortality risk. Long-term exposure to $PM_{2.5}$ elevated CVD morbidity (RR per 10 μg/m^3 increase:1.131, 95% CI 1.057–1.210) and mortality (RR:1.092, 95% CI 1.030–1.159). High and low temperatures and long-term solid fuel use were linked to CVD deaths. The bulk of studies were from mainland China (72%), which may not accurately reflect the situation in other LMICs. Sub-Saharan Africa was particularly lacking, representing a major research gap.

CORRESPONDING AUTHOR:
Stephaney Gyaase
Kintampo Health Research Centre, Research and Development Division, Ghana Health Service, Kintampo, Ghana; Julius Global Health, Department of Global Public Health and Bioethics, Julius Center for Health Sciences, University Medical Center Utrecht, Utrecht University, Utrecht, The Netherlands
stephaney.gyaase@kintampo-hrc.org; s.gyaase@umcutrecht.nl

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INTRODUCTION

The World Health Organization (WHO) estimates that cardiovascular diseases (CVD) are responsible for approximately 32% of all deaths, with more than 75% of these deaths occurring in low- and middle-income countries (LMICs). Within the regions of Sub-Saharan Africa, cardiovascular diseases are the most common cause of noncommunicable diseases (NCDs), with a regional burden that is anticipated to double by the year 2030 (1–3).

Climatic and environmental disruptions to health can be observed via multiple systems and pathways, affecting people throughout the life course. It is estimated that every year, air pollution is responsible for approximately 7 million premature deaths around the world, with cardiovascular diseases being among the top four diseases related to air and other environmental exposures (4–8). Several lines of evidence have demonstrated that increasing and ongoing exposure to climatic features such as heat waves, air pollution, and household air pollution can cause or are strongly related to myriad adverse long- and short-term health outcomes such as CVD, respiratory disorders, elevated blood pressure, malignancies, heart disease, and death (4, 9–24).

However, the majority of these estimates are based on studies from high-income countries. As such, there is very little in terms of evidence synthesis from a primarily LMIC context. With the burden of CVD anticipated to double by the year 2030 (25), the limited health care infrastructure in LMIC settings and substantial differences between pollutant sources, extrapolations of evidence from high-income settings are of limited use. The purpose of this review, therefore, is to examine and synthesize the evidence related to key indicators of climate, household/ambient air pollution, and their association with all-cause CVD morbidity and mortality in LMICs. We will also evaluate relevant research gaps in this setting related to the link between climatic indicators and all-cause CVD morbidity and mortality in LMICs.

METHODS

SEARCH STRATEGY

The systematic review and meta-analysis protocol followed PRISMA guidelines and was registered with PROSPERO (registered ID: CRD42022373943). We searched seven electronic databases, including PubMed, Embase, SCOPUS, LILACS, AIM, Web of Science, and Global Health. Specific search terms for each database are included in the appendix.

ELIGIBILITY CRITERIA

Studies were eligible for inclusion in the current study if they contained information related to climate and environmental exposures and their effect on all-cause cardiovascular disease morbidity and mortality amongst adults (i.e., 18 years and older) in low- and middle-income countries. A wide range of reporting all-cause CVD morbidity/mortality was allowed, including physician diagnosis, self-report, national disease surveillance database, hospital records, verbal autopsies, and death certificates. The definition of LMIC was based on the World Bank definition at the time of the literature search. Studies that did not primarily examine environmental conditions, examine pediatric populations, have a high-income-country focus, or were restricted to specific cardiovascular conditions (e.g., hypertension alone) were not included.

There was no restriction on the publication date. The search was initially performed on November 20, 2023, and updated on June 15, 2024.

ARTICLE SELECTION AND DATA EXTRACTION

All articles identified by the initial searches were exported to Rayyan (26) for deduplication. Following this, the remaining articles were imported to ASReview lab version 1.1.1 (27) for title and abstract screening. ASReview is an artificial intelligence tool that utilizes a TF-IDF, Naïve Bayes, mixed sampling model to rank titles and abstracts based on their probability of being relevant. This probability is initially based on positive examples provided by the reviewer and subsequently refined following inclusion or exclusion decisions. Titles that are less likely to qualify for the current review are ranked lower, with the ranking being dynamically updated following each decision. A stopping rule based on a data-driven strategy was employed by two reviewers (SG and GD) and set at 250 consecutive irrelevant articles. Any disagreement about

Table 1 Description of included articles on CVD morbidity/mortality and environmental factors.

AUTHOR & YEAR	LOCATION	STUDY DESIGN	MAIN EXPOSURE(S)	OUTCOME AND DEFINITION	MAIN FINDINGS	STUDY QUALITY
Buadong et al., 2009 (33)	Bangkok, Thailand	Time-series	PM_{10}, O_3	Morbidity – daily hospital visits	There was no significant association for either PM_{10} or O_3 on CVD morbidity in the 3-day cumulative lag model.	Fair
Dong et al., 2013 (56)	Liaoning Province, China	Cross-sectional	PM_{10}, SO_2, NO_2, O_3	Morbidity – Positive response from questionnaire	No significant association was found between any of the air pollutants and CVD morbidity	Fair
Tong et al., 2014 (36)	Tianjin Municipality, China	Time-series	PM_{10}, SO_2, NO_2	Morbidity – Database	A 10 μg/m³ increase in the 2-day average concentration of PM_{10} and SO_2 were associated with a 0.19% (0.08–0.31) and 0.43% (0.03–0.84) increase in CVD morbidity respectively. No significant association was found for NO_2.	Fair
Giang et al., 2014 (31)	Thai Nguyen, Vietnam	Time-series	Temperature	Morbidity – Hospital admission	Over a 0–30-day lag period, there was a 12% (1%–25%) increase in CVD hospital admissions per 1 degree below the temperature threshold. A positive, yet non-significant association was observed for increased temperature.	Fair
Su et al, 2016 (34)	Haidian District, Beijing, China	Time-series	PM_{10}, $PM_{2.5}$, SO_2, NO_2	Morbidity – Medical records of emergency visits	In the 0–7-day cumulative lag model, no significant association between $PM_{2.5}$, PM_{10}, SO_2, or NO_2, and CVD morbidity was observed.	Fair
de Freitas et al., 2016 (35)	Victoria, Brazil	Time-series	PM_{10}, O_3, SO_2	Morbidity – Hospital records	In the 0–5-day cumulative lag model, CVD events increased by 2.11% (1.06–3.18) per 10 μg/m³ increase in O_3. No significant association was observed for PM_{10} and SO_2.	Poor
Phung et al., 2016 (39)	Vietnam	Time-series	PM_{10}, SO_2, NO_2, O_3	Morbidity – Hospital admission	In the lag-3 model, neither PM_{10}, NO_2, SO_2 or O_3 had a statistically significant association with CVD morbidity.	Fair
Ma et al., 2017 (42)	Beijing, China	Time-series	PM_{10}, SO_2, NO_2	Morbidity – Hospital admission	For a 10 μg/m³ increase in NO_2, ER cardiovascular admission increased by 1.4% (RR:0.986; 95%CI:0.976–0.996) in the 0–6-day cumulative lag model. There was no association between CVD admission and PM_{10} or SO_2.	Fair
Liu et al., 2018 (46)	Mainland China	Case crossover	CO	Morbidity – Health database	A 1 mg/m³ increase in the same day CO was associated with a 4.39% (4.07–4.70) increase in CVD.	Fair
Li et al., 2018 (47)	Beijing, China	Case crossover	CO	Morbidity – Health database	A 1 mg/m³ increase in the 2-day moving average of CO was associated with a 2.8% (2.2–3.3) increase in daily hospital CVD admissions.	Fair
Phosri et al., 2019 (38)	Bangkok, Thailand	Time-series	SO_2, NO_2, O_3, CO	Morbidity – Daily hospital admission	A 10 μg/m³ increase in PM_{10}, SO_2, and NO_2 corresponded to 0.6% (0.10–1.00), 5.3% (2.42–8.21), and 0.6% (0.06–1.09) increases in total CVD admission in the 0–4-day cumulative lag models, respectively. A 1 mg/m³ increase in CO increased CVD admission by 4.2% (1.35–7.26). No significant association with O_3 was observed.	Fair
Yao et al., 2019 (86)	Yichang Province, China	Time-series	PM_{10}, $PM_{2.5}$	Morbidity – Daily inpatient records	There was no statistically significant association between PM_{10} or $PM_{2.5}$ and CVD admission in the lag 7 model.	Fair
Amsalu et al., 2019 (32)	Beijing, China	Time-series	$PM_{2.5}$	Morbidity – Daily hospital admission	In the 0–3-day lag model, a 10 μg/m³ increase in $PM_{2.5}$ was associated with a 0.7% (0.4–0.9) increase in CVD hospital admissions.	Fair
Cheng et al., 2019 (48)	Lanzhou city, China	Time-series	CO	Morbidity – Daily CVD hospitalization	In the lag 0–4 model, a 1 mg/m³ increase in CO was associated with an 11% increase (95%CI: 3%–20%) in CVD hospitalization.	Fair
Khan et al., 2019 (45)	Dhaka, Bangladesh	Case crossover	$PM_{2.5}$	Morbidity – Emergency room visit	An IQR increase (103 μg/m) of $PM_{2.5}$ corresponded to a 15% increase (1–30) in CVD emergency room visits in the 3–5-day lag model.	Fair
Phosri et al., 2020 (43)	Bangkok, Thailand	Time-series	Temperature	Morbidity – Daily hospital admission	In the 0–21 lag models, an "extremely high" diurnal temperature range (11.6°C) was associated with a 20.6% (0.2–45.2) increase in CVD hospital admissions.	Fair

(Contd.)

AUTHOR & YEAR	LOCATION	STUDY DESIGN	MAIN EXPOSURE(S)	OUTCOME AND DEFINITION	MAIN FINDINGS	STUDY QUALITY
Rahman et al., 2022 (40)	Dhaka, Bangladesh	Time-series	Temperature	Morbidity – Count of CVD from Database	There was no association between a 1°C increase in temperature variability and ED visits for cardiovascular disease.	Fair
Karbakhsh et al., 2022 (44)	Iran	Case crossover	PM_{10}, $PM_{2.5}$, PM_{coarse}	Morbidity – CVD admitted	An IQR increase in PM_{coarse} (IQR: 55 μg/m³) and PM_{10} (IQR: 71 μg/m³) was associated with an increase in CVD admission (OR:1.02; 95% CI: 1.00–1.05 and 1.02; 95% CI:1.01–1.04) respectively in the lag 0–1–2 model. No significant effect was observed for $PM_{2.5.}$	Fair
Makunyane et al., 2023 (37)	Cape Town, South Africa	Time-series	Temperature	Morbidity – Daily counts of hospital admission	An IQR (6.4°C) increase in temperature variability of TV was associated with a 2.61% (1.15–4.08) increase in hospital admissions.	Fair
Ji et al., 2021 (49)	Mainland China	Cohort	Solid fuel	Morbidity – Response from questionnaire	Individuals using solid fuels at baseline had a higher risk of non-fatal CVD event than those using clean fuels (HR:1.18; 95% CI:1.05–1.32).	Fair
Liu et al., 2021 (50)	Mainland China	Cohort	$PM_{2.5}$	Morbidity – Based on Disease classification	An IQR increase in $PM_{2.5}$ (27.9 μg/m³) increased the risk of CVD morbidity (HR:1.291, 95% CI: 1.147–1.54).	Fair
Mai et al., 2032 (51)	Mainland China	Cohort	$PM_{2.5}$	Morbidity – Response from questionnaire	A 10 μg/m³ increase in $PM_{2.5}$ was associated with an increased risk of CVD morbidity (OR:1.18 95% CI: 1.12–1.26).	Fair
Wen et al., 2023 (52)	Mainland China	Cohort	Solid fuel	Morbidity – Self Assessment	Treatment effect of cardiovascular disease after implementation of coal-to-gas/electricity project was not statistically significant.	Fair
Wang et al., 2023 (53)	Mainland China	Cohort	NO_2	Morbidity – Questionnaire	A 10 μg/m³ increase in NO_2 resulted in an elevated risk of CVD morbidity (HR:1.558 95% CI: 1.477–1.642).	Fair
Liu et al., 2023 (54)	Mainland China	Cohort	Solid fuel	Morbidity – Response from questionnaire	The use of solid fuel for cooking and heating versus clean fuel increased the risk of nonfatal CVD incident by 43.0% [HR:1.43 (1.07–1.92)].	Fair
Zhu et al., 2024 (55)	Mainland China,	Cohort	O_3	Morbidity – Questionnaire	A 10 μg/m³ increase in long-term O_3 exposure was positively associated with incident of CVD (HR:1.078 95% CI: 1.050–1.106).	Fair
Xia et al., 2023 (85)	Mainland China	Cohort	$PM_{2.5}$	Morbidity & Mortality – Questionnaire	A 10 μg/m³ increase in $PM_{2.5}$ was positively associated with total CVD morbidity (HR:1.12, 95% CI: 1.11–1.14) and CVD mortality (HR:1.12 95% CI: 1.08–1.15).	Good
Liang et al., 2020 (84)	Mainland China	Cohort	$PM_{2.5}$	Morbidity & Mortality – Extracted from questionnaire	A 10 μg/m³ increase in $PM_{2.5}$ gave HRs for CVD incidence and mortality of 1.25(1.22–1.28) and 1.16 (1.12–1.21), respectively.	Good
Jalali et al., 2021 (23)	Isfahan, Iran	Cohort	$PM_{2.5}$	Morbidity & Mortality – Questionnaire & health records	The risk of CVD event increased by 2.6% (OR:1.026, 95% CI:1.016–1.036) for a 10 μg/m³ increase in $PM_{2.5}$. No significant association was observed between $PM_{2.5}$ and CVD mortality.	Fair
Zhang et al., 2006 (57)	Shanghai, China	Time-series	O_3	Mortality – Database	An increase of 10 μg/m³ in the 4-day O_3 average corresponded to a 0.9% increase (95% CI: 0.5–1.4) in total cardiovascular mortality.	Fair
Tam et al., 2010 (58)	Hong Kong Administrative Region	Time-series	Temperature	Mortality – Database	In the 0–3 lag model, a 1°C increase in diurnal temperature range resulted in a 1.7% increase in cardiovascular mortality (RR:1.017, 95% CI: 1.003–1.033)	Poor
Yang et al., 2012 (87)	Suzhou Province, China	Time-series	O_3	Mortality – Database	An IQR increase in the 24-hour average concentration of O_3 (33.3 μg/m³) was associated with a 3.33% (95% CI: 0.50–6.16) increase in CVD mortality.	Fair
Chen et al., 2012 (60)	Mainland China	Time series	SO_2	Mortality – Database	A 10 μg/m³ increase in the 2-day moving average of SO_2 was associated with a 0.83% increase in cardiovascular mortality (95% PI:0.47–1.19).	Fair
Wichmann & Voyi, 2012 (76)	South Africa	Case crossover	PM_{10}, SO_2, NO_2	Mortality – Database	There was a 3.4% (0.3–6.6) and 2.6% (0.1–5.2) increase in cardiovascular mortality per IQR increase in NO_2 (IQR: 12 μ/m³) and SO_2 (IQR: 8 μg/m³), respectively. No significant effect of PM_{10} was observed.	Fair

(Contd.)

AUTHOR & YEAR	LOCATION	STUDY DESIGN	MAIN EXPOSURE(S)	OUTCOME AND DEFINITION	MAIN FINDINGS	STUDY QUALITY
Fuhai Geng et al., 2013 (61)	Shanghai, China	Time-series	BC & $PM_{2.5}$	Mortality – Database	An IQR increase in the mean daily concentrations of BC (IQR: 2.7 μg/m³) and $PM_{2.5}$ (IQR: 41.8 μg/m³) corresponded to a 3.2% (0.6–5.7) and 3.3% (0.4–6.1) increase in total cardiovascular mortality, respectively.	Fair
Wang et al., 2014 (62)	Suzhou Province, China	Time-series	Temperature	Mortality – Database	In the 0–28 lag model, extreme cold (1st centile: –0.3°C) and hot (99th centile: 32.6°C) temperatures were positively associated with cardiovascular mortality with RRs of 2.67 (1.64–4.33) and 1.62 (1.21–2.17), respectively.	Fair
Han et al., 2017 (63)	Jinan Province, China	Time-series	Temperature	Mortality – Database	Cold spells (3 consecutive days below –3.8°C) and heat waves (3 consecutive days above 29°C) were associated with CVD mortality RRs of 1.06 (1.03–1.10) and 1.03 (1.00–1.06), respectively	Fair
Chen et al., 2018 (65)	Mainland China	Time-series	NO_2	Mortality – Database	A 10 μg/m³ increase in the 2-day average concentration of NO_2 would increase total cardiovascular mortality by 0.9% (0.7–1.2)	Fair
Chen et al., 2018 (64)	Mainland China	Time-series	$PM_{2.5}$	Mortality – Database	In the 0–2 lag model, no significant association between $PM_{2.5}$ and cardiovascular mortality was observed.	Fair
Liu et al., 2018 (66)	Mainland China	Time-series	CO	Mortality – Database	In the 0–1 lag model, a 1 mg/ m³ increase in CO was associated with a 1.12% (PI:0.42–1.83) increase in cardiovascular mortality	Fair
Wu et al., 2018 (67)	Guangzhou Province, China	Time-series	$PM_{2.5}$, PM_{10} & $PM_{10-2.5}$	Mortality – Database	In the lag 06 model, a 10 μg/m³ increase in $PM_{2.5}$, PM coarse, and PM_{10} was associated with an excess risk for CVD mortality of 1.15% (95% CI: 0.68, 1.62), 1.64% (95% CI: 0.86, 2.43), and 0.82% (95% CI: 0.49, 1.14), respectively.	Fair
Zhang et al., 2019 (41)	Jiangsu Province, China	Time-series	O_3	Mortality – Database	In the lag 0–3 model, a 10 μg/m³ increase in O_3 was associated with a 0.983% (0.588–1.3770) increase in CVD-related death.	Fair
Liu et al., 2019 (68)	Shenyang Province, China	Time-series	PM_{10}, $PM_{2.5}$, SO_2, NO_2, O_3, CO	Mortality – Death registry	In the lag 05 model, 10 μg/m³ increases in $PM_{2.5}$, PM_{10}, SO_2, and NO_2 were associated with RRs for CVD mortality of 1.004 (1.001, 1.008), 1.003 (1.001, 1.006), 1.005 (1.001, 1.009), and 1.016 (1.005, 1.028), respectively. A 1 mg/m³ increase in CO was associated with an RR of 1.066 (1.025, 1.108). No significant association was observed for O_3.	Fair
Duan et al., 2019 (69)	Shenzhen Province, China	Time-series	NO_2	Mortality – Database	In the lag 0–5-day model, a 10 μg/m³ increase in NO_2 was associated with a 3.41% (1.55–5.30) increase in cardiovascular mortality.	Fair
Iranpour et al., 2020 (70)	Ahvaz, Iran	Time-series	Temperature	Mortality – Database	In the 0–28-day lag model, no association between heat above the 99th centile (41.2°C) or below the 1st centile (9.3°C), and CVD mortality was observed.	Fair
Khosravi et al., 2020 (71)	Mashhad, Iran	Time-series	PM_{10}, $PM_{2.5}$, NO_2, O_3, CO	Mortality – Database	None of the five pollutants assessed were associated with cardiovascular mortality.	Fair
Zhou et al., 2021 (72)	Taiyuan Province, China	Time-series	PM_{10}, $PM_{2.5}$	Mortality – Database	In the 0–30 lag model, a 10 μg/m³ increase in $PM_{2.5}$ and PM_{10} was associated with a 3.10% (0.86–5.38) and 1.61% (0.69–2.54) increase in cardiovascular mortality.	Fair
Li et al., 2021 (73)	Guangzhou Province, China	Time-series	O_3	Mortality – Registry	In the 0–3 lag model, a 10 μg/m³ increase in O_3 was associated with a 0.59% (0.30–0.88) increase in CVD mortality.	Fair
Olutola et al., 2023 (75)	South Africa	Case crossover	PM_{10}, SO_2, NO_2	Mortality – Database	In the 0–6-day lag model, none of the examined pollutants were associated with increased CVD mortality.	Fair
Xia et al., 2023 (74)	Chengdu, China	Time-series	Temperature	Mortality – Database	In the 0–14-day lag model, extreme heat (99th centile, >29 °C) and extreme cold (1st centile, < 3°C) were both associated with increased CVD mortality, with RRs of 1.28 (1.14–1.43) and 1.45 (1.24–1.68), respectively.	Fair

(Contd.)

AUTHOR & YEAR	LOCATION	STUDY DESIGN	MAIN EXPOSURE(S)	OUTCOME AND DEFINITION	MAIN FINDINGS	STUDY QUALITY
Cao et al., 2011 (59)	Mainland China	Cohort	SO_2, TSP, NO_X	Mortality – Hospital records	A 10 μg/m³ increase in TSP, SO_2, and NOx corresponded to 0.9% (95% CI: 0.3, 1.5), 3.2% (95% CI: 2.3, 4.0), and 2.3% (95% CI:0.6, 4.1) increases in cardiovascular mortality, respectively.	Fair
Wong et al., 2015 (77)	Hong Kong, Administrative Region	Cohort	$PM_{2.5}$	Mortality – Death registry	A 10 μg/m³ increase in $PM_{2.5}$ exposure was associated with a 22% increase in cardiovascular mortality [HR:1.22 (1.08–1.39)].	Fair
Yu et al., 2018 (78)	Mainland China	Cohort	Solid fuel	Mortality – Questionnaire	Solid fuel use for cooking or heating was significantly associated with higher risk of cardiovascular mortality [HR:1.20 (1.02–1.41)] and [HR:1.29 (1.06–1.55)], respectively.	Fair
Yang et al., 2018 (79)	Mainland China	Cohort	$PM_{2.5}$, NO_2 & BC	Mortality – Database	An IQR increase in $PM_{2.5}$ (5.5 μg/m³) or BC (9.6 μg/m³) was associated with increased HRs for CVD mortality (1.06 [1.02–1.10] and 1.07 [1.02–1.11], respectively. No significant association was observed for NO_2.	Fair
Arku et al., 2020 (80)	China, India, South Africa and Tanzania	Cohort	Kerosene	Mortality – Hospital records, Death certificate and Verbal autopsies	Household cooking primary with kerosene had a 34% [HR:1.34 (1.08–1.66)] increase in major cardiovascular disease mortality.	Fair
Liang et al., 2022 (81)	Mainland China	Cohort	$PM_{2.5}$	Mortality – Death registry	A 10 μg/m³ increase in $PM_{2.5}$ was associated with a HR for cardiovascular mortality of 1.02 (1.00–1.05).	Good
Liu et al., 2022 (82)	Yinzhou Province, China	Cohort	O_3	Mortality – Death registry	A 10 μg/m³ increase in long-term annual average of O_3 increased cardiovascular mortality by approximately 22% [HR:1.22 (1.12–1.33)].	Good
Niu et al., 2022 (83)	Mainland China	Cohort	O_3	Mortality – Death registry	A 10 μg/m³ increase in O_3 was associated with an elevated risk of cardiovascular mortality [HR:1.093 (1.046–1.142)].	Good

the articles selected was discussed, and an agreement was reached. Articles identified through title/abstract screening subsequently underwent full-text screening. Articles retained following full-text screening underwent data extraction for information on author, title, publication year, study location, study period, study design, outcome type, mean/median exposure, comorbidities controlled for, total population, and type of pollution or climatic factor exposure studied.

RISK OF BIAS ASSESSMENT

The quality and risk of bias of the identified studies were evaluated by two reviewers (SG and GD) using the study Quality Assessment Tool of the National Health Institute/National Heart, Lung and Blood Institute (NHI/NLBI) (28). The tool has a rating of good, fair, and poor based on fourteen criteria assessments. Ratings of poor quality are associated with high risk of bias, with fair and good being associated with medium and low risks of bias, respectively.

STATISTICAL ANALYSIS/META-ANALYSIS

Studies were pooled and examined based on whether they examined either short (e.g., time-series analysis) or long (e.g., cohort) term exposures. In addition, studies examining similar environmental components and designs were pooled via random-effect meta-analysis. When examining short-term exposures, the longest combined (i.e., cumulative or pooled) lag effect (e.g., pooled lag over days 0–7) reported was retained for analysis. This decision was made to avoid selecting only lag estimates with positive findings. Effect estimates (Risk Ratio (RR)/Odds Ratio (OR), Hazard Ratio (HR), percentages) and 95% confidence intervals (95% CI) or sufficient information included for estimates calculation were extracted and configured to indicate the impact per specific increment in exposure. Exposures to PM_{10}, $PM_{2.5}$, NO_2, SO_2, BC, and O_3 were pooled for a 10 μg/m³ increment, and CO exposure was pooled for a one part per million (ppm) increment. Exposure to solid fuel was based on solid fuel versus clean fuel. Studies reporting percentage change were converted to RR using the below formula:

$$RR = \frac{\text{Percentage change}}{100} + 1$$

A forest plot was used to visualize the summaries of the included studies. Both visual inspection of the forest plot and I^2 statistics were used to assess the degree of heterogeneity of the true effect. Results of $I^2 < 30\%$, 30%–50%, and >50% were interpreted to indicate no, moderate, and substantial heterogeneity, respectively. Begg's and Egger's tests were used to assess publication bias and small study effects for meta-analysis involving five or more studies (29). As the association between temperature and morbidity/mortality tends to follow a U or J shape, meta-analysis was not performed. Instead, we described these effects at high and low temperatures. All analyses were conducted using R version 4.3.1 (30), and a two-sided $P < 0.05$ was deemed statistically significant.

RESULTS

In total, the search returned 7,306 articles across the seven databases. After duplicate removal, 6,540 articles remained. After title and abstract screening, 58 papers were retained for data extraction and analysis—26 of which examined morbidity, 29 examined mortality, and 3 examined both. For details regarding article selection, see Figure 1. Nine different exposure parameters were examined (PM_{10}, $PM_{2.5}$, SO_2, NO_2, O_3, temperature variation, CO_2, Black Carbon, and solid fuel), with the number examined per paper ranging from one to six (the average examined was approximately two). Single-exposure models were most used, with a smaller number of articles utilizing multi-exposure models in secondary analysis. We therefore primarily focused on the findings of single exposure models. A variety of methods of reporting CVD morbidity/mortality were used, including physician diagnosis, self-report, national disease surveillance database, verbal autopsy, death certificate, and hospital records. In terms of study location, the majority (n = 42, 72%) of studies were conducted in Mainland China. Regarding other regions, 4 studies were conducted in Iran, 3 each in Thailand and South Africa, 2 each in Vietnam and Bangladesh, and 1 in Brazil. Only one study was conducted in multiple countries, thus; China, India, South Africa, and Tanzania. Most (n = 53) papers had a moderate to low risk of bias, with 51 papers being determined as a 'fair' quality and 5 as 'good' (Table 1).

The relationship between environmental exposure(s) and CVD morbidity/mortality was examined either through the relationship between short-term changes in exposure and acute events or through long-term exposures and CVD disease. Short-term exposures were typically examined through a lag of up to 7 days, except for studies examining temperature, where lags of up to 28 days were also observed. Of the twenty-six articles examining cardiovascular morbidity, 17 assessed the effect of short-term exposures (of which 13 used time series (31–43), and 4 used a case-crossover design (44–47)). Among the 9 studies examining long-term exposures, 8 utilized cohort studies (48–55), and 1 used a cross-sectional approach (56). Of the 29 articles examining cardiovascular mortality, 21 examined short-term effects (of which 19 used a time-series design (41, 57–74) and 2 used a case-crossover design (75, 76), with the remaining 8 articles examining long-term effects by use of a cohort study design (59, 77–83). The 3 articles assessing the effect on both morbidity and mortality all examined long-term effects by use of a cohort design (23, 84, 85).

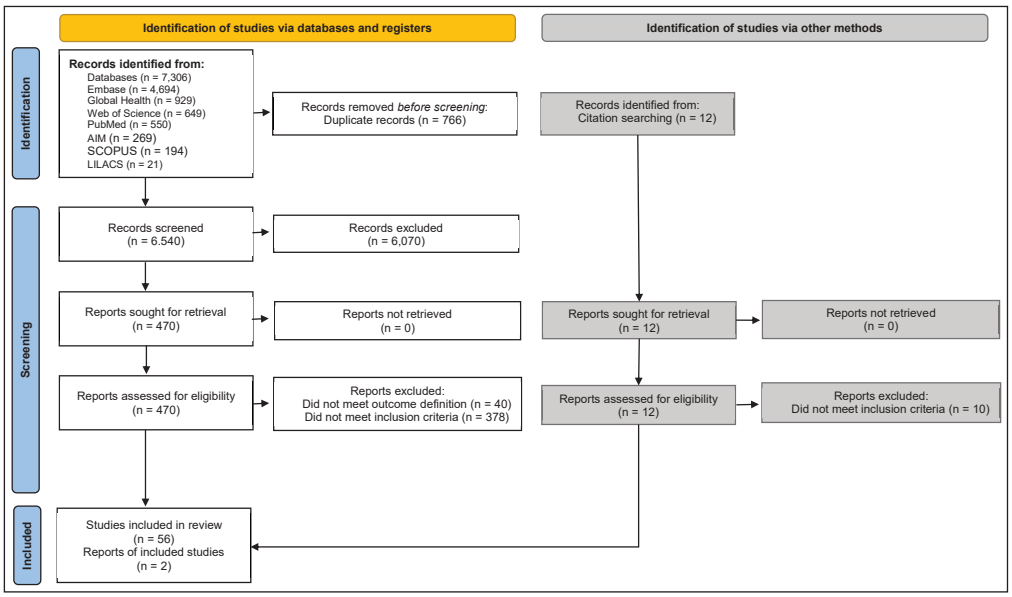


Figure 1 Description of the articles selection processes.

1.1: THE EFFECT OF SHORT-TERM EXPOSURES ON CARDIOVASCULAR MORBIDITY AND MORTALITY

1.1.1: Exposure to PM_{10}

The effects of short-term exposure to PM_{10} on CVD morbidity and mortality were reported by nine and six articles, respectively, typically showing a combination of increased or null likelihoods of disease or mortality. Of the nine morbidity articles, eight (33–36, 38, 39, 42, 86) utilized a time series design, with the remaining article utilizing a case-crossover design (44). The time-series articles were retained for meta-analysis. The case-crossover study reported that for a 10 μg/m³ increase in PM_{10}, the risk of CVD morbidity increases by 0.6% (95% CI: 0.4–0.8) (44). In the meta-analysis, a 10 μg/m³ increase of PM_{10} was found to increase short-term CVD morbidity by 0.1% (i.e., an RR of 1.001) with a 95% confidence interval (CI) of 0.0% to 0.3%. There was no evidence of publication bias for morbidity outcomes (Begg's test, p = 0.4885, and Egger's test, p = 0.3988).

With regards to the six articles examining short-term exposure to PM_{10} and CVD mortality, four utilized a time series design (67, 68, 71, 72) and were included in the meta-analysis. The remaining two (33, 76) utilized a case-crossover design, neither of which displayed significant results in their maximal lag models. The pooled meta-analysis found that, for a 10 μg/m³ increase in PM_{10}, the risk of CVD-related death increases by 0.7% (RR: 1.007 95% CI: 1.000–1.014)]. Publication bias was not assessed for mortality due to the relatively small number of papers. Further details are presented in Supplementary Figure A1.

1.1.2: Exposure to $PM_{2.5}$

Short-term exposure to $PM_{2.5}$ and its effects on CVD morbidity were assessed by four articles (32, 34, 44, 86), and its effects on mortality were assessed by six (61, 64, 67, 68, 71, 72), with studies tending to show positive associations, albeit with a combination of significant and non-significant effects. Of the four morbidity studies, three (32, 34, 86) represented time-series design and were included in the meta-analysis (the remaining case-crossover study did not identify a significant relationship between $PM_{2.5}$ and CVD morbidity). The pooled meta-analysis found that a 10 μg/m³increase in $PM_{2.5}$ was associated with a 0.6% increase in CVD morbidity (RR: 1.006, 95% CI: 1.003–1.009). Due to the small number of articles examining morbidity, a test of publication bias was not performed, and no heterogeneity was observed.

For the effects of short-term $PM_{2.5}$ exposure on CVD-related mortality, all six studies utilized a time-series design and were included in the meta-analysis. The overall pooled results indicated that a 10 μg/m³increase in $PM_{2.5}$ corresponded to a 0.7% increase in CVD mortality (RR: 1.007, 95% CI: 1.002–1.012). There was some evidence of publication bias (Begg's test, p = 0.015; Egger's test, p = 0.7194), and substantial heterogeneity was observed. Further details are presented in Figure 2.

1.1.3: Exposure to NO_2

The short-term effects of NO_2 exposure on CVD morbidity and mortality were evaluated by five and six studies, respectively. Overall, the association between NO_2 and CVD morbidity was mixed, with a more positive association observed with mortality. All five studies examining CVD morbidity were of time-series design and thus included in the meta-analysis (34, 36, 38, 39, 42). In pooled meta-analysis, no significant association between NO_2 exposure and CVD morbidity was observed [RR: 1.00 (95% CI: 0.991–1.008)]. No publication bias was observed (Begg's test, p = 0.5109, and Egger's test, p = 0.2333).

When examining the effect of NO_2 on CVD mortality, four out of the six studies utilized a time-series design and were included in the meta-analysis. The remaining two articles, utilizing a case-crossover design, showed no association between NO_2 and mortality in their maximal lag models (75, 76). Meta-analysis found that a 10 μg/m³ increase in NO_2 resulted in a 1.9% [RR: 1.019 (95% CI: 1.005–1.032)] increase in CVD-related deaths. Some evidence of publication bias was observed (Begg's test, p < 0.0001, and Egger's test, p = 0.0833). Further details are presented in Figure 3.

1.1.4: Exposure to O_3

The effects of O_3 exposure on CVD morbidity and mortality were assessed by four and six articles, respectively, with limited evidence being observed for an association between O_3 and morbidity, although there was more consistent evidence for an increased association with CVD mortality. All four articles examining morbidity utilized a time-series design and were included

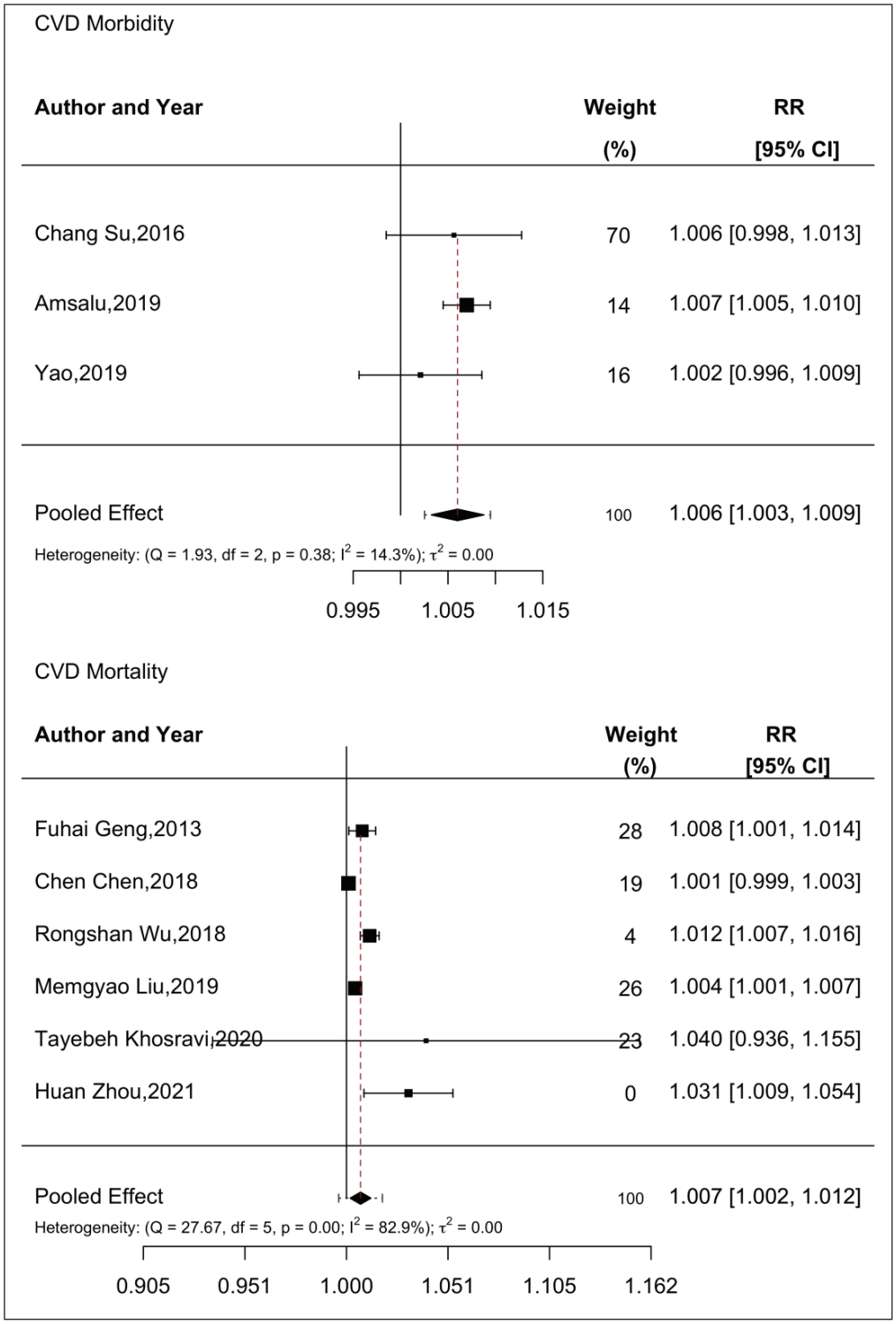


Figure 2 Meta-analysis of short-term $PM_{2.5}$ exposure and CVD morbidity and mortality.

in the meta-analysis (33, 35, 38, 39), which found no overall association between a 10 μg/m³ increase in O_3 exposure and CVD morbidity (RR: 1.004, 95% CI: 0.995–1.014) (35).

For CVD mortality, all six articles utilized a time-series design and were thus included in the meta-analysis (41, 57, 68, 71, 73, 87), which indicated that a 10 μg/m³ increase in O_3 exposure was associated with a 0.9% increase in CVD-related mortality [RR: 1.009 (95% CI: 1.006–1.012)]. No evidence of publication bias was found in the mortality outcomes (Begg's test, p = 0.1949, and Egger's test, p = 1.7194). Further details are presented in Figure 4.

1.1.5: Exposure to SO_2

Four and six articles examined the short-term effects of SO_2 on CVD morbidity and mortality, respectively. All six morbidity articles incorporated a time-series design and were included in the meta-analysis (34–36, 38, 39, 42), which did not show a significant pooled association (RR: 1.006 95% CI: 0.993–1.020). No evidence of publication bias was observed (Begg's test, p = 0.0492, and Egger's test, p = 0.4694). Details of the meta-analysis are found in Supplementary Figure A2.

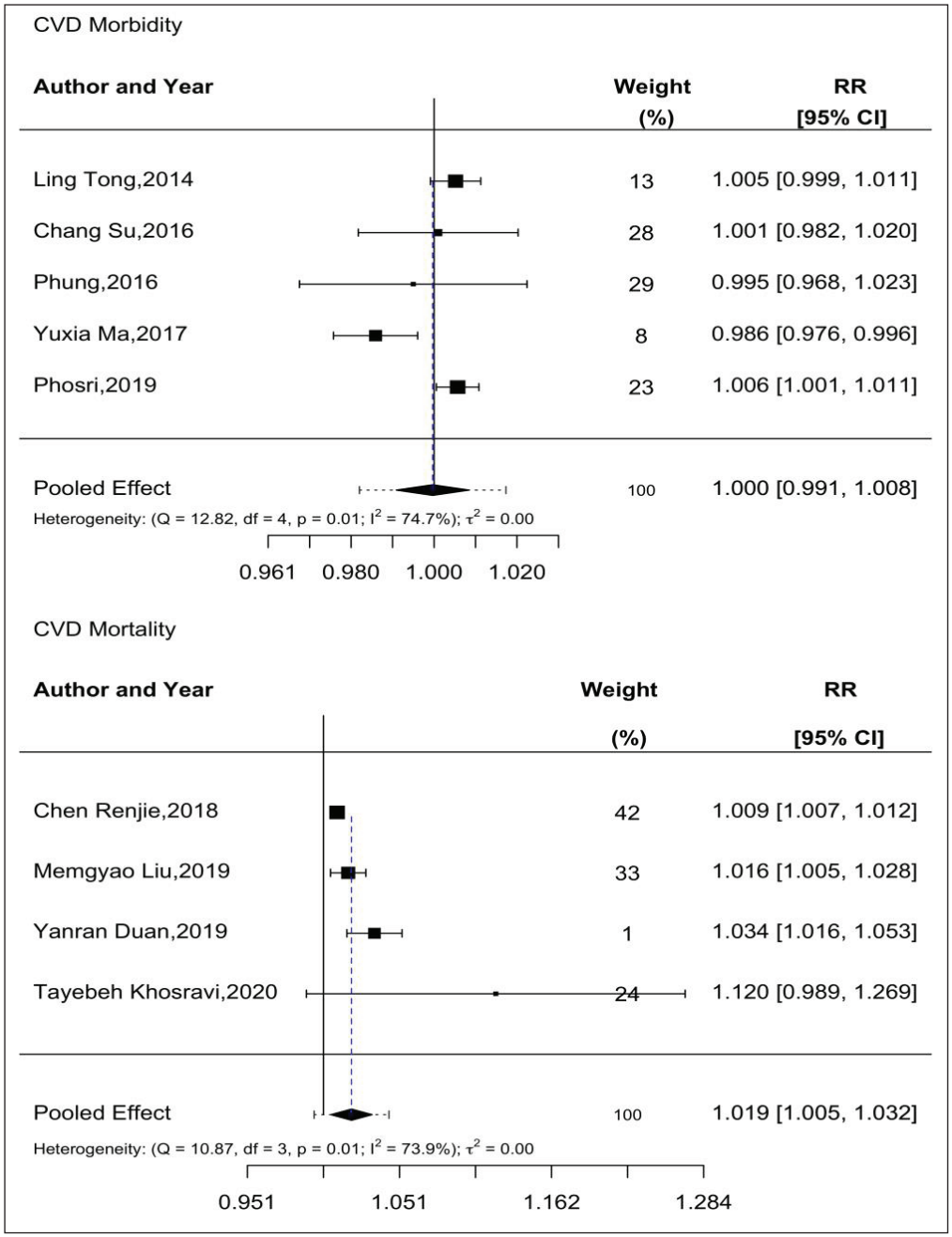


Figure 3 Meta-analysis of short-term NO_2 exposure and CVD morbidity and mortality.

Meta-analysis was not performed to examine the pooled effect of SO_2 on CVD mortality as two papers utilized time-series design and the other two case-crossover. However, three of the four articles reported a positive and significant association (60, 68, 76), with effect sizes ranging from 0.8% (95% CI: 0.47–1.19) to 3.3% (95% CI: 0.06–7.9) per 10 μg/m^3 increment, with the fourth reporting no significant association (75).

1.1.6: Exposure to CO

Two articles examined the impact of CO on CVD morbidity, and three examined mortality. Due to the limited number of articles, a meta-analysis was not performed. Both articles examining morbidity reported a positive association with a 1 ppm increase in CO exposure increasing morbidity by 4.2% (95% CI: 1.35–7.26%) and 11% (3–20%). Two of the three articles examining the effect of CO on mortality reported a positive effect (66, 68), with results ranging from 1.1% (0.42–1.83%) to 6.5% (2.5–10.8%). The final article observed no significant association between CO and CVD mortality.

1.1.7: Temperature exposure

Four and five articles assessed the effect of temperature variation on CVD morbidity and mortality, respectively, with effects observed at temperatures that were both higher and lower than normal temperatures. Out of the four articles examining temperature variation on CVD

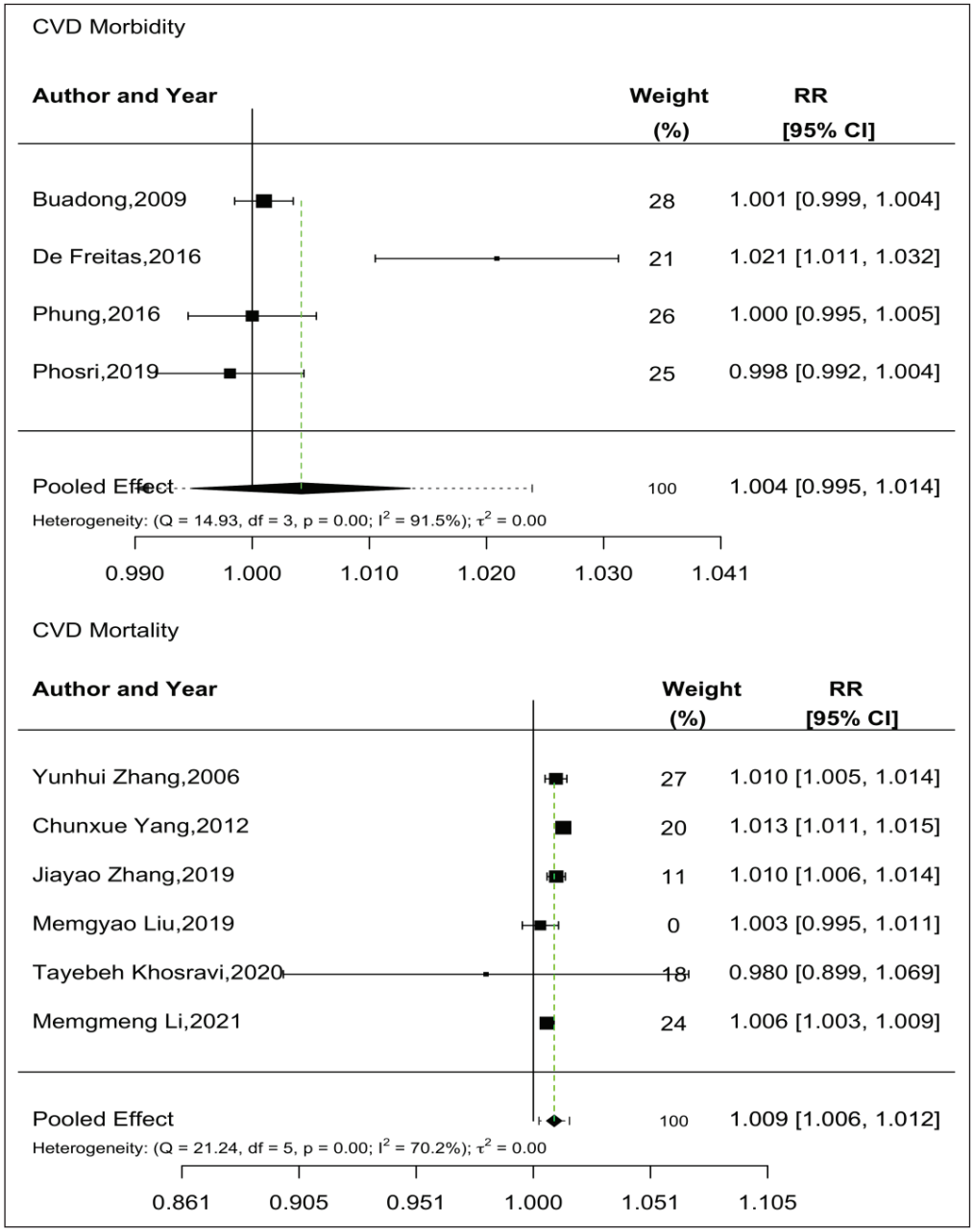


Figure 4 Meta-analysis of short-term O_3 exposure and CVD morbidity and mortality.

morbidity, two reported a significant association between higher-than-normal temperatures and CVD morbidity (37, 43). One reported that lower-than-normal temperatures increased CVD morbidity (with no significant effect for hot temperatures reported) (31). The final article reported no relationship between temperature variation and CVD morbidity (40).

Among the five articles examining temperature and CVD mortality, three reported significantly increased mortality associated with both abnormally high and low temperatures. One article reported an association only for increased temperature, and one reported no association between temperature and mortality in its maximally lag-adjusted model.

1.1.8: Other components

One article examined the impact of Black Carbon exposure on CVD mortality, reporting that an IQR increase (2.7 μg/m³) in BC was associated with a 3.2% (95% CI: 0.6–5.7%) increase in CVD mortality. Two articles examined PMcoarse, one examining morbidity and the other mortality. Both articles reported a positive association between exposure and morbidity/mortality.

1.2: THE EFFECT OF LONG-TERM EXPOSURES ON CARDIOVASCULAR MORBIDITY AND MORTALITY

1.2.1: Exposure to PM_{10}

Only one article assessed the long-term effect of PM_{10} on CVD morbidity, reporting no effect in cross-sectional analysis (56). The impact of PM_{10} on CVD mortality was not assessed.

1.2.2: Exposure to $PM_{2.5}$

CVD morbidity and mortality in relation to long-term $PM_{2.5}$ exposure was assessed by five and six articles, respectively, consistently showing increased associations between $PM_{2.5}$ and CVD morbidity/mortality. All five articles evaluating morbidity utilized a cohort design and were included in the meta-analysis (23, 50, 51, 84, 85), finding that a 10 μg/m³ increase in $PM_{2.5}$ exposure increased CVD morbidity by approximately 13.1% [RR: 1.131 (95% CI: 1.057–1.210)]. No evidence of publication bias was observed (Begg's test, p = 0.4522, and Egger's test, p = 0.8167).

All six articles examining mortality also employed cohort design (23, 77, 79, 81, 84, 85), with meta-analysis indicating that a 10 μg/m³ increase in $PM_{2.5}$ exposure increased CVD-related mortality by 9.2% [RR: 1.092 (95% CI: 1.030–1.159)]. However, some evidence of publication bias was observed (Begg's test, p = 0.0401, and Egger's test, p = 0.2722). Details are given in Figure 5.

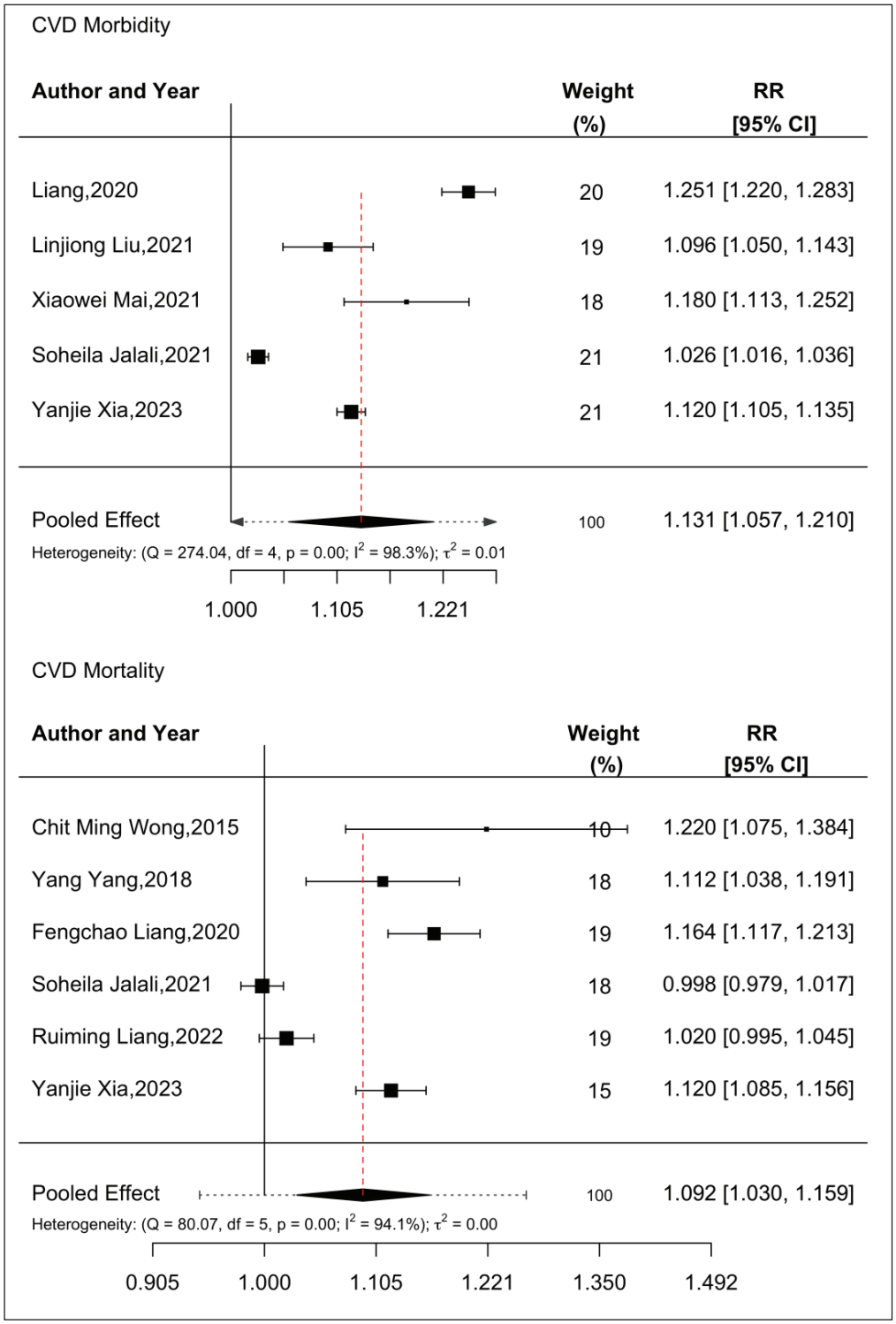


Figure 5 Meta-analysis of long-term $PM_{2.5}$ exposure and cardiovascular disease morbidity and mortality.

1.2.3: Exposure to SO_2

One article examined the long-term effects of SO_2 on CVD morbidity, reporting no association in a cross-sectional analysis (56). In contrast, one article, utilizing a cohort design, investigated the effect of long-term exposure to SO_2 on CVD mortality, reporting that a 10 μg/m^3 increase in SO_2 exposure was associated with a 3.2% (95% CI: 2.3–4.0%) increase in mortality.

1.2.4: Exposure to NO_2

Two articles assessed the long-term effects of NO_2 exposure on CVD morbidity (53, 56). One, in a cross-sectional analysis, reported no association between NO_2 and CVD morbidity. By contrast, the second article, employing a cohort design, reported that a 10 μg/m^3 increase in long-term NO_2 was associated with a large increase in CVD risk morbidity (RR: 1.558, 95% CI: 1.477–1.642) (53). With respect to mortality, one article examined the impact of NO_2 exposure on CVD mortality, reporting a relative risk of approximately 1.00.

1.2.5: Exposure to O_3

Two articles evaluated the long-term effect of O_3 on CVD morbidity, with a null association observed in cross-sectional analysis (55, 56). A cohort study examining O_3 exposure and CVD morbidity, however, reported that a 10 μg/m^3 increase in O_3 was associated with a 7.8% (95% CI: 5.0–10.6) increase in CVD morbidity (55). Two articles assessed the effect of O_3 on CVD mortality (82, 83), both reporting significant associations between O_3 and CVD mortality, with a 10 μg/m^3 increase being associated with a 22% (95% CI: 12%–33%) or 9% (95% CI: 4.6%–14.2%) increase in mortality.

1.2.6: Use of solid fuels

Three articles evaluated the long-term effect of using solid/polluting fuels versus clean fuel on CVD morbidity (49, 52, 54). Two of these studies reported that the long-term use of solid fuels was associated with increased risks of cardiovascular events. One article, examining the implementation of a coal-to-gas/electricity project, did not observe a significant change in cardiovascular morbidity. Two articles examined fuel use and mortality, one examining the use of kerosene in a multi-center study reported that kerosene usage (compared to clean alternatives) was associated with a 34% increase in mortality (95% CI: 8–66%). The other article reported that cooking on solid fuels was associated with a CVD mortality HR of 1.20 (95% CI 1.02–1.41), whereas using them for heating was associated with an HR of 1.29 (95% CI: 1.06–1.55).

1.2.7: Other pollutants

One study assessed the effect of Black Carbon on CVD mortality (50), reporting that an IQR increase in BC (9.6 μg/m^3) was associated with a 7% (95% CI: 2–11%) increase in CVD mortality.

DISCUSSION

This review and meta-analysis sought to summarize the available evidence regarding climatic and environmental exposures and their association with CVD morbidity and/or mortality in LMICs. Among the main findings were that both short- and long-term exposure to a variety of air pollutants was associated with both CVD morbidity and mortality. Of note, short- and long-term exposure to $PM_{2.5}$, a well-recognized air contaminant, was consistently associated with increased CVD morbidity and mortality. In addition, short-term disruptions to temperature (both above and below normal) were also associated with morbidity and mortality. Additionally, short-term exposure to NO_2 and O_3 was associated with CVD mortality. The long-term use of solid or other polluting fuels was also found to be associated with CVD morbidity and mortality. The vast majority of studies in this review were conducted in China. Other LMIC regions, especially Africa, are significantly understudied, limiting the generalizability of our findings.

Particulate matter (PM) is a commonly used proxy for air pollution. It is a complex mixture of particles that vary widely in size, shape, and chemical composition, which, at smaller sizes, can penetrate the respiratory system. Consistent with other epidemiological studies, we observed $PM_{2.5}$ to be consistently associated with adverse health effects (88). In this review, the overall risk ratio of long-term $PM_{2.5}$ exposure on CVD mortality in LMICs was 1.092 (95% CI: 1.030–

1.159) per 10 μg/m³ increase. This is comparable to the findings of Guo et al. (2022), who, in their study of LMICs, reported a risk ratio of 1.10 (95% CI: 1.06–1.14) (89) and another study in the United States, which reported a hazard ratio of 1.10 (95% CI: 1.05–1.15) (90).

Many gaseous pollutants such as SO_2, NO_2, O_3, and CO can be classified as short-term exposures due to their brief presence in the atmosphere and temporal variability. Accordingly, the majority of the studies in this review examined the short-term impact of these air pollutants. Of these, NO_2 and O_3 were most commonly studied. In general, short-term NO_2 exposure did not appear to influence CVD morbidity, a finding comparable to findings from high-income countries (91–93). In contrast, short-term exposure to NO_2 was associated with an increase in CVD mortality, with a pooled RR of 1.019 (95% CI: 1.005–1.032), an effect higher than what is seen in higher-income countries (94, 95).

A similar phenomenon was observed when examining ozone, where the pooled analysis did not suggest an association with CVD morbidity but did for mortality. This may be indicative of differences in short-term biological effects of these agents or of health care challenges contributing to higher mortality patterns. Compared with results from higher-income countries, this review had divergent results on the effect of ozone on CVD morbidity (92, 96).

The use of solid fuels for household heating and cooking is another well-established risk factor for mortality worldwide. The findings from this review largely affirm this finding, showing consistently increased risks of CVD morbidity and mortality in relation to solid fuel use (97, 98).

Ongoing climate change means that average temperatures are likely to continue to rise for the foreseeable future. LMICs can be especially vulnerable to the effects of rising temperature, as reflected by the findings from this review, where higher temperatures were consistently associated with increased risks of CVD morbidity and mortality. The overall LMIC research identified in this review showed patterns consistent with findings from high-income countries (99–102), where both extreme highs and lows of temperature would drive disease morbidity and mortality.

While this review identified nearly 58 articles, a substantial research gap remains, particularly in Sub-Saharan Africa. Most studies identified in this review were conducted in mainland China, which may not accurately reflect other LMICs. The Sub-Saharan Africa region faces distinct climatic/environmental and health challenges, including higher levels of poverty, varying pollution sources, and low-resourced healthcare infrastructures, making increased research crucial. Increased research on environmental health impacts within LMICs, and Sub-Saharan Africa in particular, is crucial for several reasons. First, the sources and types of air pollution can differ by geographic region due to factors such as widespread use of biomass for cooking, dust from unpaved roads, and unregulated emissions from industry. Again, focusing on LMICs can provide comprehensive data for tailored interventions and policies, contributing to more effective public health strategies and global health equity.

The review examined how various environmental exposures affect health in LMICs by examining a wide range of databases. Additionally, this review highlights a major research gap regarding environmental exposure and cardiovascular disease, emphasizing the need for more research, especially in Sub-Saharan African countries. Limitations of this review relate to the relative lack of long-term studies on the effect of climate/air pollution and cardiovascular disease, the lack of studies reporting on specific diagnoses, and the predominance of studies from Asia, hampering our ability to generalize the findings beyond the Asian region. Also, since the study only explored all-cause CVD, we were unable to explore the association of environmental constituents with specific CVD conditions, meaning that specific associations may have been overlooked.

CONCLUSION

Short- and long-term exposure to various environmental components was significantly associated with CVD morbidity and mortality in LMICs. Most notably, both short- and long-term exposure to $PM_{2.5}$ was associated with CVD morbidity and mortality, a finding reflected elsewhere in the literature in a variety of settings. In addition, both high and low-temperature extremes were associated with increased morbidity and mortality, and the long-term use of solid (or

other polluting) fuels was found to increase CVD mortality. A major research gap was identified where most LMIC research comes from the Asia region, and China in particular, meaning that other regions, especially Sub-Saharan Africa, are markedly understudied. Therefore, context-specific research is needed to understand better the role of environmental disruptions in these understudied regions. Future work will also benefit from examining the association between environmental changes and specific CVD conditions.

ADDITIONAL FILES

The additional files for this article can be found as follows:

- **Supplementary Document 1.** *Review search terms*. DOI: https://doi.org/10.5334/gh.1409.s1
- **Supplementary Figure A1.** Meta-analysis of short-term PM_{10} exposure and CVD morbidity and mortality. DOI: https://doi.org/10.5334/gh.1409.s2
- **Supplementary Figure A2.** Meta-analysis of SO_2 exposure and cardiovascular disease morbidity. DOI: https://doi.org/10.5334/gh.1409.s3

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COMPETING INTERESTS

The authors have no competing interests to declare.

AUTHOR CONTRIBUTIONS

SG, GSD, and KKG designed the study and advised the analyses plans; SG and GSD led the data collection and analysis. SG, GSD, and KKG co-drafted the manuscript, which was reviewed and edited by SG, KKG, SN, KPA, and GSD. All the authors approved the final version of the manuscript.

AUTHOR AFFILIATIONS

Stephaney Gyaase orcid.org/0000-0003-2389-2307
Kintampo Health Research Centre, Research and Development Division, Ghana Health Service, Kintampo, Ghana; Julius Global Health, Department of Global Public Health and Bioethics, Julius Center for Health Sciences, University Medical Center Utrecht, Utrecht University, Utrecht, The Netherlands

Solomon Nyame orcid.org/0000-0003-0419-7237
Kintampo Health Research Centre, Research and Development Division, Ghana Health Service, Kintampo, Ghana; Julius Global Health, Department of Global Public Health and Bioethics, Julius Center for Health Sciences, University Medical Center Utrecht, Utrecht University, Utrecht, The Netherlands

Kerstin Klipstein-Grobusch orcid.org/0000-0002-5462-9889
Julius Global Health, Department of Global Public Health and Bioethics, Julius Center for Health Sciences, University Medical Center Utrecht, Utrecht University, Utrecht, The Netherlands; Division of Epidemiology and Biostatistics, School of Public Health, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa

Kwaku Poku Asante orcid.org/0000-0001-9158-351X
Kintampo Health Research Centre, Research and Development Division, Ghana Health Service, Kintampo, Ghana

George S. Downward orcid.org/0000-0001-6642-7048
Julius Global Health, Department of Global Public Health and Bioethics, Julius Center for Health Sciences, University Medical Center Utrecht, Utrecht University, Utrecht, The Netherlands; Institute for Risk Assessment Sciences, Utrecht University, The Netherlands

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