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# Long-term exposure to particulate matter on cardiovascular and respiratory diseases in low- and middle-income countries: A systematic review and meta-analysis

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**Background:** Long-term exposure to particulate matter (PM) has essential and profound effects on human health, but most current studies focus on high-income countries. Evidence of the correlations between PM and health effects in low- and middle-income countries (LMICs), especially the risk factor $PM_1$ (particles $<1\,\mu m$ in size), remains unclear.

**Objective:** To explore the effects of long-term exposure to particulate matter on the morbidity and mortality of cardiovascular and respiratory diseases in LMICs.

**Methods:** A systematic search was conducted in the PubMed, Web of Science, and Embase databases from inception to May 1, 2022. Cohort studies and case-control studies that examine the effects of $PM_1$, $PM_{2.5,}$ and $PM_{10}$ on the morbidity and mortality of cardiovascular and respiratory diseases in LMICs were included. Two reviewers independently selected the studies, extracted the data, and assessed the risk of bias. Outcomes were analyzed *via* a random effects model and are reported as the relative risk (RR) with 95% CI.

**Results:** Of the 1,978 studies that were identified, 38 met all the eligibility criteria. The studies indicated that long-term exposure to $PM_{2.5}$, $PM_{10}$, and $PM_1$ was associated with cardiovascular and respiratory diseases: (1) Long-term exposure to $PM_{2.5}$ was associated with an increased risk of cardiovascular morbidity (RR per 1.11 $\mu g/m^3$, 95% CI: 1.05, 1.17) and mortality (RR per 1.10 $\mu g/m^3$, 95% CI: 1.06, 1.14) and was significantly associated with respiratory mortality (RR 1.31, 95% CI: 1.25, 1.38) and morbidity (RR 1.08, 95% CI: 1.02, 1.04); (2) An increased risk of respiratory mortality was observed in the elderly (65+ years) (RR 1.21, 95% CI: 1.00, 1.47) with long-term exposure to $PM_{2.5}$; (3) Long-term exposure to $PM_{10}$ was associated with cardiovascular morbidity (RR 1.07, 95% CI 1.01, 1.13), respiratory morbidity (RR 1.43, 95% CI: 1.21, 1.69) and respiratory mortality (RR 1.28, 95% CI 1.10, 1.49); (4) A significant association between long-term exposure to $PM_1$ and cardiovascular disease was also observed.

**Conclusions:** Long-term exposure to $PM_{2.5}$, $PM_{10}$ and $PM_1$ was all related to cardiovascular and respiratory disease events. $PM_{2.5}$ had a greater effect than $PM_{10}$, especially on respiratory diseases, and the risk of respiratory mortality was significantly higher for LMICs than high-income countries. More studies are needed to confirm the effect of $PM_1$ on cardiovascular and respiratory diseases.

KEYWORDS

**particulate matter, cardiovascular diseases, respiratory diseases, low- and middle-income countries, long-term exposure**

## Introduction

Air pollution has long been recognized as both a public health problem and a social problem, and air pollutants are classified as carcinogens by the International Agency for Research on Cancer (IARC) (1). According to the latest urban air quality database information from the World Health Organization (WHO), 56 percent of cities in high-income countries with a population over 100,000 do not comply with WHO air quality guidelines, but in low- and middle-income countries (LMICs), the figure is 98%. In the past few years, air pollution has become increasingly serious. The public health significance of PM pollution is much greater than that of other air pollutants. PM pollution is associated with haze, and of all the air pollutants, it is most closely connected to adverse health effects (2). Epidemiological research has suggested that particulate air pollution is associated with many adverse health outcomes, including increased mortality and morbidity caused by lung and heart diseases (3). In the 2005 revision of the Air Quality Guidelines (AQG), the WHO defined PM as a major global air pollutant. PM pollution can result in multi-system damage, especially to the respiratory and cardiovascular systems. The evidence of the respiratory and cardiovascular disease effects of respirable PM with aerodynamic diameters below 2.5 and 10 mm (i.e., $PM_{2.5,}$ and $PM_{10}$) is growing (4).

Several studies have reported a global correlation between PM and respiratory and cardiovascular diseases (5–7). In fact, short-term exposure to $PM_{10}$ and $PM_{2.5}$ has been associated with respiratory and cardiovascular mortality, as well as daily all-cause mortality, in over 600 cities (8). Current research has concentrated on the acute health effects of PM pollutants. However, long-term effects remain a significant issue, particularly for decision-making regarding better air pollution control and assessing the long-term effects on public health (9).

The WHO estimates that air pollution results in over approximately one million premature deaths throughout the world each year (10). According to a recent report on the global burden of disease, particulate air pollution leads to 3.1 million deaths worldwide each year, and 22% of disability-adjusted life years (DALYs) are caused by cardiovascular disease (11).

LMICs have poor health care capabilities, but they bear a high proportion of the global morbidity and mortality caused by air pollution. Increased exposure to risk factors throughout life (e.g., particulate pollution and smoking) is associated with higher cardiovascular and respiratory disease prevalence in LMICs, but the lack of treatment availability increases the avoidable harm. Numerous current studies have shown the effects of $PM_{2.5}$ and $PM_{10}$ in high-income countries; however, less attention is paid to LMICs, particularly the effects of $PM_1$. This study aims to comprehensively review existing efforts in order to facilitate future studies.

## Methods

A PRISMA 2020 (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement was utilized as a guide for reporting this systematic review (12, 13). We used data extracted from published articles; therefore, this study has no discernible ethical issues.

### Search strategy

Systematic reviews offer a unique advantage in decision-making in health care (12). PubMed, Embase and Web of Science databases were systematically searched utilizing following terms: (air pollution OR particulate matter) AND (respiratory* OR cardiovascular*) AND (morbidit* OR hospitalization* OR hospitalization* OR death* OR mortalit* OR outpatien*) AND (case-control OR cohort) AND (developing country). We restricted the search from inception to May 1, 2022, and no limitations were placed on the publication dates. Furthermore, we manually searched the lists of references contained in the studies to determine additional relevant studies. The details for each database's search strategy can be found in the online Supplementary material. All manuscripts were uploaded to Rayyan and screened independently by two reviewers (XF and ZL). Any disagreements were resolved through discussion and consultation with a third member (XH) of the review team until a consensus was reached.

### Selection of studies

The titles and abstracts of all independently acquired articles were reviewed by two of the study authors (XF and ZL), and the

relevant studies were then identified through full-text assessment. The reasons for exclusion during the full-text screening were recorded. Any disagreements that arose were resolved through discussion and, if necessary, with the involvement of the third author. Case-control or cohort studies assessing the effects of $PM_{10}$, $PM_{2.5}$ and $PM_1$ on the morbidity and mortality of cardiovascular and respiratory diseases in LMICs were enrolled. The studies were included if the following criteria were met: (1) the type of study was limited to cohort and case-control studies; (2) studies in which $PM_1$, $PM_{2.5}$ and $PM_{10}$ were included as pollutants and studies reporting long-term exposure (months to years) to ambient air $PM_1$, $PM_{2.5}$, and $PM_{10}$ expressed as a concentration unit ($\mu g/m^3$) were included; (3) the study locations were low- and middle-income countries (LMICs); (4) the studies were conducted according to the International Classification of Diseases (ICD), 9th or 10th Revision, and included cardiovascular disease (ICD-9 codes 390-459, ICD-10 codes I00-I99) or respiratory disease (ICD-9 codes 460-519, ICD-10 codes J00-J99); (5) the studies included morbidity or mortality as an outcome; (6) estimates were expressed as the relative risk (RR), OR or HR with 95% CI, or sufficient information was included for calculation; (7) the publication language was limited to English.

Articles were excluded according to the following: (1) studies reporting occupational exposure (measured in the workplace) or exclusively indoor exposure to $PM_1$, $PM_{2.5}$ and $PM_{10}$ were excluded; (2) studies evaluating disease progression in patients suffering from respiratory or cardiovascular diseases [for instance, asthma or chronic obstructive pulmonary disease (COPD)] and exposed to pollutants; (3) studies linked to seasonality; (4) duplicate studies, commentaries, summaries, editorials, letters, and conference abstracts; (5) the information provided in the results was insufficient for data extraction.

## Extraction of data

XF and ZL independently extracted the indicated data from the included cohort and case-control studies. If disputes remained after discussion, a third investigator (XH) was engaged to resolve the conflict. The following data were extracted from all included studies and entered into a Microsoft Excel database (Version 2014 Microsoft, USA): author, location, year of publication, study design, study duration, study group, pollutant, type of disease, number of events, health outcomes, and specific risk estimates.

## Risk of bias assessment

Two reviewers (JG and XF) evaluated the underlying risk of bias independently for all the included studies with the Newcastle-Ottawa Quality Assessment Scale (NOS) (14); disagreements were discussed and resolved by consensus with the third review author (XH). The NOS provides scores of 0–9 according to selection, comparability, and outcome evaluation. Studies with scores of 0–3, 4–6, and 7–9 were respectively considered to be low-, medium-, and high-quality studies.

## Statistical methods

For meta-analysis, RR was used as an effect estimate, and OR for case crossover studies and HR for cohort studies were considered equivalent to RR (15, 16). Where multiple estimates existed in the primary study, maximum adjusted model estimates were extracted to minimize the risk of underlying unmeasured confounding. RR for morbidity and mortality was used as impact values and was converted to a standardized increment (10 $\mu g/m^3$) for PM concentration. The following formula was used to calculate the standardized risk estimates:

$$RR_{(standardised)} = RR_{(original)}^{Increment(10)/Increment(original)} \quad (1)$$

For this meta-analysis, a random-effects model was constructed to anticipate significant heterogeneity among studies. We used the $I^2$ statistic to estimate the degree of heterogeneity for each analysis. Values of $I^2 < 25\%$, 25–50%, and >50% respectively represent low, moderate, and high heterogeneity. If we identified substantial unexplained heterogeneity, we reported it and explored potential influencing factors with a prespecified subgroup analysis of the results of each data-sufficient synthesis, including sex (male vs. female), age (<65 years vs. >65 years), type of study (cohort vs. case-control), and type of disease. If a study reported subgroup data separately, we directly used the corresponding data for our analysis. Publication bias was assessed by Egger's regression test when the outcome included more than 10 studies.

All analyses were carried out with Stata software (Version 15.0, Stata Corp., College Station, TX, USA), and statistical significance was deemed to be two-sided $P < 0.05$.

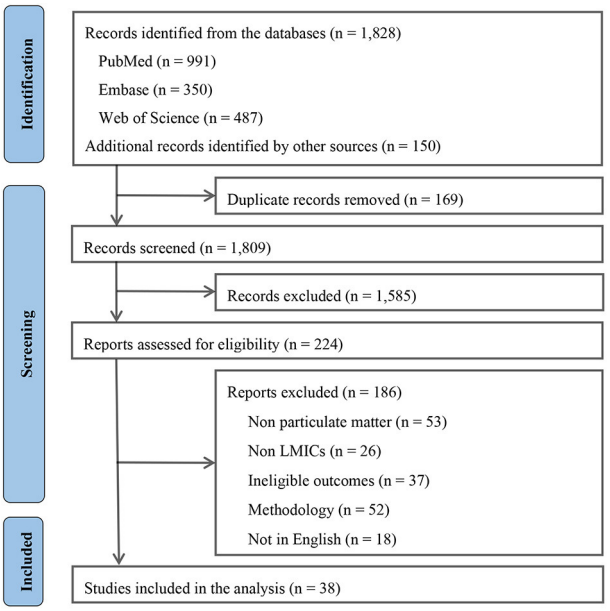


FIGURE 1
Flow chart for study inclusion.

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TABLE 1 Features of the included studies regarding long-term PM exposure.

| References | Area | Species | Mean/median exposure ($\mu g/m^3$) | Study period | Study design | Sample size | Age (years) | Disease(s) | Outcome(s) | NOS score |
|---|---|---|---|---|---|---|---|---|---|---|
| Zhang et al. (17) | Northern China | $PM_{10}$ | 154.0 | 1998–2009 | Cohort study | 12,584 | 35–103 | CVD | Mortality | 7 |
| Dong et al. (19) | Shenyang, China | $PM_{10}$ | 154.0 | 1998–2009 | Cohort study | 9,941 | ≥25 | RSD | Mortality | 8 |
| Zhang et al. (18) | Northern China | $PM_{10}$ | 144.0 | 1998–2009 | Cohort study | 39,054 | ≥40 | CVD | Mortality | 7 |
| Zhou et al. (7) | 25 cities in China | $PM_{10}$ | 104.0 | 1990–1991 | Cohort study | 71,431 | ≥40 | CVD and RSD | Mortality | 5 |
| Tseng et al. (52) | Taiwan, China | $PM_{2.5}$ | 30.5 | 1989–2008 | Cohort study | 43,227 | ≥26 | CVD | Mortality | 7 |
| Hwang et al. (21) | Taiwan, China | $PM_{10}$ | 60.3 | 2001–2007 | Case-control study | 1,087 | Infants | CVD | Morbidity | 6 |
| Yin et al. (22) | 44 areas in China | $PM_{2.5}$ | 47.3 | 2000–2005 | Cohort study | 186,399 | 40–79 | CVD | Mortality | 5 |
| Lai et al. (23) | Taiwan, China | $PM_{2.5}$ | 27.8 | 2005–2012 | Cohort study | 106,678 | ≥18 | RSD | Morbidity | 5 |
| Jin et al. (20) | Lanzhou, China | $PM_{10}$ | 143.8 | 2010–2012 | Cohort study | 8,969 | Infants | CVD | Morbidity | 7 |
| Liu et al. (24) | Shanghai, China | $PM_{10}$ | 82.0 | 2011–2012 | Cohort study | 3,358 | 4–6 | RSD | Morbidity | 5 |
| Peng et al. (25) | Shanghai, China | $PM_{2.5}$ | 53.5 | 2003–2013 | Cohort study | 4,444 | ≥14 | RSD | Mortality | 6 |
| Chen et al. (6) | Northern China | $PM_{10}$ | 44.3 | 1998–2009 | Cohort study | 39,054 | Mean 44.29 | RSD | Mortality | 7 |
| Wong et al. (26) | Hongkong, China | $PM_{2.5}$ | 33.7 | 1998–2001 | Cohort study | 66,820 | ≥65 | RSD | Mortality | 5 |
| Deng et al. (27) | Changsha, China | $PM_{10}$ | 90.0 | 2011–2012 | Cohort study | 2,598 | 3–6 | RSD | Morbidity | 7 |
| Zhang et al. (28) | Wuhan, China | $PM_{2.5}$, $PM_{10}$ | 65.6/101.7 | 2012–2013 | Cohort study | 105,988 | Infants | CVD | Morbidity | 8 |
| Chen et al. (29) | Four cities in China | $PM_{10}$ | 144.3 | 1999–2009 | Cohort study | 39,054 | ≥42 | RSD | Mortality | 7 |
| Yin et al. (30) | 45 areas in China | $PM_{2.5}$ | 43.7 | 1990–1991 | Cohort study | 189,793 | ≥40 | CVD and RSD | Mortality | 7 |
| Ren et al. (31) | Beijing, China | $PM_{10}$ | 104.1 | 2009–2012 | Cohort study | 30,669 | Infants | CVD | Morbidity | 5 |
| Jiang et al. (32) | Changsha, China | $PM_{10}$ | 110.0 | 2011–2012 | Cohort study | 2,598 | 3-6 | RSD | Morbidity | 6 |
| Yang et al. (33) | Hongkong, China | $PM_{2.5}$ | 42.2 | 1998–2011 | Cohort study | 61,386 | ≥65 | CVD | Mortality | 8 |
| Huang et al. (34) | Taiwan, China | $PM_{2.5}$, $PM_{10}$ | 30.6/53.0 | 2007–2014 | Case-control study | 5,474 | Infants | CVD | Morbidity | 7 |
| Huang et al. (35) | 15 provinces in China | $PM_{2.5}$ | 64.9 | 1992–2008 | Cohort study | 117,575 | ≥18 | CVD | Morbidity | 6 |
| Huang et al. (36) | China | $PM_{2.5}$ | 77.7 | 2014–2015 | Cohort study | 59,456 | ≥18 | CVD | Morbidity | 8 |
| Chen et al. (37) | China | $PM_1$, $PM_{2.5}$, $PM_{10}$ | 63.3/80.6/134.9 | 2007–2008 | Case-control study | 12,291 | ≥18 | CVD | Mortality | 6 |

*(Continued)*

TABLE 1 (Continued)

| References | Area | Species | Mean/median exposure ($\mu g/m^3$) | Study period | Study design | Sample size | Age (years) | Disease(s) | Outcome(s) | NOS score |
|---|---|---|---|---|---|---|---|---|---|---|
| Mao et al. (38) | Henan, China | $PM_{2.5}$, $PM_{10}$ | 72.8/131.5 | 2015–2017 | Cohort study | 39,259 | 18-79 | CVD | Morbidity | 7 |
| Sun et al. (39) | Hongkong, China | $PM_{2.5}$ | 35.3 | 1998–2001 | Cohort study | 58,643 | ≥65 | RSD | Mortality | 8 |
| Yang et al. (40) | Northeastern China | $PM_1$, $PM_{2.5}$ | 65.9/82.0 | 2006–2008 | Cohort study | 24,845 | 18-74 | CVD | Mortality | 6 |
| Bo et al. (41) | Hongkong, China | $PM_{2.5}$ | 26.6 | 2001–2014 | Cohort study | 134,978 | ≥18 | CVD | Morbidity | 7 |
| Hystad et al. (42) | Multiple countries | $PM_{2.5}$ | 47.5 | 2003–2018 | Cohort study | 157,436 | 35-70 | CVD | Morbidity, mortality | 8 |
| Ruchiraset et al. (43) | Thailand | $PM_{10}$ | 74.0 | 2003–2014 | Cohort study | 41,085 | ≥18 | RSD | Morbidity | 5 |
| Li et al. (44) | China | $PM_{2.5}$ | 65.0 | 2000–2015 | Cohort study | 118,551 | ≥18 | RSD | Morbidity, mortality | 7 |
| Liang et al. (45) | China | $PM_{2.5}$ | 67.4 | 2000–2015 | Cohort study | 127,840 | ≥18 | CVD | Morbidity, mortality | 8 |
| Yang et al. (46) | China | $PM_{2.5}$ | 64.9 | 2000–2015 | Cohort study | 116,821 | ≥18 | CVD | Mortality | 7 |
| Yang et al. (47) | Foshan, China | $PM_{2.5}$ | 39.2 | 2015–2019 | Cohort study | 61,884 | ≥18 | CVD | Morbidity | 5 |
| Lin et al. (48) | Taiwan, China | $PM_{2.5}$ | 32.5 | 2005–2011 | Cohort study | 140,911 | Infants | RSD | Morbidity | 7 |
| Yang et al. (49) | Northern China | $PM_{2.5}$ | 66.3 | – | Cohort study | 38,140 | ≥18 | CVD | Mortality | 5 |
| Paoin et al. (51) | Thailand | $PM_{10}$ | 44.4 | 2005–2013 | Cohort study | 25,532 | ≥18 | CVD | Morbidity | 8 |
| Shi et al. (50) | China | $PM_{2.5}$, $PM_{10}$ | 52.1/93.0 | 2016–2018 | Cohort study | 4,866 | Average 65.2 | CVD and RSD | Morbidity, mortality | 7 |

CVD, Cardiovascular disease; RSD, Respiratory disease; CHD, Congenital heart disease.



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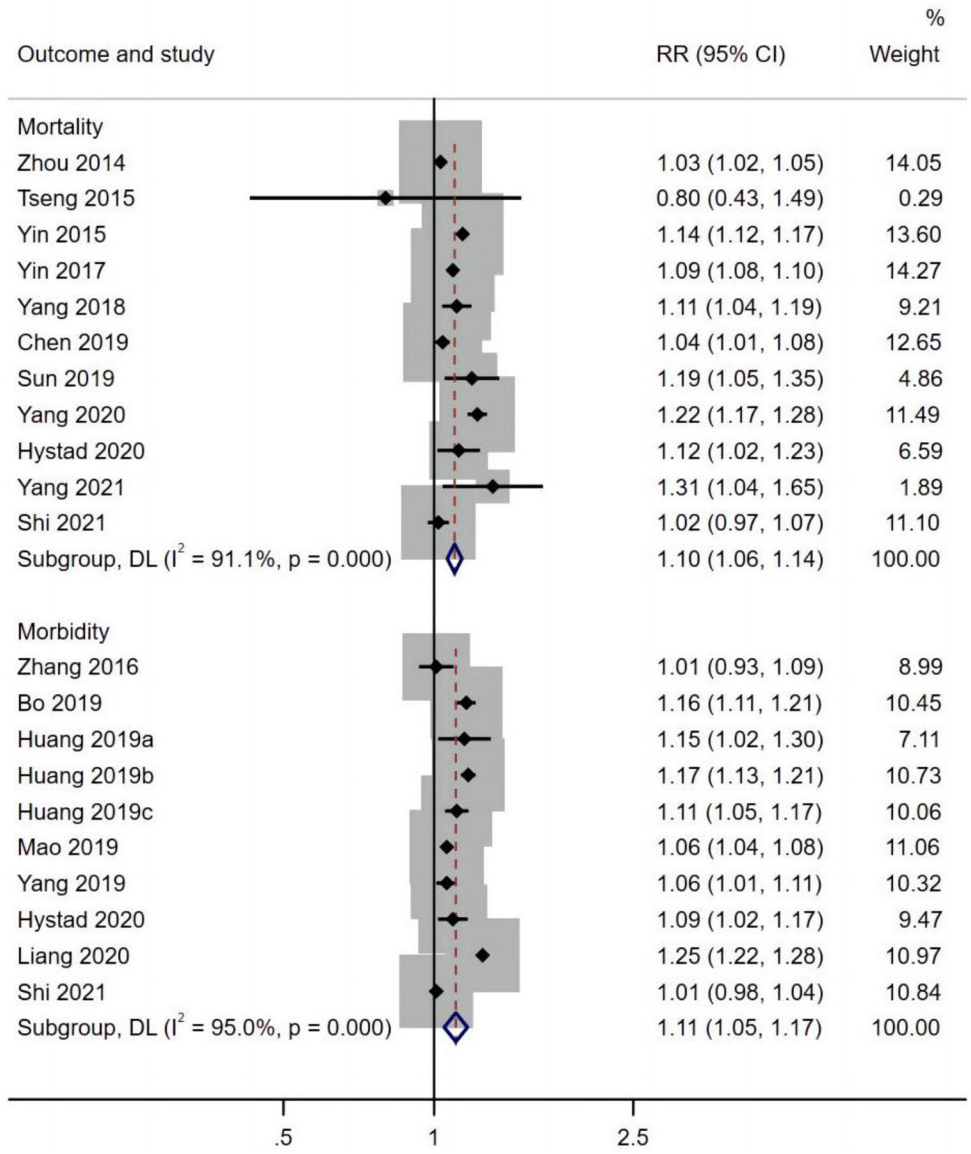


FIGURE 2
$PM_{2.5}$ effects on cardiovascular disease mortality and morbidity.

## Results

Our search yielded 1,978 unique records, of which 224 were potentially eligible and subjected to further full-text review. Ultimately, 38 studies (6, 7, 17–51) of long-term PM exposure met the criteria and were chosen for meta-analysis (Figure 1).

Table 1 presents the main characteristics of the included studies. A number of studies assessed the morbidity and mortality effects of long-term exposure to $PM_{2.5}$ ($n$ = 24) (22, 23, 25, 26, 28, 30, 33–42, 44–50, 52) or $PM_{10}$ ($n$ = 19) (6, 7, 17–21, 24, 27–29, 31, 32, 34, 37, 38, 43, 50, 51), but there were few studies of $PM_1$ ($n$ = 2) (37, 40). The vast majority utilized a cohort study design ($n$ = 35) (6, 7, 17–20, 22–33, 35, 36, 38–51), and only three articles (21, 34, 37) used a case-control study design. Three studies (7, 30, 50) analyzed both cardiovascular and respiratory diseases; 22 studies (17, 18, 20–22, 28, 31, 33–38, 40–42, 45–47, 49, 51) investigated only cardiovascular diseases, and 13 studies (6, 19, 23–27, 29, 32, 39, 43, 44, 48) assessed respiratory diseases. Seventeen (20, 21, 23, 24, 27, 28, 31, 32, 34–36, 38, 41, 43, 47, 48, 51) of the 38 studies reported morbidity as an outcome variable; 17 studies (6, 7, 17–20, 22, 25, 26, 29, 30, 33, 37, 39, 40, 46, 49) reported mortality, and 4 studies (42, 44, 45, 50) reported both morbidity and mortality. Thirty-five studies were conducted in China (6, 7, 17–41, 44–50); 2 studies were performed in Thailand (43, 51), and the remaining study (42) used data from 21 different countries.

Table 1 presents the risk-of-bias assessments. Twenty-five studies were rated as "low risk." However, 15 studies were rated as "medium risk" due to inadequate adjustment for potential confounders in the analysis and a lack of

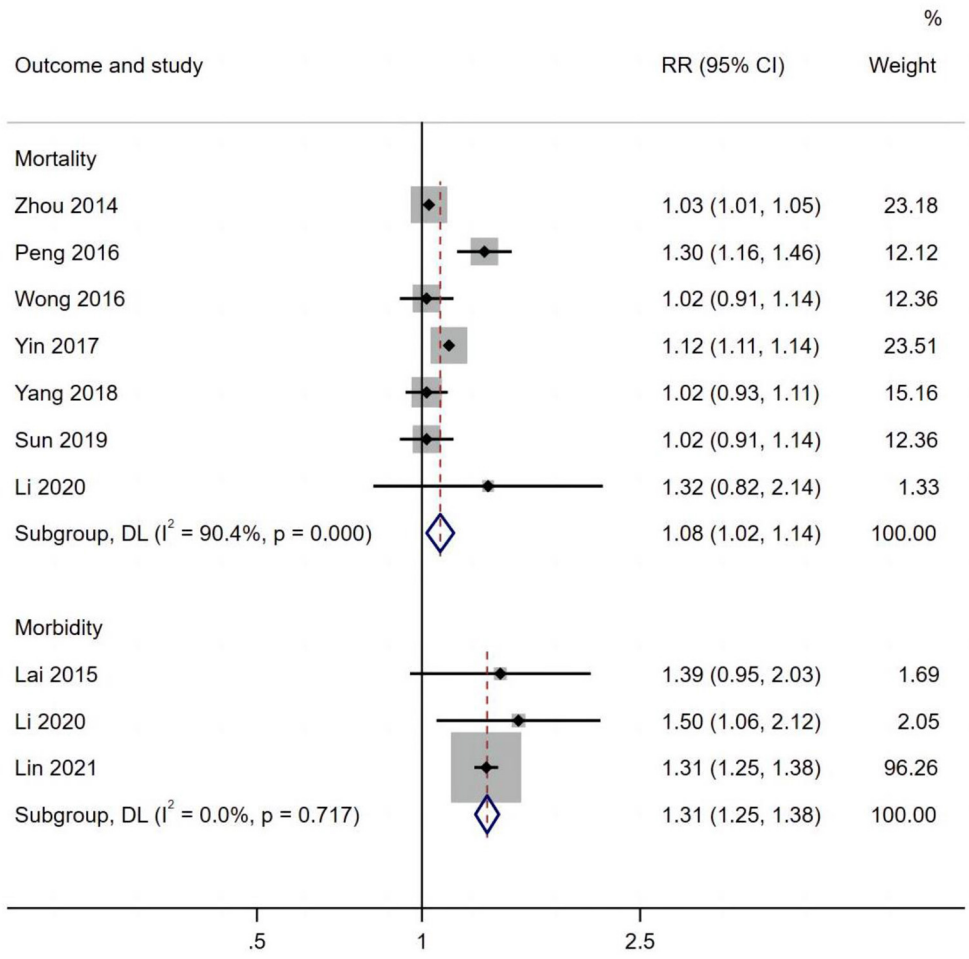


FIGURE 3
$PM_{2.5}$ effects on respiratory mortality and morbidity.

exposure assessment, mainly because pollutants were measured once over a large geographical area and not measured at least daily.

## Effects of $PM_{2.5}$ per 10 μg/m$^3$ increment on cardiovascular and respiratory diseases

Included in the meta-analysis were 22 cohort studies (22, 23, 25, 26, 28, 30, 33, 35, 36, 38–42, 44–50, 52) and two case-control studies (35, 37) published after 2014 that evaluated the mortality and morbidity attributed to the long-term effects of $PM_{2.5}$.

Figure 2 presents the pooled estimates of the correlation between exposure to $PM_{2.5}$ and cardiovascular disease. Overall, long-term exposure to $PM_{2.5}$ per 10 μg/m$^3$ increment was associated with an increased risk of cardiovascular morbidity (RR 1.11, 95% CI: 1.05, 1.17) and mortality (RR 1.10, 95% CI: 1.06, 1.14). Furthermore, exposure to $PM_{2.5}$ per 10 μg/m$^3$ increment was significantly associated with an increased risk of respiratory mortality (RR 1.31, 95% CI: 1.25, 1.38) and morbidity (RR 1.08, 95% CI: 1.02, 1.04) (Figure 3).

Table 2 shows that the morbidity of stroke (RR 1.09, 95% CI: 1.06, 1.12) was related to $PM_{2.5}$ exposure per 10 μg/m$^3$ increment. A significant association between $PM_{2.5}$ andcardiovascular morbidity was observed in both males (RR 1.08, 95% CI: 1.06, 1.10) and females (RR 1.14, 95% CI: 1.12, 1.17). In addition, the mortality rates for COPD (RR 1.12, 95% CI: 1.11, 1.14), tuberculosis (RR 1.22, 95% CI: 1.09, 1.36), and lung cancer (RR 1.12, 95% CI: 1.09, 1.16) were all associated with long-term exposure to $PM_{2.5}$, and an increased risk of respiratory mortality was observed in elderly persons over 65 years old (RR 1.21, 95% CI: 1.00, 1.47).

## Effects of $PM_{10}$ per 10 μg/m$^3$ increment on cardiovascular and respiratory diseases

Ten studies assessed the long-term exposure to $PM_{10}$ and cardiovascular diseases. A positive association was observed

TABLE 2 Subgroup analysis of the effects of $PM_{2.5}$ per 10 $\mu g/m^3$ increment on cardiovascular and respiratory diseases.

| Characteristics | *n* | RR (95%CI) | $I^2$ | *P* | *P*-interaction |
|---|---|---|---|---|---|
| cardiovascular morbidity | | | | | |
| Type of study | | | | | |
| Cohort | 8 (28, 35, 36, 41, 42, 45, 47, 50) | 1.07 (1.06, 1.09) | 99.1 | <0.001 | 0.264 |
| Case-control | 1 (34) | 1.15 (1.02, 1.30) | - | 0.024 | |
| Sex | | | | | |
| Male | 3 (38, 42, 45) | 1.08 (1.06, 1.10) | 98.2 | <0.001 | <0.001 |
| Female | 3 (38, 42, 45) | 1.14 (1.12, 1.17) | 96.4 | <0.001 | |
| Type of disease | | | | | |
| Stroke | 4 (35, 42, 45, 46) | 1.09 (1.06, 1.12) | 78 | <0.001 | <0.001 |
| CHD | 2 (28, 34) | 1.01 (0.96, 1.08) | 75.2 | 0.635 | |
| TF | 2 (35, 42) | 1.07 (0.92, 1.24) | 0 | 0.379 | |
| Hypertension | 2 (36, 41) | 1.14 (1.09, 1.19) | 35.8 | 0.212 | |
| Respiratory mortality | | | | | |
| Type of disease | | | | | |
| COPD | 2 (30, 33) | 1.12 (1.11, 1.14) | 0 | <0.001 | 0.36 |
| Tuberculosis | 2 (23, 25) | 1.22 (1.09, 1.36) | 0 | 0.001 | |
| Lung cancer | 3 (26, 30, 44) | 1.12 (1.09, 1.16) | 0 | <0.001 | |
| Age | | | | | |
| ≥65 | 4 (7, 26, 33, 39) | 1.21 (1.00, 1.47) | 84.6 | <0.001 | <0.001 |
| <65 | 3 (25, 30, 44) | 1.13 (0.82, 1.55) | 55.4 | 0.106 | |

CHD, Congenital heart disease; TF, Tetralogy of Fallot; COPD, Chronic obstructive pulmonary disease.

between $PM_{10}$ andcardiovascular morbidity (RR 1.07, 95% CI 1.01, 1.13) (Figure 4).

Figure 5 shows that respiratory morbidity (RR 1.43, 95% CI: 1.21, 1.69) and mortality (RR 1.28, 95% CI 1.10, 1.49) were both related to long-term exposure to $PM_{10}$.

Subgroup analyses of type of disease, sex, population, and country were performed for morbidity and mortality (Table 3). The risk of VSD morbidity (RR 1.03, 95% CI: 1.02, 1.04) increased per 10 $\mu g/m^3$ increment of $PM_{10}$. A significant association between $PM_{10}$ and cardiovascular mortality was observed for both males (RR 1.06, 95% CI: 1.04, 1.07) and females (RR 1.15, 95% CI: 1.13, 1.17).

Very few studies of the effects of long-term exposure to $PM_{10}$ on respiratory diseases have been carried out. Two studies assessed long-term exposure to $PM_{10}$ and lung cancer, and a positive association was observed (RR 1.04, 95% CI: 1.02, 1.06).

## Effects of $PM_1$ per 10 $\mu g/m^3$ increment on cardiovascular diseases

Two studies (29, 41) assessed long-term exposure to $PM_1$ and cardiovascular diseases. One study assessed long-term exposure to $PM_1$ per 10 $\mu g/m^3$ increment and cardiovascular disease mortality, and a positive association was observed (RR 1.06, 95% CI: 1.03, 1.10). Another study assessed long-term exposure to $PM_1$ per 10 $\mu g/m^3$ increment andcardiovascular morbidity and similarly found a positive association (RR 1.11, 95% CI: 1.01, 1.22). A forest plot of the effects of $PM_1$ on cardiovascular diseases can be found in the online Supplementary material.

## Publication bias

Egger's test ($p = 0.\ 0.615$, $n = 11$) was conducted for the literature regarding the effects of $PM_{2.5}$ on cardiovascular disease mortality, and no publication bias was found. Publication bias was not assessed for $PM_{10}$ and $PM_1$ because fewer than 10 studies were considered in the meta-analysis.

# Discussion

To the best of our knowledge, this is the first systematic review and meta-analysis to explore the effects of long-term exposure to particulate matter on the morbidity and mortality of cardiovascular and respiratory diseases in LMICs. Increased risk for CVD and respiratory disease events was associated with increased $PM_{2.5}$ and $PM_{10}$ concentrations. The results regarding the effects of $PM_1$ were not remarkable because of the small sample size; thus, more studies are needed.

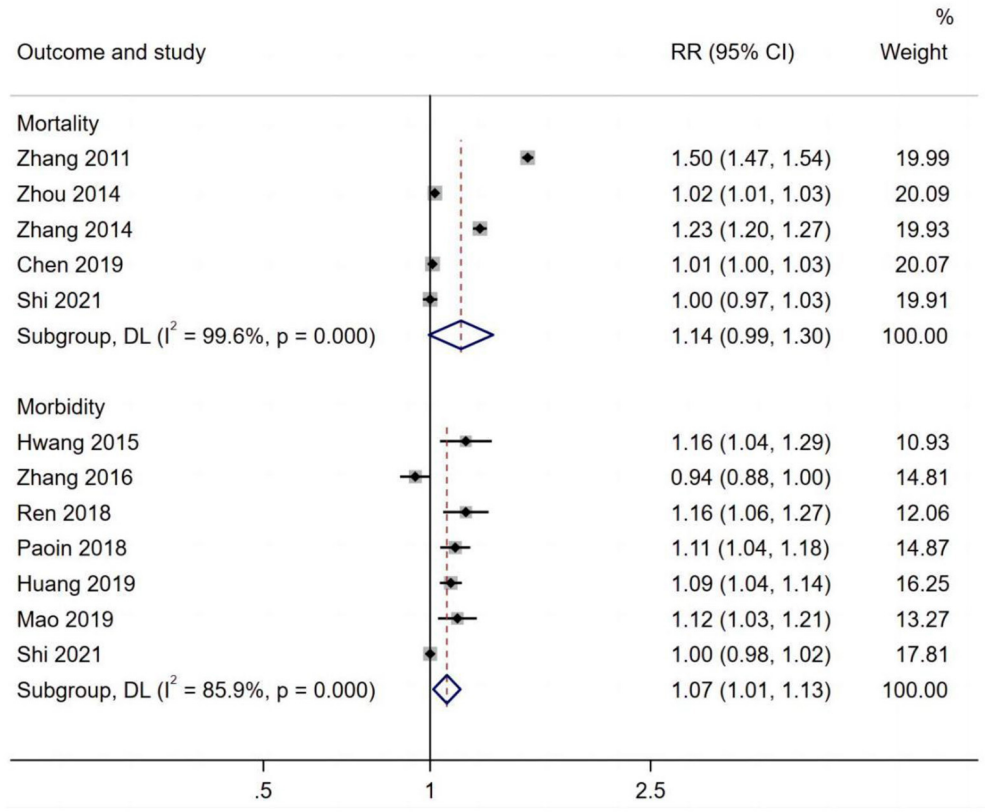


FIGURE 4
$PM_{10}$ effects on cardiovascular disease mortality and morbidity.

PM pollution has considerable effects on the cardiovascular and respiratory systems. Atmospheric PM exposure, even at very low concentrations, could seriously affect the health of humans. Due to its small particle size, $PM_1$ stays in the atmosphere for a long time; these particles have a long transport distance and comprise many harmful and toxic substances, such as polycyclic aromatic hydrocarbons, which can have harmful human health effects. Although its effects on health are significant (53, 54), few studies focus on $PM_1$ pollution. In contrast, there are many studies about the effects of $PM_{2.5}$ and $PM_{10}$ on human health (55, 56). Some studies have shown that $PM_{10}$ is made up of fine ($PM_{2.5}$) and coarse particles. Unfortunately, the presented effect estimates for $PM_{2.5}$ and $PM_{10}$ cannot be compared as the applied increment of 10 $\mu g/m^3$ represents a larger contrast for $PM_{2.5}$ than $PM_{10}$. The biological mechanisms by which PM affects cardiovascular health include metabolic activation, oxidative stress, genotoxicity, inflammation, and autophagy interference (57). Cells involved in these physiological and biochemical processes affect cardiovascular and respiratory system functions in target cells and result in pathophysiological changes, such as cardiac autonomic nervous system adjustments, high blood pressure, metabolic disorders, atherosclerosis and deterioration, inflammatory injury, mutagenicity, and airway epithelial defense function defects, eventually leading to a series of cardiovascular and respiratory events and even death.

This pattern is consistent with the findings of previous studies. Momtazan et al.'s results showed that high levels of particulate matter in the air drastically increased the number of people with cardiovascular diseases (58). In Chen and Hoek (15), a systematic review and meta-analysis evaluated long-term exposure to PM and all-cause and cause-specific mortality; clear evidence showed that both $PM_{2.5}$ and $PM_{10}$ were associated with increased all cause, cardiovascular disease, and respiratory mortality, but $PM_{2.5}$ had a greater effect than $PM_{10}$, especially on respiratory diseases. In this study, the combined risk ratio (RR) for $PM_{2.5}$ and respiratory mortality in LMICs was 1.31, (95% CI: 1.25, 1.38) per 10 $\mu g/m^3$ increase; compared with Chen's study, this result is significantly higher than the research results for the global area (RR 1.10, 95% CI: 1.03, 1.18) and even higher than those of high-income countries (RR 1.04, 95% CI: 1.03, 1.06).

Ambient particulate matter air pollution has increasingly significant effects on health in LMICs. Compared to those in high-income countries, populations in LMICs are burdened with a greater proportion of PM, leading to their extensive distribution as anthropogenic PM increases (59). Management of PM pollution is a challenging process, especially for LMICs with serious economic and health resource problems. Compared to that of the last WHO global assessment, the evidence available has increased considerably (60–66); nevertheless, studies carried out in LMICs remain rare. Studies on the effects of PM on the health of LMICs' populations

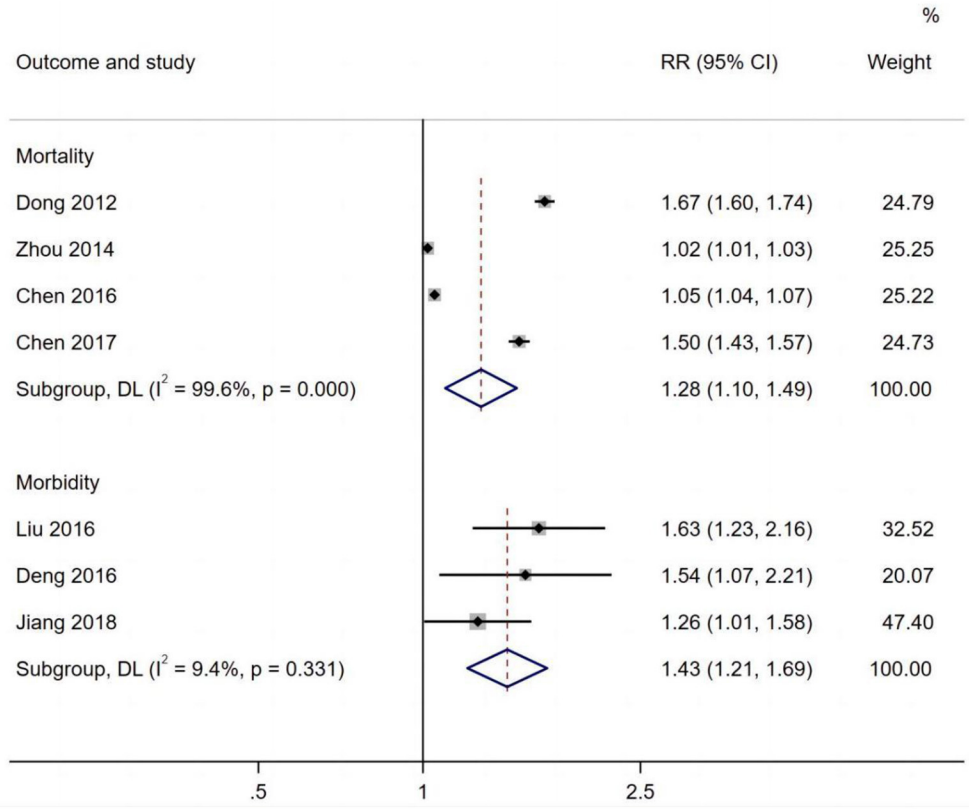


FIGURE 5
$PM_{10}$ effects on respiratory mortality and morbidity.

are scarce. LMICs may have published relevant articles in their own national languages, but the language issue prevents many of these studies from being included. Through systematic analysis, we can obtain effect data for LMICs to provide support for the formulation of appropriate improvement policies. These findings are essential to inform policymakers and eventually alleviate the burden of PM ambient air pollution in LMICs.

## Strengths and limitations

This systematic review and meta-analysis provide comprehensive and current evidence of the effects of long-term exposure to particulate matter on the morbidity and mortality of cardiovascular and respiratory diseases in LMICs. However, our study has some limitations. First, significant heterogeneity for the pooled estimates was noted in the meta-analysis; this finding might be due to the high variability in the study populations, outcomes, and geographical locations. Therefore, subgroup analyses of sex (male vs. female), population age (<65 years vs. >65 years), study type (cohort study vs. case-control), and disease type were conducted to further investigate the potential contributing sources. Second, most of the papers included in our study were from China; this parameter affects the pooled estimates, although it is an inherent and inevitable selection bias. Third, we found that relatively few studies were performed in LMICs. The earliest included studies of the chronic effects of PM pollution on respiratory and cardiovascular diseases were reported in 2011. Results from individual studies may not be representative, and the limited sample size cannot yield statistically significant conclusions. To support health effects assessments in LMICs and global burden of disease assessments, new studies in LMICs are needed.

## Suggestions for further research

First, the present evidence regarding long-term exposure to particulate matter in LMICs was mainly from China. Studies assessing the effects in other geographical locations are suggested and could contribute to the evaluation of the potentially different effects of particulate matter on different continents. Second, $PM_1$ is the smallest particle, and its health effects should not be understated. Future studies should monitor the chronic effects of $PM_1$ on health status for longer. Third, a greater number of studies are needed to prove the association between long-term exposure to particulates and cardiovascular and respiratory diseases in vulnerable populations; special attention should be paid

TABLE 3 Subgroup analysis of the effects of $PM_{10}$ per 10 $\mu g/m^3$ increment on cardiovascular and respiratory diseases.

| Characteristic | n | RR (95%CI) | $I^2$ | *P* | *P*-interaction |
|---|---|---|---|---|---|
| $PM_{10}$ effects on cardiovascular morbidity and mortality | | | | | |
| Morbidity | | | | | |
| Type of disease | | | | | |
| CHD | 3 (28, 31, 34) | 1.02 (0.99, 1.06) | 87.5 | <0.001 | 0.386 |
| VSD | 3 (21, 28, 35) | 1.03 (1.02, 1.04) | 98.6 | <0.001 | |
| ASD | 2 (21, 35) | 1.02 (1.01, 1.03) | 9.7 | 0.293 | |
| TF | 3 (21, 28, 34) | 1.01 (0.99, 1.03) | 52.3 | 0.123 | |
| Mortality | | | | | |
| Sex | | | | | |
| Male | 3 (17, 18, 37) | 1.06 (1.04, 1.07) | 98.4 | <0.001 | <0.001 |
| Female | 3 (17, 18, 37) | 1.15 (1.13, 1.17) | 99.5 | <0.001 | |
| $PM_{10}$ effects on respiratory morbidity and mortality | | | | | |
| Morbidity | | | | | |
| Disease | | | | | |
| Pneumonia | 2 (32, 43) | 1.01 (1.00, 1.01) | 0 | 0.358 | 0.013 |
| AR | 1 (27) | 3.34 (1.42, 7.88) | 0 | - | |
| Asthma | 1 (24) | 0.85 (0.62, 1.16) | 0 | - | |
| Mortality | | | | | |
| Disease | | | | | |
| COPD | 2 (6, 29) | 1.02 (0.99, 1.06) | 95.3 | <0.001 | 0.443 |
| Lung cancer | 2 (6, 7) | 1.04 (1.02, 1.06) | 99.3 | <0.001 | |

CHD, Congenital heart disease; VSD, Ventricular septal defect; ASD, Atrial septal defect; TF, Tetralogy of Fallot; AR, Allergic rhinitis; COPD, Chronic obstructive pulmonary disease.

to the relationship between long-term exposure to particulates and pregnant women, newborn diseases, mental disorders, and infectious diseases.

## Conclusions

Long-term exposure to $PM_{2.5}$, $PM_{10}$, and $PM_1$ was all related to cardiovascular and respiratory disease events. $PM_{2.5}$ had a greater effect than $PM_{10}$, especially on respiratory diseases, and the risk of respiratory mortality was significantly higher for LMICs than high-income countries. More studies are needed to confirm the effect of $PM_1$ on cardiovascular and respiratory diseases.

## Data availability statement

The original contributions presented in the study are included in the article/Supplementary material, further inquiries can be directed to the corresponding authors.

## Author contributions

Criteria setting were performed by XS and XH. The data were collected by JG, XF, and ZL. The first draft of the manuscript was written by JG. GC and KY were the instructors. All authors contributed to the study conception, design, read, and approved the final manuscript.

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## Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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## Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2023.1134341/full#supplementary-material

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