

BMJ Open is committed to open peer review. As part of this commitment we make the peer review history of every article we publish publicly available.

When an article is published we post the peer reviewers' comments and the authors' responses online. We also post the versions of the paper that were used during peer review. These are the versions that the peer review comments apply to.

The versions of the paper that follow are the versions that were submitted during the peer review process. They are not the versions of record or the final published versions. They should not be cited or distributed as the published version of this manuscript.

BMJ Open is an open access journal and the full, final, typeset and author-corrected version of record of the manuscript is available on our site with no access controls, subscription charges or pay-per-view fees (http://bmjopen.bmj.com).

If you have any questions on BMJ Open's open peer review process please email <a href="mailto:info.bmjopen@bmj.com">info.bmjopen@bmj.com</a>

# **BMJ Open**

# Short-term and Long-term Exposure to Black Carbon and Cardiovascular and Respiratory Diseases: A Systematic Review and Meta-Analysis

Journal:	BMJ Open
Manuscript ID	bmjopen-2021-049516
Article Type:	Original research
Date Submitted by the Author:	29-Jan-2021
Complete List of Authors:	Song, Xuping; Lanzhou University, School of Public Health Hu, Yue; Lanzhou University, School of Public Health Ma, Yan; Lanzhou University, School of Public Health Jiang, Liangzhen; Lanzhou University, School of Public Health Wang, Xinyi; Lanzhou University, Second Clinical College Shi, Anchen; Xi'an Jiaotong University Medical College First Affiliated Hospital, Department of General Surgery Zhao, Junxian; Lanzhou University, School of Public Health Liu, Yunxu; Lanzhou University, School of Public Health Liu, Yafei; Lanzhou University, School of Public Health Tang, Jing; Lanzhou University, School of Public Health Li, Xiayang; Lanzhou University, School of Public Health Zhang, Xiaoling; Chengdu University of Information Technology, College of Atmospheric Sciences Guo, Yong; Guizhou Province Wang, Shigong; Chengdu University of Information Technology, College of Atmospheric Sciences
Keywords:	PUBLIC HEALTH, RESPIRATORY MEDICINE (see Thoracic Medicine), CARDIOLOGY

SCHOLARONE™ Manuscripts



I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

# **Title Page**

#### Title:

Short-term and Long-term Exposure to Black Carbon and Cardiovascular and

Respiratory Diseases: A Systematic Review and Meta-Analysis

#### **Author names and affiliations:**

1. Xuping Song<sup>a</sup> E-mail: songxp@lzu.edu.cn

2. Yue Hu<sup>a</sup> E-mail: huy20@lzu.edu.cn

3. Yan Ma<sup>a</sup> E-mail: may2020@lzu.edu.cn

4. Liangzhen Jiang<sup>a</sup> E-mail: jianglzh19@lzu.edu.cn

5. Xinyi Wang<sup>c</sup> E-mail: wangxinyi17@lzu.edu.cn

6. Anchen Shi<sup>d</sup> E-mail: 3120115202@stu.xjtu.edu.cn

7. Junxian Zhao<sup>a</sup> E-mail:zhaojx2017@lzu.edu.cn

8. Yunxu Liu<sup>a</sup> E-mail:yxliu17@lzu.edu.cn

9. Yafei Liu<sup>a</sup> E-mail:isak-even@qq.com

10. Jing Tang<sup>a</sup> E-mail: tangj19@lzu.edu.cn

11. Xiayang Li<sup>a</sup> E-mail: lixiayang18@lzu.edu.cn

10. Xiaoling Zhang<sup>b</sup> E-mail: xlzhang@ium.cn

11. Yong Guo<sup>e</sup> E-mail:gycau@qq.com

12. Shigong Wang<sup>b</sup> E-mail: wangsg@lzu.edu.cn

Chengdu 610000, China;

<sup>&</sup>lt;sup>a</sup> School of Public Health, Lanzhou University, Lanzhou 730000, China;

<sup>&</sup>lt;sup>b</sup> College of Atmospheric Sciences, Chengdu University of Information Technology,

<sup>c</sup> Second Clinical College, Lanzhou University, Lanzhou 730000, China;

<sup>d</sup> Department of General Surgery, The First Affiliated Hospital of Xi'an Jiao Tong

University, Shaanxi 710061, China;

<sup>e</sup> Department of Civil Affairs in Guizhou Province, Guiyang 550004, China.

### **Corresponding author 1:**

Name: Xiaoling Zhang

Postal Address: College of Atmospheric Sciences, Chengdu University of Information

Technology, Chengdu 610000, Sichuan, China

E-mail address: xlzhang@ium.cn

Fax: 028-85966502

## **Corresponding author 2:**

Name: Shigong Wang

Postal Address: College of Atmospheric Sciences, Chengdu University of Information

Technology, Chengdu 610000, Sichuan, China

E-mail address: wangsg@cuit.edu.cn

Fax: 028-85966502

#### **Abstract**

**Background:** Adverse health effects of fine particles (PM<sub>2.5</sub>) have been well documented by a large number of studies. However, evidence on the impact of black carbon (BC) or elemental carbon (EC) on health is limited. The systematic review and meta-analysis provided comprehensive and current evidence on health impact of BC or EC, which could support the update of the World Health Organization Global Air Quality Guidelines. The objectives were (i) to explore the effects of BC and EC on cardiovascular and respiratory morbidity and mortality; (ii) to conduct stratified analyses that could explain the observed heterogeneity.

Methods: PubMed, Embase, and Web of Science were searched. Two reviewers independently selected studies for inclusion, extracted data, and assessed risk of bias. Outcomes were analyzed via a random effects model and reported as relative risk (RR) with 95% confidence interval (CI). Adapted Grading of Recommendations assessment, Development and Evaluation (GRADE) was used to assess the certainty of evidence.

Results: Sixty-one studies met our inclusion criteria. (i) Short-term exposure to BC or EC were associated with 1.6% (95% CI: 0.4%-2.9%) increase in cardiovascular diseases and 3.8% (95% CI: 0.6%-7.1%) increase in respiratory diseases per 1 μg/m³ in the elderly; (ii) Impact of short-term exposure to BC or EC on cardiovascular morbidity was stronger than mortality; (iii) Increased risk of asthma morbidity was observed in children with short-term exposure to BC or EC, while no statistical significance was found in adults; (iv) A positive association between long-term

exposure to BC or EC and cardiovascular diseases was observed.

Conclusions: Overall, short-term exposure to BC or EC were related with both cardiovascular and respiratory diseases in the elderly. In addition, impact of short-term exposure to BC or EC on cardiovascular morbidity was stronger than mortality and the association differ across continents.

Keywords: Black carbon, Cardiovascular disease, Respiratory disease, Systematic review

# Strengths and limitations of this study

- 1.The study provided a comprehensive and current evidence for the health effects of BC.
- 2. PM2.5-adjusted estimates and PM2.5-unadjusted estimates were combined respectively to investigate the robustness of results.
- 3. The elderly and children were more vulnerable to the effects of BC.
- 4. Impact of short-term exposure to BC on cardiovascular morbidity was stronger than mortality.
- 5. Compared with Europe and America, a stronger association between BC and cardiovascular mortality was noted in Asia.

# 1. Background

Black carbon (BC), a ubiquitous component of particulate matter, is usually measured through optical absorption.<sup>[1]</sup> Elemental carbon (EC), another carbonaceous material with a graphitic structure, is commonly measured by thermal or thermo-optical methods. [1, 2] Although the measurement methods are different, BC and EC are often considered interchangeable. BC is mainly emitted from traffic and combustion-related sources, and is a measured component of the particulate matter (PM). The adverse health effects of PM, especially of PM<sub>2.5</sub>, are well documented. In 2017, a total of 2.94 million deaths resulted from ambient PM worldwide. [3-5] PM<sub>2.5</sub> is composed of various constituents, in which some of them are more toxic and hypothesized as the main cause of the adverse effects of PM<sub>2.5</sub>. A growing body of studies indicates a potential role of BC among these more toxic constituents. [6, 7] In addition, some reviews demonstrated that BC is a better indicator of adverse effects of PM from combustion sources according to robust associations from epidemiological studies.<sup>[8, 9]</sup> The underlying pathological mechanisms of BC include oxidative stress, inflammation and gene mutations.[10-12]

Due to its association with adverse health and climate effects, the number of studies exploring the effects of BC on cardiorespiratory diseases has rapidly increased in recent years. Cardiovascular and respiratory diseases are common diseases worldwide, with a heavy disease burden and major implications in clinical practice and public health. The Global burden of disease study 2017 indicated that

cardiovascular and respiratory-related death ranked first and third respectively among non-communicable diseases.<sup>[4]</sup> Health effects of acute and chronic exposure to BC have been widely reported. Despite there are some epidemiological evidences that BC was associated with cardiorespiratory diseases, in other studies, no statistical significance was observed.

Some systematic reviews analyzed the impact of BC on health. Nevertheless, quantitative associations between BC exposure and cardiovascular and respiratory diseases have not been well-characterized due to the different objectives of the reviews focused on.<sup>[13, 14]</sup> In addition, a series of eligible studied published recently have not been considered and Grade (Grading of Recommendations assessment, Development and Evaluation) framework was not adopted in previous systematic reviews. Therefore, a systematic review and meta-analysis was performed to further elucidate the health effects of BC or EC. The objectives of this study were (1) to investigate the association of short-term and long-term exposure to BC or EC with the respiratory and circulatory morbidity and mortality; (2) to conduct stratified analyses that could explain the observed heterogeneity.

#### 2. Methods

The protocol for this systematic review was registered and published online on PROSPERO (International Prospective Register of Systematic Reviews), under registration number CRD42020186244.

#### 2.1 Patient and public involvement

Patients or the public were not involved in this study.

#### 2.2 Database

Articles were identified using PubMed, Web of Science, and Embase databases up to August 6<sup>th</sup>, 2019. Original articles were searched using the following U.S. National Library of Medicine's Medical Subject Headings (MeSH) terms and keywords: "(black carbon\* or elemental carbon\*) AND (respiratory\* or cardiovascular\*) AND (morbidit\* or hospitalization\* or death\* or mortalit\* or outpatien\*) AND (time series\* or case cross\* or cohort\*)". In addition, the reference lists of the included studies and related reviews were manually evaluated to identify additional relevant studies. The details of the search strategy in PubMed are shown in Supplementary Table S1.

#### 2.3 Inclusion and exclusion criteria

A time series study, case crossover study and cohort study that evaluated the impact of BC or EC on cardiovascular or respiratory diseases were included in this systematic review and meta-analysis. Studies were considered eligible for inclusion if they fulfilled the inclusion criteria as follows: (1) study types restricted to time series, case crossover or cohort studies; (2) studies considering BC or EC as air pollutants; (3) based on the International Classification of Diseases (ICD) 9<sup>th</sup> or 10<sup>th</sup> revision, diseases included respiratory diseases, wheeze, other respiratory distress insufficiency or respiratory cancer (ICD-9 codes 460–519, 786.07, 786.09 or 162; ICD-10 codes J00–J99, R06.251, R06.001 or C34) or cardiovascular diseases (ICD-9 codes 390–459, ICD-10 codes I00–I99); (4) studies considering morbidity or mortality as outcome; (5) estimates were odds ratio (OR), relative risk (RR) or hazard ratio (HR)

with 95% confidence interval (CI) or enough information for calculation; (6) publication language was restricted to English.

The exclusion criteria were as follows: (1) studies on soot or black smoke were excluded, because the definition of such components usually lacked precision. (2) studies assessing the disease progression exposure to pollutants in individuals with cardiovascular or respiratory diseases (for example chronic obstructive pulmonary disease and asthma); (3) studies focusing on particular populations (for example pregnant women and miners) or population living in specific environments with high pollution concentration (for example residential area near industrial complexes, population exposed to sugar cane burning and neighborhoods that expose many streets); (4) studies focusing on seasonality; (5) conference abstracts; (6) study period less than 1 year.

#### 2.4 Selection of articles and extraction of data

To identify eligible studies, two investigators independently screened titles and abstracts. Studies which relevance could not be determined by titles and abstracts were subjected to full text screening. Any disagreement was resolved by discussion. A third investigator was involved in the discussion when a consensus could not be reached between the two investigators.

Two reviewers independently extracted the following items from each included study and record them in a pre-designed table: first author, publication year, country, study design, diagnosis standard, time periods, population age, statistical models, air pollutants, outcomes, and number of events. If the reported data of the included

studies were unclear or missing, the first author or corresponding author was contacted by e-mail. Any conflicts were resolved by the involvement of a third investigator if the controversy was not solved after the discussion.

#### 2.5 Data synthesis

Regarding the meta-analysis, the RR was used as an effect estimate, and the OR in case crossover study and HR in cohort study were considered equivalent to RR. Estimates from the maximally adjusted model in the cohort study were extracted when multiple estimates were present in the original study to reduce the risk of potential unmeasured confounding. [15] In addition, the estimate was converted to a standardized increment (1  $\mu$ g/m³) of RR. The following formula was used to calculate the standardized risk estimates:

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

Two studies did not show the overall risk, while stratified risk estimates by age and location were reported.<sup>[16, 17]</sup> In this case, the stratified estimates were pooled. One study presented the estimates of both morbidity and mortality, which were combined in the overall analysis.<sup>[18]</sup> In addition, the same cohort data were analyzed in different studies and the latest studies were included in the systematic review and meta-analysis.<sup>[19-21]</sup>

#### 2.6 Risk of bias assessment

The risk of bias was assessed for each study according to the Office of Health Assessment and Translation (OHAT) tool and the Navigation Guide tool.<sup>[13, 22, 23]</sup> Risk of bias evaluation was conducted as follows: exposure assessment, outcome

assessment, confounding bias, selection bias, incomplete outcome data, selective reporting, conflict of interest and other bias. Each domain was considered as "low", "probably low", "probably high", "high", or "not applicable" criteria. Two investigators conducted the risk of bias evaluation. Any inconsistency between the investigators was discussed and a third researcher was involved to resolve any disagreement.

#### 2.7 Evaluation of certainty of evidence

An adaptation of the Grade (Grading of Recommendations assessment, Development and Evaluation) framework, formulated by the WHO (World Health Organization) global air quality guidelines working group, was used to evaluate the overall certainty of evidence. [24] The rating process on the certainty of evidence was started at moderate. The certainty was graded into four levels: "high", "moderate", "low" and "very low". Five reasons were used to downgrading the certainty of evidence: limitations in studies, indirectness, inconsistency, imprecision, and publication bias; 3 reasons were used to upgrade the certainty of evidence: large magnitude of effect size, all plausible confounding shifts the relative risk towards the null and concentration-response gradient. To evaluate the magnitude of the effect size, the E-value was calculated using the following formula: RR+sqrt{RR\*(RR-1)}

#### 2.8 Statistical analysis

Statistical analysis was performed using STATA (version12.0, Stata Corp, College Station, TX, USA). In this meta-analysis, the random-effects model was conducted for anticipating significant heterogeneity among studies. Heterogeneity

among trials was assessed by the Chi-square test and the extent of inconsistency was evaluated by the  $I^2$ . An 80% prediction interval (PI) of meta-estimate was calculated to assess the inconsistency. To assess potential sources of heterogeneity, subgroup analyses were performed on outcome (morbidity and mortality), single lag days (0, 1 and 2 days), study area (Europe, America, and Asia) and season (warm and cold). The estimates from BC and EC were combined, since both of them are indicators of carbon-rich combustion sources, and are usually considered interchangeable in medical research.

Estimates were pooled separately where more than three estimates were available. Most studies presented estimates for single lags and the estimate of shortest lag was used to combine the estimates (RRs) of shortest lag in meta-analysis. However, only few studies presented cumulative lags, and the estimates of shortest cumulative lags were used in the meta-analysis. In addition, Mostofsky et al. indicated that PM<sub>2.5</sub> is a potential confounder in assessing the health effects of PM<sub>2.5</sub> constituents.<sup>[7]</sup> For overall and outcome analysis, PM<sub>2.5</sub>-adjusted estimates and PM<sub>2.5</sub>-unadjusted estimates in the models were combined, respectively where more Regarding than three estimates were available. the subgroup analysis. PM<sub>2.5</sub>-unadjusted estimates were analyzed, while PM<sub>2.5</sub>-adjusted estimates were not presented due to the limited number of included studies. Moreover, primary data of the included studies could not be obtained, hence it was not possible to evaluate whether the same patients were repeatedly included across multiple studies. Therefore, the sensitivity analysis was performed on all age populations to investigate

the robustness of the aggregation results by the removal of studies with partial temporal overlap from the same geographical location. The majority of the included studies analyzed and presented results of cardiovascular or respiratory system diseases, hence systematic diseases were analyzed in the acute effect analysis except for the chronic effect analysis. Publication bias was assessed by Egger's regression test when the outcome included more than 10 studies. Trim and fill method were used to correct on asymmetry for the outcome with publication bias. p < 0.05 was considered statistically significant.

#### 3. Results

A total of 1308 studies were initially identified and 107 were reviewed in depth. Of these, 61 fulfilled the inclusion criteria (Figure 1). Of the 61 included studies, 53 estimated the short-term effects of BC or EC using a time series design or case crossover design, while 8 studies explored the long-term effects of BC or EC using a cohort design. Thirty of the 61 studies reported morbidity as the outcome variable, 24 studies reported mortality, and 7 studies reported both morbidity and mortality. Thirty-three studies analyzed both cardiovascular and respiratory diseases, 13 studies merely investigated cardiovascular diseases, and 14 studies assessed respiratory diseases. Thirty-six studies were conducted in the United States, 13 in China, 3 in Canada, 2 in the United Kingdom, 2 in Korea, 1 in Serbia, Denmark, and the Netherlands. The remaining 2 studies collected data from two different countries: one from Spain and Greece, the other one from Spain and Italy. Twenty-seven studies classified the diseases using the ICD-9 codes, 23 used the ICD-10 codes, and 8 used

both the ICD-9 and ICD-10 codes. However, the remaining 3 studies did not employ the ICD standards (Supplementary Table S2). In addition, the authors of 33 studies were contacted, but only 19 answered to our request (response rate: 57.6%).

#### 3.1 Short-term effect of BC or EC on cardiovascular and respiratory diseases

Overall, short-term exposure to BC or EC was associated with an increased risk of cardiovascular diseases (RR = 1.007 per 1  $\mu$ g/m³, 95% CI: 1.003–1.011) (adjusted by trim and fill method), but had no impact on respiratory diseases (RR = 1.010 per 1  $\mu$ g/m³, 95% CI: 0.996–1.025) in overall analyses (Table 1). However, both cardiovascular (RR = 1.016 per 1  $\mu$ g/m³, 95% CI: 1.004–1.029) and respiratory diseases (RR = 1.038 per 1  $\mu$ g/m³, 95% CI: 1.006–1.071) were associated with BC or EC in the elderly (65+ years) (Figure 2 and Figure 3).

The stratification analysis by outcome indicated that the effect estimates of BC or EC on cardiovascular morbidity (RR = 1.022 per 1  $\mu$ g/m³, 95% CI: 1.016–1.029) were higher compared to their effect on mortality (RR = 1.003 per 1  $\mu$ g/m³, 95% CI: 1.001–1.006). The impact of BC or EC on cardiovascular diseases was related to the exposure lag. The estimates of the association were strongest on the day of the event (lag 0) (RR = 1.011 per 1  $\mu$ g/m³, 95% CI: 1.006–1.016), and then diminished on lag 1 (RR = 1.005 per 1  $\mu$ g/m³, 95% CI: 1.002–1.008) and lag 2 (RR = 1.002 per 1  $\mu$ g/m³, 95% CI: 0.999–1.005) (Supplementary Table S3). The subgroup analysis on the geographical location was performed for morbidity and mortality, respectively. Significant association between BC or EC and cardiovascular mortality was observed in Asia (RR = 1.003, 95% CI: 1.001–1.004). However, no association was found in

America (RR = 1.017, 95% CI: 0.998–1.037) and Europe (RR = 0.990, 95% CI: 0.979–1.002) (Supplementary Figure S1). On the other hand, an increased risk on cardiovascular morbidity was observed in America (RR = 1.022, 95% CI: 1.016–1.029) with short-term exposure to BC or EC, while only one study performed in Europe (RR = 1.026, 95% CI: 1.006–1.047) investigated the short-term effect of BC or EC on cardiovascular morbidity.<sup>[18]</sup> In addition, just one study in Asia was performed assessing the short-term effects of BC or EC on stroke morbidity<sup>[25]</sup> (Supplementary Figure S2).

No association was observed between short-term exposure of BC and EC and respiratory morbidity (RR = 1.012, 95% CI:0.993–1.031) and mortality (RR = 1.013, 95% CI:0.997–1.030) (Table 1). In addition, the pooled effect estimates of BC or EC on asthma morbidity indicated an increased risk in children of 0-18 years (RR = 1.020, 95% CI:1.006–1.035), while no statistical significance was observed in populations older than 18 years (RR = 1.011, 95% CI:0.998–1.025) (Supplementary Figure S3).

Table 1. Short-term impacts of BC or EC on cardiovascular and respiratory diseases in different models

Table 1. Short-term impacts of BC or EC on cardiov	vasculai ali	u respiratory	diseases in different if	lodeis		9			
	PM <sub>2.5</sub> -unadjusted model						PM <sub>2.5</sub> -adjusted model		
Subgroup Analysis	No. of Studies	No. of Estimates	Relative Risk (95%CI)	$I^2$	Egger regression test (p value)		Estimates	Relative Risk (95%CI)	$I^2$
Cardiovascular Diseases						22. C			
Age						Jowr			
All population	20	22	1.008 (1.004, 1.012)	63.80%	0.011	6 ac	7	1.014 (1.001, 1.027)	50.40%
Relative risk adjusted for publication bias with trim and fill method	24	26	1.007(1.003, 1.011)	_	_	Downloaded from	_	_	_
Sensitive analysis on study of partial temporal overlap from the same geographical location	16	16	1.006 (1.002, 1.010)	60.00%	0.020	— m http	_	_	_
≥65 years	5	6	1.016 (1.004, 1.029)	87.80%	_	— <sup>()</sup> bn	_	_	_
Outcome						njop			
Morbidity	12	12	1.022 (1.016, 1.029)	37.20%	0.163	4 en.b	5	1.018 (1.006, 1.031)	39.50%
Mortality	14	15	1.003 (1.001, 1.006)	29.70%	0.266	http://bmjopen.bmj.com/	4	1.006 (0.993, 1.019)	42.90%
Respiratory Diseases						)m/ o			
Age						on A			
All population	16	18	1.010 (0.996, 1.025)	86.80%	0.627	April 19,	8	1.002 (0.990, 1.014)	42.70%
Sensitive analysis on study of partial temporal overlap from the same geographical location	12	12	1.008 (0.992, 1.023)	90.30%	0.449			_	_
≥65	3	4	1.038 (1.006, 1.071)	83.30%	_	2024 by	_	_	_
Outcome						guest.			
Morbidity	10	10	1.012 (0.993, 1.031)	91.80%	0.671	3 E	5	0.996 (0.987, 1.004)	0
Mortality	10	11	1.013 (0.997, 1.030)	66.40%	0.328		3	1.017 (0.985, 1.050)	48.30%
						rotected by copyr			
						′ соруг			

#### 3.2 Long-term impact of BC or EC on cardiovascular and respiratory diseases

Seven studies assessed the long-term exposure to BC or EC and cardiovascular diseases, and a positive association was observed (RR = 1.052, 95% CI: 1.021-1.183) (Supplementary Figure S4). On the other hand, 3 studies assessed the long-term exposure to BC or EC and respiratory mortality. Meta analysis was not performed due to limited included studies. no association was observed among the three include studies.<sup>[20, 26, 27]</sup> However, one study analyzed COPD. It indicated that long-term exposure to BC or EC was associated with an increased risk of chronic obstructive pulmonary disease (COPD) morbidity (RR=1.060, 95%CI: 1.020-1.100), while no impact was observed for COPD mortality (RR=1.070, 95%CI: 1.000-1.140).<sup>[19]</sup>

#### 3.3 Results from the PM<sub>2.5</sub>-adjusted model

In the PM<sub>2.5</sub>-adjusted model, six studies were included in the meta-analysis of short-term exposure to BC or EC and cardiovascular diseases (RR = 1.014 per 1  $\mu$ g/m³, 95% CI: 1.001-1.027) (Supplementary Figure S5). The meta-analysis indicated that the association was robust compared to the results of the PM<sub>2.5</sub>-unadjusted model. In addition, the impact of BC or EC on cardiovascular morbidity in the PM<sub>2.5</sub>-adjusted model (RR = 1.018 per 1  $\mu$ g/m³, 95% CI: 1.006-1.031) was consistent with the results in the PM<sub>2.5</sub>-unadjusted model (RR = 1.022 per 1  $\mu$ g/m³, 95% CI: 1.016-1.029). However, an increased risk was found between BC or EC and cardiovascular mortality in the PM<sub>2.5</sub>-unadjusted model (RR = 1.003 per 1  $\mu$ g/m³, 95% CI: 1.001-1.006), while no association was observed in the PM<sub>2.5</sub>-adjusted model (RR = 1.006 per 1  $\mu$ g/m³, 95% CI: 0.993-1.019) (Table 1). On the other hand, consistent

results (RR = 1.002 per 1  $\mu$ g/m³, 95% CI: 0.990-1.014) were observed in the meta-analysis of the PM<sub>2.5</sub>-adjusted models for respiratory diseases (Supplementary Figure S6). In addition, results of BC or EC on respiratory morbidity and mortality in the PM<sub>2.5</sub>-adjusted models were also consistent with the results in the PM<sub>2.5</sub>-unadjusted model (Table 1).

#### 3.4 Sensitive analysis

In the sensitive analysis, similar results were observed from the overall analysis of all age populations. Increased risk of cardiovascular diseases after exposure to BC or EC was found (RR = 1.006 per 1  $\mu$ g/m³, 95% CI: 1.002-1.010) by eliminating studies with partial overlap from the same geographical location.<sup>[16, 18, 28, 29]</sup> In addition, no statistical significance was observed (RR = 1.008 per 1  $\mu$ g/m³, 95% CI: 0.992-1.023) between respiratory diseases and BC or EC after eliminating overlapped studies<sup>[16, 18, 30, 31]</sup> (Table 1).

#### 3.5 Risk of bias and certainty of evidence

The risk of bias assessment of the included studies is shown in Table 2 and more analytically in Supplementary Table S4. In general, the majority of the included studies were rated as "low risk" in the items of outcome assessment, selection bias, incomplete outcome data, conflict of interest and other bias. The confounding bias and selective reporting were mostly rated as "probably low". However, 5 studies were rated as "probably high" risk because not all critical potential confounders were adjusted in the analysis.<sup>[7, 19, 21, 32, 33]</sup> In addition, the majority of the included studies on the exposure assessment were assessed as "probably low" and "probably high",

and in some cases studies were rated as "high" risk. Two studies were rated as "high risk" on exposure assessment mainly because pollutant were measured with a single monitoring over a large geographical area and not measured at least daily.<sup>[34, 35]</sup>

The certainty of the evidence on the acute effects of BC or EC on cardiovascular diseases in the PM<sub>2.5</sub>-adjusted model was rated as "high", and "moderate" for respiratory diseases in all population as assessed by the adapted GRADE. The evidence on the chronic effects of BC or EC on cardiovascular diseases was evaluated as "high" certainty (Supplementary Table S5). 

Table 2. Results of risk of bias assessment

			Key criteria		Other criteria				
No.	Study	Exposure	Outcome	Confounding	Selection	Incomplete	Selective	Conflict of	Other
		assessment	assessment	bias	bias	outcome data	reporting	interest	Other
1	Atkinson et al. 2016								
2	Bell et al. 2014								
3	Cai et al. 2014								
4	Geng et al. 2013								
5	Hua et al. 2014								
6	Ostro et al. 2015a								
7	Samoli et al. 2016								
8	Zanobetti and Schwartz 2006								
9	Liu et al. 2016a								
10	Liu et al. 2016b								
11	Sarnat et al. 2015								
12	Kim et al. 2012								
13	Ostro et al. 2009								
14	Kim et al. 2015								
15	Huang et al. 2012								
16	Peng et al. 2009					•			
17	Levy et al. 2012								
18	Son et al. 2012								
19	Heo et al. 2014								
20	Basagaña et al. 2015								
21	Dai et al. 2014								
22	Lin et al. 2016a								
23	Cao et al. 2012								
24	Klemm et al. 2011								
25	Zhou et al. 2011								
26	Winquist et al. 2015								
27	Ostro et al. 2007								
28	Tolbert et al. 2000								
29	Wang and Lin 2016								
30	Darrow et al. 2014								
31	Metzger et al. 2004								
32	Mar et al. 2000								
33	Wang et al. 2019								
34	Lin et al. 2016b								
35	Ostro et al. 2008								

**Table 2.** Results of risk of bias assessment (continued)

			Key criteria	1	Other criteria						
No.	Study	Exposure	Outcome	Confounding	Selection	Incomplete	Selective	Conflict	0.0		
		assessment	assessment	bias	bias	outcome data	reporting	of interest	Other		
36	Ito et al. 2011										
37	Chen et al. 2014										
38	Tomic'-Spiric' et al. 2019										
39	Maynard et al. 2007										
40	Sinclair et al. 2010										
41	Krall et al. 2013										
42	Cakmak et al. 2009										
43	Tolbert et al. 2007										
44	Lall et al. 2011										
45	Jung and Lin 2017										
46	Gong et al. 2019										
47	Mostofsky et al. 2012										
48	Krall et al. 2017										
49	O'Lenick et al. 2017										
50	Pearce et al. 2015										
51	Strickland et al. 2010										
52	Strickland et al. 2014										
53	Ito et al. 2013										
54	Ostro et al. 2015b										
55	Gan et al. 2013										
56	Hvidtfeldt et al. 2019										
57	Thurston et al. 2016										
58	Yang et al. 2018										
59	Gan et al. 2011										
60	De Kluizenaar et al. 2013										
61	Vedal et al. 2013										
	Risk of bias rating:	Low		Probably Low		Probably High		High			

#### 4. Discussion

A comprehensive search of three electronic databases was performed using a well-defined search strategy. Finally, 61 studies assessing the short-term and long-term impacts of BC or EC on cardiovascular and respiratory morbidity and mortality were included. The pooled effect estimates indicated that the short-term exposure to BC or EC was associated with an increased risk of cardiovascular diseases, but had no impact on respiratory diseases in all populations. However, BC or EC was related with both cardiovascular and respiratory diseases in the elderly (65+ years). Impact of short-term exposure to BC or EC on cardiovascular morbidity was stronger than mortality. In addition, association between short-term exposure to BC or EC and cardiovascular diseases differ across continents.

# 4.1 Short-term exposure to BC or EC were related with both cardiovascular and respiratory diseases in the elderly

Overall, the meta-analysis results indicated that short-term exposure to BC or EC was associated with an increased risk of cardiovascular diseases, but had no impact on respiratory diseases in all populations. In general, consistent results in the PM<sub>2.5</sub>-adjusted model were obtained in the PM<sub>2.5</sub>-unadjusted model and sensitivity analysis showed that the associations were robust. In addition, the association of short-term exposure to BC or EC on cardiovascular morbidity was stronger than mortality. However, the association between BC or EC and cardiovascular mortality should be further explored by further studies, which should pay more attention to the PM<sub>2.5</sub>-adjusted model. The subgroup analysis indicated that the effects of BC or EC

on cardiovascular diseases were the most significant on the current day and the impacts were decreased with lag days. In addition, the association between BC or EC and cardiovascular mortality in the cold season was stronger than that in the warm season. A potential reason could be that the concentration of BC or EC in the cold season was higher than that in the warm season.<sup>[36-38]</sup> Subgroup analysis on pollutant (BC and EC) indicated that the results from the PM<sub>2.5</sub>-unadjusted model and PM<sub>2.5</sub>-adjusted model were not consistent. Furthermore, the sensitivity analysis on omitting a single study showed that the results were not robust (data not shown). An essential reason could be that BC and EC were considered interchangeable. Three included studies simultaneously assessed the effects of BC and EC on cardiovascular diseases. [17, 39, 40] The results in Winguist et al [40] show that the impact of EC (RR =1.048, 95% CI: 1.012-1.085) on cardiovascular morbidity was higher than that of BC (RR = 1.040, 95% CI: 1.011–1.071) in the  $PM_{2.5}$ -unadjusted model. However, in the PM<sub>2.5</sub>-adjusted model, no statistically significant difference was observed between EC (RR =1.039, 95% CI: 0.993-1.083) and cardiovascular morbidity. In addition, Samoli et al<sup>[17]</sup> illustrated that the impact of BC and EC on cardiovascular morbidity differed in the elderly and other age groups, while Atkinson et al<sup>[39]</sup> indicated no statistically significant difference between BC or EC and cardiovascular mortality in both the PM<sub>2.5</sub>-adjusted model and PM<sub>2.5</sub>-unadjusted model. On the other hand, increased risk of long-term exposure to BC or EC and cardiovascular diseases was observed. However, in this meta-analysis, due to the limited number of included studies, only short-term exposure to asthma morbidity was evaluated. In addition, a

subgroup analysis on the chronic effects of BC or EC on cardiovascular and respiratory diseases was not performed as well because of the limited number of included studies.

The overall quality of the acute effects of BC or EC on cardiovascular diseases in all populations in the PM<sub>2.5</sub>-unadjusted model was evaluated as "moderate" certainty. We downgraded one level for publication bias, hence the estimate was adjusted using the trim and fill method. Several pieces of evidence (acute effects of BC or EC on cardiovascular diseases in all populations in PM<sub>2.5</sub>-unadjusted/adjusted model and chronic effects of BC or EC on cardiovascular diseases in PM<sub>2.5</sub>-unadjusted model) upgrade one level on concentration-response gradient for an increase in risk with increasing BC or EC.<sup>[24]</sup> In addition, inconsistency was not downgraded because 80% PI does not include unity, or it include unity but less than twice the 95% CI.

#### 4.2 Vulnerable populations

This meta-analysis revealed that BC or EC have acute effects on cardiovascular and respiratory diseases in the elderly. Different indoor or outdoor activity patterns, occupational exposure, and social network make the elderly at higher risk of BC exposure. In addition, lung function and mucociliary clearance decline with long-term exposure to pollutants and increasing age. These factors contribute to make the elderly more vulnerable to BC. On the other hand, this meta-analysis indicated that an increased risk was observed between BC or EC and asthma morbidity in children of 0-18 years, while no statistical significance was observed in populations older than 18 years. Asthma, a chronic airway disorder, is a serious health

disease and previous studies indicated that children had higher PM<sub>2.5</sub> deposition rather than the adults, and BC is an essential constituent of PM<sub>2.5</sub>. In addition, BC activates macrophages from the lung cells, which release pro-inflammatory mediators, finally leading to an accumulation of inflammatory cells.<sup>[43]</sup> Persistent airway inflammation is a pathological feature of asthma.<sup>[44]</sup>

#### 4.3 Underlying pathological mechanism

In our study, the pooled effect estimate indicated that short-term and long-term exposure to BC or EC was associated with an increased risk of cardiovascular diseases. A series of studies explored the underlying mechanisms between BC and cardiovascular diseases. An animal study conducted by Niwa et al revealed that BC accelerated atherosclerotic plaque formation.<sup>[45]</sup> Yamawaki et al found that BC directly impacts the vascular endothelium, causing inflammatory responses, cytotoxic injury, and inhibition of cell growth.<sup>[46]</sup> These responses contribute to the progression of atherosclerosis, leading to cardiovascular disease.<sup>[46]</sup> Furthermore, a human panel study was performed to assess whether the patients with IHD experience change in the repolarization parameters exposure to rising concentration of pollutants.<sup>[47]</sup> The results indicated that the variability of the T-wave complexity increased with increasing EC during periods of 0-5 hours, 12-17 hours and 0-2 hours before ECG measurement.<sup>[47]</sup>

#### 4.4 Suggestions for further research

First, critical potential confounders (temperature, seasonality, day of the week, and long-term trends) and other potential confounders (holidays and influenza epidemics) should be considered in time series and case crossover studies, especially

for influenza epidemics. Influenza epidemics are factors usually neglected in short-term studies. Second, studies should adjust PM<sub>2.5</sub> when assessing the health effect of PM<sub>2.5</sub> constituents. Mostofsky et al. proved that PM<sub>2.5</sub> may be associated with both health and its constituents. Constituent having closer association with PM<sub>2.5</sub> may illustrate a stronger association with diseases. Therefore, the results of PM<sub>2.5</sub>-unadjusted model could introduce bias.<sup>[7]</sup> Third, further studies are suggested to evaluate the health effects of long-term exposure to BC, especially for morbidity. An essential difficulty that needs to be acknowledged is the availability of the disease data. Emergency department visits and outpatient are more time-sensitive data than mortality; hence these indicators are more representative to some extent in investigating the health effects of environmental factors. However, the data of emergency department visits and outpatient generally from medical institutions are more difficult to obtain than data on mortality, with a large portion of mortality data arriving from departments of disease control institutions in China. Forth, the present evidence on the health effects of BC was mainly confined in America and Asia. Studies assessing the association in other geographical locations are suggested, which might contribute the evaluation of the potentially different effects of BC in different continents.

#### 4.5 Strength and limitation

This systematic review and meta-analysis provided a comprehensive and current evidence for the short-term and long-term exposure to BC or EC on cardiorespiratory morbidity and mortality. Adapted GRADE framework was used to assess the certainty

of the evidence. The evidence can support the update of the WHO Global Air Quality Guidelines. Potential limitations in our study are as follows. A significant heterogeneity for the pooled estimates was noticed in the meta-analysis, which might be due to the high variability in the study population, outcome, and geographical locations. Therefore, subgroup analyses on age of the population (all and older than 65 years old), outcomes (morbidity and mortality), geological locations (Europe, America and Asia) and lag days (0, 1, 2 days) was conducted for a further investigation of the potential sources in conditions more than 3 estimates. In addition, consistent results of cardiovascular and respiratory diseases exposure to BC or EC were observed by eliminating studies with partial overlap from the same geographical location

#### 5. Conclusions

Overall, the short-term exposure to BC or EC was associated with an increased risk of cardiovascular and respiratory disease in the elderly and childhood asthma. In addition, short-term exposure to BC or EC-related cardiovascular diseases attributable to morbidity was higher than the one attributable to mortality, and the associations differ across continents.

# Acknowledgements

We would like to thank the authors of the original studies for their contribution to our systematic review and meta-analysis, especially those authors who provided their raw data for the analysis.



# **Contributorship statement**

SW, XZ and XS developed the research design. XS, YH, YM and LJ analysed the data and interpreted the results. XS, YH and YM drafted manuscript. All authors contributed to drafting the manuscript. The final manuscript was approved by all authors.



# **Funding**

The work was supported by the National Key Research and Development Program of China (No. 2016YFA0602004) and Innovation Fund Project on Public Meteorological Service Center of China Meteorological Administration in 2020 (Grant numbers: K2020010).



### **Competing interests**

We declare that all authors have no competing interests.



# **Data sharing statement**

All data relevant to the study are included in the article or uploaded as supplementary information.



#### Reference

- [1] BOND T C, DOHERTY S J, FAHEY D W, et al. Bounding the role of black carbon in the climate system: A scientific assessment [J]. Journal of geophysical research: Atmospheres, 2013, 118(11): 5380-552.
- [2] ZENCAK Z, ELMQUIST M, GUSTAFSSON Ö. Quantification and radiocarbon source apportionment of black carbon in atmospheric aerosols using the CTO-375 method [J]. Atmospheric Environment, 2007, 41(36): 7895-906.
- [3] ATKINSON R, KANG S, ANDERSON H, et al. Epidemiological time series studies of PM2. 5 and daily mortality and hospital admissions: a systematic review and meta-analysis [J]. Thorax, 2014, 69(7): 660-5.
- [4] BOURNE R R, COLLABORATORS G R F. Global, regional, and national comparative risk assessment of 84 behavioural, environmental and occupational, and metabolic risks or clusters of risks for 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017 [J]. The Lancet, 2018, 392(10159): 1923-94.
- [5] ROSS M A. Integrated science assessment for particulate matter [J]. US Environmental Protection Agency: Washington DC, USA, 2009, 61-161.
- [6] BELL M L, DOMINICI F, EBISU K, et al. Spatial and temporal variation in PM2. 5 chemical composition in the United States for health effects studies [J]. Environmental health perspectives, 2007, 115(7): 989-95.
- [7] MOSTOFSKY E, SCHWARTZ J, COULL B A, et al. Modeling the association between particle constituents of air pollution and health outcomes [J]. American journal of epidemiology, 2012, 176(4): 317-26.
- [8] GRAHAME T J, KLEMM R, SCHLESINGER R B. Public health and components of particulate matter: the changing assessment of black carbon [J]. Journal of the Air & Waste Management Association, 2014, 64(6): 620-60.
- [9] JANSSEN N, GERLOFS-NIJLAND M, LANKI T, et al. Health effects of black carbon, The WHO European Centre for Environment and Health, Bonn, Germany [J]. World Health Organisation Regional Office for Europe, Copenhagen, Denmark, 2012,
- [10] BüCHNER N, ALE-AGHA N, JAKOB S, et al. Unhealthy diet and ultrafine carbon black

particles induce senescence and disease associated phenotypic changes [J]. Exp Gerontol, 2013, 48(1): 8-16.

- [11] COLICINO E, GIULIANO G, POWER M C, et al. Long-term exposure to black carbon, cognition and single nucleotide polymorphisms in microRNA processing genes in older men [J]. Environ Int, 2016, 88(86-93.
- [12] HUSAIN M, KYJOVSKA Z O, BOURDON-LACOMBE J, et al. Carbon black nanoparticles induce biphasic gene expression changes associated with inflammatory responses in the lungs of C57BL/6 mice following a single intratracheal instillation [J]. Toxicol Appl Pharmacol, 2015, 289(3): 573-88.
- [13] ACHILLEOS S, KIOUMOURTZOGLOU M-A, WU C-D, et al. Acute effects of fine particulate matter constituents on mortality: A systematic review and meta-regression analysis [J]. Environment international, 2017, 109(89-100.
- [14] LUBEN T J, NICHOLS J L, DUTTON S J, et al. A systematic review of cardiovascular emergency department visits, hospital admissions and mortality associated with ambient black carbon [J]. Environment international, 2017, 107(154-62.
- [15] CUMBERBATCH M G, ROTA M, CATTO J W, et al. The role of tobacco smoke in bladder and kidney carcinogenesis: a comparison of exposures and meta-analysis of incidence and mortality risks [J]. European urology, 2016, 70(3): 458-66.
- [16] OSTRO B, HU J, GOLDBERG D, et al. Associations of mortality with long-term exposures to fine and ultrafine particles, species and sources: results from the California Teachers Study Cohort [J]. Environ Health Perspect, 2015, 123(6): 549-56.
- [17] SAMOLI E, ATKINSON R W, ANALITIS A, et al. Associations of short-term exposure to traffic-related air pollution with cardiovascular and respiratory hospital admissions in London, UK [J]. Occup Environ Med, 2016, 73(5): 300-7.
- [18] BASAGANA X, JACQUEMIN B, KARANASIOU A, et al. Short-term effects of particulate matter constituents on daily hospitalizations and mortality in five South-European cities: results from the MED-PARTICLES project [J]. Environ Int, 2015, 75(151-8.
- [19] GAN W Q, FITZGERALD J M, CARLSTEN C, et al. Associations of ambient air pollution with chronic obstructive pulmonary disease hospitalization and mortality [J]. Am J Respir Crit Care Med, 2013, 187(7): 721-7.

- [20] OSTRO B, TOBIAS A, KARANASIOU A, et al. The risks of acute exposure to black carbon in Southern Europe: results from the MED-PARTICLES project [J]. Occup Environ Med, 2015, 72(2): 123-9.
- [21] THURSTON G D, BURNETT R T, TURNER M C, et al. Ischemic Heart Disease Mortality and Long-Term Exposure to Source-Related Components of U.S. Fine Particle Air Pollution [J]. Environ Health Perspect, 2016, 124(6): 785-94.
- [22] National Toxicology Program. Handbook for conducting a literature-based health assessment using OHAT approach for systematic review and evidence integration. Office of Health Assessment and Translation (OHAT), Division of the National Toxicology Program, National Institute of Environmental Health Sciences <a href="https://ntpniehsnihgov/ntp/ohat/">https://ntpniehsnihgov/ntp/ohat/</a> pubs/ handbookjan2015 508pdf 2015. [J]. 2015,
- [23] LAM J, SUTTON P, KALKBRENNER A, et al. A systematic review and meta-analysis of multiple airborne pollutants and autism spectrum disorder [J]. PloS one, 2016, 11(9): e0161851.
- [24] MORGAN R L, THAYER K A, SANTESSO N, et al. A risk of bias instrument for non-randomized studies of exposures: a users' guide to its application in the context of GRADE [J]. Environment international, 2019, 122(168-84.
- [25] CHEN S Y, LIN Y L, CHANG W T, et al. Increasing emergency room visits for stroke by elevated levels of fine particulate constituents [J]. Sci Total Environ, 2014, 473-474(446-50.
- [26] HVIDTFELDT U A, SORENSEN M, GEELS C, et al. Long-term residential exposure to PM2.5, PM10, black carbon, NO2, and ozone and mortality in a Danish cohort [J]. Environ Int, 2019, 123(265-72.
- [27] YANG Y, TANG R, QIU H, et al. Long term exposure to air pollution and mortality in an elderly cohort in Hong Kong [J]. Environ Int, 2018, 117(99-106.
- [28] METZGER K B, TOLBERT P E, KLEIN M, et al. Ambient air pollution and cardiovascular emergency department visits [J]. Epidemiology, 2004, 15(1): 46-56.
- [29] TOLBERT P E, KLEIN M, PEEL J L, et al. Multipollutant modeling issues in a study of ambient air quality and emergency department visits in Atlanta [J]. J Expo Sci Environ Epidemiol, 2007, 17 Suppl 2(S29-35.
- [30] KIM S Y, DUTTON S J, SHEPPARD L, et al. The short-term association of selected components of fine particulate matter and mortality in the Denver Aerosol Sources and Health

- (DASH) study [J]. Environ Health, 2015, 14(49.
- [31] KIM S Y, PEEL J L, HANNIGAN M P, et al. The temporal lag structure of short-term associations of fine particulate matter chemical constituents and cardiovascular and respiratory hospitalizations [J]. Environ Health Perspect, 2012, 120(8): 1094-9.
- [32] GAN W Q, KOEHOORN M, DAVIES H W, et al. Long-term exposure to traffic-related air pollution and the risk of coronary heart disease hospitalization and mortality [J]. Environ Health Perspect, 2011, 119(4): 501-7.
- [33] TOMIC-SPIRIC V, KOVACEVIC G, MARINKOVIC J, et al. Evaluation of the Impact of Black Carbon on the Worsening of Allergic Respiratory Diseases in the Region of Western Serbia: A Time-Stratified Case-Crossover Study [J]. Medicina (Kaunas), 2019, 55(6):
- [34] KRALL J R, ANDERSON G B, DOMINICI F, et al. Short-term exposure to particulate matter constituents and mortality in a national study of U.S. urban communities [J]. Environ Health Perspect, 2013, 121(10): 1148-53.
- [35] OSTRO B, ROTH L, MALIG B, et al. The effects of fine particle components on respiratory hospital admissions in children [J]. Environ Health Perspect, 2009, 117(3): 475-80.
- [36] ANAND A, PHULERIA H C. Spatial and seasonal variation of outdoor BC and PM 2.5 in densely populated urban slums [J]. Environmental Science and Pollution Research, 2020, 1-12.
- [37] CHEN P, KANG S, GUL C, et al. Seasonality of carbonaceous aerosol composition and light absorption properties in Karachi, Pakistan [J]. Journal of Environmental Sciences, 2020, 90(286-96.
- [38] YANG Y, XU X, ZHANG Y, et al. Seasonal size distribution and mixing state of black carbon aerosols in a polluted urban environment of the Yangtze River Delta region, China [J]. Science of The Total Environment, 2019, 654(300-10.
- [39] ATKINSON R W, ANALITIS A, SAMOLI E, et al. Short-term exposure to traffic-related air pollution and daily mortality in London, UK [J]. J Expo Sci Environ Epidemiol, 2016, 26(2): 125-32.
- [40] WINQUIST A, SCHAUER J J, TURNER J R, et al. Impact of ambient fine particulate matter carbon measurement methods on observed associations with acute cardiorespiratory morbidity [J]. J Expo Sci Environ Epidemiol, 2015, 25(2): 215-21.
- [41] BELL M L, ZANOBETTI A, DOMINICI F. Evidence on vulnerability and susceptibility to 36

health risks associated with short-term exposure to particulate matter: a systematic review and meta-analysis [J]. American journal of epidemiology, 2013, 178(6): 865-76.

- [42] SINHARAY R, GONG J, BARRATT B, et al. Respiratory and cardiovascular responses to walking down a traffic-polluted road compared with walking in a traffic-free area in participants aged 60 years and older with chronic lung or heart disease and age-matched healthy controls: a randomised, crossover study [J]. The Lancet, 2018, 391(10118): 339-49.
- [43] CHENG Z, CHU H, WANG S, et al. TAK1 knock-down in macrophage alleviate lung inflammation induced by black carbon and aged black carbon [J]. Environmental Pollution, 2019, 253(507-15.
- [44] BATEMAN E D, HURD S, BARNES P, et al. Global strategy for asthma management and prevention: GINA executive summary [J]. European Respiratory Journal, 2008, 31(1): 143-78.
- [45] NIWA Y, HIURA Y, MURAYAMA T, et al. Nano-sized carbon black exposure exacerbates atherosclerosis in LDL-receptor knockout mice [J]. Circulation journal, 2007, 71(7): 1157-61.
- [46] YAMAWAKI H, IWAI N. Mechanisms underlying nano-sized air-pollution-mediated progression of atherosclerosis [J]. Circulation Journal, 2006, 70(1): 129-40.
- [47] HENNEBERGER A, ZAREBA W, IBALD-MULLI A, et al. Repolarization changes induced by air pollution in ischemic heart disease patients [J]. Environmental health perspectives, 2005, 113(4): 440-6.
- [48] LEVY J I, DIEZ D, DOU Y, et al. A meta-analysis and multisite time-series analysis of the differential toxicity of major fine particulate matter constituents [J]. Am J Epidemiol, 2012, 175(11): 1091-9.
- [49] LIU S, GANDUGLIA C M, LI X, et al. Fine particulate matter components and emergency department visits among a privately insured population in Greater Houston [J]. Sci Total Environ, 2016, 566-567(521-7.
- [50] LIU S, GANDUGLIA C M, LI X, et al. Short-term associations of fine particulate matter components and emergency hospital admissions among a privately insured population in Greater Houston [J]. Atmospheric Environment, 2016, 147(369-75.
- [51] NAYEBARE S R, ABURIZAIZA O S, SIDDIQUE A, et al. Association of fine particulate air pollution with cardiopulmonary morbidity in Western Coast of Saudi Arabia [J]. Saudi Med J, 2017, 38(9): 905-12.

- [52] PEARCE J L, WALLER L A, MULHOLLAND J A, et al. Exploring associations between multipollutant day types and asthma morbidity: epidemiologic applications of self-organizing map ambient air quality classifications [J]. Environ Health, 2015, 14(55.
- [53] PENG R D, BELL M L, GEYH A S, et al. Emergency admissions for cardiovascular and respiratory diseases and the chemical composition of fine particle air pollution [J]. Environ Health Perspect, 2009, 117(6): 957-63.
- [54] PHALEN R F, OLDHAM M J, KLEINMAN M T, et al. Tracheobronchial deposition predictions for infants, children and adolescents [M]. Inhaled Particles VI. Elsevier. 1988: 11-21.
- [55] STRICKLAND M J, DARROW L A, MULHOLLAND J A, et al. Implications of different approaches for characterizing ambient air pollutant concentrations within the urban airshed for time-series studies and health benefits analyses [J]. Environmental Health, 2011, 10(1): 36.
- [56] TOLBERT P E, KLEIN M, METZGER K B, et al. Interim results of the study of particulates and health in Atlanta (SOPHIA) [J]. Journal of Exposure Science and Environmental Epidemiology, 2000, 10(5): 446-60.
- [57] VEDAL S, CAMPEN M J, MCDONALD J D, et al. National Particle Component Toxicity (NPACT) initiative report on cardiovascular effects [J]. Research Report (Health Effects Institute), 2013, 178): 5-8.

# **Table captions**

**Table 1** Short-term impact of BC or EC on cardiovascular and respiratory diseases in different models.

**Table 2** Results of risk of bias assessment.



# Figure captions

- Fig. 1. Flow diagram of literature screening process.
- **Fig. 2.** Impact of short-term exposure to BC or EC on cardiovascular diseases in the PM<sub>2.5</sub>-unadjusted model.
- Fig. 3. Impact of short-term exposure to BC or EC on respiratory diseases in the PM<sub>2.5</sub>-unadjusted model.

# Appendix A. Supplementary data

- Table S1 Search strategy in PubMed.Table
- **Table S2** Characteristics of the included studies in the systematic review and meta-analysis.
- **Table S3** Subgroup analysis on short-term effects of BC or EC on cardiovascular and respiratory diseases.
- **Table S4** Assessment of certainty of evidence for the outcomes.
- **Table S5** Details of risk of bias assessment.
- **Fig. S1.** Impact of short-term exposure to BC or EC on cardiovascular mortality stratified by geographical locations.
- **Fig. S2.** Impact of short-term exposure to BC or EC on cardiovascular morbidity stratified by geographical locations.
- **Fig. S3.** Impact of short-term exposure to BC or EC on asthma morbidity in different age groups.
- **Fig. S4.** Impact of long-term exposure to BC or EC on cardiovascular diseases.
- **Fig. S5.** Impact of short-term exposure to BC or EC on cardiovascular diseases in the PM<sub>2.5</sub>-adjusted model.
- **Fig. S6.** Impact of short-term exposure to BC or EC on respiratory diseases in the PM<sub>2.5</sub>-adjusted model.

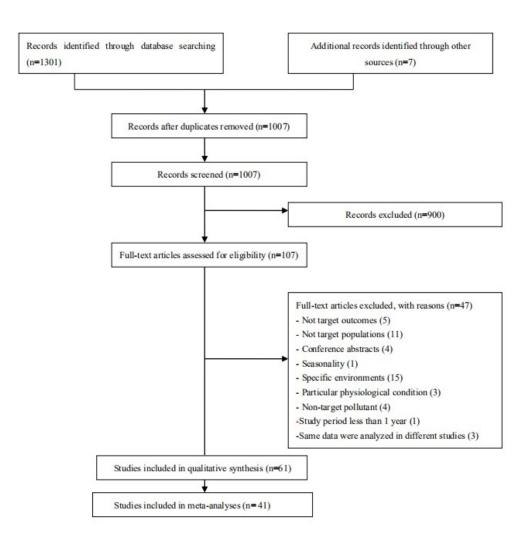


Fig. 1. Flow diagram of literature screening process  $170 \times 169 \text{mm}$  (96 x 96 DPI)

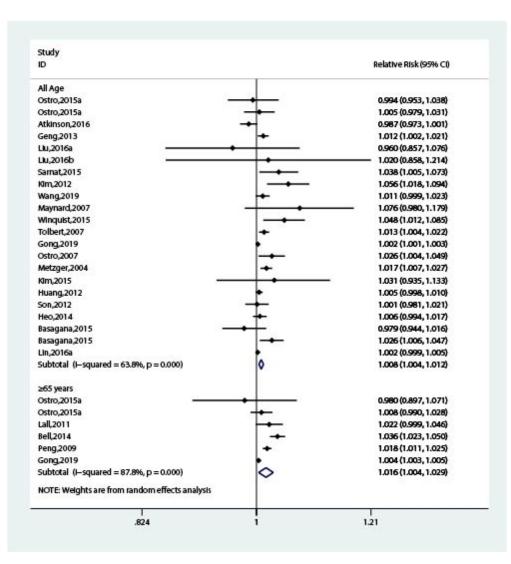


Fig. 2. Impact of short-term exposure to BC or EC on cardiovascular diseases in the PM2.5-unadjusted model.

176x188mm (72 x 72 DPI)

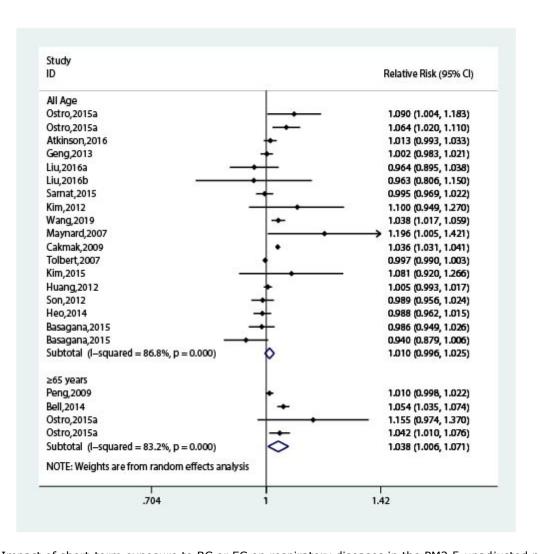


Fig. 3. Impact of short-term exposure to BC or EC on respiratory diseases in the PM2.5-unadjusted model.  $176x178mm (72 \times 72 DPI)$ 

#### SUPPLEMENTARY APPENDIX

# Short-term and Long-term Exposure to Black Carbon and Cardiovascular and Respiratory Diseases: A

# Systematic Review and Meta-Analysis

Xuping Song<sup>a</sup>, Yue Hu<sup>a</sup>, Yan Ma<sup>a</sup>, Liangzhen Jiang<sup>a</sup>, Xinyi Wang<sup>c</sup>, Anchen Shi<sup>d</sup>, Junxian Zhao<sup>a</sup>, Yunxu Liu<sup>a</sup>, Yafei Liu<sup>a</sup>, Jing Tang<sup>a</sup>, Xiayang Li<sup>a</sup>, Xiaoling Zhang<sup>\*b</sup>, Yong Guo<sup>e</sup>, Shigong Wang<sup>\*b</sup>

### **Corresponding author 1:**

Name: Xiaoling Zhang

Postal Address: College of Atmospheric Sciences, Chengdu University of Information

Technology, Chengdu 610000, Sichuan, China

E-mail address: xlzhang@ium.cn

Fax: 028-85966502 Corresponding author 2: Name: Shigong Wang

Postal Address: College of Atmospheric Sciences, Chengdu University of Information

Technology, Chengdu 610000, Sichuan, China

E-mail address: wangsg@cuit.edu.cn

Fax: 028-85966502

<sup>&</sup>lt;sup>a</sup> School of Public Health, Lanzhou University, Lanzhou 730000, China;

<sup>&</sup>lt;sup>b</sup> College of Atmospheric Sciences, Chengdu University of Information Technology, Chengdu 610000, China;

<sup>&</sup>lt;sup>c</sup> Second Clinical College, Lanzhou University, Lanzhou 730000, China;

<sup>&</sup>lt;sup>d</sup> Department of General Surgery, The First Affiliated Hospital of Xi'an Jiao Tong University, Shaanxi 710061, China;

<sup>&</sup>lt;sup>e</sup> Department of Civil Affairs in Guizhou Province, Guiyang 550004, China.

# Supplementary data

- Table S1 Search strategy in PubMed
- **Table S2** Characteristics of the included studies in the systematic review and meta-analysis.
- **Table S3** Subgroup analysis on short-term effects of BC or EC on cardiovascular and respiratory diseases.
- **Table S4** Assessment of certainty of evidence for the outcomes
- Table S5 Details of risk of bias assessment.
- **Fig. S1.** Impact of short-term exposure to BC or EC on cardiovascular mortality stratified by geographical locations.
- **Fig. S2.** Impact of short-term exposure to BC or EC on cardiovascular morbidity stratified by geographical locations.
- **Fig. S3.** Impact of short-term exposure to BC or EC on asthma morbidity in different age groups.
- **Fig. S4.** Impact of long-term exposure to BC or EC on cardiovascular diseases.
- **Fig. S5.** Impact of short-term exposure to BC or EC on cardiovascular diseases in the PM<sub>2.5</sub>-adjusted model.
- **Fig. S6.** Impact of short-term exposure to BC or EC on respiratory diseases in the PM<sub>2.5</sub>-adjusted model.

 Table S1. Search Strategy for PubMed

Table	e S1. Search Strategy for PubMed
No.	Search Strategy ω
#1	particulate matter/or aerosols.sh.
#2	particulate matter/or aerosols.sh.  particulate matter*/or "PM10"/or "PM2.5"/or fine particle*/or thoracic particle*/or ultrafine/or aerosol*/or carbon*/or soot*.ti,ab.  "PM".tw.
#3	"PM".tw. N
#4	
#5	or/1,2,3  "EC" /or "BC".tw. and/4,5  black carbon*/or elemental carbon*.ti,ab.
#6	and/4,5
#7	
#8	or/6,7
#9	respiratory tract disease.sh.
#10	respirat*/or pulmonary disease*/or lung/or chest infection*/or airway/or asthma*/or pneumonia*/or "chronic obstructive pulmonary disease"/or COPD.ti,ab.
#11	cardiovascular diseases.sh.
#12	cardio*/or cardiop*/or cardior*/or heart/or coronary/or vascular/or blood/or cardiac.ti,ab.
#13	or/9,10,11,12
#14	morbidity/or hospitalization/or death/or mortality/or outpatient.sh
#15	morbidit*/or hospitalisation*/or hospitalization*/or death*/or mortalit*/or outpatien*/or emergency room*/or emergency department*/69 emergency admi*/or hospital
π15	admission*.ti,ab.
#16	or/14,15
#17	epidemiologic studies/or cross over study.sh.
#18	time series*/or timeseries*/or case cross*/or casecross*.tw.
	generalized additive model/or generalised additive model/or generalized linear model/or generalised linear model/or distributed lag nor ginear model/or ginear mod
#19	model/or distributed lag model/or quasipoisson*/or poisson*/or generalized estimating equation/or generalised estimating equation/or Am/or GLM/or DLNM/or GEE/or DLM/or
	ARIMA.tw.
#20	cohort*/or follow up*/or observational/or longitudinal/or case control*/or epidemiologic/or population
#20	stud*/or prospective*/or retrospective*.tw.
#21	or/17,18,19,20 and/8,13,16,21
#22	
	by cop
	CO OF

**Table S2.** Characteristics of included studies in the systematic review and meta analysis

9 of 122						В	МЈ Ореі	36/bmjopen-2021-049516
Table S2. Characterist	Study	ded studies in	Study	w and meta ar  Outcome	nalysis Age	Pollutant	ICD	Siseases
Atkinson et al. 2016	Design TS	UK	2011-2012	Mortality	All	BC,EC	Code ICD-10	CVD(ICD-10:I00-I99),RES(ICD-10:J00-J99) 8
Bell et al. 2014	TS	USA	2000-2004	Morbidity	≥65	BC	ICD-9	RES[COPD(ICD-9-CM:490-492,RTI(ICD-9-CM:464-466, 480-487)];CVD[HF(ICD-9-CM:428),Heart Rhythm Disturbances(ICD-9-CM:426-427), Cerebrovascular vents(ICD-9-CM:430-438),IHD(ICD-9-CM:410-414,
Cai et al. 2014	TS	China	2005-2011	Morbidity	≥18	ВС	ICD-10	429),PVD(ICD-9-CM:440–448)]  Asthma(ICD-10:J45)
Geng et al. 2013	TS	China	2007-2008	Mortality	All	BC	ICD-10	CVD(ICD-10:I00-I99),RES(ICD-10:J00-J98)
Hua et al. 2014	TS	China	2007-2012	Morbidity	0-14	BC	ICD-10	
Ostro et al. 2015a	CS	Spain, Greece	2008-2009 (Athens), 2009-2010(Barc elona)	Mortality	All	ВС	ICD-10	Asthma(ICD-10:J45)  CVD(ICD-10:I00-I99),RES(ICD-10:J00-J99)
Samoli et al. 2016	TS	UK	2011-2012	Morbidity	≥15(CVD), all (RES)	BC,EC	ICD-10	CVD(ICD-10:I00-I99),RES(ICD-10:J00-J99)
Zanobetti and Schwartz 2006	CS	USA	1995-1999	Morbidity	≥65	ВС	ICD-9	MI(ICD-9:410),Pneumonia (ICD-9: 480–487)
Liu et al. 2016a	TS	USA	2008-2013	Morbidity	All	EC	ICD-9	CVD(ICD-9:390-429),Stroke(ICD-9:430-438),RES(10-9:460-519),COPD(ICD-9:490-492,494,496),Pneumonia(ICD-9:480-486),Asthma(ICD-9:493),SSID(ICD-9:786799)
Liu et al. 2016b	TS	USA	2008-2013	Morbidity	All	EC	ICD-9	CVD(ICD-9:390-429),Stroke(ICD-9:430-438),RESR CD-9:460-519),COPD(ICD-9:490-492,494,496),Pneumonia (ICD-9:480-486),Asthma(ICD-9:493)
Sarnat et al. 2015	TS	USA	2001-2003	Morbidity	All	EC	ICD9	CVD[IHD(ICD9:410–414),Cardiac Dysrhythmias(ICD9:427),CHF(ICD9:428),Other CVD (ICD-9:433-437,440,443-445,451-453)],RES[Pneumonia(ICD9:480-486),COPD (ICD:491,492,496),Asthma/Wheeze (ICD9:493,786.07),Other RES(ICD9:460–466,477)]
Kim et al. 2012	TS	USA	2003-2007	Morbidity	All	EC	ICD-9	CVD(ICD-9:390-459),RES(ICD-9:460-519)
								соругід

						В	MJ Oper	36/bmjopen
Table S2. Characteris	stics of inclu	ded studies in th	ne systematic revi	ew and meta anal	ysis			36/bmjopen-2021-049516 on
Study	Study Design	Country	Study Period	Outcome	Age	Pollutant	ICD code	ω Diseases Diseases
Ostro et al. 2009	TS	USA	2000-2003	Morbidity	<19	EC	ICD9	RES(ICD-9:460-519),Asthma(ICD-9:493),Acute broth hitis(ICD-9:466),Pneumonia(ICD-9:480-486)
Kim et al. 2015	TS	USA	2003-2007	Mortality	All	EC	ICD-10	CVD,RES ?
Huang et al. 2012	TS	China	2004-2008	Mortality	All	EC	ICD-10	RES(ICD-10:I00-I98),CVD(ICD-10:I00-I99)
								CVD[Cardiac Dysrhythmias(ICD-9:428),Heart Rhytten Disturbances(ICD-9:426-427),Cerebrovascular Events
Peng et al. 2009	TS	USA	2000-2006	Morbidity	≥65	EC	ICD-9	(ICD-9:430-438),IHD (ICD-9:410-414,
								429),PVD(ICD-9:440-448)],RES[COPD(ICD-9:490
Levy et al. 2012	TS	USA	2000-2008	Morbidity	≥65	EC	ICD-9	CVD(ICD-9:390-459),RES(ICD-9:464-466 and 480-487).
Son et al. 2012	TS	Korea	2008-2009	Mortality	All	EC	ICD-10	CVD(ICD-10:100-I99),RES(ICD-10:J00-J99)
Heo et al. 2014	TS	Korea	2003-2007	Mortality	All	EC	ICD-10	CVD(ICD-10:I00-I99),RES(ICD-10:J00-J98)
Basagaña et al. 2015	CS	Spain, Italy	2003-2013	Morbidity,  Mortality	All	EC	ICD-9,	CVD(ICD-9:390-459,ICD-10:100-199),RES(ICD-9:480-519,ICD-10:J00-J99)
Dai et al. 2014	TS	USA	2000-2006	Mortality	All	EC	ICD-10	CVD(ICD-10:101-159),RES(ICD-10:J00-J99),MI(ICD-10:121-122),Stroke(ICD-10:I60-I69)
Lin et al. 2016a	TS	China	2007-2011	Mortality	All	EC	ICD-10	CVD(ICD-10:100-199)
Cao et al. 2012	TS	China	2004-2008	Mortality	All	EC	ICD-10	
Klemm et al. 2011	TS	USA	1998-2007	Mortality	≥65	EC	ICD-10	CVD(ICD-10:100-I99),RES(ICD-10:J00-J98)  CVD(ICD-10:I00-I99),RES(ICD-10:J00-J99)
Zhou et al. 2011	TS	USA	2002-2004	Mortality	All	EC	ICD-10	CVD(ICD-10:101-199),RES(ICD-10:J00-J99)
Winquist et al. 2015	TS	USA	2001-2003	Morbidity	All	BC,EC	ICD-9	CVD(ICD-10:I01-I99),RES(ICD-10:J00-J99)  RES(ICD-9:460-465,466.0,466.1,466.11,466.19,477, \$\frac{1}{2}\text{80}\text{-486,491,492,493,496,786.07},CVD(ICD-9:410-414,427, 428,433-437,440,443-445,451-453)
Ostro et al. 2007	TS	USA	2000-2003	Mortality	All	EC	ICD-10	428,433-437,440,443-445,451-453)  CVD(ICD-10:100-I99),RES(ICD-10:J00-J98)
Tolbert et al. 2000	TS	USA	1998-2000	Morbidity	All	EC	ICD-9	CVD(ICD-9:402,410-414,427,428,433-437,440,444,441,1453),RES(ICD-9:460-466,477,480-486,491,492,493,496,
								786.09) (ec ed by copyright.

**Table S2.** Characteristics of included studies in the systematic review and meta analysis

Table S2. Characteris			•				ICD	9
Study	Study	Country	Study	Outcome	Age	Pollutant		Siseases .ag
	Design		Period				code	
				Morbidity,				202:
Wang and Lin 2016	TS	China	2004-2010	Mortality	≥65(mortality),	EC	ICD-9	CVD(ICD-9-CM:390-459),RES(ICD-9-CM:460-519) □
					all(morbidity)			D w
Darrow et al. 2014	TS	USA	1993-2010	Morbidity	0–4	EC	ICD-9	Acute Bronchitis or Bronchiolitis(ICD-9:466),Pneumonia(ICD-9:480-486),URI(ICD-9:460-465)
						EC		CVD[IHD(ICD-9:410-414),AMI(ICD-9:410),cardia@
Metzger et al. 2004	TS	USA	1993-2000	Morbidity	All		ICD-9	dysrhythmias(ICD-9:427),CA(ICD-9:427.5),CHF(ICD-9:428),PVD and cerebrovascular
								events(ICD-9:433-437,440,443-444,451-453),CHD(IGD-9:440),Stroke(ICD-9:436)]
Mar et al. 2000	TS	USA	1995-1997	Mortality	All	EC	ICD-9	CVD(ICD-9:390-448.9)
Wang et al. 2019	TS	China	2013-2015	Mortality	All	EC	ICD-10	CVD(ICD-9:390-448.9)  CVD(ICD-10:I00-I99),RES(ICD-10:J00-J99)  Stroke(ICD-10:I60-I66)
Lin et al. 2016b	TS	China	2007-2011	Mortality	All	EC	ICD-10	Stroke(ICD-10:I60-I66)
Ostro et al. 2008	TS	USA	2000-2003	Mortality	All	EC	ICD-10	CVD(ICD-10:100-I99)
		USA		Morbidity, 2006 Mortality	≥40	EC		CVD[Hypertensive Diseases(ICD-9:402,ICD-10:I11] MI(ICD-9:410;ICD-10:I21-I22),IHD
Ito et al. 2011	TS		2000-2006					(ICD-9:414,ICD-10:I25),Dysrhythmias(ICD-9:427,ICD-10:I48),HF(ICD-9:428,ICD-10:I50),Stroke(ICD-9:430-43
							ICD-10	9,ICD-10:I60-I69)] > O
Chen et al. 2014	TS	China	2004-2008	Morbidity	All	EC	ICD-9	Stroke[Ischemic Stroke(ICD-9:433-434),Hemorrhagiestroke(ICD-9:430-432)]
Tomic'-Spiric' et al.	CS	Serbia	2012-2014	Morbidity	≥18	ВС	ICD-10	Allers in DEGLAD/ICD 10.1.20.4) AA/ICD 10.1.45 of
2019	CS	Seroia	2012-2014	Morbialty	≥18	ьс	ICD-10	Allergic RES[AR(ICD-10:J.30.4),AA(ICD-10:J.45.0)
		***	1995-1997,			D.G.	ICD-9,	CVD(ICD-9:390-429,ICD-10:I01-I52),Stroke(ICD-9:30-438,ICD-10:I60-I69),RES(ICD-9:460-519,ICD-10:J00-J
Maynard et al. 2007	CS	USA	1999-2002	Mortality	All	BC	ICD-10	99) <b>es</b> t.
Sinclair et al. 2010	TS	USA	1998-2002	Morbidity	All	EC	NR	
Krall et al. 2013	TS	USA	2000-2005	Mortality	All	EC	NR	CVD and RES(NR)
Cakmak et al. 2009	TS	Canada	2001-2006	Morbidity	All	EC	ICD-9	CVD and RES(NR)  RES(ICD-9:460-519)
								βy

**Table S2.** Characteristics of included studies in the systematic review and meta analysis

						В	MJ Oper	36/bmjopen-2021-049516
Table S2. Characterist	Study Design	ded studies in	the systematic revie	w and meta anal	lysis <b>Age</b>	Pollutant	ICD code	1-0 4951 60 n Wiscases
Tolbert et al. 2007	TS	USA	1993-2004	Morbidity	All	EC	ICD-9	CVD[IHD(ICD-9:410-414),Cardiac Dysrhythmias(ICD-9:427),CHF(ICD-9:428),PVD and Cerebrovascular  Events(ICD-9:433-437,440,443-445,451-453)],  RES[Asthma(ICD-9:493,786.07,786.09),COPD(ICD 2:491,492,496),URTI(ICD-9:460-465,460.0,477),Pneumonia (ICD-9:480-486),Bronchiolitis(ICD-9:466.1,466.11,466.11)]
Lall et al. 2011	TS	USA	2001-2002	Morbidity	≥65	EC	ICD-9	RES[Pneumonia(ICD-9:480-486),COPD(ICD-9:490 92,496),Acute Bronchitis and Bronchiolitis(ICD-9:466),Asthma(ICD-9:493)],CVDBysrhythmia(ICD-9:427),IHD(ICD-9:410-414),HF(ICD-9:428),Stroke(ICD-9:431-437)]
Jung and Lin 2017	CS	China	2000-2010	Morbidity	0-20	BC	ICD-9	Asthma(ICD-9-CM:493)
Gong et al. 2019	TS	China	2006-2011	Mortality	All	ВС	ICD-10	CVD(ICD-10:I00-I99)
Mostofsky et al. 2012	CS	USA	2003-2008	Morbidity	≥21	BC	NO	Acute Ischemic Stroke
Krall et al. 2017	TS	USA	1999-2009(Atlan ta,Georgia), 2004-010(Birmi ngham,Alabama, 2001-2007(St.Lo uis, Missouri), 2006-2009(Dalla s,Texas)	Morbidity	All	EC	ICD-9	Asthma(ICD-9-CM:493)  CVD(ICD-10:100-199)  Acute Ischemic Stroke  RES[Pneumonia(ICD-9:480-486),COPD(ICD-9:491 22,496),URTI(ICD-9:460-465,466.0,477),Asthma and/or Wheeze(ICD-9:493,786.07)]  Wheeze(ICD-9:493,786.07)]
O'Lenick et al. 2017	CS	USA	2001-2008	Morbidity	5-18	EC	ICD-9	Asthma(ICD-9:493.0-493.9),Wheeze(ICD-9:786.07)
Pearce et al. 2015	TS	USA	1999-2008	Morbidity	5–17	EC	ICD-9	Asthma(ICD-9:493.0-493.9),Wheeze(ICD-9:786.07)
Strickland et al. 2010	CS	USA	1993-2004	Morbidity	5-17	EC	ICD-9	Asthma(ICD-9:493.0-493.9),Wheeze(ICD-9:786.09)

**Table S2.** Characteristics of included studies in the systematic review and meta analysis

CAJ.	Study	Ct	Study	0	A	Pollutant	ICD	S ₩iseases
Study	Design	Country	Period	Outcome	Age	Pollutant	code	inseases D
Strickland et al. 2014	TS	USA	2000-2010	Morbidity	2-16	EC	ICD-9	Asthma(codes beginning with 493),Wheeze (ICD-9: 26.07)
Ito et al. 2013	TS	USA	2001-2006	Morbidity,	all (mortality),	EC	ICD-9,	CVD(ICD-10:I01-I79),RES(ICD-10:J00-J99)
110 Ct al. 2013	13	USA	2001-2000	Mortality	≥65(morbidity)	EC	ICD-10	CVD(ICD-10:I01-I79),RES(ICD-10:J00-J99)
Ostro et al. 2015b	Co	USA	2001-2007	Mortality	≥30	EC	ICD-10	CVD(ICD-10:I00-I99),IHD(ICD-10:I20-I25),Pulmorary(ICD-10:C34,J00-J98)
Gan et al. 2013	Co	Canada	1999-2002	Morbidity,	45-85	ВС	ICD-9,	COPD(ICD-9:490-492,496,ICD10:J40-J44)
Gair et al. 2013		Canada	1777-2002	Mortality	45-65	ВС	ICD-10	To B
Hvidtfeldt et al. 2019	Co	Denmark	1993-2015	Mortality	50 -64	BC	ICD-10	CVD(ICD-10:I00-I99),RES(ICD-10:J00-J99,C34)
Thurston et al. 2016	Co	USA	1988-2004	Mortality	≥30	EC	ICD-9,	HD0CD-9-410-414 (CD-10-120-125)
Thurston et al. 2010		CS/1	1700-2004	Wiortanty		LC	ICD-10	IHD(ICD-9:410-414,ICD-10:120-125)  CVD(ICD-10:100-199),RES(ICD-10:J00-J47,J80-J990
Yang et al. 2018	Co	China	1998-2011	Mortality	≥65	BC	ICD-10	CVD(ICD-10:I00-I99),RES(ICD-10:J00-J47,J80-J999
Gan et al. 2011	Co	Canada	1999-2002	Morbidity,	45–85	ВС	ICD-9,	CHD(ICD-9:410-414,429.2 ),(ICD-10:120-125)
Gair et al. 2011	Co	Canada	1999-2002	Mortality	45-65	ВС	ICD-10	CHD(ICD-9:410-414,429.2 ),(ICD-10:120-125)
De Kluizenaar et al.	Co	Netherlands	1991-2003	Morbidity	15-74	EC	ICD-9	IHD(ICD-9:410-414),CHD(ICD-9:430-438)
2013	Co	recticitates	1771-2003	Morbianty	15-74	LC	ICD-)	A Pri:
Vedal et al. 2013	Co	USA	1994-2005	Morbidity,	50-79	FC	ICD-9	CVD (ICD 0:CM 410 452)
		USA	1994-2005	Mortality	30-17	EC	ICD-9	φ <u>Σ</u>

Abbreviations: NR: Not Reported; TS: Time-Series; CS: Case-Crossover; Co: Cohort; ICD: International Classification of Diseases; MI: Myocardial infarction; CHD: Coronary heart disease; CVD: Cardiovascular disease; RES: respiratory diseases; IHD: Ischemic Heart Disease; ARI: acute respiratory illness; HF: heart failure; CHF: congestive heart failure; PVD: peripheral vascular disease; AA: allergic asthma; AR: allergic rhinitis; AMI: acute metal infarction; CA: cardiac arrest; RTI: respiratory tract infection; URTI: Upper Respiratory Infection; LRTI: Lower Respiratory Infection; ARTI: Acute respiratory infections.

Table S3. Subgroup analysis on short-term effects of BC or EC on cardiovascular and respiratory diseases

Subgroup Analysis	No. of	No. of	Relative Risk	$\mathbf{I}^2$	Egger Regression Test
Subgroup Analysis	Studies	Estimates	(95%CI)	Г	(p value)
Cardiovascular Diseases					
Lag Days					
Lag 0d	15	18	1.011 (1.006, 1.016)	76.00%	0.038
Lag 1d	12	15	1.005 (1.002, 1.008)	32.70%	0.299
Lag 2d	11	14	1.002 (0.999, 1.005)	73.80%	0.969
Geographical Location (Mortality)					
Asia	7	7	1.003 (1.001, 1.004)	38.30%	_
Europe	3	4	0.990 (0.979, 1.002)	0	_
America	4	4	1.017 (0.998, 1.037)	21.30%	_
Geographical Location (Morbidity)					
Asia	_	_	_	_	_
Europe	_	_	_	_	_
America	11	11	1.022 (1.016, 1.029)	41.70%	0.207
Disease					
Congestive heart failure (Morbidity)	3	3	1.076 (1.021, 1.134)	64.70%	_
Season (Mortality)					
Warm season	3	3	1.002 (0.995, 1.010)	0	_
Cold season	3	3	1.014 (1.008, 1.019)	0	_
Respiratory Diseases					
Asthma (Morbidity)					
Asthma 0-18	5	6	1.020 (1.006, 1.035)	68.40%	_
	3	4	1.011 (0.998, 1.025)	14.20%	_

**Table S4.** Details of risk of bias assessment

6 7 8 9	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete ⇔ Soutcome data N		Conflict of interest	Other
10	1	Atkinson	Probably Low	Low	Probably Low	Low	Low 82	Probably Low	Low	Low
11		et al. 2016	All of the pollutants were	Death data for the period	Adjusted for time	Study included	Daily counts	There was	The authors	No other
12			measured at the central	1 January 2011 to 31	(seasonality,	daily counts of	for death were	insufficient	declare no	potential
13 14			London background	December 2012 were	long-term trend),	deaths in	obtained, so	information	conflict of	sources of
15			monitoring site at North	obtained from the Office	temperature,	London, United	likely have all	about	interest.	bias
16			Kensington. All	for National Statistics.	humidity, day of	Kingdom for the	outcome data.	selective		identified.
17 18			measurements were 24-h	Daily counts of deaths in	week and public	period 1 January	However, any	outcome to		
19			averages except for CO.	London, United Kingdom	holidays.	2011 to 31	potential errors	judge for low		
20			The number of all	were classified as all	1/0	December 2012.	or missing data	risk, but		
21 22			observations was 621-693	disease-related causes,	(0)	•	did not depend	indirect		
23			(<25% missing data).	cardiovascular			on air pollution	evidence that		
24				(International		'01.	levels.	suggests study		
25 26				Classification of			on	was free of		
27				Diseases,10th			Apr	selective		
28				revision-ICD10: I00-I99)			119	report.		
29				and respiratory (ICD10:			, 20			
30 31				J00-J99) diseases.			24 b			
32							y gi			
33							Jest			
34 35							19, 2024 by guest. Protected			
36							otec			
37										
38					l		\$	l		

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome dataω		Conflict of interest	Other
8 9	2	Bell et al.	Probably High	Low	Probably Low	Low	Low	Probably Low	Low	Low
10		2014	BC measured from filters	The study used the	Models adjusted	Data obtained	Daily counts 8	There was	The authors	No other
11			collected daily using	Medicare beneficiary	for time	from records of	for hospital	insufficient	declare no	potential
12			optical reflectance.	denominator file from the	(seasonality,	individuals ≥65	admissions \(\frac{8}{2}\)	information	conflict of	sources of
13 14			Monitors from 5 sites	Centers for Medicare and	long-term trend),	years of age	were obtained,	about	interest.	bias
15			across 4 counties were	Medicaid Services. Cause	day of week,	enrolled in the	so likely have	selective		identified.
16			used. Sampling occurred	of admission was	temperature, and	Medicare	all outcome	outcome to		
17 18			daily, with some missing	determined by principal	dew point.	fee-for-service	data. However,	judge for low		
19			periods, for Hartford,	discharge diagnosis code		plan during	any potential	risk, but		
20			New Haven, and	according to International	1	August 2000 to	errors or	indirect		
21 22			Springfield, and every	Classification of	(4)	February 2004.	missing data	evidence that		
23			third day for Bridgeport	Diseases, Ninth Revision,			did not depend	suggests study		
24			and Danbury. Days with	Clinical Modification		'01.	on air pollution	was free of		
25 26			missing data were	(ICD-9-CM; National			levels.	selective		
27			omitted from analysis	Center for Health			April 19,	report.		
28			(the number of missing	Statistics 2006).			119			
29			data was not reported).				, 20			
30 31							24 b			
32							ע פֿר			
33							Jest.			
34 35							. Prc			
36							2024 by guest. Protected b			
37							ted -			
38 <sup>1</sup>				1	1		Ý	1	<u> </u>	
39							сор			

36/bmjopen-2021-0495<mark>1</mark>

2	
2	
3	
4	
5	
6	
7	
8	H
5 6 7 8 9	
10	
10 11	
11	
12	
13	
14	
12 13 14 15 16 17 18	
16	
17	
18	
19 20	
20	
21	
22	
23	
22 23 24 25 26	
24 25 26 27 28 29 30	
25	
20	
2/	
28	
29	
31	
32	
31 32 33	
34	
35	
36	
37	
34 35 36 37 38	

5 5 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on the outcome data ≤		Conflict of interest	Other
3	3	Cai et al.	Probably Low	Low	Probably Low	Low	Low 2	Probably Low	Low	Low
0		2014	Daily concentrations of	Asthmatic hospitalization	Adjusted for time	Study included	Daily counts 82	There was	Authors	No other
1			BC were measured at a	data was obtained from	(seasonality,	all asthmatic	for asthmatic	insufficient	declared no	potential
2			fixed-site station. Daily	the Shanghai Health	long-term trend),	hospitalization	hospitalization	information	competing	sources of
3 4			data was available and no	Insurance Bureau	temperature,	for adult	were obtained,	about	financial	bias
5			missing data was	(SHIB). The causes of	relative humidity	residents living	so likely have	selective	interests.	identified.
6			reported.	hospital admission were	and day of the	in the nine urban	all outcome	outcome to		
7 8				coded according to	week.	districts between	data. However,	judge for low		
9				International		January 1, 2005	any potential	risk, but		
0				Classification of	' /	and December	errors or	indirect		
21				Diseases, Revision 10	(0)	31, 2011(2922	missing data	evidence that		
23				(ICD-10): Asthma (J45).		days) from the	did not depend	suggests study		
24						Shanghai Health	on air pollution	was free of		
25						Insurance	levels.	selective		
26 27						Bureau.	Apr	report.		
8							April 19,			
9										
0							124			
2							ру д			
3							2024 by guest. Protected			
34							t. Pr			
35 36							otec			
37							ted			
8 L							\$	1		

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on the outcome data ≤		Conflict of interest	Other
8 9			Probably High	Low	Probably Low	Low	Low by	Probably Low	Low	Low
10	4	Geng et al.	Single, central-site	Health data were	Models included	Data consisted of	Daily counts 8	There was	The authors	No other
11		2013	monitor. Daily BC and	obtained from Shanghai	time (seasonality,	all causes	for death were	insufficient	declare no	potential
12			PM <sub>2.5</sub> were measured	Municipal Center of	long-term trend),	(excluding	obtained, so	information	conflict of	sources of
13 14			continuously and 24hr	Disease Control and	temperature,	accidents or	likely have all	about	interest.	bias
15			averaged was estimated	Prevention database. The	humidity and day	injuries) deaths	outcome data.	selective		identified.
16			if >75% of the 1hr values	causes of death were	of week.	during over the	However, any	outcome to		
17 18			was available for that	coded according to the	<b>'</b> O.	course of the	potential errors	judge for low		
19			day. Missing data was not	International		study.	or missing data	risk, but		
20			replaced by other values.	Classification of	' /		did not depend	indirect		
21 22				Diseases, Revision 10	(4)		on air pollution	evidence that		
23				(ICD 10).			levels.	suggests study		
24						'61.	òm	was free of		
25 26							on on	selective		
27							Apr	report.		
28							ii 19			
29							, 20			
30 31							24 b			
32							יץ פוי			
33							Jest			
34 35							. Prc			
36							otec			
37							ted t			
			1	1	L	ı	~	ı		
36							on April 19, 2024 by guest. Protected by cop			

36/bmjopen-2021-0495<mark>1</mark>

2	
2	
3	
4	
5	
6	
7	
3 4 5 6 7 8	
u	
10	
11	
12	
13	
14	
15	
16	
17	
18	
10 11 12 13 14 15 16 17 18 19	
20	
21	
22	
23	
24	
22 23 24 25 26 27 28	
26	
27	
28	
29	
29 30	
31	
32	
32 33 34 35 36 37	
34	
35	
36	
37	
37 38	

	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete $\stackrel{1}{\circ}_{\circ}$ outcome data $\stackrel{2}{\circ}$		Conflict of interest	Other
			Probably High	Low	Probably Low	Low	Low ay	Probably Low	Low	Low
0	5	Hua et al.	Daily 24h average PM <sub>2.5</sub>	Daily asthma hospital	Adjusted for	Study included	Daily counts 8	There was	Authors	No other
1		2014	and BC data was obtained	admission data was	long-term and	all asthma	for asthma	insufficient	declared no	potential
2			from a fixed-site station.	obtained from Shanghai	seasonal trend, day	hospital	hospital 💆	information	competing	sources of
3 4			The study only used the	Children's Medical	of week,	admissions of	admissions of	about	financial	bias
5			actual collected data and	Center. Dates of	temperature and	children ≤ 14	children were	selective	interests.	identified.
6			did not fill in the missing	admission and discharge,	relative humidity.	years of age from	obtained, so	outcome to		
7 8			data for PM <sub>2.5</sub> and black	and diagnoses using the	<b>'</b> O.	Shanghai	likely have all	judge for low		
9			carbon.	International		Children's	outcome data.	risk, but		
0				Classification of	1	Medical Center	However, any	indirect		
1				Diseases, Revision 10.	' 01	between1	potential errors	evidence that		
2						January 2007 and	or missing data	suggests study		
4						31 July 2012 in	did not depend	was free of		
5						nine urban	on air pollutions	selective		
.6 .7						districts of	levels.	report.		
8						Shanghai.	119,			
9										
0							2024 by			
2							ру д			
3							lues			
4							guest. Protected			
5							otec			
7							cted			
8 L							9			

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data ≤		Conflict of interest	Other
8			Probably Low	Low	Low	Low	Low 2	Probably Low	Low	Low
10	6	Ostro et	Daily 24hr average BC	For both cities daily	Adjusted for long	Study population	Daily counts 82	There was	Authors	No other
11		al. 2015a	concentrations were	counts of all-cause	term and seasonal	consisted of daily	for death were	insufficient	declared no	potential
12			obtained from one station	mortality for all ages	(year, month, day	counts of	obtained, so	information	competing	sources of
13 14			in Barcelona and Athens.	were collected (excluding	of week) trends,	all-cause	likely have all	about	interests.	bias
15			Daily data was available	deaths from external	temperature,	mortality for all	outcome data.	selective		identified.
16			and no missing data was	causes, International	holidays, summer	ages and daily	However, any	outcome to		
17 18			reported.	Classification of	vacations and	counts of	potential errors	judge for low		
19				Disease-ICD9: 001799,	influenza.	cardiovascular,	or missing data	risk, but		
20				ICD10 A00R99), as well	1	respiratory and	did not depend	indirect		
21 22				as daily counts of	(0)	all-cause	on air pollution	evidence that		
23				cardiovascular (ICD9:		mortality for	levels.	suggests study		
24				390459, ICD10: I00I99),		those greater	ióm/	was free of		
25 26				respiratory		than age 65.	on	selective		
27				(ICD9:460519,			Apri	report.		
28				ICD10:J00J99) and			119,			
29 30				all-cause mortality for			202			
31				those greater than age 65.			24 b			
32							y gu			
33							lest.			
34 35							April 19, 2024 by guest. Protected			
36							tect			
37							ed b			
38 <sup>1</sup> 39							у сор			

36/bmjopen-2021-0495<mark>1</mark>

2	
3	
4	
5	
6	
6 7 8	
8	Ī
9	
10	
11	
12	
13	
12 13 14 15 16 17 18	
15	
16	
17	
18	
19	
20	
21	
22	
23	
24 25	
25	
26 27	
27	
28	
29	
20	
30	
2.1	
31 32	
31 32 33	
31 32 33	
31 32 33	
31 32 33 34 35 36	
31 32 33	

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete $\stackrel{\circlearrowleft}{\circ}$ outcome data $\overset{\circlearrowleft}{\simeq}$		Conflict of interest	Other
3			Low	Low	Probably Low	Low	Low $\overset{\text{as}}{\searrow}$	Probably Low	Low	Low
10	7	Samoli et	Daily concentrations of	Based on the primary	Adjusted for long	Study included	Daily counts 8	There was	Authors	No other
11		al. 2016	BC and EC were	discharge diagnosis, daily	term and seasonal	all	for all	insufficient	declared no	potential
12			collected from the	numbers of admissions	trends,	cardiovascular	emergency $\frac{8}{2}$	information	competing	sources of
13 14			ClearfLo project,	for cardiovascular disease	temperature,	and respiratory	hospital o	about	interests.	bias
15			supplemented by local	(International	relative humidity,	hospital	admissions	selective		identified.
16			measurements made at	Classification of	regulated	admissions in	were obtained,	outcome to		
17 18			the North Kensington	Diseases, 10th	pollutants (PM <sub>10</sub> ,	London, UK	so likely have	judge for low		
19			urban background site.	revision-ICD-10:	PM <sub>2.5</sub> , NO <sub>2</sub> , SO <sub>2</sub>	between 2011	all outcome			
20			Number of days of	I00-I99) for those aged	and O <sub>3</sub> ), day of the	and 2012.	data. However,	indirect		
21 22			observation for BC: 629	15-64 (adult) and 65+	week and public		any potential	evidence that		
22			(BC urban in PM <sub>2.5</sub> ) and	years (elderly), and	holidays.		errors or	suggests study		
24			702 (BC in PM <sub>2.5</sub> )	respiratory diseases		<b>'</b> 01.	missing data	was free of		
25			between 2011 and 2012	(ICD-10: J00-J99) for			did not depend9	selective		
26 27			(<25% missing data).	those aged 0-14 years			on air pollution	report.		
28				(paediatric), adult and the			levels.			
29				elderly were calculated.						
30 31							)24			
32							by g			
33							ues			
34							t. Pr			
35 36							otec			
30 37							2024 by guest. Protected by copyright.			
38 <sup>L</sup>							, and the second			
39 40							зору			
+0 41							⁄righ			
12							7			

Page 62 of 122

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on the outcome data of the outcome		Conflict of interest	Other
8 9			Probably High	Low	Probably Low	Low	Low ay 2	Probably Low	Low	Low
10	8	Zanobetti	Ambient BC from one	The study extracted data	Adjusted for	Data consisted of	Daily counts 8	There was	Authors	No other
11		and	monitor. The hourly	on all hospital admissions	temperature, day	all U.S. Medicare	for hospital	insufficient	declared no	potential
12 13		Schwartz	measurements for BC and	for residents of the	of the week,	hospital	admissions \frac{\S}{2}	information	competing	sources of
14		2006	PM <sub>2.5</sub> were not complete.	Boston Metropolitan area	seasonality,	admissions in the	were obtained,	about	interests.	bias
15			Missing values were	who were admitted to the	long-term trends,	Boston	so likely have	selective		identified.
16			replaced with the	hospital (in the Boston	humidity,	Metropolitan	all outcome	outcome to		
17 18			predicted values.	area) with a primary	barometric	area for	data. However,	judge for low		
19			Additionally BC data was	diagnosis of MI	pressure, and the	myocardial	any potential	risk, but		
20			missing from March 1997	(International	extinction	infarction during	errors or	indirect		
21 22			to March 1999 and was	Classification of	coefficient.	the study	missing data	evidence that		
23			not included in the study.	Diseases, 9th		duration.	did not depend	suggests study		
24				revision-ICD-9:410), and		'01.	on air pollution	was free of		
25 26				pneumonia (ICD-9:			levels.	selective		
27				480–487), from Medicare			April 19,	report.		
28				billing records for the			ii 19			
29				years 1995–1999.						
30 31							24 b			
32							y gi			
33							Jest			
34 35							Pr			
36							otec			
37							2024 by guest. Protected b			
38				<u> </u>	<u>I</u>	<u> </u>	~	<u> </u>		<u>l</u>
39							сор			

2	
3	
4	
5	
6	
7	
8	
9	
10	
11	
12	
13	
14	
15	
16	
16 17	
18	
19	
20	
21	
22	
23	
24	
25	
26	
27	
28	
29	
30	
31	
32	
33	
34	
35	
36	
37	
38	

Page 63	of 122			BMJ Oper	ו	36/bmJopen			
 <u>2</u>  }						Incomplete			
No	. Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on the outcome data	Selective reporting	Conflict of interest	Other
3		Probably High	Low	Probably Low	Low	Low	Probably Low	Low	Low
9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 33 33 34 33 34 35 36 37	Liu et al. 2016a	EC were collected from a single monitor on a one-in-three or one-in-six day schedule. EC were measured for 566 days from April 02, 2009, to December 30, 2013, <25% missing for the frequency of sampling.	Emergency department visit data was obtained from the Blue Cross Blue Shield Texa. International Classification of Diseases 9th Revision (ICD-9) diagnosis codes were used to classify outcome groups.	Adjusted for time (long-term and seasonal trend), day of week, temperature, dew point and population growth.	Study included daily counts of emergency department visits for Greater Houston from claims data insured from January 1, 2008 through December 31, 2013.	Daily counts for emergency department visits were obtained, so likely have all outcome data. However, any potential errors or missing data did not depend on air pollution levels. Protected	insufficient information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of selective report.	Authors declared no potential competing financial interests.	No other potential sources of bias identified.
38 39 40 41 42						Protected by copyright.			

•	
2	
3	
4	
5	
6	
7	
8	ŀ
7 8 9	
11 12	
12	
14	
15	
16	
17	
14 15 16 17 18	
19	
20	
19 20 21 22	
22 23	
23	
24	
25	
26	
27	
25 26 27 28	
29	
30	
31	
37	
33	
29 30 31 32 33 34	
34 35 36 37 38	
36	
37	
38	
50	

No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome dataω		Conflict of interest	Other
3		Probably High	Low	Probably Low	Low	Low by	Probably Low	Low	Low
10 10	Liu et al.	EC were collected from a	Hospital admission data	Adjusted for time,	Study included	Daily counts &	There was	Authors	No other
11	2016b	single monitor on a	was obtained from the	day of week,	all hospital	for HA were	insufficient	declared no	potential
2		one-in-three or one-in-six	Blue Cross Blue Shield	temperature,	admissions	obtained, so	information	competing	sources of
13  4		day schedule. EC were	Texa. International	seasonaility,	obtained from	likely have all	about	financial	bias
15		measured for 566 days	Classification of Diseases	humidity and	billing claims of	outcome data.	selective	interests.	identified.
6		from April 02, 2009, to	9th Revision (ICD-9)	population growth.	Blue Cross Blue	However, any	outcome to		
7		December 30, 2013,	diagnosis codes were		Shield Texa	potential errors	judge for low		
8  9		<25% missing for the	used to classify outcome		enrollees for	or missing data			
20		frequency of sampling.	groups.	1/6	Greater Houston	did not depend	indirect		
21				' (2)	from January 1,	on air pollution	evidence that		
22 23					2008 to	levels.	suggests study		
24					December 31,	con	was free of		
25					2013.	or or	selective		
26						Αp			
27 28						April 19, 2024 by			
29						9, 2			
30						024			
1						by			
3						guest.			
34									
5						Prot			
36						Protected			
37 <u> </u>						0			
39						y copyright.			
10						pyrii			
l1 l2						ght.			

2	
4	
5	
6	
7 8	
8	
9	
10	
11	
12	
13	
10 11 12 13 14 15	
15	
16 17 18 19	
1/	
18	
19	
20 21 22 23	
21	
22	
23 24	
25	
26 27	
28	
29	
30	
31	
32 33	
2 <i>1</i>	
25 25	
34 35 36	
37	
3/	

Page 6	65 of	122			BMJ Open BMJ open					
1 2 3 4							36/bmjopen-2021-0495			
7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome dataω		Conflict of interest	Other
8			Probably Low	Low	Probably Low	Low	Probably Low	Probably Low	Low	Low
9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38	1	Sarnat et al. 2015	24hr average concentration of PM <sub>2.5</sub> were obtained from a Supersite (single, central site monitoring location). The observations of EC was 666 days during 1 June 2001-30 April 2003 (missing data <25%).	Computerized billing records were obtained from the Missouri Hospital Association (MHA) for emergency department visits. The outcome groups were identified using primary International Classification of Diseases 9th Revision (ICD9) codes.	Models adjusted for season, day of week, holidays, time trends (using cubic splines for day of visit with monthly knots), and temperature	Data consisted of all emergency department visits during the study period for cardiovascular disease outcomes.	Daily counts for emergency of department visits were obtained, hence from http://tc one hospital not providing data after 26	There was insufficient information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of selective report.	The authors declare they have no actual or potential competing financial interests.	No other potential sources of bias identified.

Page 66 of 122

4 5 6 7	No.	Study	Exposure assessment	Outcome assessment	<b>Confounding bias</b>	Selection bias	Incomplete on outcome data ≤	Selective reporting	Conflict of interest	Other
8			Probably Low	Low	Probably Low	Low	Low ay	Probably Low	Low	Low
10	12	Kim et al.	PM <sub>2.5</sub> mass and chemical	All individual hospital	Model adjusted for	Data consisted of	Daily counts 8	There was	The authors	No other
11		2012	constituents were	admission records during	days from the start	all	for hospital	insufficient	declare they	potential
12			measured daily at one	the study period were	of the study, day of	cardiovascular	admission wer	information	have no	sources of
13 14			residential monitoring	extracted from	week, seasonality,	hospital	obtained, so	about	actual or	bias
15			station located on the roof	nonelective hospital	long-term trends,	admissions over	likely have all	selective	potential	identified.
16			of an elementary school	admission discharge data	daily average	the course of the	outcome data. $\frac{8}{3}$	outcome to	competing	
17 18			building in Denver. The	obtained from the	temperature and	study.	However, any	judge for low	financial	
19			observations of EC was	Colorado Hospital	relative humidity.		potential errors	risk, but	interests.	
20			1809 days during	Association. The	' /		or missing data	indirect		
21 22			2003-2007 (missing data	International	' (2)		did not depend	evidence that		
23			<25%).	Classification of			on air pollution	suggests study		
24				Diseases, Ninth		'01.	levels.	was free of		
25 26				Revision(ICD-9) codes			on on	selective		
27				were used to define			Apr	report.		
28				cardiovascular hospital			ii 19			
29				admissions (codes			, 20			
30 31				390-459) and respiratory			24 b			
32				hospital admissions			א פו			
33				(codes 460–519).			Jest			
34 35							Ρπ			
36							on April 19, 2024 by guest. Protected b			
37							ted			
38 <sup>L</sup> 39							by cop			

2	
2	
3 4	
5	
6	
7	
, δ	ŀ
9	
10	
11	
12	
13	
14	
15	
16	
17	
18	
19	
20	
21	
22	
23	
24	
25	
26	
27	
28	
29	
30	
31	
32	
33	
34	
35	
36	
37	

Pag	Page 67 of 122 BMJ Open 99.09									
1 2 3 4							36/bmjopen-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on the outcome data of the outcome	Selective reporting	Conflict of interest	Other
8			High	Low	Probably Low	Low	Low ay	Probably Low	Low	Low
9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37	13	Ostro et al. 2009	EC were generally recorded every 3 days from two co-located monitors or one monitor in 6 counties. The number of available days of data over the 4-year period ranged from 227 to 381 (some counties had >25% missing for the frequency of sampling).	Data for hospitalizations were obtained from the Office of Statewide Health Planning and Development, Healthcare Quality and Analysis Division. Hospital admissions for children <19 years of age were classified into one or more categories: all respiratory disease (International Classification of Diseases, Ninth Revision-ICD-9 codes 460–519), asthma (ICD-9 code 493), acute bronchitis (ICD-9 code 466), and pneumonia (ICD-9 codes 480–486).	Adjusted for time, day of the week, temperature, seasonality, relative humidity and pollutant.	Study included all hospitalizations for children < 19 and < 5 years of age for total respiratory diseases and several subcategories including pneumonia, acute bronchitis, and asthma for six California counties from 2000 through 2003.	Daily counts for hospitalizations of children were obtained, from http://bmjopen.bmj.com/ of children were obtained, so likely have all outcome data. However, any potential errors or missing data did not depend on air pollutions levels.  Protected by guest. Protected by guest. Protected by guest.	insufficient information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of selective report.	Authors declared no competing financial interests.	No other potential sources of bias identified.
38 <sup>1</sup> 39 40 41 42							by copyright.			

Page 68 of 122

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome dataω	Selective reporting	Conflict of interest	Other
8 9			Probably Low	Low	Probably Low	Low	Low ay 2	Probably Low	Low	Low
10	14	Kim et al.	Daily 24-hour composite	Daily mortality counts for	Models adjusted	Data consisted of	Daily counts 8	There was	None of the	No other
11		2015	PM <sub>2.5</sub> samples were	metropolitan Denver	for longer-term	all deaths over	for death were	insufficient	authors has	potential
12			collected from single,	were computed from the	temporal trend, as	the course of the	obtained, so	information	any actual	sources of
13 14			central-site monitor. The	Colorado Health	time since the	study in a	likely have all	about	or potential	bias
15			observations of EC was	Information Dataset	study began, day	defined	outcome data.	selective	competing	identified.
16			1809 days from 2003	compiled by the Colorado	of week, and daily	geographical	However, any	outcome to	interests.	
17 18			through 2007 (missing	Department of Public	temperature and	area.	potential errors	judge for low		
19			data <25%).	Health and Environment.	humidity.		or missing data	risk, but		
20				Data included cause of	' /	ieh	did not depend	indirect		
21				death by the International	. 61		on air pollution	evidence that		
22 23				Classification of Diseases			levels.	suggests study		
24				10th Revision (ICD-10)		<b>101</b>	com	was free of		
25				code.			/ on	selective		
26 27							Apı	report.		
28							1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1			
29							9, 20			
30 31							)24			
32							by g			
33							ues			
34							t. Pr			
35 36							ote			
37							on April 19, 2024 by guest. Protected b			
38							5			

36/bmjopen-2021-0495<mark>1</mark>

2	
3	
4	
5	
6	
7	
8	
9	
10	
11	
12	
13	
14	
15	
16	
17	
18	
19	
20	
21	
22	
23	
24	
25	
26	
27	
28	
29	
30	
31	
32	
33	
34	
35	
36	
37	
38	

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete 9 outcome data ≤		Conflict of interest	Other
3			Probably Low	Low	Probably Low	Probably Low	Low 2	Probably Low	Low	Low
10	15	Huang et	Daily average	Daily mortality data were	Models adjusted	The author	Daily counts 82	There was	No	No other
11		al. 2012	concentrations of PM <sub>2.5</sub>	obtained from the Xi'an	for calendar time	removed the	for death were	insufficient	competing	potential
12			were obtained from a	Center for Disease	(seasonality,	death counts on	obtained, so	information	financial	sources of
13   14			single, central-site	Control and Prevention.	long-term trends),	December 31 and	likely have all	about	interests.	bias
15			monitor. Daily average	The International	weather(temperatu	January 1 of each	outcome data. ≟	selective		identified.
16			concentrations of EC in	Classification of	re, relative	year.	However, any	outcome to		
17 18			PM <sub>2.5</sub> samples were	Diseases, Tenth Revision	humidity), year,		potential errors			
19			further analyzed. Daily	(ICD-10), codes of	day of week.		or missing data	risk, but		
20			data was available and no	mortality were as	'/		did not depend	indirect		
21			missing data was	follows: all natural causes	. 61		on air pollution	evidence that		
22			reported.	(ICD-10 codes			levels.	suggests study		
24				A00–R99), respiratory		<b>10</b> 1.	com	was free of		
25				diseases (ICD-10 codes			v on	selective		
26   27				I00–I98), and			Ap	report.		
28				cardiovascular diseases						
29				(ICD-10 codes I00–I99).			9, 20			
30				, , ,			024			
31   32							by g			
33							jues			
34							ř <del>.</del> D			
35							rote			
36   37							ctec			
38 L							.com/ on April 19, 2024 by guest. Protected by copyright.			
39							cop			
40 41							yrigl			
17 12							.∺			

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on the outcome data ≤		Conflict of interest	Other
8			Probably High	Low	Probably Low	Low	Low 2	Probably Low	Low	Low
10	16	Peng et al.	Ambient EC obtained	Daily counts of hospital	Model adjusted for	Data consisted of	Daily counts 82	There was	The authors	No other
11		2009	from Speciation Trends	admissions were obtained	weather (i.e.,	all	for hospital	insufficient	declare they	potential
12			Network monitors and	from billing claims of	temperature, dew	cardiovascular	admission were	information	have no	sources of
13 14			either from central site or	enrollees in the U.S.	point temperature),	hospital	obtained, so	about	competing	bias
15			averaged over a county.	Medicare system. Each	day of week,	admissions	likely have all	selective	financial	identified.
16			Air pollution	billing claim contains the	unobserved	during over the	outcome data.	outcome to	interests.	
17 18			concentrations were	date of service, disease	seasonal factors,	course of the	However, any	judge for low		
19			measured on a 1-in-3-day	classification using	and long-term	study.	potential errors	risk, but		
20			schedule in the national	International	trends.		or missing data	indirect		
21 22			air monitoring stations	Classification of	(4)	•	did not depend	evidence that		
23			and on a 1-in-6-day	Diseases, 9th Revision			on air pollution	suggests study		
24			schedule in the state and	(ICD-9) codes (Centers		'01.	levels.	was free of		
25 26			local air monitoring	for Disease Control and			on	selective		
27			stations. Study removed	Prevention 2008).			Apr	report.		
28			suspect data and extreme				119			
29			values from the original				, 20			
30 31			monitor records; monitors				24 b			
32			with very little data were				ง อเ			
33			omitted altogether.				Jest			
34 35			Missing data was not				. Prc			
36			replaced by other values.				April 19, 2024 by guest. Protected			
37							ted b			
38 <sup>L</sup> 39				1	L	ı	<	ı		
39							сор			

36/bmjopen-2021-0495<mark>1</mark>

3	
4 5 6 7 8 9 10 11 12	
5	
6	
7	
8	ŀ
9	
10	
11	
12	
13	
14	
15	
15 16 17 18	
17	
18	
19	
20	
21 22 23 24 25 26 27	
22	
23	
24	
25	
20	
26 27 28	
20	
29 30 31	
31	
32	
32 33	
34	
34 35 36 37 38	
36	
37	
38	
39	

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data ≤		Conflict of interest	Other
8 9			Probably High	Low	Probably Low	Low	Low <sup>ay</sup> 2	Probably Low	Low	Low
10	17	Levy et al.	The U.S. Environmental	Hospital admissions data	Adjusted for time	Study included	Daily counts of	There was	No	No other
11		2012	Protection Agency	were obtained from	(seasonality,	people who died	hospital 🖔	insufficient	competing	potential
12			established the PM	billing claims information	long-term trends),	any day between	admissions	information	financial	sources of
13 14			Speciation Trends	for US Medicare	seasonality, day of	2000 and 2008 in	were obtained a	about	interests.	bias
15			Network (STN) to	enrollees in 119 counties	the week and	119 US counties.	from billing	selective		identified.
16			measure more than 50	for the years 2000–2008.	dew-point		claims $\stackrel{\circ}{\exists}$	outcome to		
17 18			PM <sub>2.5</sub> chemical	The Medicare billing	temperature.		information, so	judge for low		
19			components, in addition	claims data were			likely have all	risk, but		
20			to total mass. The STN	classified into disease	' /		outcome data.	indirect		
21			includes > 50 national air	categories according to	(0)	•	However, any	evidence that		
23			monitoring stations	their International			potential errors	suggests study		
24			(NAMS) and $> 200$ state	Classification of		<b>'01.</b>	or missing data	was free of		
25			and local air monitoring	Diseases, Ninth Revision			did not depend?	selective		
26 27			stations (SLAMS). Air	(ICD-9), codes.			on air pollution	report.		
28			pollution concentrations				levels.			
29			were typically measured							
30 31			on a 1-in-3-day schedule				124 h			
32			in the NAMS and on a				у д			
33			1-in-6-day schedule in				2024 by guest.			
34			the SLAMS. There was							
35 36			no information about				Protected			
37			missing data.				ted			
88 -			-				9	1		

Page 72 of 122

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome dataω	Selective reporting	Conflict of interest	Other
8 9			Probably Low	Low	Probably Low	Low	Low $\stackrel{\mathbf{a}}{\checkmark}$	Probably Low	Low	Low
10	18	Son et al.	Hourly air samples were	Daily death counts were	Models adjusted	Data consisted of	Daily counts 8	There was	The authors	No other
11		2012	obtained from a single,	obtained from the	for time (long-term	all	for death were	insufficient	declare they	potential
12 13			central-site monitor. The	National Statistical	trends and	cardiovascular	obtained, so ≦	information	have no	sources of
14			monitoring system	Office. The study	seasonality), day	deaths over the	likely have all	about	actual or	bias
15			produces hourly estimates	classified mortality data	of week,	course of the	outcome data.	selective	potential	identified.
16			of PM <sub>2.5</sub> total mass, and	into all causes of death	temperature and	study.	However, any	outcome to	competing	
17 18			PM <sub>2.5</sub> levels of EC. Daily	[International	relative humidity.		potential errors	judge for low	financial	
19			data was available and no	Classification of			or missing data	risk, but	interests.	
20			missing data was	Diseases, 10th Revision	1		did not depend	indirect		
21 22			reported.	(ICD-10; codes	(0)	•	on air pollution	evidence that		
23				A00–R99),		ien	levels.	suggests study		
24				cardiovascular causes		'61'	, mo	was free of		
25 26				(codes I00–I99), and			on	selective		
27				respiratory causes (codes			Apri	report.		
28				J00–J99)] (World Health			1119			
29				Organization 2007).			, 20:			
30 31							24 b			
32							y gu			
33							uest.			
34 35							. Pro			
36							otect			
37							on April 19, 2024 by guest. Protected b			
38 39				1	1	1	~		<u> </u>	
39							сор			

2	
4	
5	
6	
/	L
8	
9	
10	
11	
12	
13	
14 1 <i>E</i>	
16	
10	
10	
10	
19	
20	
21	
22	
าว	
23	
23 24	
<ul><li>23</li><li>24</li><li>25</li><li>26</li></ul>	
<ul><li>23</li><li>24</li><li>25</li><li>26</li><li>27</li></ul>	
23 24 25 26 27	
23 24 25 26 27 28	
23 24 25 26 27 28 29	
23 24 25 26 27 28 29 30	
23 24 25 26 27 28 29 30 31	
23 24 25 26 27 28 29 30 31 32	
23 24 25 26 27 28 29 30 31 32 33	
23 24 25 26 27 28 29 30 31 32 33 34	
23 24 25 26 27 28 29 30 31 32 33 34 35	
23 24 25 26 27 28 29 30 31 32 33 34 35 36	
3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 33 33 34 35 36 36 37 37 38 37 38 37 37 37 37 37 37 37 37 37 37 37 37 37	

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete of outcome dataω		Conflict of interest	Other
8 9			Probably High	Low	Low	Low	Low $\overset{\mathbf{a}}{\searrow}$	Probably Low	Low	Low
10	19	Heo et al.	Ambient air samples	Seoul daily mortality data	Adjusted for	Study included	Daily counts 8	There was	Authors	No other
11		2014	were collected over a	were obtained from the	long-term trends,	all death for	for death were	insufficient	declared no	potential
12			24-hour period at 3-day	Korea National Statistical	seasonality,	all-cause,	obtained, so	information	competing	sources of
13 14			intervals from a single	Office. Using the	temperature and	cardiovascular,	likely have all	about	financial	bias
15			monitor. Missing data	International	humidity, day of	and respiratory in	outcome data.	selective	interests.	identified.
16			<25% for the frequency	Classification of Disease,	the week, holiday	Seoul during	However, any	outcome to		
17 18			of EC samples.	10th Revision (ICD-10;	and influenza	2003–2007.	potential errors	judge for low		
19				World Health	epidemics.		or missing data	risk, but		
20				Organization 1993), the	' /		did not depend	indirect		
21				mortality data were	' (2)		on air pollution	evidence that		
22				classified as all			levels.	suggests study		
24				nonaccidental causes		(0)	соп	was free of		
25				(codes A00-R99),			v or	selective		
26   27				cardiovascular disease			Αp	report.		
28				(codes I00-I99),				•		
29				respiratory disease (codes			9, 2			
30				J00-J98), and injury			024			
31				(S00-T98).			by (			
33				(200 170).			on April 19, 2024 by guest.			
34										
35							Protected			
36							ecte			
37   38							<u>م</u>			

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome dataω	Selective reporting	Conflict of interest	Other
8			Probably High	Low	Probably Low	Low	Low ay 2	Probably Low	Low	Low
10	20	Basagaña	Single central-site	Daily mortality counts for	Models adjusted	Data consisted of	Daily counts 22	There was	The authors	No other
11		et al. 2015	monitor in each city. For	all non-external causes	for holidays,	all deaths over	for death and	insufficient	have no	potential
12			each city, PM	[International	summer	the course of the	emergency §	information	conflicts of	sources of
13 14			constituents with >20%	Classification of	population	study in a	hospital	about	interest to	bias
15			of the values below the	Diseases, 9th Revision	decrease, influenza	defined	admissions	selective	disclose.	identified.
16			detection limit or missing	(ICD9) codes 001–799;	epidemics,	geographical	were obtained, 3	outcome to		
17 18			were excluded.	10th revision (ICD10)	seasonality,	area.	so likely have	judge for low		
19			Otherwise,	codes A00–R99],	long-term trends		all outcome	risk, but		
20			non-detectable were	cardiovascular (ICD9	and temperature.		data. However,	indirect		
21 22			replaced by half the limit	codes 390–459, ICD-10			any potential	evidence that		
23			of detection. Air pollution	codes I00–I99) and			errors or	suggests study		
24			data was collected daily	respiratory (ICD9 codes		Ch	missing data	was free of		
25 26			in Bologna (n=472),	460–519, ICD10 codes			did not depend9	selective		
27			twice a week in	J00–J99) were collected.			on air pollution	report.		
28			Barcelona (n=736) and	Cardiovascular and			levels.			
29			Madrid (n=104), and	respiratory			, 20:			
30 31			once a week in Huelva	hospitalizations were			24 b			
32			(n=406). There was no	defined on the basis of			יץ פר			
33			information about	the primary discharge			uest.			
34 35			missing data.	diagnosis using the same			. Prc			
36				ICD codes defined above.			19, 2024 by guest. Protected by			
37							led F			
38 <u> </u> 39							оу сор			

2	
2	
<b>3</b>	
4	
5 6 7 8	
0	
/	L
8	
9	
10	
11	
12	
13	
14	
15	
16	
17	
9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31	
19	
20	
21	
22	
23	
24	
25	
26	
27	
28	
29	
30	
31	
31 32 33	
33	
34	
32 33 34 35 36 37	
36	
37	
38	

age	e 75 of	75 of 122 BMJ Open								
							36/bmjopen-2021-049516 o	Selective	Conflict of	
	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	outcome data <sup>ω</sup>		interest	Other
,			Probably High	Low	Probably Low	Low	Low by 2	Probably Low	Low	Low
, 0 1 2 3 4 5 6 7 8 9 20 1 22 23 4 25 26 27 8 9 30 31 32 33 4 35	21	Dai et al. 2014	EC were measured on a 1-in-3 or 1-in-6 day schedule. Most of the cities had a single monitor. For every species, the study calculated the monthly average species-to-PM <sub>2.5</sub> proportions for each month as a solution to the missing speciation data problem due to the 1-in-6 or 1-in-3 day sampling frequency. There was no information of missing data for that sampling frequency.	Daily mortality data were obtained from National Center for Health Statistics. The study examined nonaccidental deaths due to all causes and specific diseases, derived from the International Statistical Classification of Disease, 10th Revision (World Health Organization 2007).	Adjusted for time, temperature, day of the week, and season.	Study included all death for all causes, cardiovascular disease, myocardial infarction, stroke, and respiratory diseases from National Center for Health Statistics in 75 U.S. cities between 2000 and 2006.	Daily counts for death were obtained, so likely have all outcome data. However, any potential errors or missing data did not depended on air pollution levels.	insufficient information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of selective	The authors declare they have no actual or potential competing financial interests.	No other potential sources of bias identified.
6 17 18							ected by			

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome dataω	Selective reporting	Conflict of interest	Other
8 9			Probably Low	Low	Low	Low	Low ay	Probably Low	Low	Low
9 10	22	Lin et al.	The concentrations of	Daily mortality data from	Adjusted for	Study included	Daily counts 82	There was	The authors	No other
11		2016a	different particle size	1 January 2007 to 31	public holidays,	daily	for death were	insufficient	declare they	potential
12			fractions and PM <sub>2.5</sub>	December 2011 were	day of the week,	cardiovascular	obtained, so	information	have no	sources of
13 14			chemical constituents	obtained from	influenza	mortality data	likely have all	about	actual or	bias
15			were measured at two air	Guangdong Provincial	outbreaks,	from 1 January	outcome data.	selective	potential	identified.
16			monitoring stations. EC	Center for Disease	seasonal patterns	2007 to 31	However, any	outcome to	competing	
17 18			were measured for four	Control and Prevention.	and long-term	December 2011	potential errors	judge for low	financial	
19			months of each year from	The cause of death was	trends, temperature	in Guangzhou.	or missing data	risk, but	interests.	
20			2007 through 2010.	coded using the	and relative		did not depend	indirect		
21 22			During the period	International	humidity.		on air pollution	evidence that		
23			2009-2011, the	Classification of			levels.	suggests study		
24			proportion of missing	Diseases, Tenth Revision		<b>101</b>	com	was free of		
25			data was very low	(ICD-10). Mortality from			/ on	selective		
26 27			(ranging from 1% to 2%).	cardiovascular diseases			Apr	report.		
28			There were about 20 days	(ICD-10:I00-I99) were			April 19,			
29			without chemical	extracted to construct the			9, 20			
30			constituents records and	time series.			2024 by			
31 32			were treated as missing				by g			
33			observations.				guest.			
34							ř <del>.</del> P			
35							rote			
36 37							tected			
37 38							<u>\$</u>			

by copyright.

2	
3	
4	
5	
6	
7	
8	H
9	
10	
11	
12	
13	
14	
15	
16	
17	
18	
19	
20	
21	
つつ	
23	
24	
24 25	
26	
27	
26 27 28	
29	
30	
31	
32	
33	
2/	
35	
36	
36 37 38	
38	
39	

41 42 43

	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome dataω	Selective reporting	Conflict of interest	Other
			Probably Low	Low	Probably Low	Low	Low ay 2	Probably Low	Low	Low
0	23	Cao et al.	Daily concentrations of	The study obtained	Model adjusted for	Data consisted of	Daily counts 22	There was	The authors	No other
1		2012	EC was obtained from a	numbers of deaths in	long-term and	all nonaccidental	for death were	insufficient	declare they	potential
2			single monitoring site.	Xi'an for each day from	seasonal trends,	causes deaths	obtained, so	information	have no	sources of
3			The observations of EC	the Shanxi Provincial	day of week,	during over the	likely have all	about	actual or	bias
5			was 1749 in 1827 days	Center for Disease	temperature,	course of the	outcome data.	selective	potential	identified.
6			(missing data <25%).	Control and Prevention	humidity, and SO <sub>2</sub>	study.	However, any	outcome to	competing	
7 8				(SPCDCP). SPCDCP	and NO <sub>2</sub>		potential errors	judge for low	financial	
9				staff then classify the	concentrations.		or missing data	risk, but	interests.	
0				cause of death according	' /		did not depend	indirect		
1				to the International	' 01		on air pollution	evidence that		
2 3 4				Classification of			levels.	suggests study		
4				Diseases, 10th Revision		<b>'</b> 01.	com	was free of		
5				[ICD-10; World Health			/ on	selective		
6 7				Organization (WHO)			Apr	report.		
8				1992] as due to total			il 19			
9				nonaccidental causes			9, 20			
0				(ICD-10 codes			)24			
2				A00–R99),			эу <u>д</u>			
3				cardiovascular diseases			ues			
4				(I00–I99), respiratory			April 19, 2024 by guest. Protected			
5				diseases(J00–J98), or			otec			
7				injury (S00–T98).			ted			

4 5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on the outcome data S		Conflict of interest	Other
8 9			Probably Low	Low	Probably Low	Low	Low by 2	Probably Low	Low	Low
10	24	Klemm et	Daily 24-hr average EC	Records of individual	Adjusted for time	Study included	Daily counts &	There was	Authors	No other
11		al. 2011	measurements are	deaths were provided by	(seasonality,	all nonaccidental	for death were	insufficient	declared no	potential
12 13			available for Atlanta	the Georgia Department	long-term trends),	deaths during	obtained, so	information	competing	sources of
4			during the study period.	of Human Resources.	temperature, and	over the course	likely have all	about	financial	bias
5			The observations of EC	Cause of death is	day of the week.	of the study.	outcome data.	selective	interests.	identified.
6			was 3317 days from	categorized using the			However, any	outcome to		
8			August 1998 to	International	<b>'</b> O.		potential errors	judge for low		
9			December 31, 2007.	Classification of			or missing data	risk, but		
20			Missing data <25%.	Diseases, 10th edition	1/0		did not depend	indirect		
21			There was no information	(ICD-10), including	' 01	•	on air pollution	evidence that		
23			for monitor stations.	circulatory conditions			levels.	suggests study		
24				(I00–I99), respiratory	er rel	'01.	, and the same of	was free of		
25 26				conditions (J00–J99),			on	selective		
27				malignant neoplasm			Apr	report.		
28				(cancer; C00–D48), or			April 19, 2024			
29				other nonaccidental			, 20			
0				causes (A00-R99,			24 b			
32				excluding cardiovascular,			у д			
33				respiratory, or cancer			by guest.			
34				causes).						
35 36							Protected			
37							ted			
38 <sup>L</sup> 39			<u> </u>	<u> </u>			by cop	<u> </u>		

2	
3	
4	
5	
6	
7	
8	
9	
10	
11	
12	
13	
14	
15	
16	
17	
18	
19	
20	
21	
22	
23	
24	
25	
26	
27	
28	
29	
30	
31	
32	
33	
34	
35	
36	
37	
38	
39	

5   5   7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome dataω	Selective reporting	Conflict of interest	Other
3			Probably Low	Low	Probably Low	Low	Low 2	Probably Low	Low	Low
0	25	Zhou et al.	24hr PM <sub>2.5</sub> samples were	Using codes from the	Models adjusted	Data consisted of	Daily counts 82	There was	The authors	No other
1		2011	obtained from a single,	International	for time,	all	for death were	insufficient	declare they	potential
2			central-site monitor.	Classification of	seasonality and	cardiovascular	obtained, so	information	have no	sources of
3 4			Daily data was available	Diseases, version 10	long-term trends,	deaths over the	likely have all	about	actual or	bias
5			and no missing data was	(ICD10; World Health	day of week,	course of the	outcome data.		potential	identified.
6			reported.	Organization 2007), daily	temperature, and	study.	However, any	outcome to	competing	
7				death counts were	humidity.		potential errors		financial	
9				aggregated to			or missing data	risk, but	interests.	
20				nonaccidental allcause	' /		did not depend	indirect		
21				deaths (ICD10, codes	. 01	•	on air pollution	evidence that		
22				A00 through R99),			levels.	suggests study		
24				cardiovascular deaths		<b>101</b>	com	was free of		
25				(ICD10, codes I01			/ on	selective		
26 27				through I99), and			Арі	report.		
28				respiratory deaths (ICD-			111111111111111111111111111111111111111			
29				10, codes J00 through			9, 20			
30				J99).			)24			
31   32							by g			
33							ues			
34							April 19, 2024 by guest. Protected			
35 36							oter			
37							cted			
38 L										

Page 80 of 122

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data ≤	Selective reporting	Conflict of interest	Other
8 9			Probably Low	Low	Probably Low	Low	Low $\overset{\mathbf{a}}{\searrow}$	Probably Low	Low	Low
10	26	Winquist	Daily EC and BC were	Individual-level data	Adjusted for time	Study included	Daily counts 8	There was	Authors	No other
11		et al. 2015	from a single monitor	were obtained from the	trends, day of	emergency	for emergency 💆	insufficient	declared no	potential
12			site. All species of	Missouri Hospital	week, holidays,	department visits	department \(\frac{8}{2}\)	information	competing	sources of
13 14			pollutant statistics are	Association for all	season,	in St Louis	visit were	about	financial	bias
15			missing less than 5%.	emergency department	temperature and	metropolitan	obtained, so	selective	interests.	identified.
16				visits to 36 of 43	dew point.	statistical area	likely have all $\frac{8}{3}$	outcome to		
17 18				acute-care non-federal	<b>'</b> O.	during 1 June	outcome data.	judge for low		
19				hospitals with emergency		2001 through 30	However, any	risk, but		
20				department visits in the	' /	April 2003.	potential errors	indirect		
21 22				16-county St Louis	. 61		or missing data	evidence that		
23				metropolitan statistical			did not depend	suggests study		
24				area during 1 June 2001		'01.	on air pollution	was free of		
25 26				through 30 April 2003.			levels. 9	selective		
27				Cardiorespiratory			Apr	report.		
28				outcomes of interest were			19			
29				defined based on the			April 19, 2024			
30 31				primary ICD-9			24 b			
32				(International			by guest.			
33				Classification of			Jest			
34 35				Diseases, version 9)						
36				diagnosis code for the			Protected			
37				visit.			ted =			
38 <sup>L</sup> 39				<u>'</u>			у сор			

2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 33 33 34 35 36 36 37 37 37 37 37 37 37 37 37 37 37 37 37	
5	
6	
7	
8	
9	
10	
11	
12	
14	
15	
16	
17	
18	
19	
20	
21	
22	
23	
24	
25	
26	
2/	
28	
29	
3U 21	
37	
33	
34	
35	
36	
37	
38	

I	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete of outcome dataω		Conflict of interest	Other
			Probably High	Low	Probably Low	Low	Low <sup>ay</sup> 2	Probably Low	Low	Low
0 2	.7	Ostro et	Each of the six counties	Daily mortality data were	Adjusted for time	Data consisted of	Daily counts 8	There was	The authors	No other
1		al. 2007	had two monitors	obtained from the	trend, day of week,	all	for death were	insufficient	declare they	potential
2			measuring PM <sub>2.5</sub>	California Department of	seasonality,	cardiovascular	obtained, so	information	have no	sources of
3 4			components and mass.	Health Services, Center	long-term trends,	deaths over the	likely have all	about	competing	bias
5			Fresno, Kern, Riverside,	for Health Statistics. The	temperature and	course of the	outcome data.	selective	financial	identified.
б			and Sacramento Counties	study determined daily	humidity.	study.	However, any	outcome to	interests.	
7 8			reported data every third	total mortality counts for	<b>'</b> O.		potential errors	judge for low		
9			day, whereas San Diego	those > 65 years of age			or missing data	risk, but		
0			and Santa Clara Counties	and for deaths from	' /		did not depend	indirect		
1			reported data every sixth	respiratory disease	' 01	•	on air pollution	evidence that		
2   3			day. For the speciation	[International			levels.	suggests study		
4			analyses, the number of	Classification of		101.	com	was free of		
5			observation days	Diseases, 10th Revision			on /	selective		
б 7			available ranged from	(ICD10; World Health			Apr	report.		
8 9			243 (San Diego County)	Organization 1993) codes			April 19,			
			to 395 (Sacramento	J00–J98] and			), 20			
0			County) from 2000 to	cardiovascular disease			24 k			
2			2003. There was no	(codes I00–I99).			ру д			
3			specific information				2024 by guest.			
4			about missing data.				t. Pr			
5 6			-				Protected			
7							cted			
₃∟									1	

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome dataω	Selective reporting	Conflict of interest	Other
8 9			Probably Low	Low	Probably Low	Low	Low S	Probably Low	Low	Low
10	28	Tolbert et	Daily 24h EC from a	Computerized billing	Adjusted for time	Study included	Daily count for	There was	Authors	No other
11		al. 2000	single monitor site. The	record data are being	(seasonality,	emergency	emergency $\bigcirc$	insufficient	declared no	potential
12			observation of EC was	obtained from the	long-term trends),	department visits	department \frac{8}{2}	information	competing	sources of
13 14			356 in 365 days, missing	emergency department	temperature, dew	of the	visits were	about	financial	bias
15			data <25%.	visits participating in the	point, and day of	participating	obtained, so	selective	interests.	identified.
16				study. Several case	week.	hospitals in the	likely have all	outcome to		
17 18				groups are being defined	<b>'</b> O.	Atlanta	outcome data.	judge for low		
19				using the primary ICD-9	(*/* .	Metropolitan	However, any	risk, but		
20				(International	1/0	Statistical Area,	potential errors	indirect		
21 22				Classification of	(4)	including 33	or missing data	evidence that		
23				Diseases, 9th Revision)		hospitals	did not depend	suggests study		
24				diagnostic code.		between January	on air pollution	was free of		
25 26						1 1993-August	levels.	selective		
27						31 2000, 4	Apr	report.		
28						hospitals	119			
29						between January	, 20			
30 31						1 1993-February	24 b			
32						30 2000.	א פו			
33							Jest			
34 35							. Pr			
36							otec			
37							April 19, 2024 by guest. Protected by			
38				I .	1		<del>by</del> c		l	
39							сор			

2 3 4	
5	
4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 29 20 20 20 20 20 20 20 20 20 20 20 20 20	
7	
8	f
9	
10	
11	
12	
13	
14	
15	
16	
17	
18	
19	
20	
21	
22	
23	
24	
25	
20	
2/	
20	
20 20	
31 32 33 34 35 36 37	
32	
33	
34	
35	
36	
37	
3 <i>/</i> 38	

Lin 2016 simply averaged to calculate the daily average data for PM <sub>10</sub> , PM <sub>25</sub> monitored at 13 general air quality monitoring stations located in a densely populated area in Taipei. Hourly concentrations of EC were detected by series 5400 Monitor. Very few missing values in the database were omitted as the daily average was calculated.  Lin 2016 simply averaged to calculate the daily average data for PM <sub>10</sub> , PM <sub>25</sub> monitored at 13 general air quality monitoring stations located in a densely populated area in Taipei. Hourly concentrations of EC were detected by series 5400 Monitor. Very few missing values in the database were omitted as the daily average was calculated.  Classification of Diseases with Clinical Modification, Ninth Revision (ICD-9 CM).	; ;	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on the outcome data ≤		Conflict of interest	Other
Lin 2016 simply averaged to calculate the daily average data for PM <sub>10</sub> , PM <sub>2.5</sub> monitored at 13 general air quality monitoring stations located in a densely populated area in Taipei. Hourly concentrations of EC were detected by series 5400 Monitor. Very few missing values in the database were omitted as the daily average was the daily average was  Lin 2016 simply averaged to calculate the daily averaged to calculate the daily universal health insurance claims from the National Health Research Institute (Claims from the National Health Research Institute (Claims from the National Health Research Institute (Claims from the National Health Research Institute (NHRI) and vital statistics from the Ministry of Health and located in a densely populated area in Taipei. Hourly concentrations of EC were detected by series 5400 Monitor. Very few missing values in the database were omitted as the daily average was diagnoses were based on the database were omitted as the daily average was diagnoses were based on the database were omitted as the daily average was diagnoses were based on the database were omitted as the daily average was diagnoses were based on the database were omitted as the daily average was diagnoses were based on the database were omitted as the daily average was diagnoses were based on the database were omitted as the daily average was diagnoses were based on the database were omitted as the daily average was diagnoses were based on the database were omitted as the daily average was diagnoses were based on the database were omitted as the daily average was diagnoses were based on the daily average was diagnoses were based on the daily average was diagnoses were based on the database were omitted as the daily average was diagnoses were based on the database were omitted as the daily average was diagnoses were based on the database were omitted as the daily average was diagnoses were based on the database were only the database were omitted as the daily average was diagnoses were based on the database wer				Low	Low	Probably Low	Low	Low	Probably Low	Low	Low
<i>,</i> ∪	9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 22 25 26 27 28 29 30 31 33 34 35 36 37 37 38 38 38 38 38 38 38 38 38 38 38 38 38	29	Ü	The hourly data were simply averaged to calculate the daily average data for PM <sub>10</sub> , PM <sub>2.5</sub> monitored at 13 general air quality monitoring stations located in a densely populated area in Taipei. Hourly concentrations of EC were detected by series 5400 Monitor. Very few missing values in the database were omitted as the daily average was	This study obtained universal health insurance claims from the National Health Research Institute (NHRI) and vital statistics from the Ministry of Health and Welfare from 2004 to 2008. Death causes were coded according to the diagnoses of the 9th revision of International Classification of Diseases (ICD-9). Disease diagnoses were based on the International Classification of Diseases with Clinical Modification, Ninth	Adjusted for temperature, relative humidity, wind speed, barometric pressure, holidays, day of the week, pneumonia and	Study included elderly (≥65 years) mortality from 2004 to 2008 and all population EVR from 2004 to 2010 in Taipei,	Daily counts for elderly mortality and all population emergency room visits were obtained, so likely have all outcome data. However, any potential errors or missing data did not dependent on air pollution	There was insufficient information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of selective report.	Authors declared no competing financial	No other potential sources of bias

5 5 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome dataω	Selective reporting	Conflict of interest	Other
3			Low	Low	Low	Low	Probably Low	Probably Low	Low	Low
10	30	Darrow et	Daily 24-hour average	Health data were	Adjusted for dew	Study included	Daily counts 8	There was	Authors	No other
11		al. 2014	EC was from ambient	obtained from 41	point, temperature,	daily emergency	for emergency 🖯	insufficient	declared no	potential
12			monitoring networks.	metropolitan Atlanta	seasonality,	department visit	department \(\frac{8}{2}\)	information	competing	sources of
13 14			Missing data <1%.	hospitals and the Georgia	long-term trends,	data from 41	visit were	about	financial	bias
15				Hospital Association. The	day of week,	metropolitan	obtained. In the	selective	interests.	identified.
16				diagnoses of respiratory	holiday and	Atlanta hospitals	earliest years	outcome to		
17 18				infection were based on	influenza	for the period	of the study,	judge for low		
19				International	epidemics.	January 1, 1993,	not all	risk, but		
20				Classification of	' /	to December 31,	hospitals were	indirect		
21				Diseases, 9th Revision	(0)	2004 (not all	participating.	evidence that		
22				(ICD-9), diagnosis codes:		hospitals	However, any	suggests study		
24				acute bronchitis or		contributed the	potential errors	was free of		
25				bronchiolitis (code 466);		full period), and	or missing data	selective		
26 27				pneumonia (codes		from the Georgia	did not depend ≧	report.		
28				480–486); and upper		Hospital	نے on air pollution			
29				respiratory infection		Association for				
30 31				(codes 460–465).		the period	)24			
32						January 1, 2005,	by g			
33						to June 30, 2010.	ues			
34						·	t. Pr			
35 36							oter			
37							2024 by guest. Protected			
38 L							\$			

2	
4	
6	
7	
8	H
9	
10	
11	
12	
13	
14	
15	
16	
17	
18	
19	
20	
21	
22	
23	
24	
25	
26	
27	
28	
29	
30	
31	
32	
33	
34 35	
35 36	
30 37	
38	
20	

	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete 9 outcome dataω		Conflict of interest	Other
			Probably High	Low	Probably Low	Low	Low 2	Probably Low	Low	Low
0	31	Metzger et	Ambient 24hr average	The study asked 41	Model adjusted for	Data consisted of	Daily counts 8	There was	No	No other
1		al. 2004	EC were obtained from	hospitals with emergency	temporal trends,	all	for emergency 🖯	insufficient	competing	potential
2			one monitor. On days	departments that serve	meteorological	cardiovascular	department \( \frac{\blue{2}}{2} \)	information	financial	sources of
3 4			when measurements were	the 20-county Atlanta	conditions (i.e.,	hospital	visits were	about	interests.	bias
5			missing at the central site,	metropolitan statistical	temperature, dew	admissions over	obtained, so	selective		identified.
6			data for the pollutant	area (MSA) to provide	point temperature),	the course of the	likely have all	outcome to		
7			were imputed using an	computerized billing data	day of week,	study.	outcome data.			
8 9			algorithm that modeled	for all emergency	hospital entry and	-	However, any	risk, but		
0			measurements. The	department visits between	exit, and federally		potential errors	indirect		
1			observations of EC was	January 1, 1993, and	observed holidays.		or missing data	evidence that		
2			714 days during the	August 31, 2000. Using			did not depend			
4			period August 1,	the primary International		101	on air pollution			
5			1998–August 31, 2000	Classification of			levels.	selective		
6 7			(missing data >25%).	Diseases, 9th Revision				report.		
8				(ICD-9) diagnosis code,						
9				the study defined several			9, 21			
0				cardiovascular disease			024			
1 2				(cardiovascular disease)			by g			
3				groups based largely on			Jues			
4				ICD-9 diagnosis codes.						
5				> diagnosis codes.			rote			
6 7							ctec			
, 8							l g			
9							April 19, 2024 by guest. Protected by copyright.			
0							yrigl			
12							Ę.			

Page 86 of 122

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome dataω	Selective reporting	Conflict of interest	Other
8 9			Probably Low	Low	Probably Low	Low	Low ay 2	Probably Low	Low	Low
10	32	Mar et al.	Hourly PM <sub>2.5</sub> chemical	Mortality data for all of	Adjusted for time	Data consisted of	Daily counts 8	There was	No	No other
11		2000	composition data from a	Maricopa County from	trend, seasonality,	all	for death were	insufficient	competing	potential
12 13			single, central-site	1995 to 1997 were	day of week,	cardiovascular	obtained, so	information	financial	sources of
14			monitor. Daily data was	obtained from the	temperature and	deaths during	likely have all	about	interests.	bias
15			available and no missing	Arizona Center for	relative humidity.	over the course	outcome data.	selective		identified.
16			data was reported.	Health Statistics in		of the study.	However, any	outcome to		
17 18				Phoenix. Death certificate	ertel		potential errors	judge for low		
19				data included residence			or missing data	risk, but		
20				zip code and the primary	' /		did not depend	indirect		
21 22				cause of death as	. 61		on air pollution	evidence that		
23				identified by the			levels.	suggests study		
24				International		'01.	com	was free of		
25				Classification of			on /	selective		
26 27				Diseases, Ninth Revision			Apr	report.		
28				(ICD-9, World Health			ii 19			
29				Organization, Geneva).			, 20			
30 31							24 b			
32							y gi			
33							April 19, 2024 by guest.			
34 35										
36							Protected			
37							ted_			
38				1	1		\$	1		<u> </u>

2	
3	
4	
5	
6 7	
7	
8	Ī
9	
10	
11	
12	
13	
14 15 16 17 18	
15	
16	
17	
18	
19	
20	
21	
22 23 24	
23	
24	
25 26 27	
26	
27	
28	
29	
30	
31	
32	
33	
32 33 34 35 36 37 38	
35	
36	
37	
38	

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete 9 outcome data ≤		Conflict of interest	Other
			Low	Low	Probably Low	Low	Low 2	Probably Low	Low	Low
8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 33 33 33 33 33 33 33 33 33 33 33 33 33	33	Wang et al. 2019	Hourly data of PM <sub>2.5</sub> were collected at 10 Chinese air quality monitoring sites in Shanghai. Hourly mass concentrations of PM <sub>2.5</sub> and EC were predicted in Shanghai by using a Community Multiscale Air Quality model. The study included continuous daily data from 2013 to 2015 (1095 days). Daily data was available and no missing data was reported.	Low  The daily mortality data were obtained from the system of Disease  Monitoring Point belonged to the Chinese Center for Disease  Control and Prevention (China CDC). Deaths were classified according to the 10th revised  International Statistical  Classification of Disease (ICD-10), all-cause mortality (A00-R99), circulatory disease mortality (I00-I99, the circulatory disease is also known as cardiovascular disease) and respiratory disease mortality (J00-J99).	Probably Low  Adjusted for long term trends, seasonal influence, day of the week, holidays, temperature and relative humidity.	Low Study included daily mortality data in Huangpu district from January 1, 2013 to December 31, 2015.	Daily counts for death were obtained, so likely have all outcome data. However, any potential errorssing data did not dependent on air pollution levels.  Protected by copyright.	There was insufficient information about selective outcome to judge for low risk, but indirect evidence that suggests study	No competing financial interests.	Low  No other potential sources of bias identified.
38 39 40 41							y copyright.			

Page 88 of 122

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data ≤		Conflict of interest	Other
8			Probably High	Low	Probably Low	Low	Low ay 2	Probably Low	Low	Low
10	34	Lin et al.	EC was from a single	Daily mortality data were	Adjusted for	Study included	Daily counts 22	There was	Authors	No other
11		2016b	monitor site for four	obtained from the death	long-term trends,	the residents who	for death were	insufficient	declared no	potential
12 13			months of each year from	registry system. The	seasonality,	died of ischemic	obtained, so	information	conflict of	sources of
14			2007 to 2010. Missing	cause of death was coded	temperature,	or hemorrhagic	likely have all	about	interest.	bias
15			data for the particle	using the International	humidity, day of	strokes in urban	outcome data.	selective		identified.
16			concentration was very	Classification of	week and public	districts of	However, any	outcome to		
17 18			low (ranging from 1% to	Diseases, Tenth Revision	holidays.	Guangzhou	potential errors	judge for low		
19			2%).	(ICD-10). Mortality from		between 2007	or missing data	risk, but		
20				stroke (ICD-10:I60–I66),		and 2011.	did not depend	indirect		
21 22				and sub-categories,			on air pollution	evidence that		
23				including ischemic stroke			levels.	suggests study		
24				(ICD-10:I63–I66), and		'61'	ým/	was free of		
25 26				hemorrhagic stroke			on	selective		
27				(ICD-10: I60–I62) were			Apri	report.		
28				extracted to construct the			119			
29				time series.			, 20			
30 31							24 b			
32							יץ פוי			
33							uest.			
34 35							. Pro			
36							April 19, 2024 by guest. Protected			
37							ted b			
38 <sup>L</sup> 39				1			су сор	1		

2	
3	
4	
5	
6	
6 7 8	
8	
9	
10	
11	
12	
13	
14	
10 11 12 13 14 15 16 17 18	
16	
17	
18	
19	
20	
20 21 22 23	
22	
23	
24 25	
25	
26 27	
27	
28	
29	
30	
31	
32	
33	
34	
35	
34 35 36 37	
37	
38	

Lin et al. 2016b   Each of the six counties had two monitors measuring components of PM2.5. Fresno, Kern, Riverside and Sacramento counties reported 24-hour average EC in PM2.5 every third day; San Diego and Santa Clara counties reported data every sixth day. The study included only species for which at least 50% of the observations were above the level of detection.  Probably Low   Low   Adjusted for time, temperature, humidity and day of the week.   Study included daily cardiovascular displayed and the montality for all California cardiovascular obtained, so obtained,	Incomplete of Selective outcome data reporting	Selection bias	Confounding bias	Outcome assessment	Exposure assessment	Study	No.
had two monitors measuring components of PM2.5. Fresno, Kern, Riverside and Sacramento counties reported 24-hour average EC in PM2.5 every third day; San Diego and Santa Clara counties reported data every sixth day. The study included only species for which at least can be a species for which at least can be a species for which at least can be a species of the study included only species for which at least can be a species of the study included only species for which at least can be a species of the study included only species for which at least can be a species of the study included only species for which at least can be a species of the study included only species for which at least can be a species of the study included only species for which at least can be a species of the study included only species for which at least can be a species of the study included only species for which at least can be a species of the study included only species for which at least can be a special to the measuring components of the measuring them the california residents were obtained, so likely have all good about selective outcome data. The humidity and day of the week.  California residents were obtained, so likely have all good about selective outcome data. The humidity and day or ardiovascular on the munidity and day or ardiovascular outcome data. The humidity and day or ardiovascular outcome data.  California residents were obtained, so likely have all good about selective outcome of the week.  California residents were obtained, so likely have all good about selective outcome or missing data outcome of the week.  California residents were obtained, so likely have all good about selective outcome or missing data outcome of the week.  California residents were obtained, so likely have all good outcome of the week.  California resid	Low S Probably Low	Low	Probably Low	Low	Probably High		
st. Protected by co	Daily counts for death were obtained, so likely have all outcome data. However, any potential errors or missing data on air pollution levels.  There was insufficient insufficient information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of selective	Study included daily cardiovascular mortality for all California residents from 1 January 2000 to 31 December	Adjusted for time, temperature, humidity and day	Daily mortality for all California residents were obtained from the California Department of Health Services, Center for Health Statistics. Daily counts of deaths from cardiovascular disease (International Classification of Diseases, Tenth Revision (ICD10) =I00–I99) were	Each of the six counties had two monitors measuring components of PM <sub>2.5</sub> . Fresno, Kern, Riverside and Sacramento counties reported 24-hour average EC in PM <sub>2.5</sub> every third day; San Diego and Santa Clara counties reported data every sixth day. The study included only species for which at least 50% of the observations were above the level of		1 2 3 4 5 6 7 8 9 0 1 2 3 4 5 6 7 8 9 0 1 2 3 4 5 6 7 8 9 0 1 1 2 3 4 5 6 7 8 8 9 0 1 1 2 3 4 4 5 6 6 7 8 8 9 8 9 8 9 8 9 8 9 8 9 8 9 8 8 8 9 8 8 8 9 8 8 8 8 9 8

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on the second seco		Conflict of interest	Other
8 9			Probably Low	Low	Probably Low	Low	Low 2	Probably Low	Low	Low
10	36	Ito et al.	Ambient EC obtained	Hospitalizations and	Model adjusted for	Data consisted of	Daily counts 8	There was	The authors	No other
11		2011	from multiple monitors	mortality data were	temporal trends	all	for death and	insufficient	declare they	potential
12			and the average of data	available at the New York	and seasonal	cardiovascular	hospitalization	information	have no	sources of
13 14			from multiple monitors	City Department of	cycles, immediate	hospital	were obtained,	about	actual or	bias
15			was computed using the	Health and Mental	and delayed	admissions over	so likely have	selective	potential	identified.
16			24hr average values. The	Hygiene. The relevant	temperature	the course of the	all outcome	outcome to	competing	
17 18			sampling frequency of	variables available in the	effects, and day of	study.	data. However,	judge for low	financial	
19			the chemical speciation	electronic discharge	the week.		any potential	risk, but	interests.	
20			data was every third day.	abstract for each patient	' /		errors or	indirect		
21			Daily data was available	included date of	. 01	•	missing data	evidence that		
22 23			and no missing data was	admission and			did not depend	suggests study		
24			reported.	International		'01.	on air pollution	was free of		
25				Classification of			levels.	selective		
26 27				Diseases, Nine Revision			Apr	report.		
28				(ICD9) discharge			iil 19,			
29				diagnosis code. The						
30 31				International			124			
32				Classification of			ру д			
33				Diseases, Tenth Revision			2024 by guest.			
34				(ICD10) codes for			Р			
35 36				determining cause of			rotected			
37				death.			ted			
38				ı	L	<u> </u>	9	1	<u> </u>	

2	
<b>o</b> ⊿	
5	
6	
7	
8	ŀ
9	
10	
11	
12	
	I
13 14 15	
15 16 17 18	
16	
17	
18	
19 20	
20	
21 22	
23	
24	
25 26	
26	
27 28 29	
28	
29	
30	
31	
32	
31 32 33	
34 35 36 37 38	I
35	
36	
37	
38	

5	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on the outcome data ≤	Selective reporting	Conflict of interest	Other
			Probably Low	Low	Probably Low	Low	Low ay 2	Probably Low	Low	Low
0	37	Chen et al.	Hourly mass	The counts of daily	Models adjusted	Data consisted of	Daily counts 8	There was	No	No other
1		2014	concentrations of PM <sub>2.5</sub>	emergency room visits	for time, day of	all emergency	for emergency 🖯	insufficient	competing	potential
2			and the four PM <sub>2.5</sub>	were obtained from the	week, temperature,	department visits	room visit wer	information	financial	sources of
3 4			constituents obtained	National Taiwan	seasonality and	during the study	obtained, so	about	interests.	bias
5			from a Supersite (single,	University Hospital. The	relative humidity.	period for	likely have all			identified.
6			central site monitoring	emergency room visit		ischemic and	outcome data.	outcome to		
7 8			location). The	data were coded		hemorrhagic	However, any	judge for low		
9			observations of EC was	regarding the discharge		stroke.	potential errors	risk, but		
0			1599 in 1705 days	diagnosis using the	'/		or missing data	indirect		
1			(missing data <25%).	International	. 61		did not depend	evidence that		
2				Classification of Disease,			on air pollution			
4				9th revision (ICD-9).		<b>101.</b>	levels.	was free of		
5							/ on	selective		
6							1 Ap	report.		
8								-		
9							9, 2			
0							024			
1 2							by (			
3							gues			
4							; <del>;</del>			
5							rote			
6 7							cter			
' L							d by			
9							on April 19, 2024 by guest. Protected by copyright.			
0							byriç			
1							ht.			

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data ≤	Selective reporting	Conflict of interest	Other
8 9			Low	Low	Probably High	Low	Low ay 2	Probably Low	Low	Low
10	38	Tomic´-Sp	Average daily	Emergency department	Adjusted for	Study included	All counts for 82	There was	Authors	No other
11		iric´et al.	concentrations of BC in	visits data were obtained	temperature,	emergency	emergency $\bigcirc$	insufficient	declared no	potential
12		2019	micrograms per cubic	from the Health Center	humidity, and air	department visit	department department	information	competing	sources of
13 14			meter were measured by	Užice, either from the	pressure.	for allergic	visits were	about	financial	bias
15			three automatic ambient	emergency department		rhinitis and	obtained, so	selective	interests.	identified.
16			air quality monitoring	visits in Užice, Sevojno,		allergic asthma	likely have all	outcome to		
17 18			stations. There was no	and Kosjeri´c, or from a		from 1 July 2012	outcome data.	judge for low		
19			information about	general hospital in Užice.		to 30 June 2014	However, any	risk, but		
20			missing data.	The inclusion criteria	' /	in the Zlatibor	potential errors	indirect		
21 22				were adults aged 18 years	. 01	District, Western	or missing data	evidence that		
23				and older with the		Serbia.	did not depend	suggests study		
24				diagnosis of allergic		<b>101</b>	on air pollution	was free of		
25				rhinitis (International			levels.	selective		
26 27				Classification of			Арі	report.		
28				Diseases, 10th revision,			ii 19			
29				code J.30.4), allergic			9, 20			
30				asthma (International			)24			
31 32				Classification of			by g			
33				Diseases, 10th revision,			lues			
34				code J.45.0), or asthma			it. Pi			
35 36				with coexisting allergic			rote			
37				rhinitis.			on April 19, 2024 by guest. Protected			
38				**			by			

2	
3	
4	
5 6	
8	-
7 8 9	
10	
11	
12	
13	
14	
13 14 15 16 17 18	
16	
17	
18	
19	
20	
21	
22 23	
24	
25	
27	
25 26 27 28	
29	
30	
31	
32	
33	
34	
34 35 36 37 38	
36	
37	
38	

I	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete $\stackrel{\circlearrowleft}{\circ}$ outcome data $\stackrel{\hookrightarrow}{\simeq}$		Conflict of interest	Other
			Probably Low	Low	Probably Low	Low	Low ay 2	Probably Low	Low	Low
0 3	39	Maynard	Daily measurements of	Individual mortality	Adjusted for	Study included	Daily counts 8	There was	Authors	No other
1		et al. 2007	BC were obtained from a	records were obtained	season and long	all death for all	for individual	insufficient	declared no	potential
2   3			single monitor site. In	from the Massachusetts	term trend,	causes,	mortality 💆	information	competing	sources of
4			order to predict local BC	Department of Public	temperature, dew	cardiovascular,	records were	about	financial	bias
5			level, the study used a	Health, for the years	point and day of	respirator, stroke,	obtained, so	selective	interests.	identified.
6			validated	1995–2002. Specific	week.	and diabetes	likely have all	outcome to		
7 8			spatial-temporal land use	cause mortality was	<b>'</b> O.	diseases in	outcome data.	judge for low		
9			regression model to	derived from the		Boston	However, any	risk, but		
0			predict 24-hr measures of	International	1	metropolitan area	potential errors	indirect		
1 2			traffic exposure data (BC)	Classification of Diseases	(0)	from the	or missing data	evidence that		
3			at $> 80$ locations in the	(ICD) codes [9th		Massachusetts	did not depend	suggests study		
4			Boston area.	Revision before 1999		Department of	on air pollution	was free of		
5 6				(World Health		Public Health	levels. 음	selective		
7				Organization 1975) and		between	April 19,	report.		
8				10th Revision 1999 to		1995–1997 and	ii 19			
9				2002 World Health		1999–2002.	, 20			
0   1				Organization 1993)].			24 k			
2							у д			
3							2024 by guest. Protected b			
4							: P			
5 6							otec			
7							ted			
<sub>8</sub> └─					l		<u> </u>	l	l	1

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0		Conflict of interest	Other
8 9			Probably Low	Probably Low	Probably Low	Low	Low 2	Probably Low	Low	Low
10	40	Sinclair et	Daily 24-hr averages EC	Daily outpatient visits	Adjusted for	Study included	Daily counts 82	There was	No	No other
11		al. 2010	was from a single	were obtained from the	season, day of	daily outpatient	for outpatient	insufficient	competing	potential
12			monitor site. The total	electronic patient data	week, federal	visits for acute	visits were	information	financial	sources of
13 14			observed rate of EC was	warehouse of a	holidays, study	respiratory	obtained, so	about	interests.	bias
15			95.2%.	not-for-profit,	month, time,	diseases from the	likely have all	selective		identified.
16				group-model managed	temperature and	electronic patient	outcome data. $\frac{9}{3}$	outcome to		
17 18				care organization (MCO)	dew point.	data warehouse	However, any	judge for low		
19				in the metropolitan		of a	potential errors	risk, but		
20				Atlanta area between	1/0	not-for-profit,	or missing data	indirect		
21 22				August 1, 1998 and	(4)	group-model	did not depend	evidence that		
23				December 31, 2002.		managed care	on air pollution	suggests study		
24				Visits that met acute visit		organization	levels.	was free of		
25 26				definition and that had a		(MCO) in the	on	selective		
27				visit diagnosis code of		metropolitan	Apr	report.		
28				asthma, upper respiratory		Atlanta area	ii 19			
29				infection (URI), or lower		between August	, 20			
30 31				respiratory infection		1, 1998 and	24 b			
32				(LRI) were included in		December 31,	ง อูเ			
33				the study.		2002.	Jest .			
34 35							. Pro			
36							otec			
37							April 19, 2024 by guest. Protected b			
38 <sup>1</sup> 39				I	l		by cop	I		I.

2	
3	
4	
5	
6	
7	
8	
9	
10	
11	
12	
13	
14	
15	
16	
17	
18	
19	
20	
21	
22	
23	
24	
25	
26	
27	
28	
29	
30	
31	
32	
33	
34	
35	
36	
37	
38	
39	

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome dataω		Conflict of interest	Other
8 9			High	Probably Low	Probably Low	Low	Low $\overset{a}{\searrow}$	Probably Low	Low	Low
10	41	Krall et al.	Monitors typically	All-cause mortality data	Adjusted for	Study included	Daily counts 8	There was	The authors	No other
11		2013	measure PM <sub>2.5</sub>	(excluding accidental	temperature, day	all death	for death were	insufficient	declare they	potential
12			constituent	deaths) were aggregated	of week, long-term	(excluding	obtained, so	information	have no	sources of
13 14			concentrations every third	from death certificate	and seasonal	accidental	likely have all	about	actual or	bias
15			or sixth day. Some	data obtained from the	trends.	deaths) for 108	outcome data.	selective	potential	identified.
16			communities with a	National Center for		urban	However, any	outcome to	competing	
17 18			single monitor. The	Health Statistics for 2000		communities	potential errors	judge for low	financial	
19			observation of EC was	to 2005.		from 2000 to	or missing data	risk, but	interests.	
20			58-921 days,some		' /	2005.	did not depend	indirect		
21			communities had >25%		. 01		on air pollution	evidence that		
22 23			missing data.				levels.	suggests study		
24						<b>101</b>	com	was free of		
25							on	selective		
26 27							Api	report.		
28										
29							9, 20			
30							)24			
31 32							by g			
33							April 19, 2024 by guest.			
34										
35							Protected			
36 37							ctec			
38 38										

Page 96 of 122

No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data		Conflict of interest	Other
		Probably High	Low	Probably Low	Low	Low	Probably Low	Low	Low
42	Cakmak et	Daily PM <sub>2.5</sub> aerosol	Diseases were coded	Adjusted for	Study included	Daily counts 8	There was	No	No other
	al. 2009	samples approximately 1	using the WHO	temperature and	all emergency	for emergency	insufficient	competing	potential
		of every 4 days from a	International	humidity, day of	department visits	department \( \frac{\delta}{2} \)	information	financial	sources of
		single monitor site.	Classification of Disease,	week, long-term	obtained from	visit were	about	interests.	bias
		Sampling occurred daily	9th Revision (ICD-9).	and seasonal	the	obtained, so	selective		identified.
		during the cold season	The daily number of	trends.	Departamento de	likely have all	outcome to		
		(April through	emergency department	<b>'</b> O.	Es-tad' isticas e	outcome data.	judge for low		
		September) and alternate	visits for all		InformaciónenSa	However, any	risk, but		
		days during the warm	nonaccidental (ICD-9 <	' /	lud (DEIS) of the	potential errors	indirect		
		season (October through	800) and respiratory	. 01	Ministry of	or missing data	evidence that		
		March). Missing data	(ICD-9 460–519) causes		Health from	did not depend	suggests study		
		<25% for that frequency.	in Santiago Centro,		April 2001	on air pollution	was free of		
			Cerrillos, and Pudahuel		through August	levels.	selective		
			were obtained from the		2006.	Apr	report.		
			Departamento de Estad´						
			ısticas e			), 20			
			InformaciónenSalud			24 5			
			(DEIS) of the Ministry of			у g			
			Health from April 2001			uest			
			through August 2006.			: P			
						otec			
						April 19, 2024 by guest. Protected b			
						by cop			

2	
3	
4	
5	
6	
7	
8	
9	
10	
11	
12	
13	
14 15	
15	
16 17	
17	
18	
19	
20	
21 22 23	
22	
23	
24	
25	
26 27	
27	
28	
29	
30	
31	
32	
33	
34	
35	
36	
35 36 37 38	
38	

	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on the outcome data of the outcome		Conflict of interest	Other
			Low	Low	Probably Low	Low	Low ay	Probably Low	Low	Low
0   4	43	Tolbert et	Daily ambient EC	Computerized billing	Model adjusted for	Data consisted of	Daily counts 8	There was	No	No other
1		al. 2007	obtained from multiple	records for all emergency	long-term and	all	for emergency	insufficient	competing	potential
2   3			monitors and a single	department visits between	seasonal trends,	cardiovascular	department \frac{8}{2}	information	financial	sources of
4			concentration obtained by	January 1, 1993 and	daily average	disease and	visit were	about	interests.	bias
5			averaging across	December 31, 2004 were	temperature, dew	respiratory	obtained, so	selective		identified.
6			monitors. The	collected, including the	point, day of week,	disease hospital	likely have all	outcome to		
7 8			observations of EC was	following data for each	federal holiday,	admissions	outcome data.	judge for low		
9			2258 during the period	visit: primary	and hospital entry	during the period	However, any	risk, but		
0			August 1, 1998 to	International	and exit.	1993 to 2004	potential errors	indirect		
1 2			December 31, 2004	Classification of Diseases	(0)	over the course	or missing data	evidence that		
3			(missing data <25%).	9th Revision (ICD-9)		of the study.	did not depend	suggests study		
4				diagnostic code,		'01.	on air pollution	was free of		
5 6				secondary ICD-9			levels.	selective		
7				diagnosis codes.			Apr	report.		
8							April 19,			
9										
0   1							24 k			
2							ру д			
3							uest			
4							: P			
5 6							otec			
7							2024 by guest. Protected b			
<sub>8</sub> L						<u> </u>	ā.		l .	

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data ≤	Selective reporting	Conflict of interest	Other
8 9			Low	Low	Probably Low	Low	Low ay 2	Probably Low	Low	Low
9 10	44	Lall et al.	Daily EC data were	The categorization of the	Model adjusted for	Data consisted of	Daily counts 8	There was	The authors	No other
11		2011	obtained from two	admissions data was	season, wintertime	all	for hospital	insufficient	declare they	potential
12			monitors. Daily data was	based on codes from the	influenza episode,	cardiovascular	admission wer	information	have no	sources of
13 14			available and no missing	International	weather, day of	hospital	obtained, so	about	actual or	bias
15			data was reported.	Classification of	week, and other	admissions over	likely have all	selective	potential	identified.
16				Diseases, revision 9	possible	the course of the	outcome data.	outcome to	competing	
17 18				(ICD-9).	confounders (e.g.,	study.	However, any	judge for low	financial	
19					federal holidays).		potential errors	risk, but	interests.	
20					' /		or missing data	indirect		
21					. 61	•	did not depend	evidence that		
22 23						ien,	on air pollution	suggests study		
24						<b>101</b>	levels.	was free of		
25							/ on	selective		
26 27							Apı	report.		
28							<b>/</b>			
29							9, 20			
30							)24			
31 32							by ç			
33							Jues			
34							it. P			
35							rote			
36 37							on April 19, 2024 by guest. Protected b			
38							l by			

2	
3	
4	
5	
6	
7	
0	L
7 8 9	
9	
10	
10 11 12 13	
12	
13	
13 14 15 16 17 18	
15	
16	
17	
12	
19	
19 20 21	
21	
22	
22 23	
23	
24	
25	
25 26	
27	
28	
29	
30	
31	
32	
33	
34	
35	
29 30 31 32 33 34 35 36 37 38	
37	
20	
38	

	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete 9 outcome data ≤		Conflict of interest	Other
			Probably High	Low	Probably Low	Low	Low 2	Probably Low	Low	Low
o   '	45	Jung and	A total of 153 daily	The health data used in	Adjusted for	Study included	Daily counts 82	There was	No	No other
1		Lin 2017	samples (approximately 4	the study were sourced	seasonal trend, day	all asthma	for asthma	insufficient	competing	potential
2			weeks per season) from a	from Longitudinal Health	of week,	outpatient visits	outpatient \( \frac{8}{2} \)	information	financial	sources of
3 4			single monitor site were	Insurance Database 2000.	temperature,	(0-20 years old)	visits (0-20	about	interests.	bias
5			collected. Multiple linear	Daily outpatient visits for	precipitation and	in Shalu district	years old) data	selective		identified.
6			regression models were	asthma (International	wind vectors.	from	were obtained,	outcome to		
7			used to back extrapolate	Classification of	<b>'</b> O.	Longitudinal	so likely have	judge for low		
9			the historic concentration	Diseases, Ninth Revision,		Health Insurance	all outcome	risk, but		
0			of individual components	Clinical Modification,	' /	Database 2000	data. However,	indirect		
1 2			of PM <sub>2.5</sub> from 2000	ICD-9-CM code 493)	. 61	during January 1,	any potential	evidence that		
3			through to 2010,	data was obtained from		2000 to	errors or	suggests study		
4			including BC.	Longitudinal Health		December 31,	missing data	was free of		
5				Insurance Database 2000.		2010.	did not depend을	selective		
6							on air pollution	report.		
8							levels.			
9										
0							24 b			
2							y gi			
3							2024 by guest. Protected			
5							. Pr			
6							otec			
7							ted			
8 └							<u> </u>	l		

Page 100 of 122

No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete of outcome dataω		Conflict of interest	Other
		Probably Low	Low	Probably Low	Low	Low 2	Probably Low	Low	Low
46	Gong et	The 24-h mean BC	The disease data used in	Adjusted for	Study included	Daily counts 8	There was	Authors	No other
	al. 2019	concentrations data were	this study were collected	calendar effects,	all	for all deaths	insufficient	declared no	potential
		obtained from a single	from the Chinese Center	long-term trends,	cardiovascular	were obtained, $\frac{5}{2}$	information	conflict of	sources of
		monitor site. During the	for Disease Control and	temperature,	mortality in	so likely have	about	interest.	bias
		study period (2091 days),	Prevention, and included	humidity, day of	Beijing obtained	all outcome	selective		identified.
		missing rate of BC was	all deaths in Beijing from	week, NO2 and	from the Chinese	data. However,	outcome to		
		0.68%.	January 1, 2006 to	$SO_2$ .	Center for	any potential	judge for low		
			December 31, 2011.		Disease Control	errors or	risk, but		
			Causes of death were	' /	and Prevention	missing data	indirect		
			classified according to	(0)	during January 1,	did not depend	evidence that		
			the International		2006 to	on air pollution	suggests study		
			Classification of		December 31,	levels.	was free of		
			Diseases, 10th Edition		2011.	on	selective		
			(ICD-10) and data on			Apr	report.		
			cardiovascular diseases			ii 19			
			(ICD-10 code: I00–I99)			, 20			
			were obtained.			24 b			
						งy gเ			
						Jest			
						. Pr.			
						otec			
						ted I			
			I			~	1		
		46 Gong et	Probably Low  The 24-h mean BC concentrations data were obtained from a single monitor site. During the study period (2091 days), missing rate of BC was	Probably Low  The 24-h mean BC concentrations data were obtained from a single monitor site. During the study period (2091 days), missing rate of BC was 0.68%.  Probably Low  The disease data used in this study were collected from the Chinese Center for Disease Control and Prevention, and included all deaths in Beijing from January 1, 2006 to December 31, 2011.  Causes of death were classified according to the International Classification of Diseases, 10th Edition (ICD-10) and data on cardiovascular diseases (ICD-10 code: I00–I99)	Probably Low  The 24-h mean BC concentrations data were obtained from a single monitor site. During the study period (2091 days), missing rate of BC was 0.68%.  Probably Low  The disease data used in this study were collected from the Chinese Center for Disease Control and Prevention, and included all deaths in Beijing from January 1, 2006 to December 31, 2011.  Causes of death were classified according to the International Classification of Diseases, 10th Edition (ICD-10) and data on cardiovascular diseases (ICD-10 code: 100–199)	Probably Low  The 24-h mean BC concentrations data were obtained from a single monitor site. During the study period (2091 days), missing rate of BC was 0.68%.  Probably Low  The disease data used in this study were collected from the Chinese Center for Disease Control and Prevention, and included all deaths in Beijing from January 1, 2006 to December 31, 2011.  Causes of death were classified according to the International Classification of Diseases, 10th Edition (ICD-10) and data on cardiovascular diseases (ICD-10 code: I00–I99)  Probably Low  Adjusted for calendar effects, long-term trends, temperature, humidity, day of week, NO2 and SO2.  Study included all cardiovascular mortality in Beijing obtained from the Chinese Center for Disease Control and Prevention during January 1, 2006 to December 31, 2011.	Probably Low  The 24-h mean BC concentrations data were obtained from a single monitor site. During the study period (2091 days), missing rate of BC was 0.68%.  The 28-h mean BC concentrations data were obtained from the Chinese Center for Disease Control and prevention, and included all deaths in Beijing from January 1, 2006 to December 31, 2011.  Causes of death were classified according to the International Classification of Diseases, 10th Edition  Probably Low  Low  Adjusted for calendar effects, long-term trends, temperature, humidity, day of week, NO2 and SO2.  Center for Disease Control and prevention and Prevention during January 1, 2006 to December 31, 2011.  Causes of death were classified according to the International Classification of Diseases, 10th Edition  Probably Low  Low  Low  Study included all cardiovascular mortality in Beijing obtained from the Chinese data. However, and included all outcome data.  Solve International Classification of December 31, 2011.	Probably Low  In this study were collected from the Chinese Center for Disease Control and Indiated all deaths in Beijing from January 1, 2006 to December 31, 2011.  Causes of death were classification of Diseases, 10th Edition (ICD-10) and data on cardiovascular diseases (ICD-10 code: 100-199) were obtained.  Probably Low  In the diseases data used in this study were collected from the Chinese Center for Disease Control and Included all deaths in Beijing from January 1, 2006 to December 31, 2011.  Causes of death were classification of Diseases, 10th Edition (ICD-10) and data on cardiovascular diseases (ICD-10 code: 100-199) were obtained.  Probably Low  Low  Low  Low  Low  Low  Low  Study included all deaths or cardiovascular mortality in so likely have got likely have	Probably Low The 24-h mean BC concentrations data were obtained from a single monitor site. During the study period (2091 days), missing rate of BC was 0.68%.  December 31, 2011. Causes of death were classified according to the International Classification of Diseases, 10th Edition (ICD-10) and data on cardiovascular diseases (ICD-10 code: 100-199) were obtained.  Probably Low The 24-h mean BC concentrations data were obtained from a single monitor site. During the study period (2091 days), missing rate of BC was 0.68%.  December 31, 2011. Causes of death were classified according to the International Classification of Diseases, 10th Edition (ICD-10) and data on cardiovascular diseases (ICD-10 code: 100-199) were obtained.  Probably Low

2	
3	
4	
5	
6	
7	
8	
9	
10	
11	
12	
13	
14	
15	
16	
17	
18	
19	
20	
21	
22	
23	
24	
25	
26	
27	
28	
29	
30	
31	
32	
33	
34	
35	
36	
37 38	
38	
39	

	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete $\stackrel{\text{do}}{\circ}$ outcome data $^{\omega}$		Conflict of interest	Other
			Probably Low	Probably Low	Probably High	Low	Low <sup>ay</sup> 2	Probably Low	Low	Low
0	47	Mostofsky	Ambient EC obtained	Patients potentially	Model adjusted for	Population	Daily counts 8	There was	No	No other
1		et al. 2012	from one monitor. BC	eligible for this study	seasonality,	consisted of	for emergency	insufficient	competing	potential
2			concentrations were	were identified by	time-trends,	patients ≥21	department \frac{8}{2}	information	financial	sources of
3 4			measured continuously.	reviewing daily	temperature, dew	years of age	admission were	about	interests.	bias
5			Daily data was available	emergency department	point temperature,	admitted to the	obtained, so	selective		identified.
6			and no missing data was	admission logs, stroke	barometric	hospital with	likely have all	outcome to		
7 8			reported.	service admission logs,	pressure and	neurologist-confi	outcome data.	judge for low		
9				stroke service consult	chronic and	rmed ischemic	However, any	risk, but		
0				logs, and hospital	slowly-varying	stroke and	potential errors	indirect		
1 2				electronic discharge	potential	residing in the	or missing data	evidence that		
3				records.	confounders.	Boston	did not depend	suggests study		
4						metropolitan	on air pollution	was free of		
5						region. Also	levels.	selective		
6 7						patients had to	April	report.		
8						reside within 40	ii 19,			
9						km of the air				
0						pollution	)24			
1 2						monitor.	2024 by guest. Protected			
3							lues			
4							t. Pr			
5 6							oter			
7							cted			
$_{3}$ $\Box$							<u></u>			

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome dataω		Conflict of interest	Other
8			Probably High	Low	Probably Low	Low	Low $\overset{\mathbf{a}}{\searrow}$	Probably Low	Low	Low
9 10	48	Krall et al.	PM <sub>2.5</sub> constituents from	The study obtained	Adjusted for	Study included	Daily counts 82	There was	The authors	No other
11		2017	one urban, ambient	electronic billing data for	holidays,	all emergency	for emergency 🖯	insufficient	declare they	potential
12			monitor located in each	respiratory disease	long-term trends,	department visits	department \( \frac{8}{2} \)	information	have no	sources of
13 14			city. Daily pollution data	emergency department	day of the week,	for respiratory	visits of	about	actual or	bias
15			were available in Atlanta;	visits for all ages at acute	season,	disease at acute	respiratory	selective	potential	identified.
16			however, data were only	care hospitals. Using	hospitalsreporting	care hospitals in	disease were	outcome to	competing	
17 18			available approximately	diagnosis codes from the	data, temperature	the 20-county	obtained, so	judge for low	financial	
19			every third day in the	International	and dew point.	Atlanta	likely have all	risk, but	interests.	
20			remaining three cities.	Classification of	' /	metropolitan	outcome data.	indirect		
21 22			There was no information	Diseases, 9th Revision	. 61	area, the	However, any	evidence that		
23			about missing data.	(ICD-9), the study		7-county	potential errors	suggests study		
24				considered subcategories		Birmingham	or missing data	was free of		
25 26				of respiratory diseases		metropolitan	did not depend9	selective		
27				including pneumonia		area, the 8	on air pollution€	report.		
28				(ICD-9 codes 480–486),		Missouri and 8	levels.			
29				chronic obstructive		Illinois counties	, 20			
30 31				pulmonary disease		in the St. Louis	24 b			
32				(491,492,496), upper		metropolitan	y gi			
33				respiratory infection		area, and the	uest			
34 35				(URI) (460–465, 466.0,		12-county Dallas	Pr			
36				477), and asthma and/or		metropolitan	2024 by guest. Protected			
37				wheeze (493, 786.07).		area.		_		
38 39							by cop			

2	
4	
4 5 6 7 8 9 10	
7	
8	H
9	
10	
11	
12	
13	
12 13 14 15 16 17 18 19 20 21 22 23	
15	
16	
17	
18	
19	
20	
21	
22	
23	
24 25 26 27 28 29 30	
25	
26	
27	
20	
30	
31	
31 32 33	
33	
34	
35	
33 34 35 36 37	
37	
37 38	

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data ≤	Selective reporting	Conflict of interest	Other
8 9			Probably Low	Low	Probably Low	Low	Low ay	Probably Low	Low	Low
9 10	49	O'Lenick	The 24-hour average	Patient-level emergency	Adjusted for	Study included	Daily counts 22	There was	Competing	No other
11		et al. 2017	concentration of EC was	department visit data	season, periods of	all emergency	for emergency	insufficient	interests:	potential
12			evaluated. Pollutant	from 1 January 2002 to	hospital	department visit	department $\frac{8}{2}$	information	None	sources of
13 14			concentration estimates	31 December 2008 were	participation and	data acquired	visit were	about	declared.	bias
15			were obtained by fusing	acquired from hospitals	holidays,	directly from	obtained, so	selective		identified.
16			observational data from	located within the	temperature and	hospitals	likely have all	outcome to		
17 18			available network	20-county metropolitan	mean dew point,	(2002–2004	outcome data.	judge for low		
19			monitors with pollutant	area of Atlanta; Relevant	interaction terms	period) and the	However, any	risk, but		
20			concentration simulations	data elements included	between season	Georgia Hospital	potential errors	indirect		
21			from the Community	admission date,	and maximum	Association	or missing data	evidence that		
22 23			Multi-Scale Air Quality	International	temperature and	(2005–2008	did not depend	suggests study		
24			emissions-based chemical	Classification of Diseases	day of year.	period) located	on air pollution	was free of		
25			transport model at	Ninth Revision (ICD-9)	, ,	within the	levels.	selective		
26 27			12×12km grids over	diagnosis codes, age and		20-county		report.		
28			Atlanta. 24-hour average	ZIP code of patient		metropolitan area		•		
29			EC were evaluated. Daily	residence.		of Atlanta.	9, 20			
30			data was available and no				024			
31 32			missing data was				by g			
33			reported.				jues			
34							it. P			
35							rote			
36 37							ctec			
38							April 19, 2024 by guest. Protected by copyright.			
39							сор			
40 41							yrig			
41 42							ht.			

Page 104 of 122

5 6 7	No.	Study	Exposure assessment	Outcome assessment	<b>Confounding bias</b>	Selection bias	Incomplete on the outcome data of the outcome data on the outcome data of the outcome data on the outcome data outcome data on the outcome data on the outcome data on the outcome data on the outcome data of the outcome data o		Conflict of interest	Other
8 9			Probably Low	Low	Probably Low	Low	Low	Probably Low	Low	Low
9 10	50	Pearce et	Daily EC data were	The study obtained	Adjusted for year,	Study included	Daily counts 8	There was	The authors	No other
11		al. 2015	obtained from a central	aggregate daily counts for	season, month, day	all emergency	for pediatric	insufficient	declare that	potential
12			monitoring location in	pediatric asthma related	of the week,	department visits	asthma related	information	they have	sources of
13 14			Atlanta. Daily data was	emergency department	hospital, holidays,	for pediatric	emergency of	about	no	bias
15			available and no missing	visits for children ages 5	temperature and	asthma of	department $\frac{\omega}{\exists}$	selective	competing	identified.
16			data was reported.	to 18 years from 41	dew point.	children ages 5	visits were	outcome to	interests.	
17 18				hospitals within	<b>'</b> O.	to 18 years from	obtained, so	judge for low		
19				metropolitan Atlanta; and		41 hospitals	likely have all	risk, but		
20				defined emergency	' /	within	outcome data.	indirect		
21 22				department visits for	' 01	metropolitan	However, any	evidence that		
23				pediatric asthma as all		Atlanta for study	potential errors	suggests study		
24				visits with a code for		period.	or missing data	was free of		
25				asthma (493.0–493.9) or			did not depend9	selective		
26 27				wheeze (786.07) using			on air pollution€	report.		
28				the International			levels.			
29				Classification of						
30 31				Diseases, 9th Revision.			2024 by guest.			
32							у д			
33							uest			
34 35										
36							Protected			
37							ted			
38			<u> </u>	L	<u> </u>	L	by c	<u>I</u>		<u> </u>
39							' cop			

2	
3	
4	
5	
6	
7	
8	
9	
10	
11	
13	
14	
14 15	
16	
17	
16 17 18	
19	
20	
21 22 23 24 25	
22	
23	
24	
25	
26	
26 27	
28	
29	
30	
31 32	
32	
33	
33 34 35 36 37 38	
35	
36	
37	
38	

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome dataω	Selective reporting	Conflict of interest	Other
8			Low	Low	Probably Low	Low	Low $\overset{a}{\searrow}$	Probably Low	Low	Low
10	51	Strickland	24-hour average EC were	Daily counts of	Adjusted for	Study included	Daily counts 8	There was	No conflict	No other
11		et al. 2010	obtained from 6 monitors.	emergency department	season, dew point,	all emergency	for emergency 🖯	insufficient	of interests.	potential
12			Missing data <1%.	visits for asthma or	temperature, year,	department visits	room visits of	information		sources of
13 14				wheeze among children	month, day of	for asthma or	asthma or	about		bias
15				were collected from 41	week, hospital,	wheeze among	wheeze disease	selective		identified.
16				Metropolitan Atlanta	upper respiratory	children aged 5	were obtained,	outcome to		
17 18				hospitals during	infections (the	to 17 years from	so likely have	judge for low		
19				1993-2004. Using the	logarithm of the	metropolitan	all outcome	risk, but		
20				International	daily count of	Atlanta hospitals	data. However,	indirect		
21				Classification of	upper respiratory	during	any potential	evidence that		
23				Diseases, 9th Revision,	infections) and	1993–2004.	errors or	suggests study		
24				the study defined	pollen	<b>101.</b>	missing data	was free of		
25				emergency department	concentrations		did not depend9	selective		
26 27				visits for pediatric asthma	(various lags of		on air pollution	report.		
28				as all visits with a code	ambient ragweed,		levels.			
29				for asthma (493.0–493.9)	pine, oak, juniper,		9, 20			
30   31				or wheeze (786.09 before	grass and birch		024			
32				October 1, 1998; 786.07	concentrations).		р д			
33				after October 1, 1998).			2024 by guest.			
34				·			t. Pr			
35 36							oter)			
37							Protected			
38 L							<del>-</del>			

Page 106 of 122

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data ≤		Conflict of interest	Other
8 9			Low	Low	Probably Low	Low	Low ay 2	Probably Low	Low	Low
10	52	Strickland	24-hour average EC were	Daily counts of	Adjusted for	Study included	Daily counts 8	There was	No conflict	No other
11		et al. 2014	obtained from 6 monitors.	emergency department	season, dew point,	all emergency	for emergency 🞖	insufficient	of interests.	potential
12			Missing data was 1%.	visits for asthma or	temperature, day	department visits	room visits of	information		sources of
13 14				wheeze among children	of week, and	for asthma or	asthma or	about		bias
15				aged 2 to 16 years were	holiday.	wheeze among	wheeze disease	selective		identified.
16				collected from the		children 2 to 16	were obtained, §	outcome to		
17 18				Georgia Hospital	<b>'</b> O.	years of age from	so likely have	judge for low		
19				Association from 1		the Georgia	all outcome	risk, but		
20				January 2002 through 30	' /	Hospital	data. However,	indirect		
21 22				June 2010. The study	(0)	Association.	any potential	evidence that		
23				identified all emergency			errors or	suggests study		
24				department visits with an		'01.	missing data	was free of		
25 26				International			did not depend9	selective		
27				Classification of			on air pollution	report.		
28				Diseases, 9th revision			levels.			
29				(ICD-9) code for asthma			, 20			
30 31				(codes beginning with			24 b			
32				493) or wheeze (code			יץ פוי			
33				786.07) present in any			uest.			
34 35				diagnosis field.			. Pro			
36							oteci			
37							2024 by guest. Protected b			
38 <sup>L</sup>				1	1		dy cop	1	<u> </u>	ı

36/bmjopen-2021-0495

2	
3	
4	
5	
6	
7	
8	
9	
10	
11	
12	
13	
14	
15	
16 17	
17	
18	
19	
20	
21	
22	
23	
24	
25	
26	
2/	
28	
29	
30	
31	
32	
33	
34	
35 36	
36	
. 7 /	
38	

5	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome dataω		Conflict of interest	Other
3 [			Probably High	Low	Probably Low	Low	Low 2	Probably Low	Low	Low
0	53	Ito et al.	The study chose 150 U.S.	Using International	Adjusted for	Study included	Daily counts 82	There was	No conflict	No other
1		2013	metropolitan statistical	Classification of	modeling of	all nonaccidental	for death and	insufficient	of interests.	potential
2			areas where the data from	Diseases, 10th Revision	confounding	all-cause,	emergency <u>S</u>	information		sources of
3 4			at least one Chemical	(ICD-10) codes, the study	temporal trends	cardiovascular	hospitalization o	about		bias
5			Species Network monitor	aggregated daily death	(annual cycles and	disease and	were obtained, =	selective		identified.
6			were available. The	counts for the	influenza	respiratory	so likely have	outcome to		
7 8			Chemical Species	nonaccidental all-cause,	epidemics),	deaths and	all outcome	judge for low		
9			Network data for PM <sub>2.5</sub>	cardiovascular disease	day-of-week	emergency	data. However,	risk, but		
0			components were	and respiratory deaths.	patterns and	hospitalizations	any potential	indirect		
1			available either every	Using International	temperature.	for the elderly	errors or	evidence that		
2			third day or every sixth	Classification of		(those 65 and	missing data	suggests study		
4			day. There was no	Diseases, 9th Revision		older) of	did not depend	was free of		
25			information about	(ICD-9) codes,		cardiovascular	on air pollution			
26 27			missing data.	emergency		disease and	levels. ≱on			
8				hospitalizations for the		respiratory	ril 19,			
9				elderly (those 65 and		diseases.	9, 20			
0				older) data were divided			024			
1				into cardiovascular			by g			
3				disease and respiratory			jues			
4				categories.			it. P			
5							rote			
6 7							ctec			
8 L							2024 by guest. Protected by copyright.			
9							ဝဓု			
·0 ·1							yrigl			
12							;÷			

5	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data ≤	Selective reporting	Conflict of interest	Other
			Probably Low	Low	Probably Low	Low	Probably Low	Probably Low	Low	Low
o :	54	Ostro et	The model calculations	Deaths were assigned	ge, race, marital	Data obtained for	There was no 8	There was	The authors	No other
1		al. 2015b	track the mass and	codes based on the	status, smoking	a cohort of	information on	insufficient	declare they	potential
2			concentrations of the PM	International	status, pack-years	female teachers	the rate of lost	information	have no	sources of
3			constituents in particle	Classification of	of smoking,	≥30 years old.	follow up.	about	actual or	bias
5			diameters ranging from	Diseases, 10th Revision	secondhand smoke		ed fr	selective	potential	identified.
6			0.01 to 10μm through	(ICD-10) for the	exposure, body		óm	outcome to	competing	
7			calculations that describe	following outcomes:	mass index,		http	judge for low	financial	
9			emissions, transport,	all-cause deaths	lifetime physical		://br	risk, but	interests.	
0			diffusion, deposition,	excluding those with an	activity, alcohol		njop	indirect		
1 2			coagulation, gas- and	external cause	consumption,		en.k	evidence that		
3			particle-phase chemistry,	(A00–R99),	average daily		omj.	suggests study		
4			and gas-to-particle	cardiovascular deaths	dietary intake of	Ch.	com	was free of		
5			conversion. The	(I00-I99), Ischemic heart	fat, calories,		/ on	selective		
6			University of California	disease deaths (I20–I25),	menopausal status,		Apr	report.		
8			Davis/California Institute	and pulmonary deaths	family history of		11 19			
9			of Technology model was	(C34, J00–J98).	myocardial		April 19, 2024 by			
0			used to estimate		infarction, stroke,		24 k			
2			ground-level		use of blood		у д			
3			concentrations of 50 PM		pressure		guest.			
4			constituents over the		medication,					
6			major population regions		aspirin; living		Protected			
7			in California.		conditions		ted			
8 🗀							у			

36/bmjopen-2021-0495

1 2 3 4	
5	
6	
7	
8	
9	
10	
11	
12 13	
13 14	
15	
16	
17	
17 18	l
19	
20	
21	
22	
23	
24	
25	
26	
27 28	
28	
29	
30	
31	
32 33	
34	۱
35	۱
36	۱
27	۱
38	•

ably Low Low	Low
e was	No other
ficient declare they	potential
nation have no	sources of
actual or	bias
ive potential	identified.
me to competing	
for low financial	
out interests.	
ect	
nce that	
ests study	
ree of	
ive	
t.	
neresuff formout lect atco dge sk, l directide gge as f	nere was The authors declare they formation have no actual or potential atcome to declare they formation have no actual or potential atcome to competing dige for low financial

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome dataω	Selective reporting	Conflict of interest	Other
8 9			Probably Low	Low	Probably Low	Low	Probably Low	Probably Low	Low	Low
9 10	56	Hvidtfeldt	The PM, NO <sub>2</sub> , BC, and	Participants who died	Age, sex,	Data obtained for	There was no 8	There was	The authors	No other
11		et al. 2019	O <sub>3</sub> concentrations at	from external causes such	educational	a cohort of men	information on	insufficient	declare they	potential
12			residential addresses of	as injuries, accidents and	attainment,	and women aged	the rate of lost	information	have no	sources of
13 14			the cohort members were	suicides (International	occupational	50–64 years	follow up.	about	competing	bias
15			derived by a	Classification of	status, marital	residing in the	ed fr	selective	financial	identified.
16			high-resolution	Diseases, 10th	status, smoking	areas of	o M	outcome to	interests.	
17 18			dispersion modelling	Revision-ICD-10 codes	(status, intensity,	Copenhagen and	http:	judge for low		
19			system which	S–Z) were censored at	and duration),	Aarhus.	://bn	risk, but		
20			incorporates	date of death. In addition,	environmental		Ŋop	indirect		
21 22			contributions from local,	the study investigated	tobacco smoke	•	en.b	evidence that		
23			urban, and regional	cardiovascular (ICD10	(ETS), alcohol		<u>)</u> .	suggests study		
24			sources of precursors to	codes I00–I99) and	consumption, body	'01.	SOM.	was free of		
25			PM, NO <sub>2</sub> , BC, and O <sub>3</sub> .	respiratory (ICD10 codes	mass index, waist		on on	selective		
26   27				J00–J99 and C34)	circumference,		April	report.		
28				subgroups of mortality.	fruit consumption,		ii 19,			
29					vegetable		, 20			
30 31					consumption,		2024 by			
32					physical activity;		у 9			
33					neighborhood		guest.			
34					level		: · P			
35 36					socioeconomic		otec			
37					status (SES).		otected			
38				ı			бу			

2 3 4	
5	
6	
7	
4 5 6 7 8 9	l
9	
10	
11	
12	
13	
14	
11 12 13 14 15 16 17 18	
16	
17	
18	
19	
20	
21	
22 23 24	
23	
24	
25 26	
26	
27 28	
28	
29	
30	
31	
32	
33	
32 33 34 35 36 37 38	
35	
36	
37	
38	ĺ

Pag	je 111 d	of 122		BMJ Open pp						
1 2 3 4							36/bmjopen-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome dataω	Selective reporting	Conflict of interest	Other
8 9			Probably Low	Probably Low	Probably High	Low	Probably High	Probably Low	Low	Low
10	57	Thurston	The mean concentrations	More than 99% of known	Active smoking	Data obtained for	The analytic &	There was	No	No other
11		et al. 2016	of PM <sub>2.5</sub> mass and trace	deaths were assigned a	and former	a cohort of	cohort included	insufficient	competing	potential
12			constituents were	cause using the	smoking, passive	persons at least	445,860	information	financial	sources of
13 14			obtained from U.S.	International	smoke exposure,	30 years of age,	participants,	about	interests.	bias
15			Environmental Protection	Classification of	possible workplace	in households	with 34,408	selective		identified.
16 17			Agency Air Quality	Diseases, 9th and 10th	exposure to PM,	including	Ischemic heart	outcome to		
17			System. These PM <sub>2.5</sub>	Revision (ICD-9 codes	occupational	someone at least	disease deaths	judge for low		
19			constituent data were	410–414; ICD-10 codes	dirtiness index,	45 years of age	(of a total of	risk, but		
20			analyzed to derive	I20–I25).	marital status,	and resided in all	157,572 deaths	indirect		
21 22			estimates of source		education, BMI	50 states, the	from all	evidence that		
23			apportioned PM <sub>2.5</sub> mass		and BMI <sup>2</sup> ,	District of	causes)	suggests study		
24			exposure concentrations		consumption of	Columbia, and		was free of		
25 26			using the absolute		beer, wine, and	Puerto Rico.	during 9	selective		
27			principal component		other alcohol,		follow-up. <u>₽</u>	report.		
28			analysis (APCA) PM <sub>2.5</sub>		quintile of dietary		19,			
29 30			source apportionment		fat consumption,		19, 2024 by guest			
31			method.		quintile of		i4 by			
32					combined dietary		/ gu			
33 34					vegetable, fruit,		est.			
35					fiber consumption;		Prof			
36					Six ecologic		tecte			
37 38					covariates.		Protected by			
39			<u> </u>	<u>l</u>	<u> </u>	<u> </u>				
40							copyright.			
41 42							jht.			

4 5 6 7	No.	Study	Exposure assessment	Outcome assessment	<b>Confounding bias</b>	Selection bias	Incomplete on the outcome data S		Conflict of interest	Other
8 9			Probably Low	Low	Probably Low	Low	Probably Low	Probably Low	Low	Low
10	58	Yang et al.	Land use regression	Deaths were coded	Age at entry,	Data obtained for	There was no	There was	The authors	No other
11		2018	models were derived	according to the	gender, individual	a cohort of	information on	insufficient	declare they	potential
12			from street level	International	smoking status,	people who were	the rate of lost	information	have no	sources of
13 14			measurements collected	classification of Diseases,	body mass index	older than or	follow up.	about	actual or	bias
15			during two sampling	10th Revision (ICD-10;	(BMI), physical	equal to 65 years	ed fr	selective	potential	identified.
16			campaigns conducted in	WHO 2010) including	activity, education	old.	om.	outcome to	competing	
17 18			2014 and 2015.	natural cause mortality	level and monthly		http:	judge for low	financial	
19				(A00–R99), overall	expenses;		://bn	risk, but	interests.	
20				cardiovascular disease	percentage of		njop	indirect		
21 22				(I00–I99) and overall	participants who		en.b	evidence that		
23				respiratory disease	were equal to or		<u>m</u>	suggests study		
24				(J00–J47 and J80–J99).	older than 65 years	"eh	, and the same of	was free of		
25 26				Subcategories included	old, percentage of		on	selective		
27				Ischemic heart disease	participants whose		Apr	report.		
28				(IHD) (I20–I25),	educational level		April 19, 2024			
29				cerebrovascular disease	was higher than		, 20			
30 31				(I60–I69), Pneumonia	secondary school,		24 b			
32				(J12–J18) and chronic	average income		y gu			
33				obstructive pulmonary	per month and		by guest.			
34 35				disease (COPD) (J40–I44	percentage of					
36				and I47).	smokers.		Protected			
37							ted			
38 <sup>L</sup> 39				<u> </u>		<u>I</u>	by cop	<u> </u>		

36/bmjopen-2021-0495<mark>1</mark>

3 4	
5	Ī
6	I
7	I
8	ŀ
9	I
10	I
11	I
12	I
13	I
14	I
15	I
16	I
17	I
17 18	I
19	I
20	I
21	I
22	I
23	I
24	I
25	I
26	I
27	I
28	I
29	I
30	I
31	I
32	I
33	I
34	I
35	I
31 32 33 34 35 36 37 38 39	I
3/ عو	Ĺ
38 20	
22	

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome dataω		Conflict of interest	Other
8 9			Probably Low	Low	Probably High	Low	Probably Low	Probably Low	Low	Low
10	59	Gan et al.	Land use regression to	A coronary heart disease	Model adjusted for	Study provided	During the 22	There was	The authors	No other
11		2011	estimate air pollution	hospitalization case is a	age, sex,	total number of	4-year	insufficient	declare they	potential
12			concentrations and	record of hospitalization	preexisting	subjects along	follow-up	information	have no	sources of
13 14			exposure assigned to	with the following	comorbidity, and	with those lost	period, 17,542 g	about	actual or	bias
15			residential centroid.	International Statistical	neighborhood	during the	$(3.9\%)$ moved $\stackrel{\text{def}}{\Rightarrow}$	selective	potential	identified.
16				Classification of	socioeconomic	follow-up period.	out of the	outcome to	competing	
17 18				Diseases, 9th Revision	status. No		province and	judge for low	financial	
19				codes, ICD-9, 410-414	individual data on		16,367 (3.6%)	risk, but	interests.	
20				and 429.2or 10th	behavioral risk		died from other	indirect		
21				Revision (ICD-10),	factors.		diseases,	evidence that		
23				I20–I25, as the principal			leaving $\frac{3}{2}$	suggests study		
24				diagnosis (the most		'01.	418,826	was free of		
25				responsible diagnosis) for			(9 <sub>2.5</sub> %) subject§	selective		
26 27				a hospital admission in			at the end of $\frac{\triangleright}{\square}$	report.		
28				the hospitalization			follow-up.			
29				database. A coronary			), 20			
30				heart disease death is a			024 1			
32				death record with			оу <u>д</u>			
33				coronary heart disease as			2024 by guest.			
34				the cause of death in the						
35 36				provincial death			Protected			
37				registration database.			ted by			

Page 114 of 122

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data ≤	Selective reporting	Conflict of interest	Other
8 9			Probably High	Low	Probably Low	Low	Probably Low	Probably Low	Low	Low
9 10	60	De	Used black smoke (BS)	The study obtained	Individual-level	Data obtained for	There was no $\frac{02}{2}$	There was	No	No other
11		Kluizenaa	as an indicator of EC	information on the	covariates: age,	a cohort of	information on	insufficient	competing	potential
12		r et al.	concentrations. Derived	incidence of	gender, marital	27,070	the rate of lost	information	financial	sources of
13 14		2013	background EC	hospital-based Ischemic	status, education,	non-institutionali	follow up.	about	interests.	bias
15			concentrations from BS	heart disease	smoking, alcohol	zed subjects.	ed fr	selective		identified.
16			measured at two regional	(International	use, physical		Öm	outcome to		
17 18			monitoring sites. Local	Classification of Diseases	activity, body mass		http	judge for low		
19			traffic-related EC	[ICD9] 410-414) and	index, living		://br	risk, but		
20			emission contributions	cerebrovascular disease	conditions		njop	indirect		
21			were estimated based on	(ICD9 430-438) in the	(employment		en.k	evidence that		
22 23			fuel-specific EC content	study population.	status, financial	1eh	omj.	suggests study		
24			of exhaust PM <sub>10</sub>		problems).	<b>101.</b>	com	was free of		
25			emission. Used the				/ on	selective		
26 27			traffic-related EC				Apr	report.		
28			emissions as input to				April 19,			
29			calculate local EC				9, 20			
30 31			concentrations, assuming				2024 by			
31   32			absence of other local EC				ру д			
33			sources. Also assumed				guest.			
34			that dispersion dynamics				t. Pr			
35 36			of EC are identical to				otec			
37			those of $PM_{10}$ .				tected			
38 🖁							<u> </u>			

36/bmjopen-2021-0495

2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35

5,	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome dataω	Selective reporting	Conflict of interest	Other
3			Probably Low	Probably Low	Probably Low	Low	Probably Low	Probably Low	Low	Low
0	61	Vedal et	The exposure estimation	All outcomes were	Individual-level	Data obtained for	There was no $\frac{8}{2}$	There was	No financial	No other
1		al. 2013	were used the national	reported via questionnaire	covariates: age,	a cohort of	information on		interests.	potential
2			spatial model predictions	and assessed via	body mass index,	postmenopausal	the rate of lost on follow up.	information		sources of
3 4			and secondary exposure	physician-adjudicator	smoking status,	women.	follow up.	about		bias
5			measures of citywide	review of medical records	cigarettes smoked		ed fr	selective		identified.
6			average exposures and	following established	per day and years		om.	outcome to		
7 8			distance to major	protocols.	of smoking,		from http://bmjop	judge for low		
9			roadways.		systolic blood		://br	risk, but		
0					pressure, history of		njop	indirect		
1					hypertension,	•	en.	evidence that		
2					hypercholesterole		omj.	suggests study		
4					mia, history of	(0)	соп	was free of		
25					diabetes,		n/ or	selective		
6					education,	'eh,	Ар	report.		
8					household income			_		
29					level, and race.		9, 20			
30 <sup>L</sup>							)24			
1 2							by g			
3							lues			
4							:t P			
5 6							ote.			
7							bmj.com/ on April 19, 2024 by guest. Protected by copyright.			
8							lby			
							сор			
10 11							yrigi			
+ I 12							ht.			

51'a	ble	S5.	Asses	ssment	of	certainty	of	evid	ence	for	outco	me

4		
5 Fable S5. Assessment of certainty of evidence for outcome  6 Reasons for downgrading Reasons for ungrading		Final
Evidence  A1 Rationale A2 Rationale A3 Rationale A4 Rationale A5 Rationale B1 Rationale B2 Rationale B3 Rat	Overall	certainty assessment
Risk estimates publication bias  All included studies  All included studies  80% PI 1.005 (95%CI: reported by the exised, RR  13	sk with 0	Moderate
Risk estimates  Acute effects of BC 18 BC or EC on CVD 19 10 10 10 10 10 10 10 10 10 10 10 10 10	sk with +1	High
All included studies  All included studies  All included studies  BOW PI 1.011(95% CI: reported by the PECOS  PECOS  PECOS  All included studies  All included studies  BOW PI 1.011(95% CI: reported by the include are 0 publication bias precise  PECOS  PECOS  BOW PI 1.010 (95% CI: Risk estimates precise  All included studies  PECOS  BOW PI 1.010 (95% CI: Risk estimates precise)  All included studies  PECOS  BOW PI 1.010 (95% CI: Risk estimates precise)  All included studies  PECOS  BOW PI 1.010 (95% CI: Risk estimates precise)  All included studies  PECOS  BOW PI 1.010 (95% CI: Risk estimates precise)  All included studies  PECOS  BOW PI 1.010 (95% CI: Risk estimates precise)  All included studies  PECOS  BOW PI 1.010 (95% CI: Risk estimates precise)  No evidence of Insufficient basis for publication bias precise  No evidence of Insufficient basis for publication bias pupgrading  No evidence of publication bias pupgrading  No evidence of publication bias pupgrading  No evidence of publication bias pupgrading  PECOS	ing risk 0	Moderate
30 Actute effects of BC 31 All included studies 31 Operation of the overall effect of th	ing risk 0	Moderate

5Table S5. Assessment of certainty of evidence for outcome

6 7	Reasons for downgrading											⊖ GReasons for upgrading						Final
8 Evidence 9	A1	Rationale	A2	Rationale	А3	Rationale	A4	Rationale	A5	Rationale	B1	Rationale	Иау≌20	Rationale	В3	Rationale	Overall	certainty assessment
10 1Chronic effects of  1B2: or EC on CVD  13 in PM <sub>2.5</sub> -unadjusted 14 1Sedel	0	Little influence on the overall effect	0	All included studies were consistent with our prespecified PECOS	0	80% PI 1.052 (95% CI: 1.001, 1.104) does not include unity	0	Risk estimates reported by the studies are sufficiently precise	0	No evidence of publication bias	0	Insufficient basis for upgrading	22. Downtoaded fro	Confounders would shift the RR in both directions	+1	No evidence of a clear increasing risk with exposure	+1	High

17 Abbreviations: BC: Black carbon; EC: Elemental carbon; CVD: cardiovascular diseases; RES: respiratory diseases; IHD: ischemic heart diseases; PI: prediction interval; CI: confidence interval; A1 = limitations in studies (risk of bias); A2 =

18 indirectness; A3 = inconsistency; A4 = imprecision; A5 = publication bias; B1 = large RR; B2 = all confounding decreases observed RR; B3 = concentration-response gradient.

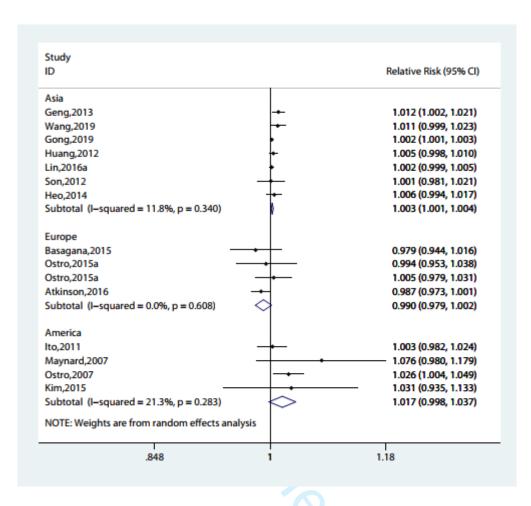


Fig. S1. Impact of short-term exposure to BC or EC on cardiovascular mortality stratified by geographical locations.

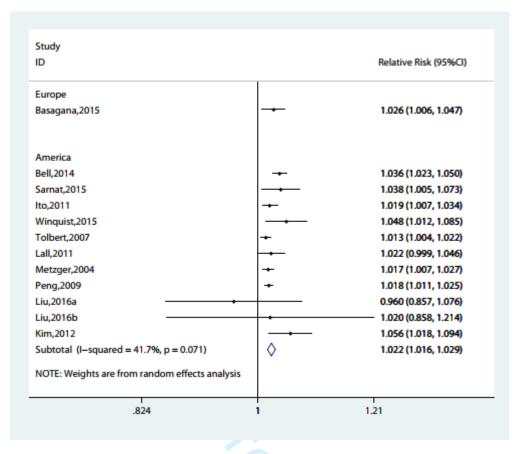


Fig. S2. Impact of short-term exposure to BC or EC on cardiovascular morbidity stratified by geographical locations.

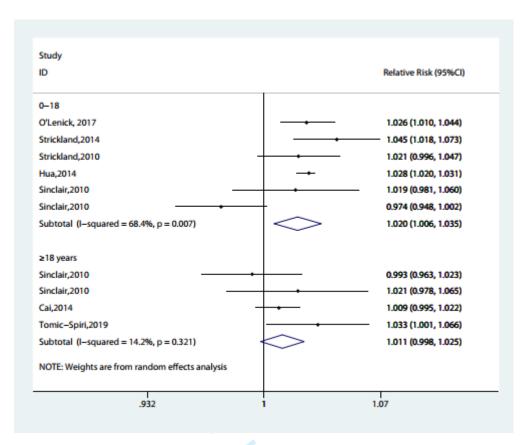


Fig. S3. Impact of short-term exposure to BC or EC on asthma morbidity in different age groups.

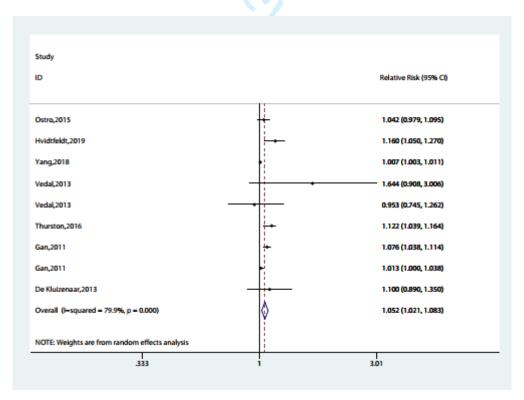


Fig. S4. Impact of long-term exposure to BC or EC on cardiovascular diseases.

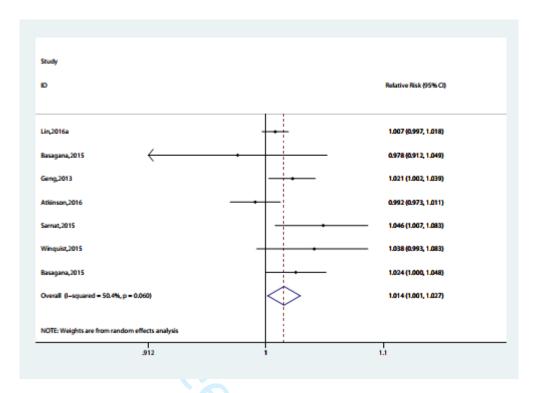


Fig. S5. Impact of short-term exposure to BC or EC on cardiovascular diseases in the PM<sub>2.5</sub>-adjusted model.

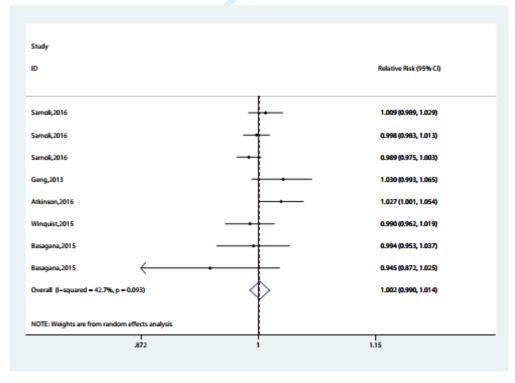


Fig. S6. Impact of short-term exposure to BC or EC on respiratory diseases in the PM<sub>2.5</sub>-adjusted model.



## PRISMA 2009 Checklist

		.0 2	
Section/topic	#	Checklist item 495	Reported on page #
TITLE		99 91	
Title	1	Identify the report as a systematic review, meta-analysis, or both.	#1
ABSTRACT		y 20	
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; sonclusions and implications of key findings; systematic review registration number.	#3-4
INTRODUCTION		a de	
Rationale	3	Describe the rationale for the review in the context of what is already known.	#6
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	#7
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	#7
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	#8-9
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with stud authors to identify additional studies) in the search and date last searched.	#8
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	#8
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	#9
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duple attemption and confirming data from investigators.	#9-10
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and simplifications made.	#14
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	#10
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	#11
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I²) for each meta-analysis, or peer review orlly - http://bmjopen.bmj.com/site/about/guidelines.xhtml	#11



## **PRISMA 2009 Checklist**

		Page 1 of 2	
Section/topic	#	Checklist item 255	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	#18
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	#18
RESULTS		Doy	
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with easons for exclusions at each stage, ideally with a flow diagram.	#13
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICSS, follow-up period) and provide the citations.	#14
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment see item 12).	#18
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	#14
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	#14-16
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	#18-19
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regisession [see Item 16]).	#18
DISCUSSION		Apri	
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; cogsider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	#22
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., not be identified research, reporting bias).	#26
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	#27
FUNDING		Prot	
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of da ); role of funders for the systematic review.	#30

41 From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The RISMA Statement. PLoS Med 6(6): e1000097. 42 doi:10.1371/journal.pmed1000097

## **BMJ Open**

# Short-term and Long-term Exposure to Black Carbon and Cardiovascular and Respiratory Diseases: A Systematic Review and Meta-Analysis

Journal:	BMJ Open
Manuscript ID	bmjopen-2021-049516.R1
Article Type:	Original research
Date Submitted by the Author:	19-Aug-2021
Complete List of Authors:	Song, Xuping; Lanzhou University, School of Public Health Hu, Yue; Lanzhou University, School of Public Health Ma, Yan; Lanzhou University, School of Public Health Jiang, Liangzhen; Lanzhou University, School of Public Health Wang, Xinyi; Lanzhou University, Second Clinical College Shi, Anchen; Xi'an Jiaotong University Medical College First Affiliated Hospital, Department of General Surgery Zhao, Junxian; Lanzhou University, School of Public Health Liu, Yunxu; Lanzhou University, School of Public Health Tang, Jing; Lanzhou University, School of Public Health Li, Xiayang; Lanzhou University, School of Public Health Li, Xiayang; Chengdu University of Information Technology, College of Atmospheric Sciences Guo, Yong; Guizhou Province Wang, Shigong; Chengdu University of Information Technology, College of Atmospheric Sciences
<b>Primary Subject Heading</b> :	Public health
Secondary Subject Heading:	Cardiovascular medicine, Respiratory medicine
Keywords:	PUBLIC HEALTH, RESPIRATORY MEDICINE (see Thoracic Medicine), CARDIOLOGY

SCHOLARONE™ Manuscripts



I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

### **Title Page**

#### Title:

Short-term and Long-term Exposure to Black Carbon and Cardiovascular and

Respiratory Diseases: A Systematic Review and Meta-Analysis

#### **Author names and affiliations:**

1. Xuping Song<sup>a</sup> E-mail: songxp@lzu.edu.cn

2. Yue Hu<sup>a</sup> E-mail: huy20@lzu.edu.cn

3. Yan Ma<sup>a</sup> E-mail: may2020@lzu.edu.cn

4. Liangzhen Jiang<sup>a</sup> E-mail: jianglzh19@lzu.edu.cn

5. Xinyi Wang<sup>c</sup> E-mail: wangxinyi17@lzu.edu.cn

6. Anchen Shi<sup>d</sup> E-mail: 3120115202@stu.xjtu.edu.cn

7. Junxian Zhao<sup>a</sup> E-mail: zhaojx2017@lzu.edu.cn

8. Yunxu Liu<sup>a</sup> E-mail: yxliu17@lzu.edu.cn

9. Yafei Liu<sup>a</sup> E-mail: isak-even@qq.com

10. Jing Tang<sup>a</sup> E-mail: tangj19@lzu.edu.cn

11. Xiayang Li<sup>a</sup> E-mail: lixiayang 18@lzu.edu.cn

10. Xiaoling Zhang<sup>b</sup> E-mail: xlzhang@ium.cn

11. Yong Guo<sup>e</sup> E-mail: gycau@qq.com

12. Shigong Wang<sup>b</sup> E-mail: wangsg@lzu.edu.cn

Chengdu 610000, China;

<sup>&</sup>lt;sup>a</sup> School of Public Health, Lanzhou University, Lanzhou 730000, China;

<sup>&</sup>lt;sup>b</sup> College of Atmospheric Sciences, Chengdu University of Information Technology,

<sup>c</sup> Second Clinical College, Lanzhou University, Lanzhou 730000, China;

<sup>d</sup> Department of General Surgery, The First Affiliated Hospital of Xi'an Jiao Tong

University, Shaanxi 710061, China;

<sup>e</sup> Department of Civil Affairs in Guizhou Province, Guiyang 550004, China.

#### **Corresponding author 1:**

Name: Xiaoling Zhang

Postal Address: College of Atmospheric Sciences, Chengdu University of Information

Technology, Chengdu 610000, Sichuan, China

E-mail address: xlzhang@ium.cn

Fax: 028-85966502

#### **Corresponding author 2:**

Name: Shigong Wang

Postal Address: College of Atmospheric Sciences, Chengdu University of Information

Technology, Chengdu 610000, Sichuan, China

E-mail address: wangsg@cuit.edu.cn

Fax: 028-85966502

#### **Abstract**

**Background** Adverse health effects of fine particles (PM<sub>2.5</sub>) have been well documented by a large number of studies. However, evidence on the impact of black carbon (BC) or elemental carbon (EC) on health is limited. The systematic review and meta-analysis provided comprehensive and current evidence on health impact of BC or EC, which could support the update of the World Health Organization Global Air Quality Guidelines.

**Objectives** (i) To explore the effects of BC and EC on cardiovascular and respiratory morbidity and mortality; (ii) To conduct stratified analyses that could explain the observed heterogeneity.

Methods PubMed, Embase and Web of Science were searched. Two reviewers independently selected studies for inclusion, extracted data and assessed risk of bias. Outcomes were analyzed via a random effects model and reported as relative risk (RR) with 95% confidence interval (CI). Adapted Grading of Recommendations assessment, Development and Evaluation (GRADE) was used to assess the certainty of evidence.

Results Seventy studies met our inclusion criteria. (i) Short-term exposure to BC or EC was associated with 1.6% (95% CI: 0.4%-2.8%) increase in cardiovascular diseases per 1 μg/m³ in the elderly; (ii) Impact of short-term exposure to BC or EC on cardiovascular morbidity was stronger than cardiovascular mortality; (iii) Short-term exposure to BC or EC was observed with 1.1% (95% CI: 0-2.1%) increase in children asthma morbidity; (iv) Long-term exposure to BC or EC was associated with 6.8%

(95% CI: 0.4%-13.5%) increase in cardiovascular diseases.

**Conclusions** Both short-term and long-term exposure to BC or EC were related with cardiovascular diseases and the association differs across continents. There is still not enough evidence on respiratory diseases in vulnerable groups, which requires further investigation.

**Keywords** Black carbon, Cardiovascular disease, Respiratory disease, Systematic review

PROSPERO registration number CRD42020186244.

#### Strengths and limitations of this study

- 1. Adapted GRADE (Grading of Recommendations assessment, Development and Evaluation) framework, formulated by the WHO global air quality guidelines working group, was used to evaluate the certainty of evidence.
- 2. The Systematic Review and Meta-Analysis on Short-term and Long-term Exposure to Black Carbon and Cardiorespiratory Diseases incorporated a detailed search strategy, explicit inclusion and exclusion criteria, literature screening, data extraction and risk of bias assessment.
- 3. The study populations, outcomes, and geographical locations were the possible reasons for heterogeneity in the pooled estimates.

#### 1. Background

Black carbon (BC), a ubiquitous component of particulate matter, is usually measured through optical absorption. Elemental carbon (EC), another carbonaceous material with a graphitic structure, is commonly measured by thermal or thermo-optical methods.<sup>1, 2</sup> Although the measurement methods are different, BC and EC are often considered interchangeable. BC is mainly emitted from traffic and combustion-related sources, and is a measured component of the particulate matter (PM). The adverse health effects of PM, especially of PM<sub>2.5</sub>, are well documented. In 2017, a total of 2.94 million deaths resulted from ambient PM worldwide.<sup>3-5</sup> PM<sub>2.5</sub> is composed of various constituents, in which some of them are more toxic and hypothesized as the main cause of the adverse effects of PM<sub>2.5</sub>. A growing body of studies indicates a potential role of BC among these more toxic constituents.<sup>6, 7</sup> In addition, some reviews demonstrated that BC is a better indicator of adverse effects of PM from combustion sources according to robust associations from epidemiological studies.<sup>8, 9</sup> The underlying pathological mechanisms of BC include oxidative stress, inflammation and gene mutations. 10-12

Due to its association with adverse health and climate effects, the number of studies exploring the effects of BC on cardiorespiratory diseases has rapidly increased in recent years. Cardiovascular and respiratory diseases are common diseases worldwide, with a heavy disease burden and major implications in clinical practice and public health. The Global burden of disease study 2017 indicated that

cardiovascular and respiratory-related death ranked first and third respectively among non-communicable diseases.<sup>4</sup> Health effects of acute and chronic exposure to BC have been widely reported. Despite there are some epidemiological evidences that BC was associated with cardiorespiratory diseases, in other studies, no statistical significance was observed.

Some systematic reviews analyzed the impact of BC on health. Nevertheless, quantitative associations between BC exposure and cardiovascular and respiratory diseases have not been well-characterized due to the different objectives of the reviews focused on.<sup>13, 14</sup> In addition, a series of eligible studied published recently have not been considered and GRADE (Grading of Recommendations assessment, Development and Evaluation) framework was not adopted in previous systematic reviews. Therefore, a systematic review and meta-analysis was performed to further elucidate the health effects of BC or EC. The objectives of this study were (1) to investigate the association of short-term and long-term exposure to BC or EC with the respiratory and circulatory morbidity and mortality; (2) to conduct stratified analyses that could explain the observed heterogeneity.

#### 2. Methods

The protocol for this systematic review was registered and published online on PROSPERO (International Prospective Register of Systematic Reviews), under registration number CRD42020186244.

#### 2.1 Patient and public involvement

Patients or the public were not involved in this study.

#### 2.2 Database

Articles were identified using PubMed, Web of Science and Embase databases up to July 19th, 2021. Original articles were searched using the following U.S. National Library of Medicine's Medical Subject Headings (MeSH) terms and keywords: "(black carbon\* or elemental carbon\*) AND (respiratory\* or cardiovascular\*) AND (morbidit\* or hospitalization\* or death\* or mortalit\* or outpatien\*) AND (time series\* or case cross\* or cohort\*)". In addition, the reference lists of the included studies and related reviews were manually evaluated to identify additional relevant studies. The details of the search strategy in PubMed are shown in Supplementary Table S1.

#### 2.3 Inclusion and exclusion criteria

A time series study, case crossover study and cohort study that evaluated the impact of BC or EC on cardiovascular or respiratory diseases were included in this systematic review and meta-analysis. Studies were considered eligible for inclusion if they fulfilled the inclusion criteria as follows: (1) study types restricted to time series, case crossover or cohort studies; (2) studies considering BC or EC as air pollutants; (3) based on the International Classification of Diseases (ICD) 9<sup>th</sup> or 10<sup>th</sup> revision, diseases included respiratory diseases, wheeze, other respiratory distress insufficiency or respiratory cancer (ICD-9 codes 460–519, 786.07, 786.09 or 162; ICD-10 codes J00–J99, R06.251, R06.001 or C34) or cardiovascular diseases (ICD-9 codes 390–459, ICD-10 codes I00–I99); (4) studies considering morbidity or mortality as outcome; (5) estimates were odds ratio (OR), relative risk (RR) or hazard ratio (HR)

with 95% confidence interval (CI) or enough information for calculation; (6) publication language was restricted to English.

The exclusion criteria were as follows: (1) studies on soot or black smoke were excluded, because the definition of such components usually lacked precision; (2) studies assessing the disease progression exposure to pollutants in individuals with cardiovascular or respiratory diseases (for example chronic obstructive pulmonary disease and asthma); (3) studies focusing on particular populations (for example pregnant women and miners) or population living in specific environments with high pollution concentration (for example residential area near industrial complexes, population exposed to sugar cane burning and neighborhoods that expose many streets); (4) studies focusing on seasonality; (5) conference abstracts; (6) study period less than 1 year.

#### 2.4 Selection of articles and extraction of data

To identify eligible studies, two investigators independently screened titles and abstracts. Studies which relevance could not be determined by titles and abstracts were subjected to full text screening. Any disagreement was resolved by discussion. A third investigator was involved in the discussion when a consensus could not be reached between the two investigators.

Two reviewers independently extracted the following items from each included study and record them in a pre-designed table: first author, publication year, country, study design, diagnosis standard, time periods, population age, statistical models, air pollutants, outcomes and number of events. If the reported data of the included studies

were unclear or missing, the first author or corresponding author was contacted by e-mail. Any conflicts were resolved by the involvement of a third investigator if the controversy was not solved after the discussion.

#### 2.5 Data synthesis

Regarding the meta-analysis, the RR was used as an effect estimate, and the OR in case crossover study and HR in cohort study were considered equivalent to RR. Estimates from the maximally adjusted model in the cohort study were extracted when multiple estimates were present in the original study to reduce the risk of potential unmeasured confounding. In addition, the estimate was converted to a standardized increment (1  $\mu$ g/m³) of RR. The following formula was used to calculate the standardized risk estimates:

$$RR_{(standardized)} = RR_{(original)}^{Increment(1)/Increment(original)}$$

Two studies did not show the overall risk, while stratified risk estimates by age and location were reported. <sup>16, 17</sup> In this case, the stratified estimates were pooled. One study presented the estimates of both morbidity and mortality, which were combined in the overall analysis. <sup>18</sup> In addition, the same cohort data were analyzed in different studies and the latest studies were included in the systematic review and meta-analysis. <sup>19-21</sup>

#### 2.6 Risk of bias assessment

The risk of bias was assessed for each study according to the Office of Health Assessment and Translation (OHAT) tool and the Navigation Guide tool. 13, 22, 23 Risk of bias evaluation was conducted as follows: exposure assessment, outcome

assessment, confounding bias, selection bias, incomplete outcome data, selective reporting, conflict of interest and other bias. Each domain was considered as "low", "probably low", "probably high", "high", or "not applicable" criteria. Two investigators conducted the risk of bias evaluation. Any inconsistency between the investigators was discussed and a third researcher was involved to resolve any disagreement.

#### 2.7 Evaluation of certainty of evidence

An adaptation of the GRADE (Grading of Recommendations assessment, Development and Evaluation) framework, formulated by the WHO (World Health Organization) global air quality guidelines working group, was used to evaluate the overall certainty of evidence.<sup>24</sup> The rating process on the certainty of evidence was started at moderate. The certainty was graded into four levels: "high", "moderate", "low" and "very low". Five reasons were used to downgrading the certainty of evidence: limitations in studies, indirectness, inconsistency, imprecision, and publication bias; 3 reasons were used to upgrade the certainty of evidence: large magnitude of effect size, all plausible confounding shifts the relative risk towards the null and concentration-response gradient. To evaluate the magnitude of the effect size, the E-value was calculated using the following formula: RR+sqrt{RR\*(RR-1)}.

#### 2.8 Statistical analysis

Statistical analysis was performed using STATA (version12.0, Stata Corp, College Station, TX, USA). In this meta-analysis, the random-effects model was conducted for anticipating significant heterogeneity among studies. Heterogeneity

among trials was assessed by the Chi-square test and the extent of inconsistency was evaluated by the  $I^2$ . An 80% prediction interval (PI) of meta-estimate was calculated to assess the inconsistency. To assess potential sources of heterogeneity, subgroup analyses were performed on outcomes (morbidity and mortality), single lag days (0, 1 and 2 days), study areas (Europe, America, and Asia) and seasons (warm and cold). The estimates from BC and EC were combined, since both of them are indicators of carbon-rich combustion sources, and are usually considered interchangeable in medical research.

Estimates were pooled separately where more than three estimates were available. Most studies presented estimates for single lags and the estimate of shortest lag was used to combine the estimates (RRs) of shortest lag in meta-analysis. However, only few studies presented cumulative lags, and the estimates of shortest cumulative lags were used in the meta-analysis. In addition, Mostofsky et al. indicated that PM<sub>2.5</sub> is a potential confounder in assessing the health effects of PM<sub>2.5</sub> constituents.<sup>7</sup> For overall and outcome analysis, PM<sub>2.5</sub>-adjusted estimates and PM<sub>2.5</sub>-unadjusted estimates in the models were combined, respectively where more Regarding than three estimates were available. the subgroup analysis. PM<sub>2.5</sub>-unadjusted estimates were analyzed, while PM<sub>2.5</sub>-adjusted estimates were not presented due to the limited number of included studies. Moreover, primary data of the included studies could not be obtained, hence it was not possible to evaluate whether the same patients were repeatedly included across multiple studies. Therefore, the sensitivity analysis was performed on all age populations to investigate

the robustness of the aggregation results by the removal of studies with partial temporal overlap from the same geographical location. The majority of the included studies analyzed and presented results of cardiovascular or respiratory system diseases, hence systematic diseases were analyzed in the acute effect analysis except for the chronic effect analysis. Publication bias was assessed by Egger's regression test when the outcome included more than 10 studies. Trim and fill method was used to correct on asymmetry for the outcome with publication bias. p < 0.05 was considered statistically significant.

#### 3. Results

A total of 1694 studies were initially identified and 129 were reviewed in depth. We excluded the studies which study period less than 1 year or same data were analyzed in different studies.<sup>25, 26</sup> Of these, 70 fulfilled the inclusion criteria (Figure 1).<sup>7, 16-21, 27-89</sup> Of the 70 included studies, 56 estimated the short-term effects of BC or EC using a time series design or case crossover design, while 14 studies explored the long-term effects of BC or EC using a cohort design. Thirty-seven of the 70 studies reported morbidity as the outcome variable, 25 studies reported mortality, and 8 studies reported both morbidity and mortality. Thirty-five studies analyzed both cardiovascular and respiratory diseases, 18 studies merely investigated cardiovascular diseases, and 17 studies assessed respiratory diseases. Thirty-seven studies were conducted in the United States, 14 in China, 4 in Canada, 2 in the United Kingdom, Sweden, Korea and Serbia, 1 in Denmark, Iran, Germany and the Netherlands. The remaining 3 studies collected data from two different countries: Spain and Greece,

Spain and Italy, Sweden and Denmark. Twenty-seven studies classified the diseases using the ICD-9 codes, 26 used the ICD-10 codes, and 10 used both the ICD-9 and ICD-10 codes. However, the remaining 7 studies did not employ the ICD standards (Supplementary Table S2). In addition, the authors of 33 studies were contacted, but only 19 answered to our request (response rate: 57.6%).

#### 3.1 Short-term effect of BC or EC on cardiovascular and respiratory diseases

Overall, short-term exposure to BC or EC was associated with an increased risk of cardiovascular diseases (RR=1.007 per 1  $\mu$ g/m³, 95% CI: 1.002–1.011) (adjusted by trim and fill method), but had no impact on respiratory diseases (RR=1.010 per 1  $\mu$ g/m³, 95% CI: 0.996–1.025) in overall analyses (Table 1, Figure 2 and Figure 3). Cardiovascular diseases (RR=1.016 per 1  $\mu$ g/m³, 95% CI: 1.004–1.028) were associated with BC or EC in the elderly (65+ years), but sensitive analysis of respiratory diseases showed that the association was uncertain. (Figure 2 and Figure S1).

The stratification analysis by outcome indicated that the effect estimates of BC or EC on cardiovascular morbidity (RR=1.022 per 1  $\mu$ g/m³, 95% CI: 1.016–1.029) were higher compared to their effect on mortality (RR=1.003 per 1  $\mu$ g/m³, 95% CI: 1.001–1.006). Impact of BC or EC on cardiovascular diseases was related to the exposure lag. The estimates of the association were strongest on the day of the event (lag 0) (RR=1.011 per 1  $\mu$ g/m³, 95% CI: 1.006–1.016), and then diminished on lag 1 (RR=1.005 per 1  $\mu$ g/m³, 95% CI: 1.002–1.008) and lag 2 (RR=1.002 per 1  $\mu$ g/m³, 95% CI: 0.999–1.005) (Supplementary Table S3). The subgroup analysis on the

geographical location was performed for morbidity and mortality, respectively. Significant association between BC or EC and cardiovascular mortality was observed in Asia (RR=1.003, 95% CI: 1.001–1.005). However, no association was found in America (RR=1.017, 95% CI: 0.998–1.037) and Europe (RR=0.990, 95% CI: 0.979–1.001) (Supplementary Figure S2). On the other hand, an increased risk of cardiovascular morbidity was observed in America (RR=1.022, 95% CI: 1.016–1.029) with short-term exposure to BC or EC, while only one study performed in Europe (RR=1.026, 95% CI: 1.006–1.047) investigated the short-term effect of BC or EC on cardiovascular morbidity. In addition, just one study in Asia was performed assessing the short-term effects of BC or EC on stroke morbidity (Supplementary Figure S3). 59

No association was observed between short-term exposure of BC and EC and respiratory morbidity (RR=1.012, 95% CI: 0.993–1.031) and mortality (RR=1.013, 95% CI: 0.997–1.030) (Table 1). In addition, the pooled effect estimates of BC or EC on asthma morbidity indicated an increased risk in children of 0-18 years (RR=1.021, 95% CI: 1.006–1.035) (Supplementary Figure S4).

Table 1 Short-term impacts of BC or EC on cardiovascular and respiratory diseases in different models

		PM <sub>2.5</sub> -1	unadjusted model				PM <sub>2.5</sub> -adjusted model			
Subgroup Analysis	No. of No. of Relative Risk Studies Estimates (95%CI)		$I^2$	Egger regression test (p value)	No. of⊗ Studies	Estimates	Relative Risk (95%CI)	$I^2$		
Cardiovascular Diseases						22. [				
Age						Oowr				
All population	20	22	1.008 (1.004, 1.012)	64.40%	0.007	6 ac	7	1.014 (1.001, 1.027)	51.00%	
Relative risk adjusted for publication bias with trim and fill method	24	26	1.007 (1.002, 1.011)	_	_	Downloaded from	_	_	_	
Sensitive analysis on study of partial temporal overlap from the same geographical location	16	16	1.006 (1.002, 1.010)	60.00%	0.020			_	_	
≥65 years	5	6	1.016 (1.004, 1.028)	87.40%	_	— i//br	_	_	_	
Outcome						http://bmjopen.bmj.com/ 				
Morbidity	12	12	1.022 (1.016, 1.029)	37.20%	0.163	4 en.b	. 5	1.018 (1.006, 1.031)	39.50%	
Mortality	14	15	1.003 (1.001, 1.006)	29.70%	0.266	4 0	4	1.006 (0.993, 1.019)	42.90%	
Respiratory Diseases										
Age						on A				
All population	16	18	1.010 (0.996, 1.025)	87.20%	0.627	April 1	8	1.002 (0.990, 1.014)	43.80%	
Sensitive analysis on study of partial temporal overlap from the same geographical location	12	12	1.008 (0.992, 1.023)	90.30%	0.449	9, 2024		_	_	
≥65	3	4	1.038 (1.006, 1.071)	82.90%	_	— by	_	_	_	
Outcome						guest.				
Morbidity	10	10	1.012 (0.993, 1.031)	91.80%	0.671	3 E	5	0.996 (0.987, 1.004)	0	
Mortality	10	11	1.013 (0.997, 1.030)	66.40%	0.328	3 rote		1.017 (0.985, 1.050)	48.30%	
						cted				
						by соругі				
						ν				

#### 3.2 Long-term impact of BC or EC on cardiovascular and respiratory diseases

Five studies assessed the long-term exposure to BC or EC and cardiovascular diseases, and a positive association was observed (RR=1.068, 95% CI: 1.004-1.135) (Supplementary Figure S5). Three studies assessed the long-term exposure to BC or EC and ischemic heart disease (IHD), and a positive association was observed (RR=1.066, 95% CI: 1.009-1.127). On the other hand, 4 studies assessed the long-term exposure to BC or EC and respiratory mortality. Meta-analysis was not performed due to limited included studies and no association was observed among the include studies.<sup>20, 53, 61, 68</sup> However, one study analyzed COPD. It indicated that long-term exposure to BC or EC was associated with an increased risk of chronic obstructive pulmonary disease (COPD) morbidity (RR=1.060, 95% CI: 1.020-1.100), while no impact was observed for COPD mortality (RR=1.070, 95% CI: 1.000-1.140).<sup>19</sup>

#### 3.3 Results from the PM<sub>2.5</sub>-adjusted model

In the PM<sub>2.5</sub>-adjusted model, six studies were included in the meta-analysis of short-term exposure to BC or EC and cardiovascular diseases (RR=1.014 per 1  $\mu$ g/m³, 95% CI: 1.001-1.027) (Supplementary Figure S6). The meta-analysis indicated that the association was robust compared to the results of the PM<sub>2.5</sub>-unadjusted model. In addition, the impact of BC or EC on cardiovascular morbidity in the PM<sub>2.5</sub>-adjusted model (RR=1.018 per 1  $\mu$ g/m³, 95% CI: 1.006-1.031) was consistent with the results in the PM<sub>2.5</sub>-unadjusted model (RR=1.022 per 1  $\mu$ g/m³, 95% CI: 1.016-1.029). However, an increased risk was found between BC or EC and cardiovascular

mortality in the  $PM_{2.5}$ -unadjusted model (RR=1.003 per 1  $\mu g/m^3$ , 95% CI: 1.001-1.006), while no association was observed in the  $PM_{2.5}$ -adjusted model (RR=1.006 per 1  $\mu g/m^3$ , 95% CI: 0.993-1.019) (Table 1). On the other hand, consistent results (RR=1.002 per 1  $\mu g/m^3$ , 95% CI: 0.990-1.014) were observed in the meta-analysis of the  $PM_{2.5}$ -adjusted models for respiratory diseases (Supplementary Figure S7). In addition, results of BC or EC on respiratory morbidity and mortality in the  $PM_{2.5}$ -adjusted models were also consistent with the results in the  $PM_{2.5}$ -unadjusted model (Table 1).

#### 3.4 Sensitive analysis

In the sensitive analysis, similar results were observed from the overall analysis of all age populations. Increased risk of cardiovascular diseases after exposure to BC or EC was found (RR=1.006 per 1  $\mu$ g/m³, 95% CI: 1.002-1.010) by eliminating studies with partial overlap from the same geographical location. <sup>16, 18, 31, 73</sup> In addition, no statistical significance was observed (RR=1.008 per 1  $\mu$ g/m³, 95% CI: 0.992-1.023) between respiratory diseases and BC or EC after eliminating overlapped studies (Table 1). <sup>16, 18, 81, 87</sup>

#### 3.5 Risk of bias and certainty of evidence

The risk of bias assessment of the included studies is shown in Table 2 and more analytically in Supplementary Table S4. In general, the majority of the included studies were rated as "low risk" in the items of outcome assessment, selection bias, incomplete outcome data, conflict of interest and other bias. The confounding bias and selective reporting were mostly rated as "probably low". However, 7 studies were

rated as "probably high" risk because not all critical potential confounders were adjusted in the analysis.<sup>7, 19, 21, 39, 48, 67, 84</sup> In addition, the majority of the included studies on the exposure assessment were assessed as "probably low" and "probably high", and in some cases studies were rated as "high" risk. Three studies were rated as "high risk" on exposure assessment mainly because pollutant were measured with a single monitoring over a large geographical area, not measured at least daily.<sup>46, 78, 85</sup>

The certainty of the evidence on the acute effects of BC or EC on cardiovascular diseases in the PM<sub>2.5</sub>-adjusted model was rated as "high", and "moderate" for respiratory diseases in all population as assessed by the adapted GRADE. The evidence on the chronic effects of BC or EC on cardiovascular diseases was evaluated as "high" certainty (Supplementary Table S5).

Table 2 Results of risk of bias assessment

			Key criteria			Otl	ner criteria		
No.	Study	Exposure	Outcome	Confounding	Selection	Incomplete	Selective	Conflict of	Other
		assessment	assessment	bias	bias	outcome data	reporting	interest	Other
1	Atkinson et al. 2016								
2	Bell et al. 2014								
3	Cai et al. 2014								
4	Geng et al. 2013								
5	Hua et al. 2014								
6	Ostro et al. 2015a								
7	Samoli et al. 2016								
8	Zanobetti and Schwartz 2006								
9	Liu et al. 2016a								
10	Liu et al. 2016b								
11	Sarnat et al. 2015								
12	Kim et al. 2012								
13	Ostro et al. 2009								
14	Kim et al. 2015								
15	Huang et al. 2012								
16	Peng et al. 2009					•			
17	Levy et al. 2012								
18	Son et al. 2012								
19	Heo et al. 2014								
20	Basagaña et al. 2015								
21	Dai et al. 2014								
22	Lin et al. 2016a								
23	Cao et al. 2012								
24	Klemm et al. 2011								
25	Zhou et al. 2011								
26	Winquist et al. 2015								
27	Ostro et al. 2007								
28	Tolbert et al. 2000								
29	Wang and Lin 2016								
30	Darrow et al. 2014								
31	Metzger et al. 2004								
32	Mar et al. 2000								
33	Wang et al. 2019a								
34	Lin et al. 2016b								
35	Ostro et al. 2008								

Table 2 Results of risk of bias assessment (continued)

			Key criteria	1		Ot	her criteria		
No.	Study	Exposure	Outcome	Confounding	Selection	Incomplete	Selective	Conflict	Othon
		assessment	assessment	bias	bias	outcome data	reporting	of interest	Other
36	Ito et al. 2011								
37	Chen et al. 2014								
38	Tomic'-Spiric' et al. 2019								
39	Maynard et al. 2007								
40	Sinclair et al. 2010								
41	Krall et al. 2013								
42	Cakmak et al. 2009								
43	Tolbert et al. 2007								
44	Lall et al. 2011								
45	Jung and Lin 2017								
46	Gong et al. 2019								
47	Mostofsky et al. 2012								
48	Krall et al. 2017								
49	O'Lenick et al. 2017								
50	Pearce et al. 2015								
51	Strickland et al. 2010								
52	Strickland et al. 2014								
53	Ito et al. 2013								
54	Ostro et al. 2015b								
55	Gan et al. 2013								
56	Hvidtfeldt et al. 2019								
57	Thurston et al. 2016								
58	Yang et al. 2018								
59	Gan et al. 2011								
60	De Kluizenaar et al. 2013								
61	Vedal et al. 2013								
62	Rahmatinia et al. 2021								
63	Liu et al. 2021b								
64	Lavigne et al. 2021								
65	Rodins et al. 2020								
66	Kovačević et al. 2020								
67	Hasslöf et al. 2020								
68	Wang et al. 2019b								
69	Ljungman et al. 2019								
70	Liu et al. 2021a								
	Risk of bias rating:	Low		Probably Low		Probably High		High	

# 4. Discussion

A comprehensive search of three electronic databases was performed using a well-defined search strategy. Finally, 70 studies assessing the short-term and long-term impacts of BC or EC on cardiovascular and respiratory morbidity and mortality were included. The pooled effect estimates indicated that the short-term exposure to BC or EC was associated with an increased risk of cardiovascular diseases, but had no impact on respiratory diseases in all populations. BC or EC was related with cardiovascular diseases in the elderly (65+ years). Impact of short-term exposure to BC or EC on cardiovascular morbidity was stronger than mortality. In addition, association between short-term exposure to BC or EC and cardiovascular diseases differ across continents.

# 4.1 Short-term exposure to BC or EC was related with cardiovascular diseases in the elderly

Overall, the meta-analysis results indicated that short-term exposure to BC or EC was associated with an increased risk of cardiovascular diseases, but had no impact on respiratory diseases in all populations. In general, consistent results in the PM<sub>2.5</sub>-adjusted model were obtained in the PM<sub>2.5</sub>-unadjusted model and sensitivity analysis showed that the associations were robust. In addition, the association of short-term exposure to BC or EC on cardiovascular morbidity was stronger than mortality. However, the association between BC or EC and cardiovascular mortality should be further explored by further studies, which should pay more attention to the PM<sub>2.5</sub>-adjusted model. Subgroup analysis indicated that the effects of BC or EC on

cardiovascular diseases were the most significant on the current day and the impacts were decreased with lag days. In addition, the association between BC or EC and cardiovascular mortality in the cold season was stronger than that in the warm season. A potential reason could be that the concentration of BC or EC in the cold season was higher than that in the warm season. 90-92 Subgroup analysis on pollutant (BC and EC) indicated that the results from the PM<sub>2.5</sub>-unadjusted model and PM<sub>2.5</sub>-adjusted model were not consistent. Furthermore, the sensitivity analysis on omitting a single study showed that the results were not robust (data not shown). An essential reason could be that BC and EC were considered interchangeable. Three included studies simultaneously assessed the effects of BC and EC on cardiovascular diseases. 17, 56, 86 The results in Winguist et al show that the impact of EC (RR=1.048, 95% CI: 1.012– 1.085) on cardiovascular morbidity was higher than that of BC (RR=1.040, 95% CI: 1.011–1.071) in the PM<sub>2.5</sub>-unadjusted model. <sup>56</sup> However, in the PM<sub>2.5</sub>-adjusted model, no statistically significant difference was observed between EC (RR=1.039, 95% CI: 0.993-1.083) and cardiovascular morbidity. In addition, Samoli et al illustrated that the impact of BC and EC on cardiovascular morbidity differed in the elderly and other age groups, while Atkinson et al indicated no statistically significant difference between BC or EC and cardiovascular mortality in both the PM2.5-adjusted model and PM<sub>2.5</sub>-unadjusted model.<sup>17, 78</sup> On the other hand, increased risk of long-term exposure to BC or EC and cardiovascular diseases was observed. However, in this meta-analysis, due to the limited number of included studies, only short-term exposure to asthma morbidity was evaluated. In addition, a subgroup analysis on the chronic effects of BC or EC on cardiovascular and respiratory diseases was not performed as well because of the limited number of included studies.

The overall quality of the acute effects of BC or EC on cardiovascular diseases in all populations in the PM<sub>2.5</sub>-unadjusted model was evaluated as "moderate" certainty. We downgraded one level for publication bias, hence the estimate was adjusted using the trim and fill method. Several pieces of evidence (acute effects of BC or EC on cardiovascular diseases in all populations in PM<sub>2.5</sub>-unadjusted/adjusted model and chronic effects of BC or EC on cardiovascular diseases in PM<sub>2.5</sub>-unadjusted model) upgrade one level on concentration-response gradient for an increase in risk with increasing BC or EC.<sup>24</sup> In addition, inconsistency was not downgraded because 80% PI does not include unity, or it include unity but less than twice the 95% CI.

#### 4.2 Vulnerable populations

This meta-analysis revealed that BC or EC has acute effects on cardiovascular diseases in the elderly. Different indoor or outdoor activity patterns, occupational exposure, and social network make the elderly at higher risk of BC exposure. In addition, lung function and mucociliary clearance decline with long-term exposure to pollutants and increasing age. In these factors contribute to make the elderly more vulnerable to BC. On the other hand, this meta-analysis indicated that an increased risk was observed between BC or EC and asthma morbidity in children of 0-18 years. Asthma, a chronic airway disorder, is a serious health disease and previous studies indicated that children had higher PM<sub>2.5</sub> deposition rather than the adults, and BC is an essential constituent of PM<sub>2.5</sub>. In addition, BC activates macrophages from the

lung cells, which release pro-inflammatory mediators, finally leading to an accumulation of inflammatory cells. Persistent airway inflammation is a pathological feature of asthma. 97

#### 4.3 Underlying pathological mechanism

In our study, the pooled effect estimate indicated that short-term and long-term exposure to BC or EC was associated with an increased risk of cardiovascular diseases. A series of studies explored the underlying mechanisms between BC and cardiovascular diseases. An animal study conducted by Niwa et al revealed that BC accelerated atherosclerotic plaque formation. Yamawaki et al found that BC directly impacts the vascular endothelium, causing inflammatory responses, cytotoxic injury, and inhibition of cell growth. These responses contribute to the progression of atherosclerosis, leading to cardiovascular disease. Furthermore, a human panel study was performed to assess whether the patients with IHD experience change in the repolarization parameters exposure to rising concentration of pollutants. The results indicated that the variability of the T-wave complexity increased with increasing EC during periods of 0-5 hours, 12-17 hours and 0-2 hours before ECG measurement.

#### 4.4 Suggestions for further research

First, critical potential confounders (temperature, seasonality, day of the week, and long-term trends) and other potential confounders (holidays and influenza epidemics) should be considered in time series and case crossover studies, especially for influenza epidemics. Influenza epidemics are factors usually neglected in short-term studies. Second, studies should adjust PM<sub>2.5</sub> when assessing the health

effect of PM<sub>2.5</sub> constituents. Mostofsky et al. proved that PM<sub>2.5</sub> may be associated with both health and its constituents. Constituent having closer association with PM<sub>2.5</sub> may illustrate a stronger association with diseases. Therefore, the results of PM<sub>2.5</sub>-unadjusted model could introduce bias.<sup>7</sup> Third, further studies are suggested to evaluate the health effects of long-term exposure to BC, especially for morbidity. An essential difficulty that needs to be acknowledged is the availability of the disease data. Emergency department visits and outpatient are more time-sensitive data than mortality; hence these indicators are more representative to some extent in investigating the health effects of environmental factors. However, the data of emergency department visits and outpatient generally from medical institutions are more difficult to obtain than data on mortality, with a large portion of mortality data arriving from departments of disease control institutions in China. Forth, the present evidence on the health effects of BC was mainly confined in America and Asia. Studies assessing the association in other geographical locations are suggested, which might contribute the evaluation of the potentially different effects of BC in different continents. Fifth, more studies need to provide evidence to prove the association between BC or EC and respiratory diseases in vulnerable populations.

#### 4.5 Strength and limitation

This systematic review and meta-analysis provided a comprehensive and current evidence for the short-term and long-term exposure to BC or EC on cardiorespiratory morbidity and mortality. Adapted GRADE framework was used to assess the certainty of the evidence. The evidence can support the update of the WHO Global Air Quality

Guidelines. Potential limitations in our study are as follows. A significant heterogeneity for the pooled estimates was noticed in the meta-analysis, which might be due to the high variability in the study population, outcomes, and geographical locations. Therefore, subgroup analyses on age of the population (all and older than 65 years old), outcomes (morbidity and mortality), geological locations (Europe, America and Asia) and lag days (0, 1, 2 days) were conducted for a further investigation of the potential sources in conditions more than 3 estimates. Most of the included literatures in our study were from the US or China, which affected the pooled estimates, although it is an inherent and inevitable selection bias. We have extracted and calculated the regional distribution of BC concentration of included studies. It showed that the mean BC concentration is highest in Asia, which maybe an essential reason of the results. In addition, consistent results of cardiovascular and respiratory diseases exposure to BC or EC were observed by eliminating studies with partial overlap from the same geographical locations.

#### 5. Conclusions

Both short-term and long-term exposure to BC or EC were related with cardiovascular diseases and the association differs across continents. The short-term exposure to BC or EC was associated with an increased risk of cardiovascular diseases in the elderly and childhood asthma. In addition, short-term exposure to BC or EC-related cardiovascular diseases attributable to morbidity was higher than the one attributable to mortality, and the associations differ across continents.

# Acknowledgements

We would like to thank the authors of the original studies for their contributions to our systematic review and meta-analysis, especially authors who provided their raw data for the analysis.



# **Contributorship statement**

SW, XZ and XS developed the research design. XS, YH, YM and LJ analyzed the data and interpreted the results. XS, YH, YM, XW and JZ drafted manuscript. AS, YuL, YaL, JT, XL and YG did literature screening and data extraction. All of the authors contributed to drafting the manuscript. The final manuscript was approved by TO CORRECTION ONLY all authors.

# **Funding**

The work was supported by the National Key Research and Development Program of China (No.2016YFA0602004) and Innovation Fund Project on Public Meteorological Service Center of China Meteorological Administration in 2020 (Grant numbers: K2020010).



# **Competing interests**

We declare that all authors have no competing interests.



# **Data sharing statement**

All data relevant to the study are included in the article or uploaded as supplementary information.



#### Reference

- 1. Bond TC, Doherty SJ, Fahey DW. Bounding the role of black carbon in the climate system: A scientific assessment. *Journal of geophysical research: Atmospheres*. 2013;118(11):5380-552.
- 2. Zencak Z, Elmquist M, Gustafsson Ö. Quantification and radiocarbon source apportionment of black carbon in atmospheric aerosols using the CTO-375 method. *Atmospheric Environment*. 2007;41(36):7895-906.
- 3. Atkinson RW, Kang S, Anderson HR, et al. Epidemiological time series studies of PM2.5 and daily mortality and hospital admissions: a systematic review and meta-analysis. *Thorax*. 2014;69(7):660-5.
- 4. Global, regional, and national comparative risk assessment of 84 behavioural, environmental and occupational, and metabolic risks or clusters of risks for 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet*. 2018;392(10159):1923-94.
- 5. Ross MA. Integrated science assessment for particulate matter. *US Environmental Protection Agency: Washington DC, USA*. 2009:61-161.
- 6. Bell ML, Dominici F, Ebisu K, et al. Spatial and temporal variation in PM(2.5) chemical composition in the United States for health effects studies. *Environ Health Perspect*. 2007;115(7):989-95.
- 7. Mostofsky E, Schwartz J, Coull BA, et al. Modeling the association between particle constituents of air pollution and health outcomes. *Am J Epidemiol*. 2012;176(4):317-26.
- 8. Janssen N, Gerlofs NM, Lanki T. Health effects of black carbon, The WHO European Centre for Environment and Health, Bonn, Germany. World Health Organisation Regional Office for Europe, Copenhagen, Denmark. 2012.
- 9. Grahame TJ, Klemm R, Schlesinger RB. Public health and components of particulate matter: the changing assessment of black carbon. *J Air Waste Manag Assoc.* 2014;64(6):620-60.
- 10. Husain M, Kyjovska ZO, Bourdon-Lacombe J, et al. Carbon black nanoparticles induce biphasic gene expression changes associated with inflammatory responses in the lungs of C57BL/6 mice following a single intratracheal instillation. *Toxicol Appl Pharmacol*. 2015;289(3):573-88.

- 11. Colicino E, Giuliano G, Power MC, et al. Long-term exposure to black carbon, cognition and single nucleotide polymorphisms in microRNA processing genes in older men. *Environ Int*. 2016;88:86-93.
- 12. Büchner N, Ale-Agha N, Jakob S, et al. Unhealthy diet and ultrafine carbon black particles induce senescence and disease associated phenotypic changes. *Exp Gerontol*. 2013;48(1).
- 13. Achilleos S, Kioumourtzoglou M-A, Wu C-D, et al. Acute effects of fine particulate matter constituents on mortality: A systematic review and meta-regression analysis. *Environ Int.* 2017;109.
- 14. Luben TJ, Nichols JL, Dutton SJ, et al. A systematic review of cardiovascular emergency department visits, hospital admissions and mortality associated with ambient black carbon. *Environ Int.* 2017;107:154-62.
- 15. Cumberbatch MG, Rota M, Catto JWF, et al. The Role of Tobacco Smoke in Bladder and Kidney Carcinogenesis: A Comparison of Exposures and Meta-analysis of Incidence and Mortality Risks. *Eur Urol.* 2016;70(3):458-66.
- 16. Ostro B, Hu J, Goldberg D, et al. Associations of mortality with long-term exposures to fine and ultrafine particles, species and sources: results from the California Teachers Study Cohort. *Environ Health Perspect*. 2015;123(6):549-56.
- 17. Samoli E, Atkinson RW, Analitis A, et al. Associations of short-term exposure to traffic-related air pollution with cardiovascular and respiratory hospital admissions in London, UK. *Occup Environ Med.* 2016;73(5):300-7.
- 18. Basagaña X, Jacquemin B, Karanasiou A, et al. Short-term effects of particulate matter constituents on daily hospitalizations and mortality in five South-European cities: results from the MED-PARTICLES project. *Environ Int.* 2015;75:151-8.
- 19. Gan WQ, FitzGerald JM, Carlsten C, et al. Associations of ambient air pollution with chronic obstructive pulmonary disease hospitalization and mortality. *Am J Respir Crit Care Med*. 2013;187(7):721-7.
- 20. Ostro B, Tobias A, Karanasiou A, et al. The risks of acute exposure to black carbon in Southern Europe: results from the MED-PARTICLES project. *Occup Environ Med*. 2015;72(2):123-9.
- 21. Thurston GD, Burnett RT, Turner MC, et al. Ischemic Heart Disease Mortality and 34

- Long-Term Exposure to Source-Related Components of U.S. Fine Particle Air Pollution. *Environ Health Perspect*. 2016;124(6):785-94.
- 22. National Toxicology Program. Handbook for conducting a literature-based health assessment using OHAT approach for systematic review and evidence integration. Office of Health Assessment and Translation (OHAT), Division of the National Toxicology Program, National Institute of Environmental Health Sciences <a href="https://ntpniehsnihgov/ntp/ohat/">https://ntpniehsnihgov/ntp/ohat/</a> pubs/handbookjan2015 508pdf 2015.
- 23. Lam J, Sutton P, Kalkbrenner A, et al. A Systematic Review and Meta-Analysis of Multiple Airborne Pollutants and Autism Spectrum Disorder. *PLoS One*. 2016;11(9):e0161851.
- 24. Morgan RL, Thayer KA, Santesso N, et al. A risk of bias instrument for non-randomized studies of exposures: A users' guide to its application in the context of GRADE. *Environ Int.* 2019;122:168-84.
- 25. Strickland MJ, Darrow LA, Mulholland JA, et al. Implications of different approaches for characterizing ambient air pollutant concentrations within the urban airshed for time-series studies and health benefits analyses. *Environ Health*. 2011;10:36.
- 26. Nayebare SR, Aburizaiza OS, Siddique A, et al. Association of fine particulate air pollution with cardiopulmonary morbidity in Western Coast of Saudi Arabia. *Saudi Med J*. 2017;38(9):905-12.
- 27. Cai J, Zhao A, Zhao J, et al. Acute effects of air pollution on asthma hospitalization in Shanghai, China. *Environ Pollut*. 2014;191:139-44.
- 28. Hua J, Yin Y, Peng L, et al. Acute effects of black carbon and PM<sub>2.5</sub> on children asthma admissions: a time-series study in a Chinese city. *Sci Total Environ*. 2014;481:433-8.
- 29. Darrow LA, Klein M, Flanders WD, et al. Air pollution and acute respiratory infections among children 0-4 years of age: an 18-year time-series study. *Am J Epidemiol*. 2014;180(10):968-77.
- 30. Zanobetti A, Schwartz J. Air pollution and emergency admissions in Boston, MA. *J Epidemiol Community Health*. 2006;60(10):890-5.
- 31. Metzger KB, Tolbert PE, Klein M, et al. Ambient air pollution and cardiovascular emergency department visits. *Epidemiology*. 2004;15(1):46-56.
- 32. O'Lenick CR, Winquist A, Mulholland JA, et al. Assessment of neighbourhood-level 35

socioeconomic status as a modifier of air pollution-asthma associations among children in Atlanta. *J Epidemiol Community Health.* 2017;71(2):129-36.

- 33. Mar TF, Norris GA, Koenig JQ, et al. Associations between air pollution and mortality in Phoenix, 1995-1997. *Environ Health Perspect*. 2000;108(4):347-53.
- 34. Krall JR, Mulholland JA, Russell AG, et al. Associations between Source-Specific Fine Particulate Matter and Emergency Department Visits for Respiratory Disease in Four U.S. Cities. *Environ Health Perspect*. 2017;125(1).
- 35. Gong T, Sun Z, Zhang X, et al. Associations of black carbon and PM2.5 with daily cardiovascular mortality in Beijing, China. *Atmospheric Environment*. 2019;214:116876.
- 36. Wang Y, Shi Z, Shen F, et al. Associations of daily mortality with short-term exposure to PM and its constituents in Shanghai, China. *Chemosphere*. 2019;233:879-87.
- 37. Dai L, Zanobetti A, Koutrakis P, et al. Associations of fine particulate matter species with mortality in the United States: a multicity time-series analysis. *Environ Health Perspect*. 2014;122(8):837-42.
- 38. Bell ML, Ebisu K, Leaderer BP, et al. Associations of  $PM_{2.5}$  constituents and sources with hospital admissions: analysis of four counties in Connecticut and Massachusetts (USA) for persons  $\geq$  65 years of age. *Environ Health Perspect*. 2014;122(2):138-44.
- 39. Wang M, Hopke PK, Masiol M, et al. Changes in triggering of ST-elevation myocardial infarction by particulate air pollution in Monroe County, New York over time: a case-crossover study. *Environmental Health*. 2019;18(1).
- 40. Son JY, Lee JT, Kim KH, et al. Characterization of fine particulate matter and associations between particulate chemical constituents and mortality in Seoul, Korea. *Environ Health Perspect*. 2012;120(6):872-8.
- 41. Cakmak S, Dales RE, Gultekin T, et al. Components of particulate air pollution and emergency department visits in Chile. *Arch Environ Occup Health*. 2009;64(3):148-55.
- 42. Geng F, Hua J, Mu Z, et al. Differentiating the associations of black carbon and fine particle with daily mortality in a Chinese city. *Environ Res.* 2013;120:27-32.
- 43. Lin H, Tao J, Du Y, et al. Differentiating the effects of characteristics of PM pollution on mortality from ischemic and hemorrhagic strokes. *Int J Hyg Environ Health*. 2016;219(2):204-11.
- 44. Lall R, Ito K, Thurston GD. Distributed lag analyses of daily hospital admissions and

source-apportioned fine particle air pollution. Environ Health Perspect. 2011;119(4):455-60.

- 45. Ostro B, Feng WY, Broadwin R, et al. The effects of components of fine particulate air pollution on mortality in california: results from CALFINE. *Environ Health Perspect*. 2007;115(1):13-9.
- 46. Ostro B, Roth L, Malig B, et al. The effects of fine particle components on respiratory hospital admissions in children. *Environ Health Perspect*. 2009;117(3):475-80.
- 47. Peng RD, Bell ML, Geyh AS, et al. Emergency admissions for cardiovascular and respiratory diseases and the chemical composition of fine particle air pollution. *Environ Health Perspect*. 2009;117(6):957-63.
- 48. Tomić-Spirić V, Kovačević G, Marinković J, et al. Evaluation of the Impact of Black Carbon on the Worsening of Allergic Respiratory Diseases in the Region of Western Serbia: A Time-Stratified Case-Crossover Study. *Medicina (Kaunas)*. 2019;55(6).
- 49. Pearce JL, Waller LA, Mulholland JA, et al. Exploring associations between multipollutant day types and asthma morbidity: epidemiologic applications of self-organizing map ambient air quality classifications. *Environ Health*. 2015;14:55.
- 50. Heo J, Schauer JJ, Yi O, et al. Fine particle air pollution and mortality: importance of specific sources and chemical species. *Epidemiology*. 2014;25(3):379-88.
- 51. Liu S, Ganduglia CM, Li X, et al. Fine particulate matter components and emergency department visits among a privately insured population in Greater Houston. *Sci Total Environ*. 2016;566-567:521-7.
- 52. Sarnat SE, Winquist A, Schauer JJ, et al. Fine particulate matter components and emergency department visits for cardiovascular and respiratory diseases in the St. Louis, Missouri-Illinois, metropolitan area. *Environ Health Perspect*. 2015;123(5):437-44.
- 53. Lavigne É, Talarico R, van Donkelaar A, et al. Fine particulate matter concentration and composition and the incidence of childhood asthma. *Environ Int.* 2021;152:106486.
- 54. Cao J, Xu H, Xu Q, et al. Fine particulate matter constituents and cardiopulmonary mortality in a heavily polluted Chinese city. *Environ Health Perspect*. 2012;120(3):373-8.
- 55. Ito K, Mathes R, Ross Z, et al. Fine particulate matter constituents associated with cardiovascular hospitalizations and mortality in New York City. *Environ Health Perspect*. 2011;119(4):467-73.

- 56. Winquist A, Schauer JJ, Turner JR, et al. Impact of ambient fine particulate matter carbon measurement methods on observed associations with acute cardiorespiratory morbidity. *J Expo Sci Environ Epidemiol*. 2015;25(2):215-21.
- 57. Ostro BD, Feng WY, Broadwin R, et al. The impact of components of fine particulate matter on cardiovascular mortality in susceptible subpopulations. *Occup Environ Med*. 2008;65(11):750-6.
- 58. Klemm RJ, Thomas EL, Wyzga RE. The impact of frequency and duration of air quality monitoring: Atlanta, GA, data modeling of air pollution and mortality. *J Air Waste Manag Assoc*. 2011;61(11):1281-91.
- 59. Chen SY, Lin YL, Chang WT, et al. Increasing emergency room visits for stroke by elevated levels of fine particulate constituents. *Sci Total Environ*. 2014;473-474:446-50.
- 60. Tolbert PE, Klein M, Metzger KB, et al. Interim results of the study of particulates and health in Atlanta (SOPHIA). *J Expo Anal Environ Epidemiol*. 2000;10(5):446-60.
- 61. Yang Y, Tang R, Qiu H, et al. Long term exposure to air pollution and mortality in an elderly cohort in Hong Kong. *Environ Int.* 2018;117.
- 62. Hasslöf H, Molnár P, Andersson EM, et al. Long-term exposure to air pollution and atherosclerosis in the carotid arteries in the Malmö diet and cancer cohort. *Environ Res*. 2020;191:110095.
- 63. Rodins V, Lucht S, Ohlwein S, et al. Long-term exposure to ambient source-specific particulate matter and its components and incidence of cardiovascular events The Heinz Nixdorf Recall study. *Environ Int.* 2020;142.
- 64. Liu L, Zhang Y, Yang Z, et al. Long-term exposure to fine particulate constituents and cardiovascular diseases in Chinese adults. *Journal of Hazardous Materials*. 2021;416.
- 65. Liu S, Jorgensen JT, Ljungman P, et al. Long-term exposure to low-level air pollution and incidence of chronic obstructive pulmonary disease: The ELAPSE project. *Environ Int.* 2021;146.
- 66. Ljungman PLS, Andersson N, Stockfelt L, et al. Long-Term Exposure to Particulate Air Pollution, Black Carbon, and Their Source Components in Relation to Ischemic Heart Disease and Stroke. *Environ Health Perspect*. 2019;127(10):107012.
- 67. Gan WQ, Koehoorn M, Davies HW, et al. Long-term exposure to traffic-related air pollution and the risk of coronary heart disease hospitalization and mortality. *Environ Health Perspect*.

2011;119(4):501-7.

- 68. Hvidtfeldt UA, Sørensen M, Geels C, et al. Long-term residential exposure to PM2.5, PM10, black carbon, NO2, and ozone and mortality in a Danish cohort. *Environ Int.* 2019;123:265-72.
- 69. Levy JI, Diez D, Dou Y, et al. A meta-analysis and multisite time-series analysis of the differential toxicity of major fine particulate matter constituents. *Am J Epidemiol*. 2012;175(11):1091-9.
- 70. Strickland MJ, Klein M, Flanders WD, et al. Modification of the effect of ambient air pollution on pediatric asthma emergency visits: susceptible subpopulations. *Epidemiology*. 2014;25(6):843-50.
- 71. Wang YC, Lin YK. Mortality and emergency room visits associated with ambient particulate matter constituents in metropolitan Taipei. *Sci Total Environ*. 2016;569-570:1427-34.
- 72. Maynard D, Coull BA, Gryparis A, et al. Mortality risk associated with short-term exposure to traffic particles and sulfates. *Environ Health Perspect*. 2007;115(5):751-5.
- 73. Tolbert PE, Klein M, Peel JL, et al. Multipollutant modeling issues in a study of ambient air quality and emergency department visits in Atlanta. *J Expo Sci Environ Epidemiol*. 2007;17 Suppl 2:S29-S35.
- 74. Vedal S, Campen MJ, McDonald JD, et al. National Particle Component Toxicity (NPACT) initiative report on cardiovascular effects. *Res Rep Health Eff Inst*. 2013(178):5-8.
- 75. Ito K, Ross Z, Zhou J, et al. NPACT Study 3. Time-Series Analysis of Mortality, Hospitalizations, and Ambient PM2.5 and Its Components. In: National Particle Component Toxicity (NPACT) Initiative: Integrated Epidemiologic and Toxicologic Studies of the Health Effects of Particulate Matter Components. Research Report 177. Health Effects Institute, Boston, MA. *Res Rep Health Eff Inst.* 2013.
- 76. Lin H, Tao J, Du Y, et al. Particle size and chemical constituents of ambient particulate pollution associated with cardiovascular mortality in Guangzhou, China. *Environ Pollut*. 2016;208(Pt B):758-66.
- 77. Jung CR, Young LH, Hsu HT, et al. PM components and outpatient visits for asthma: A time-stratified case-crossover study in a suburban area. *Environ Pollut*. 2017;231(Pt 1):1085-92.
- 78. Rahmatinia M, Hadei M, Hopke PK, et al. Relationship between ambient black carbon and daily mortality in Tehran, Iran: a distributed lag nonlinear time series analysis. *Journal of*

environmental health science & engineering. 2021;19(1):907-16.

- 79. de Kluizenaar Y, van Lenthe FJ, Visschedijk AJH, et al. Road traffic noise, air pollution components and cardiovascular events. *Noise Health*. 2013;15(67):388-97.
- 80. Huang W, Cao J, Tao Y, et al. Seasonal variation of chemical species associated with short-term mortality effects of PM(2.5) in Xi'an, a Central City in China. *Am J Epidemiol*. 2012;175(6):556-66.
- 81. Kim SY, Dutton SJ, Sheppard L, et al. The short-term association of selected components of fine particulate matter and mortality in the Denver Aerosol Sources and Health (DASH) study. *Environ Health*. 2015;14:49.
- 82. Strickland MJ, Darrow LA, Klein M, et al. Short-term associations between ambient air pollutants and pediatric asthma emergency department visits. *Am J Respir Crit Care Med*. 2010;182(3):307-16.
- 83. Liu S, Ganduglia CM, Li X, et al. Short-term associations of fine particulate matter components and emergency hospital admissions among a privately insured population in Greater Houston. *Atmospheric Environment*. 2016;147:369-75.
- 84. Kovacevic G, Spiric VT, Marinkovic J, et al. Short-Term effects of air pollution on exacerbations of allergic asthma in uzice region, serbia. *Postepy Dermatologii i Alergologii*. 2020;37(3):377-83.
- 85. Krall JR, Anderson GB, Dominici F, et al. Short-term exposure to particulate matter constituents and mortality in a national study of U.S. urban communities. *Environ Health Perspect*. 2013;121(10):1148-53.
- 86. Atkinson RW, Analitis A, Samoli E, et al. Short-term exposure to traffic-related air pollution and daily mortality in London, UK. *J Expo Sci Environ Epidemiol*. 2016;26(2):125-32.
- 87. Kim SY, Peel JL, Hannigan MP, et al. The temporal lag structure of short-term associations of fine particulate matter chemical constituents and cardiovascular and respiratory hospitalizations. *Environ Health Perspect*. 2012;120(8):1094-9.
- 88. Zhou J, Ito K, Lall R, et al. Time-series analysis of mortality effects of fine particulate matter components in Detroit and Seattle. *Environ Health Perspect*. 2011;119(4):461-6.
- 89. Sinclair AH, Edgerton ES, Wyzga R, et al. A two-time-period comparison of the effects of ambient air pollution on outpatient visits for acute respiratory illnesses. *J Air Waste Manag Assoc*.

2010;60(2):163-75.

- 90. Anand A, Phuleria HC. Spatial and seasonal variation of outdoor BC and PM 2.5 in densely populated urban slums. *Environ Sci Pollut Res Int*. 2021;28(2):1397-408.
- 91. Chen P, Kang S, Gul C, et al. Seasonality of carbonaceous aerosol composition and light absorption properties in Karachi, Pakistan. *J Environ Sci (China)*. 2020;90:286-96.
- 92. Yang Y, Xu X, Zhang Y, et al. Seasonal size distribution and mixing state of black carbon aerosols in a polluted urban environment of the Yangtze River Delta region, China. *Sci Total Environ*. 2019;654:300-10.
- 93. Bell ML, Zanobetti A, Dominici F. Evidence on vulnerability and susceptibility to health risks associated with short-term exposure to particulate matter: a systematic review and meta-analysis. *Am J Epidemiol*. 2013;178(6):865-76.
- 94. Sinharay R, Gong J, Barratt B, et al. Respiratory and cardiovascular responses to walking down a traffic-polluted road compared with walking in a traffic-free area in participants aged 60 years and older with chronic lung or heart disease and age-matched healthy controls: a randomised, crossover study. *Lancet*. 2018;391(10118):339-49.
- 95. Phalen RF, Oldham MJ, Kleinman MT, et al. TRACHEOBRONCHIAL DEPOSITION PREDICTIONS FOR INFANTS, CHILDREN AND ADOLESCENTS. In: Dodgson J, McCallum RI, Bailey MR, Fisher DR, editors. Inhaled Particles VI: Pergamon; 1988. p. 11-21.
- 96. Cheng Z, Chu H, Wang S, et al. TAK1 knock-down in macrophage alleviate lung inflammation induced by black carbon and aged black carbon. *Environ Pollut*. 2019;253:507-15.
- 97. Bateman ED, Hurd SS, Barnes PJ, et al. Global strategy for asthma management and prevention: GINA executive summary. *Eur Respir J.* 2008;31(1):143-78.
- 98. Niwa Y, Hiura Y, Murayama T, et al. Nano-sized carbon black exposure exacerbates atherosclerosis in LDL-receptor knockout mice. *Circ J.* 2007;71(7):1157-61.
- 99. Yamawaki H, Iwai N. Mechanisms underlying nano-sized air-pollution-mediated progression of atherosclerosis: carbon black causes cytotoxic injury/inflammation and inhibits cell growth in vascular endothelial cells. *Circ J.* 2006;70(1):129-40.
- 100. Henneberger A, Zareba W, Ibald-Mulli A, et al. Repolarization changes induced by air pollution in ischemic heart disease patients. *Environ Health Perspect*. 2005;113(4):440-6.

#### **Table captions**

**Table 1** Short-term impact of BC or EC on cardiovascular and respiratory diseases in different models.

Table 2 Results of risk of bias assessment.

## Figure captions

Figure 1 Flow diagram of literature screening process.

**Figure 2** Impact of short-term exposure to BC or EC on cardiovascular diseases in the  $PM_{2.5}$ -unadjusted model.

**Figure 3** Impact of short-term exposure to BC or EC on respiratory diseases in the PM<sub>2.5</sub>-unadjusted model.

# Appendix A. Supplementary data

 Table S1 Search strategy in PubMed.

**Table S2** Characteristics of the included studies in the systematic review and meta-analysis.

**Table S3** Subgroup analysis on short-term effects of BC or EC on cardiovascular and respiratory diseases.

**Table S4** Assessment of certainty of evidence for the outcomes.

**Table S5** Details of risk of bias assessment.

**Figure S1** Impact of short-term exposure to BC or EC on respiratory diseases in 65+ years age group in the PM<sub>2.5</sub>-unadjusted model.

**Figure S2** Impact of short-term exposure to BC or EC on cardiovascular mortality stratified by geographical locations.

**Figure S3** Impact of short-term exposure to BC or EC on cardiovascular morbidity stratified by geographical locations.

**Figure S4** Impact of short-term exposure to BC or EC on asthma morbidity in different age groups.

Figure S5 Impact of long-term exposure to BC or EC on cardiovascular diseases.

**Figure S6** Impact of short-term exposure to BC or EC on cardiovascular diseases in the  $PM_{2.5}$ -adjusted model.

**Figure S7** Impact of short-term exposure to BC or EC on respiratory diseases in the PM<sub>2.5</sub>-adjusted model.

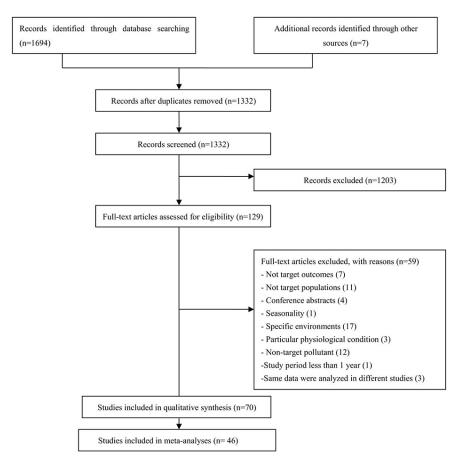


Fig. 1. Flow diagram of literature screening process

Figure 1 Flow diagram of literature screening process.

90x90mm (300 x 300 DPI)

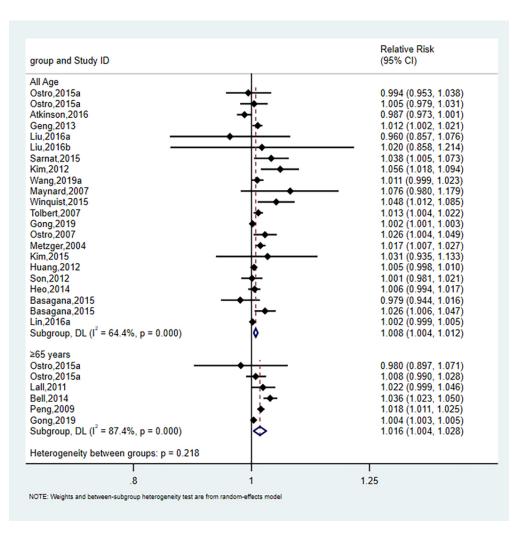


Figure 2 Impact of short-term exposure to BC or EC on cardiovascular diseases in the PM2.5-unadjusted model.

90x90mm (300 x 300 DPI)

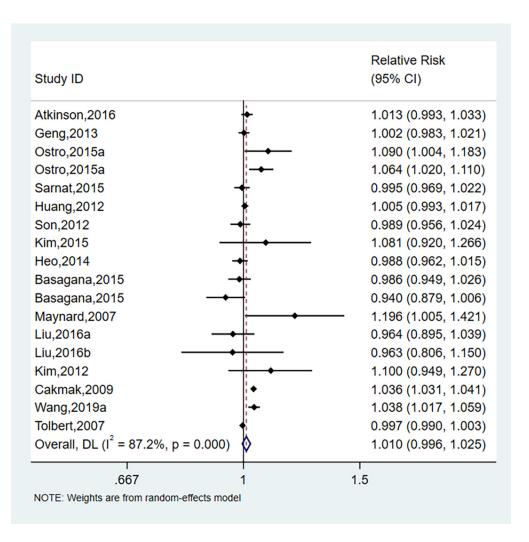


Figure 3 Impact of short-term exposure to BC or EC on respiratory diseases in the PM2.5-unadjusted model.  $90x90mm (300 \times 300 DPI)$ 

#### SUPPLEMENTARY APPENDIX

# Short-term and Long-term Exposure to Black Carbon and Cardiovascular and Respiratory

# Diseases: A Systematic Review and Meta-Analysis

Xuping Song<sup>a</sup>, Yue Hu<sup>a</sup>, Yan Ma<sup>a</sup>, Liangzhen Jiang<sup>a</sup>, Xinyi Wang<sup>c</sup>, Anchen Shi<sup>d</sup>, Junxian Zhao<sup>a</sup>, Yunxu Liu<sup>a</sup>, Yafei Liu<sup>a</sup>, Jing Tang<sup>a</sup>, Xiayang Li<sup>a</sup>, Xiaoling Zhang\*<sup>b</sup>, Yong Guo<sup>e</sup>, Shigong Wang\*<sup>b</sup>

- <sup>a</sup> School of Public Health, Lanzhou University, Lanzhou 730000, China;
- <sup>b</sup> College of Atmospheric Sciences, Chengdu University of Information Technology, Chengdu 610000, China;
- <sup>c</sup> Second Clinical College, Lanzhou University, Lanzhou 730000, China;
- <sup>d</sup> Department of General Surgery, The First Affiliated Hospital of Xi'an Jiao Tong University, Shaanxi 710061, China;
- <sup>e</sup> Department of Civil Affairs in Guizhou Province, Guiyang 550004, China.

#### **Corresponding author 1:**

Name: Xiaoling Zhang

Postal Address: College of Atmospheric Sciences, Chengdu University of Information

Technology, Chengdu 610000, Sichuan, China

E-mail address: xlzhang@ium.cn

Fax: 028-85966502 Corresponding author 2: Name: Shigong Wang

Postal Address: College of Atmospheric Sciences, Chengdu University of Information

Technology, Chengdu 610000, Sichuan, China

E-mail address: wangsg@cuit.edu.cn

Fax: 028-85966502

#### Supplementary data

- Table S1 Search strategy in PubMed
- **Table S2** Characteristics of the included studies in the systematic review and meta-analysis.
- **Table S3** Subgroup analysis on short-term effects of BC or EC on cardiovascular and respiratory diseases.
- Table S4 Assessment of certainty of evidence for the outcomes
- **Table S5** Details of risk of bias assessment.
- **Figure S1** Impact of short-term exposure to BC or EC on respiratory diseases in 65+ years age group in the PM<sub>2.5</sub>-unadjusted model.
- **Figure S2** Impact of short-term exposure to BC or EC on cardiovascular mortality stratified by geographical locations.
- **Figure S3** Impact of short-term exposure to BC or EC on cardiovascular morbidity stratified by geographical locations.
- **Figure S4** Impact of short-term exposure to BC or EC on asthma morbidity in different age groups.
- Figure S5 Impact of long-term exposure to BC or EC on cardiovascular diseases.
- **Figure S6** Impact of short-term exposure to BC or EC on cardiovascular diseases in the PM<sub>2.5</sub>-adjusted model.
- **Figure S7** Impact of short-term exposure to BC or EC on respiratory diseases in the PM<sub>2.5</sub>-adjusted model.

# Table S1 Search Strategy for PubMed

	BMJ Open  BMJ Open  Popen  2021-0495  S1 Search Strategy for PubMed
	) 02
	<b>1-</b> 02
Table	<u>Q</u>
No.	Search Strategy $\omega$
#1	particulate matter/or aerosols.sh.  particulate matter*/or "PM10"/or "PM2.5"/or fine particle*/or thoracic particle*/or ultrafine/or aerosol*/or carbon*/or soot*.ti,ab.  "PM".tw.
#2	particulate matter*/or "PM10"/or "PM2.5"/or fine particle*/or thoracic particle*/or ultrafine/or aerosol*/or carbon*/or soot*.ti,ab.
#3	
#4	or/1,2,3
#5	or/1,2,3 "EC" /or "BC".tw. and/4,5 black carbon*/or elemental carbon*.ti,ab.
#6	and/4,5
#7	black carbon*/or elemental carbon*.ti,ab.
#8	or/6,7
#9	respiratory tract disease.sh.
#10	respirat*/or pulmonary disease*/or lung/or chest infection*/or airway/or asthma*/or pneumonia*/or "chronic obstructive pulmonary disease"/or COPD.ti,ab.
#11	cardiovascular diseases.sh.
#12	cardio/vascular diseases.sn.  cardio*/or cardiop*/or cardior*/or heart/or coronary/or vascular/or blood/or cardiac.ti,ab.  or/9 10 11 12
#13	or/9,10,11,12
#14	morbidity/or hospitalization/or death/or mortality/or outpatient.sh
#15	morbidit*/or hospitalisation*/or hospitalization*/or death*/or mortalit*/or outpatien*/or emergency room*/or emergency department*/g emergency admi*/or hospital admission*.ti,ab.
#16	
#17	epidemiologic studies/or cross over study.sh.
#18	time series*/or timeseries*/or case cross*/or casecross*.tw.
	generalized additive model/or generalised additive model/or generalized linear model/or generalised linear model/or distributed lag non-
#19	model/or distributed lag model/or quasipoisson*/or poisson*/or generalized estimating equation/or generalised estimating equation/or GLM/or DLNM/or GEE/or DLM/or
	ARIMA.tw.
	cohort*/or follow up*/or observational/or longitudinal/or case control*/or epidemiologic/or population
#20	stud*/or prospective*/or retrospective*.tw.
#21	or/17,18,19,20 and/8,13,16,21
#22	and/8,13,16,21
	by c

Table S2 Characteristics of included studies in the systematic review and meta-analysis

Study	Study Design	Country	Study Period	Outcome	Age	Pollutant	ICD code	Siseases
Atkinson et al. 2016	TS	UK	2011-2012	Mortality	All	BC,EC	ICD-10	CVD(ICD-10:100-199),RES(ICD-10:J00-J99) 8
Atkinson et al. 2010	13	OK	2011-2012	Wiortanty	All	ВС,ЕС	ICD-10	RES[COPD(ICD-9-CM:490–492,RTI(ICD-9-CM:464–466, 480–487)];CVD[HF(ICD-9-CM:428),Heart Rhythm
D. II. 4. 1. 2014	TO	TIC A	2000 2004	M 1117	> 65	D.C.	ICD 0	
Bell et al. 2014	TS	USA	2000-2004	Morbidity	≥65	ВС	ICD-9	Disturbances(ICD-9-CM:426-427), Cerebrovascular vents(ICD-9-CM:430-438),IHD(ICD-9-CM:410-414,
	ma	au :				n.a		429),PVD(ICD-9-CM:440–448)]
Cai et al. 2014	TS	China	2005-2011	Morbidity	≥18	BC	ICD-10	
Geng et al. 2013	TS	China	2007-2008	Mortality	All	ВС	ICD-10	CVD(ICD-10:I00-I99),RES(ICD-10:J00-J98)
Hua et al. 2014	TS	China	2007-2012	Morbidity	0-14	BC	ICD-10	Asthma(ICD-10:J45)
Ostro et al. 2015a	CS	Spain, Greece	2008-2009 (Athens), 2009-2010(Barc elona)	Mortality	All	ВС	ICD-10	CVD(ICD-10:100-199),RES(ICD-10:J00-J98)  Asthma(ICD-10:J45)  CVD(ICD-10:100-I99),RES(ICD-10:J00-J99)  CVD(ICD-10:100-I99),RES(ICD-10:J00-J99)
Samoli et al. 2016	TS	UK	2011-2012	Morbidity	≥15(CVD), all ( RES )	BC,EC	ICD-10	CVD(ICD-10:I00-I99),RES(ICD-10:J00-J99)
Zanobetti and Schwartz 2006	CS	USA	1995-1999	Morbidity	≥65	ВС	ICD-9	MI(ICD-9:410),Pneumonia (ICD-9: 480–487)
Lin et al. 2016	TS	USA	2009 2012	Mandai dien	All	EC	ICD-9	CVD(ICD-9:390-429),Stroke(ICD-9:430-438),RES(1CD-9:460-519),COPD(ICD-9:490-492,494,496),Pneumonia(I
Liu et al. 2016a	15	USA	2008-2013	Morbidity	All	EC	ICD-9	CD-9:480-486),Asthma(ICD-9:493),SSID(ICD-9:78
	ma	***			. 11			CVD(ICD-9:390-429),Stroke(ICD-9:430-438),RESRECD-9:460-519),COPD(ICD-9:490-492,494,496),Pneumonia
Liu et al. 2016b	TS	USA	2008-2013	Morbidity	All	EC	ICD-9	(ICD-9:480-486),Asthma(ICD-9:493)
								CVD[IHD(ICD9:410–414),Cardiac Dysrhythmias(ICD9:427),CHF(ICD9:428),Other CVD (ICD-
Sarnat et al. 2015	TS	USA	2001-2003	Morbidity	All	EC	ICD9	9:433-437,440,443-445,451-453)],RES[Pneumonia(IPD):480-486),COPD (ICD:491,492,496),Asthma/Wheeze
								(ICD9:493,786.07),Other RES(ICD9:460–466,477)]
Kim et al. 2012	TS	USA	2003-2007	Morbidity	All	EC	ICD-9	
								CVD(ICD-9:390-459),RES(ICD-9:460-519)

36/bmjopen-2021-04951

Son et al. 2012 TS Korea  Heo et al. 2014 TS Korea  Basagaña et al. 2015 CS Spain, Italy  Dai et al. 2014 TS USA  Lin et al. 2016a TS China  Cao et al. 2012 TS USA  Klemm et al. 2011 TS USA	Period  2000-2003  2003-2007  2004-2008  2000-2006  2000-2008  2008-2009  2003-2007	Morbidity  Mortality  Morbidity  Morbidity  Morbidity	<19 All All ≥65	EC EC EC	ICD9 ICD-10 ICD-10 ICD-19	RES(ICD-9:460-519), Asthma(ICD-9:493), Acute broghitis(ICD-9:466), Pneumonia(ICD-9:480-486)  CVD, RES  RES(ICD-10:100-198), CVD(ICD-10:100-199)  CVD[Cardiac Dysrhythmias(ICD-9:428), Heart Rhythen Disturbances(ICD-9:426-427), Cerebrovascular Events (ICD-9:430-438), IHD (ICD-9:410-414,
Huang et al. 2012 TS China  Peng et al. 2009 TS USA  Levy et al. 2012 TS USA  Son et al. 2012 TS Korea  Heo et al. 2014 TS Korea  Basagaña et al. 2015 CS Spain, Italy  Dai et al. 2014 TS USA  Lin et al. 2016a TS China  Cao et al. 2012 TS China  Klemm et al. 2011 TS USA	2004-2008 2000-2006 2000-2008 2008-2009	Mortality  Morbidity  Morbidity  Mortality	All ≥65 ≥65	EC EC	ICD-10	RES(ICD-10:100-198),CVD(ICD-10:100-199 )  CVD[Cardiac Dysrhythmias(ICD-9:428),Heart Rhytlen Disturbances(ICD-9:426-427),Cerebrovascular Events (ICD-9:430-438),IHD (ICD-9:410-414,
Peng et al. 2009 TS USA  Levy et al. 2012 TS USA  Son et al. 2012 TS Korea  Heo et al. 2014 TS Korea  Basagaña et al. 2015 CS Spain, Italy  Dai et al. 2014 TS USA  Lin et al. 2016a TS China  Cao et al. 2012 TS USA  Klemm et al. 2011 TS USA	2000-2006 2000-2008 2008-2009	Morbidity  Morbidity  Mortality	≥65 ≥65	EC		CVD[Cardiac Dysrhythmias(ICD-9:428),Heart Rhytlen Disturbances(ICD-9:426-427),Cerebrovascular Events (ICD-9:430-438),IHD (ICD-9:410-414,
Levy et al. 2012 TS USA  Son et al. 2012 TS Korea  Heo et al. 2014 TS Korea  Basagaña et al. 2015 CS Spain, Italy  Dai et al. 2014 TS USA  Lin et al. 2016a TS China  Cao et al. 2012 TS USA  Klemm et al. 2011 TS USA	2000-2008 2008-2009	Morbidity  Mortality	≥65		ICD-9	(ICD-9:430-438),IHD (ICD-9:410-414,
Son et al. 2012 TS Korea  Heo et al. 2014 TS Korea  Basagaña et al. 2015 CS Spain, Italy  Dai et al. 2014 TS USA  Lin et al. 2016a TS China  Cao et al. 2012 TS China  Klemm et al. 2011 TS USA	2008-2009	Mortality		EC		429),PVD(ICD-9:440-448)],RES[COPD(ICD-9:490 3)2),RES(ICD-9:464-466,480-487)]
Heo et al. 2014 TS Korea  Basagaña et al. 2015 CS Spain, Italy  Dai et al. 2014 TS USA  Lin et al. 2016a TS China  Cao et al. 2012 TS China  Klemm et al. 2011 TS USA		-	, 11	EC	ICD-9	CVD(ICD-9:390-459),RES(ICD-9:464-466 and 480-487).
Basagaña et al. 2015 CS Spain, Italy  Dai et al. 2014 TS USA  Lin et al. 2016a TS China  Cao et al. 2012 TS China  Klemm et al. 2011 TS USA	2003-2007	3.6 (12)	All	EC	ICD-10	CVD(ICD-10:100-199),RES(ICD-10:J00-J99)
Dai et al. 2014         TS         USA           Lin et al. 2016a         TS         China           Cao et al. 2012         TS         China           Klemm et al. 2011         TS         USA		Mortality	All	EC	ICD-10	CVD(ICD-10:100-199),RES(ICD-10:J00-J98)
Lin et al. 2016a TS China Cao et al. 2012 TS China Klemm et al. 2011 TS USA	2003-2013	Morbidity,  Mortality	All	EC	ICD-9, ICD-10	CVD(ICD-9:390-459,ICD-10:I00-I99),RES(ICD-9:480-519,ICD-10:J00-J99)
Cao et al. 2012 TS China Klemm et al. 2011 TS USA	2000-2006	Mortality	All	EC	ICD-10	CVD(ICD-10:I01-I59),RES(ICD-10:J00-J99),MI(IC  10:I21-I22),Stroke(ICD-10:I60-I69)
Klemm et al. 2011 TS USA	2007-2011	Mortality	All	EC	ICD-10	CVD(ICD-10:100-199)
	2004-2008	Mortality	All	EC	ICD-10	CVD(ICD-10:I00-I99),RES(ICD-10:J00-J98)
Zhou et al. 2011 TS USA	1998-2007	Mortality	≥65	EC	ICD-10	CVD(ICD-10:100-199),RES(ICD-10:J00-J98)  CVD(ICD-10:100-199),RES(ICD-10:J00-J99)
	2002-2004	Mortality	All	EC	ICD-10	CVD(ICD-10:I01-I99),RES(ICD-10:J00-J99)
Winquist et al. 2015 TS USA	2001-2003	Morbidity	All	BC,EC	ICD-9	RES(ICD-9:460-465,466.0,466.1,466.11,466.19,477, \$\frac{\textbf{N}}{\textbf{N}}\text{0-486,491,492,493,496,786.07), CVD(ICD-9:410-414,400)}
Ostro et al. 2007 TS USA	2000-2003	Mortality	All	EC	ICD-10	428,433-437,440,443-445,451-453)  CVD(ICD-10:I00-I99),RES(ICD-10:J00-J98)
Tolbert et al. 2000 TS USA	1998-2000	Morbidity	All	EC	ICD-9	CVD(ICD-9:402,410-414,427,428,433-437,440,444,491-453),RES(ICD-9:460-466,477,480-486,491,492,493,400)

**Table S2** Characteristics of included studies in the systematic review and meta-analysis

Study	Study Design	Country	Study Period	Outcome	Age	Pollutant	ICD code	On Siscases Jaj
Wang and Lin 2016	TS	China	2004-2010	Morbidity,	≥65(mortality), all(morbidity)	EC	ICD-9	CVD(ICD-9-CM:390-459),RES(ICD-9-CM:460-519) Ow
Darrow et al. 2014	TS	USA	1993-2010	Morbidity	0–4	EC	ICD-9	Acute Bronchitis or Bronchiolitis(ICD-9:466),Pneumonia(ICD-9:480-486),URI(ICD-9:460-465)
Metzger et al. 2004	TS	USA	1993-2000	Morbidity	All	EC	ICD-9	CVD[IHD(ICD-9:410-414),AMI(ICD-9:410),cardiacoddysrhythmias(ICD-9:427),CA(ICD-9:427.5),CHF(ICodd).  events(ICD-9:433-437,440,443-444,451-453),CHD(IGD-9:440),Stroke(ICD-9:436)]
Mar et al. 2000	TS	USA	1995-1997	Mortality	All	EC	ICD-9	CVD(ICD-9:390-448.9)
Wang et al. 2019a	TS	China	2013-2015	Mortality	All	EC	ICD-10	CVD(ICD-9:390-448.9 )  CVD(ICD-10:100-199),RES(ICD-10:J00-J99)  Stroke(ICD-10:I60-I66)
Lin et al. 2016b	TS	China	2007-2011	Mortality	All	EC	ICD-10	Stroke(ICD-10:I60-I66)
Ostro et al. 2008	TS	USA	2000-2003	Mortality	All	EC	ICD-10	CVD(ICD-10:100-199)
Ito et al. 2011	TS	USA	2000-2006	Morbidity, Mortality	≥40	EC	ICD-9, ICD-10	CVD[Hypertensive Diseases(ICD-9:402,ICD-10:I11] MI(ICD-9:410;ICD-10:I21-I22),IHD  (ICD-9:414,ICD-10:I25),Dysrhythmias(ICD-9:427,ICD-10:I48),HF(ICD-9:428,ICD-10:I50),Stroke(ICD-9:430-43-43-43-43-43-43-43-43-43-43-43-43-43-
Chen et al. 2014	TS	China	2004-2008	Morbidity	All	EC	ICD-9	Stroke[Ischemic Stroke(ICD-9:433-434),Hemorrhagie Stroke(ICD-9:430-432)]
Tomic'-Spiric' et al. 2019	CS	Serbia	2012-2014	Morbidity	≥18	ВС	ICD-10	Allergic RES[AR(ICD-10:J.30.4),AA(ICD-10:J.45.0)
Maynard et al. 2007	CS	USA	1995-1997, 1999-2002	Mortality	All	ВС	ICD-9, ICD-10	CVD(ICD-9:390-429,ICD-10:101-152),Stroke(ICD-9-330-438,ICD-10:160-169),RES(ICD-9:460-519,ICD-10:J00-J
Sinclair et al. 2010	TS	USA	1998-2002	Morbidity	All	EC	NR	Asthma,URII,LRII
Krall et al. 2013	TS	USA	2000-2005	Mortality	All	EC	NR	CVD and RES(NR)  RES(ICD-9:460-519)
Cakmak et al. 2009	TS	Canada	2001-2006	Morbidity	All	EC	ICD-9	RES(ICD-9:460-519)
								by со

**Table S2** Characteristics of included studies in the systematic review and meta-analysis

Study	Study	Country	Study	Outcome	Age	Pollutant	ICD	O Wiseases
	Design		Period				code	
								CVD[IHD(ICD-9:410-414),Cardiac Dysrhythmias(IO)-9:427),CHF(ICD-9:428),PVD and Cerebrovascular
Tolbert et al. 2007	TS	USA	1993-2004	Morbidity	All	EC	ICD-9	Events(ICD-9:433-437,440,443-445,451-453)],
								RES[Asthma(ICD-9:493,786.07,786.09),COPD(ICD <b>2</b> :491,492,496),URTI(ICD-9:460-465,460.0,477),Pneumon
								(ICD-9:480-486),Bronchiolitis(ICD-9:466.1,466.11,466.19)]
								RES[Pneumonia(ICD-9:480-486),COPD(ICD-9:490 392,496),Acute Bronchitis and
Lall et al. 2011	TS	USA	2001-2002	Morbidity	≥65	EC	ICD-9	$Bronchiolitis (ICD-9:466), Asthma (ICD-9:493)], CVD \\ \underbrace{ Dysrhythmia (ICD-9:427), IHD (ICD-9:410-414), HF (ICD-9:493), CVD}_{DS-PS-PS-PS-PS-PS-PS-PS-PS-PS-PS-PS-PS-PS$
								28),Stroke(ICD-9:431-437)]
Jung and Lin 2017	CS	China	2000-2010	Morbidity	0-20	BC	ICD-9	Asthma(ICD-9-CM:493)
Gong et al. 2019	TS	China	2006-2011	Mortality	All	ВС	ICD-10	Asthma(ICD-9-CM:493)  CVD(ICD-10:100-199)  Acute Ischemic Stroke
Mostofsky et al. 2012	CS	USA	2003-2008	Morbidity	≥21	BC	NO	Acute Ischemic Stroke
			1999-2009(Atlan					<u>a</u>
			ta,Georgia),					<b>/m</b>
	TS	S USA	2004-010(Birmi			EC	ICD-9	on A
			ngham,Alabama,					RES[Pneumonia(ICD-9:480-486),COPD(ICD-9:491, 22,496),URTI(ICD-9:460-465,466.0,477),Asthma and/or
Krall et al. 2017			2001-2007(St.Lo	Morbidity	All			Wheeze(ICD-9:493,786.07)]
			uis, Missouri ),					200
			2006-2009(Dalla					4 7
			s,Texas)					2024 by gue
O'Lenick et al. 2017	CS	USA	2001-2008	Morbidity	5–18	EC	ICD-9	Asthma(ICD-9:493.0-493.9),Wheeze(ICD-9:786.07)
Pearce et al. 2015	TS	USA	1999-2008	Morbidity	5–17	EC	ICD-9	Asthma(ICD-9:493.0-493.9),Wheeze(ICD-9:786.07)
Strickland et al. 2010	CS	USA	1993-2004	Morbidity	5-17	EC	ICD-9	Asthma(ICD-9:493.0-493.9),Wheeze(ICD-9:786.09) (ICD-9:460.0-466.0)
								<u> </u>
								by сор

Table S2 Characteristics of included studies in the systematic review and meta-analysis

Table 52 Charac						<i>J</i> =		<u> </u>
Study	Study	Country	Study	Outcome	Age	Pollutant	ICD	iseases Diseases
	Design		Period				code	Aay
Strickland et al. 2014	TS	USA	2000-2010	Morbidity	2-16	EC	ICD-9	Asthma(codes beginning with 493),Wheeze (ICD-9:28.07)
T 1 2012	TO.	110.4	2001 2006	Morbidity,	all (mortality),	FG	ICD-9,	N
Ito et al. 2013	TS	USA	2001-2006	Mortality	≥65(morbidity)	EC	ICD-10	CVD(ICD-10:I01-I79),RES(ICD-10:J00-J99)
Ostro et al. 2015b	Co	USA	2001-2007	Mortality	≥30	EC	ICD-10	CVD(ICD-10:100-199),IHD(ICD-10:120-125),Pulmorary(ICD-10:C34,J00-J98)
			4000 0000	Morbidity,	4.5.0.5		ICD-9,	ā e C
Gan et al. 2013	Со	Canada	1999-2002	Mortality	45-85	BC	ICD-10	COPD(ICD-9:490-492,496,ICD10:J40-J44)
Hvidtfeldt et al. 2019	Co	Denmark	1993-2015	Mortality	50 –64	BC	ICD-10	CVD(ICD-10:100-199),RES(ICD-10:J00-J99,C34)
Thurston et al. 2016	Co	USA	1988-2004	Mantalita	≥30	EC	ICD-9,	HID/ICD 0.410 414 ICD 10.120 125)
Thurston et al. 2016	Co	USA	1988-2004	Mortality	≥30	EC	ICD-10	CVD(ICD-10:100-199),RES(ICD-10:J00-J99,C34)  IHD(ICD-9:410-414,ICD-10:I20-I25)  CVD(ICD-10:100-I99),RES(ICD-10:J00-J47,J80-J999
Yang et al. 2018	Co	China	1998-2011	Mortality	≥65	BC	ICD-10	CVD(ICD-10:100-I99),RES(ICD-10:J00-J47,J80-J999
Gan et al. 2011	Co	Canada	1999-2002	Morbidity,	45–85	ВС	ICD-9,	CHD(ICD-9:410-414,429.2 ),(ICD-10:120-125)
Gail et al. 2011	Co	Canada	1999-2002	Mortality	43-63	ьс	ICD-10	CHD(ICD-9:410-414,429.2),(ICD-10:120-125)  IHD(ICD-9:410-414),CHD(ICD-9:430-438)  CVD (ICD-9:CM 410-452)
De Kluizenaar et al.	C	V 4 1 1	1001 2002	M. Lilli	15-74	EC	ICD 0	HIDACD 9 419 4140 CADACD 9 409 4090
2013	Со	Netherlands	1991-2003	Morbidity	15-74	EC	ICD-9	IHD(ICD-9:410-414),CHD(ICD-9:430-438)
Vedal et al. 2013	C-	USA	1004 2005	Morbidity,	50-79	EC	ICD-9	CVD (ICD 0.CM 410 452).
Vedai et al. 2013	Со	USA	1994-2005	Mortality	50-79	EC	ICD-9	CVD (ICD-9:CM 410-452)
Rahmatinia et al. 2021	TS	Iran	2014-2017	Mortality	All	BC	ICD-10	RES(ICD10:J00- J99),CVD(ICD10:I00-I99),IHD(IC 10:I20-I25)
Liu et al. 2021b	Co	China	2010–2017	Morbidity	All	ВС	NR	CVD(including but not limited to hypertension and stocke)
Lavigne et al. 2021	Co	Canada	2006-2014	Morbidity	≤6	BC	ICD-10	Asthma(ICD-10:J45)
Rodins et al. 2020	Co	Germany	2000-2015	Morbidity	All	EC	NR	
Kovačević et al. 2020	CS	Serbia	2012-2014	Morbidity	≥18	BC	ICD-10	AA(ICD-10:J45.0) or asthma with coexisting AR Atherosclerosis in the carotid arteries
Hasslöf et al. 2020	Co	Sweden	1991-1994	Morbidity	All	BC	NR	
								ρ

**Table S2** Characteristics of included studies in the systematic review and meta-analysis

Gr. 1	Study	G	Study	0.4		D.II.4.4	ICD	S ₩ ₩iscases
Study	Design	Country	Period	Outcome	Age	Pollutant	code	weases a
Wang et al. 2019b	CS	USA	2005-2016	Morbidity	All	ВС	NR	STEMI 20
Ljungman et al. 2019	Co	Sweden	1990-2011	Morbidity, Mortality	All	ВС	ICD-9, ICD-10	IHD(ICD-9:410–414 and ICD-10:120-25);stroke(ICD <b>=9</b> :431–436 and ICD-10:161–165)
Liu et al. 2021a	Co	Sweden, Denmark	1992-2004	Morbidity	All	ВС	ICD-9, ICD-10	COPD(ICD-9:490–492, and 494–496, or ICD-10:J40014)

Abbreviations: NR: Not Reported; TS: Time-Series; CS: Case-Crossover; Co: Cohort; ICD: International Classification of Diseases; MI: Myocardial infarction; CHD: Coronary heart disease; CVD: ardiovascular disease; RES: respiratory diseases; IHD: Ischemic Heart Disease; ARI: acute respiratory illness; HF: heart failure; CHF: congestive heart failure; PVD: peripheral vascular disease; AR: allergic asthma; AR: allergic rhinitis; AMI: acute myocardial infarction; CA: cardiac arrest; STEMI: ST segment elevation myocardial infarction; RTI: respiratory tract infection; URTI: Upper Respiratory Infection; LRTI: Lower Respiratory Infection; ARTI: Acute respiratory infections.

Table S3 Subgroup analysis on short-term effects of BC or EC on cardiovascular and respiratory diseases

Cub Au abuda	No. of	No. of	Relative Risk	$I^2$	Egger Regression Test
Subgroup Analysis	Studies	Estimates	(95%CI)	l²	(p value)
Cardiovascular Diseases					
Lag Days					
Lag 0d	15	18	1.013 (1.006, 1.020)*	77.30%	0.024
Lag 1d	12	15	1.005 (1.002, 1.008)	32.70%	0.299
Lag 2d	11	14	1.002 (0.999, 1.005)	73.80%	0.969
Geographical Location (Mortality)					
Asia	8	8	1.004 (1.002, 1.006)*	70.00%	_
Europe	4	5	0.991 (0.983, 0.999)	0	_
America	4	4	1.017 (0.998, 1.037)	20.80%	_
Geographical Location (Morbidity)					
Asia	_	_	_	_	_
Europe	_	_	_	_	_
America	12	12	1.023 (1.016, 1.030)	46.00%	0.078
Disease					
Congestive heart failure (Morbidity)	3	3	1.076 (1.021, 1.134)*	64.70%	_
Season (Mortality)					
Warm season	3	3	1.002 (0.995, 1.010)	0	_
Cold season	3	3	1.014 (1.008, 1.019)*	0	_
Respiratory Diseases					
Asthma (Morbidity)					
Asthma 0-18	5	6	1.021 (1.006, 1.035)*	69.10%	_
Asthma ≥18	4	5	1.011 (1.000, 1.021)	0	_

Annotation: "\*" means the data were statistically significant.

Page 58 of 136

Table S4 Details of risk of bias assessment

6 7 8	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete Soutcome data	Selective	Conflict of interest	Other
9 10	1	Atkinson	Probably Low	Low	Probably Low	Low	Low	Probably Low	Low	Low
11		et al. 2016	All of the pollutants were	Death data for the period	Adjusted for time	Study included	Daily counts	There was	The authors	No other
12			measured at the central	1 January 2011 to 31	(seasonality,	daily counts of	for death were $\frac{8}{2}$	insufficient	declare no	potential
13 14			London background	December 2012 were	long-term trend),	deaths in	obtained, so	information	conflict of	sources of
15			monitoring site at North	obtained from the Office	temperature,	London, United	likely have all	about	interest.	bias
16			Kensington. All	for National Statistics.	humidity, day of	Kingdom for the	outcome data.	selective		identified.
17 18			measurements were 24-h	Daily counts of deaths in	week and public	period 1 January	However, any	outcome to		
18			averages except for CO.	London, United Kingdom	holidays.	2011 to 31	potential errors	judge for low		
20			The number of all	were classified as all		December 2012.	or missing data	risk, but		
21			observations was	disease-related causes,	(0)		did not depend	indirect		
22 23			621-693 (<25% missing	cardiovascular			on air pollution			
24			data).	(International		(0)	levels.	suggests study		
25				Classification of			n/ or	was free of		
26 27				Diseases,10th			1 Ap	selective		
28				revision-ICD10: I00-I99)				report.		
29				and respiratory (ICD10:			9, 2	1		
30				J00-J99) diseases.			024			
31 32				,			by g			
33							Jues			
34							<u>ب</u> ت			
35							April 19, 2024 by guest. Protected by			
36 37							) Ctec			
38							<u> </u>			

Bell et al. 2014  Bell et al. 2014  Be measured from filters collected daily using optical reflectance. Monitors from 5 sites across 4 counties were used. Sampling occurred daily, with some missing periods, for Hartford, New Haven, and Springfield, and every third day for Bridgeport and Danbury. Days with missing data were omitted from analysis (the number of missing data wars not reported).  Bell et al. 2014  Be measured from filters collected daily using optical reflectance. Models adjusted from records of individuals 265 and missions was determined by principal deshared daily, with some missing periods, for Hartford, New Haven, and Springfield, and every third day for Bridgeport and Danbury. Days with missing data were omitted from analysis (the number of missing data wars not reported).  Be measured from filters collected daily using optical reflectance. Models adjusted from records of individuals 265 admissions was determined by principal deshared daily, with some missing data were omitted from analysis (the number of missing data wars not reported).  Cause of the form the (seasonality, long-term trend), day of week, temperature, and determined by principal deshared daily, with some missing data were omitted from analysis (the number of missing data wars not reported).  Cause of the form the (seasonality, long-term trend), day of week, temperature, and determined by principal deshared daily, with some missing data were omitted from analysis (the number of missing data wars not reported).  Cause of the form the (seasonality, long-term trend), day of week, temperature, and determined by principal dew point.  Cause of the form the (seasonality, long-term trend), day of week, temperature, and dew point.  Cause of the form the (seasonality, long-term trend), day of week, temperature, and determined by principal dew point.  Cause of the form the (seasonality, long-term trend), day of week, temperature, and dew point.  Cause of the form the form the (seasonality, long-term trend), day of week, and using a day of	5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data		Conflict of interest	Other
BC measured from filters collected daily using optical reflectance.  Monitors from 5 sites across 4 counties were used. Sampling occurred daily, with some missing periods, for Hartford, New Haven, and Springfield, and every third day for Bridgeport and Danbury. Days with missing data were omitted from analysis (the number of missing data was not reported).  BC measured from filters declare hedicare baneficiary denominator file from the denominator file from the denominator file from the (seasonality, long-term trend), day of week, temperature, and dew point.  BC measured from filters declare no optential for time (seasonality, long-term trend), day of week, temperature, and dew point.  BC measured from filters declare no optential of from records of individuals 265 years of age enrolled in the development of all outcome and point of the point of time (seasonality, long-term trend), day of week, temperature, and dew point.  BC centers for Medicare and Medicare and determined by principal discharge diagnosis code according to International Classification of (ICD-9-CM; National Center for Health Statistics 2006).  Center for Health Statistics 2006).		2	Bell et al.	Probably High	Low	Probably Low	Low	Low	Probably Low	Low	Low
Collected daily using optical reflectance. Monitors from 5 sites across 4 counties were used. Sampling occurred daily, with some missing periods, for Hartford, New Haven, and Springfield, and every third day for Bridgeport and Danbury. Days with missing data were omitted from analysis (the number of missing data was not reported).   Medicare beneficiary denominator file from the (seasonality, leave denominator file from the (seasonality, leave denominator file from the (seasonality, leave denominator file from the (seasonality, law of week, were obtained, get about selective all outcome and were obtained, get about selective all outcome and dew point.   Medicare all outcome and dew point.   Medicare all outcome and part of fee-for-service plan during August 2000 to February 2004.   Medicare all outcome and part of fee-for-service plan during August 2000 to February 2004.   Medicare all outcome and pound of fee-for-service plan during August 2000 to February 2004.   Medicare all outcome and pound of fee-for-service plan during August 2000 to February 2004.   Medicare all outcome and pound of fee-for-service plan during August 2000 to February 2004.   Medicare all outcome and pound of fee-for-service plan during August 2000 to February 2004.   Medicare all outcome and pound of fee-for-service plan during August 2000 to February 2004.   Medicare all outcome and pound of fee-for-service plan during and pound o			2014	BC measured from filters	The study used the	Models adjusted	Data obtained	Daily counts	There was	The authors	No other
Monitors from 5 sites across 4 counties were used. Sampling occurred daily, with some missing periods, for Hartford, New Haven, and Springfield, and every third day for Bridgeport and Danbury. Days with missing data were omitted from analysis (the number of missing data was not reported).  Center for Health Statistics 2006).  Center for Health Statistics 2006).  Center for Medicare and Medicaid Services. Cause of admission was determined by principal discharge diagnosis code according to International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM; National Center for Health Statistics 2006).  Center for Health Statistics 2006).  Center for Health Statistics 2006).				collected daily using	Medicare beneficiary	for time	from records of	for hospital	insufficient	declare no	potential
Monitors from 5 sites across 4 counties were used. Sampling occurred daily, with some missing periods, for Hartford, New Haven, and Springfield, and every third day for Bridgeport and Danbury. Days with missing data were omitted from analysis (the number of missing data was not reported).  Centers for Medicare and Iong-term frend), day of week, temperature, and day of week, temperature, and devery plan during any potential givensory of aging was free of selective plan during any potential givensory on air pollutions on air pollutions (the number of missing data was not reported).  Centers for Medicare and Iong-term frend), day of week, temperature, and devery plan during any potential givensory on air pollutions (ICD-9-CM; National Center for Health Statistics 2006).  Centers for Medicare and Iong-term frend), day of week, temperature, and development and pollutions of admission was determined by principal discharge diagnosis code according to International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM; National Center for Health Statistics 2006).  Centers for Medicare and Iong-term frend), day of week, temperature, and dew point.  August 2000 to February 2004.  February 2004.  February 2004.  Selective missing data were on air pollutions on air pollutions on air pollutions on air pollutions of the policy of the plan during any potential given any potential of the missing data. However, all outcome to data. However, and were of the plan during any potential of the missing data. However, and on air pollutions of the policy have the plan during any potential of the missing data. However, all outcome to data. However, all outcome to data. However, and pour pollutions on air pollutions on air pollutions on air pollutions of the pollutions				optical reflectance.	denominator file from the	(seasonality,	individuals ≥65	admissions 💆	information	conflict of	sources of
across 4 counties were used. Sampling occurred daily, with some missing periods, for Hartford, New Haven, and Springfield, and every third day for Bridgeport and Danbury. Days with missing data were omitted from analysis (the number of missing data was not reported).  Medicaid Services. Cause of admission was determined by principal discharge diagnosis code according to International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM; National Center for Health Statistics 2006).  Medicaid Services. Cause of admission was determined by principal determ				Monitors from 5 sites	Centers for Medicare and	long-term trend),	years of age	were obtained,	about	interest.	bias
daily, with some missing periods, for Hartford, New Haven, and Springfield, and every third day for Bridgeport and Danbury. Days with missing data were omitted from analysis (the number of missing data was not reported).  determined by principal discharge diagnosis code according to International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM; National Center for Health Statistics 2006).  dew point.  dew point.  fee-for-service plan during August 2000 to February 2004.  fee-for-service plan during any potential did not depend on air pollutions on air pollutions (indirect evidence that suggests study was free of selective report.  Center for Health Statistics 2006).				across 4 counties were	Medicaid Services. Cause	day of week,	enrolled in the	so likely have	selective		identified.
daily, with some missing periods, for Hartford, New Haven, and Springfield, and every third day for Bridgeport and Danbury. Days with missing data were omitted from analysis (the number of missing data was not reported).    Canter for Health Statistics 2006).   Canter for Health Statistics 2006).				used. Sampling occurred	of admission was	temperature, and	Medicare	all outcome	outcome to		
periods, for Hartford, New Haven, and Springfield, and every third day for Bridgeport and Danbury. Days with missing data were omitted from analysis (the number of missing data was not reported).    19				daily, with some missing	determined by principal	dew point.	fee-for-service	data. However,	judge for low		
New Haven, and Springfield, and every third day for Bridgeport and Danbury. Days with missing data were omitted from analysis (the number of missing data was not reported).  New Haven, and Springfield, and every third day for Bridgeport and Danbury. Days with missing data were omitted from analysis (the number of missing data was not reported).  New Haven, and Springfield, and every third day for Bridgeport and Danbury. Days with missing data were omitted from analysis (the number of missing data was not reported).  New Haven, and Springfield, and every third day for Bridgeport and Danbury. Days with missing data were omitted from analysis (the number of missing data was not reported).  New Haven, and Springfield, and every third day for Bridgeport and Danbury. Days with missing data were of indirect evidence that suggests study on air pollutions levels.  Center for Health Statistics 2006).  Statistics 2006).				periods, for Hartford,	discharge diagnosis code		plan during	any potential	risk, but		
third day for Bridgeport and Danbury. Days with missing data were omitted from analysis (the number of missing data was not reported).  Statistics 2006).  Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM; National Center for Health Statistics 2006).  Statistics 2006).	20			New Haven, and	according to International	'/	August 2000 to	errors or	indirect		
third day for Bridgeport and Danbury. Days with missing data were omitted from analysis (the number of missing data was not reported).  Diseases, Ninth Revision, Clinical Modification (ICD-9-CM; National Center for Health Statistics 2006).  Diseases, Ninth Revision, Clinical Modification (ICD-9-CM; National Center for Health Statistics 2006).				Springfield, and every	Classification of	' (%)	February 2004.	missing data	evidence that		
and Danbury. Days with missing data were omitted from analysis (the number of missing data was not reported).  Clinical Modification (ICD-9-CM; National Center for Health Statistics 2006).  Center for Health Statistics 2006).				third day for Bridgeport	Diseases, Ninth Revision,			did not depend	suggests study		
omitted from analysis (the number of missing data was not reported).  Center for Health Statistics 2006).  Center for Health Statistics 2006).				and Danbury. Days with	Clinical Modification			l 0			
omitted from analysis (the number of missing data was not reported).  Center for Health Statistics 2006).  Statistics 2006).  Protection of missing data was not reported.				missing data were	(ICD-9-CM; National			levels.	selective		
28 (the number of missing data was not reported).  Statistics 2006).  Statistics 2006).  Protection of missing data was not reported by guest.  Protection of missing data was not reported by guest.  Protection of missing data was not reported by guest.  Protection of missing data was not reported by guest.  Protection of missing data was not reported by guest.				omitted from analysis	Center for Health			1 Ap	report.		
data was not reported).  data was not reported).  data was not reported).  Protected  30 20 21 22 32 33 34 35 36 37				-	Statistics 2006).				:		
32 33 34 35 36 37				data was not reported).	ŕ			9, 2			
32 33 34 35 36 37				1				024			
33								by	-		
35   Protected       Protected     Protected     Protected     Protected     Protected     Protected     Protected     Protected     Protected       Protected     Protected     Protected     Protected     Protected     Protected     Protected     Protected     Protected       Protected     Protected     Protected     Protected     Prote								gue			
35											
								ro			
	37   38							ed 5			

BMJ Open

No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data		Conflict of interest	Other
3	Cai et al.	Probably Low	Low	Probably Low	Low	Low	Probably Low	Low	Low
	2014	Daily concentrations of	Asthmatic hospitalization	Adjusted for time	Study included	Daily counts	There was	Authors	No other
		BC were measured at a	data was obtained from	(seasonality,	all asthmatic	for asthmatic	insufficient	declared no	potential
		fixed-site station. Daily	the Shanghai Health	long-term trend),	hospitalization	hospitalization \( \frac{5}{2} \)	information	competing	sources of
		data was available and no	Insurance Bureau	temperature,	for adult	were obtained,	about	financial	bias
		missing data was	(SHIB). The causes of	relative humidity	residents living	so likely have	selective	interests.	identified.
		reported.	hospital admission were	and day of the	in the nine urban	all outcome	outcome to		
			coded according to	week.	districts between	data. However,	judge for low		
			International		January 1, 2005	any potential	risk, but		
			Classification of	'/	and December	errors or	indirect		
			Diseases, Revision 10	. 01	31, 2011(2922	missing data	evidence that		
			(ICD-10): Asthma (J45).		days) from the	did not depend	suggests study		
					Shanghai Health	on air pollution			
					Insurance	levels.	selective		
					Bureau.	Αþ	report.		
						, <u>,</u> ,			
						)24			
						by g			
						Jues			
						;; 			
						rote			
						April 19, 2024 by guest. Protected by			
						l by cop			

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data ≤		Conflict of interest	Other
8 9			Probably High	Low	Probably Low	Low	Low ay	Probably Low	Low	Low
10	4	Geng et	Single, central-site	Health data were	Models included	Data consisted of	Daily counts 8	There was	The authors	No other
11		al. 2013	monitor. Daily BC and	obtained from Shanghai	time (seasonality,	all causes	for death were	insufficient	declare no	potential
12			PM <sub>2.5</sub> were measured	Municipal Center of	long-term trend),	(excluding	obtained, so	information	conflict of	sources of
13 14			continuously and 24hr	Disease Control and	temperature,	accidents or	likely have all	about	interest.	bias
15			averaged was estimated if	Prevention database. The	humidity and day	injuries) deaths	outcome data.			identified.
16			>75% of the 1hr values	causes of death were	of week.	during over the	However, any	outcome to		
17			was available for that	coded according to the		course of the	potential errors			
18 19			day. Missing data was not	International	C/-	study.	or missing data	risk, but		
20			replaced by other values.	Classification of	' /_	-	did not depend	indirect		
21				Diseases, Revision 10	(0)		on air pollution			
22 23				(ICD 10).			levels.	suggests study		
24							.con	was free of		
25							n/ 0i	selective		
26							n Ap			
27 28								Toport.		
29							9,			
30							2024			
31							by			
32 33							gue			
34							April 19, 2024 by guest. Protected			
35							Prot			
36							ecte			
37   38							ed b			
38							Ý			

BMJ Open

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data		Conflict of interest	Other
8 9			Probably High	Low	Probably Low	Low	Low ay	Probably Low	Low	Low
10	5	Hua et al.	Daily 24h average PM <sub>2.5</sub>	Daily asthma hospital	Adjusted for	Study included	Daily counts	There was	Authors	No other
11		2014	and BC data was	admission data was	long-term and	all asthma	for asthma	insufficient	declared no	potential
12			obtained from a fixed-site	obtained from Shanghai	seasonal trend, day	hospital	hospital <u>\text{\tin}\exittet{\texi}\text{\text{\text{\text{\text{\text{\text{\ter{\text{\texi}\text{\text{\texi}\text{\texi}\text{\texi}\text{\ti}\text{\text{\texi}\text{\texi{\text{\text{\text{\text{\ti</u>	information	competing	sources of
13 14			station. The study only	Children's Medical	of week,	admissions of	admissions of 8	about	financial	bias
15			used the actual collected	Center. Dates of	temperature and	children ≤ 14	children were	selective	interests.	identified.
16			data and did not fill in the	admission and discharge,	relative humidity.	years of age from	obtained, so	outcome to		
17			missing data for PM <sub>2.5</sub>	and diagnoses using the	<b>'</b> O	Shanghai	likely have all	judge for low		
18 19			and black carbon.	International	C/	Children's	outcome data.	risk, but		
20				Classification of	' / <sub>0</sub>	Medical Center	However, any	indirect		
21				Diseases, Revision 10.	' (%)	between1	potential errors.	evidence that		
22 23				·		January 2007 and	or missing data			
24						31 July 2012 in	did not depend			
25						nine urban	on air pollution			
26						districts of	levels.			
27 28						Shanghai.	<i>]</i>			
29							19, 2			
30							2024 by			
31   32							by :	•		
32   33							' guest.			
34										
35							rote			
36 37							Protected			
38							d by			

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete 9		Conflict of interest	Other
8 9			Probably Low	Low	Low	Low	Low ay	Probably Low	Low	Low
10	6	Ostro et	Daily 24hr average BC	For both cities daily	Adjusted for long	Study population	Daily counts	There was	Authors	No other
11		al. 2015a	concentrations were	counts of all-cause	term and seasonal	consisted of daily	for death were	insufficient	declared no	potential
12			obtained from one station	mortality for all ages	(year, month, day	counts of	obtained, so ≦	information	competing	sources of
13 14			in Barcelona and Athens.	were collected (excluding	of week) trends,	all-cause	likely have all	about	interests.	bias
15			Daily data was available	deaths from external	temperature,	mortality for all	outcome data.	selective		identified.
16			and no missing data was	causes, International	holidays, summer	ages and daily	However, any	outcome to		
17 18			reported.	Classification of	vacations and	counts of	potential errors	judge for low		
19				Disease-ICD9: 001799,	influenza.	cardiovascular,	or missing data	risk, but		
20				ICD10 A00R99), as well	' /	respiratory and	did not depend	indirect		
21				as daily counts of	' (0)	all-cause	on air pollution	evidence that		
22 23				cardiovascular (ICD9:		mortality for	levels.	suggests study		
24				390459, ICD10: I00I99),		those greater than	com	was free of		
25				respiratory		age 65.	n/ or	selective		
26 27				(ICD9:460519,			ı Ap	report.		
28				ICD10:J00J99) and				: 1		
29				all-cause mortality for			19, 2			
30				those greater than age 65.			2024 by			
31 32							by (			
33							' guest.			
34										
35							Protected			
36 37							cte			
38							<u> </u>			

No. Study  Exposure assessment  Outcome assessment  Confounding bias  Selection bias  Low  Low  Probably Low  Low  Adjusted for long all cardiovascular for all cardiovascular for all remaind seasonal temperature, supplemented by local measurements made at the North Kensington urban background site.  No. Study  Exposure assessment  Outcome assessment  Confounding bias  Selection bias  Incomplet outcome day  Adjusted for long discharge diagnosis, daily term and seasonal trends, regulated pollutarity temperature, relative humidity, regulated pollutants (PM <sub>10</sub> , between 2011 and missions in admissions in pollutants (PM <sub>10</sub> , between 2011 and 2012.  Number of days of observation for BC: 629  Discases, 10th pollutants (PM <sub>10</sub> , between 2011 and 2012.  Number of days of observation for BC: 629  Discassification of pollutants (PM <sub>10</sub> , between 2011 and 2012.  Number of days of observation for BC: 629  Discasses, 10th pollutants (PM <sub>10</sub> , between 2011 and 2012.  Number of days of observation for BC: 629  Discasses, 10th pollutants (PM <sub>10</sub> , between 2011 and 2012.  Number of days of observation for BC: 629  Discasses, 10th pollutants (PM <sub>10</sub> , between 2011 and 2012.  Number of days of observation for BC: 629  Discasses, 10th pollutants (PM <sub>10</sub> , between 2011 and 2012.  Number of days of observation for BC: 629  Discasses, 10th pollutants (PM <sub>10</sub> , between 2011 and 2012.  Number of days of observation of BC: 629  Discasses, 10th pollutants (PM <sub>10</sub> , between 2011 and 2012.  Number of days of observation for BC: 629  Discasses, 10th pollutants (PM <sub>10</sub> , between 2011 and 2012.  Number of days of observation of BC: 629  Discasses, 10th pollutants (PM <sub>10</sub> , between 2011 and 2012.	וכ				
Low Low Adjusted for long Study included Daily counts for all cardiovascular for all collected from the ClearfLo project, supplemented by local measurements made at the North Kensington urban background site.  Number of days of Observation for BC: 629  Low Low Low Low Low Low Low Low Low Daily counts Adjusted for long study included all cardiovascular for all term and seasonal term and respiratory term and respiratory hospital and respiratory hospital admissions in regulated pollutants (PM <sub>10</sub> , pollut		e o	Selective	Conflict of	Other
Samoli et al. 2016  Based on the primary discharge diagnosis, daily term and seasonal collected from the collected from the supplemented by local measurements made at the North Kensington urban background site.  Number of days of collected for BC: 629  Samoli et al. 2016  Based on the primary discharge diagnosis, daily term and seasonal term and respiratory term and respiratory hospital and respiratory hospital admissions in admissions in London, UK between 2011 and 2012.  Samoli et al. 2016  Based on the primary discharge diagnosis, daily term and seasonal trends, temperature, relative humidity, regulated pollutants (PM <sub>10</sub> , between 2011 and 2012.  Number of days of observation for BC: 629  Samoli et al. 2016  Based on the primary discharge diagnosis, daily term and seasonal term and respiratory hospital and respiratory hospital admissions in London, UK between 2011 and 2012.	taω ≤	ta <sup>ω</sup> ≤	reporting	interest	Other
Samoli et al. 2016 BC and EC were collected from the ClearfLo project, supplemented by local measurements made at the North Kensington urban background site. Number of days of observation for BC: 629  Samoli et al. 2016 Based on the primary discharge diagnosis, daily numbers of admissions term and seasonal trends, term and seasonal trends, term and respiratory hospital and respiratory hospital admissions in London, UK between 2011 and 2012.  Samoli et al. 2016 BC and EC were discharge diagnosis, daily numbers of admissions (International pollutants (PM <sub>10</sub> , PM <sub>2.5</sub> , NO <sub>2</sub> , SO <sub>2</sub> and O <sub>3</sub> ), day of the week and public were any potential admissions in data. However, any potential admissions and 2012.	ay 2		Probably Low	Low	Low
(BC urban in PM <sub>2.5</sub> ) and 702 (BC in PM <sub>2.5</sub> ) between 2011 and 2012 (<25% missing data).  (BC urban in PM <sub>2.5</sub> ) and respiratory diseases (ICD-10: J00-J99) for those aged 0-14 years (paediatric), adult and the elderly were calculated.  (a) the property diseases (ICD-10: J00-J99) for those aged 0-14 years (paediatric), adult and the elderly were calculated.	2. Downloaded from http://bmjopen.bmj.com/ on	Downloaded from http://bmjopen.bmj.com/ on April	There was insufficient information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of selective report.	Authors declared no competing interests.	No other potential sources of bias identified.

Page 65 of 136

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on the outcome data		Conflict of interest	Other
8 9			Probably High	Low	Probably Low	Low	Low	Probably Low	Low	Low
10	8	Zanobetti	Ambient BC from one	The study extracted data	Adjusted for	Data consisted of	Daily counts	There was	Authors	No other
11		and	monitor. The hourly	on all hospital admissions	temperature, day	all U.S. Medicare	for hospital	insufficient	declared no	potential
12		Schwartz	measurements for BC and	for residents of the	of the week,	hospital	admissions 💆	information	competing	sources of
13 14		2006	PM <sub>2.5</sub> were not complete.	Boston Metropolitan area	seasonality,	admissions in the	were obtained,	about	interests.	bias
15			Missing values were	who were admitted to the	long-term trends,	Boston	so likely have	selective		identified.
16			replaced with the	hospital (in the Boston	humidity,	Metropolitan	all outcome	outcome to		
17 18			predicted values.	area) with a primary	barometric	area for	data. However,	judge for low		
19			Additionally BC data was	diagnosis of MI	pressure, and the	myocardial	any potential	risk, but		
20			missing from March 1997	(International	extinction	infarction during	errors or	indirect		
21 22			to March 1999 and was	Classification of	coefficient.	the study	missing data	evidence that		
23			not included in the study.	Diseases, 9th		duration.	did not depend	suggests study		
24				revision-ICD-9:410), and		<b>'</b> 0/.	on air pollution	was free of		
25				pneumonia (ICD-9:			levels.	selective		
26 27				480–487), from Medicare			Apr	report.		
28				billing records for the						
29				years 1995–1999.			9, 20			
30 31							)24			
32							оу д			
33							ues			
34							ָּרָ בָּי			
35 36							otec			
37							April 19, 2024 by guest. Protected by			
38 <sup>l</sup>									<u> </u>	
39							сор			

Probably High Liu et al.  2016a  Probably High EC were collected from a single monitor on a one-in-three or one-in-six day schedule. EC were measured for 566 days from April 02, 2009, to December 30, 2013, was detained of frequency of sampling.  Probably High Low Probably Low Low Study included day counts of one mergency department visit data was obtained one-in-three or one-in-six day schedule. EC were measured for 566 days from April 02, 2009, to December 30, 2013, was obtained of frequency of sampling.  Probably Low Low Study included day counts of or emergency department visit day counts of or emergency department visits were obtained, so obtained, so obtained, so obtained, so outcome data interests.  Probably Low Low Study included day counts of or emergency department visits day counts of or emergency department visits were obtained, so obtained, so outcome data interests.  Probably Low Low Study included day counts of or emergency department visits were obtained, so obtained, so obtained, so outcome data insured from I selective or missing data for Greater point and population growth.  Probably Low Low Study included day of week, temperature, dew point and population growth.  Information potential sources of obtained, so outcome data insured from I selective or missing data did not dependant evidence that did not dependant evidence that did not dependant on air pollution	5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on the outcome data		Conflict of interest	Other
Second properties   EC were collected from a single monitor on a one-in-three or one-in-six day schedule. EC were measured for 566 days from April 02, 2009, to December 30, 2013, < 25% missing for the frequency of sampling.   Second properties				Probably High	Low	Probably Low	Low	Low ay	Probably Low	Low	Low
single monitor on a one-in-three or one-in-six day schedule. EC were measured for 566 days from April 02, 2009, to December 30, 2013, <25% missing for the frequency of sampling.  2016  Single monitor on a one-in-three or one-in-six day schedule. EC were measured for 566 days from April 02, 2009, to December 30, 2013, <25% missing for the frequency of sampling.  2017  2018  Single monitor on a one-in-three or one-in-six day schedule. EC were measured for 566 days from April 02, 2009, to December 30, 2013, <25% missing for the frequency of sampling.  2018  Single monitor on a one-in-three or one-in-six day schedule. EC were measured for 566 days from April 02, 2009, to December 30, 2013, <25% missing for the frequency of sampling.  2019  Single monitor on a one-in-three or one-in-six day schedule. EC were measured for 566 days from April 02, 2009, to December 30, 2013, <25% missing for the frequency of sampling.  2019  Single monitor on a one-in-three or one-in-six day schedule. EC were measured for 566 days from April 02, 2009, to December 30, 2013, <25% missing for the frequency of sampling.  2019  Single monitor on one-in-six day schedule. EC were measured for 566 days from Me Eluc Cross Blue temperature, department visits were and population growth.  Schedule. EC were measured for 566 days for Greater point and population growth.  Schedule Size of Greater population growth.  S	- 1	9	Liu et al.	EC were collected from a	Emergency department	Adjusted for time	Study included	Daily counts	There was	Authors	No other
day schedule. EC were measured for 566 days from April 02, 2009, to December 30, 2013, <25% missing for the frequency of sampling.    Shield Texa. International Classification of Diseases from April 02, 2009, to December 30, 2013, <25% missing for the frequency of sampling.    Shield Texa. International Classification of Diseases 9th Revision (ICD-9) diagnosis codes were used to classify outcome groups.    Shield Texa. International Classification of Diseases 9th Revision (ICD-9) diagnosis codes were used to classify outcome groups.    Shield Texa. International Classification of Diseases 9th Revision (ICD-9) diagnosis codes were used to classify outcome groups.    Shield Texa. International Classification of Diseases 9th Revision (ICD-9) diagnosis codes were used to classify outcome groups.    Shield Texa. International Classification of Diseases 9th Revision (ICD-9) diagnosis codes were used to classify outcome groups.    Shield Texa. International Classification of Diseases 9th Revision (ICD-9) diagnosis codes were used to classify outcome groups.    Shield Texa. International classification of Diseases 9th Revision (ICD-9) diagnosis codes were used to classify outcome groups.    Shield Texa. International classification of Diseases 9th Revision (ICD-9) diagnosis codes were used to classify outcome groups.    Shield Texa. International classification of Diseases 9th Revision (ICD-9) diagnosis codes were used to classify outcome groups.    Shield Texa. International classification of Diseases 1 through obtained, so outcome data. 9 thousand population growth. 9 thousan	- 1		2016a	single monitor on a	visit data was obtained	(long-term and	daily counts of	for emergency	insufficient	declared no	potential
day schedule. EC were measured for 566 days from April 02, 2009, to December 30, 2013, 425% missing for the frequency of sampling.    15				one-in-three or one-in-six	from the Blue Cross Blue	seasonal trend),	emergency	department <u>\frac{8}{2}</u>	information	potential	sources of
measured for 566 days from April 02, 2009, to December 30, 2013, <25% missing for the frequency of sampling.  The first of the frequency of sampling are separated as a separate for 566 days from April 02, 2009, to December 30, 2013, <25% missing for the frequency of sampling.  The first of the frequency of sampling are separated as a separate for Greater from April 02, 2009, to December 30, 2013, <25% missing for the frequency of sampling.  The first of the frequency of sampling are separated as a separate for Greater from population growth. Suggests study on air pollution growth or pollution growth on air pollution growth or pollution growth or pollution growth or pollution growth or pollutio				day schedule. EC were	Shield Texa. International	day of week,	department visits	visits were	about	competing	bias
December 30, 2013,  <25% missing for the frequency of sampling.  December 30, 2013,  Claims data insured from January 1, 2008 through  December 31,  December 31,  December 30, 2013,  Claims data insured from January 1, 2008 through  December 31,  Decembe				measured for 566 days	Classification of Diseases	temperature, dew	for Greater	obtained, so =	selective	financial	identified.
diagnosis codes were used to classify outcome groups.    Section   Claims data   Section   Claims data				from April 02, 2009, to	9th Revision (ICD-9)	point and	Houston from	likely have all	outcome to	interests.	
25% missing for the frequency of sampling.   used to classify outcome groups.   linsured from January 1, 2008 through December 31, 2013.   linsured from January 1, 2008 through On air pollutiong on air pollutiong levels.   linsured from January 1, 2008 through On air pollutiong on air pollutiong levels.   linsured from January 1, 2008 through On air pollutiong on air pollutiong levels.   linsured from January 1, 2008 through On air pollutiong on air pollutiong levels.   linsured from January 1, 2008 through On air pollutiong on air pollutiong levels.   linsured from January 1, 2008 through On air pollutiong levels.   linsured from January 1, 2008 through On air pollutiong levels.   linsured from January 1, 2008 through On air pollutiong levels.   linsured from January 1, 2008 through On air pollutiong levels.   linsured from January 1, 2008 through On air pollutiong levels.   linsured from January 1, 2008 through On air pollutiong levels.   linsured from January 1, 2008 through On air pollutiong levels.   linsured from January 1, 2008 through On air pollutiong levels.   linsured from January 1, 2008 through On air pollutiong levels.   linsured from January 1, 2008 through On air pollutiong levels.   linsured from January 1, 2008 through On air pollutiong levels.   linsured from January 1, 2008 through On air pollutiong levels.   linsured from January 1, 2008 through On air pollutiong levels.   linsured from January 1, 2008 through On air pollutiong levels.   linsured from January 1, 2008 through On air pollutiong levels.   linsured from January 1, 2008 through On air pollutiong levels.   linsured from January 1, 2008 through On air pollutiong levels.   linsured from January 1, 2008 through On air pollutiong levels   linsured from January 1, 2008 through On air pollutiong levels   linsured from January 1, 2008 through On air pollutiong levels   linsured from January 1, 2008 through On air pollutiong levels   linsured from January 1, 2008 through On air pollutiong levels   linsured from January 1, 2008 through				December 30, 2013,	diagnosis codes were	population growth.	claims data	outcome data.	judge for low		
frequency of sampling.  groups.  January 1, 2008 through or missing datable did not depend levels.  2013.  January 1, 2008 through or missing datable did not depend levels.  2013.  January 1, 2008 through or missing datable did not depend levels.  2013.  January 1, 2008 through or missing datable did not depend levels.  2013.  January 1, 2008 through or missing datable did not depend levels.  2013.  January 1, 2008 through or missing datable did not depend levels.  2013.  January 1, 2008 through or missing datable did not depend levels.  2015.  January 1, 2008 through or missing datable did not depend levels.  2016.  January 1, 2008 through or missing datable did not depend levels.  2017.  2018.  January 1, 2008 through or missing datable did not depend levels.  2019.				<25% missing for the	used to classify outcome		insured from	However, any	risk, but		
December 31, did not depended a suggests study on air pollutions levels.  December 31, did not depended a suggests study on air pollutions levels.  December 31, did not depended a suggests study on air pollutions levels.  December 31, did not depended a suggests study on air pollutions levels.  December 31, did not depended a suggests study on air pollutions levels.  December 31, did not depended a suggests study on air pollutions levels.  December 31, did not depended a suggests study on air pollutions levels.  December 31, did not depended a suggests study on air pollutions levels.  December 31, did not depended a suggests study on air pollutions levels.  December 31, did not depended a suggests study on air pollutions levels.  December 31, did not depended a suggests study on air pollutions levels.  December 31, did not depended a suggests study on air pollutions levels.  December 31, did not depended a suggests study on air pollutions levels.  December 31, did not depended a suggests study on air pollutions levels.  December 31, did not depended a suggests study on air pollutions levels.  December 31, did not depended a suggests study on air pollutions levels.  December 31, did not depended a suggest study on air pollutions levels.  December 31, did not depended a suggest study on air pollutions levels.  December 31, did not depended a suggest study on air pollutions levels.  December 31, did not depended a suggest study on air pollutions levels.  December 31, did not depended a suggest study on air pollutions levels.  December 31, did not depended a suggest study on air pollutions levels.  December 31, did not depended a suggest study on air pollutions levels.  December 31, did not depended a suggest study on air pollutions levels.  December 31, did not depended a suggest study on air pollutions levels.  December 31, did not depended a suggest study on air pollutions levels.  December 31, did not depended a suggest study on air pollutions levels.  December 31, did not depended a suggest study levels.  Dece	20			frequency of sampling.	groups.	1/6	January 1, 2008	potential errors	indirect		
December 31, did not depended on air pollution levels.  2013.  December 31, did not depended on air pollution levels.  2013.  December 31, did not depended on air pollution levels.  2013.  Suggests study was free of selective report.  228						' (2)	through	or missing data	evidence that		
24							December 31,	0			
levels. on April 150, 2024 by quest. Protect							2013.	_ C			
27 28 29 30 31 32 33 33 34 35 36											
28 29 30 31 32 33 34 35 36								ı Ap	report.		
29 30 31 32 33 34 35 36									:		
32   Guestian   Guesti											
32   Guestian   Guesti								024			
33								by			
P								gue			
35 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0											
36								Prof			
37								lect			
38								ed b			

2	
3	
4	
5	
6	
7	
8	_
9	
10	
11 12 13	
12	
14	
15	
16	
17	
18	
19	
20	
21	
22	
23	
24	
25	
26	
27	
28	
29	
30	
31	
32	
33	
34	
35	
36	
37	
20	

Page 67 of 136				BMJ Open Bmjop						
1 2 3 4							36/bmjopen-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data		Conflict of interest	Other
8			Probably High	Low	Probably Low	Low	Low	Probably Low	Low	Low
9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38	10	Liu et al. 2016b	EC were collected from a single monitor on a one-in-three or one-in-six day schedule. EC were measured for 566 days from April 02, 2009, to December 30, 2013, <25% missing for the frequency of sampling.	Hospital admission data was obtained from the Blue Cross Blue Shield Texa. International Classification of Diseases 9th Revision (ICD-9) diagnosis codes were used to classify outcome groups.	Adjusted for time, day of week, temperature, seasonaility, humidity and population growth.	Study included all hospital admissions obtained from billing claims of Blue Cross Blue Shield Texa enrollees for Greater Houston from January 1, 2008 to December 31, 2013.	Daily counts for HA were obtained, so likely have all outcome data. However, any potential errors or missing data did not dependent on air pollution levels.	insufficient information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of	Authors declared no competing financial interests.	No other potential sources of bias identified.

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data ≤	Selective reporting	Conflict of interest	Other
8			Probably Low	Low	Probably Low	Low	Probably Low	Probably Low	Low	Low
9 10	11	Sarnat et	24hr average	Computerized billing	Models adjusted	Data consisted of	Daily counts	There was	The authors	No other
11		al. 2015	concentration of PM <sub>2.5</sub>	records were obtained	for season, day of	all emergency	for emergency	insufficient	declare they	potential
12			were obtained from a	from the Missouri	week, holidays,	department visits	department $\frac{8}{2}$	information	have no	sources of
13 14			Supersite (single, central	Hospital Association	time trends (using	during the study	visits were	about	actual or	bias
15			site monitoring location).	(MHA) for emergency	cubic splines for	period for	obtained,	selective	potential	identified.
16			The observations of EC	department visits. The	day of visit with	cardiovascular	hence one	outcome to	competing	
17 18			was 666 days during 1	outcome groups were	monthly knots),	disease	hospital not	judge for low	financial	
19			June 2001-30 April 2003	identified using primary	and temperature.	outcomes.	providing data	risk, but	interests.	
20			(missing data <25%).	International	' /		after 26 April 💆	indirect		
21				Classification of Diseases	' (2)		2002.	evidence that		
22 23				9th Revision (ICD9)		Ch	However, any 📜	suggests study		
24				codes.		<b>'</b> 0'.	potential errors	was free of		
25							or missing data9	selective		
26 27							did not depend ≧	report.		
28							on air pollution			
29										
30							levels. 2024 by			
31 32							by g			
33							ues			
34							guest. Protected b			
35 36							rote			
37							cted			
38							<u> </u>			

2	
3	
4	_
5	
6	
7	
8	_
9	
10	
11	
12	
13	
14	
14 15	
16	
17	
16 17 18	
19	
20	
21	
21 22 23	
23	
24	
25	
26	
27	
28	
29	
30	
31	
32	
32 33	
34	
34 35 36 37 38	
36	
37	
38	
50	

Page 69 o	69 of 136 BMJ Open								
1 2 3 4						36/bmJopen-2021-04951			
5 6 <b>No.</b> 7	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data		Conflict of interest	Other
8		Probably Low	Low	Probably Low	Low	Low	Probably Low	Low	Low
9 12 11 11 12 13 14 15 16 17 18 19 20 21 22 23 24 225 26 27 228 29 30 33 1 33 2 33 34 35 36 37 38	Kim et al. 2012	PM <sub>2.5</sub> mass and chemical constituents were measured daily at one residential monitoring station located on the roof of an elementary school building in Denver. The observations of EC was 1809 days during 2003-2007 (missing data <25%).	All individual hospital admission records during the study period were extracted from nonelective hospital admission discharge data obtained from the Colorado Hospital Association. The International Classification of Diseases, Ninth Revision(ICD-9) codes were used to define cardiovascular hospital admissions (codes 390–459) and respiratory hospital admissions (codes 460–519).	Model adjusted for days from the start of the study, day of week, seasonality, long-term trends, daily average temperature and relative humidity.	Data consisted of all cardiovascular hospital admissions over the course of the study.	Daily counts for hospital admission were obtained, so likely have all outcome data. However, any potential errors or missing data did not depend on air pollution levels.	insufficient information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of selective report.	The authors declare they have no actual or potential competing financial interests.	No other potential sources of bias identified.

Page 70 of 136

No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data		Conflict of interest	Other
		High	Low	Probably Low	Low	Low	Probably Low	Low	Low
13	Ostro et	EC were generally	Data for hospitalizations	Adjusted for time,	Study included	Daily counts	There was	Authors	No other
	al. 2009	recorded every 3 days	were obtained from the	day of the week,	all	for 5	insufficient	declared no	potential
		from two co-located	Office of Statewide	temperature,	hospitalizations	hospitalization 💆	information	competing	sources of
		monitors or one monitor	Health Planning and	seasonality,	for children < 19	s of children	about	financial	bias
		in 6 counties. The	Development, Healthcare	relative humidity	and < 5 years of	were obtained,	selective	interests.	identified.
		number of available days	Quality and Analysis	and pollutant.	age for total	so likely have	outcome to		
		of data over the 4-year	Division. Hospital	<b>'</b> O.	respiratory	all outcome	judge for low		
		period ranged from 227	admissions for children		diseases and	data. However,	risk, but		
		to 381 (some counties	<19 years of age were	' /	several	any potential	indirect		
		had >25% missing for the	classified into one or	. 61	subcategories	errors or	evidence that		
		frequency of sampling).	more categories: all		including	missing data	suggests study		
			respiratory disease		pneumonia, acute	did not depend	was free of		
			(International		bronchitis, and	on air pollution	selective		
			Classification of		asthma for six	levels. ਨੂੰ	report.		
			Diseases, Ninth		California				
			Revision-ICD-9 codes		counties from	9, 20			
			460–519), asthma (ICD-9		2000 through	124			
			code 493), acute		2003.	ру д			
			bronchitis (ICD-9 code			ues			
			466), and pneumonia			ָר. ביי			
			(ICD-9 codes 480–486).			otec			
						April 19, 2024 by guest. Protected by			
			I	l	I	by cop		I	<u> </u>

36/bmjopen-2021-0495

'	
2	
3	
4	
5	
6	
7	
8	
9	
10	
11	
12	
13	
14	
15	
16	
17	
18	
19	
20	
21	
22	
23	
24	
25	
26	
27	
28	
29	
30	
31	
32	
33	
34	
35	
36 37 38	
38	
39	

No	0.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data ≤		Conflict of interest	Other
3			Probably Low	Low	Probably Low	Low	Low $\overset{\mathbf{a}}{\searrow}$	Probably Low	Low	Low
10 14	.	Kim et al.	Daily 24-hour composite	Daily mortality counts for	Models adjusted	Data consisted of	Daily counts 8	There was	None of the	No other
1		2015	PM <sub>2.5</sub> samples were	metropolitan Denver	for longer-term	all deaths over	for death were	insufficient	authors has	potential
2			collected from single,	were computed from the	temporal trend, as	the course of the	obtained, so	information	any actual	sources of
13 14			central-site monitor. The	Colorado Health	time since the	study in a	likely have all	about	or potential	bias
15			observations of EC was	Information Dataset	study began, day	defined	outcome data.		competing	identified.
6			1809 days from 2003	compiled by the Colorado	of week, and daily	geographical	However, any	outcome to	interests.	
17			through 2007 (missing	Department of Public	temperature and	area.	potential errors	judge for low		
8  9			data <25%).	Health and Environment.	humidity.		or missing data	risk, but		
20				Data included cause of			did not depend	indirect		
21				death by the International	(0)		on air pollution			
22   23				Classification of Diseases			levels.	suggests study		
24				10th Revision (ICD-10)		10,	.con	was free of		
25				code.			no ∕u	selective		
26							n Ap			
27 28								Toport.		
29							9, 2			
30							.024			
31							by			
32 33							gue			
34							st.			
35							Prot			
36							lecti			
37 <u> </u>							April 19, 2024 by guest. Protected by			

		BMJ Open By Open							Page 72
1 2 3 4						36/bmJopen-2021-0495			
5 6 <b>No.</b> 7	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data		Conflict of interest	Other
8		Probably Low	Low	Probably Low	Probably Low	Low S	Probably Low	Low	Low
9 15 15 11 12 13 14 15 16 17 18 19 20 21 22 23 24 225 226 227 228 229 330 331 332 334 335 336 337 338	Huang et al. 2012	Daily average concentrations of PM <sub>2.5</sub> were obtained from a single, central-site monitor. Daily average concentrations of EC in PM <sub>2.5</sub> samples were further analyzed. Daily data was available and no missing data was reported.	Daily mortality data were obtained from the Xi'an Center for Disease Control and Prevention. The International Classification of Diseases, Tenth Revision (ICD-10), codes of mortality were as follows: all natural causes (ICD-10 codes A00–R99), respiratory diseases (ICD-10 codes I00–I98), and cardiovascular diseases (ICD-10 codes I00–I99).	Models adjusted for calendar time (seasonality, long-term trends), weather(temperature, relative humidity), year, day of week.	The author removed the death counts on December 31 and January 1 of each year.	Daily counts for death were obtained, so likely have all outcome data. However, any potential errors or missing data did not depend on air pollution levels.	insufficient information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of	No competing financial interests.	No other potential sources of bias identified.

36/bmjopen-2021-0495

י ר	
2	
3	
4	Ī
5	
6	
7	
8	ľ
9	
10	
11	
12	
13	
14	
15	
16	
17	
18	
19	
20	
21	
22	
23	
24	
25	
26	
27	
28	
29	
30	
31	
32	
33	
34	
35	
36	
37	
38	
39	

No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data		Conflict of interest	Other
		Probably High	Low	Probably Low	Low	Low ay 2	Probably Low	Low	Low
0 16	Peng et al.	Ambient EC obtained	Daily counts of hospital	Model adjusted for	Data consisted of	Daily counts 8	There was	The authors	No other
1	2009	from Speciation Trends	admissions were obtained	weather (i.e.,	all cardiovascular	for hospital	insufficient	declare they	potential
2		Network monitors and	from billing claims of	temperature, dew	hospital	admission were	information	have no	sources of
3 4		either from central site or	enrollees in the U.S.	point temperature),	admissions	obtained, so	about	competing	bias
5		averaged over a county.	Medicare system. Each	day of week,	during over the	likely have all		financial	identified.
5		Air pollution	billing claim contains the	unobserved	course of the	outcome data.	outcome to	interests.	
7		concentrations were	date of service, disease	seasonal factors,	study.	However, any			
8 9		measured on a 1-in-3-day	classification using	and long-term		potential errors			
0		schedule in the national	International	trends.		or missing data	indirect		
1		air monitoring stations	Classification of	(0)		did not depend			
2   3		and on a 1-in-6-day	Diseases, 9th Revision			on air pollution			
4		schedule in the state and	(ICD-9) codes (Centers		101	levels.	was free of		
5		local air monitoring	for Disease Control and			n/ or	selective		
6 7		stations. Study removed	Prevention 2008).			1 Ар	report.		
8		suspect data and extreme	,				•		
9		values from the original				9, 2			
)		monitor records;				024			
1 2		monitors with very little				by g			
3		data were omitted				Jues			
4		altogether. Missing data							
5		was not replaced by other				rote			
6 7		values.				ctec			
8						on April 19, 2024 by guest. Protected by copyright.			
9						cop			
0 1						yrigl			
2						Ę.			

2	
3	
4	
5	ĺ
6	I
_	I
7 8	ŀ
9	I
10	I
11	I
12	I
13	I
14	I
15	I
16	I
17	I
17 18	I
19	I
20	I
21	I
22	I
23	I
24	I
25	I
26 27	I
27	I
28	I
29	I
30	I
31	I
32	I
33 24	I
34 35	I
	I
36 37	I
38	ĺ
20	

No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data	Selective reporting	Conflict of interest	Other
3		Probably High	Low	Probably Low	Low	Low S	Probably Low	Low	Low
17	Levy et al.	The U.S. Environmental	Hospital admissions data	Adjusted for time	Study included	Daily counts of	There was	No	No other
1	2012	Protection Agency	were obtained from	(seasonality,	people who died	hospital	insufficient	competing	potential
2		established the PM	billing claims information	long-term trends),	any day between	admissions \(\frac{8}{2}\)	information	financial	sources of
3 4		Speciation Trends	for US Medicare	seasonality, day of	2000 and 2008 in	were obtained	about	interests.	bias
5		Network (STN) to	enrollees in 119 counties	the week and	119 US counties.	from billing	selective		identified.
6		measure more than 50	for the years 2000–2008.	dew-point		claims 3	outcome to		
17		PM <sub>2.5</sub> chemical	The Medicare billing	temperature.		information, so	judge for low		
8  9		components, in addition	claims data were	C/		likely have all			
20		to total mass. The STN	classified into disease	' / <sub>C</sub>		outcome data.	indirect		
21		includes > 50 national air	categories according to	(0)		However, any	evidence that		
22 23		monitoring stations	their International			potential errors	suggests study		
24		(NAMS) and > 200 state	Classification of		101	or missing data	1		
25		and local air monitoring	Diseases, Ninth Revision			did not depend 9			
26		stations (SLAMS). Air	(ICD-9), codes.			on air pollution			
27 28		pollution concentrations	//			levels.	1		
29		were typically measured				ي ر			
30		on a 1-in-3-day schedule				2024 by			
31 32		in the NAMS and on a				by			
33		1-in-6-day schedule in				gues			
34		the SLAMS. There was							
35		no information about				Protected			
36 37		missing data.				Cte			
87 88		imssing data.				9	•		

36/bmjopen-2021-0495

2 3 4	
5	
6	
7	
8	_
9	
10	
11	
12	
13	
14 15 16	
15	
16	
17 18	
18	
19	
20 21	
22	
23	
24	
25	
26	
27	
28	
29	
30	
31	
32	
33	
34	
35	
36	
37 38	
38	
39	
40	

41 42 43

5 5	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data S		Conflict of interest	Other
3			Probably Low	Low	Probably Low	Low	Low	Probably Low	Low	Low
0	18	Son et al.	Hourly air samples were	Daily death counts were	Models adjusted	Data consisted of	Daily counts	There was	The authors	No other
11		2012	obtained from a single,	obtained from the	for time (long-term	all cardiovascular	for death were	insufficient	declare they	potential
12			central-site monitor. The	National Statistical	trends and	deaths over the	obtained, so	information	have no	sources of
3			monitoring system	Office. The study	seasonality), day	course of the	likely have all	about	actual or	bias
14			produces hourly	classified mortality data	of week,	study.	outcome data.		potential	identified.
6			estimates of PM <sub>2.5</sub> total	into all causes of death	temperature and		However, any		competing	
7			mass, and PM <sub>2.5</sub> levels of	[International	relative humidity.		potential errors		financial	
8			EC. Daily data was	Classification of			or missing data		interests.	
20			available and no missing	Diseases, 10th Revision			did not depend			
21			data was reported.	(ICD-10; codes	(0)		on air pollution			
22			· · · · · · · · · · · · · · · · · · ·	A00–R99),			levels.	suggests study		
23				cardiovascular causes		10,	CO	was free of		
25				(codes I00–I99), and			n/ o	selective		
26				respiratory causes (codes			n A	report.		
27				J00–J99)] (World Health				Тероге.		
28 29				Organization 2007).			19, 2			
80				Organization 2007).			202			
31							4 by			
32							gue			
3							est.			
5							Pro			
86							l fect			
37							.com/ on April 19, 2024 by guest. Protected by copyright.			
88 <sup>L</sup> 89							ς S			
10							opyı			
11							righ	•		
12										

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data ≤		Conflict of interest	Other
8 9			Probably High	Low	Low	Low	Low <sup>ay</sup>	Probably Low	Low	Low
9 10	19	Heo et al.	Ambient air samples	Seoul daily mortality data	Adjusted for	Study included	Daily counts 8	There was	Authors	No other
11		2014	were collected over a	were obtained from the	long-term trends,	all death for	for death were	insufficient	declared no	potential
12			24-hour period at 3-day	Korea National Statistical	seasonality,	all-cause,	obtained, so	information	competing	sources of
13   14			intervals from a single	Office. Using the	temperature and	cardiovascular,	likely have all	about	financial	bias
15			monitor. Missing data	International	humidity, day of	and respiratory in	outcome data.	selective	interests.	identified.
16			<25% for the frequency	Classification of Disease,	the week, holiday	Seoul during	However, any	outcome to		
17 18			of EC samples.	10th Revision (ICD-10;	and influenza	2003–2007.	potential errors	judge for low		
19				World Health	epidemics.		or missing data	risk, but		
20				Organization 1993), the	' /		did not depend	indirect		
21				mortality data were	. 01		on air pollution	evidence that		
22 23				classified as all			levels.	suggests study		
24				nonaccidental causes		(0)	com	was free of		
25				(codes A00-R99),			n/ or	selective		
26   27				cardiovascular disease			ı Ap	report.		
27 28				(codes I00-I99),				•		
29				respiratory disease (codes			9, 2			
30				J00-J98), and injury			024			
31				(S00-T98).			by			
32   33				(500 190).			gue			
34							on April 19, 2024 by guest. Protected b			
35							rote			
36							ecte			
37   38							<u>a</u> by			

36/bmjopen-2021-0495

2	
3	
4	
5	
6	
7	
8	_
9	
10	
11	
12	
13	
14	
15	
16	
16 17	
18	
19	
20	
21	
22	
22 23	
24	
25	
26	
27	
28	
29	
30	
31	
32	
33	
34	
35	
36 37	
38	

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data		Conflict of interest	Other
8			Probably High	Low	Probably Low	Low	Low	Probably Low	Low	Low
9 10	20	Basagaña	Single central-site	Daily mortality counts for	Models adjusted	Data consisted of	Daily counts	There was	The authors	No other
11		et al. 2015	monitor in each city. For	all non-external causes	for holidays,	all deaths over	for death and	insufficient	have no	potential
12			each city, PM	[International	summer	the course of the	emergency	information	conflicts of	sources of
3			constituents with >20%	Classification of	population	study in a	hospital	about	interest to	bias
5			of the values below the	Diseases, 9th Revision	decrease, influenza	defined	admissions	selective	disclose.	identified.
5			detection limit or missing	(ICD9) codes 001–799;	epidemics,	geographical	were obtained,	outcome to		
7 8			were excluded.	10th revision (ICD10)	seasonality,	area.	so likely have	judge for low		
9			Otherwise,	codes A00–R99],	long-term trends		all outcome	risk, but		
o			non-detectable were	cardiovascular (ICD9	and temperature.		data. However	indirect		
			replaced by half the limit	codes 390–459, ICD-10	. 01		any potential	evidence that		
2   3			of detection. Air	codes I00–I99) and			errors or	suggests study		
4			pollution data was	respiratory (ICD9 codes		(0)	missing data	was free of		
5			collected daily in	460–519, ICD10 codes			did not depend	selective		
,			Bologna (n=472), twice a	J00–J99) were collected.			on air pollution	report.		
3			week in Barcelona	Cardiovascular and			levels			
9			(n=736) and Madrid	respiratory			No.			
0   1			(n=104), and once a week	hospitalizations were			)24			
2			in Huelva (n=406). There	defined on the basis of			oy g			
3			was no information about	the primary discharge			2024 by guest.			
4			missing data.	diagnosis using the same			ָ קַ	· ]		
5 5				ICD codes defined above.						
7							Cled			
88							by			
39 10							Proteства ву сорупдпт			
11							/rign			
12							F	•		

4 5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data ≤	Selective reporting	Conflict of interest	Other
8 9			Probably High	Low	Probably Low	Low	Low	Probably Low	Low	Low
9 10	21	Dai et al.	EC were measured on a	Daily mortality data were	Adjusted for time,	Study included	Daily counts	There was	The authors	No other
11		2014	1-in-3 or 1-in-6 day	obtained from National	temperature, day	all death for all	for death were	insufficient	declare they	potential
12			schedule. Most of the	Center for Health	of the week, and	causes,	obtained, so	information	have no	sources of
13   14			cities had a single	Statistics. The study	season.	cardiovascular	likely have all	about	actual or	bias
15			monitor. For every	examined nonaccidental		disease,	outcome data.	selective	potential	identified.
16			species, the study	deaths due to all causes		myocardial	However, any	outcome to	competing	
17   18			calculated the monthly	and specific diseases,	<b>'</b> O.	infarction, stroke,	potential errors	judge for low	financial	
19			average species-to-PM <sub>2.5</sub>	derived from the		and respiratory	or missing data	risk, but	interests.	
20			proportions for each	International Statistical	' /	diseases from	did not depend	indirect		
21   22			month as a solution to the	Classification of Disease,	. 01	National Center	on air pollution	evidence that		
23			missing speciation data	10th Revision (World		for Health	levels.	suggests study		
24			problem due to the 1-in-6	Health Organization		Statistics in 75	com	was free of		
25			or 1-in-3 day sampling	2007).		U.S. cities	on	selective		
26   27			frequency. There was no			between 2000	Apr	report.		
28			information of missing			and 2006.	ii 19			
29			data for that sampling				, 20			
30   31			frequency.				24 b			
32							)			
33							uest			
34   35							April 19, 2024 by guest. Protected b			
36							otec			
37							ted			
38 <sup>L</sup>			1				by c		<u> </u>	

2	
3	
4	
5 6	
7	
8	_
9	
10	
11	
12	
13	
14	
15	
16	
17	
18	
19	
20	
21	
22 23	
24 25	
26	
27	
28	
29	
30	
31	
32	
33	
34	
35	
36	
37	
38	
39	

age	e 79 of	79 of 136 BMJ Open								
! !							36/bmjopen-2021-049516 on Incomplete			
; ;	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete ్ల outcome data	Selective reporting	Conflict of interest	Other
; [			Probably Low	Low	Low	Low	Low ay	Probably Low	Low	Low
) 10 11 12 13 14 15 16 17 18 19 19 20 21 22 23 24 25 26 27 28 29 30 31 31 31 31 31 31 31 31 31 31	22	Lin et al. 2016a	The concentrations of different particle size fractions and PM <sub>2.5</sub> chemical constituents were measured at two air monitoring stations. EC were measured for four months of each year from 2007 through 2010. During the period 2009-2011, the proportion of missing data was very low (ranging from 1% to 2%). There were about 20 days without chemical constituents records and were treated as missing observations.	Daily mortality data from 1 January 2007 to 31 December 2011 were obtained from Guangdong Provincial Center for Disease Control and Prevention. The cause of death was coded using the International Classification of Diseases, Tenth Revision (ICD-10). Mortality from cardiovascular diseases (ICD-10:I00-I99) were extracted to construct the time series.	Adjusted for public holidays, day of the week, influenza outbreaks, seasonal patterns and long-term trends, temperature and relative humidity.	Study included daily cardiovascular mortality data from 1 January 2007 to 31 December 2011 in Guangzhou.	Daily counts for death were obtained, so likely have all outcome data. However, any potential errors or missing data did not depend on air pollution levels.  Protected by	There was insufficient information about selective outcome to judge for low risk, but indirect evidence that suggests study	The authors declare they have no actual or potential competing financial interests.	No other potential sources of bias identified.
34   35			observations.				est. Protected by			

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data ≤	Selective reporting	Conflict of interest	Other
8 9			Probably Low	Low	Probably Low	Low	Low S	Probably Low	Low	Low
10	23	Cao et al.	Daily concentrations of	The study obtained	Model adjusted for	Data consisted of	Daily counts 8	There was	The authors	No other
11		2012	EC was obtained from a	numbers of deaths in	long-term and	all nonaccidental	for death were	insufficient	declare they	potential
12			single monitoring site.	Xi'an for each day from	seasonal trends,	causes deaths	obtained, so	information	have no	sources of
13 14			The observations of EC	the Shanxi Provincial	day of week,	during over the	likely have all	about	actual or	bias
15			was 1749 in 1827 days	Center for Disease	temperature,	course of the	outcome data.    dia  dia  dia  dia  dia  dia  dia  d	selective	potential	identified.
16			(missing data <25%).	Control and Prevention	humidity, and SO <sub>2</sub>	study.	However, any	outcome to	competing	
17 18				(SPCDCP). SPCDCP	and NO <sub>2</sub>		potential errors	judge for low	financial	
19				staff then classify the	concentrations.		or missing data	risk, but	interests.	
20				cause of death according	' /		did not depend	indirect		
21				to the International	. 01		on air pollution	evidence that		
22 23				Classification of			levels.	suggests study		
24				Diseases, 10th Revision		ien,	com	was free of		
25				[ICD-10; World Health			on /	selective		
26 27				Organization (WHO)			Apr	report.		
28				1992] as due to total			ii 19			
29				nonaccidental causes			), 20			
30 31				(ICD-10 codes			24 1			
32				A00–R99),			ру д			
33				cardiovascular diseases			uesi			
34 35				(I00–I99), respiratory			[. Pr			
35 36				diseases(J00–J98), or			on April 19, 2024 by guest. Protected			
37				injury (S00–T98).			ted			
38							ру сор			
39							ဗို			

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data	Selective reporting	Conflict of interest	Other
8 9			Probably Low	Low	Probably Low	Low	Low ay	Probably Low	Low	Low
9 10	24	Klemm et	Daily 24-hr average EC	Records of individual	Adjusted for time	Study included	Daily counts	There was	Authors	No other
11		al. 2011	measurements are	deaths were provided by	(seasonality,	all nonaccidental	for death were	insufficient	declared no	potential
12			available for Atlanta	the Georgia Department	long-term trends),	deaths during	obtained, so	information	competing	sources of
13 14			during the study period.	of Human Resources.	temperature, and	over the course	likely have all	about	financial	bias
15			The observations of EC	Cause of death is	day of the week.	of the study.	outcome data.	selective	interests.	identified.
16			was 3317 days from	categorized using the			However, any S	outcome to		
17 18			August 1998 to	International			potential errors	judge for low		
19			December 31, 2007.	Classification of			or missing data	risk, but		
20			Missing data <25%.	Diseases, 10th edition	' /		did not depend	indirect		
21			There was no information	(ICD-10), including	. 01	•	on air pollution <mark>≗</mark>	evidence that		
22 23			for monitor stations.	circulatory conditions		Ch	levels.	suggests study		
24				(I00–I99), respiratory		<b>101</b>	com	was free of		
25				conditions (J00–J99),			on on	selective		
26 27				malignant neoplasm			Apı	report.		
28				(cancer; C00–D48), or			April 19, 2024 by			
29				other nonaccidental			9, 20			
30 31				causes (A00-R99,			)24			
31 32				excluding cardiovascular,			by g			
33				respiratory, or cancer			guest.			
34				causes).						
35 36							Protected			
30 37							) 			
38 <sup>l</sup>							<u> </u>			

					BMJ Oper	า	36/bmJope			Page 82
1 2 3 4							36/bmJopen-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete 9		Conflict of interest	Other
8			Probably Low	Low	Probably Low	Low	Low	Probably Low	Low	Low
9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37	25	Zhou et al. 2011	24hr PM <sub>2.5</sub> samples were obtained from a single, central-site monitor.  Daily data was available and no missing data was reported.	Using codes from the International Classification of Diseases, version 10 (ICD10; World Health Organization 2007), daily death counts were aggregated to nonaccidental allcause deaths (ICD10, codes A00 through R99), cardiovascular deaths (ICD10, codes I01 through I99), and respiratory deaths (ICD-10, codes J00 through J99).	Models adjusted for time, seasonality and long-term trends, day of week, temperature, and humidity.	Data consisted of all cardiovascular deaths over the course of the study.	Daily counts for death were obtained, so likely have all outcome data. However, any potential errors or missing data did not depend on air pollution levels.	insufficient information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of	The authors declare they have no actual or potential competing financial interests.	No other potential sources of bias identified.

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data		Conflict of interest	Other
8 9			Probably Low	Low	Probably Low	Low	Low ay	Probably Low	Low	Low
10	26	Winquist	Daily EC and BC were	Individual-level data	Adjusted for time	Study included	Daily counts	There was	Authors	No other
11		et al. 2015	from a single monitor	were obtained from the	trends, day of	emergency	for emergency	insufficient	declared no	potential
12			site. All species of	Missouri Hospital	week, holidays,	department visits	department 💆	information	competing	sources of
13 14			pollutant statistics are	Association for all	season,	in St Louis	visit were	about	financial	bias
15			missing less than 5%.	emergency department	temperature and	metropolitan	obtained, so	selective	interests.	identified.
16				visits to 36 of 43	dew point.	statistical area	likely have all	outcome to		
17 18				acute-care non-federal		during 1 June	outcome data.	judge for low		
19				hospitals with emergency		2001 through 30	However, any	risk, but		
20				department visits in the	' /	April 2003.	potential errors	indirect		
21   22				16-county St Louis	. 01		or missing data	evidence that		
23				metropolitan statistical			did not depend	suggests study		
24				area during 1 June 2001		'01.	on air pollution	was free of		
25				through 30 April 2003.			levels.	selective		
26 27				Cardiorespiratory			Apr	report.		
28				outcomes of interest were			11 19,			
29				defined based on the			, 20			
30   31				primary ICD-9			2024 by			
32				(International			by g			
33				Classification of			' guest.			
34 35				Diseases, version 9)						
35   36				diagnosis code for the			Protected			
37				visit.			ted			
38 <sup>l</sup>			<u> </u>	1			\$	1		

1 2 3 4	
5	ĺ
6	
7	ŀ
8	
10	
11	
12	
13	
14	
15	
16	
17	
18	
19 20	
21	
22	
23	
24	
25	
26	
27	
28	
29	
30 31	
32	
33	
34	
35	
36	
37 38	
38	l

5 5 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data ≤		Conflict of interest	Other
3			Probably High	Low	Probably Low	Low	Low $\overset{\mathbf{a}}{\searrow}$	Probably Low	Low	Low
o	27	Ostro et	Each of the six counties	Daily mortality data were	Adjusted for time	Data consisted of	Daily counts	There was	The authors	No other
1		al. 2007	had two monitors	obtained from the	trend, day of week,	all cardiovascular	for death were	insufficient	declare they	potential
2			measuring PM <sub>2.5</sub>	California Department of	seasonality,	deaths over the	obtained, so	information	have no	sources of
3 4			components and mass.	Health Services, Center	long-term trends,	course of the	likely have all	about	competing	bias
5			Fresno, Kern, Riverside,	for Health Statistics. The	temperature and	study.	outcome data.	selective	financial	identified.
6			and Sacramento Counties	study determined daily	humidity.		However, any	outcome to	interests.	
7 8			reported data every third	total mortality counts for			potential errors	judge for low		
9			day, whereas San Diego	those > 65 years of age			or missing data	risk, but		
20			and Santa Clara Counties	and for deaths from	' /		did not depend	indirect		
21			reported data every sixth	respiratory disease	' (0)		on air pollution	evidence that		
22			day. For the speciation	[International			levels.	suggests study		
24			analyses, the number of	Classification of		(0)	com	was free of		
25			observation days	Diseases, 10th Revision		\ \/\/	n/ or	selective		
26   27			available ranged from	(ICD10; World Health			Αp	report.		
28			243 (San Diego County)	Organization 1993) codes						
9			to 395 (Sacramento	J00–J98] and			9, 20			
80			County) from 2000 to	cardiovascular disease			024			
31   32			2003. There was no	(codes I00–I99).			by g			
33			specific information				April 19, 2024 by guest. Protected			
34			about missing data.				) ; <del>;</del>			
35							rote			
36 37							ctec			
88							9			

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on the outcome data		Conflict of interest	Other
8 9			Probably Low	Low	Probably Low	Low	Low ay	Probably Low	Low	Low
10	28	Tolbert et	Daily 24h EC from a	Computerized billing	Adjusted for time	Study included	Daily count for	There was	Authors	No other
11		al. 2000	single monitor site. The	record data are being	(seasonality,	emergency	emergency 5	insufficient	declared no	potential
12			observation of EC was	obtained from the	long-term trends),	department visits	department <u>\frac{8}{2}</u>	information	competing	sources of
13 14			356 in 365 days, missing	emergency department	temperature, dew	of the	visits were	about	financial	bias
15			data <25%.	visits participating in the	point, and day of	participating	obtained, so 🚊	selective	interests.	identified.
16				study. Several case	week.	hospitals in the	likely have all	outcome to		
17 18				groups are being defined	<b>'</b> O.	Atlanta	outcome data.	judge for low		
19				using the primary ICD-9		Metropolitan	However, any	risk, but		
20				(International	'/	Statistical Area,	potential errors	indirect		
21				Classification of	. 01	including 33	or missing data	evidence that		
22 23				Diseases, 9th Revision)		hospitals	did not depend	suggests study		
24				diagnostic code.		between January	on air pollution	was free of		
25						1 1993-August	levels. ୧	selective		
26 27						31 2000, 4	1 April	report.		
28						hospitals	rii 19,			
29						between January	9, 20			
30						1 1993-February	2024 by			
31 32						30 2000.	by g			
33							guest.			
34										
35							Protected			
36 37							Ctec			
38								1		

5 5	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data ≤		Conflict of interest	Other
3			Low	Low	Probably Low	Low	Low S	Probably Low	Low	Low
0	29	Wang and	The hourly data were	This study obtained	Adjusted for	Study included	Daily counts 2	There was	Authors	No other
1		Lin 2016	simply averaged to	universal health insurance	temperature,	11 1 (>65	for elderly	insufficient	declared no	potential
2			calculate the daily	claims from the National	relative humidity,	elderly (≧65	mortality and	information	competing	sources of
3			average data for PM <sub>10</sub> ,	Health Research Institute	wind speed,	years) mortality	all population &	about	financial	bias
5			PM <sub>2.5</sub> monitored at 13	(NHRI) and vital	barometric	from 2004 to	emergency ⊕	selective	interests.	identified.
6			general air quality	statistics from the	pressure, holidays,	2008 and all	room visits	outcome to		
7 8			monitoring stations	Ministry of Health and	day of the week,	population EVR	were obtained,	judge for low		
9			located in a densely	Welfare from 2004 to	pneumonia and	from 2004 to	so likely have	risk, but		
20			populated area in Taipei.	2008. Death causes were	influenza.	2010 in Taipei,	all outcome	indirect		
21			Hourly concentrations of	coded according to the		Taiwan.	data. However,	evidence that		
23			EC were detected by	diagnoses of the 9th			any potential	suggests study		
24			series 5400 Monitor.	revision of International		'01.	errors or	was free of		
25			Very few missing values	Classification of Diseases			missing data 9	selective		
6			in the database were	(ICD-9). Disease			did not depend ਨੂੰ	report.		
8			omitted as the daily	diagnoses were based on			en air pollution			
9			average was calculated.	the International			levels.			
0				Classification of Diseases			24 k			
2				with Clinical			ру д			
3				Modification, Ninth			2024 by guest. Protected levels.			
4				Revision (ICD-9 CM).			l. Pr			
35 36							otec			
7							ted			
s L										

2	
2	
4	
5	
6	
7	
8	-
9	
10	
11	
12	
13	
14	
5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 30 30 30 30 30 30 30 30 30 30 30 30	
16	
17	
18	
19	
20	
21	
22	
23	
24	
25	
20	
28	
29	
30	
30 31 32 33	
32	
33	
34	
35	
34 35 36 37	
37	
3 <i>/</i> 38	
20	

age 87 o	f 136			BMJ Oper	n	36/bmJopen			
No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data		Conflict of interest	Other
		Low	Low	Low	Low	Probably Low	Probably Low	Low	Low
0 30 1 2 3 4 5 6 7 8 9 0 1 2 3 4 5 6 7 8 9 0 1 2 3 4 5 6 7 8 9 0 1 2 3 4 5 6 7 7 8 9	Darrow et al. 2014	Daily 24-hour average EC was from ambient monitoring networks. Missing data <1%.	Health data were obtained from 41 metropolitan Atlanta hospitals and the Georgia Hospital Association. The diagnoses of respiratory infection were based on International Classification of Diseases, 9th Revision (ICD-9), diagnosis codes: acute bronchitis or bronchiolitis (code 466); pneumonia (codes 480–486); and upper respiratory infection (codes 460–465).	Adjusted for dew point, temperature, seasonality, long-term trends, day of week, holiday and influenza epidemics.	Study included daily emergency department visit data from 41 metropolitan Atlanta hospitals for the period January 1, 1993, to December 31, 2004 (not all hospitals contributed the full period), and from the Georgia Hospital Association for the period January 1, 2005, to June 30, 2010.	Daily counts for emergency department visit were obtained. In the earliest years of the study, not all hospitals were participating. However, any potential errorson or missing dataon did not dependent on air pollution levels.	There was insufficient information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of selective report.	Authors declared no competing financial interests.	No other potential sources of bias identified.

				BMJ Opei	1	36/bmJope			Page 88
1 2 3 3 4 5 No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete		Conflict of	Other
7	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	outcome data	reporting	interest	Other
3		Probably High	Low	Probably Low	Low	Low	Probably Low	Low	Low
31 31 31 31 31 31 31 31 31 31	Metzger et al. 2004	Ambient 24hr average EC were obtained from one monitor. On days when measurements were missing at the central site, data for the pollutant were imputed using an algorithm that modeled measurements. The observations of EC was 714 days during the period August 1, 1998–August 31, 2000 (missing data >25%).	The study asked 41 hospitals with emergency departments that serve the 20-county Atlanta metropolitan statistical area (MSA) to provide computerized billing data for all emergency department visits between January 1, 1993, and August 31, 2000. Using the primary International Classification of Diseases, 9th Revision (ICD-9) diagnosis code, the study defined several cardiovascular disease (cardiovascular disease) groups based largely on ICD-9 diagnosis codes.	Model adjusted for temporal trends, meteorological conditions (i.e., temperature, dew point temperature), day of week, hospital entry and exit, and federally observed holidays.	Data consisted of all cardiovascular hospital admissions over the course of the study.	Daily counts for emergency department visits were obtained, so likely have all outcome data. However, any potential errors or missing data did not depend on air pollution levels.  April 19, 2024 by guest. Frotected	information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of selective	No competing financial interests.	No other potential sources of bias identified.
			• •			r. Protected by c			

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data		Conflict of interest	Other
8 9			Probably Low	Low	Probably Low	Low	Low <sup>ay</sup>	Probably Low	Low	Low
10	32	Mar et al.	Hourly PM <sub>2.5</sub> chemical	Mortality data for all of	Adjusted for time	Data consisted of	Daily counts	There was	No	No other
11		2000	composition data from a	Maricopa County from	trend, seasonality,	all cardiovascular	for death were	insufficient	competing	potential
12			single, central-site	1995 to 1997 were	day of week,	deaths during	obtained, so \\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\	information	financial	sources of
13 14			monitor. Daily data was	obtained from the	temperature and	over the course	likely have all	about	interests.	bias
15			available and no missing	Arizona Center for	relative humidity.	of the study.	outcome data. Ξ	selective		identified.
16			data was reported.	Health Statistics in			However, any	outcome to		
17 18				Phoenix. Death certificate			potential errors	judge for low		
19				data included residence			or missing data	risk, but		
20				zip code and the primary			did not depend	indirect		
21				cause of death as			on air pollution	evidence that		
22 23				identified by the			levels.	suggests study		
24				International		<b>'</b> 0'.	com	was free of		
25				Classification of			on on	selective		
26 27				Diseases, Ninth Revision			Apr	report.		
28				(ICD-9, World Health			April 19,			
29				Organization, Geneva).						
30   31							24			
32							2024 by guest.			
33							ues			
34										
35 36							Protected			
37							ted			
38 <sup>l</sup>							<u> </u>	l		

BMJ Open

Page 90 of 136

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data		Conflict of interest	Other
8			Low	Low	Probably Low	Low	Low	Probably Low	Low	Low
9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39	33	Wang et al. 2019a	Hourly data of PM <sub>2.5</sub> were collected at 10 Chinese air quality monitoring sites in Shanghai. Hourly mass concentrations of PM <sub>2.5</sub> and EC were predicted in Shanghai by using a Community Multiscale Air Quality model. The study included continuous daily data from 2013 to 2015 (1095 days). Daily data was available and no missing data was reported.	The daily mortality data were obtained from the system of Disease Monitoring Point belonged to the Chinese Center for Disease Control and Prevention (China CDC). Deaths were classified according to the 10th revised International Statistical Classification of Disease (ICD-10), all-cause mortality (A00-R99), circulatory disease mortality (I00-I99, the circulatory disease is also known as cardiovascular disease) and respiratory disease mortality (J00-J99).	Adjusted for long term trends, seasonal influence, day of the week, holidays, temperature and relative humidity.	Study included daily mortality data in Huangpu district from January 1, 2013 to December 31, 2015.	Daily counts for death were obtained, so likely have all outcome data. However, any potential errors or missing data did not depend on air pollution levels.	There was insufficient information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of selective report.	No competing financial interests.	No other potential sources of bias identified.

2	
4	
5	
6	
7	
8	-
9	
10	
11	
12	
13	
14	
15	
16	
17	
17 18	
19	
20	
21	
22	
23	
24	
25	
26	
27	
28	
29	
30	
31	
32	
33	
34	
35	
36	
37	
38	
39	
22	

Page	91 of	<sup>-</sup> 136			BMJ Oper	١	do/ma/op			
1 2 3 4 _							ovamjopen-zozi-o493			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data		Conflict of interest	Other
8 9	3/1	I in at al	Probably High	Low	Probably Low	Low Study included	Low S	Probably Low	Low	Low
10 111 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 38 38 38 38 38 38 38 38 38 38 38 38	34	Lin et al. 2016b	EC was from a single monitor site for four months of each year from 2007 to 2010. Missing data for the particle concentration was very low (ranging from 1% to 2%).	Daily mortality data were obtained from the death registry system. The cause of death was coded using the International Classification of Diseases, Tenth Revision (ICD-10). Mortality from stroke (ICD-10:160–166), and sub-categories, including ischemic stroke (ICD-10:163–166), and hemorrhagic stroke (ICD-10: 160–162) were extracted to construct the time series.	Adjusted for long-term trends, seasonality, temperature, humidity, day of week and public holidays.	Study included the residents who died of ischemic or hemorrhagic strokes in urban districts of Guangzhou between 2007 and 2011.	Daily counts for death were obtained, so likely have all outcome data. However, any potential errors or missing data did not depend on air pollution levels.	insufficient information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of selective	Authors declared no conflict of interest.	No other potential sources of bias identified.

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data ≤		Conflict of interest	Other
8 9			Probably High	Low	Probably Low	Low	Low ay 2	Probably Low	Low	Low
10	35	Lin et al.	Each of the six counties	Daily mortality for all	Adjusted for time,	Study included	Daily counts 2	There was	Authors	No other
11		2016b	had two monitors	California residents were	temperature,	daily	for death were	insufficient	declared no	potential
12			measuring components of	obtained from the	humidity and day	cardiovascular	obtained, so	information	competing	sources of
13 14			PM <sub>2.5</sub> . Fresno, Kern,	California Department of	of the week.	mortality for all	likely have all	about	interests.	bias
15			Riverside and	Health Services, Center		California	outcome data.    deli	selective		identified.
16			Sacramento counties	for Health Statistics.		residents from 1	However, any	outcome to		
17 18			reported 24-hour average	Daily counts of deaths		January 2000 to	potential errors	judge for low		
19			EC in PM <sub>2.5</sub> every third	from cardiovascular		31 December	or missing data	risk, but		
20			day; San Diego and Santa	disease (International	' /	2003.	did not depend	indirect		
21 22			Clara counties reported	Classification of	' (2)		on air pollution	evidence that		
23			data every sixth day. The	Diseases, Tenth Revision			levels.	suggests study		
24			study included only	(ICD10) = I00 - I99) were			com	was free of		
25			species for which at least	calculated.			on /	selective		
26 27			50% of the observations				Apr	report.		
28			were above the level of				ii 19			
29			detection.				), 20			
30 31							24 k			
32							ру д			
33							uest			
34 35							April 19, 2024 by guest. Protected by			
36							otec			
37							ted			
38 <sup>l</sup>							<u> </u>		l	

2	
3	
4	
5	
6	
7	
8	
9	
10	
11	
12	
13	
14	
15	
16	
17	
18	
19	
20	
21	
22	
23	
24	
25	
26	
27	
28	
29	
30	
31	
32	
33	
34	
35	
36	
37	
38	
39	

Pag	e 93 o	f 136		BMJ Open Bmjope						
1 2 3 4							36/bmJopen-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data		Conflict of interest	Other
8			Probably Low	Low	Probably Low	Low	Low	Probably Low	Low	Low
9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36	36	Ito et al. 2011	Ambient EC obtained from multiple monitors and the average of data from multiple monitors was computed using the 24hr average values. The sampling frequency of the chemical speciation data was every third day. Daily data was available and no missing data was reported.	Hospitalizations and mortality data were available at the New York City Department of Health and Mental Hygiene. The relevant variables available in the electronic discharge abstract for each patient included date of admission and International Classification of Diseases, Nine Revision (ICD9) discharge diagnosis code. The International Classification of Diseases, Tenth Revision (ICD10) codes for determining cause of	Model adjusted for temporal trends and seasonal cycles, immediate and delayed temperature effects, and day of the week.	Data consisted of all cardiovascular hospital admissions over the course of the study.	Daily counts for death and hospitalization were obtained, so likely have all outcome data. However, any potential errors or missing data did not depend on air pollution levels.  Protected by	There was insufficient information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of	The authors declare they have no actual or potential competing financial interests.	No other potential sources of bias identified.
37 38				death.			ted b			

4 ,							95			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data ≤	Selective reporting	Conflict of interest	Other
8 9			Probably Low	Low	Probably Low	Low	Low ay	Probably Low	Low	Low
10	37	Chen et al.	Hourly mass	The counts of daily	Models adjusted	Data consisted of	Daily counts 2	There was	No	No other
11		2014	concentrations of PM <sub>2.5</sub>	emergency room visits	for time, day of	all emergency	for emergency	insufficient	competing	potential
12			and the four PM <sub>2.5</sub>	were obtained from the	week, temperature,	department visits	room visit	information	financial	sources of
13 14			constituents obtained	National Taiwan	seasonality and	during the study	were obtained, a	about	interests.	bias
15			from a Supersite (single,	University Hospital. The	relative humidity.	period for	so likely have	selective		identified.
16			central site monitoring	emergency room visit		ischemic and	all outcome	outcome to		
17 18			location). The	data were coded	<b>'</b> O.	hemorrhagic	data. However,	judge for low		
19			observations of EC was	regarding the discharge		stroke.	any potential	risk, but		
20			1599 in 1705 days	diagnosis using the	' /		errors or	indirect		
21 22			(missing data <25%).	International	. 01		missing data	evidence that		
23				Classification of Disease,			did not depend.	suggests study		
24				9th revision (ICD-9).		'01.	on air pollution	was free of		
25							levels.	selective		
26 27							Apr	report.		
28							11 18			
29							), 20			
30 31							)24			
32							ру д			
33							ues			
34							t. Pr			
35 36							otec			
37							on April 19, 2024 by guest. Protected b			
38 <sup>l</sup>							~			
39							8			

36/bmjopen-2021-0495

2	
3	
4	
5	I
6	I
7	I
8	ŀ
9	I
10	I
11	I
12	I
13	I
14	١
15	I
16	I
17	I
18	I
19	I
20	I
21	I
22	I
23	I
24	I
25	I
26	I
27	I
28	I
29	I
30	I
31	I
32	I
33	١
34	I
35	١
36	I
37	١
38	٤
39	

5 5 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data		Conflict of interest	Other
3			Low	Low	Probably High	Low	Low ay	Probably Low	Low	Low
0	38	Tomic'-Sp	Average daily	Emergency department	Adjusted for	Study included	All counts for	There was	Authors	No other
1		iric' et al.	concentrations of BC in	visits data were obtained	temperature,	emergency	emergency 5	insufficient	declared no	potential
2		2019	micrograms per cubic	from the Health Center	humidity, and air	department visit	department ≦	information	competing	sources of
3			meter were measured by	Užice, either from the	pressure.	for allergic	visits were	about	financial	bias
5			three automatic ambient	emergency department		rhinitis and	obtained, so	selective	interests.	identified.
6			air quality monitoring	visits in Užice, Sevojno,		allergic asthma	likely have all	outcome to		
7			stations. There was no	and Kosjeri' c, or from a		from 1 July 2012	outcome data.			
9			information about	general hospital in Užice.		to 30 June 2014	However, any	risk, but		
20			missing data.	The inclusion criteria	1/6	in the Zlatibor	potential errors	indirect		
21				were adults aged 18 years	' (%)	District, Western	or missing data	evidence that		
22				and older with the		Serbia.	did not depend			
24				diagnosis of allergic		101	on air pollution			
25				rhinitis (International			levels.	selective		
26				Classification of			ı Ap	report.		
27 28				Diseases, 10th revision,				1		
9				code J.30.4), allergic			9, 2			
30				asthma (International			024			
31 32				Classification of			by (			
33				Diseases, 10th revision,			gues			
34				code J.45.0), or asthma			;; T			
35				with coexisting allergic			April 19, 2024 by guest. Protected			
36 37				rhinitis.			Ctec			
''				illilitis.			by			

				BMJ Oper	١	86/bmJope			Page 96
No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias			Conflict of interest	Other
		Probably Low	Low	Probably Low	Low	Low	Probably Low	Low	Low
9	Maynard et al. 2007	Daily measurements of BC were obtained from a single monitor site. In order to predict local BC level, the study used a validated spatial—temporal land use regression model to predict 24-hr measures of traffic exposure data (BC) at > 80 locations in the Boston area.	Individual mortality records were obtained from the Massachusetts Department of Public Health, for the years 1995–2002. Specific cause mortality was derived from the International Classification of Diseases (ICD) codes [9th Revision before 1999 (World Health Organization 1975) and 10th Revision 1999 to 2002 World Health Organization 1993)].	Adjusted for season and long term trend, temperature, dew point and day of week.	Study included all death for all causes, cardiovascular, respirator, stroke, and diabetes diseases in Boston metropolitan area from the Massachusetts Department of Public Health between 1995–1997 and 1999–2002.	Daily counts for individual mortality records were obtained, so likely have all outcome data. However, any potential errors or missing data did not depend on air pollution	There was insufficient information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of selective	Authors declared no competing financial interests.	No other potential sources of bias identified.
		9 Maynard	Probably Low  Daily measurements of BC were obtained from a single monitor site. In order to predict local BC level, the study used a validated spatial—temporal land use regression model to predict 24-hr measures of traffic exposure data (BC) at > 80 locations in	Probably Low  Maynard et al. 2007  BC were obtained from a single monitor site. In order to predict local BC level, the study used a validated spatial—temporal land use regression model to predict 24-hr measures of traffic exposure data (BC) at > 80 locations in the Boston area.  Probably Low  Low  Individual mortality records were obtained from the Massachusetts Department of Public Health, for the years 1995—2002. Specific cause mortality was derived from the International Classification of Diseases (ICD) codes [9th Revision before 1999 (World Health Organization 1975) and 10th Revision 1999 to 2002 World Health	Probably Low Daily measurements of et al. 2007 BC were obtained from a single monitor site. In order to predict local BC level, the study used a validated spatial—temporal land use regression model to predict 24-hr measures of traffic exposure data (BC) at > 80 locations in the Boston area.  Probably Low Daily measurements of Individual mortality records were obtained from the Massachusetts Department of Public Health, for the years 1995—2002. Specific cause mortality was derived from the International Classification of Diseases (ICD) codes [9th Revision before 1999 (World Health Organization 1975) and 10th Revision 1999 to 2002 World Health	Maynard et al. 2007    Maynard et al. 2007   Daily measurements of et al. 2007   Daily measurements of BC were obtained from a single monitor site. In order to predict local BC level, the study used a validated spatial—temporal land use regression model to predict 24-hr measures of traffic exposure data (BC) at > 80 locations in the Boston area.   Revision before 1999 (World Health Organization 1975) and 10th Revision 1999 to 2002 World Health   Daily measurements of Individual mortality adjusted for season and long term trend, causes, cardiovascular, respirator, stroke, and diabetes diseases in Boston metropolitan area from the Massachusetts   Department of Diseases   Department of Public   Department of   Department of	Probably Low Daily measurements of BC were obtained from the Massachusetts Department of Public level, the study used a validated spatial—temporal land use regression model to predict 24-hr measures of traffic exposure data (BC) at > 80 locations in the Boston area.  Probably Low Low Adjusted for season and long all death for all term trend, causes, cardiovascular, records were obtained from the Massachusetts Department of Public level, the study used a validated spatial—temporal land use regression model to predict 24-hr measures of traffic exposure data (BC) at > 80 locations in the Boston area.  Confounding bias  Probably Low Adjusted for season and long term trend, temperature, dew point and day of week.  International Classification of Diseases (ICD) codes [9th Revision before 1999 (World Health)  Revision before 1999 (World Health)  Probably Low  Low Low Low Low Adjusted for season and long term trend, temperature, dew point and day of week.  International Classification of Diseases (ICD) codes [9th Revision before 1999 (World Health)  Revision before 1999 (World Health)  Probably Low  Low  Low  Low  Low  Study included all death for all term trend, temperature, dew point and day of week.  International Classification of Diseases (ICD) codes [9th Revision before 1999 (World Health)  Revision before 1999 (World Health)  Public Health   Department of public Health   Department of public Health   Department of point and day of week.  International   Department of public Health   Department of point and day of week.	Study    Probably Low   Low   Adjusted for a single monitor site. In order to predict local BC level, the study used a validated spatial—temporal land use regression model to predict 24-hr measures of traffic exposure data (BC) at > 80 locations in the Boston area.    Boston   Exposure assessment   Dutcome assessment   Dut	Probably Low Daily measurements of et al. 2007 BC were obtained from a single monitor site. In order to predict local BC level, the study used a validated spatial-temporal land use regression model to predict 24-hr measures of traffic exposure data (BC) at > 80 locations in the Boston area.  Probably Low Low Probably Low Adjusted for Study included a season and long all death for all causes, cardiovascular, respirator, stroke, week.  Adjusted for season and long all death for all causes, cardiovascular, respirator, stroke, and diabetes diseases in outcome data.  Boston However, any potential errors of traffic exposure data (BC) at > 80 locations in the Boston area.  Confounding bias  Selection bias  Probably Low Low Adjusted for Study included season and long all death for all causes, cardiovascular, respirator, stroke, week.  International Classification of Diseases (ICD) codes [9th Revision before 1999 (World Health)  Revision before 1999 (World Health)  Probably Low  Low Probably Low  Low Daily remerstree for study used a bout selective outcome to outcome to information ald eclared no information ald eclared no interest over expirator, stroke, week.  Boston However, any potential errors or missing data or missing data suggests study was free of selective.

36/bmjopen-2021-0495<mark>1</mark>

'	
2	
3	
4	ſ
5	I
6	I
7	I
8	ŀ
9	I
10	I
	I
11	I
12	I
13	١
14	١
15	١
16	I
17	I
18	I
19	I
20	I
21	I
22	I
23	I
24	I
25	I
	I
26	I
27	I
28	I
29	I
30	I
31	I
32	I
33	I
34	I
35	١
36	١
37	١
38	ĺ
39	
•	

5   5   7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data o		Conflict of interest	Other
3			Probably Low	Probably Low	Probably Low	Low	Low <sup>ay</sup>	Probably Low	Low	Low
10	40	Sinclair et	Daily 24-hr averages EC	Daily outpatient visits	Adjusted for	Study included	Daily counts 8	There was	No	No other
11		al. 2010	was from a single	were obtained from the	season, day of	daily outpatient	for outpatient	insufficient	competing	potential
12			monitor site. The total	electronic patient data	week, federal	visits for acute	visits were	information	financial	sources of
13 14			observed rate of EC was	warehouse of a	holidays, study	respiratory	obtained, so	about	interests.	bias
15			95.2%.	not-for-profit,	month, time,	diseases from the	likely have all	selective		identified.
16				group-model managed	temperature and	electronic patient	outcome data.	outcome to		
17 18				care organization (MCO)	dew point.	data warehouse	However, any	judge for low		
19				in the metropolitan		of a	potential errors	risk, but		
20				Atlanta area between	' /	not-for-profit,	or missing data	indirect		
21				August 1, 1998 and	' (2)	group-model	did not depend	evidence that		
22				December 31, 2002.		managed care	on air pollution.	suggests study		
24				Visits that met acute visit		organization	levels.	was free of		
25				definition and that had a		(MCO) in the	on	selective		
26				visit diagnosis code of		metropolitan	Apı	report.		
28				asthma, upper respiratory		Atlanta area	April 19,			
29				infection (URI), or lower		between August	9, 20			
30				respiratory infection		1, 1998 and	)24			
32				(LRI) were included in		December 31,	ру д			
33				the study.		2002.	ues			
34				-			2024 by guest. Protected			
35   36							ote			
37							cted			
8 L										

No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data	Selective reporting	Conflict of interest	Other
3		High	Probably Low	Probably Low	Low	Low S	Probably Low	Low	Low
41	Krall et al.	Monitors typically	All-cause mortality data	Adjusted for	Study included	Daily counts	There was	The authors	No other
1	2013	measure PM <sub>2.5</sub>	(excluding accidental	temperature, day	all death	for death were	insufficient	declare they	potential
2		constituent	deaths) were aggregated	of week, long-term	(excluding	obtained, so	information	have no	sources of
3  4		concentrations every	from death certificate	and seasonal	accidental	likely have all	about	actual or	bias
15		third or sixth day. Some	data obtained from the	trends.	deaths) for 108	outcome data.		potential	identified.
16		communities with a	National Center for		urban	However, any	outcome to	competing	
17		single monitor. The	Health Statistics for 2000	<b>'</b> O	communities	potential errors	judge for low	financial	
8  9		observation of EC was	to 2005.	C/	from 2000 to	or missing data		interests.	
20		58-921 days,some		' / <sub>~</sub>	2005.	did not depend	indirect		
21		communities had >25%		' (%)		on air pollution			
22 23		missing data.				levels.	suggests study		
24					10,	.con	was free of		
25					\ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \	 	selective		
26						7 A			
27 28							Toport.		
29						, ç			
30						:024			
31						by			
32 33						April 19, 2024 by guest.			
34									
35									
36						Protected			
37 38						90 8			

36/bmjopen-2021-0495

2	
3	
-	
4	
5	
7	
0	L
9	
10	
11	
12	
13	
14	
15	
16	
17	
18	
19	
20	
21	
22	
23	
24	
25	
26	
27	
28	
29	
30	
31	
32	
33	
34	
35	
36	
36 37 38	
39	

No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data ≤	Selective reporting	Conflict of interest	Other
		Probably High	Low	Probably Low	Low	Low ay 2	Probably Low	Low	Low
0 42	Cakmak et	Daily PM <sub>2.5</sub> aerosol	Diseases were coded	Adjusted for	Study included	Daily counts 8	There was	No	No other
1	al. 2009	samples approximately 1	using the WHO	temperature and	all emergency	for emergency $\bigcirc$	insufficient	competing	potential
2		of every 4 days from a	International	humidity, day of	department visits	department <u>\text{\text{\text{\text{\text{\text{\text{d}}}}}} \text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{d}}}}}}}</u>	information	financial	sources of
3 4		single monitor site.	Classification of Disease,	week, long-term	obtained from the	visit were	about	interests.	bias
5		Sampling occurred daily	9th Revision (ICD-9).	and seasonal	Departamento de	obtained, so	selective		identified.
6		during the cold season	The daily number of	trends.	Es-tad' isticas e	likely have all	outcome to		
7		(April through	emergency department		InformaciónenSa	outcome data.	judge for low		
8 9		September) and alternate	visits for all	C/-	lud (DEIS) of the	However, any	risk, but		
0		days during the warm	nonaccidental (ICD-9 <	1/	Ministry of	potential errors	indirect		
1		season (October through	800) and respiratory	(0)	Health from	or missing data			
2		March). Missing data	(ICD-9 460–519) causes		April 2001	did not depend.			
4		<25% for that frequency.	in Santiago Centro,		through August	on air pollution			
5			Cerrillos, and Pudahuel		2006.	levels.	selective		
6			were obtained from the				report.		
7 8			Departamento de Estad´				•		
9			ısticas e			9, 2			
0			InformaciónenSalud			024			
1			(DEIS) of the Ministry of			by			
2 3			Health from April 2001			gue			
4			through August 2006.			st. F			
5			unough August 2000.			rote			
6						ecte			
7 8						l g			
9						April 19, 2024 by guest. Protected by copyright.			
0						pyriį			
1 2						ght.			

Tolbert et al. 2007  Tolbert e	5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data		Conflict of interest	Other
Tolbert et al. 2007  Daily ambient EC obtained from multiple monitors and a single concentration obtained by averaging across monitors. The observations of EC was 2258 during the period August 1, 1998 to December 31, 2004  December 31, 2004  Missing data <25%).  Daily counts in a ball cardiovascular disease and trends, daily average temperature, dew point, day of week, federal holiday, and hospital entry and exit.  Model adjusted for long-term and seasonal trends, daily average temperature, dew point, day of week, federal holiday, and hospital entry and exit.  Daily counts in the competing of memergency go insufficient obtained, so ob				Low	Low	Probably Low	Low	Low 2	Probably Low	Low	Low
al. 2007 obtained from multiple monitors and a single concentration obtained by averaging across monitors. The observations of EC was 2258 during the period August 1, 1998 to December 31, 2004 (missing data <25%).  December 31, 2004 (missing data <25%).  May be a concentration obtained by averaging across monitors. The observations of EC was 2258 during the period August 1, 1998 to December 31, 2004 (missing data <25%).  May be a concentration obtained by averaging across monitors. The observations of EC was 2258 during the period August 1, 1998 to December 31, 2004 (missing data <25%).  May be a concentration obtained by averaging across monitors. The observations of EC was 2258 during the period August 1, 1998 to December 31, 2004 (missing data <25%).  May be a concentration obtained by averaging across monitors. The observations of EC was 2258 during the period August 1, 1998 to December 31, 2004 (missing data <25%).  May be a concentration obtained by average temperature, dew point, day of week, federal holiday, and hospital entry and exit.  May be a concentration obtained by obtained, so		43	Tolbert et	Daily ambient EC	Computerized billing	Model adjusted for	Data consisted of	Daily counts	There was	No	No other
concentration obtained by averaging across monitors. The observations of EC was 2258 during the period 20 August 1, 1998 to December 31, 2004 (missing data <25%).  December 31, 2004 (missing data for each violity of the study.  December 31, 2004 (missing data for each violity of the study.  December 31, 2004 (missing data for each violity of the study.  December 31, 2004 (missing data for each violity of the study.  December 31, 2004 (missing data for each violity of the study.  December 31, 2004 (missing data for each violity of the study.  December 31, 2004 (missing data for each violity of the study.  December 31, 2004 (missing data for each violity of the study.  December 31, 2004 (missing data for each violity of the study.  December 31, 2004 (missing data for each violity of the study.  December 31, 2004 (missing data for each violity of the study.  December 31, 2004			al. 2007	obtained from multiple	records for all emergency	long-term and	all cardiovascular	for emergency	insufficient	competing	potential
averaging across monitors. The observations of EC was 2258 during the period August 1, 1998 to December 31, 2004 (missing data <25%).  Missing data <25%).				monitors and a single	department visits between	seasonal trends,	disease and	department \(\frac{8}{2}\)	information	financial	sources of
averaging across monitors. The observations of EC was 2258 during the period August 1, 1998 to December 31, 2004 (missing data <25%).  December 31, 2004 (missing data				concentration obtained by	January 1, 1993 and	daily average	respiratory	visit were	about	interests.	bias
monitors. The observations of EC was 2258 during the period August 1, 1998 to December 31, 2004 (missing data <25%).  Monitors. The observations of EC was 2258 during the period August 1, 1998 to December 31, 2004 (missing data <25%).  Monitors The observations of EC was 2258 during the period August 1, 1998 to December 31, 2004 (missing data <25%).  Monitors The observations of EC was 2258 during the period August 1, 1998 to December 31, 2004 (missing data <25%).  Monitors The observations of EC was 2258 during the period August 1, 1998 to December 31, 2004 (missing data <25%).  Monitors The observations of EC was 2258 during the period August 1, 1998 to December 31, 2004 (missing data <25%).  Monitors The observations of EC was 2258 during the period August 1, 1998 to December 31, 2004 (missing data <25%).  Monitors The observations of EC was 2258 during the period August 1, 1998 to December 31, 2004 (missing data <25%).  Monitors The observations of EC was 2258 during the period August 1, 1998 to Outcome data.  Monitors The observations of EC was 2258 during the period August 1, 1998 to Outcome data.  Monitors The observations of EC was 2258 during the period August 1, 1998 to Outcome data.  Monitors The observations of EC was 2258 during the period and hospital entry and exit.  Monitors The observations of EC was 2258 during the period and hospital entry and exit.  Monitors The observations of EC was 2258 during the period and hospital entry and exit.  Monitors The observations of EC was 2258 during the period and hospital entry and exit.  Monitors The observations of EC was 2258 during the period and hospital entry and exit.  Monitors The observation of Diseases of the study.  Monitors The outcome to outcome data.  Monitors The outcome to Outcome to Outcome to Outcome data.  Monitors The outcome to Outcom				averaging across	December 31, 2004 were	temperature, dew	disease hospital	obtained, so	selective		identified.
observations of EC was 2258 during the period August 1, 1998 to December 31, 2004 (missing data <25%). Observations of EC was 2258 during the period August 1, 1998 to December 31, 2004 (missing data <25%). Observations of EC was 2258 during the period August 1, 1998 to December 31, 2004 (missing data <25%). Observations of EC was 2258 during the period visit: primary and hospital entry and exit. Observations of the study. Observations of the study. Observations of the study. Observations of EC was 258 during the period and hospital entry and exit. Observations of the study. Observations of EC was 258 during the period and hospital entry and exit. Observations of the study. Observations o	16			monitors. The	collected, including the	point, day of week,	admissions	likely have all	outcome to		
2258 during the period August 1, 1998 to December 31, 2004 (missing data <25%).  226				observations of EC was	following data for each	federal holiday,	during the period				
August 1, 1998 to December 31, 2004 (missing data <25%).  August 1, 1998 to December 31, 2004 (missing data <25%).  Potential errors of the study.  Over the course of the study.  Over th				2258 during the period	visit: primary	and hospital entry	1993 to 2004	However, any	risk, but		
22 (missing data <25%).  9th Revision (ICD-9) diagnostic code, secondary ICD-9 diagnosis codes.  9th Revision (ICD-9) diagnosis codes.  9th Revision (ICD-9) diagnosis code, selective report.				August 1, 1998 to	International	and exit.	over the course	potential errors	indirect		
(missing data <25%).  9th Revision (ICD-9) diagnostic code, secondary ICD-9 diagnosis codes.  9th Revision (ICD-9) diagnostic code, secondary ICD-9 diagnosis codes.  9th Revision (ICD-9) diagnostic code, secondary ICD-9 diagnosis codes.  9th Revision (ICD-9) diagnostic code, secondary ICD-9 diagnosis codes.  9th Revision (ICD-9) diagnostic code, secondary ICD-9 diagnosis codes.  9th Revision (ICD-9) diagnostic code, secondary ICD-9 diagnosis codes.  9th Revision (ICD-9) diagnostic code, secondary ICD-9 diagnosis codes.  9th Revision (ICD-9) diagnostic code, secondary ICD-9 diagnosis codes.  9th Revision (ICD-9) diagnostic code, secondary ICD-9 diagnosis codes.  9th Revision (ICD-9) diagnostic code, secondary ICD-9 diagnosis codes.				December 31, 2004	Classification of Diseases	(0)	of the study.	or missing data	evidence that		
diagnostic code, secondary ICD-9 diagnosis codes.  diagnosis codes.  diagnosis code, secondary ICD-9 diagnosis codes.  diagnosis codes.  diagnosis codes.  on air pollutions selective report.				(missing data <25%).	9th Revision (ICD-9)						
secondary ICD-9 diagnosis codes.  levels.    Selective report.   S					diagnostic code,		(0)	C			
diagnosis codes.  diagnosis codes.  diagnosis codes.  pril 19, 2024 by gue st. Protection of the control of the	25				secondary ICD-9			· · ·			
29 30 31 32 33 34 35 36 37					•			ı Ap	report.		
29 30 31 32 33 34 35 36 37									1		
32 33 34 35 36 37								9, 2			
32 33 34 35 36 37								024			
33								by			
35   Protection								gue			
35   70   70   70   70   70   70   70   7											
	35							rot			
								ecte			

36/bmjopen-2021-0495<mark>1</mark>

2	
3	
4	
5	
6	
7	L
8	
9	
10	
11	
12	
13	
14	
15	
16	
17	
18	
19	
20	
21	
22	
23	
24	
25	
26	
27 28	
28	
29	
30	
31	
32 33	
34 35	
36 37 38	
3/ 20	
38 39	
39	

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete 9 outcome data		Conflict of interest	Other
8			Low	Low	Probably Low	Low	Low	Probably Low	Low	Low
9 10	44	Lall et al.	Daily EC data were	The categorization of the	Model adjusted for	Data consisted of	Daily counts	There was	The authors	No other
11		2011	obtained from two	admissions data was	season, wintertime	all cardiovascular	for hospital	insufficient	declare they	potential
12			monitors. Daily data was	based on codes from the	influenza episode,	hospital	admission wer	information	have no	sources of
13 14			available and no missing	International	weather, day of	admissions over	obtained, so	about	actual or	bias
15			data was reported.	Classification of	week, and other	the course of the	likely have all	selective	potential	identified.
16				Diseases, revision 9	possible	study.	outcome data.	outcome to	competing	
17 18				(ICD-9).	confounders (e.g.,		However, any	judge for low	financial	
19					federal holidays).		potential errors	risk, but	interests.	
20					1		or missing data	indirect		
21					(0)		did not depend			
22   23						Teh,	on air pollution			
23   24						10,	levels.	was free of		
25						\ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \	√ IO /u	selective		
26							ι Ak			
27 28										
29							April 19, 2024 by			
30							024			
31							l by			
32							' guest.			
33 34							est.			
35							Pro	1		
36							Protected			
37							ed <del>-</del>			
38 <sup>L</sup>			1	1		ı	<del> </del>	1		

4 5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data		Conflict of interest	Other
8 9			Probably High	Low	Probably Low	Low	Low	Probably Low	Low	Low
10	45	Jung and	A total of 153 daily	The health data used in	Adjusted for	Study included	Daily counts	There was	No	No other
11		Lin 2017	samples (approximately 4	the study were sourced	seasonal trend, day	all asthma	for asthma	insufficient	competing	potential
12			weeks per season) from a	from Longitudinal Health	of week,	outpatient visits	outpatient \( \frac{5}{2} \)	information	financial	sources of
13 14			single monitor site were	Insurance Database 2000.	temperature,	(0-20 years old)	visits (0-20	about	interests.	bias
15			collected. Multiple linear	Daily outpatient visits for	precipitation and	in Shalu district	years old) data	selective		identified.
16			regression models were	asthma (International	wind vectors.	from	were obtained,	outcome to		
17 18			used to back extrapolate	Classification of	Ά.	Longitudinal	so likely have	judge for low		
19			the historic concentration	Diseases, Ninth Revision,		Health Insurance	all outcome	risk, but		
20			of individual components	Clinical Modification,	' /	Database 2000	data. However,	indirect		
21 22			of PM <sub>2.5</sub> from 2000	ICD-9-CM code 493)	(0)	during January 1,	any potential	evidence that		
23			through to 2010,	data was obtained from		2000 to	errors or	suggests study		
24			including BC.	Longitudinal Health		December 31,	missing data	was free of		
25 26				Insurance Database 2000.		2010.	did not depend 9	selective		
27							on air pollution	report.		
28							levels.			
29							, 20			
30 31							2024 by			
32							) g			
33							lest			
34 35							guest. Protected			
36							) 			
37							led R			
38 <sup>L</sup> 39			-				y cop	,	•	•

BMJ Open

36/bmjopen-2021-0495

1	
2	
3	
4	I
5	
6	
7	L
8	
9	
10	
11	
12	
13	
14	
15	
16	
17	
17 18	
19	
20	
21	
22	
23	
24	
25	
26	
27	
28	
29	
30	
31	
32	
33	
34	
35	
36	
37	
38	
39	
29	

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data		Conflict of interest	Other
8 9			Probably Low	Low	Probably Low	Low	Low 2	Probably Low	Low	Low
10	46	Gong et	The 24-h mean BC	The disease data used in	Adjusted for	Study included	Daily counts	There was	Authors	No other
11		al. 2019	concentrations data were	this study were collected	calendar effects,	all cardiovascular	for all deaths	insufficient	declared no	potential
12			obtained from a single	from the Chinese Center	long-term trends,	mortality in	were obtained, \(\frac{8}{2}\)	information	conflict of	sources of
13 14			monitor site. During the	for Disease Control and	temperature,	Beijing obtained	so likely have	about	interest.	bias
15			study period (2091 days),	Prevention, and included	humidity, day of	from the Chinese	all outcome	selective		identified.
16			missing rate of BC was	all deaths in Beijing from	week, NO <sub>2</sub> and	Center for	data. However, 3	outcome to		
17 18			0.68%.	January 1, 2006 to	$SO_2$ .	Disease Control	any potential	judge for low		
19				December 31, 2011.		and Prevention	errors or	risk, but		
20				Causes of death were	' /	during January 1,	missing data	indirect		
21				classified according to	. 01	2006 to	did not depend	evidence that		
22 23				the International		December 31,	on air pollution	suggests study		
24				Classification of		2011.	levels.	was free of		
25				Diseases, 10th Edition			v or	selective		
26 27				(ICD-10) and data on			ı Ap	report.		
28				cardiovascular diseases			rii 19,	1		
29				(ICD-10 code: I00–I99)						
30				were obtained.			2024 by			
31 32							by (	•		
33							guest.			
34										
35							Protected			
36 37							ecte			
37   38							ع و			

Page 104 of 136

5 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data o		Conflict of interest	Other
			Probably Low	Probably Low	Probably High	Low	Low ay	Probably Low	Low	Low
o   4	47	Mostofsky	Ambient EC obtained	Patients potentially	Model adjusted for	Population	Daily counts 8	There was	No	No other
1		et al. 2012	from one monitor. BC	eligible for this study	seasonality,	consisted of	for emergency $\triangleright$	insufficient	competing	potential
2			concentrations were	were identified by	time-trends,	patients ≥21	department \( \frac{2}{2} \)	information	financial	sources of
3 4			measured continuously.	reviewing daily	temperature, dew	years of age	admission were	about	interests.	bias
5			Daily data was available	emergency department	point temperature,	admitted to the	obtained, so	selective		identified.
6			and no missing data was	admission logs, stroke	barometric	hospital with	likely have all	outcome to		
7 8			reported.	service admission logs,	pressure and	neurologist-confi	outcome data.	judge for low		
9				stroke service consult	chronic and	rmed ischemic	However, any	risk, but		
20				logs, and hospital	slowly-varying	stroke and	potential errors	indirect		
21				electronic discharge	potential	residing in the	or missing data	evidence that		
22   23				records.	confounders.	Boston	did not depend.	suggests study		
24						metropolitan	on air pollution	was free of		
25						region. Also	levels.	selective		
26 27						patients had to	Apı	report.		
28						reside within 40	11 18			
29						km of the air	9, 20			
30						pollution	)24			
31 32						monitor.	by g			
33							lues			
84							: <del>:</del> _P			
35 36							rote			
37							April 19, 2024 by guest. Protected by			
38 39										

36/bmjopen-2021-0495

2	
3	
J ∕I	
5	
6	
7	
, δ	ŀ
9	
10	
11	
12	
13	
14	
15	
16	
17	
18	
19	
20	
21	
22	
23	
24	
25	
26	
27	
28	
29	
30	
31	
32	
33	
34	
35	
36	
37	
38	

5 5 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on the outcome data of the outcome data on the outcome data of the outcome data on the outcome		Conflict of interest	Other
3			Probably High	Low	Probably Low	Low	Low by	Probably Low	Low	Low
0	48	Krall et al.	PM <sub>2.5</sub> constituents from	The study obtained	Adjusted for	Study included	Daily counts	There was	The authors	No other
1		2017	one urban, ambient	electronic billing data for	holidays,	all emergency	for emergency	insufficient	declare they	potential
2			monitor located in each	respiratory disease	long-term trends,	department visits	department 💆	information	have no	sources of
3 4			city. Daily pollution data	emergency department	day of the week,	for respiratory	visits of	about	actual or	bias
5			were available in Atlanta;	visits for all ages at acute	season,	disease at acute	respiratory	selective	potential	identified.
6			however, data were only	care hospitals. Using	hospitalsreporting	care hospitals in	disease were	outcome to	competing	
7			available approximately	diagnosis codes from the	data, temperature	the 20-county	obtained, so	judge for low	financial	
8			every third day in the	International	and dew point.	Atlanta	likely have all	risk, but	interests.	
20			remaining three cities.	Classification of	1 /	metropolitan	outcome data.	indirect		
21			There was no information	Diseases, 9th Revision	(0)	area, the	However, any	evidence that		
22			about missing data.	(ICD-9), the study		7-county	potential errors	suggests study		
24			·	considered subcategories		Birmingham	or missing data			
25				of respiratory diseases		metropolitan	did not depend	selective		
26				including pneumonia		area, the 8	on air pollution €			
28				(ICD-9 codes 480–486),		Missouri and 8	levels ==			
9				chronic obstructive		Illinois counties	9, 20			
0				pulmonary disease		in the St. Louis	024			
31 32				(491,492,496), upper		metropolitan	by g			
33				respiratory infection		area, and the	Jues			
34				(URI) (460–465, 466.0,		12-county Dallas	2024 by guest. Protected			
35				477), and asthma and/or		metropolitan	rote			
36   37				wheeze (493, 786.07).		area.	ctec			
8							9		l	

1	
2	
3	
4	ĺ
5 6	
7	
8	l
9	
10	
11	
12	
13	
14	
15	
16	
17	
18	
19	
20	
21	
22	
23	
24	
25	
26	
27	
28	
29	
30	
31	
32	
33	
34 35	
36 37 38	
3/ 3/	l
39	
29	

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data		Conflict of interest	Other
8 9			Probably Low	Low	Probably Low	Low	Low	Probably Low	Low	Low
10	49	O'Lenick	The 24-hour average	Patient-level emergency	Adjusted for	Study included	Daily counts	There was	Competing	No other
11		et al. 2017	concentration of EC was	department visit data	season, periods of	all emergency	for emergency	insufficient	interests:	potential
12			evaluated. Pollutant	from 1 January 2002 to	hospital	department visit	department \(\frac{8}{2}\)	information	None	sources of
13 14			concentration estimates	31 December 2008 were	participation and	data acquired	visit were	about	declared.	bias
15			were obtained by fusing	acquired from hospitals	holidays,	directly from	obtained, so	selective		identified.
16			observational data from	located within the	temperature and	hospitals	likely have all	outcome to		
17			available network	20-county metropolitan	mean dew point,	(2002-2004	outcome data.	judge for low		
18 19			monitors with pollutant	area of Atlanta; Relevant	interaction terms	period) and the	However, any	risk, but		
20			concentration simulations	data elements included	between season	Georgia Hospital	potential errors	indirect		
21			from the Community	admission date,	and maximum	Association	or missing data	evidence that		
22 23			Multi-Scale Air Quality	International	temperature and	(2005–2008	did not depend	suggests study		
24			emissions-based chemical	Classification of Diseases	day of year.	period) located	on air pollution	was free of		
25			transport model at	Ninth Revision (ICD-9)		within the	levels.	selective		
26 27			12×12km grids over	diagnosis codes, age and		20-county	April	report.		
28			Atlanta. 24-hour average	ZIP code of patient		metropolitan area	rii 19,	:		
29			EC were evaluated. Daily	residence.		of Atlanta.	9, 2			
30			data was available and no				2024 by			
31 32			missing data was				by (	•		
33			reported.				guest.			
34										
35							Protected			
36 37							Ctec			
38 L							ع ا			

2	
3	
4	
5	
7	
8	-
9	
10	
11	
12	
13	
14	
15	
16	
17	
18	
19	
20	
21	
22	
23	
24	
25 26	
26 27	
28	
26 29	
30	
31	
32	
33	
34	
35	
36	
37 38	
38	
39	
40	

Page 10	7 of 136			ВМЈ Орег	n	o/Binjop			
1 2 3 4						Incomplete			
5 6 <b>No</b> 7	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data	Selective reporting	Conflict of interest	Other
8		Probably Low	Low	Probably Low	Low	Low	Probably Low	Low	Low
9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38	Pearce et al. 2015	Daily EC data were obtained from a central monitoring location in Atlanta. Daily data was available and no missing data was reported.	The study obtained aggregate daily counts for pediatric asthma related emergency department visits for children ages 5 to 18 years from 41 hospitals within metropolitan Atlanta; and defined emergency department visits for pediatric asthma as all visits with a code for asthma (493.0–493.9) or wheeze (786.07) using the International Classification of Diseases, 9th Revision.	Adjusted for year, season, month, day of the week, hospital, holidays, temperature and dew point.	Study included all emergency department visits for pediatric asthma of children ages 5 to 18 years from 41 hospitals within metropolitan Atlanta for study period.	Daily counts for pediatric asthma related emergency department visits were obtained, so likely have all outcome data. However, any potential errors or missing data did not depend on air pollution levels.	There was insufficient information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of selective report.	The authors declare that they have no competing interests.	No other potential sources of bias identified.
39 40 41 42						у сорупдпт.			

No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias		Selective reporting	Conflict of interest	Other
		Low	Low	Probably Low	Low	Low S	Probably Low	Low	Low
51	Strickland	24-hour average EC were	Daily counts of	Adjusted for	Study included	Daily counts	There was	No conflict	No other
	et al. 2010	obtained from 6	emergency department	season, dew point,	all emergency	for emergency	insufficient	of interests.	potential
		monitors. Missing data	visits for asthma or	temperature, year,	department visits	room visits of	information		sources of
		<1%.	wheeze among children	month, day of	for asthma or	asthma or	about		bias
			were collected from 41	week, hospital,	wheeze among	wheeze disease	selective		identified.
			Metropolitan Atlanta	upper respiratory	children aged 5	were obtained, 3	outcome to		
			hospitals during	infections (the	to 17 years from	so likely have	judge for low		
			1993-2004. Using the	logarithm of the	metropolitan	all outcome	risk, but		
			International	daily count of	Atlanta hospitals	data. However	indirect		
			Classification of	upper respiratory	during	l ×	evidence that		
							suggests study		
			,	ĺ ,		i .	00		
			_	•					
						_			
			•	`			i i i i i i i i i i i i i i i i i i i		
						ي ر			
			· ·			20.22			
			`			by			
			· · · · · ·	concentrations).		gue			
			after October 1, 1998).						
						 	1		
						l l			
						ed 5			
		51 Strickland	Strickland et al. 2010 Et al.	Strickland et al. 2010  Strickland et al. 2010  Low  24-hour average EC were obtained from 6 monitors. Missing data <1%.  Daily counts of emergency department visits for asthma or wheeze among children were collected from 41 Metropolitan Atlanta hospitals during 1993-2004. Using the	Strickland et al. 2010  Strickland 24-hour average EC were obtained from 6  monitors. Missing data  Visits for asthma or wheeze among children were collected from 41  Metropolitan Atlanta hospitals during infections (the logarithm of the daily count of Upper respiratory infections) and pollen concentrations  Classification of Upper respiratory infections) and pollen concentrations  Visits for pediatric asthma as all visits with a code for asthma (493.0–493.9) or wheeze (786.09 before October 1, 1998; 786.07  Strickland 24-hour average EC were obtained from 6  monitors. Missing data  Visits for asthma or wheeze among children were collected from 41  Metropolitan Atlanta hopper respiratory infections (the logarithm of the daily count of upper respiratory infections) and pollen concentrations  Various lags of ambient ragweed, pine, oak, juniper, grass and birch concentrations).	Strickland et al. 2010  Adjusted for study included all emergency department temperature, year, wheeze among children were collected from 41  Metropolitan Atlanta upper respiratory infections (the logarithm of the daily count of upper respiratory infections) and pollen concentrations  Classification of Upper respiratory infections) and pollen emergency department visits for pediatric asthma as all visits with a code for asthma (493.0–493.9) or wheeze (786.09 before October 1, 1998; 786.07  Study included sall emergency department temperature, year, month, day of week, hospital, upper respiratory infections (the daily count of upper respiratory infections) and pollen concentrations  (various lags of ambient ragweed, pine, oak, juniper, grass and birch concentrations).	Strickland et al. 2010  Adjusted for sashm in chapping all emergency department visits of season, dew point, temperature, year, month, day of week, hospital, upper respiratory infections (the law in color and pollen concentrations)  Classification of Diseases, 9th Revision, the study defined emergency department visits for pediatric asthma as all visits with a code for asthma (493.0–493.9) or wheeze (786.09 before October 1, 1998; 786.07 after October 1, 1998).	Strickland et al. 2010    Strickland et al. 2010   Low   Low   Probably Low   Probably Low   Probably Low   Low   Probably Low   Probably Low   Probably Low   Low   Probably Low   Low   Probably Low   Probably Low   Low   Probably Low   Probably Low   Low   Probably Low   Low   Low   Probably Low   Low   Low   Probably Low   Low   Low   Probably	Strickland et al. 2010   Strickland emergency department visits for asthma of week, hospital, wheeze among echildren were collected from 41 Metropolitan Atlanta hospitals during infections of upper respiratory infections) and pollen emergency department visits for pediatric asthma of week, hospital, wheeze among echildren were obtained, 30 during during during during evidence that suggests study was free of did not depends on air pollutione levels.

`	
2	
3	
4	ĺ
5	I
6	I
7	l
8	I
9	I
10	I
11	I
12	I
13	I
14	١
15	I
16	I
	I
17 18	I
19	I
20	I
21	I
22	I
23	I
24	I
25	I
26	I
27	I
28	I
29	I
30	I
31	I
32	I
33	I
34	١
35	١
36	I
37	I
37 38	ĺ
39	

Pag	je 109	109 of 136 BMJ Open								
1 2 3 4							Incomplete			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data	Selective reporting	Conflict of interest	Other
8			Low	Low	Probably Low	Low	Low	Probably Low	Low	Low
9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36	52	Strickland et al. 2014	24-hour average EC were obtained from 6 monitors. Missing data was 1%.	Daily counts of emergency department visits for asthma or wheeze among children aged 2 to 16 years were collected from the Georgia Hospital Association from 1 January 2002 through 30 June 2010. The study identified all emergency department visits with an International Classification of Diseases, 9th revision (ICD-9) code for asthma (codes beginning with 493) or wheeze (code 786.07) present in any diagnosis field.	Adjusted for season, dew point, temperature, day of week, and holiday.	Study included all emergency department visits for asthma or wheeze among children 2 to 16 years of age from the Georgia Hospital Association.	Daily counts for emergency room visits of asthma or wheeze disease were obtained, so likely have all outcome data. However, any potential errors or missing data did not depend on air pollution levels.	There was insufficient information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of selective report.	No conflict of interests.	No other potential sources of bias identified.
37 38 39 40 41 42							Protected by copyright.			

1	
2	
3	
4	Ī
5	
6	
7	
8	ŀ
9	
10	
11	
12	
13	
14	
15	
16	
17	
17 18	
10	
19 20 21	
20	
21	
22	
23	
24	
25	
26	
27	
28	
29	
30	
31	
31 32	
33	
34	
35	
36	
27	ĺ
37	ı
37 38	

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data		Conflict of interest	Other
8 9			Probably High	Low	Probably Low	Low	Low ay	Probably Low	Low	Low
10	53	Ito et al.	The study chose 150 U.S.	Using International	Adjusted for	Study included	Daily counts	There was	No conflict	No other
11		2013	metropolitan statistical	Classification of	modeling of	all nonaccidental	for death and	insufficient	of interests.	potential
12			areas where the data from	Diseases, 10th Revision	confounding	all-cause,	emergency §	information		sources of
13 14			at least one Chemical	(ICD-10) codes, the study	temporal trends	cardiovascular	hospitalization 8	about		bias
15			Species Network monitor	aggregated daily death	(annual cycles and	disease and	were obtained, $\stackrel{α}{=}$	selective		identified.
16			were available. The	counts for the	influenza	respiratory	so likely have	outcome to		
17 18			Chemical Species	nonaccidental all-cause,	epidemics),	deaths and	all outcome	judge for low		
19			Network data for PM <sub>2.5</sub>	cardiovascular disease	day-of-week	emergency	data. However,	risk, but		
20			components were	and respiratory deaths.	patterns and	hospitalizations	any potential	indirect		
21			available either every	Using International	temperature.	for the elderly	errors or	evidence that		
22 23			third day or every sixth	Classification of		(those 65 and	missing data	suggests study		
24			day. There was no	Diseases, 9th Revision		older) of	did not depend	was free of		
25			information about	(ICD-9) codes,		cardiovascular	on air pollution	selective		
26 27			missing data.	emergency		disease and	levels. $\frac{1}{2}$	report.		
28				hospitalizations for the		respiratory				
29				elderly (those 65 and		diseases.	19, 2024 by guest.			
30				older) data were divided			)24			
31 32				into cardiovascular			by g			
33				disease and respiratory			Jues			
34				categories.						
35							rote			
36 37							ctec			
38 <sup>l</sup>							Protected by copyright			
39							cop			
40 41							yrig			
42							).			

36/bmjopen-2021-0495<mark>1</mark>

•
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39

7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete 9 outcome data		Conflict of interest	Other
3			Probably Low	Low	Probably Low	Low	Probably Low	Probably Low	Low	Low
10	54	Ostro et	The model calculations	Deaths were assigned	ge, race, marital	Data obtained for	There was no	There was	The authors	No other
11		al. 2015b	track the mass and	codes based on the	status, smoking	a cohort of	information on	insufficient	declare they	potential
12			concentrations of the PM	International	status, pack-years	female teachers	the rate of lost	information	have no	sources of
13 14			constituents in particle	Classification of	of smoking,	≥30 years old.	follow up.	about	actual or	bias
15			diameters ranging from	Diseases, 10th Revision	secondhand smoke		ed #	selective	potential	identified.
16			0.01 to 10μm through	(ICD-10) for the	exposure, body		om om	outcome to	competing	
17 18			calculations that describe	following outcomes:	mass index,		http	judge for low	financial	
19			emissions, transport,	all-cause deaths	lifetime physical		://br	risk, but	interests.	
20			diffusion, deposition,	excluding those with an	activity, alcohol		njop	indirect		
21			coagulation, gas- and	external cause	consumption,		en.k	evidence that		
22			particle-phase chemistry,	(A00–R99),	average daily		) Mi	suggests study		
24			and gas-to-particle	cardiovascular deaths	dietary intake of	<b>'</b> 01.	com	was free of		
25			conversion. The	(I00-I99), Ischemic heart	fat, calories,		/ on	selective		
26 27			University of California	disease deaths (I20-I25),	menopausal status,		Apr	report.		
28			Davis/California Institute	and pulmonary deaths	family history of					
29			of Technology model was	(C34, J00–J98).	myocardial		9, 20			
30 31			used to estimate		infarction, stroke,		124			
32			ground-level		use of blood		ру д			
33			concentrations of 50 PM		pressure		ues			
34			constituents over the		medication,			,		
35 36			major population regions		aspirin; living		April 19, 2024 by guest. Protected			
37			in California.		conditions		ted by			

36/bmjopen-2021-0495

Classification of cestimate residential exposure to traffic-related air pollutants including black carbon. During the 5-year exposure period, individual exposures to ambient air pollutants were estimated at each person's residential postal code centroid using land use regression   Classification of combination of comb	5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data		Conflict of interest	Other
	10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36	55		Using high spatial resolution land use regression models to estimate residential exposure to traffic-related air pollutants including black carbon. During the 5-year exposure period, individual exposures to ambient air pollutants were estimated at each person's residential postal code centroid	The study used International Statistical Classification of Diseases, 9th Revision (ICD-9) codes 490–492 and 496 or 10th Revision (ICD-10) codes J40–J44 to identify COPD cases during the 4-year	inequality, education, population size, racial composition, unemployment).  Probably High Individual-level covariates: age, sex, preexisting comorbid conditions; and neighborhood socioeconomic	Data obtained for a cohort of people (45-85 years old) registered with the provincial health insurance plan. Study provided total number of subjects along with those lost during the	Probably Low During the 4-year follow-up period, 38,377 (8%) subjects were lost to follow-up because of moving out of the province of dying from	Probably Low There was insufficient information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of selective	The authors declare they have no actual or potential competing financial	No other potential sources of bias

36/bmjopen-2021-0495<mark>1</mark>

1 2 3 4 5	
6 7	
8	
9	
10	
11	
12	
13	
14	
15	
16	
17	
18	
19	
20	
21	
22	
23	
24	
25	
26	
27	
28	
29	
30	
31	
32	
33	
34	
35	
36	
37 38	
38	l

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data		Conflict of interest	Other
8 9 10 11 12 13 14 15			models.	Corp			lay 2022. Downloaded fro			
16 17			Probably Low	Low	Probably Low	Low	Probably Low	Probably Low	Low	Low
18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38	56	Hvidtfeldt et al. 2019	The PM, NO <sub>2</sub> , BC, and O <sub>3</sub> concentrations at residential addresses of the cohort members were derived by a high-resolution dispersion modelling system which incorporates contributions from local, urban, and regional sources of precursors to PM, NO <sub>2</sub> , BC, and O <sub>3</sub> .	Participants who died from external causes such as injuries, accidents and suicides (International Classification of Diseases, 10th Revision-ICD-10 codes S–Z) were censored at date of death. In addition, the study investigated cardiovascular (ICD10 codes I00–I99) and respiratory (ICD10 codes J00–J99 and C34) subgroups of mortality.	Age, sex, educational attainment, occupational status, marital status, smoking (status, intensity, and duration), environmental tobacco smoke (ETS), alcohol consumption, body mass index, waist circumference, fruit consumption, vegetable	Data obtained for a cohort of men and women aged 50–64 years residing in the areas of Copenhagen and Aarhus.	There was no information on April 19, 2024 by guest. Protected by follow up.	There was insufficient information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of selective report.	The authors declare they have no competing financial interests.	No other potential sources of bias identified.
39 40 41 42							copyright.			

36/bmjopen-2021-049

9	
1	0
1	1
1	2
1	
	4
1	
	6
1	
	8
	9
	0
_	1
2	1
2	2
2	3
	4
	5
2	6
2	7
	8
	9
	0
	1
3	
3	3
3	4
3	5
3	6
3	7
	8
	9
	0

physical activity; neighborhood level socioeconomic status (SES).  Probably Low Probably Low Probably High Probably High Probably Low Probably High Probably Low Low Probably Low Probably Low Probably High Probably Low Low	outcome data reporting interest  consumption, physical activity; neighborhood level socioeconomic status (SES).  Probably Low Probably Low Probably High Probably High Probably Low Probably High Probably Low Probably High Probably Low Low Low	4							5			
Consumption, physical activity; neighborhood level socioeconomic status (SES).  Probably Low Probably Low Probably High Probably High Probably Low Probably High Probably Low Probably High Probably Low Low Low	consumption, physical activity; neighborhood level socioeconomic status (SES).  Probably Low Probably High Low Probably High Probably Low Low Low	5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	outcome data∽	reporting		Other
neighborhood level socioeconomic status (SES).  Probably Low Probably High Low Probably High Probably Low Low Low	neighborhood level socioeconomic status (SES).  Probably Low Probably High Low Probably High Probably High Probably Low Low Low	8					consumption,		ау			
neighborhood level socioeconomic status (SES).  Probably Low Probably High Low Probably High Probably Low Low Low	neighborhood level socioeconomic status (SES).  Probably Low Probably High Low Probably High Probably Low Low Low	-					physical activity;		022			
level socioeconomic status (SES).  Probably Low Probably Low Probably High Low Probably High Probably Low Low Low	level socioeconomic status (SES).  Probably Low Probably High Low Probably High Probably High Probably Low Low Low	11					neighborhood		D			
Probably Low Probably Low Probably High Low Probably High Low Probably High Low	Probably Low Probably Low Probably High Low Probably High Low Probably High Low Low Low Low	12					level		own			
Probably Low Probably Low Probably High Low Probably High Low Probably High Low	Probably Low Probably Low Probably High Low Probably High Low Probably High Low Low Low Low	13				()4			loac			
Probably Low Probably Low Probably High Low Probably High Low Probably High	Probably Low Probably Low Probably High Low Probably High Low Probably High								e d			
					Probably Low	Probably Low		Low	Probably High	Probably Low	Low	Low
		19 20 21 22 23 24 25 26 27 28 29							//bmjopen.bmj.com/ on April 19, 2024 by gu			

2	
<i>J</i>	
5	
6	
7	
8	-
9	
10	
11	
12	
13	
14	
15	
16	
17	
18	
19	
20	
21	
22	
23	
24	
25	
26	
27 28	
28	
29 30	
31	
32 33	
34	
35	
36	
37	
٠,	ĺ

Pag	Page 115 of 136 BMJ Open									
1 2 3 4							36/bmJopen-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data	Selective	Conflict of interest	Other
8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36	57	Thurston et al. 2016	The mean concentrations of PM <sub>2.5</sub> mass and trace constituents were obtained from U.S. Environmental Protection Agency Air Quality System. These PM <sub>2.5</sub> constituent data were analyzed to derive estimates of source apportioned PM <sub>2.5</sub> mass exposure concentrations using the absolute principal component analysis (APCA) PM <sub>2.5</sub> source apportionment method.	More than 99% of known deaths were assigned a cause using the International Classification of Diseases, 9th and 10th Revision (ICD-9 codes 410–414; ICD-10 codes I20–I25).	Active smoking and former smoking, passive smoke exposure, possible workplace exposure to PM, occupational dirtiness index, marital status, education, BMI and BMI <sup>2</sup> , consumption of beer, wine, and other alcohol, quintile of dietary fat consumption, quintile of combined dietary vegetable, fruit, fiber consumption; Six ecologic covariates.	Data obtained for a cohort of persons at least 30 years of age, in households including someone at least 45 years of age and resided in all 50 states, the District of Columbia, and Puerto Rico.	The analytic cohort included 445,860 participants, with 34,408 Ischemic heart disease deaths (of a total of 157,572 deaths from all causes) occurring during follow-up.  Protected to the first of the f	information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of selective report.	No competing financial interests.	No other potential sources of bias identified.
37 38			Probably Low	Low	Probably Low	Low	Probably Low	Probably Low	Low	Low
39 40 41 42							copyright.	:		

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data		Conflict of interest	Other
8 9	58	Yang et	Land use regression	Deaths were coded	Age at entry,	Data obtained for	There was no $\frac{\infty}{2}$	There was	The authors	No other
10		al. 2018	models were derived	according to the	gender, individual	a cohort of	information on	insufficient	declare they	potential
11			from street level	International	smoking status,	people who were	the rate of lost	information	have no	sources of
12			measurements collected	classification of Diseases,	body mass index	older than or	follow up.	about	actual or	bias
13 14			during two sampling	10th Revision (ICD-10;	(BMI), physical	equal to 65 years	load	selective	potential	identified.
15			campaigns conducted in	WHO 2010) including	activity, education	old.	ea t	outcome to	competing	
16			2014 and 2015.	natural cause mortality	level and monthly		ro m	judge for low	financial	
17				(A00–R99), overall	expenses;		nttp	risk, but	interests.	
18 19				cardiovascular disease	percentage of		)://D	indirect		
20				(I00–I99) and overall	participants who		n ng	evidence that		
21				respiratory disease	were equal to or		Jen.	suggests study		
22 23				(J00–J47 and J80–J99).	older than 65 years		om).	was free of		
24				Subcategories included	old, percentage of	(0)	com	selective		
25				Ischemic heart disease	participants whose	\ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \	v on	report.		
26				(IHD) (I20–I25),	educational level		April			
27 28				cerebrovascular disease	was higher than			<u>:</u>		
29				(I60–I69), Pneumonia	secondary school,		9, 2			
30				(J12–J18) and chronic	average income		, 2024 by			
31   32				obstructive pulmonary	per month and		by (			
33				disease (COPD) (J40–I44	percentage of		guesi			
34				and I47).	smokers.		, ;; , τ			
35 36				,			rote			
30   37			Probably Low	Low	Probably High	Low	Probably Low	Probably Low	Low	Low
38			1 Todaviy Low	LUW	1 Tobably High	LUW	1 100a0iy L0w	- 1100abiy Low	LUW	LUW

36/bmjopen-2021-0495<mark>1</mark>

2	
3	
4	
5	
6	
7	
8	ŀ
9	
10	
11	
12	
13	
14	
15	
16	
16 17	
18	
19	
20	
21	
22	
23	
24	
25	
26	
27	
28	
29	
30	
31	
32	
33	
34	
35	
36	
37 38	
38	١
39	

No	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on the outcome data of the outcome		Conflict of interest	Other
59	Gan et al.	Land use regression to	A coronary heart disease	Model adjusted for	Study provided	During the $\frac{\omega}{2}$	There was	The authors	No other
0	2011	estimate air pollution	hospitalization case is a	age, sex,	total number of	4-year	insufficient	declare they	potential
1		concentrations and	record of hospitalization	preexisting	subjects along	follow-up	information	have no	sources of
2		exposure assigned to	with the following	comorbidity, and	with those lost	period, 17,542 <u>≸</u>	about	actual or	bias
3  4		residential centroid.	International Statistical	neighborhood	during the	$(3.9\%)$ moved $\frac{8}{2}$	selective	potential	identified.
5			Classification of	socioeconomic	follow-up period.	out of the	outcome to	competing	
16			Diseases, 9th Revision	status. No		province and	judge for low	financial	
7			codes, ICD-9, 410–414	individual data on		16,367 (3.6%)	risk, but	interests.	
8  9			and 429.2or 10th	behavioral risk		died from other	indirect		
20			Revision (ICD-10),	factors.		diseases,	evidence that		
21			I20–I25, as the principal	' (0)		leaving	suggests study		
22 23			diagnosis (the most			418,826	was free of		
24			responsible diagnosis) for			(9 <sub>2.5</sub> %)	selective		
25			a hospital admission in			subjects at the 9	report.		
26 27			the hospitalization			end of Pri			
28			database. A coronary			follow-up.			
29			heart disease death is a			9, 20			
30			death record with			)24			
31 32			coronary heart disease as			by g			
33			the cause of death in the			2024 by guest.			
34			provincial death						
35 36			registration database.			rote			
37		Probably High	Low	Probably Low	Low	Probably Low 2	Probably Low	Low	Low

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data		Conflict of interest	Other
8 9	60	De	Used black smoke (BS)	The study obtained	Individual-level	Data obtained for	There was no $\frac{\omega}{2}$	There was	No	No other
10		Kluizenaa	as an indicator of EC	information on the	covariates: age,	a cohort of	information on	insufficient	competing	potential
11		r et al.	concentrations. Derived	incidence of	gender, marital	27,070	the rate of lost	information	financial	sources of
12		2013	background EC	hospital-based Ischemic	status, education,	non-institutionali	follow up.	about	interests.	bias
13 14			concentrations from BS	heart disease	smoking, alcohol	zed subjects.	oad	selective		identified.
15			measured at two regional	(International	use, physical		ea =	outcome to		
16			monitoring sites. Local	Classification of Diseases	activity, body		ÖM	judge for low		
17 18			traffic-related EC	[ICD9] 410-414) and	mass index, living		nttp	risk, but		
19			emission contributions	cerebrovascular disease	conditions		://br	indirect		
20			were estimated based on	(ICD9 430-438) in the	(employment		njop	evidence that		
21			fuel-specific EC content	study population.	status, financial		en.r	suggests study		
22 23			of exhaust PM <sub>10</sub>		problems).		) J	was free of		
24			emission. Used the			<b>'</b> 0/.	com	selective		
25			traffic-related EC			Ch	/ on	report.		
26 27			emissions as input to							
28			calculate local EC							
29			concentrations, assuming				April 19, 2024 by			
30 31			absence of other local EC				024 1			
32			sources. Also assumed				) y g			
33			that dispersion dynamics				guesi			
34			of EC are identical to				ָר. בּי	,		
35 36			those of $PM_{10}$ .				Otec			
37			Probably Low	Probably Low	Probably Low	Low	Probably Low	Probably Low	Low	Low
38 ٔ							oy			

36/bmjopen-2021-0495<mark>16</mark>

2	
3	
4	
5	
7	
8	-
9	
10	
11	
12	
13	
14	
15	
16 17	
18	
19	
20	
21	
22	
23	
24	
25	
26	
27	
28	
29 30	
31	
32	
33	
34	
35	
36	
37 38	
38	ı

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data o		Conflict of interest	Other
8 9	61	Vedal et	The exposure estimation	All outcomes were	Individual-level	Data obtained for	There was no		No financial	No other
10		al. 2013	were used the national	reported via questionnaire	covariates: age,	a cohort of	information on S	insufficient	interests.	potential
11			spatial model predictions	and assessed via	body mass index,	postmenopausal	the rate of lost	information		sources of
12			and secondary exposure	physician-adjudicator	smoking status,	women.	follow up.	about		bias
13 14			measures of citywide	review of medical records	cigarettes smoked		follow up.	selective		identified.
15			average exposures and	following established	per day and years		led fr	outcome to		
16			distance to major	protocols.	of smoking,		rom	judge for low		
17 18			roadways.		systolic blood		http	risk, but		
19					pressure, history of		).//br	indirect		
20					hypertension,		njop	evidence that		
21					hypercholesterole		en.	suggests study		
22 23					mia, history of		omj.	was free of		
24					diabetes,	"eh	con	selective		
25					education,		v on	report.		
26 27					household income		Ap			
28					level, and race.					
29							9, 20			
30							024			
31 32							by g			
33							jues			
34							; <del>;</del>			
35 36							.com/ on April 19, 2024 by guest. Protecte			
37							ctec			
38			High	Low	Probably Low	Low	Low §	Probably Low	Low	Low
39							copyright.			
40 41							yrigl			
42							7.			

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data o	Selective reporting	Conflict of interest	Other
8	62	Rahmatini	BC were collected from	Daily non-accidental	Models adjusted	Study included	Daily counts	There was	The authors	No other
9 10		a et al.	two monitors (Sharif and	deaths were obtained	for time,	all daily	Daily counts 202 for death were 22	insufficient	of this	potential
11		2021	Setad) with data recorded	from Ministry of Health	temperature,	non-accidental	obtained, so	information	article	sources of
12			at 5 min intervals. BC	and Medical Education	relative humidity,	deaths from	likely have all 🛓	about	declare that	bias
13 14			measurements began	database. The causes of	atmospheric	Ministry of	outcome data.	selective	they have	identified.
15			from March 2017 to	death were coded	pressure, PM2.5	Health and	However, any	outcome to	no conflict	
16			August 2017. But the	according to the	data, Day of week	Medical	potential errors	judge for low	of interests.	
17			gaseous pollutant at the	International	(DOW) and public	Education	or missing data	risk, but		
18 19			Setad site were unreliable	Classification of Disease	holidays.	database from	did not depend	indirect		
20			and models utilizing the	(10th revision—ICD-10).		March 2017 to	on air pollution	evidence that		
21			2-site data were		(0)	August 2017.	levels.	suggests		
22 23			unsatisfactory. So, only				levels. n.bmj.com/	study was		
24			the Sharif data were used.			101	.con	free of		
25							n/ or	selective		
26							on April 19,	report.		
27 28								•		
29							9, 2			
30							2024 by			
31							by			
32 33							guest.			
34							st. F			
35							Prote			
36 37			Probably Low	Probably Low	Probably Low	Low	Low g	Probably Low	Low	Low
37   38			<i>J</i>	J 22.02			р В	J		

2 3 4	
5	
6	
7	
8	ŀ
9	
10	
11	
12	
13	
14	
15	
16	
16 17	
18	
19	
20	
21	
22	
23	
24	
25	
26	
27	
28	
29	
30	
31	
32	
33	
34	
35	
36	
27	L

Page 121 of 136				BMJ Open						
1 2 3 4							36/bmjopen-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data on seconds	Selective reporting	Conflict of interest	Other
8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35	63	Liu et al. 2021b	Annual county-level exposures of PM2.5 and its constituents for each participant were assessed by aggregating satellite-derived estimates at a monthly time-scale and 1 km-resolution.	The three cardiovascular events as health outcomes: 1) total cardiovascular disease, including but not limited to hypertension and stroke; 2) hypertension; 3) stroke were defined according to the Disease Classification Codebook for Chinese Family Panel Studies.	Model adjusted for age, gender, education level (illiteracy, primary to middle school, and high school or above), household income (RMB, strata of ≤ 15,000, 15, 000 − 40,000, and 40,000 +, grouped according to the upper and lower quartiles), urbanicity (urban/rural, defined by CFPS participants' home addresses).	All of participants were drawn from the China Family Panel Studies (CFPS) launched by Peking University Institute of Social Science Survey (ISSS) in 2010, an ongoing national longitudinal survey of social-demograp hy in China.	The cohort included 14,331 adults who completed from http://bmjopen.bmj.com/ on April 19, 2024 by guest. Protection follow-up.	information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of selective report.	The authors declare that they have no known competing financial interests or personal relationship s that could have appeared to influence the work reported in this paper.	No other potential sources of bias identified.
36 37 38			Probably Low	Low	Probably Low	Low	Probably Low		Low	Low

7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data ≤		Conflict of interest	Other
3	64	Lavigne et	A spatial PM2.5 surface	Incident childhood	Model adjusted for	The study used	There was no	There was	The authors	No other
0		al. 2021	gridded at a resolution of	asthma cases were	parity, child sex,	data on singleton	information on S	insufficient	declared	potential
11			approximately 1-km2	identified according to	breastfeeding	live births that	the rate of lost	information	that there is	sources of
2			was derived using	International	status at the time	occurred	follow up.	about	no conflict	bias
13 14			multiple satellite-based	Classification of Diseases	of discharge,	between April	load	selective	of interest.	identified.
15			retrievals of aerosol	[ICD]-10: J45.	maternal smoking	1st 2006 and	ed fr	outcome to		
6			optical depth in	$O_{\mathcal{L}}$	during pregnancy,	March 31st 2014	om.	judge for low		
7  8			combination with a		maternal atopy,	in the Province	http	risk, but		
19			chemical transport model,		gestational age and	of Ontario,	://br	indirect		
20			and enhanced through		birth weight.	Canada.	njop	evidence that		
21			statistical incorporation		' (2)	Mother-infant	en.l	suggests		
22			of ground- based			pair data were	<u>, on</u> .	study was		
24			observations (including			obtained from	com	free of		
25			BC).			the Better	or or	selective		
26						Outcomes	1 Ap	report.		
27 28						Registry &	April 19,			
29						Network	9, 2			
30						(BORN) Ontario,	024			
31						a province wide	by			
32						birth registry that	2024 by guest.			
34						captures	st. P			
35						perinatal health	rote			
36 37						information.	rotected			
97 ∟ 88						iiiioiiiiatioii.	<u>0</u>			

36/bmjopen-2021-0495<mark>1</mark>

2	
2	
4	
-	
2	
6	
8	L
9	
10	
11	
12	
13	
14	
15	
16	
17	
18	
19	
20	
21	
22	
23	
24	
25	
26	
27	
28	
29	
30	
31	
32	
33	
34	
35	
36	
36 37 38	
38	

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete of outcome data o		Conflict of interest	Other
8			Probably Low	Probably Low	Probably Low	Low	Probably Low	Probably Low	Low	Low
10	65	Rodins et	The study used the	Cardiovascular outcomes	Model adjusted for	The study used	There was no 8	There was	The authors	No other
11		al. 2020	validated,	in the HNR Study were	age, sex,	baseline	information on	insufficient	declare that	potential
12			time-dependent,	determined by an	individual and	(2000–2003) and	the rate of lost	information	they have	sources of
13   14			three-dimensional	independent endpoint	neighborhood	14 years	follow up.	about	no known	bias
15			European Air Pollution	committee based on	SES, BMI,	follow-up data	ed fr	selective	competing	identified.
16			Dispersion chemistry	self-reports, physician	nighttime traffic	from the German	m	outcome to	financial	
17 18			transport model	and next-of-kin	noise exposure and	HNR Study, an	http	judge for low	interests or	
19			(EURAD) to estimate the	interviews, and medical	lifestyle factors:	ongoing	://br	risk, but	personal	
20			exposure to EC.	records.	smoking, alcohol	population-based	//bmjope	indirect	relationship	
21					consumption,	prospective	en.k	evidence that	s that could	
22					physical activity	cohort study.	<u>) j</u>	suggests	have	
24					and nutritional	<b>101</b>	com	study was	appeared to	
25					pattern.		on	free of	influence	
26 27							Apı	selective	the work	
28								report.	reported in	
29							9, 20		this paper.	
30							)24			
31							by ç			
33							April 19, 2024 by guest.			
34							; <del>;</del> 			
35   36							Protected			
36 37							ctec			
38							à			

Page 124 of 136

4 5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data ≤	Selective reporting	Conflict of interest	Other
8 9			Probably Low	Low	Probably High	Low	Low <sup>ay</sup>	Probably Low	Low	Low
10	66	Kovačević	The daily average	The data of emergency	Model adjusted for	Study included	Daily counts 8	There was	The authors	No other
11		et al. 2020	concentration of BC were	department (ED) visits	seasonality,	all the data of	for emergency 🖯	insufficient	declare no	potential
12			collected from three	for allergic asthma were	long-term trends,	emergency	department \(\frac{8}{2}\)	information	conflict of	sources of
13 14			automatic ambient air	collected from the Užice	temperature,	department (ED)	(ED) visits	about	interest.	bias
15			quality monitoring	Health Centre, either	humidity, air	visits for allergic	were obtained,	selective		identified.
16			stations located in Užice,	from the EDs	pressure, air	asthma were	so likely have	outcome to		
17 18			Sevojno, and Kosjerić.	(ambulances or home	pollutants and	collected from	all outcome	judge for low		
19			BC were measured	care) in Užice, Sevojno,	pollens.	the Užice Health	data. However,	risk, but		
20			between 1st July 2012	and Kosjerić or from a	' /	Centre, either	any potential	indirect		
21 22			and 30th June 2014.	general hospital in Užice.	' (7)	from the EDs	errors or	evidence that		
23			There was no information	International		(ambulances or	missing data	suggests		
24			about missing data.	Classification of		home care) in	did not depend	study was		
25				Diseases, 10th revision,		Užice, Sevojno,	on air pollution	free of		
26 27				codes were used in the		and Kosjerić or	levels. 출	selective		
28				diagnosis of allergic		from a general	11 19	report.		
29				asthma or asthma with		hospital in Užice	, 20			
30 31				coexisting allergic rhinitis		during 1st July	124 k			
32				(AR).		2012 to 30th	у 9			
33						June 2014.	uesi			
34							April 19, 2024 by guest. Protected b			
35 36							otec			
37							ted			
38 <sup>l</sup>							\$			

2	
2	
4	
4 5 6 7 8	
6	
7	
8	L
9	
9 10 11	
11	
12	
13	
14 15	
15	
16	
17	
16 17 18 19 20	
19	
20	
21	
22	
23	
24 25 26	
25	
26	
27 28	
28	
29	
30	
31	
32 33	
34	
35	
36 37 38	
زر 20	
38	

Pag	ge 125 of 136 BMJ Open									
 <u>2</u> 3							Incomplete			
5	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data	Selective reporting	Conflict of interest	Other
;			Probably Low	Probably Low	Probably Low	Low	Probably Low	Probably Low	Low	Low
'o	67	Hasslöf et	BC levels were modelled	The outcomes were	Model adjusted for	In the	Of these, 224		The authors	No other
1		al. 2020	using EnviMan (Opsis	plaque presence and	age, sex, air	cardiovascular	were missing	insufficient	declare that	potential
2			AB, Sweden) by the	CIMT of the right carotid	pollutant,	subcohort of the	data on plaque	information	they have	sources of
3 4			Environmental	artery, which were	education level,	MDCS cohort,	and 20 on	about	no known	bias
5			Department of Malm o.	assessed by ultrasound	smoke score,	6031 participants	CIMT,	selective	competing	identified.
6 7			The program uses a	examination B-mode	apoB/apoA1 ratio,	who had a	respectively.		financial	
8			Gaussian dispersion	ultrasonography,	use of lipid	residential	Hence, the number of participants	judge for low	interests or	
9			model (AERMOD)	conducted by trained and	lowering drugs,	address within	number of	risk, but	personal	
20			combined with an	certified sonographers.	living alone,	the air pollution			relationship	
21			emission database for the		cardiovascular	modelling area.	included in the	evidence that	s that could	
23			county of Scania in		heredity, diabetes	Of these, 224	plaque analyses		have	
24			Sweden.		mellitus, waist hip	were missing	were 5807 and	study was	appeared to	
25 26					ratio, physical	data on plaque	in the CIMT 9	free of	influence	
7					activity, alcohol	and 20 on CIMT,	analyses 6011. 출	selective	the work	
8					consumption,	respectively. The	119	report.	reported in	
9					median income	number of	19, 2024 by guest		this paper.	
1					level in residential	participants	24 b			
2					area, systolic blood	included in the	y gu			
3					pressure and being	plaque analyses	lest.			
4 5					born outside of	were 5807 and in	Tro			
6					Sweden.	the CIMT	tect			
7						analyses 6011.	ed b			
8 <sup>1</sup> 89							Protected by copyright.			
Ю							р Уг			
11							ight.			
2										

Page 126 of 136

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data ≤	Selective reporting	Conflict of interest	Other
8 9			Probably High	Probably Low	Probably High	Low	Low ay	Probably Low	Low	Low
9 10	68	Wang et	BC were collected from a	All patients treated at the	Model adjusted for	Study included	Daily counts	There was	The authors	No other
11		al. 2019b	routine air quality	Cardiac Catheterization	seasonality,	all patients	for all patients	insufficient	declare that	potential
12			monitoring site operated	Laboratory (Cath Lab) at	long-term trends,	treated at the	were obtained,	information	they have	sources of
13 14			by the New York State	URMC in Rochester, NY	temperature and	Cardiac	so likely have	about	no	bias
15			Department of	for STEMI, who resided	relative humidity.	Catheterization	all outcome	selective	competing	identified.
16			Environmental	within 15 miles of the		Laboratory (Cath	data. However, 3	outcome to	interests.	
17 18			Conservation	pollution monitoring		Lab) at URMC	any potential	judge for low		
19			continuously throughout	station in Rochester were		in Rochester, NY	errors or	risk, but		
20			the study period	included. American	' /	for STEMI	missing data	indirect		
21 22			(2005–2016). There was	College of Cardiology	(0)	throughout the	did not depend	evidence that		
23			no information about	(ACC)/American Heart		study period	on air pollution.	suggests		
24			missing data.	Association (AHA)		(2005–2016).	levels.	study was		
25				guidelines were used at			on /	free of		
26 27				the time of Cath Lab			April	selective		
28				admission to diagnose				report.		
29				STEMI.			9, 20			
30 31							124			
32							ру д			
33							19, 2024 by guest.			
34										
35 36							Protected			
30 37							cted			
38							9			

36/bmjopen-2021-0495

2	
3	
4	
5 6	
7	
2	
9	
10	
11	
12	
13	
14	
15	
16	
17	
18	
19	
20	
21	
22	
23 24	
24	
26	
20	
28	
29	
30	
31	
32	
33	
34	
35	
36	
37	
38	

5 5 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data ≤		Conflict of interest	Other
3			Probably Low	Low	Probably Low	Low	Probably Low	Probably Low	Low	Low
10	69	Ljungman	Based on detailed	The International	Model adjusted for	The study	The study used	There was	The authors	No other
11		et al. 2019	emission databases,	Classification of	sex, calendar year,	included	high-quality	insufficient	declare they	potential
2			monitoring data, and	Diseases, Ninth Revision	subcohort,	individuals in	and $\sum_{i=1}^{\infty}$	information	have no	sources of
3  4			high-resolution	(ICD-9) codes 410–414	smoking status,	two cohorts from	comprehensive	about	actual or	bias
15			dispersion models, the	and ICD-10 I20-25 codes	alcohol	Gothenburg, four	national patien	selective	potential	identified.
16			study calculated source	were used to define IHD	consumption in	pooled cohorts	and death	outcome to	competing	
17 18			contributions to black	and ICD-9 codes	Stockholm and	from Stockholm,	registries,	judge for low	financial	
19			carbon (BC) from road	431–436 and ICD-10	Umeå, physical	and one cohort	minimizing 😽	risk, but	interests.	
20			wear, traffic exhaust,	codes I61– I65 were used	activity, marital	from Umeå. In	loss to	indirect		
21			residential heating, and	to define stroke.	status,	total, 114,758	follow-up for	evidence that		
22			other sources in		socioeconomic	individuals were	our outcomes	suggests		
24			Gothenburg, Stockholm,		index by	included from all	of interest.	study was		
25			and Umeå.		occupation,	study areas.	Missing 9	free of		
26 27					education level,		information for	selective		
28					occupation status,		variables ≤ 1/2 0	report.		
29					and mean			1		
30					neighborhood		specified. 22			
31					individual income		by (			
33					in persons of		5% not specified. 2024 by guest.			
34					working age by					
35					Small Areas for		Protected			
36 37					Market Statistics.		ctec			
'' [					ivial Ket Statistics.		9			

Page 128 of 136

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data o	Selective reporting	Conflict of interest	Other
8 9			Probably Low	Low	Probably Low	Low	Probably Low	Probably Low	Low	Low
9 10	70	Liu et al.	Annual mean	COPD was defined by	Model adjusted for	The study used	From a total of	There was	The authors	No other
11		2021a	concentrations of BC for	following the principal	age, sex, smoking	data from three	106,727	insufficient	declare that	potential
12			2010 were estimated at	diagnosis of International	status, smoking	cohorts within	participants $\frac{8}{2}$	information	they have	sources of
13 14			the study participants'	Classification of	duration, smoking	the ELAPSE	with complete a	about	no known	bias
15			baseline residential	Diseases, 9th Revision	intensity,	project with	air pollution	selective	competing	identified.
16			addresses, using	(ICD-9) codes 490–492,	body-mass index,	available	exposure data,	outcome to	financial	
17 18			standardized	and 494–496, or ICD-10	marital status,	information on	the study	judge for low	interests or	
19			Europe-wide hybrid land	codes J40–44.	employment	COPD hospital	excluded 633	risk, but	personal	
20			use regression (LUR)		status, educational	discharge	participants §	indirect	relationship	
21 22			models. The LUR model		level and	diagnoses. Mean	with COPD at	evidence that	s that could	
23			utilized routine		area-level annual	follow-up time is	baseline and	suggests	have	
24			monitoring data from the		year income.	16.6 years.	7,586	study was	appeared to	
25			European Environment				participants 9	free of	influence	
26 27			Agency (EEA) AirBase				with missing 출	selective	the work	
28			for PM2.5, NO2, and O3,				information on $\frac{1}{6}$	report.	reported in	
29			and ESCAPE monitoring						this paper.	
30 31			data for BC as the				24 b			
32			dependent variable. BC				у д			
33			was measured by the				uest			
34 35			reflectance of PM2.5				2024 by guest. Protected			
36			filters and expressed in				otec			
37			absorbance units.							
38 ˈ							Vo			

42 43

45 46

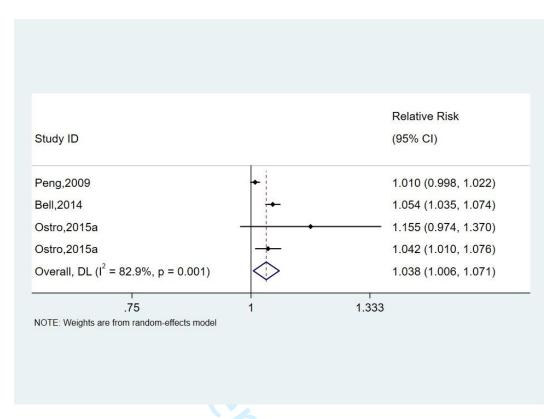
Page 129 of 130  1 2 3 4 5 6 -Table \$5 Ass		cont of certainty	v of a	evidence for outo	nome.			ВМ	МЈ Ор	en			36/bmjopen-2021-049516 on 3	sons for upgrading				
8	288111	ent of certainty	/ 01 0	Vidence for out		ons for downgrading							≥ Nea	sons for upgrading				Final
9 Evidence 10 11	A1	Rationale	A2	Rationale	A3	Rationale	A4	Rationale	A5	Rationale	B1	Rationale	2022¥ Do	Rationale	В3	Rationale	Overall	certainty assessment
12 1/8 ute effects of BC 104EC on CVD in 15 PM <sub>2.5</sub> -unadjusted 16	0	Little influence on the overall effect	0	All included studies were consistent with our prespecified PECOS	0	80% PI 1.005 (95%CI: 1.001, 1.009) does not include unity	0	Risk estimates reported by the studies are sufficiently precise	-1	publication bias exised, RR adjusted for publication bias with trim and fill.	0	Insufficient basis for upgrading	ownloaded	Confounders would shift the RR in both directions	+1	Evidence of increase in risk with increasing exposure	0	Moderate
18 19 19 19 20 BC or EC on CVD 21 20 20 20 21 20 21 20 21 20 21 20 21 21 21 22 22	Ō	Little influence on the overall effect	0	All included studies were consistent with our prespecified PECOS	0	80% PI 1.011(95%CI: 1.002, 1.020) does not include unity	0	Risk estimates reported by the studies are sufficiently precise	0	No evidence of publication bias	0	Insufficient basis for upgrading	from http://bmjopen.bmj.com/ on	Confounders would shift the RR in both directions	+1	Evidence of increase in risk with increasing exposure	+1	High
25 26 ute effects of BC 26 or EC on RES 28 10 PM2.5-unadjusted 29 30 odel	0	Little influence on the overall effect	0	All included studies were consistent with our prespecified PECOS	0	80% PI 1.010 (95%CI: 0.982, 1.040) include unity but no larger than twice the 95%CI	0	Risk estimates reported by the studies are sufficiently precise	0	No evidence of publication bias	0	Insufficient basis for upgrading	April~19, 2024	Confounders would shift the RR in both directions	0	No evidence of a clear increasing risk with exposure	0	Moderate
31 32cute effects of BC 33 34 3501_2-adjusted 360del 37 38	0	Little influence on the overall effect	0	All included studies were consistent with our prespecified PECOS	0	80% PI 1.000(95%CI: 0.991, 1.009) include unity but less than twice the 95%CI	0	Risk estimates reported by the studies are sufficiently precise	0	No evidence of publication bias	0	Insufficient basis for upgrading	by guest. ₱rotected by	Confounders would shift the RR in both directions	0	No evidence of a clear increasing risk with exposure	0	Moderate

5Table S5 Assessment of certainty of evidence for outcome

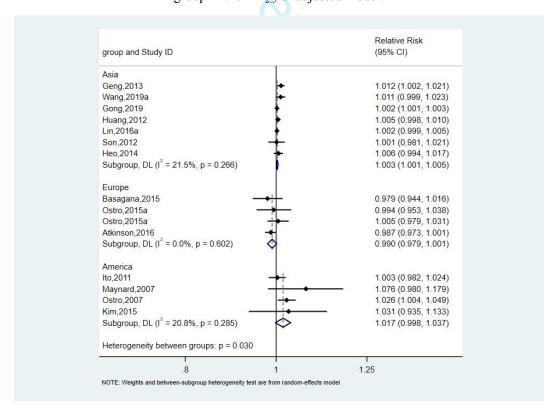
6		Reasons for downgrading										പ്പ പ്രദേശന്ദ്യ for upgrading					Final	
Evidence 8	A1	Rationale	A2	Rationale	A3	Rationale	A4	Rationale	A5	Rationale	B1	Rationale	May≊20	Rationale	В3	Rationale	Overall	certainty assessment
10 10hronic effects of 120 or EC on CVD 13hronic effects of 120 or EC on CVD 14 17bodel 16	0	Little influence on the overall effect	0	All included studies were consistent with our prespecified PECOS	0	80% PI 1.068 (95%CI: 0.965, 1.181) include unity but no larger than twice the 95%CI	0	Risk estimates reported by the studies are sufficiently precise	0	No evidence of publication bias	0	Insufficient basis for upgrading	022. Downtoaded from	Confounders would shift the RR in both directions	+1	No evidence of a clear increasing risk with exposure	+1	High

17 Abbreviations: BC: Black carbon; EC: Elemental carbon; CVD: cardiovascular diseases; RES: respiratory diseases; IHD: ischemic heart diseases; PI: prediction interval; CI: confidence interval; A1 = limitations in studies (risk of bias); A2 =

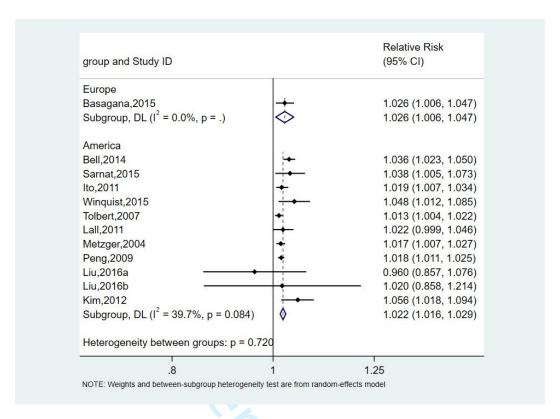
18 indirectness; A3 = inconsistency; A4 = imprecision; A5 = publication bias; B1 = large RR; B2 = all confounding decreases observed RR; B3 = concentration-response gradient.



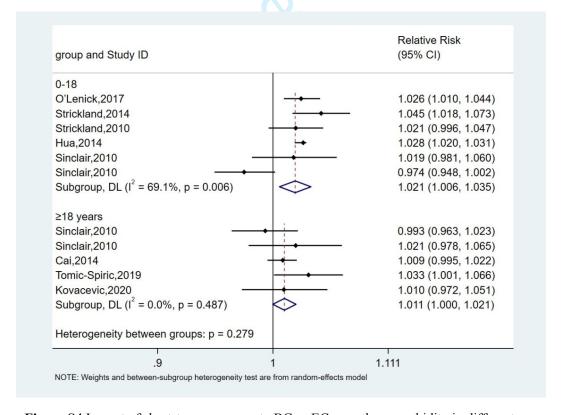
**Figure S1** Impact of short-term exposure to BC or EC on respiratory diseases in 65+ years age group in the PM<sub>2.5</sub>-unadjusted model.



**Figure S2** Impact of short-term exposure to BC or EC on cardiovascular mortality stratified by geographical locations.



**Figure S3** Impact of short-term exposure to BC or EC on cardiovascular morbidity stratified by geographical locations.



**Figure S4** Impact of short-term exposure to BC or EC on asthma morbidity in different age groups.

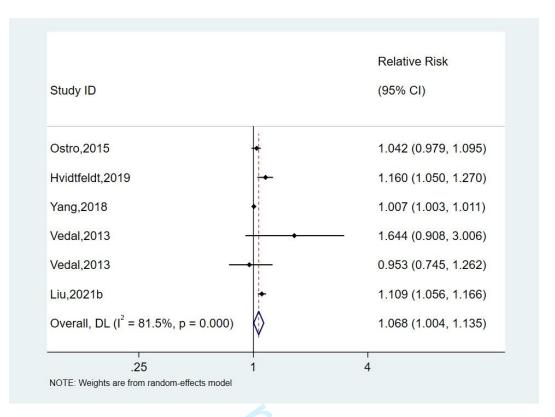


Figure S5 Impact of long-term exposure to BC or EC on cardiovascular diseases.

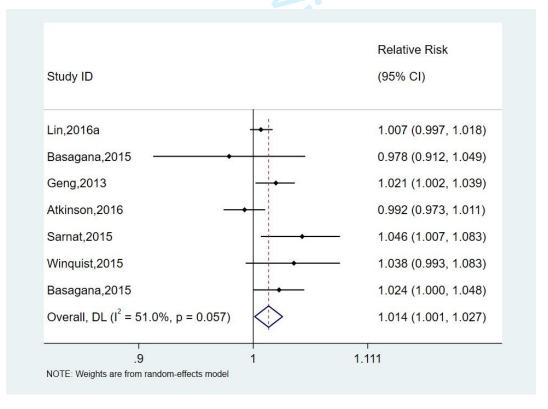
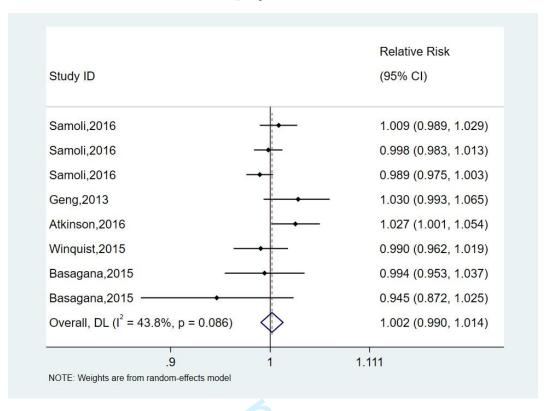


Figure S6 Impact of short-term exposure to BC or EC on cardiovascular diseases in the

#### PM<sub>2.5</sub>-adjusted model.



**Figure S7** Impact of short-term exposure to BC or EC on respiratory diseases in the PM<sub>2.5</sub>-adjusted model.



# PRISMA 2020 Checklist

Section and Topic   Time	2		n-20	
ABSTRACT Abstract 2 See the PRISMA 2020 for Abstracts checklist.  ARTODUCTION Rationate 3 Describe the rationale for the review in the context of existing knowledge.  4 Provide an explicit statement of the objective(s) or question(s) the review addresses.  5 Objectives 4 Provide an explicit statement of the objective(s) or question(s) the review addresses.  6 Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.  7 Pesent the full search strategy 5 Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.  8 Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.  9 Search strategy 7 Present the full search strategies for all databases, registers whether a study met the inclusion criteria of the review, including now many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of			Checklist item 27-04-95	where item
ABSTRACT Abstract 2 See the PRISMA 2020 for Abstracts checklist.    Abstract   2 See the PRISMA 2020 for Abstracts checklist.   \$43.4	TITLE		•	
Abstract   2   See the PRISMA 2020 for Abstracts checklist.	Title	1	Identify the report as a systematic review.	#1
Introduction   Rationale   3   Describe the rationale for the review in the context of existing knowledge.   4   Provide an explicit statement of the objective(s) or question(s) the review addresses.   47   4   4   4   4   4   4   4   4	ABSTRACT		<u>~</u>	
Rationale 3 Describe the rationale for the review in the context of existing knowledge. 4 Provide an explicit statement of the objective(s) or question(s) the review addresses. 4 Provide an explicit statement of the objective(s) or question(s) the review addresses. 4 Provide an explicit statement of the objective(s) or question(s) the review addresses. 4 Provide an explicit statement of the objective(s) or question(s) the review addresses. 4 Provide an explicit statement of the objective(s) or question(s) the review addresses. 4 Provide an explicit statement of the objective and how studies were grouped for the syntheses. 4 Provide an explicit statement of the review and how studies were grouped for the syntheses. 4 Provided and explication and exclusion criteria of the review. Including the source was last exerched or consulted. 4 Provided and exherence of the review and how studies were grouped for the syntheses. 4 Provided and exherence of searched or consulted. 4 Provided and exherence of the review and the surface of the review. Including how many reviewers consulted to the provided and each report retrieved, whether the tyw orked independently, and if applicable, details of automation tools used in the process. 4 Provided and each report retrieved, whether the tyw orked independently, and if applicable, details of automation tools used in the process. 4 Provided and each report retrieved, whether the tyw orked independently, and if applicable, details of automation tools used in the process. 4 Processes used to decide which results that were compatible with each automation tools used in the process. 4 Provided and the process. 4 Provided and the process assumptions made about any missing or unclear information. 4 Provided automation tools used in the results in the results in the included studies, including details of automation characteristics, funding sources). Describe any existing or unclear information. 4 Provided automation tools used in the results in the processes used to assess risk of bias in th	Abstract	2	See the PRISMA 2020 for Abstracts checklist.	#3-4
Dejectives   4   Provide an explicit statement of the objective(s) or question(s) the review addresses.     #7	INTRODUCTION	1	ŶO	
Eligibility criteria   5   Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.   #8   Information   6   Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to after when each source was last searched or consulted.   #8   Search strategy   7   Present the full search strategies for all databases, registers and websites, including any filters and limits used.   #8   Search strategy   7   Present the full search strategies for all databases, registers and websites, including any filters and limits used.   #8   Search strategy   7   Present the full search strategies for all databases, registers and websites, including any filters and limits used.   #8   Search strategy   7   Present the full search strategies for all databases, registers and websites, including any filters and limits used.   #8   Search strategy   7   Present the full search strategies for all databases, registers and websites, including any filters and limits used.   #8   Search strategy   7   Present the full search strategies for all databases, registers and websites, including any filters and limits used.   #8   Search strategy   7   Present the full search strategies for all databases, registers and websites, including any filters and limits used.   #8   Search strategy   7   Present the full search strategies for all databases, registers and websites, including any filters and limits used.   #9   10   Specify the methods used to cecide whether a study method strategies of all databases and strategies for all databases, registers and websites, including and provide and provides and submation tools used in the process.   #9   10   Study risk of bias   11   11   12   13   14   15   15   15   15   15   15   15	2 Rationale	3	<del>_</del>	#6-7
Filipibility criteria   5   Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.   #8	3 Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	#7
Information sources  Informati	-		olr c	
Search strategy   7   Present the full search strategies for all databases, registers and websites, including any filters and limits used.   #8	Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	#8
Selection process 8 Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.  Data collection process 9 Specify the methods used to collect data from reports, including how many reviewers collected data from each report whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.  Data items 10a List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.  Study risk of bias assessment 11 Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.  Spinthesis and the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study integention characteristics and comparing against the planned groups for each synthesis (filem #5)).  Describe any methods used to tabulate or visually display results of individual studies and syntheses.  13a Describe any methods used to abulate or visually display results of individual studies and syntheses.  13b Describe any methods used to explore possible causes of heterogeneity, and software package(s) used. The model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used. The model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used. The model(s), method(s) to identify the presence and extent of statistical hete	<i>Y</i>	6		#8
and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.  Data collection process  Specify the methods used to collect data from reports, including how many reviewers collected data from each report whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.  Data items  D	Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	#8
independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.  Data items  10a List and define all outcomes for which data were sought. Specify whether all results that were compatible with each autome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.  10b List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.  Study risk of bias assessment  11 Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.  12 Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.  13a Describe any methods used to decide which studies were eligible for each synthesis (e.g. tabulating the study interpendint characteristics and comparing against the planned groups for each synthesis (item #5)).  13b Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.  13c Describe any methods used to abulate or visually display results of individual studies and syntheses.  13d Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.  13c Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).  13d Describe any methods used to assess risk of bias due to missing results in a synthesis	Selection process	8		#9
study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which resultation collect.  10b List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.  27 Study risk of bias assessment  18 Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.  28 Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.  29 Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.  30 Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).  30 Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.  30 Describe any methods used to tabulate or visually display results of individual studies and syntheses.  31 Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.  32 Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).  33 Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).  34 Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).  34 Describe any		9	independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the	#9-10
assumptions made about any missing or unclear information.  Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.  Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.  Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.  #10  Bescribe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intergention characteristics and comparing against the planned groups for each synthesis (item #5)).  Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summany statistics, or data conversions.  Describe any methods used to tabulate or visually display results of individual studies and syntheses.  Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was periformed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.  Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).  #11-12  Reporting bias assessment  14 Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).  #13  Bescribe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).  #13  Describe any methods used to assess risk detainty (onconfidence) in the podynoficience figuriate butcoment.	25 Data items 26	10a		#9-10
study and whether they worked independently, and if applicable, details of automation tools used in the process.    Effect measures   12   Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results. #10	27 28	10b		#9-10
Synthesis methods  13a Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intergention characteristics and comparing against the planned groups for each synthesis (item #5)).  13b Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summer y statistics, or data conversions.  13c Describe any methods used to tabulate or visually display results of individual studies and syntheses.  13d Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.  13e Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).  13f Describe any sensitivity analyses conducted to assess robustness of the synthesized results.  13d Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).  13d Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).  13d Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).  13d Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).  13d Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).  13d Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).  13d Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).		11		#10-11
comparing against the planned groups for each synthesis (item #5)).  13b Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.  13c Describe any methods used to tabulate or visually display results of individual studies and syntheses.  13d Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.  13e Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).  13f Describe any sensitivity analyses conducted to assess robustness of the synthesized results.  13d Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).  13d Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).  13d Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).  13d Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).  13d Describe any methods used to assess risk of bias due to missing results in a buttoomhem!  13d Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).  13d Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).  13d Describe any methods used to assess risk of bias due to missing results in the body of exidence for all the buttoomhem.	Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	#10
Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summers y statistics, or data conversions.  Describe any methods used to tabulate or visually display results of individual studies and syntheses.  Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.  Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).  #11-12  Describe any sensitivity analyses conducted to assess robustness of the synthesized results.  #13  Reporting bias assessment  Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).  #13  Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).  #14  Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).  #15  Describe any methods used to assess reactainty (dreconfidence) in the body of evidence for all butcomems.	methods	13a		#9
Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.  Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).  Describe any sensitivity analyses conducted to assess robustness of the synthesized results.  Reporting bias assessment  Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).  #13  Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).  #13  Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).  #13  Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).  #13  Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).  #13	35 26	13b		#10
model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.  13e Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).  13f Describe any sensitivity analyses conducted to assess robustness of the synthesized results.  Reporting bias assessment  14 Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).  15 Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).  #13  #14  Certainty  15 Describe any methods used to assess resultainty (ortconfidence) in the body of evidence for all butsomem) #11	37	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	#9
Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).  13e Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).  #11-12  Reporting bias assessment  14 Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).  #13 #13 #13  Certainty  15 Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).  #14 #15 #15 #15 #15 #15 #15 #15 #15 #15 #15		13d		#11-12
13f Describe any sensitivity analyses conducted to assess robustness of the synthesized results. #11-12  Reporting bias assessment		13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	#11-12
Reporting bias assessment  Certainty  Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).  #13  #13  #13  Certainty  Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).  #13  #14  Certainty  15  Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).  #13  #14  #15	11			#11-12
15 Describe any methods use to topassess/icentainty (onconfidence) in the body of exidence for interpolation and the butsomem! #11		<del> </del>	, , , , , , , , , , , , , , , , , , ,	-
	14	15	Describe any methods used to assess/certainty (or confidence) in the body of evidence for iale but contem!	#11
	r.y. ,	I		ı



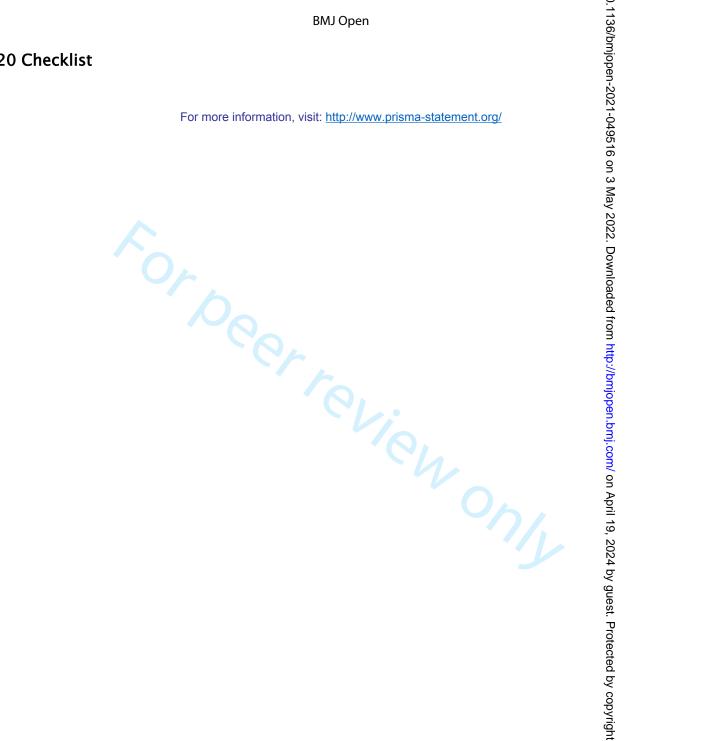
### PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
assessment		316	
RESULTS	,	) A	
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	#13
)	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	#13
Study characteristics	17	Cite each included study and present its characteristics.	#13
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	#18
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	#14-16
Results of	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	#20-21
syntheses )	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	#16
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	#18-19
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	#18
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	#18-21
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	#18-19
DISCUSSION		<u>5</u>	
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	#22-25
,	23b	Discuss any limitations of the evidence included in the review.	#26-27
	23c	Discuss any limitations of the review processes used.	#26-27
	23d	Discuss implications of the results for practice, policy, and future research.	#25-26
OTHER INFORMA	TION	9	
Registration and	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	#7
protocol	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	#7
•	24c	Describe and explain any amendments to information provided at registration or in the protocol.	#7
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the region.	#30
Competing interests	26	Declare any competing interests of review authors.	#31
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	#32

10.1136/bmj.n71

PRISMA 2020 Checklist

For more information, visit: http://www.prisma-statement.org/



# **BMJ Open**

#### Is Short-term and Long-term Exposure to Black Carbon Associated with Cardiovascular and Respiratory Diseases? A Research based on Evidence Reliability

Journal:	BMJ Open
Manuscript ID	bmjopen-2021-049516.R2
Article Type:	Original research
Date Submitted by the Author:	14-Feb-2022
Complete List of Authors:	Song, Xuping; Lanzhou University, School of Public Health Hu, Yue; Lanzhou University, School of Public Health Ma, Yan; Lanzhou University, School of Public Health Jiang, Liangzhen; Lanzhou University, School of Public Health Wang, Xinyi; Lanzhou University, Second Clinical College Shi, Anchen; Xi'an Jiaotong University Medical College First Affiliated Hospital, Department of General Surgery Zhao, Junxian; Lanzhou University, School of Public Health Liu, Yunxu; Lanzhou University, School of Public Health Tang, Jing; Lanzhou University, School of Public Health Li, Xiayang; Lanzhou University, School of Public Health Li, Xiayang; Chengdu University of Information Technology, College of Atmospheric Sciences Guo, Yong; Guizhou Province Wang, Shigong; Chengdu University of Information Technology, College of Atmospheric Sciences
<b>Primary Subject Heading</b> :	Public health
Secondary Subject Heading:	Cardiovascular medicine, Respiratory medicine
Keywords:	PUBLIC HEALTH, RESPIRATORY MEDICINE (see Thoracic Medicine), CARDIOLOGY

SCHOLARONE™ Manuscripts



I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

## **Title Page**

#### Title:

Is Short-term and Long-term Exposure to Black Carbon Associated with

Cardiovascular and Respiratory Diseases? A Research based on Evidence Reliability

#### **Author names and affiliations:**

1. Xuping Song<sup>a</sup> E-mail: songxp@lzu.edu.cn

2. Yue Hu<sup>a</sup> E-mail: huy20@lzu.edu.cn

3. Yan Ma<sup>a</sup> E-mail: may2020@lzu.edu.cn

4. Liangzhen Jiang<sup>a</sup> E-mail: jianglzh19@lzu.edu.cn

5. Xinyi Wang<sup>c</sup> E-mail: wangxinyi17@lzu.edu.cn

6. Anchen Shi<sup>d</sup> E-mail: 3120115202@stu.xjtu.edu.cn

7. Junxian Zhao<sup>a</sup> E-mail: zhaojx2017@lzu.edu.cn

8. Yunxu Liu<sup>a</sup> E-mail: yxliu17@lzu.edu.cn

9. Yafei Liu<sup>a</sup> E-mail: isak-even@qq.com

10. Jing Tang<sup>a</sup> E-mail: tangj19@lzu.edu.cn

11. Xiayang Li<sup>a</sup> E-mail: lixiayang 18@lzu.edu.cn

10. Xiaoling Zhang<sup>b</sup> E-mail: xlzhang@ium.cn

11. Yong Guo<sup>e</sup> E-mail: gycau@qq.com

12. Shigong Wang<sup>b</sup> E-mail: wangsg@lzu.edu.cn

Chengdu 610000, China;

<sup>&</sup>lt;sup>a</sup> School of Public Health, Lanzhou University, Lanzhou 730000, China;

<sup>&</sup>lt;sup>b</sup> College of Atmospheric Sciences, Chengdu University of Information Technology,

<sup>c</sup> Second Clinical College, Lanzhou University, Lanzhou 730000, China;

<sup>d</sup> Department of General Surgery, The First Affiliated Hospital of Xi'an Jiao Tong

University, Shaanxi 710061, China;

<sup>e</sup> Department of Civil Affairs in Guizhou Province, Guiyang 550004, China.

#### **Corresponding author 1:**

Name: Xiaoling Zhang

Postal Address: College of Atmospheric Sciences, Chengdu University of Information

Technology, Chengdu 610000, Sichuan, China

E-mail address: xlzhang@ium.cn

Fax: 028-85966502

#### **Corresponding author 2:**

Name: Shigong Wang

Postal Address: College of Atmospheric Sciences, Chengdu University of Information

Technology, Chengdu 610000, Sichuan, China

E-mail address: wangsg@cuit.edu.cn

Fax: 028-85966502

#### **Abstract**

**Background** Adverse health effects of fine particles (PM<sub>2.5</sub>) have been well documented by many studies. However, evidence on the impact of black carbon (BC) or elemental carbon (EC) on health is limited. This systematic review and meta-analysis provides comprehensive and current evidence on health impact of BC or EC, which could support updating of the World Health Organization Global Air Quality Guidelines.

**Objectives** (i) To explore the effects of BC and EC on cardiovascular and respiratory morbidity and mortality; (ii) To verify the reliability of the meta-analysis by p-value plots.

Methods PubMed, Embase and Web of Science were searched. Two reviewers independently selected studies for inclusion, extracted data and assessed risk of bias. Outcomes were analyzed via a random effects model and reported as relative risk (RR) with 95% confidence interval (CI). Adapted Grading of Recommendations assessment, Development and Evaluation (GRADE) was used to assess the certainty of evidence. We analyzed the reliability of Meta-analysis by drawing p-value plots.

Results Seventy studies met our inclusion criteria. (i) Short-term exposure to BC or EC was associated with 1.6% (95% CI: 0.4%-2.8%) increase in cardiovascular diseases per 1 μg/m³ in the elderly; (ii) Long-term exposure to BC or EC was associated with 6.8% (95% CI: 0.4%-13.5%) increase in cardiovascular diseases; (iii) The p-value plot analysis indicates that the association between BC or EC and respiratory diseases is consistent with randomness.

**Conclusions** Both short-term and long-term exposure to BC or EC were related with cardiovascular diseases. However, the impact of BC or EC on respiratory diseases do not present consistent evidence and further investigations are required.

**Keywords** Black carbon, Cardiovascular disease, Respiratory disease, Systematic review, P-hacking

PROSPERO registration number CRD42020186244.

#### Strengths and limitations of this study

- 1. Adapted GRADE (Grading of Recommendations assessment, Development and Evaluation) framework, formulated by the WHO global air quality guidelines working group, was used to evaluate the certainty of evidence.
- 2. The research on short-term and long-term exposure to black carbon and cardiorespiratory diseases incorporated a detailed search strategy, explicit inclusion and exclusion criteria, literature screening, data extraction and risk of bias assessment.
- 3. The p-value plot has been used to evaluate the reliability of meta-analysis.
- 4. The main limitation of search strategy was the lack of search for unpublished and/or grey literature.

#### 1. Background

Black carbon (BC), a ubiquitous component of air particulate matter, is usually measured through optical absorption. Elemental carbon (EC), another carbonaceous material with a graphitic structure, is commonly measured by thermal or thermo-optical methods.<sup>1, 2</sup> Although the measurement methods are different, BC and EC are often considered interchangeable. BC is mainly emitted from traffic and combustion-related sources and is a measured component of the particulate matter (PM). The adverse health effects of PM, especially of PM<sub>2.5</sub>, are well documented. In 2017, a total of 2.94 million deaths resulted from ambient PM worldwide.<sup>3-5</sup> PM<sub>2.5</sub> is composed of various constituents, in which some of them are more toxic and hypothesized as the main cause of the adverse effects of PM2.5. A growing body of studies indicates a potential role of BC among these more toxic constituents.<sup>6, 7</sup> In addition, some reviews demonstrated that BC is a better indicator of adverse effects of PM from combustion sources according to robust associations from epidemiological studies.<sup>8, 9</sup> The underlying pathological mechanisms of BC include oxidative stress, inflammation and gene mutations. 10-12

Due to its association with adverse health, the number of studies exploring the effects of BC on cardiorespiratory diseases has rapidly increased in recent years. Cardiovascular and respiratory diseases are common diseases worldwide, with a heavy disease burden and major implications for clinical practice and public health. The Global burden of disease study 2017 indicated that cardiovascular and respiratory-related death ranked first and third respectively among non-communicable

diseases.<sup>4</sup> Health effects of acute and chronic exposure to BC have been widely reported. Despite that there is some epidemiological evidence that BC was associated with cardiorespiratory diseases, in other studies, no statistically effects were observed.

The reliability of air quality epidemiological studies is often poor, with a serious lack of reproducibility of published findings.<sup>13</sup> If researchers run a regression with and without outliers, with and without a covariate, with one and then another dependent variable, and false positive results are much more likely to be reported. The definition of the p-value is the possibility of getting a result equal to or more extreme than what was observed, if nothing is going on. There can be a selective reporting problem (compute many tests and selectively report small p-values), which is referred to p-hacking.<sup>14</sup> P-hacking's when a study examines many questions and tests numerous statistical models, referred to as multiple testing and multiple modelling (MTMM), but does not perform multiple testing statistical corrections. 15, 16 Since the uncorrected statistical estimates derived from the original study are likely not unbiased, the results of meta-analysis are not reliable. It makes no sense to do meta-analysis and likely obtain positive results, without considering the reliability of the p-values, possible p-hacking. Therefore, it is essential to explore the p-values used in a meta-analysis.

Some systematic reviews analyzed the impact of BC on health. Nevertheless, quantitative associations between BC exposure and cardiovascular and respiratory diseases have not been well-characterized due to the different objectives of the reviews.<sup>17, 18</sup> Compared with Yang et al. 2019<sup>19</sup>, this study included recently

published eligible studies. Furthermore, meta-analysis of BC effects on vulnerable populations and across geographical regions were conducted. Moreover, the reliability of meta-analysis is here performed based on a p-value plot. In addition, a series of eligible studies published recently have not been considered. Also the GRADE (Grading of Recommendations assessment, Development and Evaluation) framework was not adopted in previous systematic reviews. Therefore, a systematic review and meta-analysis was performed to further elucidate the health effects of BC or EC in this study. The objectives of this study were (1) to investigate the association of short-term and long-term exposure to BC or EC with the respiratory and cardiovascular morbidity and mortality; (2) to verify the reliability of the meta-analysis is by p-value plots.

#### 2. Methods

The protocol for this systematic review was registered and published online on PROSPERO (International Prospective Register of Systematic Reviews), under registration number CRD42020186244. The use of p-value plots was based on recent literature.

#### 2.1 Patient and public involvement

Patients or the public were not involved in this study.

#### 2.2 Database

Articles were identified using PubMed, Web of Science and Embase databases up to July 19<sup>th</sup>, 2021. Original articles were searched using the following U.S. National Library of Medicine's Medical Subject Headings (MeSH) terms and

keywords: "(black carbon\* or elemental carbon\*) AND (respiratory\* or cardiovascular\*) AND (morbidit\* or hospitalization\* or death\* or mortalit\* or outpatien\*) AND (time series\* or case cross\* or cohort\*)". In addition, the reference lists of the included studies and related reviews were manually evaluated to identify additional relevant studies. The details of the search strategy in PubMed are shown in Table S1.

#### 2.3 Inclusion and exclusion criteria

A time series study, case crossover study or cohort study that evaluated the impact of BC or EC on cardiovascular or respiratory diseases was included in this systematic review and meta-analysis. Studies were considered eligible for inclusion if they fulfilled the inclusion criteria as follows: (1) study types restricted to time series, case crossover or cohort studies; (2) studies considering BC or EC as air pollutants; (3) based on the International Classification of Diseases (ICD) 9<sup>th</sup> or 10<sup>th</sup> revision, diseases included respiratory diseases, wheeze, other respiratory distress insufficiency or respiratory cancer (ICD-9 codes 460–519, 786.07, 786.09 or 162; ICD-10 codes J00–J99, R06.251, R06.001 or C34) or cardiovascular diseases (ICD-9 codes 390–459, ICD-10 codes I00–I99); (4) studies considering morbidity or mortality as outcome; (5) estimates were odds ratio (OR), relative risk (RR) or hazard ratio (HR) with 95% confidence interval (CI) or enough information for their calculation; (6) publication language was restricted to English.

The exclusion criteria were as follows: (1) studies on soot or black smoke were excluded, because the definition of such components usually lacked precision; (2)

studies assessing the disease progression exposure to pollutants in individuals with cardiovascular or respiratory diseases (for example chronic obstructive pulmonary disease and asthma); (3) studies focusing on particular populations (for example pregnant women and miners) or population living in specific environments with high pollution concentration (for example residential area near industrial complexes, population exposed to sugar cane burning and neighborhoods that expose many streets); (4) studies focusing on seasonality; (5) conference abstracts; (6) study period less than 1 year.

#### 2.4 Selection of articles and extraction of data

To identify eligible studies, two investigators independently screened titles and abstracts. Studies which relevance could not be determined by titles and abstracts were subjected to full text screening. Any disagreement was resolved by discussion. A third investigator was involved in the discussion when a consensus could not be reached between the two investigators.

Two reviewers independently extracted the following items from each included study and record them in a pre-designed table: first author, publication year, country, study design, diagnosis standard, time period, population age, statistical models, air pollutants, outcomes and number of events. If the reported data of the included studies were unclear or missing, the first author or corresponding author was contacted by e-mail. Any conflicts were resolved by the involvement of a third investigator if the controversy was not solved after the discussion.

#### 2.5 Data synthesis

Regarding the meta-analysis, the RR was used as an effect estimate, and the OR in case crossover study and HR in cohort study were considered equivalent to RR. Estimates from the maximally adjusted model in the cohort study were extracted when multiple estimates were present in the original study to reduce the risk of potential unmeasured confounding.<sup>20</sup> In addition, the estimate was converted to a standardized increment (1  $\mu$ g/m³) of RR. The following formula was used to calculate the standardized risk estimates:

$$RR_{(standardized)} = RR_{(original)}^{Increment(1)/Increment(original)}$$

Two studies did not show the overall risk, while stratified risk estimates by age and location were reported.<sup>21, 22</sup> In this case, the stratified estimates were pooled. One study presented the estimates of both morbidity and mortality, which were combined in the overall analysis.<sup>23</sup> In addition, if the same cohort data were analyzed in different studies and the latest studies were included in the systematic review and meta-analysis.<sup>24-26</sup>

#### 2.6 Risk of bias assessment

The risk of bias was assessed for each study according to the Office of Health Assessment and Translation (OHAT) tool and the Navigation Guide tool. 17, 27, 28 Risk of bias evaluation was conducted as follows: exposure assessment, outcome assessment, confounding bias, selection bias, incomplete outcome data, selective reporting, conflict of interest and other bias. Each domain was considered as "low", "probably low", "probably high", "high", or "not applicable" criteria. Two investigators conducted the risk of bias evaluation. Any inconsistency between the

investigators was discussed and a third researcher was involved to resolve any disagreement.

#### 2.7 Evaluation of certainty of evidence

An adaptation of the GRADE (Grading of Recommendations assessment, Development and Evaluation) framework, formulated by the WHO (World Health Organization) global air quality guidelines working group, was used to evaluate the overall certainty of evidence.<sup>29</sup> The rating process on the certainty of evidence was started at moderate. The certainty was graded into four levels: "high", "moderate", "low" and "very low". Five reasons were used to downgrading the certainty of evidence: limitations in studies, indirectness, inconsistency, imprecision, and publication bias; 3 reasons were used to upgrade the certainty of evidence: large magnitude of effect size, all plausible confounding shifts the relative risk towards the null and concentration-response gradient. To evaluate the magnitude of the effect size, the E-value was calculated using the following formula: RR+sqrt{RR\*(RR-1)}.

#### 2.8 Statistical analysis

Statistical analysis was performed using STATA (version12.0, Stata Corp, College Station, TX, USA). In this meta-analysis, the random-effects model was conducted for anticipating significant heterogeneity among studies. Heterogeneity among trials was assessed by the Chi-square test and the extent of inconsistency was evaluated by the  $I^2$ . An 80% prediction interval (PI) of meta-estimate was calculated to assess the inconsistency. To assess potential sources of heterogeneity, subgroup analyses were performed on outcomes (morbidity and mortality), single lag days (0, 1)

and 2 days), study areas (Europe, America, and Asia) and seasons (warm and cold). The estimates from BC and EC were combined, since both of them are indicators of carbon-rich combustion sources, and are usually considered interchangeable in medical research.

Estimates were pooled separately where more than three estimates were available. Most studies presented estimates for single lags and the estimate of shortest lag was used to combine the estimates (RRs) of shortest lag in meta-analysis. However, only a few studies presented cumulative lags, and the estimates of shortest cumulative lags were used in the meta-analysis. In addition, Mostofsky et al. indicated that PM<sub>2.5</sub> is a potential confounder in assessing the health effects of PM<sub>2.5</sub> constituents.<sup>7</sup> For overall and outcome analysis, PM<sub>2.5</sub>-adjusted estimates and PM<sub>2.5</sub>-unadjusted estimates in the models were combined, respectively where more three estimates were available. Regarding the subgroup PM<sub>2.5</sub>-unadjusted estimates were analyzed, while PM<sub>2.5</sub>-adjusted estimates were not presented due to the limited number of included studies. Moreover, primary data of the included studies could not be obtained, hence it was not possible to evaluate whether the same patients were repeatedly included across multiple studies. Therefore, the sensitivity analysis was performed on all age populations to investigate the robustness of the aggregation results by the removal of studies with partial temporal overlap from the same geographical location. Most of the included studies analyzed and presented results of cardiovascular or respiratory system diseases, hence systematic diseases were analyzed in the acute effect analysis except for the chronic

effect analysis. Publication bias was assessed by Egger's regression test when the outcome included more than 10 studies. Trim and fill method was used to correct on asymmetry for the outcome with publication bias. p<0.05 was considered statistically significant.

Non-traditional methods were used to assess the reliability of basic studies, which is different from mainstream environmental epidemiology. Studies with large analysis search spaces suggest the use of a large number of statistical models and statistical tests for an effect thereby allowing greater flexibility of researchers to selectively search through and only report results showing positive effects. We counted the number of outcomes, predictors, covariates, etc. available in 15 studies, which included in the meta-analysis of association between BC and cardiovascular and respiratory diseases. We computed the search spaces as follows: Space1 is outcome times predictor times lags. Space2 is 2covariate. Space3 is Space1 times Space2. Space3 is the total analysis search space. Search spaces were computed by the method introduced in Young et al, 2019.<sup>30</sup>

The p-value plot was used to inspect the distribution condition of the p-values.<sup>31</sup> Regardless of size of sample, the p-value is distributed uniformly between 0 to 1 under the null hypothesis. If the shape of p-value plot is a straight line, the p-values are in a distribution of true null hypothesis.<sup>31</sup> If the shape of p-value plot follows an approximate 45-degree line, the p-values are assumed to be random. If the shape of p-value plot is approximately a hockey stick, the p-values on the blade are unlikely due to chance. Therefore, p-value plot was used to assess the validity and reliability of

included basic studies.

P-values of included studies were computed using RR, lower confidence interval and high confidence interval. Then, the p-values were ranked from smallest to largest using 1, 2, 3... and the plots were constructed. The following formulas were used to calculate p-value:

SE = (lnCI high - lnCI low)/2/1.96

Z = lnRR/SE

 $p - value = \{1 - NORMSDIST[ABS(Z)]\} * 2$ 

#### 3. Results

A total of 1694 studies were initially identified and 129 were reviewed in depth. We excluded the studies which study period less than 1 year or same data were analyzed in different studies.<sup>32, 33</sup> Of these, 70 fulfilled the inclusion criteria (Figure 1).<sup>7, 21-26, 34-96</sup> Of the 70 included studies, 56 estimated the short-term effects of BC or EC using a time series design or case crossover design, while 14 studies explored the long-term effects of BC or EC using a cohort design. Thirty-seven of the 70 studies reported morbidity as the outcome variable, 25 studies reported mortality, and 8 studies reported both morbidity and mortality. Thirty-five studies analyzed both cardiovascular and respiratory diseases, 18 studies merely investigated cardiovascular diseases, and 17 studies assessed respiratory diseases. Thirty-seven studies were conducted in the United States, 14 in China, 4 in Canada, 2 in the United Kingdom, Sweden, Korea and Serbia, 1 in Denmark, Iran, Germany and the Netherlands. The remaining 3 studies collected data from two different countries: Spain and Greece,

Spain and Italy, Sweden and Denmark. Twenty-seven studies classified the diseases using the ICD-9 codes, 26 used the ICD-10 codes, and 10 used both the ICD-9 and ICD-10 codes. However, the remaining 7 studies did not employ the ICD standards (Table S2). In addition, the authors of 33 studies were contacted, but only 19 answered to our request (response rate: 57.6%).

#### 3.1 Short-term effect of BC or EC on cardiovascular and respiratory diseases

Overall, short-term exposure to BC or EC was associated with an increased risk of cardiovascular diseases (RR=1.007 per 1  $\mu$ g/m³, 95% CI: 1.002–1.011) (adjusted by trim and fill method) in overall analyses (Table 1 and Figure 2). Cardiovascular diseases (RR=1.016 per 1  $\mu$ g/m³, 95% CI: 1.004–1.028) were associated with BC or EC in the elderly (65+ years). (Figure 2)

Impact of BC or EC on cardiovascular diseases was related to the exposure lag. The estimates of the association were strongest on the day of the event (lag 0) (RR=1.011 per 1  $\mu$ g/m³, 95% CI: 1.006–1.016), and then diminished on lag 1 (RR=1.005 per 1  $\mu$ g/m³, 95% CI: 1.002–1.008) and lag 2 (RR=1.002 per 1  $\mu$ g/m³, 95% CI: 0.999–1.005) (Table S3). Subgroup analyses on geographical location was performed for morbidity and mortality, respectively. Significant association between BC or EC and cardiovascular mortality was observed in Asia (RR=1.003, 95% CI: 1.001–1.005). However, no association was found in America (RR=1.017, 95% CI: 0.998–1.037) and Europe (RR=0.990, 95% CI: 0.979–1.001) (Figure S1). On the other hand, an increased risk of cardiovascular morbidity was observed in America (RR=1.022, 95% CI: 1.016–1.029) with short-term exposure to BC or EC, while only

one study performed in Europe (RR=1.026, 95% CI: 1.006–1.047) investigated the short-term effect of BC or EC on cardiovascular morbidity.<sup>23</sup> In addition, just one study in Asia was performed assessing the short-term effects of BC or EC on stroke morbidity (Figure S2).<sup>66</sup>

No association was observed between short-term exposure of BC and EC and respiratory morbidity (RR=1.012, 95% CI: 0.993–1.031) and mortality (RR=1.013, 95% CI: 0.997–1.030) (Table 1).

Table 1 Short-term impacts of BC or EC on cardiovascular and respiratory diseases in different models

			uiseases in different in			9				
		PM <sub>2.5</sub> -1	ınadjusted model			<u>~~~</u>	PM <sub>2</sub>	2.5-adjusted model	del	
Subgroup Analysis	No. of Studies	No. of Estimates	Relative Risk (95%CI)	$I^2$	Egger regression test (p value)	No. of (2) Studies (2)	No. of Estimates	Relative Risk (95%CI)	I <sup>2</sup>	
Cardiovascular Diseases						22. [				
Age						Jowr				
All population	20	22	1.008 (1.004, 1.012)	64.40%	0.007	6 ac	7	1.014 (1.001, 1.027)	51.00%	
Relative risk adjusted for publication bias with trim and fill method	24	26	1.007 (1.002, 1.011)	_	_	ded fro	_	-	_	
Sensitive analysis on study of partial temporal overlap from the same geographical location	16	16	1.006 (1.002, 1.010)	60.00%	0.020	Downloaded from http://bmjopen.bmj.com/ on	_	_	_	
≥65 years	5	6	1.016 (1.004, 1.028)	87.40%	_	9://br	_	_	_	
Outcome						njop				
Morbidity	12	12	1.022 (1.016, 1.029)	37.20%	0.163	4 en.b	5	1.018 (1.006, 1.031)	39.50%	
Mortality	14	15	1.003 (1.001, 1.006)	29.70%	0.266	4 3.	4	1.006 (0.993, 1.019)	42.90%	
Respiratory Diseases						om/ o				
Age						on <u>A</u>				
All population	16	18	1.010 (0.996, 1.025)	87.20%	0.627	April 19, 5	8	1.002 (0.990, 1.014)	43.80%	
Sensitive analysis on study of partial temporal overlap from the same geographical location	12	12	1.008 (0.992, 1.023)	90.30%	0.449	9, 202	_	_	_	
≥65	3	4	1.038 (1.006, 1.071)	82.90%	_	2024 by	_	_	_	
Outcome						guest.				
Morbidity	10	10	1.012 (0.993, 1.031)	91.80%	0.671		5	0.996 (0.987, 1.004)	0	
	10	11	1.013 (0.997, 1.030)	66.40%	0.328	Protected by copy	3	1.017 (0.985, 1.050)	48.30%	

# 3.2 P-value plots of short-term exposure to BC or EC on cardiovascular and respiratory diseases in the $PM_{2.5}$ -unadjusted model

We chose at random 15 studies included in the meta-analysis of association between BC and cardiovascular and respiratory diseases. Then, we extracted analysis items (outcomes, predictors, covariates, and lags) and calculated the analysis search spaces. Table 2 listed the counts of outcomes, predictors, covariates and lags for the 15 studies. There were many thousands of possible analysis options in each of the randomly selected studies and summary statistics of the numbers of options are given in Table 3. Across the studies, the median number of possible analyses was 12,000 (interquartile range 2,688–15,360) for Space3, which took all the factors into account.

In Figure 3, the plot of cardiovascular studies showed a shape of hockey stick. There were nine p-values less than 0.05 and thirteen p-values larger than 0.05 (Table S6). The smallest p-value in cardiovascular group was 0.000087 and the largest was 0.921904, which was of a wide range. The association between BC and cardiovascular diseases are consistent with a mixture based on p-values and p-value plot. We do not find a consistent effect so there is no proof of a causal effect. The plot's shape of the impact of BC on respiratory diseases was close to 45-degree line. The calculated p-values have four p-values were less than 0.05, while fourteen were larger than 0.05 and fall on an approximate 45-degree line (Table S6). In addition, the smallest p-value was 3.2036\*10<sup>-45</sup> and the largest was 0.836403. The smallest p-value was so small that p-hacking (or even data fabrication) may exist. As the p-value plot's shape approached a 45-degree line, the impact of short-term exposure to BC or EC on

respiratory diseases was likely to be random.

Table 2 Variable counts, and analysis search spaces for the 15 studies chosen from the meta-analysis.

Number	Study	Outcome	Predictor	Covariate	Lag	Space1	Space2	Space3
1	Atkinson,2016	3	7	6	2	42	64	2688
2	Geng,2013	3	1	5	3	9	32	288
3	Sarnat,2015	8	22	5	4	704	32	22528
4	Kim,2012	3	5	6	15	225	64	14400
5	Maynard,2007	4	2	5	1	8	32	256
6	Winquist,2015	4	8	6	3	96	64	6144
7	Gong,2019	1	2	7	9	18	128	2304
8	Huang,2012	3	13	6	7	273	64	17472
9	Basagana,2015	5	16	6	3	240	64	15360
10	Son,2012	3	11	5	7	231	32	7392
11	Heo,2014	3	9	7	4	108	128	13824
12	Kim,2015	5	5	5	15	375	32	12000
13	Tolbert,2007	2	13	7	3	78	128	9984
14	Wang,2019a	3	6	6	11	198	64	12672
15	Metzger,2004	6	14	5	8	672	32	21504

**Table 3** Summary statistics for the number of possible analyses using the three search spaces.

Statistic	Space1	Space2	Space3
maximum	704	128	22528
quartile	273	64	15360
median	198	64	12000
quartile	42	32	2688
minimum	8	32	256

#### 3.3 Long-term impact of BC or EC on cardiovascular and respiratory diseases

Five studies assessed the long-term exposure to BC or EC and cardiovascular diseases, and a positive association was observed (RR=1.068, 95% CI: 1.004-1.135) (Figure S3). Three studies assessed the long-term exposure to BC or EC and ischemic heart disease (IHD), and a positive association was observed (RR=1.066, 95% CI: 1.009-1.127). On the other hand, 4 studies assessed the long-term exposure to BC or EC and respiratory mortality. Meta-analysis was not performed due to limited included studies and no association was observed among the include studies.<sup>25, 60, 68, 75</sup> However, one study analyzed COPD. It indicated that long-term exposure to BC or

EC was associated with an increased risk of chronic obstructive pulmonary disease (COPD) morbidity (RR=1.060, 95% CI: 1.020-1.100), while no impact was observed for COPD mortality (RR=1.070, 95% CI: 1.000-1.140).<sup>24</sup>

#### 3.4 Results from the PM<sub>2.5</sub>-adjusted model

In the PM<sub>2.5</sub>-adjusted model, six studies were included in the meta-analysis of short-term exposure to BC or EC and cardiovascular diseases (RR=1.014 per 1  $\mu$ g/m³, 95% CI: 1.001-1.027) (Figure S4). The meta-analysis indicated that the association was robust compared to the results of the PM<sub>2.5</sub>-unadjusted model. In addition, the impact of BC or EC on cardiovascular morbidity in the PM<sub>2.5</sub>-adjusted model (RR=1.018 per 1  $\mu$ g/m³, 95% CI: 1.006-1.031) was consistent with the results in the PM<sub>2.5</sub>-unadjusted model (RR=1.022 per 1  $\mu$ g/m³, 95% CI: 1.016-1.029). However, an increased risk was found between BC or EC and cardiovascular mortality in the PM<sub>2.5</sub>-unadjusted model (RR=1.003 per 1  $\mu$ g/m³, 95% CI: 1.001-1.006), while no association was observed in the PM<sub>2.5</sub>-adjusted model (RR=1.006 per 1  $\mu$ g/m³, 95% CI: 0.993-1.019) (Table 1).

#### 3.5 Sensitive analysis

In the sensitive analysis, similar results were observed from the overall analysis of all age populations. Increased risk of cardiovascular diseases after exposure to BC or EC was found (RR=1.006 per 1  $\mu$ g/m³, 95% CI: 1.002-1.010) by eliminating studies with partial overlap from the same geographical location.<sup>21, 23, 38, 80</sup> In addition, no statistical significance was observed (RR=1.008 per 1  $\mu$ g/m³, 95% CI: 0.992-1.023) between respiratory diseases and BC or EC after eliminating overlapped

studies (Table 1).21, 23, 88, 94

#### 3.6 Risk of bias and certainty of evidence

The risk of bias assessment of the included studies is shown in Table 4 and more analytically in Table S4. In general, the majority of the included studies were rated as "low risk" in the items of outcome assessment, selection bias, incomplete outcome data, conflict of interest and other bias. The confounding bias and selective reporting were mostly rated as "probably low". However, 7 studies were rated as "probably high" risk because not all critical potential confounders were adjusted in the analysis. <sup>7, 24, 26, 46, 55, 74, 91</sup> In addition, the majority of the included studies on the exposure assessment were assessed as "probably low" and "probably high", and in some cases studies were rated as "high" risk. Three studies were rated as "high risk" on exposure assessment mainly because pollutants were measured with a single monitoring over a large geographical area, and not measured at least daily. <sup>53, 85, 92</sup>

The certainty of the evidence on the acute effects of BC or EC on cardiovascular diseases in the  $PM_{2.5}$ -adjusted model was rated as "moderate" and in the  $PM_{2.5}$ -unadjusted model was rated as "low", which assessed by the adapted GRADE. The evidence on the chronic effects of BC or EC on cardiovascular diseases was evaluated as "moderate" certainty (Table S5).

Table 4 Results of risk of bias assessment

			Key criteria			Oth			
No.	Study	Exposure	Outcome	Confounding	Selection	Incomplete	Selective	Conflict of	0.41
		assessment	assessment	bias	bias	outcome data	reporting	interest	Other
1	Atkinson et al. 2016								
2	Bell et al. 2014								
3	Cai et al. 2014								
4	Geng et al. 2013								
5	Hua et al. 2014								
6	Ostro et al. 2015a								
7	Samoli et al. 2016								
8	Zanobetti and Schwartz 2006								
9	Liu et al. 2016a								
10	Liu et al. 2016b								
11	Sarnat et al. 2015								
12	Kim et al. 2012								
13	Ostro et al. 2009								
14	Kim et al. 2015								
15	Huang et al. 2012								
16	Peng et al. 2009								
17	Levy et al. 2012								
18	Son et al. 2012								
19	Heo et al. 2014								
20	Basagaña et al. 2015								
21	Dai et al. 2014								
22	Lin et al. 2016a								
23	Cao et al. 2012								
24	Klemm et al. 2011								
25	Zhou et al. 2011								
26	Winquist et al. 2015								
27	Ostro et al. 2007								
28	Tolbert et al. 2000								
29	Wang and Lin 2016								
30	Darrow et al. 2014								
31	Metzger et al. 2004								
32	Mar et al. 2000								
33	Wang et al. 2019a								
34	Lin et al. 2016b								
35	Ostro et al. 2008								

Table 4 Results of risk of bias assessment (continued)

No.				1	Other criteria						
	Study	Exposure	Outcome	Confounding	Selection	Incomplete	Selective	Conflict	Other		
		assessment	assessment	bias	bias	outcome data	reporting	of interest	Other		
36	Ito et al. 2011										
37	Chen et al. 2014										
38	Tomic'-Spiric' et al. 2019										
39	Maynard et al. 2007										
40	Sinclair et al. 2010										
41	Krall et al. 2013										
42	Cakmak et al. 2009										
43	Tolbert et al. 2007										
44	Lall et al. 2011										
45	Jung and Lin 2017										
46	Gong et al. 2019										
47	Mostofsky et al. 2012										
48	Krall et al. 2017										
49	O'Lenick et al. 2017										
50	Pearce et al. 2015										
51	Strickland et al. 2010										
52	Strickland et al. 2014										
53	Ito et al. 2013										
54	Ostro et al. 2015b										
55	Gan et al. 2013										
56	Hvidtfeldt et al. 2019										
57	Thurston et al. 2016										
58	Yang et al. 2018										
59	Gan et al. 2011										
60	De Kluizenaar et al. 2013										
61	Vedal et al. 2013										
62	Rahmatinia et al. 2021										
63	Liu et al. 2021b										
64	Lavigne et al. 2021										
65	Rodins et al. 2020										
66	Kovačević et al. 2020										
67	Hasslöf et al. 2020										
68	Wang et al. 2019b										
69	Ljungman et al. 2019										
70	Liu et al. 2021a										
	Risk of bias rating:	Low		Probably Low		Probably High		High			

#### 4. Discussion

A comprehensive search of three electronic databases was performed using a well-defined search strategy. Finally, 70 studies assessing the short-term and long-term impacts of BC or EC on cardiovascular and respiratory morbidity and mortality were included. Using a random effects model, the pooled effect estimates indicated that the short-term exposure to BC or EC was associated with an increased risk of cardiovascular diseases, but not on respiratory diseases in all populations. BC or EC was associated with cardiovascular diseases in the elderly (65+ years). The impact of short-term exposure to BC or EC on cardiovascular morbidity was stronger than mortality. In addition, association between short-term exposure to BC or EC and cardiovascular diseases differ across continents.

# 4.1 Short-term exposure to BC or EC was related with cardiovascular diseases in the elderly

Overall, the meta-analysis results indicated that short-term exposure to BC or EC was associated with an increased risk of cardiovascular diseases, but not on respiratory diseases in all populations. In general, the PM<sub>2.5</sub>-adjusted model and the PM<sub>2.5</sub>-unadjusted model and sensitivity analysis showed that the associations were consistent. In contrast to the meta-analysis calculations, p-value plots indicate mixed results for cardiovascular, some studies indicate an effect while others appear to be random. For respiratory effects, the p-value plot is consistent with randomness, no effect. Our counting results, Table 2 and Table 3 indicate that small p-values could be the result of multiple testing/multiple modeling.

However, the association between BC or EC and cardiovascular mortality should be further explored by further studies, which should pay more attention to the PM<sub>2.5</sub>-adjusted model. Subgroup analysis indicated that the effects of BC or EC on cardiovascular diseases were the most significant on the current day and the impacts were decreased with lag days. In addition, the association between BC or EC and cardiovascular mortality in the cold season was stronger than that in the warm season. A potential reason could be that the concentration of BC or EC in the cold season was higher than that in the warm season. 97-99 Subgroup analysis on pollutant (BC and EC) indicated that the results from the PM<sub>2.5</sub>-unadjusted model and PM<sub>2.5</sub>-adjusted model were not consistent. Furthermore, the sensitivity analysis on omitting a single study showed that the results were not robust (data not shown). An essential reason could be that BC and EC were considered interchangeable. Three included studies simultaneously assessed the effects of BC and EC on cardiovascular diseases.<sup>22, 63, 93</sup> However, in the PM<sub>2.5</sub>-adjusted model, no statistically significant difference was observed between EC (RR=1.039, 95% CI: 0.993-1.083) and cardiovascular morbidity. In addition, Samoli et al illustrated that the impact of BC and EC on cardiovascular morbidity differed in the elderly and other age groups, while Atkinson et al indicated no statistically significant difference between BC or EC and cardiovascular mortality in both the PM<sub>2.5</sub>-adjusted model and PM<sub>2.5</sub>-unadjusted model.<sup>22, 85</sup> On the other hand, increased risk of long-term exposure to BC or EC and cardiovascular diseases was observed. However, in this meta-analysis, due to the limited number of included studies, only short-term exposure to asthma morbidity was

evaluated. In addition, a subgroup analysis on the chronic effects of BC or EC on cardiovascular and respiratory diseases was not performed because of the limited number of included studies.

The overall quality of the acute effects of BC or EC on cardiovascular diseases in all populations in the PM<sub>2.5</sub>-unadjusted model was evaluated as "moderate" certainty. We downgraded one level for publication bias, hence the estimate was adjusted using the trim and fill method. Several pieces of evidence (acute effects of BC or EC on cardiovascular diseases in all populations in PM<sub>2.5</sub>-unadjusted/adjusted model and chronic effects of BC or EC on cardiovascular diseases in PM<sub>2.5</sub>-unadjusted model) upgrade one level on concentration-response gradient for an increase in risk with increasing BC or EC.<sup>29</sup> In addition, inconsistency was not downgraded because 80% PI does not include unity, or it include unity but less than twice the 95% CI.

#### 4.2 Vulnerable populations

This meta-analysis revealed that BC or EC may have acute effects on cardiovascular diseases in the elderly.<sup>100</sup> In addition, lung function and mucociliary clearance decline with long-term exposure to pollutants and increasing age.<sup>5, 101</sup> These factors contribute to make the elderly more vulnerable to BC. On the other hand, this meta-analysis indicated that an increased risk was observed between BC or EC and asthma morbidity in children of 0-18 years. Asthma, a chronic airway disorder, is a serious health disease and previous studies indicated that children had higher PM<sub>2.5</sub> deposition rather than the adults, and BC is an essential constituent of PM<sub>2.5</sub>.<sup>102</sup>

#### 4.3 Underlying pathological mechanism

In our study, the pooled effect estimate indicated that short-term and long-term exposure to BC or EC was associated with an increased risk of cardiovascular diseases. There is considerable speculative literature on possible underlying mechanisms, which we review here. An animal study conducted by Niwa et al revealed that BC accelerated atherosclerotic plaque formation. Furthermore, a human panel study was performed to assess whether the patients with IHD experience change in the repolarization parameters exposure to rising concentration of pollutants. He results indicated that the variability of the T-wave complexity increased with increasing EC during periods of 0-5 hours, 12-17 hours and 0-2 hours before ECG measurement. On the other hand, a p-value plot analysis does not support a consistent effect of BC/EC on cardiovascular disease. The original meta-analysis examined heart attacks and claim effects for PM<sub>10</sub> and PM<sub>2.5</sub>, which performed by Mustafic et al, 2012. A critique is given in Young et al, 2019, who used p-value plots to call those claims into question.

#### 4.4 Suggestions for further research

First, critical potential confounders (temperature, seasonality, day of the week, and long-term trends) and other potential confounders (holidays and influenza epidemics) should be considered in time series and case crossover studies, especially for influenza epidemics. Influenza epidemics are factors usually neglected in short-term studies. Second, studies should adjust PM<sub>2.5</sub> when assessing the health effect of PM<sub>2.5</sub> constituents. Mostofsky et al. proved that PM<sub>2.5</sub> may be associated with both health and its constituents. Constituent having closer association with PM<sub>2.5</sub>

may illustrate a stronger association with diseases. Therefore, the results of PM<sub>2.5</sub>-unadjusted model could introduce bias.<sup>7</sup> Third, further studies are suggested to evaluate the health effects of long-term exposure to BC, especially for morbidity. An essential difficulty that needs to be acknowledged is the availability of the disease data. Emergency department visits and outpatient are more time-sensitive data than mortality; hence these indicators are more representative to some extent in investigating the health effects of environmental factors. However, the data of emergency department visits and outpatient generally from medical institutions are more difficult to obtain than data on mortality, with a large portion of mortality data arriving from departments of disease control institutions in China. Forth, the present evidence on the health effects of BC was mainly from America and Asia. Studies assessing the association in other geographical locations are suggested, which might contribute the evaluation of the potentially different effects of BC in different continents. Fifth, more studies need to provide evidence to prove the association between BC or EC and respiratory diseases in vulnerable populations.

#### 4.5 Strength and limitation

This systematic review and meta-analysis provided a comprehensive and current evidence for the short-term and long-term exposure to BC or EC on cardiorespiratory morbidity and mortality. Adapted GRADE framework was used to assess the certainty of the evidence. Potential limitations in our study are as follows. A significant heterogeneity for the pooled estimates was noticed in the meta-analysis, which might be due to the high variability in the study population, outcomes, and geographical

locations. Therefore, subgroup analyses on age of the population (all and older than 65 years old), outcomes (morbidity and mortality), geological locations (Europe, America and Asia) and lag days (0, 1, 2 days) were conducted for a further investigation of the potential sources in conditions more than 3 estimates. Most of the included papers used in our study were from the US or China, which affected the pooled estimates, although it is an inherent and inevitable selection bias. We have extracted and calculated the regional distribution of BC concentration of included studies. It showed that the mean BC concentration is highest in Asia, which maybe an essential reason of the results. In addition, consistent results of cardiovascular and respiratory diseases exposure to BC or EC were observed by eliminating studies with partial overlap from the same geographical locations.

It is important to obtain reasonable results from high quality evidence. A range of challenges exist in environmental epidemiology researches, which need to be envisaged and improved. The reliability of Meta-analysis was analyzed by combining p-value plots and heterogeneity. Our findings indicated that the impact of BC on cardiovascular diseases was more reliable. However, the impact of BC on respiratory diseases was random and some reported small p-values may be the result of p-hacking. It is not appropriate to do meta-analysis blindly when researchers do not understand the limitations in the basic studies. It is important to understand the causes of limitations and draw objective conclusions.

#### 5. Conclusions

Both short-term and long-term exposure to BC or EC were related with

cardiovascular diseases, supported by meta-analysis, but not p-value plots. However, the impact of BC or EC on respiratory diseases was not supported by meta-analysis or p-value plots. The effect of p-hacking on meta-analysis should be further examined.



# Acknowledgements

We would like to thank the authors of the original studies for their contributions to our systematic review and meta-analysis, especially authors who provided their raw data for the analysis. We thank Professor S. Stanley Young and all reviewers for their helpful comments and suggestions on this manuscript.



# **Contributorship statement**

SW, XZ and XS developed the research design. XS, YH, YM and LJ analyzed the data and interpreted the results. XS, YH, YM, XW and JZ drafted manuscript. AS, YuL, YaL, JT, XL and YG did literature screening and data extraction. All of the authors contributed to drafting the manuscript. The final manuscript was approved by TO CORRECTION ONLY all authors.

# **Funding**

The work was supported by the National Key Research and Development Program of China (No.2016YFA0602004) and Innovation Fund Project on Public Meteorological Service Center of China Meteorological Administration in 2020 (Grant numbers: K2020010).



# **Competing interests**

We declare that all authors have no competing interests.



# Data sharing statement

All data relevant to the study are included in the article or uploaded as supplementary information.



#### Reference

- 1. Bond TC, Doherty SJ, Fahey DW. Bounding the role of black carbon in the climate system: A scientific assessment. *Journal of geophysical research: Atmospheres*. 2013;118(11):5380-552.
- 2. Zencak Z, Elmquist M, Gustafsson Ö. Quantification and radiocarbon source apportionment of black carbon in atmospheric aerosols using the CTO-375 method. *Atmospheric Environment*. 2007;41(36):7895-906.
- 3. Atkinson RW, Kang S, Anderson HR, et al. Epidemiological time series studies of PM2.5 and daily mortality and hospital admissions: a systematic review and meta-analysis. *Thorax*. 2014;69(7):660-5.
- 4. Global, regional, and national comparative risk assessment of 84 behavioural, environmental and occupational, and metabolic risks or clusters of risks for 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet*. 2018;392(10159):1923-94.
- 5. Ross MA. Integrated science assessment for particulate matter. *US Environmental Protection Agency: Washington DC, USA*. 2009:61-161.
- 6. Bell ML, Dominici F, Ebisu K, et al. Spatial and temporal variation in PM(2.5) chemical composition in the United States for health effects studies. *Environ Health Perspect*. 2007;115(7):989-95.
- 7. Mostofsky E, Schwartz J, Coull BA, et al. Modeling the association between particle constituents of air pollution and health outcomes. *Am J Epidemiol*. 2012;176(4):317-26.
- 8. Janssen N, Gerlofs NM, Lanki T. Health effects of black carbon, The WHO European Centre for Environment and Health, Bonn, Germany. *World Health Organisation Regional Office for Europe, Copenhagen, Denmark.* 2012.
- 9. Grahame TJ, Klemm R, Schlesinger RB. Public health and components of particulate matter: the changing assessment of black carbon. *J Air Waste Manag Assoc*. 2014;64(6):620-60.
- 10. Husain M, Kyjovska ZO, Bourdon-Lacombe J, et al. Carbon black nanoparticles induce biphasic gene expression changes associated with inflammatory responses in the lungs of C57BL/6 mice following a single intratracheal instillation. *Toxicol Appl Pharmacol*. 2015;289(3):573-88.
- 11. Colicino E, Giuliano G, Power MC, et al. Long-term exposure to black carbon, cognition and single nucleotide polymorphisms in microRNA processing genes in older men. *Environ Int.* 2016;88:86-93.
- 12. Büchner N, Ale-Agha N, Jakob S, et al. Unhealthy diet and ultrafine carbon black particles induce senescence and disease associated phenotypic changes. *Exp Gerontol*. 2013;48(1).
- 13. Young SS. Air quality environmental epidemiology studies are unreliable. *REGULATORY TOXICOLOGY AND PHARMACOLOGY*. 2017;86:177-80.
- 14. Simonsohn U, Nelson LD, Simmons JP. p-Curve and Effect Size: Correcting for Publication Bias Using Only Significant Results. *PERSPECTIVES ON PSYCHOLOGICAL SCIENCE*. 2014;9(6):666-81.
- 15. Spellman BA. The Seven Deadly Sins of Psychology: A Manifesto for Reforming the Culture of Scientific Practice. *NATURE*. 2017;544(7651):414-5.
- 16. Munafo M. Rigor Mortis: How Sloppy Science Creates Worthless Cures, Crushes Hope, and Wastes Billions. *NATURE*. 2017;543(7647):619-20.
- 17. Achilleos S, Kioumourtzoglou M-A, Wu C-D, et al. Acute effects of fine particulate matter constituents on mortality: A systematic review and meta-regression analysis. *Environ Int.* 2017;109.

- 18. Luben TJ, Nichols JL, Dutton SJ, et al. A systematic review of cardiovascular emergency department visits, hospital admissions and mortality associated with ambient black carbon. *Environ Int.* 2017;107:154-62.
- 19. Yang Y, Ruan Z, Wang X, et al. Short-term and long-term exposures to fine particulate matter constituents and health: A systematic review and meta-analysis. *ENVIRONMENTAL POLLUTION*. 2019;247:874-82.
- 20. Cumberbatch MG, Rota M, Catto JWF, et al. The Role of Tobacco Smoke in Bladder and Kidney Carcinogenesis: A Comparison of Exposures and Meta-analysis of Incidence and Mortality Risks. *Eur Urol*. 2016;70(3):458-66.
- 21. Ostro B, Hu J, Goldberg D, et al. Associations of mortality with long-term exposures to fine and ultrafine particles, species and sources: results from the California Teachers Study Cohort. *Environ Health Perspect*. 2015;123(6):549-56.
- 22. Samoli E, Atkinson RW, Analitis A, et al. Associations of short-term exposure to traffic-related air pollution with cardiovascular and respiratory hospital admissions in London, UK. *Occup Environ Med.* 2016;73(5):300-7.
- 23. Basagaña X, Jacquemin B, Karanasiou A, et al. Short-term effects of particulate matter constituents on daily hospitalizations and mortality in five South-European cities: results from the MED-PARTICLES project. *Environ Int.* 2015;75:151-8.
- 24. Gan WQ, FitzGerald JM, Carlsten C, et al. Associations of ambient air pollution with chronic obstructive pulmonary disease hospitalization and mortality. *Am J Respir Crit Care Med*. 2013;187(7):721-7.
- 25. Ostro B, Tobias A, Karanasiou A, et al. The risks of acute exposure to black carbon in Southern Europe: results from the MED-PARTICLES project. *Occup Environ Med.* 2015;72(2):123-9.
- 26. Thurston GD, Burnett RT, Turner MC, et al. Ischemic Heart Disease Mortality and Long-Term Exposure to Source-Related Components of U.S. Fine Particle Air Pollution. *Environ Health Perspect*. 2016;124(6):785-94.
- 27. National Toxicology Program. Handbook for conducting a literature-based health assessment using OHAT approach for systematic review and evidence integration. Office of Health Assessment and Translation (OHAT), Division of the National Toxicology Program, National Institute of Environmental Health Sciences <a href="https://ntpniehsnihgov/ntp/ohat/">https://ntpniehsnihgov/ntp/ohat/</a> pubs/ handbookjan2015 508pdf 2015.
- 28. Lam J, Sutton P, Kalkbrenner A, et al. A Systematic Review and Meta-Analysis of Multiple Airborne Pollutants and Autism Spectrum Disorder. *PLoS One*. 2016;11(9):e0161851.
- 29. Morgan RL, Thayer KA, Santesso N, et al. A risk of bias instrument for non-randomized studies of exposures: A users' guide to its application in the context of GRADE. *Environ Int.* 2019;122:168-84.
- 30. Stanley Young S, Kindzierski WB. Evaluation of a meta-analysis of air quality and heart attacks, a case study. *Critical reviews in toxicology*. 2019;49(1):85-94.
- 31. Schweder T, Spjotvoll E. PLOTS OF P-VALUES TO EVALUATE MANY TESTS SIMULTANEOUSLY. *BIOMETRIKA*. 1982;69(3):493-502.
- 32. Strickland MJ, Darrow LA, Mulholland JA, et al. Implications of different approaches for characterizing ambient air pollutant concentrations within the urban airshed for time-series studies and health benefits analyses. *Environ Health*. 2011;10:36.
- 33. Nayebare SR, Aburizaiza OS, Siddique A, et al. Association of fine particulate air pollution with cardiopulmonary morbidity in Western Coast of Saudi Arabia. *Saudi Med J.* 2017;38(9):905-12.

- 34. Cai J, Zhao A, Zhao J, et al. Acute effects of air pollution on asthma hospitalization in Shanghai, China. *Environ Pollut*. 2014;191:139-44.
- 35. Hua J, Yin Y, Peng L, et al. Acute effects of black carbon and PM<sub>2.5</sub> on children asthma admissions: a time-series study in a Chinese city. *Sci Total Environ*. 2014;481:433-8.
- 36. Darrow LA, Klein M, Flanders WD, et al. Air pollution and acute respiratory infections among children 0-4 years of age: an 18-year time-series study. *Am J Epidemiol*. 2014;180(10):968-77.
- 37. Zanobetti A, Schwartz J. Air pollution and emergency admissions in Boston, MA. *J Epidemiol Community Health*. 2006;60(10):890-5.
- 38. Metzger KB, Tolbert PE, Klein M, et al. Ambient air pollution and cardiovascular emergency department visits. *Epidemiology*. 2004;15(1):46-56.
- 39. O'Lenick CR, Winquist A, Mulholland JA, et al. Assessment of neighbourhood-level socioeconomic status as a modifier of air pollution-asthma associations among children in Atlanta. *J Epidemiol Community Health*. 2017;71(2):129-36.
- 40. Mar TF, Norris GA, Koenig JQ, et al. Associations between air pollution and mortality in Phoenix, 1995-1997. *Environ Health Perspect*. 2000;108(4):347-53.
- 41. Krall JR, Mulholland JA, Russell AG, et al. Associations between Source-Specific Fine Particulate Matter and Emergency Department Visits for Respiratory Disease in Four U.S. Cities. *Environ Health Perspect*. 2017;125(1).
- 42. Gong T, Sun Z, Zhang X, et al. Associations of black carbon and PM2.5 with daily cardiovascular mortality in Beijing, China. *Atmospheric Environment*. 2019;214:116876.
- 43. Wang Y, Shi Z, Shen F, et al. Associations of daily mortality with short-term exposure to PM and its constituents in Shanghai, China. *Chemosphere*. 2019;233:879-87.
- 44. Dai L, Zanobetti A, Koutrakis P, et al. Associations of fine particulate matter species with mortality in the United States: a multicity time-series analysis. *Environ Health Perspect*. 2014;122(8):837-42.
- 45. Bell ML, Ebisu K, Leaderer BP, et al. Associations of  $PM_{2.5}$  constituents and sources with hospital admissions: analysis of four counties in Connecticut and Massachusetts (USA) for persons  $\geq$  65 years of age. *Environ Health Perspect*. 2014;122(2):138-44.
- 46. Wang M, Hopke PK, Masiol M, et al. Changes in triggering of ST-elevation myocardial infarction by particulate air pollution in Monroe County, New York over time: a case-crossover study. *Environmental Health*. 2019;18(1).
- 47. Son J-Y, Lee J-T, Kim K-H, et al. Characterization of fine particulate matter and associations between particulate chemical constituents and mortality in Seoul, Korea. *Environ Health Perspect*. 2012;120(6):872-8.
- 48. Cakmak S, Dales RE, Gultekin T, et al. Components of particulate air pollution and emergency department visits in Chile. *Arch Environ Occup Health*. 2009;64(3):148-55.
- 49. Geng F, Hua J, Mu Z, et al. Differentiating the associations of black carbon and fine particle with daily mortality in a Chinese city. *Environ Res.* 2013;120:27-32.
- 50. Lin H, Tao J, Du Y, et al. Differentiating the effects of characteristics of PM pollution on mortality from ischemic and hemorrhagic strokes. *Int J Hyg Environ Health*. 2016;219(2):204-11.
- 51. Lall R, Ito K, Thurston GD. Distributed lag analyses of daily hospital admissions and source-apportioned fine particle air pollution. *Environ Health Perspect*. 2011;119(4):455-60.
- 52. Ostro B, Feng W-Y, Broadwin R, et al. The effects of components of fine particulate air pollution on mortality in california: results from CALFINE. *Environ Health Perspect*. 2007;115(1):13-9.

- 53. Ostro B, Roth L, Malig B, et al. The effects of fine particle components on respiratory hospital admissions in children. *Environ Health Perspect*. 2009;117(3):475-80.
- 54. Peng RD, Bell ML, Geyh AS, et al. Emergency admissions for cardiovascular and respiratory diseases and the chemical composition of fine particle air pollution. *Environ Health Perspect*. 2009;117(6):957-63.
- 55. Tomić-Spirić V, Kovačević G, Marinković J, et al. Evaluation of the Impact of Black Carbon on the Worsening of Allergic Respiratory Diseases in the Region of Western Serbia: A Time-Stratified Case-Crossover Study. *Medicina (Kaunas)*. 2019;55(6).
- 56. Pearce JL, Waller LA, Mulholland JA, et al. Exploring associations between multipollutant day types and asthma morbidity: epidemiologic applications of self-organizing map ambient air quality classifications. *Environ Health*. 2015;14:55.
- 57. Heo J, Schauer JJ, Yi O, et al. Fine particle air pollution and mortality: importance of specific sources and chemical species. *Epidemiology*. 2014;25(3):379-88.
- 58. Liu S, Ganduglia CM, Li X, et al. Fine particulate matter components and emergency department visits among a privately insured population in Greater Houston. *Sci Total Environ*. 2016;566-567:521-7.
- 59. Sarnat SE, Winquist A, Schauer JJ, et al. Fine particulate matter components and emergency department visits for cardiovascular and respiratory diseases in the St. Louis, Missouri-Illinois, metropolitan area. *Environ Health Perspect*. 2015;123(5):437-44.
- 60. Lavigne É, Talarico R, van Donkelaar A, et al. Fine particulate matter concentration and composition and the incidence of childhood asthma. *Environ Int*. 2021;152:106486.
- 61. Cao J, Xu H, Xu Q, et al. Fine particulate matter constituents and cardiopulmonary mortality in a heavily polluted Chinese city. *Environ Health Perspect*. 2012;120(3):373-8.
- 62. Ito K, Mathes R, Ross Z, et al. Fine particulate matter constituents associated with cardiovascular hospitalizations and mortality in New York City. *Environ Health Perspect*. 2011;119(4):467-73.
- 63. Winquist A, Schauer JJ, Turner JR, et al. Impact of ambient fine particulate matter carbon measurement methods on observed associations with acute cardiorespiratory morbidity. *J Expo Sci Environ Epidemiol*. 2015;25(2):215-21.
- 64. Ostro BD, Feng WY, Broadwin R, et al. The impact of components of fine particulate matter on cardiovascular mortality in susceptible subpopulations. *Occup Environ Med.* 2008;65(11):750-6.
- 65. Klemm RJ, Thomas EL, Wyzga RE. The impact of frequency and duration of air quality monitoring: Atlanta, GA, data modeling of air pollution and mortality. *J Air Waste Manag Assoc.* 2011;61(11):1281-91.
- 66. Chen S-Y, Lin Y-L, Chang W-T, et al. Increasing emergency room visits for stroke by elevated levels of fine particulate constituents. *Sci Total Environ*. 2014;473-474:446-50.
- 67. Tolbert PE, Klein M, Metzger KB, et al. Interim results of the study of particulates and health in Atlanta (SOPHIA). *J Expo Anal Environ Epidemiol*. 2000;10(5):446-60.
- 68. Yang Y, Tang R, Qiu H, et al. Long term exposure to air pollution and mortality in an elderly cohort in Hong Kong. *Environ Int.* 2018;117.
- 69. Hasslöf H, Molnár P, Andersson EM, et al. Long-term exposure to air pollution and atherosclerosis in the carotid arteries in the Malmö diet and cancer cohort. *Environ Res.* 2020;191:110095.
- 70. Rodins V, Lucht S, Ohlwein S, et al. Long-term exposure to ambient source-specific particulate matter and its components and incidence of cardiovascular events The Heinz Nixdorf Recall study.

Environ Int. 2020;142.

- 71. Liu L, Zhang Y, Yang Z, et al. Long-term exposure to fine particulate constituents and cardiovascular diseases in Chinese adults. *Journal of Hazardous Materials*. 2021;416.
- 72. Liu S, Jorgensen JT, Ljungman P, et al. Long-term exposure to low-level air pollution and incidence of chronic obstructive pulmonary disease: The ELAPSE project. *Environ Int.* 2021;146.
- 73. Ljungman PLS, Andersson N, Stockfelt L, et al. Long-Term Exposure to Particulate Air Pollution, Black Carbon, and Their Source Components in Relation to Ischemic Heart Disease and Stroke. *Environ Health Perspect*. 2019;127(10):107012.
- 74. Gan WQ, Koehoorn M, Davies HW, et al. Long-term exposure to traffic-related air pollution and the risk of coronary heart disease hospitalization and mortality. *Environ Health Perspect*. 2011;119(4):501-7.
- 75. Hvidtfeldt UA, Sørensen M, Geels C, et al. Long-term residential exposure to PM2.5, PM10, black carbon, NO2, and ozone and mortality in a Danish cohort. *Environ Int.* 2019;123:265-72.
- 76. Levy JI, Diez D, Dou Y, et al. A meta-analysis and multisite time-series analysis of the differential toxicity of major fine particulate matter constituents. *Am J Epidemiol*. 2012;175(11):1091-9.
- 77. Strickland MJ, Klein M, Flanders WD, et al. Modification of the effect of ambient air pollution on pediatric asthma emergency visits: susceptible subpopulations. *Epidemiology*. 2014;25(6):843-50.
- 78. Wang Y-C, Lin Y-K. Mortality and emergency room visits associated with ambient particulate matter constituents in metropolitan Taipei. *Sci Total Environ*. 2016;569-570:1427-34.
- 79. Maynard D, Coull BA, Gryparis A, et al. Mortality risk associated with short-term exposure to traffic particles and sulfates. *Environ Health Perspect*. 2007;115(5):751-5.
- 80. Tolbert PE, Klein M, Peel JL, et al. Multipollutant modeling issues in a study of ambient air quality and emergency department visits in Atlanta. *J Expo Sci Environ Epidemiol*. 2007;17 Suppl 2:S29-S35.
- 81. Vedal S, Campen MJ, McDonald JD, et al. National Particle Component Toxicity (NPACT) initiative report on cardiovascular effects. *Res Rep Health Eff Inst.* 2013(178):5-8.
- 82. Ito K, Ross Z, Zhou J, et al. NPACT Study 3. Time-Series Analysis of Mortality, Hospitalizations, and Ambient PM2.5 and Its Components. In: National Particle Component Toxicity (NPACT) Initiative: Integrated Epidemiologic and Toxicologic Studies of the Health Effects of Particulate Matter Components. Research Report 177. Health Effects Institute, Boston, MA. *Res Rep Health Eff Inst.* 2013.
- 83. Lin H, Tao J, Du Y, et al. Particle size and chemical constituents of ambient particulate pollution associated with cardiovascular mortality in Guangzhou, China. *Environ Pollut*. 2016;208(Pt B):758-66.
- 84. Jung C-R, Young L-H, Hsu H-T, et al. PM components and outpatient visits for asthma: A time-stratified case-crossover study in a suburban area. *Environ Pollut*. 2017;231(Pt 1):1085-92.
- 85. Rahmatinia M, Hadei M, Hopke PK, et al. Relationship between ambient black carbon and daily mortality in Tehran, Iran: a distributed lag nonlinear time series analysis. *Journal of environmental health science & engineering*. 2021;19(1):907-16.
- 86. de Kluizenaar Y, van Lenthe FJ, Visschedijk AJH, et al. Road traffic noise, air pollution components and cardiovascular events. *Noise Health*. 2013;15(67):388-97.
- 87. Huang W, Cao J, Tao Y, et al. Seasonal variation of chemical species associated with short-term mortality effects of PM(2.5) in Xi'an, a Central City in China. *Am J Epidemiol*. 2012;175(6):556-66.
- 88. Kim S-Y, Dutton SJ, Sheppard L, et al. The short-term association of selected components of fine

particulate matter and mortality in the Denver Aerosol Sources and Health (DASH) study. *Environ Health*. 2015;14:49.

- 89. Strickland MJ, Darrow LA, Klein M, et al. Short-term associations between ambient air pollutants and pediatric asthma emergency department visits. *Am J Respir Crit Care Med.* 2010;182(3):307-16.
- 90. Liu S, Ganduglia CM, Li X, et al. Short-term associations of fine particulate matter components and emergency hospital admissions among a privately insured population in Greater Houston. *Atmospheric Environment*. 2016;147:369-75.
- 91. Kovacevic G, Spiric VT, Marinkovic J, et al. Short-Term effects of air pollution on exacerbations of allergic asthma in uzice region, serbia. *Postepy Dermatologii i Alergologii*. 2020;37(3):377-83.
- 92. Krall JR, Anderson GB, Dominici F, et al. Short-term exposure to particulate matter constituents and mortality in a national study of U.S. urban communities. *Environ Health Perspect*. 2013;121(10):1148-53.
- 93. Atkinson RW, Analitis A, Samoli E, et al. Short-term exposure to traffic-related air pollution and daily mortality in London, UK. *J Expo Sci Environ Epidemiol*. 2016;26(2):125-32.
- 94. Kim S-Y, Peel JL, Hannigan MP, et al. The temporal lag structure of short-term associations of fine particulate matter chemical constituents and cardiovascular and respiratory hospitalizations. *Environ Health Perspect*. 2012;120(8):1094-9.
- 95. Zhou J, Ito K, Lall R, et al. Time-series analysis of mortality effects of fine particulate matter components in Detroit and Seattle. *Environ Health Perspect*. 2011;119(4):461-6.
- 96. Sinclair AH, Edgerton ES, Wyzga R, et al. A two-time-period comparison of the effects of ambient air pollution on outpatient visits for acute respiratory illnesses. *J Air Waste Manag Assoc*. 2010;60(2):163-75.
- 97. Anand A, Phuleria HC. Spatial and seasonal variation of outdoor BC and PM 2.5 in densely populated urban slums. *Environ Sci Pollut Res Int.* 2021;28(2):1397-408.
- 98. Chen P, Kang S, Gul C, et al. Seasonality of carbonaceous aerosol composition and light absorption properties in Karachi, Pakistan. *J Environ Sci (China)*. 2020;90:286-96.
- 99. Yang Y, Xu X, Zhang Y, et al. Seasonal size distribution and mixing state of black carbon aerosols in a polluted urban environment of the Yangtze River Delta region, China. *Sci Total Environ*. 2019;654:300-10.
- 100. Bell ML, Zanobetti A, Dominici F. Evidence on vulnerability and susceptibility to health risks associated with short-term exposure to particulate matter: a systematic review and meta-analysis. *Am J Epidemiol*. 2013;178(6):865-76.
- 101. Sinharay R, Gong J, Barratt B, et al. Respiratory and cardiovascular responses to walking down a traffic-polluted road compared with walking in a traffic-free area in participants aged 60 years and older with chronic lung or heart disease and age-matched healthy controls: a randomised, crossover study. *Lancet*. 2018;391(10118):339-49.
- 102. Phalen RF, Oldham MJ, Kleinman MT, et al. TRACHEOBRONCHIAL DEPOSITION PREDICTIONS FOR INFANTS, CHILDREN AND ADOLESCENTS. In: Dodgson J, McCallum RI, Bailey MR, Fisher DR, editors. Inhaled Particles VI: Pergamon; 1988. p. 11-21.
- 103. Niwa Y, Hiura Y, Murayama T, et al. Nano-sized carbon black exposure exacerbates atherosclerosis in LDL-receptor knockout mice. *Circ J.* 2007;71(7):1157-61.
- 104. Henneberger A, Zareba W, Ibald-Mulli A, et al. Repolarization changes induced by air pollution in ischemic heart disease patients. *Environ Health Perspect*. 2005;113(4):440-6.
- 105. Mustafic H, Jabre P, Caussin C, et al. Main air pollutants and myocardial infarction: a systematic

review and meta-analysis. Jama. 2012;307(7):713-21.

# **Table captions**

**Table 1** Short-term impact of BC or EC on cardiovascular and respiratory diseases in different models.

**Table 2** Variable counts, and analysis search spaces for the 15 studies chosen from the meta-analysis.

**Table 3** Summary statistics for the number of possible analyses using the three search spaces.

**Table 4** Results of risk of bias assessment.

# Figure captions

Figure 1 Flow diagram of literature screening process.

**Figure 2** Impact of short-term exposure to BC or EC on cardiovascular diseases in the  $PM_{2.5}$ -unadjusted model.

**Figure 3** P-value plots of short-term exposure to BC or EC on cardiovascular diseases (A) and respiratory diseases (B) in the PM<sub>2.5</sub>-unadjusted model.

## Appendix A. Supplementary data

**Table S1** Search strategy in PubMed.

**Table S2** Characteristics of the included studies in the systematic review and meta-analysis.

**Table S3** Subgroup analysis on short-term effects of BC or EC on cardiovascular and respiratory diseases.

**Table S4** Details of risk of bias assessment.

**Table S5** Assessment of certainty of evidence for the outcomes.

**Table S6** The p-value calculation process for each study using RR, CI low and CI high.

**Figure S1** Impact of short-term exposure to BC or EC on cardiovascular mortality stratified by geographical locations.

**Figure S2** Impact of short-term exposure to BC or EC on cardiovascular morbidity stratified by geographical locations.

Figure S3 Impact of long-term exposure to BC or EC on cardiovascular diseases.

**Figure S4** Impact of short-term exposure to BC or EC on cardiovascular diseases in the PM<sub>2.5</sub>-adjusted model.

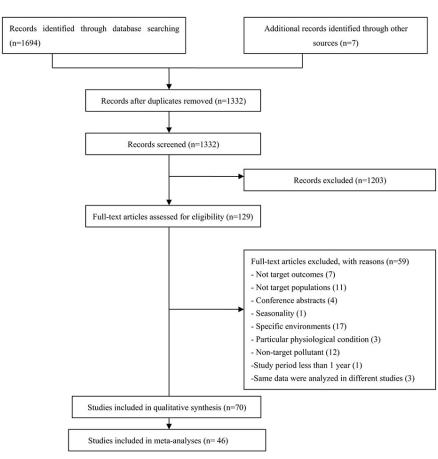


Fig. 1. Flow diagram of literature screening process

Figure 1 Flow diagram of literature screening process.

90x90mm (300 x 300 DPI)

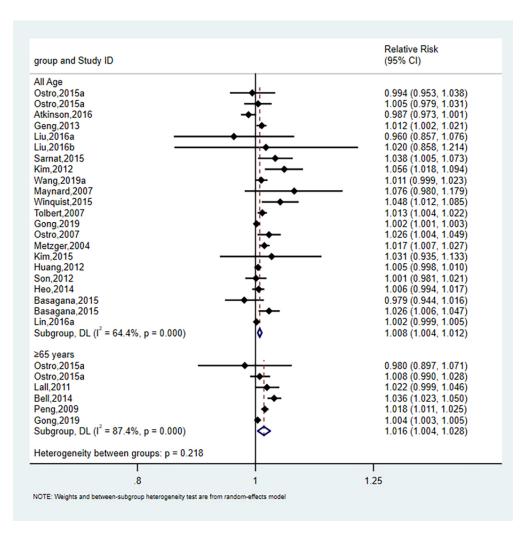


Figure 2 Impact of short-term exposure to BC or EC on cardiovascular diseases in the PM2.5-unadjusted model.

90x90mm (300 x 300 DPI)

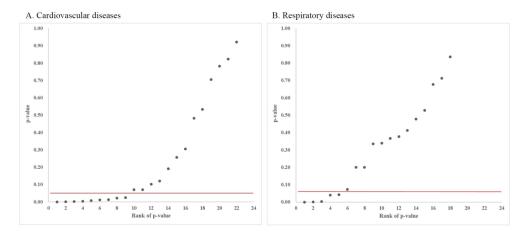


Figure 3 P-value plots of short-term exposure to BC or EC on cardiovascular diseases (A) and respiratory diseases (B) in the PM2.5-unadjusted model.

160x71mm (300 x 300 DPI)

#### SUPPLEMENTARY APPENDIX

# Is Short-term and Long-term Exposure to Black Carbon Associated with Cardiovascular and Respiratory Diseases? A Research based on Evidence Reliability

Xuping Song<sup>a</sup>, Yue Hu<sup>a</sup>, Yan Ma<sup>a</sup>, Liangzhen Jiang<sup>a</sup>, Xinyi Wang<sup>c</sup>, Anchen Shi<sup>d</sup>, Junxian Zhao<sup>a</sup>, Yunxu Liu<sup>a</sup>, Yafei Liu<sup>a</sup>, Jing Tang<sup>a</sup>, Xiayang Li<sup>a</sup>, Xiaoling Zhang\*<sup>b</sup>, Yong Guo<sup>e</sup>, Shigong Wang\*<sup>b</sup>

- <sup>a</sup> School of Public Health, Lanzhou University, Lanzhou 730000, China;
- <sup>b</sup> College of Atmospheric Sciences, Chengdu University of Information Technology, Chengdu 610000, China;
- <sup>c</sup> Second Clinical College, Lanzhou University, Lanzhou 730000, China;
- <sup>d</sup> Department of General Surgery, The First Affiliated Hospital of Xi'an Jiao Tong University, Shaanxi 710061, China;
- <sup>e</sup> Department of Civil Affairs in Guizhou Province, Guiyang 550004, China.

#### **Corresponding author 1:**

Name: Xiaoling Zhang

Postal Address: College of Atmospheric Sciences, Chengdu University of Information

Technology, Chengdu 610000, Sichuan, China

E-mail address: xlzhang@ium.cn

Fax: 028-85966502 Corresponding author 2: Name: Shigong Wang

Postal Address: College of Atmospheric Sciences, Chengdu University of Information

Technology, Chengdu 610000, Sichuan, China

E-mail address: wangsg@cuit.edu.cn

Fax: 028-85966502

## Supplementary data

- Table S1 Search strategy in PubMed.
- **Table S2** Characteristics of the included studies in the systematic review and meta-analysis.
- **Table S3** Subgroup analysis on short-term effects of BC or EC on cardiovascular and respiratory diseases.
- Table S4 Details of risk of bias assessment.
- **Table S5** Assessment of certainty of evidence for the outcomes.
- **Table S6** The p-value calculation process for each study using RR, CI low and CI high.
- **Figure S1** Impact of short-term exposure to BC or EC on cardiovascular mortality stratified by geographical locations.
- **Figure S2** Impact of short-term exposure to BC or EC on cardiovascular morbidity stratified by geographical locations.
- Figure S3 Impact of long-term exposure to BC or EC on cardiovascular diseases.
- **Figure S4** Impact of short-term exposure to BC or EC on cardiovascular diseases in the PM<sub>2.5</sub>-adjusted model.

	BMJ Open  BMJ Open  2021-044951  e S1 Search Strategy for PubMed.
	pen
	-200
	27-0
	495
Table	
No.	Search Strategy ω
#1	particulate matter/or aerosols.sh.
#2	particulate matter*/or "PM10"/or "PM2.5"/or fine particle*/or thoracic particle*/or ultrafine/or aerosol*/or carbon*/or soot*.ti,ab.
#3	particulate matter/or aerosols.sh.  particulate matter*/or "PM10"/or "PM2.5"/or fine particle*/or thoracic particle*/or ultrafine/or aerosol*/or carbon*/or soot*.ti,ab.  "PM".tw.
#4	
#5	or/1,2,3 "EC" /or "BC".tw. and/4,5 black carbon*/or elemental carbon*.ti,ab.
#6	and/4,5
#7	black carbon*/or elemental carbon*/or element carbon*.ti,ab.
#8	or/6,7
#9	respiratory tract disease.sh.
#10	respirat*/or pulmonary disease*/or lung/or chest infection*/or airway/or asthma*/or pneumonia*/or "chronic obstructive pulmonary disease"/or COPD.ti,ab.
#11	cardiovascular diseases.sh.
#12	cardio*/or cardiop*/or cardior*/or heart/or coronary/or vascular/or blood/or cardiac.ti,ab.
#13	or/9,10,11,12
#14	morbidity/or hospitalization/or death/or mortality/or outpatient.sh
#15	morbidit*/or hospitalisation*/or hospitalization*/or death*/or mortalit*/or outpatien*/or emergency room*/or emergency department*/of emergency admi*/or hospitalization*
	admission*.ti,ab.
#16	or/14,15 epidemiologic studies/or cross over study.sh.
#17	
#18	time series*/or timeseries*/or case cross*/or casecross*.tw.
	generalized additive model/or generalised additive model/or generalized linear model/or generalised linear model/or distributed lag non-ginear model/or distributed lag non-ginear model/or distributed lag non-ginear model
#19	model/or distributed lag model/or quasipoisson*/or poisson*/or generalized estimating equation/or generalised estimating equation/or GLM/or GLM/or DLNM/or GEE/or DLM/or
	ARIMA.tw.
#20	condit /of follow up /of conservational/of case condition /of epidemiologic/of population
	stud*/or prospective*/or retrospective*.tw.
#21	or/17,18,19,20 and/8,13,16,21
#22	and/8,13,16,21
	by c
	l by сору

**Table S2** Characteristics of included studies in the systematic review and meta-analysis.

Study	Study	Country	Study	Outcome	Age	Pollutant	ICD	On Siseases
	Design		Period				code	
Atkinson et al. 2016	TS	UK	2011-2012	Mortality	All	BC,EC	ICD-10	CVD(ICD-10:I00-I99),RES(ICD-10:J00-J99)
								RES[COPD(ICD-9-CM:490-492,RTI(ICD-9-CM:46)2466, 480-487)];CVD[HF(ICD-9-CM:428),Heart Rhythm
Bell et al. 2014	TS	USA	2000-2004	Morbidity	≥65	BC	ICD-9	Disturbances(ICD-9-CM:426-427), Cerebrovascular vents(ICD-9-CM:430-438),IHD(ICD-9-CM:410-414,
								429),PVD(ICD-9-CM:440–448)]
Cai et al. 2014	TS	China	2005-2011	Morbidity	≥18	BC	ICD-10	429),PVD(ICD-9-CM:440–448)]  Asthma(ICD-10:J45)
Geng et al. 2013	TS	China	2007-2008	Mortality	All	BC	ICD-10	CVD(ICD-10:100-199),RES(ICD-10:J00-J98)
Hua et al. 2014	TS	China	2007-2012	Morbidity	0-14	BC	ICD-10	Asthma(ICD-10:J45)
Ostro et al. 2015a	CS	Spain, Greece	2008-2009 (Athens), 2009-2010(Barc elona)	Mortality	All	ВС	ICD-10	Asthma(ICD-10:J45)  CVD(ICD-10:I00-I99),RES(ICD-10:J00-J99)  CVD(ICD-10:I00-I99),RES(ICD-10:J00-J99)
Samoli et al. 2016	TS	UK	2011-2012	Morbidity	≥15(CVD), all	BC,EC	ICD-10	CVD(ICD-10:100-199),RES(ICD-10:J00-J99)
Zanobetti and Schwartz 2006	CS	USA	1995-1999	Morbidity	≥65	ВС	ICD-9	MI(ICD-9:410),Pneumonia (ICD-9: 480–487)
Liu et al. 2016a	TS	USA	2008-2013	Morbidity	All	EC	ICD-9	CVD(ICD-9:390-429),Stroke(ICD-9:430-438),RES(ED-9:460-519),COPD(ICD-9:490-492,494,496),Pneumonia
Liu et al. 2016b	TS	USA	2008-2013	Morbidity	All	EC	ICD-9	CVD(ICD-9:390-429),Stroke(ICD-9:430-438),RESR&CD-9:460-519),COPD(ICD-9:490-492,494,496),Pneumon (ICD-9:480-486),Asthma(ICD-9:493)
Sarnat et al. 2015	TS	USA	2001-2003	Morbidity	All	EC	ICD9	CVD[IHD(ICD9:410–414),Cardiac Dysrhythmias(ICD9:427),CHF(ICD9:428),Other CVD (ICD-9:433-437,440,443-445,451-453)],RES[Pneumonia(ID9:480-486),COPD (ICD:491,492,496),Asthma/Wheeze (ICD9:493,786.07),Other RES(ICD9:460–466,477)]
Kim et al. 2012	TS	USA	2003-2007	Morbidity	All	EC	ICD-9	CVD(ICD-9:390-459),RES(ICD-9:460-519)
								copyrigl

36/bmjopen-2021-04951

Study	Study Design	Country	Study Period	Outcome	Age	Pollutant	ICD code	S Wiseases W
Ostro et al. 2009	TS	USA	2000-2003	Morbidity	<19	EC	ICD9	RES(ICD-9:460-519), Asthma(ICD-9:493), Acute bro hitis(ICD-9:466), Pneumonia(ICD-9:480-486)
Kim et al. 2015	TS	USA	2003-2007	Mortality	All	EC	ICD-10	CVD,RES . N
Huang et al. 2012	TS	China	2004-2008	Mortality	All	EC	ICD-10	RES(ICD-10:100-I98),CVD(ICD-10:100-I99)
Peng et al. 2009	TS	USA	2000-2006	Morbidity	≥65	EC	ICD-9	CVD[Cardiac Dysrhythmias(ICD-9:428),Heart Rhythmias(ICD-9:426-427),Cerebrovascular Events (ICD-9:430-438),IHD (ICD-9:410-414, 429),PVD(ICD-9:440-448)],RES[COPD(ICD-9:490-429),RES(ICD-9:464-466,480-487)]
Levy et al. 2012	TS	USA	2000-2008	Morbidity	≥65	EC	ICD-9	CVD(ICD-9:390-459),RES(ICD-9:464-466 and 480-287).
Son et al. 2012	TS	Korea	2008-2009	Mortality	All	EC	ICD-10	CVD(ICD-10:I00-I99),RES(ICD-10:J00-J99)
Heo et al. 2014	TS	Korea	2003-2007	Mortality	All	EC	ICD-10	CVD(ICD-10:100-199),RES(ICD-10:J00-J98)
Basagaña et al. 2015	CS	Spain, Italy	2003-2013	Morbidity, Mortality	All	EC	ICD-9, ICD-10	CVD(ICD-9:390-459,ICD-10:100-199),RES(ICD-9:480-519,ICD-10:J00-J99)
Dai et al. 2014	TS	USA	2000-2006	Mortality	All	EC	ICD-10	CVD(ICD-10:I01-I59),RES(ICD-10:J00-J99),MI(IC
Lin et al. 2016a	TS	China	2007-2011	Mortality	All	EC	ICD-10	CVD(ICD-10:I00-199)
Cao et al. 2012	TS	China	2004-2008	Mortality	All	EC	ICD-10	CVD(ICD-10:I00-I99),RES(ICD-10:J00-J98)
Klemm et al. 2011	TS	USA	1998-2007	Mortality	≥65	EC	ICD-10	CVD(ICD-10:100-199),RES(ICD-10:J00-J98)  CVD(ICD-10:100-199),RES(ICD-10:J00-J99)
Zhou et al. 2011	TS	USA	2002-2004	Mortality	All	EC	ICD-10	CVD(ICD-10:I01-I99),RES(ICD-10:J00-J99)
Winquist et al. 2015	TS	USA	2001-2003	Morbidity	All	BC,EC	ICD-9	RES(ICD-9:460-465,466.0,466.1,466.11,466.19,477, \$\) 80-486,491,492,493,496,786.07),CVD(ICD-9:410-414,466.19,477)
Ostro et al. 2007	TS	USA	2000-2003	Mortality	All	EC	ICD-10	428,433-437,440,443-445,451-453)  CVD(ICD-10:I00-I99),RES(ICD-10:J00-J98)
Tolbert et al. 2000	TS	USA	1998-2000	Morbidity	All	EC	ICD-9	CVD(ICD-9:402,410-414,427,428,433-437,440,444,491-453),RES(ICD-9:460-466,477,480-486,491,492,493,400)
								786.09) tec

Table S2 Characteristics of included studies in the systematic review and meta-analysis.

Study	Study	Country	Study	Outcome	Age	Pollutant	ICD	Siseases
	Design		Period				code	
Wang and Lin 2016	TS	China	2004-2010	Morbidity, Mortality	≥65(mortality),	EC	ICD-9	CVD(ICD-9-CM:390-459),RES(ICD-9-CM:460-519)
				11101111111	all(morbidity)			Dow
Darrow et al. 2014	TS	USA	1993-2010	Morbidity	0–4	EC	ICD-9	Acute Bronchitis or Bronchiolitis(ICD-9:466),Pneumonia(ICD-9:480-486),URI(ICD-9:460-465)
								CVD[IHD(ICD-9:410-414),AMI(ICD-9:410),cardiaco
Metzger et al. 2004	TS	USA	1993-2000	Morbidity	All	EC	ICD-9	dysrhythmias(ICD-9:427),CA(ICD-9:427.5),CHF(IC -9:428),PVD and cerebrovascular
								events(ICD-9:433-437,440,443-444,451-453),CHD(15D-9:440),Stroke(ICD-9:436)]
Mar et al. 2000	TS	USA	1995-1997	Mortality	All	EC	ICD-9	CVD(ICD-9:390-448.9)
Wang et al. 2019a	TS	China	2013-2015	Mortality	All	EC	ICD-10	CVD(ICD-9:390-448.9 )  CVD(ICD-10:100-199),RES(ICD-10:J00-J99)  Stroke(ICD-10:160-166)
Lin et al. 2016b	TS	China	2007-2011	Mortality	All	EC	ICD-10	Stroke(ICD-10:I60-I66)
Ostro et al. 2008	TS	USA	2000-2003	Mortality	All	EC	ICD-10	CVD(ICD-10:I00-I99)
				M. I. I.			ICD 0	CVD[Hypertensive Diseases(ICD-9:402,ICD-10:111] MI(ICD-9:410;ICD-10:121-122),IHD
Ito et al. 2011	TS	USA	2000-2006	Morbidity,	≥40	EC	ICD-9,	(ICD-9:414,ICD-10:125),Dysrhythmias(ICD-9:427,IGD-10:148),HF(ICD-9:428,ICD-10:150),Stroke(ICD-9:430-43
				Mortality			ICD-10	9,ICD-10:I60-I69)] > O
Chen et al. 2014	TS	China	2004-2008	Morbidity	All	EC	ICD-9	Stroke[Ischemic Stroke(ICD-9:433-434),Hemorrhagiz Stroke(ICD-9:430-432)]
Tomic'-Spiric' et al.	CS	Serbia	2012-2014	Morbidity	≥18	ВС	ICD-10	4. Allergic RES[AR(ICD-10:J.30.4),AA(ICD-10:J.45.0
2019				j				Allergic RES[AR(ICD-10:J.30.4),AA(ICD-10:J.45.0
Maynard et al. 2007	CS	USA	1995-1997,	Mortality	All	ВС	ICD-9,	CVD(ICD-9:390-429,ICD-10:101-152),Stroke(ICD-9:430-438,ICD-10:160-169),RES(ICD-9:460-519,ICD-10:J00-J
			1999-2002	,			ICD-10	99) Guest.
Sinclair et al. 2010	TS	USA	1998-2002	Morbidity	All	EC	NR	
Krall et al. 2013	TS	USA	2000-2005	Mortality	All	EC	NR	CVD and RES(NR)  RES(ICD-9:460-519)
Cakmak et al. 2009	TS	Canada	2001-2006	Morbidity	All	EC	ICD-9	RES(ICD-9:460-519)
								by сор
								ŏρ

**Table S2** Characteristics of included studies in the systematic review and meta-analysis.

Study	Study	Country	Study	Outcome	Age	Pollutant	ICD	O Suiseases
	Design		Period				code	CVD[IHD(ICD-9:410-414),Cardiac Dysrhythmias(IC)-9:427),CHF(ICD-9:428),PVD and Cerebrovascular
								Events(ICD-9:433-437,440,443-445,451-453)],
Tolbert et al. 2007	TS	USA	1993-2004	Morbidity	All	EC	ICD-9	RES[Asthma(ICD-9:493,786.07,786.09),COPD(ICD <b>9</b> :491,492,496),URTI(ICD-9:460-465,460.0,477),Pneumo
								(ICD-9:480-486),Bronchiolitis(ICD-9:466.1,466.11,466.19)]
								RES[Pneumonia(ICD-9:480-486),COPD(ICD-9:490-92,496),Acute Bronchitis and
Lall et al. 2011	TS	USA	2001-2002	Morbidity	≥65	EC	ICD-9	Bronchiolitis(ICD-9:466), Asthma(ICD-9:493)], CVD
2011 of the 2011	15	05/1	2001 2002	Moroidity	_03	Le	icb )	28\ Stroke/ICD 0:431 437\]
Jung and Lin 2017	CS	China	2000-2010	Morbidity	0-20	BC	ICD-9	Asthma(ICD-9-CM:493)
				,				//bm
Gong et al. 2019	TS	China	2006-2011	Mortality	All	ВС	ICD-10	CVD(ICD-10:100-199)
Mostofsky et al. 2012	CS	USA	2003-2008	Morbidity	≥21	BC	NO	Asthma(ICD-9-CM:493)  CVD(ICD-10:100-199)  Acute Ischemic Stroke
			1999-2009(Atlan					nj. cc
			ta,Georgia),					m/
			2004-010(Birmi				on >	
			ngham,Alabama,					RES[Pneumonia(ICD-9:480-486),COPD(ICD-9:491, 2012, 496), URTI(ICD-9:460-465, 466.0, 477), Asthma and/or
Krall et al. 2017	TS	USA	2001-2007(St.Lo	Morbidity	All	EC	ICD-9	Wheeze(ICD-9:493,786.07)]
			uis, Missouri ),					202
			2006-2009(Dalla					4 by
			s,Texas)					gue
O'Lenick et al. 2017	CS	USA	2001-2008	Morbidity	5–18	EC	ICD-9	Wheeze(ICD-9:493,786.07)]  20 24  by que  Sthma(ICD-9:493.0-493.9), Wheeze(ICD-9:786.07);
Pearce et al. 2015	TS	USA	1999-2008	Morbidity	5–17	EC	ICD-9	Asthma(ICD-9:493.0-493.9),Wheeze(ICD-9:786.07)
Strickland et al. 2010	CS	USA	1993-2004	Morbidity	5-17	EC	ICD-9	Asthma(ICD-9:493.0-493.9),Wheeze(ICD-9:786.09)

Table S2 Characteristics of included studies in the systematic review and meta-analysis.

Table 52 Charac						<i>J</i> =		<u> </u>
Study	Study	Country	Study	Outcome	Age	Pollutant	ICD	∰iseases ⊕
	Design		Period				code	ay
Strickland et al. 2014	TS	USA	2000-2010	Morbidity	2-16	EC	ICD-9	Asthma(codes beginning with 493),Wheeze (ICD-9:20.07)
Tr. 1 2012	TO	TICA	2001 2006	Morbidity,	all (mortality),	FC	ICD-9,	CVD/(CD 10 IO1 IZ) PEC/(CD 10 IO0 IO0)
Ito et al. 2013	TS	USA	2001-2006	Mortality	≥65(morbidity)	EC	ICD-10	CVD(ICD-10:I01-I79),RES(ICD-10:J00-J99)
Ostro et al. 2015b	Co	USA	2001-2007	Mortality	≥30	EC	ICD-10	CVD(ICD-10:I00-I99),IHD(ICD-10:I20-I25),Pulmorary(ICD-10:C34,J00-J98)
			4000 0000	Morbidity,	4.5.0.5		ICD-9,	ā e C
Gan et al. 2013	Со	Canada	1999-2002	Mortality	45-85	BC	ICD-10	COPD(ICD-9:490-492,496,ICD10:J40-J44)
Hvidtfeldt et al. 2019	Co	Denmark	1993-2015	Mortality	50 –64	BC	ICD-10	CVD(ICD-10:100-199),RES(ICD-10:J00-J99,C34)
Thursday et al. 2016	C-	LICA	1000 2004	Mantalita	>20	EC	ICD-9,	HIDJCD 0.410 414 JCD 10.120 125)
Thurston et al. 2016	Со	USA	1988-2004	Mortality	≥30	EC	ICD-10	IHD(ICD-9:410-414,ICD-10:120-125)
Yang et al. 2018	Co	China	1998-2011	Mortality	≥65	BC	ICD-10	CVD(ICD-10:100-199),RES(ICD-10:J00-J99,C34)  IHD(ICD-9:410-414,ICD-10:I20-I25)  CVD(ICD-10:I00-I99),RES(ICD-10:J00-J47,J80-J999
G 1 2011		G 1	1000 2002	Morbidity,	45.05	D.C.	ICD-9,	GYENGGE A MA MA MA MA A A GER TA MA MA
Gan et al. 2011	Co	Canada	1999-2002	Mortality	45–85	BC	ICD-10	CHD(ICD-9:410-414,429.2),(ICD-10:120-125)  IHD(ICD-9:410-414),CHD(ICD-9:430-438)  CVD (ICD-9:CM 410-452)  On Application of the Company of th
De Kluizenaar et al.	_							<u>ځ</u>
2013	Со	Netherlands	1991-2003	Morbidity	15-74	EC	ICD-9	IHD(ICD-9:410-414),CHD(ICD-9:430-438)
	_			Morbidity,				<u>D</u> .
Vedal et al. 2013	Co	USA	1994-2005	Mortality	50-79	EC	ICD-9	CVD (ICD-9:CM 410-452)
Rahmatinia et al. 2021	TS	Iran	2014-2017	Mortality	All	BC	ICD-10	RES(ICD10:J00- J99),CVD(ICD10:I00-I99),IHD(ICX 10:I20-I25)
Liu et al. 2021b	Co	China	2010–2017	Morbidity	All	BC	NR	CVD(including but not limited to hypertension and stocke)
Lavigne et al. 2021	Co	Canada	2006-2014	Morbidity	≤6	BC	ICD-10	Asthma(ICD-10:J45)
Rodins et al. 2020	Co	Germany	2000-2015	Morbidity	All	EC	NR	
Kovačević et al. 2020	CS	Serbia	2012-2014	Morbidity	≥18	BC	ICD-10	AA(ICD-10:J45.0) or asthma with coexisting AR Atherosclerosis in the carotid arteries
Hasslöf et al. 2020	Co	Sweden	1991-1994	Morbidity	All	BC	NR	
								δ

36/bmjopen-2021-049516

Table S2 Characteristics of included studies in the systematic review and meta-analysis.

Study	Study	Country	Study	Outcome	Amo	Pollutant	ICD	(	Diseases
Study	Design	Country	Period	Outcome	Age	ronutant	code	Š	b seases
Wang et al. 2019b	CS	USA	2005-2016	Morbidity	All	BC	NR	STEMI	N N
Linnann et al. 2010	C-	Sweden	1990-2011	Morbidity,	A 11	l BC	ICD-9,	•	7 421 427 J 10D 10 J (1 J 1/5)
Ljungman et al. 2019	Co		1990-2011	Mortality	All		ICD-10	IHD(ICD-9:410–414 and ICD-10:I20-25);stroke(ICD	37:431–430 and ICD-10:101–103)
Liu et al. 2021a	Co	Sweden,	1992-2004	Mouhidity	All	D.C.	ICD-9,	CORD/ICD 0:400, 402, and 404, 406, an ICD 10:140	5 0 0 0
Liu et ai. 2021a	Co	Denmark		Morbidity	All	ВС	ICD-10	COPD(ICD-9:490–492, and 494–496, or ICD-10:J4	5 <sup>14</sup> ) D D

Abbreviations: NR: Not Reported; TS: Time-Series; CS: Case-Crossover; Co: Cohort; ICD: International Classification of Diseases; MI: Myocardial infarction; CHD: Coronary heart disease; CVD: ardiovascular disease; RES: respiratory diseases; IHD: Ischemic Heart Disease; ARI: acute respiratory illness; HF: heart failure; CHF: congestive heart failure; PVD: peripheral vascular disease; AR: allergic asthma; AR: allergic rhinitis; AMI: acute myocardial infarction; CA: cardiac arrest; STEMI: ST segment elevation myocardial infarction; RTI: respiratory tract infection; URTI: Upper Respiratory Infection; LRTI: Lower Respiratory Infection; ARTI: Acute respiratory infections.

Table S3 Subgroup analysis on short-term effects of BC or EC on cardiovascular and respiratory diseases.

Subgroup Analysis	No. of	No. of	Relative Risk	$\mathbf{I}^2$	Egger Regression Test
Subgroup Analysis	Studies	Estimates	(95%CI)	1	(p value)
Cardiovascular Diseases					
Lag Days					
Lag 0d	15	18	1.013 (1.006, 1.020)*	77.30%	0.024
Lag 1d	12	15	1.005 (1.002, 1.008)	32.70%	0.299
Lag 2d	11	14	1.002 (0.999, 1.005)	73.80%	0.969
Geographical Location (Mortality)					
Asia	8	8	1.004 (1.002, 1.006)*	70.00%	_
Europe	4	5	0.991 (0.983, 0.999)	0	_
America	4	4	1.017 (0.998, 1.037)	20.80%	_
Geographical Location (Morbidity)					
Asia	_	_	_	_	_
Europe	_	_	_	_	_
America	12	12	1.023 (1.016, 1.030)	46.00%	0.078
Disease					
Congestive heart failure (Morbidity)	3	3	1.076 (1.021, 1.134)*	64.70%	_
Season (Mortality)					
Warm season	3	3	1.002 (0.995, 1.010)	0	_
Cold season	3	3	1.014 (1.008, 1.019)*	0	_
Respiratory Diseases					
Asthma (Morbidity)					
Asthma 0-18	5	6	1.021 (1.006, 1.035)*	69.10%	_
Asthma ≥18	4	5	1.011 (1.000, 1.021)	0	_

Annotation: "\*" means the data were statistically significant, p < 0.05.

36/bmjopen-2021-049516

**Table S4** Details of risk of bias assessment.

6 7 8	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data		Conflict of interest	Other
9 10	1	Atkinson	Probably Low	Low	Probably Low	Low	Low	Probably Low	Low	Low
11		et al. 2016	All of the pollutants were	Death data for the period	Adjusted for time	Study included	Daily counts	There was	The authors	No other
12			measured at the central	1 January 2011 to 31	(seasonality,	daily counts of	for death were $\frac{8}{2}$	insufficient	declare no	potential
13 14			London background	December 2012 were	long-term trend),	deaths in	obtained, so	information	conflict of	sources of
15			monitoring site at North	obtained from the Office	temperature,	London, United	likely have all	about	interest.	bias
16			Kensington. All	for National Statistics.	humidity, day of	Kingdom for the	outcome data.	selective		identified.
17 18			measurements were 24-h	Daily counts of deaths in	week and public	period 1 January	However, any	outcome to		
19			averages except for CO.	London, United Kingdom	holidays.	2011 to 31	potential errors	judge for low		
20			The number of all	were classified as all	'/	December 2012.	or missing data	risk, but		
21			observations was	disease-related causes,	. 01		did not depend	indirect		
22 23			621-693 (<25% missing	cardiovascular			on air pollution	evidence that		
24			data).	(International		(0)	levels.	suggests study		
25				Classification of			or or	was free of		
26 27				Diseases,10th			1 Ap	selective		
28				revision-ICD10: I00-I99)			rii 19,	report.		
29				and respiratory (ICD10:						
30				J00-J99) diseases.			2024 by guest.			
31 32				,			by g			
33							Jues			
34										
35							rote			
36 37							Protected			
38 <sup>l</sup>							l â			
39							сор			

4										,
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on the outcome data	Selective reporting	Conflict of interest	Other
8 9	2	Bell et al.	Probably High	Low	Probably Low	Low	Low 2	Probably Low	Low	Low
10		2014	BC measured from filters	The study used the	Models adjusted	Data obtained	Daily counts	There was	The authors	No other
11			collected daily using	Medicare beneficiary	for time	from records of	for hospital	insufficient	declare no	potential
12			optical reflectance.	denominator file from the	(seasonality,	individuals ≥65	admissions \( \frac{2}{5} \)	information	conflict of	sources of
13 14			Monitors from 5 sites	Centers for Medicare and	long-term trend),	years of age	were obtained,	about	interest.	bias
15			across 4 counties were	Medicaid Services. Cause	day of week,	enrolled in the	so likely have	selective		identified.
16			used. Sampling occurred	of admission was	temperature, and	Medicare	all outcome	outcome to		
17 18			daily, with some missing	determined by principal	dew point.	fee-for-service	data. However,	judge for low		
19			periods, for Hartford,	discharge diagnosis code		plan during	any potential	risk, but		
20			New Haven, and	according to International	' /	August 2000 to	errors or	indirect		
21			Springfield, and every	Classification of	. 01	February 2004.	missing data	evidence that		
22 23			third day for Bridgeport	Diseases, Ninth Revision,			did not depend.	suggests study		
24			and Danbury. Days with	Clinical Modification		(0)	on air pollution	was free of		
25			missing data were	(ICD-9-CM; National			levels.	selective		
26 27			omitted from analysis	Center for Health						
28			(the number of missing	Statistics 2006).						
29			data was not reported).				9, 20			
30 31							)24			
32							by g			
33							lues			
34							ָרָ יַדַ			
35 36							otec			
37							April 19, 2024 by guest. Protected by			
38								<u> </u>		
39							cop			

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data S		Conflict of interest	Other
8 9	3	Cai et al.	Probably Low	Low	Probably Low	Low	Low s	Probably Low	Low	Low
10		2014	Daily concentrations of	Asthmatic hospitalization	Adjusted for time	Study included	Daily counts	There was	Authors	No other
11			BC were measured at a	data was obtained from	(seasonality,	all asthmatic	for asthmatic	insufficient	declared no	potential
12			fixed-site station. Daily	the Shanghai Health	long-term trend),	hospitalization	hospitalization <u>≤</u>	information	competing	sources of
13   14			data was available and no	Insurance Bureau	temperature,	for adult	were obtained,	about	financial	bias
15			missing data was	(SHIB). The causes of	relative humidity	residents living	so likely have	selective	interests.	identified.
16			reported.	hospital admission were	and day of the	in the nine urban	all outcome	outcome to		
17 18				coded according to	week.	districts between	data. However,	judge for low		
19				International		January 1, 2005	any potential	risk, but		
20				Classification of	' /	and December	errors or	indirect		
21				Diseases, Revision 10	'(0)	31, 2011(2922	missing data	evidence that		
22   23				(ICD-10): Asthma (J45).		days) from the	did not depend	suggests study		
24						Shanghai Health	on air pollution			
25						Insurance	levels.	selective		
26						Bureau.	<u> </u>	report.		
27						Bureau.		_		
28   29							19, 2			
30							2024 by			
31							4 by			
32							/ gu			
33							guest.			
34   35										
36							Protected			
37							l ted			
38 <sup>L</sup>			l				1 8	1		

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data ≤	Selective reporting	Conflict of interest	Other
8 9			Probably High	Low	Probably Low	Low	Low <sup>ay</sup>	Probably Low	Low	Low
10	4	Geng et	Single, central-site	Health data were	Models included	Data consisted of	Daily counts	There was	The authors	No other
11		al. 2013	monitor. Daily BC and	obtained from Shanghai	time (seasonality,	all causes	for death were	insufficient	declare no	potential
12			PM <sub>2.5</sub> were measured	Municipal Center of	long-term trend),	(excluding	obtained, so	information	conflict of	sources of
13 14			continuously and 24hr	Disease Control and	temperature,	accidents or	likely have all	about	interest.	bias
15			averaged was estimated if	Prevention database. The	humidity and day	injuries) deaths	outcome data.	selective		identified.
16			>75% of the 1hr values	causes of death were	of week.	during over the	However, any	outcome to		
17 18			was available for that	coded according to the		course of the	potential errors	judge for low		
19			day. Missing data was not	International		study.	or missing data	risk, but		
20			replaced by other values.	Classification of	' /		did not depend	indirect		
21 22				Diseases, Revision 10	' (%)		on air pollution	evidence that		
23				(ICD 10).			levels.	suggests study		
24						Teh (	com	was free of		
25							on	selective		
26 27							Apr	report.		
28							ii 19			
29							on April 19, 2024 by			
30 31							24 k			
32							) 9			
33							uest			
34 35							guest. Protected			
35							otec			
37							l ted			
38 <sup>l</sup>							<u> </u>			

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete 9 outcome data		Conflict of interest	Other
8 9			Probably High	Low	Probably Low	Low	Low ay	Probably Low	Low	Low
10	5	Hua et al.	Daily 24h average PM <sub>2.5</sub>	Daily asthma hospital	Adjusted for	Study included	Daily counts	There was	Authors	No other
11		2014	and BC data was	admission data was	long-term and	all asthma	for asthma	insufficient	declared no	potential
12			obtained from a fixed-site	obtained from Shanghai	seasonal trend, day	hospital	hospital 💆	information	competing	sources of
13 14			station. The study only	Children's Medical	of week,	admissions of	admissions of a	about	financial	bias
15			used the actual collected	Center. Dates of	temperature and	$children \leq 14$	children were	selective	interests.	identified.
16			data and did not fill in the	admission and discharge,	relative humidity.	years of age from	obtained, so	outcome to		
17 18			missing data for PM <sub>2.5</sub>	and diagnoses using the	<b>'</b> O.	Shanghai	likely have all	judge for low		
19			and black carbon.	International		Children's	outcome data.	risk, but		
20				Classification of	'/	Medical Center	However, any	indirect		
21				Diseases, Revision 10.	' (2)	between1	potential errors	evidence that		
22 23						January 2007 and	or missing data	suggests study		
24						31 July 2012 in	did not depend			
25						nine urban	on air pollution			
26						districts of	levels.			
27 28						Shanghai.	rii 19,			
29						C	9, 2			
30							2024 by			
31 32							by (			
33							gues			
34							St. F			
35							rote			
36 37							rotected			
37 38							<u> </u>			

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data o		Conflict of interest	Other
8			Probably Low	Low	Low	Low	Low ay	Probably Low	Low	Low
9   10	6	Ostro et	Daily 24hr average BC	For both cities daily	Adjusted for long	Study population	Daily counts 8	There was	Authors	No other
11		al. 2015a	concentrations were	counts of all-cause	term and seasonal	consisted of daily	for death were	insufficient	declared no	potential
12			obtained from one station	mortality for all ages	(year, month, day	counts of	obtained, so	information	competing	sources of
13 14			in Barcelona and Athens.	were collected (excluding	of week) trends,	all-cause	likely have all	about	interests.	bias
15			Daily data was available	deaths from external	temperature,	mortality for all	outcome data.	selective		identified.
16			and no missing data was	causes, International	holidays, summer	ages and daily	However, any	outcome to		
17 18			reported.	Classification of	vacations and	counts of	potential errors	judge for low		
19				Disease-ICD9: 001799,	influenza.	cardiovascular,	or missing data	risk, but		
20				ICD10 A00R99), as well	' /	respiratory and	did not depend	indirect		
21				as daily counts of	' (2)	all-cause	on air pollution <mark>≗</mark>	evidence that		
22   23				cardiovascular (ICD9:		mortality for	levels.	suggests study		
24				390459, ICD10: I00I99),		those greater than	com	was free of		
25				respiratory		age 65.	v on	selective		
26 27				(ICD9:460519,			Ap	report.		
28				ICD10:J00J99) and						
29				all-cause mortality for			9, 20			
30				those greater than age 65.			)24			
31 32				_			by ç			
33							jues			
34							; <del>:</del>   ''			
35							rote			
36 37							April 19, 2024 by guest. Protected by			
38							by c			

5 No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data	Selective reporting	Conflict of interest	Other
3 9		Low	Low	Probably Low	Low	Low ex	Probably Low	Low	Low
7	Samoli et	Daily concentrations of	Based on the primary	Adjusted for long	Study included	Daily counts	There was	Authors	No other
11	al. 2016	BC and EC were	discharge diagnosis, daily	term and seasonal	all cardiovascular	for all	insufficient	declared no	potential
12		collected from the	numbers of admissions	trends,	and respiratory	emergency §	information	competing	sources of
13 14		ClearfLo project,	for cardiovascular disease	temperature,	hospital	hospital 8	about	interests.	bias
15		supplemented by local	(International	relative humidity,	admissions in	admissions	selective		identified.
16		measurements made at	Classification of	regulated	London, UK	were obtained,	outcome to		
17 18		the North Kensington	Diseases, 10th	pollutants (PM <sub>10</sub> ,	between 2011	so likely have	•		
19		urban background site.	revision-ICD-10:	PM <sub>2.5</sub> , NO <sub>2</sub> , SO <sub>2</sub>	and 2012.	all outcome	risk, but		
20		Number of days of	I00-I99) for those aged	and O <sub>3</sub> ), day of the		data. However	indirect		
21		observation for BC: 629	15-64 (adult) and 65+	week and public		any potential	evidence that		
22 23		(BC urban in PM <sub>2.5</sub> ) and	years (elderly), and	holidays.		errors or	suggests study		
24		702 (BC in PM <sub>2.5</sub> )	respiratory diseases		(0)	missing data	was free of		
25		between 2011 and 2012	(ICD-10: J00-J99) for			did not depend 9	selective		
26 27		(<25% missing data).	those aged 0-14 years			on air pollution €	report.		
28			(paediatric), adult and the			levels =			
29			elderly were calculated.			9, 20			
30						2024 by			
31 32						by g			
33						gues			
34						is:			
35						Protected			
36 37						Ctec			
38						ع ا	:		

<b>).</b>	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias			Conflict of interest	Other
		Probably High	Low	Probably Low	Low	Low ay	Probably Low	Low	Low
	Zanobetti	Ambient BC from one	The study extracted data	Adjusted for	Data consisted of	Daily counts	There was	Authors	No other
	and	monitor. The hourly	on all hospital admissions	temperature, day	all U.S. Medicare	for hospital	insufficient	declared no	potential
	Schwartz	measurements for BC and	for residents of the	of the week,	hospital	admissions 💆	information	competing	sources of
	2006	PM <sub>2.5</sub> were not complete.	Boston Metropolitan area	seasonality,	admissions in the	were obtained,	about	interests.	bias
		Missing values were	who were admitted to the	long-term trends,	Boston	so likely have	selective		identified.
		replaced with the	hospital (in the Boston	humidity,	Metropolitan	all outcome	outcome to		
		predicted values.	area) with a primary	barometric	area for	data. However,	judge for low		
		Additionally BC data was	diagnosis of MI	pressure, and the	myocardial	any potential	risk, but		
		missing from March 1997	(International	extinction	infarction during	errors or	indirect		
		to March 1999 and was	Classification of	coefficient.	the study	missing data	evidence that		
		not included in the study.	Diseases, 9th		duration.		suggests study		
		-	revision-ICD-9:410), and		(0)	_ 0			
			pneumonia (ICD-9:			levels.	selective		
			480–487), from Medicare			Ар г	report.		
			**				1		
			•			9, 2			
			J Caro 1770 1777.			024			
						by			
						gue			
						Prot			
						ecte			
						<u> </u>			
	).	Zanobetti and Schwartz	Probably High  Zanobetti and Schwartz  2006  PM <sub>2.5</sub> were not complete.  Missing values were replaced with the predicted values.  Additionally BC data was missing from March 1997 to March 1999 and was	Probably High  Zanobetti and Schwartz  2006  PM <sub>2.5</sub> were not complete. Missing values were replaced with the predicted values. Additionally BC data was missing from March 1997 to March 1999 and was not included in the study.  Probably High  Low The study extracted data on all hospital admissions for residents of the Boston Metropolitan area who were admitted to the hospital (in the Boston area) with a primary diagnosis of MI (International Classification of Diseases, 9th	Probably High  Zanobetti and Schwartz  2006  Probably High  Ambient BC from one monitor. The hourly measurements for BC and PM <sub>2.5</sub> were not complete. Missing values were replaced with the predicted values.  Additionally BC data was missing from March 1997 to March 1999 and was not included in the study.  Probably High  Low  Probably Low  Adjusted for temperature, day of the week, seasonality, long-term trends, humidity, barometric diagnosis of MI (International classification of Diseases, 9th revision-ICD-9:410), and pneumonia (ICD-9:480–487), from Medicare billing records for the	Probably High  Zanobetti and Ambient BC from one and BC schwartz 2006  Probably Low Ambient BC from one monitor. The hourly measurements for BC and PM2.5 were not complete. Missing values were replaced with the predicted values. Additionally BC data was missing from March 1997 to March 1999 and was not included in the study.  Probably Low Adjusted for temperature, day of the week, seasonality, long-term trends, humidity, barometric pressure, and the extinction coefficient.  Probably Low Adjusted for temperature, day of the week, seasonality, long-term trends, humidity, barometric pressure, and the extinction coefficient.  Classification of Diseases, 9th revision-ICD-9:410), and pneumonia (ICD-9: 480–487), from Medicare billing records for the	Probably High Low Probably Low Low Data consisted of on all hospital admissions for residents of the predicted values.  Additionally BC data was missing from March 1997 to March 1999 and was not included in the study.  Probably High Low Probably Low Low Data consisted of on all hospital admissions for residents of the Boston Metropolitan area who were admitted to the hospital (in the Boston area) with a primary diagnosis of MI (International Classification of Diseases, 9th revision-ICD-9:410), and pneumonia (ICD-9: 480–487), from Medicare billing records for the years 1995–1999.	Probably High  Zanobetti and Schwartz 2006  Probably High  Ambient BC from one monitor. The hourly measurements for BC and PM25 were not complete. Missing values were replaced with the predicted values. Additionally BC data was missing from March 1997 to March 1999 and was not included in the study.  Additionally BC data was missing from March 1997 to March 1999 and was not included in the study.  Additionally BC data was missing from March 1997 to March 1999 and was not included in the study.  Boutcome assessment outcome assessment and but composition and pneumonia (ICD-9: 480–487), from Medicare billing records for the and probably Low  Adjusted for Data consisted of all U.S. Medicare of the week, seasonality, admissions in the lospital admissions in the pressure, and the extinction coefficient.  Boston Metropolitan area for data. However, and the extinction coefficient.  Diseases, 9th revision-ICD-9:410), and pneumonia (ICD-9: 480–487), from Medicare billing records for the low outcome to judge for low missing data duration.  Additionally BC data was not included in the study.  Boston Metropolitan area for myocardial infarction during the study duration.  Boston Metropolitan and part preparting admissions in the lospital (in the Boston area) with a primary diagnosis of MI (International Classification of pneumonia (ICD-9: 480–487), from Medicare billing records for the lospital control in the study on air pollutione and duration.  Boston Metropolitan and many potential infarction during the study duration.  Boston Metropolitan and preparting admissions in the lospital admissions and ll U.S. Medicare for hospital admissions in the meek, seasonality, and posterm trends, hospital admissions in the lospital admissions in the mere data. However, and the extinction coefficient.  Boston Metropolitan and the extinction during the study duration.  Boston Metropolitan and duration area for myocardial infarction during the study duration.  Boston Metropolitan and the myocardial infarction during the study duration.  Bo	Probably High Ambient BC from one monitor. The hourly measurements for BC and Schwartz Missing values were replaced with the predicted values. Additionally BC data was missing from March 1997 to March 1999 and was not included in the study.  Additionally BC data was missing from March 1999 and was not included in the study.  Beston Metropolitan area who were admitted to the premise of the seasonality, and pneumonia (ICD-9: 480-487), from Medicare billing records for the years 1995–1999.  Probably Low Adjusted for temperature, day of the week, seasonality, long-term trends, hospital admissions in the were obtained, admissions in the were obtained. Boston Boston Metropolitan admissions in the were obtained admissions in the were obtained. Boston Metropolitan all outcome admissions in the were obtained. Boston Metropolitan all outcome all U.S. Medicare of the meek, long-term trends, hospital admissions in the were obtained. Boston Metropolitan almostors in the were obtained. Boston Metropolitan almostors in the were obtained. Boston Metropolitan almostors in the were obtained. Boston Metropolitan area for myocardial infarction during the study missing data bill infarction during the study.  Diseases, 9th revision-ICD-9:410), and pneumonia (ICD-9: 480-487), from Medicare billing records for the years 1995–1999.

36/bmjopen-2021-0495

2	
3	
4	
5	
6 7	
7	
8	
9	
10	
11	
12	
13	
14	
15 16	
16	
17	
18	
19	
20	
21 22 23	
22	
23	
24	
25	
26 27	
27	
28	
29	
30	
31	
32 33	
33	
34	
35	
36	
36 37	
38	

,	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data ≤		Conflict of interest	Other
3			Probably High	Low	Probably Low	Low	Low ay	Probably Low	Low	Low
o	9	Liu et al.	EC were collected from a	Emergency department	Adjusted for time	Study included	Daily counts 🕺	There was	Authors	No other
1		2016a	single monitor on a	visit data was obtained	(long-term and	daily counts of	for emergency	insufficient	declared no	potential
2			one-in-three or one-in-six	from the Blue Cross Blue	seasonal trend),	emergency	department 💆	information	potential	sources of
3 4			day schedule. EC were	Shield Texa. International	day of week,	department visits	visits were	about	competing	bias
5			measured for 566 days	Classification of Diseases	temperature, dew	for Greater	obtained, so 🚊	selective	financial	identified.
6			from April 02, 2009, to	9th Revision (ICD-9)	point and	Houston from	likely have all	outcome to	interests.	
7 8			December 30, 2013,	diagnosis codes were	population growth.	claims data	outcome data.			
9			<25% missing for the	used to classify outcome		insured from	However, any	risk, but		
20			frequency of sampling.	groups.	' /	January 1, 2008	potential errors	indirect		
21					' (0)	through	or missing data			
22						December 31,	did not depend	suggests study		
24						2013.	on air pollution			
25							levels.	selective		
26							_	report.		
27 28							April 19,	1		
9										
0							024			
1 2							2024 by guest.			
3							gue			
34							st. F			
35							Protected			
6							ecte			
7							9			

Probably High Low Probably Low Low Daily counts Probably Low Low EC were collected from a single monitor on a one-in-three or one-in-six day schedule. EC were measured for 566 days from April 02, 2009, to December 30, 2013, 25% missing for the frequency of sampling.  Probably High Low Probably Low Low Daily counts Probably Low Adjusted for time, day of week, all hospital for HA were by obtained, so obtained, so obtained, so obtained, so obtained from billing claims of outcome data. The probably Low Low Boundary Counts Probably Low Boundary Counts Probably Low Low Boundary Counts Probably			
Liu et al. 2016b   EC were collected from a single monitor on a one-in-three or one-in-six day schedule. EC were measured for 566 days from April 02, 2009, to December 30, 2013, company 20	Probably Low	Low	Low
single monitor on a one-in-three or one-in-six day schedule. EC were measured for 566 days from April 02, 2009, to December 30, 2013, <25% missing for the frequency of sampling.    10	There was	Authors	No other
day schedule. EC were measured for 566 days from April 02, 2009, to December 30, 2013,	insufficient	declared no	potential
day schedule. EC were measured for 566 days from April 02, 2009, to December 30, 2013,    16	information	competing	sources of
measured for 566 days from April 02, 2009, to December 30, 2013,  <25% missing for the frequency of sampling.    December 30, 2013,   Classification of Diseases   Di	about	financial	bias
December 30, 2013,  20   Greater Houston from January 1,    Construction (1693)   December 30, 2013,   December 30	selective	interests.	identified.
December 30, 2013, diagnosis codes were used to classify outcome groups.  Shield 1exa potential errors or missing data or miss	outcome to		
20	judge for low		
from January 1, on air pollution	risk, but		
22 Inom January 1, on an ponution p	indirect		
	evidence that		
	suggests study		
24 December 31,	was free of		
25 26 2013.	selective		
20 27	report.		
28			
29			
30 31			
32 9			
34 PP 0			
36			
25 26 27 28 29 30 31 32 33 34 35 36 37 38			
38 S S S S S S S S S S S S S S S S S S S			1

36/bmjopen-2021-0495

2 3 4	
5	
6	
7	L
8 9	
10	
11	
12	
13	
14	
15	
16 17	
18	
19	
20	
21	
22	
23 24	
25	
26	
27	
28	
29	
30	
31	
32	
33	
34	
35	
36	
37	
38	

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data		Conflict of interest	Other
8 9			Probably Low	Low	Probably Low	Low	Probably Low	Probably Low	Low	Low
10	11	Sarnat et	24hr average	Computerized billing	Models adjusted	Data consisted of	Daily counts	There was	The authors	No other
11		al. 2015	concentration of PM <sub>2.5</sub>	records were obtained	for season, day of	all emergency	for emergency	insufficient	declare they	potential
12			were obtained from a	from the Missouri	week, holidays,	department visits	department 💆	information	have no	sources of
13 14			Supersite (single, central	Hospital Association	time trends (using	during the study	visits were	about	actual or	bias
15			site monitoring location).	(MHA) for emergency	cubic splines for	period for	obtained, ⊕	selective	potential	identified.
16			The observations of EC	department visits. The	day of visit with	cardiovascular	hence one	outcome to	competing	
17			was 666 days during 1	outcome groups were	monthly knots),	disease	hospital not	judge for low	financial	
18 19			June 2001-30 April 2003	identified using primary	and temperature.	outcomes.	providing data	risk, but	interests.	
20			(missing data <25%).	International			after 26 April	indirect		
21				Classification of Diseases	(0)		2002.	evidence that		
22 23				9th Revision (ICD9)			However, any	suggests study		
24				codes.		(0)	potential errors	was free of		
25							or missing data	selective		
26							did not depend ≧			
27 28							on air pollution	1		
29										
30							024			
31							by			
32 33							gue			
34							st. F			
35							rote			
36 37							ecte			
38							<u> </u>			
39							2024 by guest. Protected by copyright.			
40							oyriç			
41 42							ght.			

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data		Conflict of interest	Other
8 9			Probably Low	Low	Probably Low	Low	Low	Probably Low	Low	Low
10	12	Kim et al.	PM <sub>2.5</sub> mass and chemical	All individual hospital	Model adjusted for	Data consisted of	Daily counts	There was	The authors	No other
11		2012	constituents were	admission records during	days from the start	all cardiovascular	for hospital	insufficient	declare they	potential
12			measured daily at one	the study period were	of the study, day	hospital	admission wer	information	have no	sources of
13 14			residential monitoring	extracted from	of week,	admissions over	obtained, so	about	actual or	bias
15			station located on the	nonelective hospital	seasonality,	the course of the	likely have all 🚊	selective	potential	identified.
16			roof of an elementary	admission discharge data	long-term trends,	study.	outcome data.	outcome to	competing	
17 18			school building in	obtained from the	daily average		However, any	judge for low	financial	
19			Denver. The observations	Colorado Hospital	temperature and		potential errors	risk, but	interests.	
20			of EC was 1809 days	Association. The	relative humidity.		or missing data	indirect		
21			during 2003-2007	International	' (2)		did not depend	evidence that		
22 23			(missing data <25%).	Classification of			on air pollution	suggests study		
24				Diseases, Ninth		<b>101.</b>	levels.	was free of		
25				Revision(ICD-9) codes			on	selective		
26 27				were used to define			Ap	report.		
28				cardiovascular hospital			rii 19,			
29				admissions (codes			9, 2			
30				390–459) and respiratory			2024 by guest.			
31   32				hospital admissions			by (			
33				(codes 460–519).			gue			
34				(60465 400 517).						
35							rote			
36							Protected			
37 38							9			

36/bmjopen-2021-0495

2	
3	
4	
5 6	
7	
8	_
9	
10	
11	
12	
13	
14	
15	
16	
17	
18	
19	
20	
21	
22 23	
24 25	
26	
27	
28	
29	
30	
31	
32	
33	
34	
35	
36	
37	
38	
39	

5 5 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data		Conflict of interest	Other
3			High	Low	Probably Low	Low	Low ay	Probably Low	Low	Low
10	13	Ostro et	EC were generally	Data for hospitalizations	Adjusted for time,	Study included	Daily counts	There was	Authors	No other
11		al. 2009	recorded every 3 days	were obtained from the	day of the week,	all	for 💆	insufficient	declared no	potential
12			from two co-located	Office of Statewide	temperature,	hospitalizations	hospitalization \(\frac{\zeta}{2}\)	information	competing	sources of
13 14			monitors or one monitor	Health Planning and	seasonality,	for children < 19	s of children	about	financial	bias
15			in 6 counties. The	Development, Healthcare	relative humidity	and < 5 years of	were obtained,	selective	interests.	identified.
16			number of available days	Quality and Analysis	and pollutant.	age for total	so likely have	outcome to		
17 18			of data over the 4-year	Division. Hospital		respiratory	all outcome	judge for low		
19			period ranged from 227	admissions for children		diseases and	data. However,	risk, but		
20			to 381 (some counties	<19 years of age were	1/6	several	any potential	indirect		
21			had >25% missing for the	classified into one or	' (0)	subcategories	errors or	evidence that		
22			frequency of sampling).	more categories: all		including	missing data	suggests study		
24				respiratory disease		pneumonia, acute	did not depend	was free of		
25				(International		bronchitis, and	on air pollution♀			
26 27				Classification of		asthma for six	· :			
28				Diseases, Ninth		California				
29				Revision-ICD-9 codes		counties from	9, 20			
30				460–519), asthma (ICD-9		2000 through	024			
31				code 493), acute		2003.	by g			
33				bronchitis (ICD-9 code			Jues			
34				466), and pneumonia			April 19, 2024 by guest. Protected by			
35				(ICD-9 codes 480–486).			rote			
36 37				(-12 ) (000).			ctec			
" 88							9			

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data △	Selective reporting	Conflict of interest	Other
8 9			Probably Low	Low	Probably Low	Low	Low $\overset{\mathbf{a}}{\searrow}$	Probably Low	Low	Low
10	14	Kim et al.	Daily 24-hour composite	Daily mortality counts for	Models adjusted	Data consisted of	Daily counts	There was	None of the	No other
11		2015	PM <sub>2.5</sub> samples were	metropolitan Denver	for longer-term	all deaths over	for death were	insufficient	authors has	potential
12			collected from single,	were computed from the	temporal trend, as	the course of the	obtained, so	information	any actual	sources of
13 14			central-site monitor. The	Colorado Health	time since the	study in a	likely have all	about	or potential	bias
15			observations of EC was	Information Dataset	study began, day	defined	outcome data.	selective	competing	identified.
16			1809 days from 2003	compiled by the Colorado	of week, and daily	geographical	However, any	outcome to	interests.	
17 18			through 2007 (missing	Department of Public	temperature and	area.	potential errors	judge for low		
19			data <25%).	Health and Environment.	humidity.		or missing data	risk, but		
20				Data included cause of	' /		did not depend	indirect		
21 22				death by the International	' (2)		on air pollution	evidence that		
23				Classification of Diseases			levels.	suggests study		
24				10th Revision (ICD-10)		ien	com	was free of		
25				code.			/ on	selective		
26 27							on April 19, 2024 by	report.		
28							11 19			
29							9, 20			
30							)24			
31 32							by g			
33							lues			
34							guest. Protected b			
35 36							rote			
37							ctec			
38							1 5			

36/bmjopen-2021-0495

2	
3	
4	
5	
6	
7	
8	_
9	
10	
11	
12	
13	
14	
15	
16	
16 17 18	
18	
19	
20	
21	
19 20 21 22 23	
23	
24	
25	
26	
26 27	
28	
29	
30	
31	
32	
32 33	
34 35 36 37	
36	
37	
38	
50	

5 5 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data ≤		Conflict of interest	Other
3			Probably Low	Low	Probably Low	Probably Low	Low by	Probably Low	Low	Low
0	15	Huang et	Daily average	Daily mortality data were	Models adjusted	The author	Daily counts	There was	No	No other
1		al. 2012	concentrations of PM <sub>2.5</sub>	obtained from the Xi'an	for calendar time	removed the	for death were	insufficient	competing	potential
2			were obtained from a	Center for Disease	(seasonality,	death counts on	obtained, so	information	financial	sources of
3			single, central-site	Control and Prevention.	long-term trends),	December 31 and	likely have all	about	interests.	bias
5			monitor. Daily average	The International	weather(temperatu	January 1 of each	outcome data.	selective		identified.
6			concentrations of EC in	Classification of	re, relative	year.	However, any	outcome to		
7			PM <sub>2.5</sub> samples were	Diseases, Tenth Revision	humidity), year,		potential errors	judge for low		
9			further analyzed. Daily	(ICD-10), codes of	day of week.		or missing data	risk, but		
20			data was available and no	mortality were as	'/		did not depend	indirect		
21			missing data was	follows: all natural causes	' (%)		on air pollution			
22			reported.	(ICD-10 codes			levels.	suggests study		
24				A00–R99), respiratory		(0)	com	was free of		
25				diseases (ICD-10 codes			n/ on	selective		
26 27				I00–I98), and			1 Ap	report.		
28				cardiovascular diseases						
29				(ICD-10 codes I00–I99).			9, 21			
30							024			
31 32							by (			
33							gues			
84							April 19, 2024 by guest. Protected			
35							rote			
36 37							ecte			
38 L										

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data ≤	Selective reporting	Conflict of interest	Other
8 9			Probably High	Low	Probably Low	Low	Low $\stackrel{\mathbf{a}}{\checkmark}$	Probably Low	Low	Low
10	16	Peng et al.	Ambient EC obtained	Daily counts of hospital	Model adjusted for	Data consisted of	Daily counts	There was	The authors	No other
11		2009	from Speciation Trends	admissions were obtained	weather (i.e.,	all cardiovascular	for hospital	insufficient	declare they	potential
12			Network monitors and	from billing claims of	temperature, dew	hospital	admission wer	information	have no	sources of
13 14			either from central site or	enrollees in the U.S.	point temperature),	admissions	obtained, so	about	competing	bias
15			averaged over a county.	Medicare system. Each	day of week,	during over the	likely have all	selective	financial	identified.
16			Air pollution	billing claim contains the	unobserved	course of the	outcome data.	outcome to	interests.	
17 18			concentrations were	date of service, disease	seasonal factors,	study.	However, any	judge for low		
19			measured on a 1-in-3-day	classification using	and long-term		potential errors	risk, but		
20			schedule in the national	International	trends.		or missing data	indirect		
21 22			air monitoring stations	Classification of	. 01	•	did not depend	evidence that		
23			and on a 1-in-6-day	Diseases, 9th Revision			on air pollution.	suggests study		
24			schedule in the state and	(ICD-9) codes (Centers		'01.	levels.	was free of		
25			local air monitoring	for Disease Control and			/ on	selective		
26 27			stations. Study removed	Prevention 2008).				report.		
28			suspect data and extreme				110			
29			values from the original				, 20			
30 31			monitor records;				24 b			
32			monitors with very little				) 9			
33			data were omitted				uest			
34 35			altogether. Missing data				April 19, 2024 by guest. Protected by			
36			was not replaced by other				otec			
37			values.				ed ed			
38 <sup>l</sup>					<u> </u>		<u> </u>		I	

36/bmjopen-2021-0495<mark>1</mark>

2	
3	
4	
5	
6	
7	
8	H
9	
10	
11	
12	
13	
14	
15	
16	
16 17	
18	
19	
20	
21	
22 23	
22	
24	
24	
25	
26 27	
27	
28	
29	
30	
31	
32	
33	
34	
35	
36 37	
37 38	
38	

5 5 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete ్ల outcome data		Conflict of interest	Other
3 [			Probably High	Low	Probably Low	Low	Low	Probably Low	Low	Low
10	17	Levy et al.	The U.S. Environmental	Hospital admissions data	Adjusted for time	Study included	Daily counts of	There was	No	No other
11		2012	Protection Agency	were obtained from	(seasonality,	people who died	hospital 💆	insufficient	competing	potential
2			established the PM	billing claims information	long-term trends),	any day between	admissions 💆	information	financial	sources of
3  4			Speciation Trends	for US Medicare	seasonality, day of	2000 and 2008 in	were obtained	about	interests.	bias
5			Network (STN) to	enrollees in 119 counties	the week and	119 US counties.	from billing	selective		identified.
6			measure more than 50	for the years 2000–2008.	dew-point		claims S	outcome to		
7  8			PM <sub>2.5</sub> chemical	The Medicare billing	temperature.		information, so	judge for low		
9			components, in addition	claims data were			likely have all	risk, but		
20			to total mass. The STN	classified into disease	'/_		outcome data.	indirect		
21			includes > 50 national air	categories according to	. 01		However, any	evidence that		
22			monitoring stations	their International			potential errors	suggests study		
24			(NAMS) and $> 200$ state	Classification of		<b>101</b>	or missing data	was free of		
25			and local air monitoring	Diseases, Ninth Revision			did not depend 9	selective		
26 27			stations (SLAMS). Air	(ICD-9), codes.			on air pollution €	report.		
28			pollution concentrations				levels.			
29			were typically measured				9, 20			
30   31			on a 1-in-3-day schedule				)24			
32			in the NAMS and on a				by g			
33			1-in-6-day schedule in				2024 by guest. Protected			
34			the SLAMS. There was				<u></u>			
35 36			no information about				roteo			
37			missing data.				cted			

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data ≤	Selective reporting	Conflict of interest	Other
8 9			Probably Low	Low	Probably Low	Low	Low $\overset{\mathbf{a}}{\overset{\mathbf{b}}{\overset{\mathbf{c}}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}}{\overset{\mathbf{c}}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}}{\overset{\mathbf{c}}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{c}}}{\overset{\mathbf{c}}{\overset{c}}}{\overset{\mathbf{c}}{\overset{c}}}{\overset{c}}{\overset{c}}{\overset{c}}{\overset{c}}{\overset{c}}{\overset{c}}{\overset{c}}{\overset{c}}{\overset{c}}{\overset{c}}{\overset{c}}{\overset{c}}}{\overset{c}}{\overset{c}}{\overset{c}}{\overset{c}}}{\overset{c}}{\overset{c}}{\overset{c}}{\overset{c}}{\overset{c}}}{\overset{c}}{\overset{c}}}{\overset{c}}{\overset{c}}}{\overset{c}}}}{\overset{c}}}{\overset{c}}}{\overset{c}}{\overset{c}}{\overset{c}}{\overset{c}}}{\overset{c}}}}}{\overset{c}}}{\overset{c}}}{\overset{c}}{\overset{c}}{\overset{c}}{\overset{c}}}{\overset{c}}}}{\overset{c}}}{\overset{c}}}{\overset{c}}}{\overset{c}}}{\overset{c}}}{\overset{c}}}}{\overset{c}}{\overset{c}}}{\overset{c}}}}}}}}$	Probably Low	Low	Low
10	18	Son et al.	Hourly air samples were	Daily death counts were	Models adjusted	Data consisted of	Daily counts	There was	The authors	No other
11		2012	obtained from a single,	obtained from the	for time (long-term	all cardiovascular	for death were	insufficient	declare they	potential
12			central-site monitor. The	National Statistical	trends and	deaths over the	obtained, so	information	have no	sources of
13 14			monitoring system	Office. The study	seasonality), day	course of the	likely have all	about	actual or	bias
15			produces hourly	classified mortality data	of week,	study.	outcome data.	selective	potential	identified.
16			estimates of PM <sub>2.5</sub> total	into all causes of death	temperature and		However, any	outcome to	competing	
17 18			mass, and PM <sub>2.5</sub> levels of	[International	relative humidity.		potential errors	judge for low	financial	
19			EC. Daily data was	Classification of			or missing data	risk, but	interests.	
20			available and no missing	Diseases, 10th Revision	' /		did not depend	indirect		
21   22			data was reported.	(ICD-10; codes	(0)		on air pollution	evidence that		
23				A00–R99),			levels.	suggests study		
24				cardiovascular causes		101.	com	was free of		
25				(codes I00-I99), and		ien	on /	selective		
26 27				respiratory causes (codes			Apr	report.		
28				J00–J99)] (World Health			111111111111111111111111111111111111111			
29				Organization 2007).			9, 20			
30 31							)24			
32							оу д			
33							ues			
34							ָרָ קַ			
35 36							on April 19, 2024 by guest. Protected			
37							cted			
38 <sup>l</sup>							<u>\$</u>			

2	
3	
4	
5	
7	
8	-
9	
10	
11	
12	
13	
14	
15	
16	
17	
18	
19	
20	
21	
22	
23	
24	
25 26	
26 27	
28	
26 29	
30	
31	
32	
33	
34	
35	
36	
37 38	
38	
39	
40	

Page 77	of 136			BMJ Oper	า	86/bmJopen			
						Incomplete			
No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data	Selective reporting	Conflict of interest	Other
		Probably High	Low	Low	Low	Low	Probably Low	Low	Low
19 11 22 33 44 55 66 77 88 99 90 11 12 23 33 44 14 15 16 16 17 18 18 18 18 18 18 18 18 18 18 18 18 18	Heo et al. 2014	Ambient air samples were collected over a 24-hour period at 3-day intervals from a single monitor. Missing data <25% for the frequency of EC samples.	Seoul daily mortality data were obtained from the Korea National Statistical Office. Using the International Classification of Disease, 10th Revision (ICD-10; World Health Organization 1993), the mortality data were classified as all nonaccidental causes (codes A00-R99), cardiovascular disease (codes I00-I99), respiratory disease (codes J00-J98), and injury (S00-T98).	Adjusted for long-term trends, seasonality, temperature and humidity, day of the week, holiday and influenza epidemics.	Study included all death for all-cause, cardiovascular, and respiratory in Seoul during 2003–2007.	Daily counts for death were obtained, so likely have all outcome data. However, any potential errors or missing data did not depend on air pollution levels.	There was insufficient information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of selective report.	Authors declared no competing financial interests.	No other potential sources of bias identified.
9 -0 -1						y copyrigni.			

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data ≤	Selective reporting	Conflict of interest	Other
8 9			Probably High	Low	Probably Low	Low	Low ay	Probably Low	Low	Low
10	20	Basagaña	Single central-site	Daily mortality counts for	Models adjusted	Data consisted of	Daily counts	There was	The authors	No other
11		et al. 2015	monitor in each city. For	all non-external causes	for holidays,	all deaths over	for death and	insufficient	have no	potential
12			each city, PM	[International	summer	the course of the	emergency <u>S</u>	information	conflicts of	sources of
13 14			constituents with >20%	Classification of	population	study in a	hospital a	about	interest to	bias
15			of the values below the	Diseases, 9th Revision	decrease, influenza	defined	admissions 🚊	selective	disclose.	identified.
16			detection limit or missing	(ICD9) codes 001–799;	epidemics,	geographical	were obtained,	outcome to		
17 18			were excluded.	10th revision (ICD10)	seasonality,	area.	so likely have	judge for low		
19			Otherwise,	codes A00-R99],	long-term trends		all outcome	risk, but		
20			non-detectable were	cardiovascular (ICD9	and temperature.		data. However,	indirect		
21			replaced by half the limit	codes 390–459, ICD-10	. 01		any potential	evidence that		
22 23			of detection. Air	codes I00-I99) and			errors or	suggests study		
24			pollution data was	respiratory (ICD9 codes		<b>101</b>	missing data	was free of		
25			collected daily in	460-519, ICD10 codes			did not depend	selective		
26 27			Bologna (n=472), twice a	J00–J99) were collected.			on air pollution ≧	report.		
28			week in Barcelona	Cardiovascular and			levels.			
29			(n=736) and Madrid	respiratory			3, 20			
30   31			(n=104), and once a week	hospitalizations were			024 1			
32			in Huelva (n=406). There	defined on the basis of			ру д			
33			was no information about	the primary discharge			uesi			
34			missing data.	diagnosis using the same			9, 2024 by guest. Protected by			
35 36				ICD codes defined above.			otec			
37							ted.			
38 [ 39							by co			

2	
3	
4	
5	
6	
7	
8	-
9	
10	
11	
12	
13	
14	
15	
16	
16 17	
18	
19	
20	
21	
22	
23	
24	
25	
26	
27	
28	
29	
30	
31	
32	
33	
34	
35	
36 37	
38	
20	

ag	e 79 of	f 136	BMJ Open  BMJ Open  The second							
	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	outcome data⇔ ≤	reporting	Conflict of interest	Other
0 1 2 3 4 5 6 7 8 9 0 1 2 3 4 5 6 7 8 9 0 1 2 3	21	Dai et al. 2014	Probably High  EC were measured on a 1-in-3 or 1-in-6 day schedule. Most of the cities had a single monitor. For every species, the study calculated the monthly average species-to-PM <sub>2.5</sub> proportions for each month as a solution to the missing speciation data problem due to the 1-in-6 or 1-in-3 day sampling frequency. There was no information of missing data for that sampling frequency.	Low Daily mortality data were obtained from National Center for Health Statistics. The study examined nonaccidental deaths due to all causes and specific diseases, derived from the International Statistical Classification of Disease, 10th Revision (World Health Organization 2007).	Probably Low Adjusted for time, temperature, day of the week, and season.	Low Study included all death for all causes, cardiovascular disease, myocardial infarction, stroke, and respiratory diseases from National Center for Health Statistics in 75 U.S. cities between 2000 and 2006.	Daily counts for death were obtained, so likely have all outcome data. However, any potential errors or missing data did not depend on air pollution levels.	insufficient information about selective outcome to judge for low risk, but indirect evidence that	Low The authors declare they have no actual or potential competing financial interests.	No other potential sources of bias identified.
4   5   6   7							st. Protected by			

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data S		Conflict of interest	Other
8 9			Probably Low	Low	Low	Low	Low ay	Probably Low	Low	Low
10	22	Lin et al.	The concentrations of	Daily mortality data from	Adjusted for	Study included	Daily counts	There was	The authors	No other
11		2016a	different particle size	1 January 2007 to 31	public holidays,	daily	for death were	insufficient	declare they	potential
12			fractions and PM <sub>2.5</sub>	December 2011 were	day of the week,	cardiovascular	obtained, so	information	have no	sources of
13 14			chemical constituents	obtained from	influenza	mortality data	likely have all	about	actual or	bias
15			were measured at two air	Guangdong Provincial	outbreaks,	from 1 January	outcome data.	selective	potential	identified.
16			monitoring stations. EC	Center for Disease	seasonal patterns	2007 to 31	However, any S	outcome to	competing	
17 18			were measured for four	Control and Prevention.	and long-term	December 2011	potential errors	judge for low	financial	
19			months of each year from	The cause of death was	trends, temperature	in Guangzhou.	or missing data	risk, but	interests.	
20			2007 through 2010.	coded using the	and relative		did not depend	indirect		
21			During the period	International	humidity.		on air pollution	evidence that		
22			2009-2011, the	Classification of			levels.	suggests study		
24			proportion of missing	Diseases, Tenth Revision			com	was free of		
25			data was very low	(ICD-10). Mortality from			on on	selective		
26 27			(ranging from 1% to 2%).	cardiovascular diseases			Api	report.		
28			There were about 20 days	(ICD-10:I00-I99) were			April 19,			
29			without chemical	extracted to construct the			9, 20			
30			constituents records and	time series.			2024 by guest.			
31			were treated as missing				by g			
33			observations.				Jues			
34										
35 36							Protected			
36   37							ctec			
38							l by			

5 5 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data	Selective reporting	Conflict of interest	Other
3 9			Probably Low	Low	Probably Low	Low	Low 2	Probably Low	Low	Low
10	23	Cao et al.	Daily concentrations of	The study obtained	Model adjusted for	Data consisted of	Daily counts 2	There was	The authors	No other
11		2012	EC was obtained from a	numbers of deaths in	long-term and	all nonaccidental	for death were	insufficient	declare they	potential
12			single monitoring site.	Xi'an for each day from	seasonal trends,	causes deaths	obtained, so	information	have no	sources of
13 14			The observations of EC	the Shanxi Provincial	day of week,	during over the	likely have all ଥୁ	about	actual or	bias
15			was 1749 in 1827 days	Center for Disease	temperature,	course of the	outcome data.		potential	identified.
6			(missing data <25%).	Control and Prevention	humidity, and SO <sub>2</sub>	study.	However, any	outcome to	competing	
7				(SPCDCP). SPCDCP	and NO <sub>2</sub>		potential errors		financial	
18 19				staff then classify the	concentrations.		or missing data	risk, but	interests.	
20				cause of death according	1		did not depend	indirect		
21				to the International	. 01		on air pollution	evidence that		
22   23				Classification of			levels.	suggests study		
24				Diseases, 10th Revision		(0)	com	was free of		
25				[ICD-10; World Health			n/ or	selective		
26 27				Organization (WHO)			ı Ap	report.		
28				1992] as due to total				-		
29				nonaccidental causes			9, 20			
30				(ICD-10 codes			024			
31 32				A00–R99),			by g			
33				cardiovascular diseases			Jues			
34				(I00–I99), respiratory			on April 19, 2024 by guest. Protected			
35				diseases(J00–J98), or			rote			
36   37				injury (S00–T98).			ctec			
38 38				mjarj (500 170).			by			

7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data		Conflict of interest	Other
8   9			Probably Low	Low	Probably Low	Low	Low S	Probably Low	Low	Low
$\frac{9}{10}$ 2	4	Klemm et	Daily 24-hr average EC	Records of individual	Adjusted for time	Study included	Daily counts	There was	Authors	No other
11		al. 2011	measurements are	deaths were provided by	(seasonality,	all nonaccidental	for death were	insufficient	declared no	potential
12			available for Atlanta	the Georgia Department	long-term trends),	deaths during	obtained, so	information	competing	sources of
13 14			during the study period.	of Human Resources.	temperature, and	over the course	likely have all	about	financial	bias
15			The observations of EC	Cause of death is	day of the week.	of the study.	outcome data.	selective	interests.	identified.
16			was 3317 days from	categorized using the			However, any	outcome to		
17 18			August 1998 to	International	<b>'</b> O.		potential errors	judge for low		
19			December 31, 2007.	Classification of			or missing data	risk, but		
20			Missing data <25%.	Diseases, 10th edition	' /		did not depend	indirect		
21 22			There was no information	(ICD-10), including	. 61		on air pollution <mark>≗</mark>	evidence that		
23			for monitor stations.	circulatory conditions			levels.	suggests study		
24				(I00–I99), respiratory	er rel	'01.	com	was free of		
25				conditions (J00–J99),			on	selective		
26 27				malignant neoplasm			Apr	report.		
28				(cancer; C00–D48), or			100			
29				other nonaccidental			, 20			
30 31				causes (A00-R99,			24 k			
32				excluding cardiovascular,			у g			
33				respiratory, or cancer			uest			
34 35				causes).			. Pr			
36							otec			
37							on April 19, 2024 by guest. Protected by			
38 └─ 39							by cop			

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data ≤		Conflict of interest	Other
3			Probably Low	Low	Probably Low	Low	Low <sup>ay</sup>	Probably Low	Low	Low
10	25	Zhou et al.	24hr PM <sub>2.5</sub> samples were	Using codes from the	Models adjusted	Data consisted of	Daily counts 8	There was	The authors	No other
11		2011	obtained from a single,	International	for time,	all cardiovascular	for death were	insufficient	declare they	potential
12			central-site monitor.	Classification of	seasonality and	deaths over the	obtained, so	information	have no	sources of
13   14			Daily data was available	Diseases, version 10	long-term trends,	course of the	likely have all	about	actual or	bias
15			and no missing data was	(ICD10; World Health	day of week,	study.	outcome data.    dia  dia  dia  dia  dia  dia  dia  d	selective	potential	identified.
16			reported.	Organization 2007), daily	temperature, and		However, any	outcome to	competing	
17 18				death counts were	humidity.		potential errors	judge for low	financial	
19				aggregated to			or missing data	risk, but	interests.	
20				nonaccidental allcause	' /		did not depend	indirect		
21				deaths (ICD10, codes	. 01	•	on air pollution	evidence that		
22				A00 through R99),			levels.	suggests study		
24				cardiovascular deaths		<b>10</b> 1.	com	was free of		
25				(ICD10, codes I01			on on	selective		
26   27				through I99), and			Ap	report.		
28				respiratory deaths (ICD-						
29				10, codes J00 through			9, 20			
30				J99).			)24			
31							by g			
33							jues			
34							on April 19, 2024 by guest. Protected			
35							rote			
36 37							ctec			
38 L							<u> </u>			

4 5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data	Selective reporting	Conflict of interest	Other
8 9			Probably Low	Low	Probably Low	Low	Low ay	Probably Low	Low	Low
9 10	26	Winquist	Daily EC and BC were	Individual-level data	Adjusted for time	Study included	Daily counts 2	There was	Authors	No other
11		et al. 2015	from a single monitor	were obtained from the	trends, day of	emergency	for emergency $\bigcirc$	insufficient	declared no	potential
12			site. All species of	Missouri Hospital	week, holidays,	department visits	department $\frac{8}{2}$	information	competing	sources of
13 14			pollutant statistics are	Association for all	season,	in St Louis	visit were	about	financial	bias
15			missing less than 5%.	emergency department	temperature and	metropolitan	obtained, so =	selective	interests.	identified.
16				visits to 36 of 43	dew point.	statistical area	likely have all	outcome to		
17 18				acute-care non-federal	<b>'</b> O.	during 1 June	outcome data.	judge for low		
19				hospitals with emergency		2001 through 30	However, any	risk, but		
20				department visits in the	' /	April 2003.	potential errors	indirect		
21 22				16-county St Louis	. 01		or missing data	evidence that		
23				metropolitan statistical			did not depend.	suggests study		
24				area during 1 June 2001		'01.	on air pollution	was free of		
25				through 30 April 2003.			levels.	selective		
26 27				Cardiorespiratory			Apr	report.		
28				outcomes of interest were			ii 19			
29				defined based on the			), 20			
30 31				primary ICD-9			24 k			
32				(International			ру д			
33				Classification of			uesi			
34 35				Diseases, version 9)			April 19, 2024 by guest. Protected			
35 36				diagnosis code for the			otec			
37				visit.			ted			
38 <sup>l</sup>				1			\$			

Page 85 of 136

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data ≤		Conflict of interest	Other
8			Probably High	Low	Probably Low	Low	Low ay	Probably Low	Low	Low
9 10	27	Ostro et	Each of the six counties	Daily mortality data were	Adjusted for time	Data consisted of	Daily counts 2	There was	The authors	No other
11		al. 2007	had two monitors	obtained from the	trend, day of week,	all cardiovascular	for death were	insufficient	declare they	potential
12			measuring PM <sub>2.5</sub>	California Department of	seasonality,	deaths over the	obtained, so	information	have no	sources of
13 14			components and mass.	Health Services, Center	long-term trends,	course of the	likely have all	about	competing	bias
15			Fresno, Kern, Riverside,	for Health Statistics. The	temperature and	study.	outcome data.	selective	financial	identified.
16			and Sacramento Counties	study determined daily	humidity.		However, any	outcome to	interests.	
17 18			reported data every third	total mortality counts for			potential errors	judge for low		
19			day, whereas San Diego	those > 65 years of age			or missing data	risk, but		
20			and Santa Clara Counties	and for deaths from	' /		did not depend	indirect		
21 22			reported data every sixth	respiratory disease	(0)		on air pollution	evidence that		
23			day. For the speciation	[International			levels.	suggests study		
24			analyses, the number of	Classification of			com	was free of		
25			observation days	Diseases, 10th Revision			on /	selective		
26 27			available ranged from	(ICD10; World Health			Apr	report.		
28			243 (San Diego County)	Organization 1993) codes			ii 19			
29			to 395 (Sacramento	J00-J98] and			, 20			
30 31			County) from 2000 to	cardiovascular disease			24 k			
32			2003. There was no	(codes I00–I99).			у д			
33			specific information				uest			
34 35			about missing data.				on April 19, 2024 by guest. Protected b			
36							otec			
37							ted			
38			1				<u> </u>	l		

4							51			
5 6	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data o	Selective reporting	Conflict of interest	Other
7 8			Probably Low	Low	Probably Low	Low	Low S	Probably Low	Low	Low
9	28	Tolbert et	Daily 24h EC from a	Computerized billing	Adjusted for time	Study included	Daily count for		Authors	No other
10 11		al. 2000	single monitor site. The	record data are being	(seasonality,	emergency	emergency	insufficient	declared no	potential
12		ai. 2000	observation of EC was	obtained from the	long-term trends),		اکِ ت	information		sources of
13					"	department visits	department N		competing	
14			356 in 365 days, missing	emergency department	temperature, dew	of the	visits were	about	financial	bias
15			data <25%.	visits participating in the	point, and day of	participating	obtained, so	selective	interests.	identified.
16				study. Several case	week.	hospitals in the	likely have all	outcome to		
17 18				groups are being defined	<b>'</b> O.	Atlanta	outcome data.	judge for low		
19				using the primary ICD-9		Metropolitan	However, any	risk, but		
20				(International	' / <sub>~</sub>	Statistical Area,	potential errors	indirect		
21				Classification of	(0)	including 33	or missing data	evidence that		
22				Diseases, 9th Revision)		hospitals	did not depend.	suggests study		
23 24				diagnostic code.		between January	on air pollution	was free of		
25				diagnostic code.		1 1993-August	_	selective		
26										
27						31 2000, 4	pril	report.		
28						hospitals	19,			
29 30						between January	202			
31						1 1993-February	24 b			
32						30 2000.	) 9			
33							ues			
34							÷. P			
35							rote			
36 37							cted			
38							April 19, 2024 by guest. Protected by			
20							, c			

36/bmjopen-2021-0495

2	
3	
4	
5	
6	
7	
8	
9	
10	
11	
12	
13	
14	
15 16	
16 17	
18	
19	
20	
21	
22	
23	
24	
25	
26	
27	
28	
29	
30	
31	
32	
33	
34	
35	
36	
37 38	
38	

5 5	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data		Conflict of interest	Other
3			Low	Low	Probably Low	Low	Low 2	Probably Low	Low	Low
0	29	Wang and	The hourly data were	This study obtained	Adjusted for	Study included	Daily counts	There was	Authors	No other
1		Lin 2016	simply averaged to	universal health insurance	temperature,	11 1 005	for elderly	insufficient	declared no	potential
2			calculate the daily	claims from the National	relative humidity,	elderly (≧65	mortality and ≦	information	competing	sources of
3			average data for PM <sub>10</sub> ,	Health Research Institute	wind speed,	years) mortality	all population	about	financial	bias
5			PM <sub>2.5</sub> monitored at 13	(NHRI) and vital	barometric	from 2004 to	emergency $\stackrel{\omega}{\exists}$	selective	interests.	identified.
6			general air quality	statistics from the	pressure, holidays,	2008 and all	room visits	outcome to		
7  8			monitoring stations	Ministry of Health and	day of the week,	population EVR	were obtained,	judge for low		
9			located in a densely	Welfare from 2004 to	pneumonia and	from 2004 to	so likely have	risk, but		
20			populated area in Taipei.	2008. Death causes were	influenza.	2010 in Taipei,	all outcome	indirect		
21			Hourly concentrations of	coded according to the	' (2)	Taiwan.	data. However,	evidence that		
22			EC were detected by	diagnoses of the 9th			any potential	suggests study		
24			series 5400 Monitor.	revision of International		<b>101</b>	errors or	was free of		
25			Very few missing values	Classification of Diseases			missing data 9	selective		
26 27			in the database were	(ICD-9). Disease			did not depend ≧	report.		
28			omitted as the daily	diagnoses were based on			on air pollution			
9			average was calculated.	the International			, ,	1		
30			_	Classification of Diseases			)24			
31 32				with Clinical			by g			
33				Modification, Ninth			2024 by guest. Protected			
34				Revision (ICD-9 CM).			;; 			
35							rote			
36   37							ctec			
88										

5 5 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data ≤		Conflict of interest	Other
3			Low	Low	Low	Low	Probably Low	Probably Low	Low	Low
10	30	Darrow et	Daily 24-hour average	Health data were	Adjusted for dew	Study included	Daily counts 8	There was	Authors	No other
11		al. 2014	EC was from ambient	obtained from 41	point, temperature,	daily emergency	for emergency $\bigcirc$	insufficient	declared no	potential
2			monitoring networks.	metropolitan Atlanta	seasonality,	department visit	department <u>§</u>	information	competing	sources of
13 14			Missing data <1%.	hospitals and the Georgia	long-term trends,	data from 41	visit were	about	financial	bias
15				Hospital Association. The	day of week,	metropolitan	obtained. In the	selective	interests.	identified.
6				diagnoses of respiratory	holiday and	Atlanta hospitals	earliest years	outcome to		
17 18				infection were based on	influenza	for the period	of the study,	judge for low		
19				International	epidemics.	January 1, 1993,	not all	risk, but		
20				Classification of	1/6	to December 31,	hospitals were	indirect		
21				Diseases, 9th Revision	' (2)	2004 (not all	participating.	evidence that		
22				(ICD-9), diagnosis codes:		hospitals	However, any	suggests study		
24				acute bronchitis or		contributed the	potential errors			
25				bronchiolitis (code 466);		full period), and	or missing data	selective		
26 27				pneumonia (codes		from the Georgia	did not depend ≧			
28				480–486); and upper		Hospital	on air pollution			
29				respiratory infection		Association for				
30				(codes 460–465).		the period	)24			
31   32						January 1, 2005,	by g			
33						to June 30, 2010.	Jues			
34						·	2024 by guest. Protected levels.			
35 36							rote			
37							cted			
38							<u>\$</u>			

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on the outcome data		Conflict of interest	Other
8 9			Probably High	Low	Probably Low	Low	Low 2	Probably Low	Low	Low
10	31	Metzger et	Ambient 24hr average	The study asked 41	Model adjusted for	Data consisted of	Daily counts	There was	No	No other
11		al. 2004	EC were obtained from	hospitals with emergency	temporal trends,	all cardiovascular	for emergency	insufficient	competing	potential
12			one monitor. On days	departments that serve	meteorological	hospital	department 💆	information	financial	sources of
13 14			when measurements were	the 20-county Atlanta	conditions (i.e.,	admissions over	visits were	about	interests.	bias
15			missing at the central site,	metropolitan statistical	temperature, dew	the course of the	obtained, so	selective		identified.
16			data for the pollutant	area (MSA) to provide	point temperature),	study.	likely have all	outcome to		
17 18			were imputed using an	computerized billing data	day of week,		outcome data.	judge for low		
19			algorithm that modeled	for all emergency	hospital entry and		However, any	risk, but		
20			measurements. The	department visits between	exit, and federally		potential errors	indirect		
21			observations of EC was	January 1, 1993, and	observed holidays.		or missing data	evidence that		
22 23			714 days during the	August 31, 2000. Using			did not depend	suggests study		
24			period August 1,	the primary International		<b>101.</b>	on air pollution	was free of		
25			1998–August 31, 2000	Classification of			levels.	selective		
26 27			(missing data >25%).	Diseases, 9th Revision			Apr	report.		
28				(ICD-9) diagnosis code,			il 19,			
29				the study defined several						
30 31				cardiovascular disease			2024 by			
32				(cardiovascular disease)			by g			
33				groups based largely on			guest.			
34				ICD-9 diagnosis codes.						
35 36							Protected			
30   37							ctec			
38							l by			

BMJ Open

5 5	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data ≤		Conflict of interest	Other
3 [			Probably Low	Low	Probably Low	Low	Low S	Probably Low	Low	Low
0	32	Mar et al.	Hourly PM <sub>2.5</sub> chemical	Mortality data for all of	Adjusted for time	Data consisted of	Daily counts	There was	No	No other
1		2000	composition data from a	Maricopa County from	trend, seasonality,	all cardiovascular	for death were	insufficient	competing	potential
2			single, central-site	1995 to 1997 were	day of week,	deaths during	obtained, so	information	financial	sources of
3			monitor. Daily data was	obtained from the	temperature and	over the course	likely have all	about	interests.	bias
5			available and no missing	Arizona Center for	relative humidity.	of the study.	outcome data.	selective		identified.
6			data was reported.	Health Statistics in			However, any	outcome to		
7				Phoenix. Death certificate			potential errors	judge for low		
8   9				data included residence	er rei		or missing data	risk, but		
0				zip code and the primary	1/6		did not depend	indirect		
1				cause of death as	(0)		on air pollution			
22				identified by the			levels.	suggests study		
4				International		101	.con	was free of		
5				Classification of			n∕ or	selective		
6				Diseases, Ninth Revision			Ap	report.		
7 8				(ICD-9, World Health						
9				Organization, Geneva).			9, 2			
0				organization, coneva).			024			
1							by			
2							April 19, 2024 by guest. Protected			
4							st. F			
5							rot			
6							ecte			
7							ğ İ			

36/bmjopen-2021-0495

2	
3	
4 5	
<i>5</i>	
7 8	_
9	
10	
11 12	
13	
14	
15	
16	
16 17 18	
18 19	
20	
21	
22	
23	
24	
25	
26 27	
28	
29	
30	
31	
32	
33 34	
35	
36 37	
37	
38	

]	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data ≤		Conflict of interest	Other
			Low	Low	Probably Low	Low	Low ay 2	Probably Low	Low	Low
0 3	33	Wang et	Hourly data of PM <sub>2.5</sub>	The daily mortality data	Adjusted for long	Study included	Daily counts	There was	No	No other
1		al. 2019a	were collected at 10	were obtained from the	term trends,	daily mortality	for death were	insufficient	competing	potential
2			Chinese air quality	system of Disease	seasonal influence,	data in Huangpu	obtained, so		financial	sources of
3 4			monitoring sites in	Monitoring Point	day of the week,	district from	likely have all	about	interests.	bias
5			Shanghai. Hourly mass	belonged to the Chinese	holidays,	January 1, 2013	outcome data.	selective		identified.
б			concentrations of PM <sub>2.5</sub>	Center for Disease	temperature and	to December 31,	However, any	outcome to		
7 8			and EC were predicted in	Control and Prevention	relative humidity.	2015.	potential errors	judge for low		
9			Shanghai by using a	(China CDC). Deaths			or missing data	risk, but		
0			Community Multiscale	were classified according	' /		did not depend	indirect		
1			Air Quality model. The	to the 10th revised	. 01		on air pollution	evidence that		
2   3			study included	International Statistical			levels.	suggests study		
4			continuous daily data	Classification of Disease		(0).	com	was free of		
5			from 2013 to 2015 (1095	(ICD-10), all-cause			on on	selective		
6 7			days). Daily data was	mortality (A00-R99),			Apr	report.		
8			available and no missing	circulatory disease			111111111111111111111111111111111111111			
9			data was reported.	mortality (I00-I99, the			9, 20			
0				circulatory disease is also			)24			
2				known as cardiovascular			by g			
2				disease) and respiratory			on April 19, 2024 by guest. Protected b			
4				disease mortality			t. Pr			
5 6				(J00-J99).			oter -			
7							cted			
<sub>8</sub> L							<u> </u>			

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data		Conflict of interest	Other
8 9			Probably High	Low	Probably Low	Low	Low ay	Probably Low	Low	Low
10	34	Lin et al.	EC was from a single	Daily mortality data were	Adjusted for	Study included	Daily counts	There was	Authors	No other
11		2016b	monitor site for four	obtained from the death	long-term trends,	the residents who	for death were	insufficient	declared no	potential
12			months of each year from	registry system. The	seasonality,	died of ischemic	obtained, so	information	conflict of	sources of
13 14			2007 to 2010. Missing	cause of death was coded	temperature,	or hemorrhagic	likely have all	about	interest.	bias
15			data for the particle	using the International	humidity, day of	strokes in urban	outcome data.	selective		identified.
16			concentration was very	Classification of	week and public	districts of	However, any	outcome to		
17 18			low (ranging from 1% to	Diseases, Tenth Revision	holidays.	Guangzhou	potential errors	judge for low		
19			2%).	(ICD-10). Mortality from		between 2007	or missing data	risk, but		
20				stroke (ICD-10:I60–I66),	'/	and 2011.	did not depend	indirect		
21				and sub-categories,	' (%)		on air pollution	evidence that		
22				including ischemic stroke			levels.	suggests study		
24				(ICD-10:I63–I66), and			con	was free of		
25				hemorrhagic stroke			or or	selective		
26				(ICD-10: I60–I62) were			Ap			
27 28				extracted to construct the			April 19, 2024 by	1		
29				time series.			9, 2			
30				VIIII 0 001100.			024			
31							by			
32 33							guest.			
34										
35							Protected			
36							lect			
37   38							<u>a</u>			

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data ≤	Selective reporting	Conflict of interest	Other
8 9			Probably High	Low	Probably Low	Low	Low <sup>ay</sup>	Probably Low	Low	Low
10	35	Lin et al.	Each of the six counties	Daily mortality for all	Adjusted for time,	Study included	Daily counts	There was	Authors	No other
11		2016b	had two monitors	California residents were	temperature,	daily	for death were	insufficient	declared no	potential
12			measuring components of	obtained from the	humidity and day	cardiovascular	obtained, so	information	competing	sources of
13 14			PM <sub>2.5</sub> . Fresno, Kern,	California Department of	of the week.	mortality for all	likely have all	about	interests.	bias
15			Riverside and	Health Services, Center		California	outcome data.	selective		identified.
16			Sacramento counties	for Health Statistics.		residents from 1	However, any	outcome to		
17 18			reported 24-hour average	Daily counts of deaths	<b>'</b> O.	January 2000 to	potential errors	judge for low		
19			EC in PM <sub>2.5</sub> every third	from cardiovascular	C/	31 December	or missing data	risk, but		
20			day; San Diego and Santa	disease (International	1 /	2003.	did not depend	indirect		
21			Clara counties reported	Classification of	. 01		on air pollution	evidence that		
22 23			data every sixth day. The	Diseases, Tenth Revision			levels.	suggests study		
24			study included only	(ICD10) =I00–I99) were		(0)	com	was free of		
25			species for which at least	calculated.			/ on	selective		
26 27			50% of the observations				Api	report.		
28			were above the level of				11 19			
29			detection.				9, 20			
30 31							)24			
32							by g			
33							ues			
34							[			
35 36							rote			
37							on April 19, 2024 by guest. Protected by			
38										
39							сор			

BMJ Open

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data		Conflict of interest	Other
8 9			Probably Low	Low	Probably Low	Low	Low s	Probably Low	Low	Low
9 10	36	Ito et al.	Ambient EC obtained	Hospitalizations and	Model adjusted for	Data consisted of	Daily counts	There was	The authors	No other
11		2011	from multiple monitors	mortality data were	temporal trends	all cardiovascular	for death and	insufficient	declare they	potential
12			and the average of data	available at the New	and seasonal	hospital	hospitalization <u>\text{\tin}\text{\te}\}}}}}}}}}}}}}}}}}}}}}}}}}}}}}}}}}</u>	information	have no	sources of
13 14			from multiple monitors	York City Department of	cycles, immediate	admissions over	were obtained,	about	actual or	bias
15			was computed using the	Health and Mental	and delayed	the course of the	so likely have	selective	potential	identified.
16			24hr average values. The	Hygiene. The relevant	temperature	study.	all outcome	outcome to	competing	
17 18			sampling frequency of	variables available in the	effects, and day of		data. However,	judge for low	financial	
19			the chemical speciation	electronic discharge	the week.		any potential	risk, but	interests.	
20			data was every third day.	abstract for each patient	1/6		errors or	indirect		
21			Daily data was available	included date of	. 01		missing data	evidence that		
22 23			and no missing data was	admission and			did not depend.	suggests study		
24			reported.	International			on air pollution	was free of		
25				Classification of			levels.	selective		
26 27				Diseases, Nine Revision			Api	report.		
28				(ICD9) discharge			April 19,			
29				diagnosis code. The			9, 20			
30 31				International			2024 by			
32				Classification of			by g			
33				Diseases, Tenth Revision			' guest.			
34				(ICD10) codes for						
35 36				determining cause of			Protected			
30 37				death.			cted			
38 <sup>ˈ</sup>			ı				<u>,                                    </u>	<u>I</u>		

Page 95 of 136

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data ≤		Conflict of interest	Other
8 9			Probably Low	Low	Probably Low	Low	Low ay	Probably Low	Low	Low
10	37	Chen et al.	Hourly mass	The counts of daily	Models adjusted	Data consisted of	Daily counts 2	There was	No	No other
11		2014	concentrations of PM <sub>2.5</sub>	emergency room visits	for time, day of	all emergency	for emergency	insufficient	competing	potential
12			and the four PM <sub>2.5</sub>	were obtained from the	week, temperature,	department visits	room visit	information	financial	sources of
13 14			constituents obtained	National Taiwan	seasonality and	during the study	were obtained,	about	interests.	bias
15			from a Supersite (single,	University Hospital. The	relative humidity.	period for	so likely have	selective		identified.
16			central site monitoring	emergency room visit		ischemic and	all outcome	outcome to		
17 18			location). The	data were coded	<b>'</b> O.	hemorrhagic	data. However,	judge for low		
19			observations of EC was	regarding the discharge		stroke.	any potential	risk, but		
20			1599 in 1705 days	diagnosis using the			errors or	indirect		
21 22			(missing data <25%).	International	. 01		missing data	evidence that		
23				Classification of Disease,			did not depend.	suggests study		
24				9th revision (ICD-9).		.617	on air pollution	was free of		
25 26							levels.	selective		
27							Apri	report.		
28							119			
29 30							20:			
31							24 b			
32							у дг			
33							Jest.			
34 35							Pro			
36							otect			
37							April 19, 2024 by guest. Protected b			
38 <sup>1</sup> 39							y cop			

Page 96 of 136

4 5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data ≤	Selective reporting	Conflict of interest	Other
8 9			Low	Low	Probably High	Low	Low $\overset{\mathbf{a}}{\searrow}$	Probably Low	Low	Low
10	38	Tomic'-Sp	Average daily	Emergency department	Adjusted for	Study included	All counts for	There was	Authors	No other
11		iric' et al.	concentrations of BC in	visits data were obtained	temperature,	emergency	emergency 💆	insufficient	declared no	potential
12		2019	micrograms per cubic	from the Health Center	humidity, and air	department visit	department $\frac{8}{2}$	information	competing	sources of
13 14			meter were measured by	Užice, either from the	pressure.	for allergic	visits were	about	financial	bias
15			three automatic ambient	emergency department		rhinitis and	obtained, so	selective	interests.	identified.
16			air quality monitoring	visits in Užice, Sevojno,		allergic asthma	likely have all	outcome to		
17 18			stations. There was no	and Kosjeri' c, or from a	<b>'</b> O.	from 1 July 2012	outcome data.	judge for low		
19			information about	general hospital in Užice.		to 30 June 2014	However, any	risk, but		
20			missing data.	The inclusion criteria	' /	in the Zlatibor	potential errors	indirect		
21				were adults aged 18 years	' (2)	District, Western	or missing data	evidence that		
22   23				and older with the		Serbia.	did not depend.	suggests study		
24				diagnosis of allergic		'01.	on air pollution	was free of		
25				rhinitis (International			levels.	selective		
26 27				Classification of			Apr	report.		
28				Diseases, 10th revision,			April 19, 2024 by			
29				code J.30.4), allergic			9, 20			
30   31				asthma (International			)24			
32				Classification of			оу д			
33				Diseases, 10th revision,			ues			
34				code J.45.0), or asthma			guest. Protected			
35 36				with coexisting allergic			otec			
37				rhinitis.			cted			
38			<u> </u>	ı	<u>I</u>		y		<u> </u>	

2	
3	
4	
5	
6	
7 8	
9	
10 11	
12	
13	
14	
15	
16 17 18	
19	
20	
21 22	
22	
23	
25	
26 27	
28	
29	
30	
31	
32	
33	
34	
35	
36 37	
38	
20	

5 5	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data		Conflict of interest	Other
3			Probably Low	Low	Probably Low	Low	Low ay	Probably Low	Low	Low
0	39	Maynard	Daily measurements of	Individual mortality	Adjusted for	Study included	Daily counts	There was	Authors	No other
1		et al. 2007	BC were obtained from a	records were obtained	season and long	all death for all	for individual	insufficient	declared no	potential
2			single monitor site. In	from the Massachusetts	term trend,	causes,	mortality <u>§</u>	information	competing	sources of
3  4			order to predict local BC	Department of Public	temperature, dew	cardiovascular,	records were	about	financial	bias
15			level, the study used a	Health, for the years	point and day of	respirator, stroke,	obtained, so	selective	interests.	identified.
16			validated	1995–2002. Specific	week.	and diabetes	likely have all	outcome to		
17 18			spatial-temporal land use	cause mortality was		diseases in	outcome data.			
19			regression model to	derived from the		Boston	However, any	risk, but		
20			predict 24-hr measures of	International	1/6	metropolitan area	potential errors	indirect		
21			traffic exposure data	Classification of Diseases	' (2)	from the	or missing data	evidence that		
22			(BC) at $> 80$ locations in	(ICD) codes [9th		Massachusetts	did not depend	suggests study		
24			the Boston area.	Revision before 1999		Department of	on air pollution	was free of		
25				(World Health		Public Health	levels.	selective		
26   27				Organization 1975) and		between	Ap	report.		
28				10th Revision 1999 to		1995–1997 and				
29				2002 World Health		1999–2002.	9, 20			
30				Organization 1993)].			)24			
31   32				/-			by g			
33							Jues			
34							April 19, 2024 by guest. Protected			
35							rote			
36   37							ctec			
38 L							<u>\$</u>			

Page 98 of 136

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data ≤	Selective reporting	Conflict of interest	Other
8			Probably Low	Probably Low	Probably Low	Low	Low $\overset{\mathbf{a}}{\searrow}$	Probably Low	Low	Low
9 10	40	Sinclair et	Daily 24-hr averages EC	Daily outpatient visits	Adjusted for	Study included	Daily counts	There was	No	No other
11		al. 2010	was from a single	were obtained from the	season, day of	daily outpatient	for outpatient	insufficient	competing	potential
12			monitor site. The total	electronic patient data	week, federal	visits for acute	visits were	information	financial	sources of
13 14			observed rate of EC was	warehouse of a	holidays, study	respiratory	obtained, so	about	interests.	bias
15			95.2%.	not-for-profit,	month, time,	diseases from the	likely have all	selective		identified.
16				group-model managed	temperature and	electronic patient	outcome data.	outcome to		
17 18				care organization (MCO)	dew point.	data warehouse	However, any	judge for low		
19				in the metropolitan		of a	potential errors	risk, but		
20				Atlanta area between	' /	not-for-profit,	or missing data	indirect		
21				August 1, 1998 and	. 01	group-model	did not depend	evidence that		
22 23				December 31, 2002.		managed care	on air pollution.	suggests study		
24				Visits that met acute visit		organization	levels.	was free of		
25				definition and that had a		(MCO) in the	v on	selective		
26 27				visit diagnosis code of		metropolitan		report.		
28				asthma, upper respiratory		Atlanta area	11 12			
29				infection (URI), or lower		between August	9, 20			
30 31				respiratory infection		1, 1998 and	)24			
32				(LRI) were included in		December 31,	оу д			
33				the study.		2002.	ues			
34							April 19, 2024 by guest. Protected b			
35 36							otec			
37							ted			
38 <sup>[</sup>							<u> </u>			

36/bmjopen-2021-0495<mark>1</mark>

2	
4	
5	
6	
7	
8	_
9	
10	
11	
12	
13	
14	
15	
16	
17	
18	
19	
20	
21	
22	
23	
24	
25	
26	
27	
28	
29	
30	
31	
32	
33	
34	
35	
36 37	
37 38	
38 39	
29	

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data		Conflict of interest	Other
8 9			High	Probably Low	Probably Low	Low	Low 2	Probably Low	Low	Low
9 10	41	Krall et al.	Monitors typically	All-cause mortality data	Adjusted for	Study included	Daily counts 2	There was	The authors	No other
11		2013	measure PM <sub>2.5</sub>	(excluding accidental	temperature, day	all death	for death were	insufficient	declare they	potential
12			constituent	deaths) were aggregated	of week, long-term	(excluding	obtained, so		have no	sources of
13 14			concentrations every	from death certificate	and seasonal	accidental	likely have all	about	actual or	bias
15			third or sixth day. Some	data obtained from the	trends.	deaths) for 108	outcome data.	selective	potential	identified.
16			communities with a	National Center for		urban	However, any	outcome to	competing	
17 18			single monitor. The	Health Statistics for 2000		communities	potential errors	judge for low	financial	
19			observation of EC was	to 2005.		from 2000 to	or missing data	risk, but	interests.	
20			58-921 days,some			2005.	did not depend	indirect		
21			communities had >25%			•	on air pollution	evidence that		
22 23			missing data.				levels.	suggests study		
24						<b>10</b> 1.	com	was free of		
25							) or	selective		
26 27							Ap	report.		
28								_		
29							9, 20			
30							024			
31 32							by g			
33							Jues			
34							; <del>;</del> 			
35							rote			
36 37							ctec			
38 <sup>l</sup>							.com/ on April 19, 2024 by guest. Protected by copyright.			
39							СОР			
40 41							yrigi			
41 42							ᇎ			

1
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22 23
-
24 25
26
27
28
29
30
31
32
33
34
35
36
37 38
38

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data	Selective reporting	Conflict of interest	Other
8 9			Probably High	Low	Probably Low	Low	Low ay	Probably Low	Low	Low
10	42	Cakmak et	Daily PM <sub>2.5</sub> aerosol	Diseases were coded	Adjusted for	Study included	Daily counts	There was	No	No other
11		al. 2009	samples approximately 1	using the WHO	temperature and	all emergency	for emergency	insufficient	competing	potential
12			of every 4 days from a	International	humidity, day of	department visits	department <u>\frac{8}{2}</u>	information	financial	sources of
13 14			single monitor site.	Classification of Disease,	week, long-term	obtained from the	visit were	about	interests.	bias
15			Sampling occurred daily	9th Revision (ICD-9).	and seasonal	Departamento de	obtained, so 🚊	selective		identified.
16			during the cold season	The daily number of	trends.	Es-tad' isticas e	likely have all	outcome to		
17 18			(April through	emergency department		InformaciónenSa	outcome data.	judge for low		
19			September) and alternate	visits for all		lud (DEIS) of the	However, any	risk, but		
20			days during the warm	nonaccidental (ICD-9 <	1/6	Ministry of	potential errors	indirect		
21			season (October through	800) and respiratory	' (2)	Health from	or missing data	evidence that		
22 23			March). Missing data	(ICD-9 460–519) causes		April 2001	did not depend	suggests study		
24			<25% for that frequency.	in Santiago Centro,		through August	on air pollution	was free of		
25				Cerrillos, and Pudahuel		2006.	levels.	selective		
26 27				were obtained from the			1 Ap	report.		
28				Departamento de Estad'			rii 19,			
29				ısticas e			9, 20			
30				InformaciónenSalud			2024 by			
31 32				(DEIS) of the Ministry of			by g			
33				Health from April 2001			guest.			
34				through August 2006.						
35							Protected			
36 37							cte			
38 L							<u> </u>			

1	
2	
3 4	
5	
6	
7	
8	-
9	
10	
11	
12	
13	
14	
15	
16	
17	
18	
19	
20	
21	
22	
23	
24	
25	
26	
27	
28	
29	
30	
31	
32	
33	
34	
35	
36	
37 38	
39	

Page 101	of 136		BMJ Open						
2 3 4 5 5						Incomplete			
No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data		Conflict of interest	Other
3		Low	Low	Probably Low	Low	Low	Probably Low	Low	Low
9 10 43 43 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 33 34 35 36 37 37 38 38 38 38 38 38 38 38 38 38	Tolbert et al. 2007	Daily ambient EC obtained from multiple monitors and a single concentration obtained by averaging across monitors. The observations of EC was 2258 during the period August 1, 1998 to December 31, 2004 (missing data <25%).	Computerized billing records for all emergency department visits between January 1, 1993 and December 31, 2004 were collected, including the following data for each visit: primary International Classification of Diseases 9th Revision (ICD-9) diagnostic code, secondary ICD-9 diagnosis codes.	Model adjusted for long-term and seasonal trends, daily average temperature, dew point, day of week, federal holiday, and hospital entry and exit.	Data consisted of all cardiovascular disease and respiratory disease hospital admissions during the period 1993 to 2004 over the course of the study.	Daily counts for emergency department visit were obtained, so likely have all outcome data. However, any potential errorspoor or missing data did not depend on air pollution levels.	insufficient information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of selective	No competing financial interests.	No other potential sources of bias identified.

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data ≤		Conflict of interest	Other
8			Low	Low	Probably Low	Low	Low $\overset{\mathbf{a}}{\searrow}$	Probably Low	Low	Low
9 10	44	Lall et al.	Daily EC data were	The categorization of the	Model adjusted for	Data consisted of	Daily counts 2	There was	The authors	No other
11		2011	obtained from two	admissions data was	season, wintertime	all cardiovascular	for hospital	insufficient	declare they	potential
12			monitors. Daily data was	based on codes from the	influenza episode,	hospital	admission wer	information	have no	sources of
13 14			available and no missing	International	weather, day of	admissions over	obtained, so	about	actual or	bias
15			data was reported.	Classification of	week, and other	the course of the	likely have all 🚊	selective	potential	identified.
16				Diseases, revision 9	possible	study.	outcome data.	outcome to	competing	
17 18				(ICD-9).	confounders (e.g.,		However, any		financial	
19					federal holidays).		potential errors	risk, but	interests.	
20					'/		or missing data	indirect		
21					' (%)		did not depend			
22 23							on air pollution.			
24							levels.	was free of		
25							n∕ or	selective		
26 27							1 Ар	report.		
28								•		
29							9, 2			
30							024			
31 32							by (			
33							gues			
34							st. F			
35							rote			
36 37							on April 19, 2024 by guest. Protected			
38							d by			

2	
3	
4	
5	
6	
7	
8	-
9	
10 11	
11	
12	
13	
14	
15 16	
16	
17 18	
18	
19 20 21	
20	
21	
22	
23	
24	
25 26	
26	
27 28	
26 29	
30	
31	
32	
33	
34	
35	
36	
37	
37 38	

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data		Conflict of interest	Other
8 9			Probably High	Low	Probably Low	Low	Low 2	Probably Low	Low	Low
10	45	Jung and	A total of 153 daily	The health data used in	Adjusted for	Study included	Daily counts	There was	No	No other
11		Lin 2017	samples (approximately 4	the study were sourced	seasonal trend, day	all asthma	for asthma	insufficient	competing	potential
12			weeks per season) from a	from Longitudinal Health	of week,	outpatient visits	outpatient $\frac{8}{2}$	information	financial	sources of
13 14			single monitor site were	Insurance Database 2000.	temperature,	(0-20 years old)	visits (0-20	about	interests.	bias
15			collected. Multiple linear	Daily outpatient visits for	precipitation and	in Shalu district	years old) data ⊕	selective		identified.
16			regression models were	asthma (International	wind vectors.	from	were obtained,	outcome to		
17 18			used to back extrapolate	Classification of		Longitudinal	so likely have	judge for low		
19			the historic concentration	Diseases, Ninth Revision,		Health Insurance	all outcome	risk, but		
20			of individual components	Clinical Modification,	' /	Database 2000	data. However,	indirect		
21 22			of PM <sub>2.5</sub> from 2000	ICD-9-CM code 493)	. 01	during January 1,	any potential	evidence that		
23			through to 2010,	data was obtained from		2000 to	errors or	suggests study		
24			including BC.	Longitudinal Health		December 31,	missing data	was free of		
25				Insurance Database 2000.		2010.	did not depend 9	selective		
26 27							on air pollution≧	report.		
28							levels.			
29							9, 20			
30 31							2024 by			
32							оу д			
33							guest.			
34										
35 36							Protected			
37							cted			
38 <sup> </sup>							9	•		

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data		Conflict of interest	Other
8 9			Probably Low	Low	Probably Low	Low	Low ay	Probably Low	Low	Low
10	46	Gong et	The 24-h mean BC	The disease data used in	Adjusted for	Study included	Daily counts	There was	Authors	No other
11		al. 2019	concentrations data were	this study were collected	calendar effects,	all cardiovascular	for all deaths	insufficient	declared no	potential
12			obtained from a single	from the Chinese Center	long-term trends,	mortality in	were obtained, 💆	information	conflict of	sources of
13 14			monitor site. During the	for Disease Control and	temperature,	Beijing obtained	so likely have	about	interest.	bias
15			study period (2091 days),	Prevention, and included	humidity, day of	from the Chinese	all outcome 🚊	selective		identified.
16			missing rate of BC was	all deaths in Beijing from	week, NO <sub>2</sub> and	Center for	data. However,∃	outcome to		
17 18			0.68%.	January 1, 2006 to	$SO_2$ .	Disease Control	any potential	judge for low		
19				December 31, 2011.		and Prevention	errors or	risk, but		
20				Causes of death were	' /	during January 1,	missing data	indirect		
21				classified according to	. 01	2006 to	did not depend	evidence that		
22 23				the International		December 31,	on air pollution	suggests study		
24				Classification of		2011.	levels.	was free of		
25				Diseases, 10th Edition			v or	selective		
26 27				(ICD-10) and data on			1 Ap	report.		
28				cardiovascular diseases			rii 19,			
29				(ICD-10 code: I00–I99)						
30				were obtained.			)24			
31 32							by g			
33							2024 by guest.			
34										
35							rote			
36 37							Protected			
38							l by			

36/bmjopen-2021-0495<mark>1</mark>

2	
3	
4	
5	
6	
7	L
8	
9	
10 11	
12	
13	
14	
15	
16	
17	
18	
19	
20	
21	
22 23	
24	
25	
26	
27 28	
28	
29 30	
31	
32	
33	
34	
35	
36	
37 38	
39	

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data ≤	Selective reporting	Conflict of interest	Other
8			Probably Low	Probably Low	Probably High	Low	Low ay	Probably Low	Low	Low
10	47	Mostofsky	Ambient EC obtained	Patients potentially	Model adjusted for	Population	Daily counts 2	There was	No	No other
11		et al. 2012	from one monitor. BC	eligible for this study	seasonality,	consisted of	for emergency $\bigcirc$	insufficient	competing	potential
12			concentrations were	were identified by	time-trends,	patients ≥21	department $\frac{8}{2}$	information	financial	sources of
13 14			measured continuously.	reviewing daily	temperature, dew	years of age	admission were	about	interests.	bias
15			Daily data was available	emergency department	point temperature,	admitted to the	obtained, so 🚊	selective		identified.
16			and no missing data was	admission logs, stroke	barometric	hospital with	likely have all	outcome to		
17 18			reported.	service admission logs,	pressure and	neurologist-confi	outcome data.	judge for low		
19				stroke service consult	chronic and	rmed ischemic	However, any	risk, but		
20				logs, and hospital	slowly-varying	stroke and	potential errors	indirect		
21				electronic discharge	potential	residing in the	or missing data	evidence that		
22				records.	confounders.	Boston	did not depend.	suggests study		
24						metropolitan	on air pollution			
25						region. Also	levels.	selective		
26 27						patients had to	Ap	report.		
28						reside within 40				
29						km of the air	9, 20			
30						pollution	)24			
31   32						monitor.	by g			
33							Jues			
34							April 19, 2024 by guest. Protected			
35							rote			
36   37							ctec			
38 L							9			

Page 106 of 136

one urban, ambient monitor located in each city. Daily pollution data were available in Atlanta; however, data were only available approximately  one urban, ambient monitor located in each city. Daily pollution data were only available approximately  one urban, ambient monitor located in each city. Daily pollution data were only available approximately  electronic billing data for respiratory disease long-term trends, day of the week, season, hospitalsreporting data, temperature  holidays, long-term trends, day of the week, season, hospitalsreporting data, temperature  holidays, long-term trends, department visits of respiratory disease at acute care hospitals in the 20-county  obtained, so judge for low	Conflict of interest Other		Incomplete outcome data	Selection bias	Confounding bias	Outcome assessment	Exposure assessment	Study	No.
Krall et al. 2017	Low Low	Probably Low	Low	Low	Probably Low	Low	Probably High		
one urban, ambient monitor located in each city. Daily pollution data were available in Atlanta; however, data were only available approximately  2017 one urban, ambient monitor located in each city. Daily pollution data were available in Atlanta; however, data were only available approximately  2017 one urban, ambient monitor located in each city. Daily pollution data emergency department visits of all emergency department day of the week, season, hospitalsreporting data, temperature data, temperature  2018 one urban, ambient monitor located in each city. Daily pollution data emergency department visits of about selective outcome to judge for low insufficient information about selective outcome to judge for low	The authors No other	There was	Daily counts	Study included	Adjusted for	The study obtained	PM <sub>2.5</sub> constituents from	Krall et al.	10
city. Daily pollution data were available in Atlanta; however, data were only available approximately  little label of the week of the week, and the label of the week of the week, and the label of the week of the week, and the label of the week of the week, and the label of the week of the week, and the label of the week of the week, and the label of the week of the week, and the label of the week of the week, and the label of the week of the week, and the label of the week of the week, and the label of the week of the week, and the label of the week of the week, and the label of the week of the week, and the label of the week of the	declare they potential	insufficient	for emergency	all emergency	holidays,	electronic billing data for	one urban, ambient	2017	
were available in Atlanta; were available approximately large available available approximately large available avai	have no sources of	information	department \(\frac{8}{2}\)	department visits	long-term trends,	respiratory disease	monitor located in each		
were available in Atlanta; however, data were only available approximately available approximately were available in Atlanta; visits for all ages at acute care hospitals. Using diagnosis codes from the data, temperature data, te	actual or bias	about	visits of	for respiratory	day of the week,	emergency department	city. Daily pollution data		
available approximately diagnosis codes from the data, temperature the 20-county obtained, so judge for low	potential identified.	selective	respiratory $\frac{6}{2}$	disease at acute	season,	visits for all ages at acute	were available in Atlanta;		
available approximately diagnosis codes from the data, temperature the 20-county obtained, so judge for low	competing	outcome to	disease were	care hospitals in	hospitalsreporting	care hospitals. Using	however, data were only		
	financial	judge for low	obtained, so	the 20-county	data, temperature	diagnosis codes from the	available approximately		
every third day in the   International   and dew point.   Atlanta   likely have all $\frac{1}{2}$ risk, but	interests.	risk, but	likely have all	Atlanta	and dew point.	International	every third day in the		
remaining three cities. Classification of metropolitan outcome data. indirect		indirect	outcome data.	metropolitan	' /	Classification of	remaining three cities.		20
There was no information Diseases, 9th Revision area, the However, any evidence that		evidence that	However, any	area, the	. 01	Diseases, 9th Revision	There was no information		
about missing data. (ICD-9), the study 7-county potential errors suggests study		suggests study	potential errors.	7-county		(ICD-9), the study	about missing data.		
considered subcategories Birmingham or missing data was free of		was free of	or missing data	Birmingham		considered subcategories			
of respiratory diseases metropolitan did not depend selective		selective	did not depend	metropolitan		of respiratory diseases			
including pneumonia area, the 8 on air pollution report.		report.	on air pollution₫	area, the 8		including pneumonia			
(ICD-9 codes 480–486), Missouri and 8 levels.			levels.	Missouri and 8		(ICD-9 codes 480–486),			
			-	Illinois counties		chronic obstructive			
chronic obstructive pulmonary disease in the St. Louis  (491 492 496) upper			)24	in the St. Louis		pulmonary disease			
(491,492,496), upper metropolitan			оу 9	metropolitan		(491,492,496), upper			
respiratory infection area, and the			lues	area, and the		respiratory infection			
				12-county Dallas					
(URI) (460–465, 466.0, 477), and asthma and/or wheeze (493, 786.07).			 	1		` ' '			
wheeze (493, 786.07).			cted			·			

2	
4	
5 6	
6	
7	
7 8 9	
9	
10	
11	
12	
13	
14	
13 14 15 16 17 18	
16	
17	
18	
19	
20	
21	
22	
23	
24	
25	
26	
27	
25 26 27 28 29	
29	
30	
31	
31 32	
33	
34	
34 35 36 37 38	
36	
37	
38	

5 5 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data		Conflict of interest	Other
3			Probably Low	Low	Probably Low	Low	Low	Probably Low	Low	Low
0	49	O'Lenick	The 24-hour average	Patient-level emergency	Adjusted for	Study included	Daily counts	There was	Competing	No other
11		et al. 2017	concentration of EC was	department visit data	season, periods of	all emergency	for emergency	insufficient	interests:	potential
12			evaluated. Pollutant	from 1 January 2002 to	hospital	department visit	department §	information	None	sources of
13 14			concentration estimates	31 December 2008 were	participation and	data acquired	visit were	about	declared.	bias
15			were obtained by fusing	acquired from hospitals	holidays,	directly from	obtained, so	selective		identified.
16			observational data from	located within the	temperature and	hospitals	likely have all	outcome to		
17 18			available network	20-county metropolitan	mean dew point,	(2002–2004	outcome data.	•		
19			monitors with pollutant	area of Atlanta; Relevant	interaction terms	period) and the	However, any	risk, but		
20			concentration simulations	data elements included	between season	Georgia Hospital	potential errors	indirect		
21			from the Community	admission date,	and maximum	Association	or missing data			
22			Multi-Scale Air Quality	International	temperature and	(2005–2008	did not depend	suggests study		
24			emissions-based chemical	Classification of Diseases	day of year.	period) located	on air pollution			
25			transport model at	Ninth Revision (ICD-9)		within the	levels. 9	selective		
26   27			12×12km grids over	diagnosis codes, age and		20-county	April	report.		
28			Atlanta. 24-hour average	ZIP code of patient		metropolitan area		_		
29			EC were evaluated. Daily	residence.		of Atlanta.	9, 20			
30			data was available and no				)24			
31   32			missing data was				by g			
33			reported.				19, 2024 by guest. Protected			
34			•				;; D			
35							rote			
36   37							ctec			
38 L							<u></u>			

Page 108 of 136

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data ≤		Conflict of interest	Other
8			Probably Low	Low	Probably Low	Low	Low ay 2	Probably Low	Low	Low
10	50	Pearce et	Daily EC data were	The study obtained	Adjusted for year,	Study included	Daily counts 8	There was	The authors	No other
11		al. 2015	obtained from a central	aggregate daily counts for	season, month, day	all emergency	for pediatric	insufficient	declare that	potential
12			monitoring location in	pediatric asthma related	of the week,	department visits	asthma related	information	they have	sources of
13 14			Atlanta. Daily data was	emergency department	hospital, holidays,	for pediatric	emergency a	about	no	bias
15			available and no missing	visits for children ages 5	temperature and	asthma of	department	selective	competing	identified.
16			data was reported.	to 18 years from 41	dew point.	children ages 5 to	visits were	outcome to	interests.	
17 18				hospitals within		18 years from 41	obtained, so	judge for low		
19				metropolitan Atlanta; and		hospitals within	likely have all	risk, but		
20				defined emergency	' /	metropolitan	outcome data.	indirect		
21 22				department visits for	' (2)	Atlanta for study	However, any	evidence that		
23				pediatric asthma as all		period.	potential errors	suggests study		
24				visits with a code for		<b>101</b>	or missing data	was free of		
25				asthma (493.0–493.9) or			did not depend	selective		
26 27				wheeze (786.07) using			on air pollution €	report.		
28				the International			levels.			
29				Classification of			16 VCIS.			
30 31				Diseases, 9th Revision.			)24			
32							by g			
33							lues			
34							: 			
35 36							rote			
37							2024 by guest. Protected b			
38 <sup>l</sup>							\$			

2	
3	
4	
5	
6	
7	
8	
9	
10	
11	
12	
13	
14	
15	
16	
17	
18	
19	
20	
21	
22	
23	
24	
25	
26	
27	
28	
29	
30	
31	
32	
33	
34	
35	
36	
37 38	
38	ĺ
39	

7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on the outcome data of the outcome		Conflict of interest	Other
3			Low	Low	Probably Low	Low	Low 2	Probably Low	Low	Low
0	51	Strickland	24-hour average EC were	Daily counts of	Adjusted for	Study included	Daily counts 8	There was	No conflict	No other
1		et al. 2010	obtained from 6	emergency department	season, dew point,	all emergency	for emergency	insufficient	of interests.	potential
2			monitors. Missing data	visits for asthma or	temperature, year,	department visits	room visits of	information		sources of
3			<1%.	wheeze among children	month, day of	for asthma or	asthma or	about		bias
5				were collected from 41	week, hospital,	wheeze among	wheeze disease diseas	selective		identified.
6				Metropolitan Atlanta	upper respiratory	children aged 5	were obtained,	outcome to		
7  8				hospitals during	infections (the	to 17 years from	so likely have	judge for low		
9				1993-2004. Using the	logarithm of the	metropolitan	all outcome	risk, but		
20				International	daily count of	Atlanta hospitals	data. However,	indirect		
21				Classification of	upper respiratory	during	any potential	evidence that		
22				Diseases, 9th Revision,	infections) and	1993–2004.	errors or	suggests study		
24				the study defined	pollen		missing data	was free of		
25				emergency department	concentrations		did not depend	selective		
26				visits for pediatric asthma	(various lags of		on air pollution €	report.		
28				as all visits with a code	ambient ragweed,		levels.			
9				for asthma (493.0–493.9)	pine, oak, juniper,		9, 20			
0				or wheeze (786.09 before	grass and birch		)24			
31 32				October 1, 1998; 786.07	concentrations).		by g			
33				after October 1, 1998).	-		2024 by guest.			
34										
35 36							Protected			
37							cted			
8 L							<u> </u>			

			BMJ Oper	1	i6/bmJope			Page 110
					_		Conflict of	
Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias			interest	Other
	Low	Low	Probably Low	Low	Low	Probably Low	Low	Low
Strickland et al. 2014	24-hour average EC were obtained from 6 monitors. Missing data was 1%.	Daily counts of emergency department visits for asthma or wheeze among children aged 2 to 16 years were collected from the Georgia Hospital Association from 1 January 2002 through 30 June 2010. The study identified all emergency department visits with an International Classification of Diseases, 9th revision (ICD-9) code for asthma (codes beginning with 493) or wheeze (code 786.07) present in any diagnosis field.	Adjusted for season, dew point, temperature, day of week, and holiday.	Study included all emergency department visits for asthma or wheeze among children 2 to 16 years of age from the Georgia Hospital Association.	room visits of asthma or wheeze disease were obtained, so likely have all outcome data. However, any potential errors or missing data did not depend on air pollutions	information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of selective report.	No conflict of interests.	No other potential sources of bias identified.
	Strickland	Strickland et al. 2014 Detailed from 6 monitors. Missing data	Strickland et al. 2014  Strickland et al. 2014  Daily counts of emergency department visits for asthma or wheeze among children aged 2 to 16 years were collected from the Georgia Hospital Association from 1  January 2002 through 30  June 2010. The study identified all emergency department visits with an International Classification of Diseases, 9th revision (ICD-9) code for asthma (codes beginning with 493) or wheeze (code 786.07) present in any	Strickland et al. 2014  Strickland et al. 2014  Strickland et al. 2014  Daily counts of emergency department visits for asthma or wheeze among children aged 2 to 16 years were collected from the Georgia Hospital Association from 1  January 2002 through 30  June 2010. The study identified all emergency department visits with an International Classification of Diseases, 9th revision (ICD-9) code for asthma (codes beginning with 493) or wheeze (code 786.07) present in any	Strickland et al. 2014    Strickland et al. 2014   Daily counts of obtained from 6 monitors. Missing data was 1%.   Daily counts of emergency department visits for asthma or wheeze among children aged 2 to 16 years were collected from the Georgia Hospital Association from 1 January 2002 through 30 June 2010. The study identified all emergency department visits with an International Classification of Diseases, 9th revision (ICD-9) code for asthma (codes beginning with 493) or wheeze (code 786.07) present in any   Probably Low   Low    Adjusted for study identified sall emergency department visits temperature, day of week, and holiday.   department visits of week, and holiday.    It was 1%.   Study included all emergency department visits of week, and holiday.    It was 1%.   Study included sall emergency department visits of week, and holiday.    It was 1%.   Study included sall emergency department visits of week, and holiday.    It was 1%.   Study included sall emergency department visits of week, and holiday.    It was 1%.   Study included sall emergency department visits of week, and holiday.    It was 1%.   Study included sall emergency department visits week, and holiday.    It was 1%.   Study included sall emergency department visits week, and holiday.    It was 1%.   Study included sall emergency department visits week, and holiday.    It was 1%.   Study included all emergency department visits week, and holiday.    It was 1%.   Study included all emergency department visits week, and holiday.    It was 1%.   Study included all emergency department visits week, and holiday.    It was 1%.   Study included all emergency department visits week, and holiday.    It was 1%.   Study included all emergency department visits week, and holiday.    It was 1%.   Study included all emergency department visits week, and holiday.    It was 1%.   Study included all emergency department visits week, and holiday.    It was 1%.   Study included all emergency department visits week, and holiday.    It was 1%.   Study includ	Exposure assessment    Confounding bias   Selection bias   Confounding bias	Study Exposure assessment Outcome assessment Confounding bias Selection bias Outcome data Value of Probably Low Low Strickland et al. 2014  Strickland et al. 2014  24-hour average EC were obtained from 6 emergency department visits for asthma or wheeze among children aged 2 to 16 years were collected from the Georgia Hospital Association from 1 January 2002 through 30 June 2010. The study identified all emergency department visits with an International Classification of Diseases, 9th revision (ICD-9) code for asthma (codes beginning with 493) or wheeze (code 786.07) present in any	Strickland et al. 2014  Strick

2	
3	
4	
5	
6	
7	
8	ŀ
9	
10	
11	
12	
13	
14	
15	
16	
17	
18	
19	
20	
21	
22	
23	
24	
25	
26	
27	
28	
29	
30	
31	
32	
33	
34	
35	
36	
37 38	
38	
39	

5 5 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data on seconds		Conflict of interest	Other
3			Probably High	Low	Probably Low	Low	Low 2	Probably Low	Low	Low
10	53	Ito et al.	The study chose 150 U.S.	Using International	Adjusted for	Study included	Daily counts 8	There was	No conflict	No other
11		2013	metropolitan statistical	Classification of	modeling of	all nonaccidental	for death and	insufficient	of interests.	potential
12			areas where the data from	Diseases, 10th Revision	confounding	all-cause,	emergency §	information		sources of
13   14			at least one Chemical	(ICD-10) codes, the study	temporal trends	cardiovascular	hospitalization	about		bias
15			Species Network monitor	aggregated daily death	(annual cycles and	disease and	were obtained,	selective		identified.
16			were available. The	counts for the	influenza	respiratory	so likely have	outcome to		
7  8			Chemical Species	nonaccidental all-cause,	epidemics),	deaths and	all outcome	judge for low		
19			Network data for PM <sub>2.5</sub>	cardiovascular disease	day-of-week	emergency	data. However,	risk, but		
20			components were	and respiratory deaths.	patterns and	hospitalizations	any potential	indirect		
21			available either every	Using International	temperature.	for the elderly	errors or	evidence that		
22			third day or every sixth	Classification of		(those 65 and	missing data	suggests study		
24			day. There was no	Diseases, 9th Revision		older) of	did not depend	was free of		
25			information about	(ICD-9) codes,		cardiovascular	on air pollution	selective		
26 27			missing data.	emergency		disease and	levels. ≱	report.		
28				hospitalizations for the		respiratory				
29				elderly (those 65 and		diseases.	9, 20			
30   31				older) data were divided			124			
32				into cardiovascular			оу д			
33				disease and respiratory			ues			
34				categories.			19, 2024 by guest. Protected			
35   36							oter -			
37							cted			
88 <sup>L</sup>							<u> </u>			

Page 112 of 136

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data ≤		Conflict of interest	Other
8 9			Probably Low	Low	Probably Low	Low	Probably Low	Probably Low	Low	Low
10	54	Ostro et	The model calculations	Deaths were assigned	ge, race, marital	Data obtained for	There was no 22	There was	The authors	No other
11		al. 2015b	track the mass and	codes based on the	status, smoking	a cohort of	information on	insufficient	declare they	potential
12			concentrations of the PM	International	status, pack-years	female teachers	the rate of lost	information	have no	sources of
13 14			constituents in particle	Classification of	of smoking,	≥30 years old.	follow up.	about	actual or	bias
15			diameters ranging from	Diseases, 10th Revision	secondhand smoke		ed fr	selective	potential	identified.
16			0.01 to 10µm through	(ICD-10) for the	exposure, body		om	outcome to	competing	
17 18			calculations that describe	following outcomes:	mass index,		http	judge for low	financial	
19			emissions, transport,	all-cause deaths	lifetime physical		://bn	risk, but	interests.	
20			diffusion, deposition,	excluding those with an	activity, alcohol		njop	indirect		
21 22			coagulation, gas- and	external cause	consumption,		en.b	evidence that		
23			particle-phase chemistry,	(A00–R99),	average daily		)mj.c	suggests study		
24			and gas-to-particle	cardiovascular deaths	dietary intake of	'61.	com	was free of		
25			conversion. The	(I00-I99), Ischemic heart	fat, calories,		on /	selective		
26 27			University of California	disease deaths (I20–I25),	menopausal status,		Apr	report.		
28			Davis/California Institute	and pulmonary deaths	family history of		ii 19			
29			of Technology model was	(C34, J00–J98).	myocardial		, 20			
30 31			used to estimate		infarction, stroke,		24 b			
32			ground-level		use of blood		y gu			
33			concentrations of 50 PM		pressure		on April 19, 2024 by guest.			
34 35			constituents over the		medication,		. Pro			
36			major population regions		aspirin; living		Protected			
37 38			in California.		conditions		ted by			

1 2 3 4
5
6 7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30 31
31 32
33
34
35
36
37
38
39

5 5 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data	reporting	Conflict of interest	Other
3					(income, income		ay 2			
0					inequality,		2022.			
1					education,		: D	,		
2					population size,		OWN			
13				Oh	racial composition,		oad			
14   15					unemployment).		Downloaded from			
16				0,			rom			
17							nttp			
18 - 19			Probably Low	Low	Probably High	Low	Probably Low	Probably Low	Low	Low
20	55	Gan et al.	Using high spatial	The study used	Individual-level	Data obtained for	During the	There was	The authors	No other
21		2013	resolution land use	International Statistical	covariates: age,	a cohort of	4-year	insufficient	declare they	potential
22			regression models to	Classification of	sex, preexisting	people (45-85	follow-up	information	have no	sources of
24			estimate residential	Diseases, 9th Revision	comorbid	years old)	period, 38,377	about	actual or	bias
25			exposure to traffic-related	(ICD-9) codes 490–492	conditions; and	registered with	(8%) subjects 9	selective	potential	identified.
26 27			air pollutants including	and 496 or 10th Revision	neighborhood	the provincial	were lost to	outcome to	competing	
28			black carbon. During the	(ICD-10) codes J40–J44	socioeconomic	health insurance	follow-up	judge for low	financial	
29			5-year exposure period,	to identify COPD cases	status (SES).	plan. Study	because of	risk, but	interests.	
30			individual exposures to	during the 4-year		provided total	moving out of 4	indirect		
32			ambient air pollutants	follow-up period.		number of	the province or	evidence that		
33			were estimated at each			subjects along	dying from	suggests study		
34			person's residential			with those lost	other diseases.	was free of		
35   36			postal code centroid			during the	otec	selective		
37			using land use regression			follow-up period.	Sted	report.		
88 <sup>-</sup>				1			9	-		

5 6 <b>No</b> .	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data		Conflict of interest	Other
8 9 10 11 12 13 14 15		models.	Corp			ay 2022. Downloaded fro			
16		Probably Low	Low	Probably Low	Low	Probably Low	Probably Low	Low	Low
18 56 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39	Hvidtfeldt et al. 2019	The PM, NO <sub>2</sub> , BC, and O <sub>3</sub> concentrations at residential addresses of the cohort members were derived by a high-resolution dispersion modelling system which incorporates contributions from local, urban, and regional sources of precursors to PM, NO <sub>2</sub> , BC, and O <sub>3</sub> .	Participants who died from external causes such as injuries, accidents and suicides (International Classification of Diseases, 10th Revision-ICD-10 codes S–Z) were censored at date of death. In addition, the study investigated cardiovascular (ICD10 codes I00–I99) and respiratory (ICD10 codes J00–J99 and C34) subgroups of mortality.	Age, sex, educational attainment, occupational status, marital status, smoking (status, intensity, and duration), environmental tobacco smoke (ETS), alcohol consumption, body mass index, waist circumference, fruit consumption, vegetable	Data obtained for a cohort of men and women aged 50–64 years residing in the areas of Copenhagen and Aarhus.	There was no information on April 19, 2024 by guest. Protected by cop	There was insufficient information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of selective report.	The authors declare they have no competing financial interests.	No other potential sources of bias identified.

17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34

						<u> </u>			
No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data S	reporting	Conflict of interest	Other
				consumption,		May 2022.			
				physical activity;		202			
0				neighborhood		5.			
2				-		Oow			
2 3				level		/nlo			
4				socioeconomic		ade			
5			-/ h	status (SES).		ed =			
6		Probably Low	Probably Low	Probably High	Low	Probably High	Probably Low	Low	Low
7				Probably High					
8						)://c			
9 0						<u>ğ</u>			
1						эре			
2						n.b			
3						<u> </u>			
1 2 3 4 5 6 7						COM			
5						0 /			
6						n A	•		
7							:		
8 9						19,			
9						20			
0						124			
1						ittp://bmjopen.bmj.com/ on April 19, 2024 by guest. Protected	•		
2						gue			
3 4 5 6						t.			
<del>-</del> 5						Pro	1		
6						otec			
7						ted			

5 No	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data		Conflict of interest	Other
57	Thurston	The mean concentrations	More than 99% of known	Active smoking	Data obtained for	The analytic	There was	No	No other
10	et al. 2016	of PM <sub>2.5</sub> mass and trace	deaths were assigned a	and former	a cohort of	cohort included	insufficient	competing	potential
11		constituents were	cause using the	smoking, passive	persons at least	445,860	information	financial	sources of
12		obtained from U.S.	International	smoke exposure,	30 years of age,	participants,	about	interests.	bias
3  4		Environmental Protection	Classification of	possible workplace	in households	with 34,408	selective		identified.
5		Agency Air Quality	Diseases, 9th and 10th	exposure to PM,	including	Ischemic heart	outcome to		
16		System. These PM <sub>2.5</sub>	Revision (ICD-9 codes	occupational	someone at least	disease deaths	judge for low		
17		constituent data were	410–414; ICD-10 codes	dirtiness index,	45 years of age	(of a total of	risk, but		
18 19		analyzed to derive	I20–I25).	marital status,	and resided in all	157,572 deaths	indirect		
20		estimates of source	,	education, BMI	50 states, the	from all	evidence that		
21		apportioned PM <sub>2.5</sub> mass		and BMI <sup>2</sup> ,	District of	causes)	suggests study		
22		exposure concentrations		consumption of	Columbia, and	occurring	was free of		
23 24		using the absolute		beer, wine, and	Puerto Rico.	during	selective		
25		principal component		other alcohol,		follow-up.	report.		
26		analysis (APCA) PM <sub>2.5</sub>		quintile of dietary			'  *		
27 28		source apportionment		fat consumption,		April	_		
29		method.		quintile of		, ,			
30		metriod.		combined dietary		2024 by			
31						+ by			
32				vegetable, fruit,		gue			
33   34				fiber consumption;		SSI.			
35				Six ecologic		ן			
36				covariates.		l			
37		D. 1.11 T.	т .	D. 1.11 I	т.	D. 1.11 I	D. 1.11 I	T	т.
38 [ 39		Probably Low	Low	Probably Low	Low	Probably Lows	Probably Low	Low	Low

36/bmjopen-2021-0495<mark>1</mark>

2
3
4
5
6
7
8
8 9
10
11
12
13
14
15
16
16 17 18
18
19
20
21
21 22
23 24
24
25
25 26
27 28
28
29
30
31
32
33
34
35
36 37 38
38
38 39

5 1	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data		Conflict of interest	Other
3 4	58	Yang et	Land use regression	Deaths were coded	Age at entry,	Data obtained for	There was no	There was	The authors	No other
10		al. 2018	models were derived	according to the	gender, individual	a cohort of	information on	insufficient	declare they	potential
1			from street level	International	smoking status,	people who were	the rate of lost	information	have no	sources of
2			measurements collected	classification of Diseases,	body mass index	older than or	follow up.	about	actual or	bias
3			during two sampling	10th Revision (ICD-10;	(BMI), physical	equal to 65 years	follow up.	selective	potential	identified.
14			campaigns conducted in	WHO 2010) including	activity, education	old.	ed	outcome to	competing	
6			2014 and 2015.	natural cause mortality	level and monthly		rom	judge for low	financial	
7				(A00–R99), overall	expenses;		i h	risk, but	interests.	
18 19				cardiovascular disease	percentage of		o://b	indirect		
20				(I00–I99) and overall	participants who		mjo	evidence that		
21				respiratory disease	were equal to or		pen	suggests study		
22				(J00–J47 and J80–J99).	older than 65 years		.bm	was free of		
23   24				Subcategories included	old, percentage of	10,	j. cor	selective		
25				Ischemic heart disease	participants whose		m/ 0			
26				(IHD) (I20–I25),	educational level		on A	тероге.		
27				cerebrovascular disease	was higher than					
28				(I60–I69), Pneumonia	secondary school,		19, 2			
30				(J12–J18) and chronic	•		202			
31				·	average income		4 by			
32				obstructive pulmonary	per month and		gue			
33 34				disease (COPD) (J40–I44	percentage of		est.			
35				and I47).	smokers.		April 19, 2024 by guest. Protec			
6							tect			
37 <u> </u>			Probably Low	Low	Probably High	Low	Probably Low	Probably Low	Low	Low

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data se		Conflict of interest	Other
8 9	59	Gan et al.	Land use regression to	A coronary heart disease	Model adjusted for	Study provided	During the	There was	The authors	No other
10		2011	estimate air pollution	hospitalization case is a	age, sex,	total number of	4-year $\stackrel{\circ}{\sim}$	insufficient	declare they	potential
11			concentrations and	record of hospitalization	preexisting	subjects along	follow-up	information	have no	sources of
12			exposure assigned to	with the following	comorbidity, and	with those lost	period, 17,542 <u>₹</u>	about	actual or	bias
13 14			residential centroid.	International Statistical	neighborhood	during the	(3.9%) moved 8	selective	potential	identified.
15				Classification of	socioeconomic	follow-up period.	out of the	outcome to	competing	
16				Diseases, 9th Revision	status. No		province and	judge for low	financial	
17				codes, ICD-9, 410–414	individual data on		16,367 (3.6%)	risk, but	interests.	
18 19				and 429.2or 10th	behavioral risk		died from other			
20				Revision (ICD-10),	factors.		diseases,	evidence that		
21				I20–I25, as the principal	(0)		leaving 👱	suggests study		
22 23				diagnosis (the most		ien	418,826 (9 <sub>2.5</sub> %)	was free of		
24				responsible diagnosis) for		(0)	(9 <sub>2.5</sub> %)	selective		
25				a hospital admission in			subjects at the 9	report.		
26 27				the hospitalization			end of →			
28				database. A coronary			follow-up.			
29				heart disease death is a			9, 20			
30				death record with			024			
31 32				coronary heart disease as			by g			
33				the cause of death in the			end of follow-up. 2024 by guest.			
34				provincial death						
35 36				registration database.			Prote			
37			Probably High	Low	Probably Low	Low	Probably Low	Probably Low	Low	Low
38 <sup>°</sup> 39							by cop			

36/bmjopen-2021-0495

3	
4	ſ
5	I
6	I
7	I
8	ľ
9	I
10	I
11	I
12	I
13	I
14	I
15	I
16	I
17	I
18	I
19	I
20	I
21	I
22	I
23	I
24	I
25	I
26	I
27	I
28	I
29	I
30	I
31	I
32	I
33	I
34	I
35	I
	١
36 37 38	ľ
38	ĺ
39	
40	

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data		Conflict of interest	Other
8 9	60	De	Used black smoke (BS)	The study obtained	Individual-level	Data obtained for	There was no	There was	No	No other
10		Kluizenaa	as an indicator of EC	information on the	covariates: age,	a cohort of	information on	insufficient	competing	potential
11		r et al.	concentrations. Derived	incidence of	gender, marital	27,070	the rate of lost	information	financial	sources of
12		2013	background EC	hospital-based Ischemic	status, education,	non-institutionali	follow up.	about	interests.	bias
13 14			concentrations from BS	heart disease	smoking, alcohol	zed subjects.	follow up.	selective		identified.
15			measured at two regional	(International	use, physical		ed f	outcome to		
16			monitoring sites. Local	Classification of Diseases	activity, body		rom	judge for low		
17 18			traffic-related EC	[ICD9] 410-414) and	mass index, living		http:/	risk, but		
19			emission contributions	cerebrovascular disease	conditions		://br	indirect		
20			were estimated based on	(ICD9 430-438) in the	(employment		njop	evidence that		
21			fuel-specific EC content	study population.	status, financial		en.r	suggests study		
22			of exhaust PM <sub>10</sub>		problems).		<u>)</u>	was free of		
24			emission. Used the			<b>101</b>	com	selective		
25			traffic-related EC			Ch,	v on	report.		
26 27			emissions as input to				Api			
28			calculate local EC							
29			concentrations, assuming				9, 20			
30			absence of other local EC				)24			
32			sources. Also assumed				by g			
33			that dispersion dynamics				ues			
34			of EC are identical to				on April 19, 2024 by guest. Prote			
35 36			those of $PM_{10}$ .				otec			
37 38			Probably Low	Probably Low	Probably Low	Low	Probably Low	Probably Low	Low	Low

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data		Conflict of interest	Other
8	61	Vedal et	The exposure estimation	All outcomes were	Individual-level	Data obtained for	There was no	There was	No financial	No other
9 10		al. 2013	were used the national	reported via questionnaire	covariates: age,	a cohort of	information on	insufficient	interests.	potential
11			spatial model predictions	and assessed via	body mass index,	postmenopausal	the rate of lost	information		sources of
12			and secondary exposure	physician-adjudicator	smoking status,	women.	follow up.	about		bias
13 14			measures of citywide	review of medical records	cigarettes smoked		load	selective		identified.
15			average exposures and	following established	per day and years		ean	outcome to		
16			distance to major	protocols.	of smoking,		l rom	judge for low		
17			roadways.		systolic blood		) ng	risk, but		
18 19					pressure, history of		0://b	indirect		
20					hypertension,		njop	evidence that		
21					hypercholesterole		Jen.	suggests study		
22 23					mia, history of		om).	was free of		
24					diabetes,	10,	.con	selective		
25					education,	\ \/_	or or	report.		
26					household income		1 Ap	•		
27 28					level, and race.		リカノ	<u>:</u>		
29							19, 2			
30							2024 by guest.			
31 32							by			
33							Jues			
34							τ	<b>J</b>		
35							rotec			
36 37							)Cled			
38			High	Low	Probably Low	Low	Low Ş		Low	Low
39							S			

2	
3	
4	ſ
5	I
6	I
7	I
Q	ŀ
9	I
10	I
10 11 12	I
12	I
13	I
14	I
15	I
16	I
17	I
18	I
19	I
20	I
21	I
22	I
23	I
24	I
25	I
26	I
27	I
28	I
29	I
30	I
31	I
32	I
33	I
34	I
35	I
36	ŀ
37 38	١
38	
39	
40	

Page 1	121 c	of 136			BMJ Oper	١	86/bmJop			
2 3 4 5 <b>N</b>	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data	Selective	Conflict of	Other
9 110 111 12 13 14 15 16 17 18 19 20 21 22 22		a et al. 2021	two monitors (Sharif and Setad) with data recorded at 5 min intervals. BC measurements began from March 2017 to August 2017. But the gaseous pollutant at the Setad site were unreliable and models utilizing the 2-site data were unsatisfactory. So, only	deaths were obtained from Ministry of Health and Medical Education database. The causes of death were coded according to the International Classification of Disease (10th revision—ICD-10).	for time, temperature, relative humidity, atmospheric pressure, PM2.5 data, Day of week (DOW) and public holidays.	all daily non-accidental deaths from Ministry of Health and Medical Education database from March 2017 to August 2017.	Daily counts for death were obtained, so likely have all outcome data. However, any potential errors or missing data did not depend on air pollution	information about selective outcome to judge for low risk, but indirect evidence that suggests	of this article declare that they have no conflict of interests.	potential sources of bias identified.
24 25 26 27 28 29 30 31 32 33 34 35			the Sharif data were used.				bmJ.com/ on April 19, 2024 by guest. Protected Low	free of selective report.		
7 8			Probably Low	Probably Low	Probably Low	Low	Low g	Probably Low	Low	Low

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data ≤	Selective reporting	Conflict of interest	Other
8	63	Liu et al.	Annual county-level	The three cardiovascular	Model adjusted for	All of	The cohort	There was	The authors	No other
9 10		2021b	exposures of PM2.5 and	events as health	age, gender,	participants were	included 8	insufficient	declare that	potential
11			its constituents for each	outcomes: 1) total	education level	drawn from the	14,331 adults	information	they have	sources of
12			participant were assessed	cardiovascular disease,	(illiteracy, primary	China Family	who completed <u>≤</u>	about	no known	bias
13 14			by aggregating	including but not limited	to middle school,	Panel Studies	three waves of $\frac{8}{2}$	selective	competing	identified.
15			satellite-derived estimates	to hypertension and	and high school or	(CFPS) launched	follow-up.	outcome to	financial	
16			at a monthly time-scale	stroke; 2) hypertension;	above), household	by Peking	rom	judge for low	interests or	
17 18			and 1 km-resolution.	3) stroke were defined	income (RMB,	University	http	risk, but	personal	
18				according to the Disease	strata of ≤	Institute of	s://bi	indirect	relationship	
20				Classification Codebook	15,000, 15,	Social Science	njop	evidence that	s that could	
21				for Chinese Family Panel	000 - 40,000, and	Survey (ISSS) in	oen.	suggests	have	
22 23				Studies.	40,000 +, grouped	2010, an ongoing	bmj	study was	appeared to	
24					according to the	national	com	free of	influence	
25					upper and lower	longitudinal	n/ or	selective	the work	
26 27					quartiles),	survey of	1 Ар	report.	reported in	
28					urbanicity	social-demograp	April 19,	_	this paper.	
29					(urban/rural,	hy in China.	9, 2			
30					defined by CFPS		2024 by guest.			
31 32					participants' home		by (			
33					addresses).		Jues			
34										
35							Protec			
36 37			D. 1.11 T.	T .	D. 1.11 I	т.	<del></del>	D. 1 11 1	Τ.,	т.
38			Probably Low	Low	Probably Low	Low	Probably Low	Probably Low	Low	Low
39							сор			

1	
2	
3 4	
4	ĺ
5	I
0	I
/	ŀ
8	I
9	I
10	I
11	I
12	I
13	I
14 15	I
13	I
16	I
17	I
17 18	I
19	I
20	I
21	I
22	I
23	I
24	I
25	I
26	I
27	I
28	I
29	I
30	I
31	I
32	I
33	I
34	I
35	I
36	١
37	١
38	•
39	

Page 123 of 136 BMJ Open					Incomplete				
No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data	Selective reporting	Conflict of interest	Other
64 64 64 64 64 64 64 64 64 64	Lavigne et al. 2021	A spatial PM2.5 surface gridded at a resolution of approximately 1-km2 was derived using multiple satellite-based retrievals of aerosol optical depth in combination with a chemical transport model, and enhanced through statistical incorporation of ground- based observations (including BC).	Incident childhood asthma cases were identified according to International Classification of Diseases [ICD]-10: J45.	Model adjusted for parity, child sex, breastfeeding status at the time of discharge, maternal smoking during pregnancy, maternal atopy, gestational age and birth weight.	The study used data on singleton live births that occurred between April 1st 2006 and March 31st 2014 in the Province of Ontario, Canada. Mother-infant pair data were obtained from the Better Outcomes Registry & Network (BORN) Ontario, a province wide birth registry that captures perinatal health information.	There was no information on the rate of lost follow up.  There was no information on the rate of lost follow up.  There was no information on April 19, 2024 by guest. Protected the rate of lost follow up.	information about selective	The authors declared that there is no conflict of interest.	No other potential sources of bias identified.

4,							51			
5 5 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on the outcome data of the outcome	Selective reporting	Conflict of interest	Other
3			Probably Low	Probably Low	Probably Low	Low	Probably Low	Probably Low	Low	Low
10	65	Rodins et	The study used the	Cardiovascular outcomes	Model adjusted for	The study used	There was no	There was	The authors	No other
11		al. 2020	validated,	in the HNR Study were	age, sex,	baseline	information on	insufficient	declare that	potential
12			time-dependent,	determined by an	individual and	(2000–2003) and	the rate of lost	information	they have	sources of
3  4			three-dimensional	independent endpoint	neighborhood	14 years	follow up.	about	no known	bias
5			European Air Pollution	committee based on	SES, BMI,	follow-up data	ed fr	selective	competing	identified.
6			Dispersion chemistry	self-reports, physician	nighttime traffic	from the German	om om	outcome to	financial	
7  8			transport model	and next-of-kin	noise exposure and	HNR Study, an	http	judge for low	interests or	
9			(EURAD) to estimate the	interviews, and medical	lifestyle factors:	ongoing	://bn	risk, but	personal	
20			exposure to EC.	records.	smoking, alcohol	population-based	njop	indirect	relationship	
21					consumption,	prospective	en.k	evidence that	s that could	
22					physical activity	cohort study.	ļ <u>j</u>	suggests	have	
24					and nutritional	<b>101.</b>	com	study was	appeared to	
25					pattern.		on	free of	influence	
26 27							Apı	selective	the work	
28								report.	reported in	
9							9, 20		this paper.	
30							)24			
31 32							by g			
33							April 19, 2024 by guest.			
34										
35							rote			
36 37							Protected			
38							l d			
39							S			

2	
4	
4 5 6	
6	
7	
7 8 9	_
9	
10	
11	
12	
13	
13 14	
15	
16	
17	
15 16 17 18	
19	
20	
21	
22	
23	
23 24 25	
25	
25 26	
27	
27 28	
29	
30	
31	
32	
33	
34	
34 35 36 37 38	
36	
37	
38	

Pag	e 125 (	of 136			BMJ Oper	١	36/bmJop			
I <u>2</u> 3							Incomplete			
5	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data	Selective reporting	Conflict of interest	Other
3			Probably Low	Low	Probably High	Low	Low	Probably Low	Low	Low
9 10 11 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 33 34 35 36 36 37 37 37 37 37 37 37 37 37 37 37 37 37	66	Kovačević et al. 2020	The daily average concentration of BC were collected from three automatic ambient air quality monitoring stations located in Užice, Sevojno, and Kosjerić. BC were measured between 1st July 2012 and 30th June 2014. There was no information about missing data.	The data of emergency department (ED) visits for allergic asthma were collected from the Užice Health Centre, either from the EDs (ambulances or home care) in Užice, Sevojno, and Kosjerić or from a general hospital in Užice. International Classification of Diseases, 10th revision, codes were used in the diagnosis of allergic asthma or asthma with coexisting allergic rhinitis (AR).	Model adjusted for seasonality, long-term trends, temperature, humidity, air pressure, air pollutants and pollens.	Study included all the data of emergency department (ED) visits for allergic asthma were collected from the Užice Health Centre, either from the EDs (ambulances or home care) in Užice, Sevojno, and Kosjerić or from a general hospital in Užice during 1st July 2012 to 30th June 2014.	Daily counts for emergency department (ED) visits were obtained, so likely have all outcome data. However, any potential errors or missing data did not depend on air pollution levels.	There was insufficient information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of selective report.	The authors declare no conflict of interest.	No other potential sources of bias identified.
38 <sup>1</sup> 39 10 11 12							Protected by copyright.	:		

Page 126 of 136

5	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data ≤	Selective reporting	Conflict of interest	Other
3 [			Probably Low	Probably Low	Probably Low	Low	Probably Low	Probably Low	Low	Low
0	67	Hasslöf et	BC levels were modelled	The outcomes were	Model adjusted for	In the	Of these, 224	There was	The authors	No other
1		al. 2020	using EnviMan (Opsis	plaque presence and	age, sex, air	cardiovascular	were missing	insufficient	declare that	potential
2			AB, Sweden) by the	CIMT of the right carotid	pollutant,	subcohort of the	data on plaque	information	they have	sources of
3 4			Environmental	artery, which were	education level,	MDCS cohort,	and 20 on	about	no known	bias
5			Department of Malm"o.	assessed by ultrasound	smoke score,	6031 participants	CIMT,	selective	competing	identified.
6			The program uses a	examination B-mode	apoB/apoA1 ratio,	who had a	respectively.	outcome to	financial	
7 8			Gaussian dispersion	ultrasonography,	use of lipid	residential	Hence, the	judge for low	interests or	
9			model (AERMOD)	conducted by trained and	lowering drugs,	address within	number of	risk, but	personal	
0			combined with an	certified sonographers.	living alone,	the air pollution	participants 3	indirect	relationship	
11			emission database for the		cardiovascular	modelling area.	included in the	evidence that	s that could	
2			county of Scania in		heredity, diabetes	Of these, 224	plaque analyses.	suggests	have	
4			Sweden.		mellitus, waist hip	were missing	were 5807 and	study was	appeared to	
.5					ratio, physical	data on plaque	in the CIMT	free of	influence	
6					activity, alcohol	and 20 on CIMT,	analyses 6011. ⋛	selective	the work	
8					consumption,	respectively. The	ril 19,	report.	reported in	
9					median income	number of			this paper.	
0					level in residential	participants	)24			
1					area, systolic blood	included in the	by g			
3					pressure and being	plaque analyses	Jues			
4					born outside of	were 5807 and in	2024 by guest. Protected			
5					Sweden.	the CIMT	otec			
7						analyses 6011.	cted			
88 <sup>L</sup>							\$			

BMJ Open

2	
3	
4	I
5 6	
7	
, 8	
9	
10	
11	
12	
13	
14	
15	
16	
17	
18	
19	
20	
21	
22	
23	
24	
25	
26	
2/	
28 29	
30	
31	
37	
33	
34	
35	ĺ
36	
37	ĺ
38	

5 5	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data ≤		Conflict of interest	Other
3			Probably High	Probably Low	Probably High	Low	Low S	Probably Low	Low	Low
0	68	Wang et	BC were collected from a	All patients treated at the	Model adjusted for	Study included	Daily counts 8	There was	The authors	No other
1		al. 2019b	routine air quality	Cardiac Catheterization	seasonality,	all patients	for all patients	insufficient	declare that	potential
2			monitoring site operated	Laboratory (Cath Lab) at	long-term trends,	treated at the	were obtained, \sum_{\frac{8}{2}}	information	they have	sources of
3  4			by the New York State	URMC in Rochester, NY	temperature and	Cardiac	so likely have $\frac{6}{2}$	about	no	bias
5			Department of	for STEMI, who resided	relative humidity.	Catheterization	all outcome	selective	competing	identified.
6			Environmental	within 15 miles of the		Laboratory (Cath	data. However, $\stackrel{\circ}{\exists}$	outcome to	interests.	
7			Conservation	pollution monitoring	<b>'</b> O.	Lab) at URMC	any potential	judge for low		
9			continuously throughout	station in Rochester were		in Rochester, NY	errors or	risk, but		
20			the study period	included. American	1/6	for STEMI	missing data	indirect		
21			(2005–2016). There was	College of Cardiology	(0)	throughout the	did not depend	evidence that		
22			no information about	(ACC)/American Heart		study period	on air pollution.			
24			missing data.	Association (AHA)		(2005–2016).	levels.	study was		
25				guidelines were used at			n on	free of		
26				the time of Cath Lab				selective		
27 28				admission to diagnose				report.		
29				STEMI.			9, 2			
30							024			
31   32							by			
33							April 19, 2024 by guest. Protected			
34							St. F			
35							rote			
36   37							ecte			
37   38							d by			

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data se		Conflict of interest	Other
8 9			Probably Low	Low	Probably Low	Low	Probably Low	Probably Low	Low	Low
10	69	Ljungman	Based on detailed	The International	Model adjusted for	The study	The study used	There was	The authors	No other
11		et al. 2019	emission databases,	Classification of	sex, calendar year,	included	high-quality	insufficient	declare they	potential
12			monitoring data, and	Diseases, Ninth Revision	subcohort,	individuals in	and $\frac{\delta}{2}$	information	have no	sources of
13 14			high-resolution	(ICD-9) codes 410–414	smoking status,	two cohorts from	comprehensive	about	actual or	bias
15			dispersion models, the	and ICD-10 I20-25 codes	alcohol	Gothenburg, four	national patien	selective	potential	identified.
16			study calculated source	were used to define IHD	consumption in	pooled cohorts	and death	outcome to	competing	
17 18			contributions to black	and ICD-9 codes	Stockholm and	from Stockholm,	registries,	judge for low	financial	
19			carbon (BC) from road	431–436 and ICD-10	Umeå, physical	and one cohort	minimizing	risk, but	interests.	
20			wear, traffic exhaust,	codes I61– I65 were used	activity, marital	from Umeå. In	loss to	indirect		
21 22			residential heating, and	to define stroke.	status,	total, 114,758	follow-up for	evidence that		
23			other sources in		socioeconomic	individuals were	our outcomes	suggests		
24			Gothenburg, Stockholm,		index by	included from all	of interest.	study was		
25 26			and Umeå.		occupation,	study areas.	Missing 9	free of		
27					education level,		information for	selective		
28					occupation status,		variables $\leq \frac{1}{2}$	report.		
29					and mean					
30 31					neighborhood		specified.			
32					individual income		y gi			
33					in persons of		uest			
34 35					working age by		P <sub>R</sub>			
36					Small Areas for		otec			
37					Market Statistics.		5% not specified. 2024 by guest. Protected by			
38 <sup>l</sup> 39			1	I	1	l	by cop	1		

2	
3	
-	
4	
5	
7	
0	L
9	
10	
11	
12	
13	
14	
15	
16 17	
18	
19	
20	
21	
22	
23	
24	
25	
26	
27	
28	
29	
30	
31	
32	
33	
34	
25	
36	
36 37	
38	L
39	

No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data ≤		Conflict of interest	Other
		Probably Low	Low	Probably Low	Low	Probably Low	Probably Low	Low	Low
0 70	Liu et al.	Annual mean	COPD was defined by	Model adjusted for	The study used	From a total of	There was	The authors	No other
1	2021a	concentrations of BC for	following the principal	age, sex, smoking	data from three	106,727	insufficient	declare that	potential
2		2010 were estimated at	diagnosis of International	status, smoking	cohorts within	participants	information	they have	sources of
3 4		the study participants'	Classification of	duration, smoking	the ELAPSE	with complete	about	no known	bias
5		baseline residential	Diseases, 9th Revision	intensity,	project with	air pollution	selective	competing	identified.
6		addresses, using	(ICD-9) codes 490–492,	body-mass index,	available	exposure data,	outcome to	financial	
7 8		standardized	and 494–496, or ICD-10	marital status,	information on	the study	judge for low	interests or	
9		Europe-wide hybrid land	codes J40-44.	employment	COPD hospital	excluded 633	risk, but	personal	
О		use regression (LUR)		status, educational	discharge	participants	indirect	relationship	
1		models. The LUR model		level and	diagnoses. Mean	with COPD at	evidence that	s that could	
2 3		utilized routine		area-level annual	follow-up time is	baseline and	suggests	have	
4		monitoring data from the		year income.	16.6 years.	7,586	study was	appeared to	
5		European Environment				participants 9	free of	influence	
6 7		Agency (EEA) AirBase				with missing 출	selective	the work	
8		for PM2.5, NO2, and O3,				information on ≟	report.	reported in	
9		and ESCAPE monitoring				, , , , , , , , , , , , , , , , , , ,		this paper.	
0 1		data for BC as the				confounders. 2024			
2		dependent variable. BC				ру д			
3		was measured by the				by guest.			
4		reflectance of PM2.5							
5 6		filters and expressed in				Protected			
7		absorbance units.				ted			

45

7Table S5 Assessment of certainty of evidence for the outcomes.

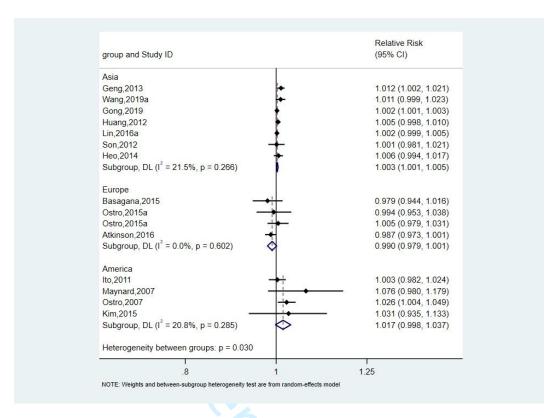
8	Reasons for downgrading											© ≤Reasons for upgrading N					Final	
10 Evidence	A1	Rationale	A2	Rationale	A3	Rationale	A4	Rationale	A5	Rationale	B1	Rationale	∑ 82 Ra	tionale	В3	Rationale	Overall	certainty
11 12 1/3 ute effects of BC 1/4 EC on CVD in 1,5 1,5 1,7 1,7 1,6 1,7 1,7 1,7 1,7 1,7 1,7 1,7 1,7 1,7 1,7	0	Little influence on the overall effect	0	All included studies were consistent with our prespecified PECOS	0	80% PI 1.005 (95%CI: 1.001, 1.009) does not include unity	0	Risk estimates reported by the studies are sufficiently precise	-1	publication bias exised, RR adjusted for publication bias with trim and fill.	0	Insufficient basis for upgrading	shift the	nders would e RR in both ections	0	Evidence of increase in risk with increasing exposure	-1	Low
18 1Acute effects of BC 20 BC or EC on CVD 21 2pPM <sub>2.5</sub> -adjusted 23bdel 24	Ō	Little influence on the overall effect	Ō	All included studies were consistent with our prespecified PECOS	0	80% PI 1.011(95%CI: 1.002, 1.020) does not include unity	0	Risk estimates reported by the studies are sufficiently precise	0	No evidence of publication bias	0	Insufficient basis for upgrading	Confou	nders would e RR in both ections	0	Evidence of increase in risk with increasing exposure	0	Moderate
25 26 ronic effects of 2√ or EC on CVD 28 rin PM2.5-unadjusted 29 300 del 31	0	Little influence on the overall effect	0	All included studies were consistent with our prespecified PECOS	0	80% PI 1.068 (95%CI: 0.965, 1.181) include unity but no larger than twice the 95%CI	0	Risk estimates reported by the studies are sufficiently precise	0	No evidence of publication bias	0	Insufficient basis for upgrading	Shift the	nders would RR in both ections	0	No evidence of a clear increasing risk with exposure	0	Moderate
32 Abbreviations:						diseases; RES: respirato							Al = limital	ions in studio	es (risk	of bias); A2 =		

Table S6 The p-value calculation process for each study using RR, CI low and CI high.

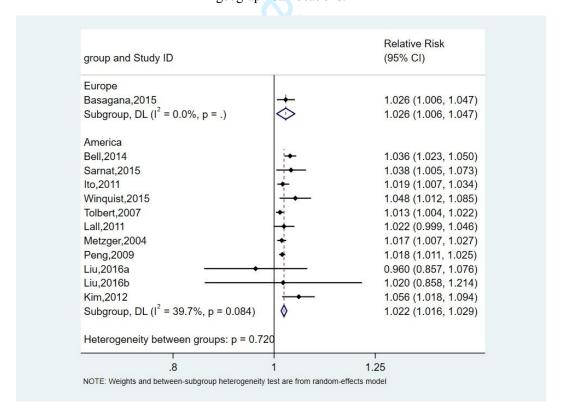
	Number	Study ID	RR	CI low	CI high	InRR	lnCI low	lnCI high	ω ≤SE a	Z	p-values
	1	Ostro,2015a	0.994000	0.953000	1.038000	0.006018	0.048140	0.037296	<b>≥</b> 0.021795	0.276122	0.782454
	2	Ostro,2015a	1.005000	0.979000	1.031000	0.004988	0.021224	0.030529	$\aleph_{0.013202}$	0.377780	0.705594
	3	Atkinson,2016	0.987000	0.973000	1.001000	0.013085	0.027371	0.001000	Q 0.007237	1.807997	0.070607
	4	Geng,2013	1.012000	1.002000	1.021000	0.011929	0.001998	0.020783	0.004792	2.489281	0.012800
	5	Liu,2016a	0.960000	0.857000	1.076000	0.040822	0.154317	0.073250	0.058053	0.703185	0.481941
	6	Liu,2016b	1.020000	0.858000	1.214000	0.019803	0.153151	0.193921	ਰੋ 0.088539	0.223661	0.823021
	7	Sarnat,2015	1.038000	1.005000	1.073000	0.037296	0.004988	0.070458	3 <sub>0.016702</sub>	2.233044	0.025546
	8	Kim,2012	1.056000	1.018000	1.094000	0.054488	0.017840	0.089841	0.018368	2.966547	0.003012
	9	Wang,2019a	1.011000	0.999000	1.023000	0.010940	0.001001	0.022739	0.006056	1.806427	0.070852
	10	Maynard,2007	1.076000	0.980000	1.179000	0.073250	0.020203	0.164667	0.047161	1.553215	0.120372
	11	Winquist,2015	1.048000	1.012000	1.085000	0.046884	0.011929	0.081580	<b>5</b> 0.017768	2.638621	0.008324
Cardiovascular Diseases	12	Tolbert,2007	1.013000	1.004000	1.022000	0.012916	0.003992	0.021761	0.004533	2.849359	0.004381
	13	Gong,2019	1.002000	1.001000	1.003000	0.001998	0.001000	0.002996	0.000509	3.923916	0.000087
	14	Ostro,2007	1.026000	1.004000	1.049000	0.025668	0.003992	0.047837	9 0.011185	2.294831	0.021743
	15	Metzger,2004	1.017000	1.007000	1.027000	0.016857	0.006976	0.026642	<u>5</u> .0.005017	3.360055	0.000779
	16	Kim,2015	1.031000	0.935000	1.133000	0.030529	0.067209	0.124869	0.048999	0.623052	0.533250
	17	Huang,2012	1.005000	0.998000	1.010000	0.004988	0.002002	0.009950	0.003049	1.635761	0.101890
	18	Son,2012	1.001000	0.981000	1.021000	0.001000	0.019183	0.020783	<b>5</b> 0.010195	0.098036	0.921904
	19	Heo,2014	1.006000	0.994000	1.017000	0.005982	0.006018	0.016857	<u>e</u> 0.005836	1.025116	0.305308
	20	Basagana,2015	0.979000	0.944000	1.016000	0.021224	0.057629	0.015873	Φ 0.018751	1.131889	0.257681
	21	Basagana,2015	1.026000	1.006000	1.047000	0.025668	0.005982	0.045929	ਰ 0.010191	2.518785	0.011776
	22	Lin,2016a	1.002000	0.999000	1.005000	0.001998	0.001001	0.004988	0.001528	1.307969	0.190884
									ed by copyri		

**Respiratory Diseases** 

1	Atkinson,2016	1.013000	0.993000	1.033000	0.012916	0.007025	0.032467	6 0.010074	1.282079	0.199815
2	Geng,2013	1.002000	0.983000	1.021000	0.001998	0.017146	0.020783	On ω 0.009676	0.206497	0.836403
3	Ostro,2015a	1.090000	1.004000	1.183000	0.086178	0.003992	0.168054	<b>≦</b> 0.041852	2.059084	0.039486
4	Ostro,2015a	1.064000	1.020000	1.110000	0.062035	0.019803	0.104360	20.021571	2.875902	0.004029
5	Sarnat,2015	0.995000	0.969000	1.022000	0.005013	0.031491	0.021761	No.013585	0.368983	0.712140
6	Huang,2012	1.005000	0.993000	1.017000	0.004988	0.007025	0.016857	0.006092	0.818666	0.412977
7	Son,2012	0.989000	0.956000	1.024000	0.011061	0.044997	0.023717	<u>0.017529</u>	0.631007	0.528036
8	Kim,2015	1.081000	0.920000	1.266000	0.077887	0.083382	0.235862	0.081440	0.956370	0.338885
9	Heo,2014	0.988000	0.962000	1.015000	0.012073	0.038741	0.014889	ਰੋ <sup>0.013681</sup>	0.882435	0.377541
10	Basagana,2015	0.986000	0.949000	1.026000	0.014099	0.052346	0.025668	₹ <sub>0.019902</sub>	0.708432	0.478677
11	Basagana,2015	0.940000	0.879000	1.006000	0.061875	0.128970	0.005982	0.034427	1.797311	0.072286
12	Maynard,2007	1.196000	1.005000	1.421000	0.178983	0.004988	0.351361	0.088361	2.025595	0.042806
13	Liu,2016a	0.964000	0.895000	1.039000	0.036664	0.110932	0.038259	0.038059	0.963352	0.335371
14	Liu,2016b	0.963000	0.806000	1.150000	0.037702	0.215672	0.139762	0.090672	0.415806	0.677552
15	Kim,2012	1.100000	0.949000	1.270000	0.095310	0.052346	0.239017	0.074327	1.282302	0.199737
16	Cakmak,2009	1.036000	1.031000	1.041000	0.035367	0.030529	0.040182	0.002462	14.36291	3.2036*10-45
17	Wang,2019a	1.038000	1.017000	1.059000	0.037296	0.016857	0.057325	9 0.010323	3.612723	0.000303
18	Tolbert,2007	0.997000	0.990000	1.003000	0.003005	0.010050	0.002996	<u>P</u> 0.003328	0.902791	0.366637
								19, 2024 by guest. Protected by copyright.		



**Figure S1** Impact of short-term exposure to BC or EC on cardiovascular mortality stratified by geographical locations.



**Figure S2** Impact of short-term exposure to BC or EC on cardiovascular morbidity stratified by geographical locations.

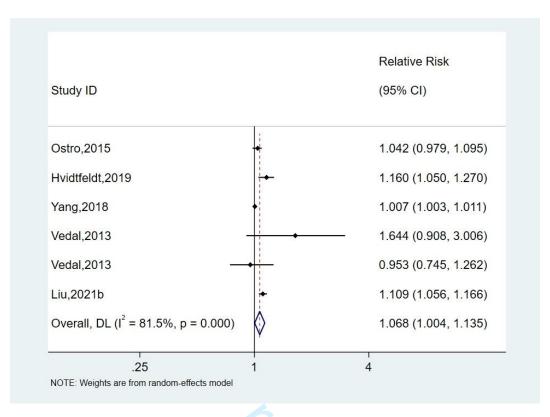
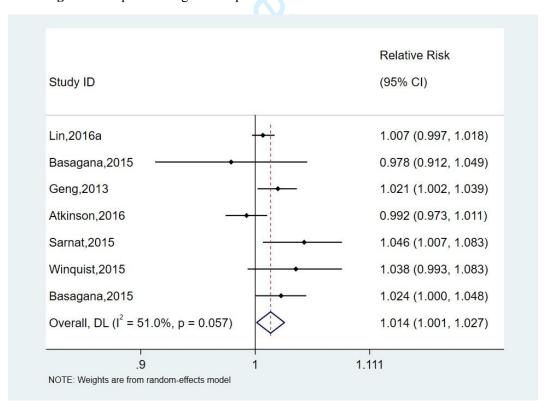


Figure S3 Impact of long-term exposure to BC or EC on cardiovascular diseases.



**Figure S4** Impact of short-term exposure to BC or EC on cardiovascular diseases in the PM<sub>2.5</sub>-adjusted model.



# PRISMA 2020 Checklist

		n-20	
Section and Topic	Item #	Checklist item 27-04 95	Location where item is reported
TITLE		50	
Title	1	Identify the report as a systematic review.	#1
ABSTRACT	I		
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	#3-4
INTRODUCTION			W0.0
2 Rationale	3	Describe the rationale for the review in the context of existing knowledge.	#6-8
3 Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	#8
METHODS			"0
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	#9
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to Hentify studies. Specify the date when each source was last searched or consulted.	#8-9
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	#8-9
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	#10
2 Data collection 3 process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each reports whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	#10-11
5 Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	#10-11
27 28	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	#10-11
9 Study risk of bias 0 assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	#11-12
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	#11
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	#11
5	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	#11, 14-15
7	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	#11
3	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	#11-12
9 . <b>0</b>	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	#11-12
-1	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	#11-12
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	#12
Certainty	15	Describe any methods usethtopassess/certainty (drtcpnfildenjce)-in.the/bodyn/driev/ldence/fon/ah-butcomhem/	#11
6	l .	- Francis A. Calante Management and an administration	



47

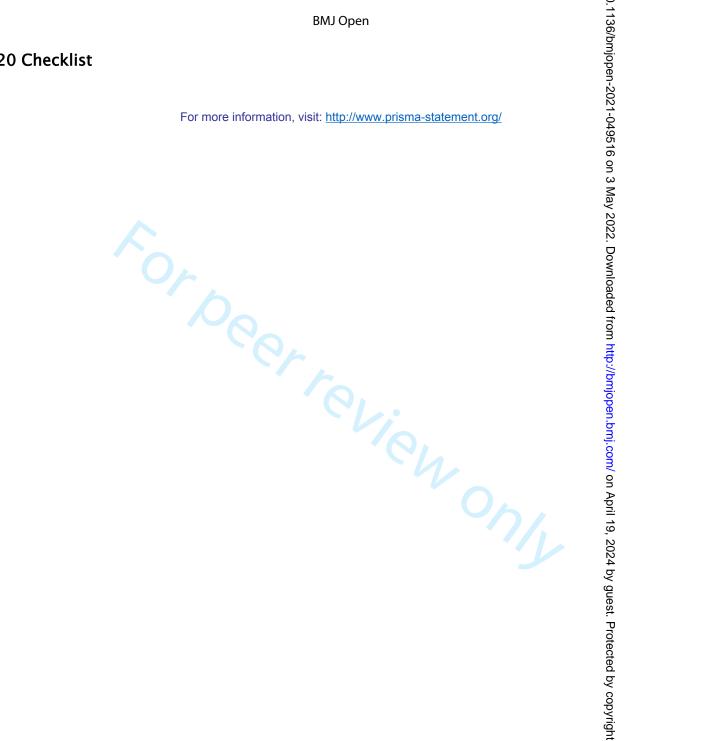
# PRISMA 2020 Checklist

		BMJ Open 33	Page 136 of 13
PRIS	SMA 2	2020 Checklist	
Section and Topic	Item #	Checklist item Checklist item	Location where item is reported
assessment			
RESULTS		0	
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	#15
<b>0</b> 1	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	#15
Study characteristics	17	Cite each included study and present its characteristics.	#15
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	#22
6 Results of rindividual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	#15-18
Results of	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	#23-24
syntheses	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	#18
1	20c	Present results of all investigations of possible causes of heterogeneity among study results.	#19-21
<del>2</del> 3	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	#21
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	#22-24
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	#22
DISCUSSION		<u> </u>	
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	#25-29
9	23b	Discuss any limitations of the evidence included in the review.	#29-30
1	23c	Discuss any limitations of the review processes used.	#29-30
2	23d	Discuss implications of the results for practice, policy, and future research.	#28-29
OTHER INFORMA	TION	<u>Q</u>	
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	#8
protocol	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	#8
<b>7</b>	24c	Describe and explain any amendments to information provided at registration or in the protocol.	#8
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the rediew.	#34
Competing interests	26	Declare any competing interests of review authors.	#35
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	#36

10.1136/bmj.n71

PRISMA 2020 Checklist

For more information, visit: http://www.prisma-statement.org/



# **BMJ Open**

### Is Short-term and Long-term Exposure to Black Carbon Associated with Cardiovascular and Respiratory Diseases? A Systematic Review and Meta-Analysis based on Evidence Reliability

Journal:	BMJ Open			
Manuscript ID	bmjopen-2021-049516.R3			
Article Type:	Original research			
Date Submitted by the Author:	18-Mar-2022			
Complete List of Authors:	Song, Xuping; Lanzhou University, School of Public Health Hu, Yue; Lanzhou University, School of Public Health Ma, Yan; Lanzhou University, School of Public Health Jiang, Liangzhen; Lanzhou University, School of Public Health Wang, Xinyi; Lanzhou University, Second Clinical College Shi, Anchen; Xi'an Jiaotong University Medical College First Affiliated Hospital, Department of General Surgery Zhao, Junxian; Lanzhou University, School of Public Health Liu, Yunxu; Lanzhou University, School of Public Health Tang, Jing; Lanzhou University, School of Public Health Li, Xiayang; Lanzhou University, School of Public Health Li, Xiayang; Chengdu University of Information Technology, College of Atmospheric Sciences Guo, Yong; Guizhou Province Wang, Shigong; Chengdu University of Information Technology, College of Atmospheric Sciences			
<b>Primary Subject Heading</b> :	Public health			
Secondary Subject Heading:	Cardiovascular medicine, Respiratory medicine			
Keywords:	PUBLIC HEALTH, RESPIRATORY MEDICINE (see Thoracic Medicine), CARDIOLOGY			

SCHOLARONE™ Manuscripts



I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

# **Title Page**

#### Title:

Is Short-term and Long-term Exposure to Black Carbon Associated with

Cardiovascular and Respiratory Diseases? A Systematic Review and Meta-Analysis

based on Evidence Reliability

# **Author names and affiliations:**

1. Xuping Song<sup>a</sup> E-mail: songxp@lzu.edu.cn

2. Yue Hu<sup>a</sup> E-mail: huy20@lzu.edu.cn

3. Yan Ma<sup>a</sup> E-mail: may2020@lzu.edu.cn

4. Liangzhen Jiang<sup>a</sup> E-mail: jianglzh19@lzu.edu.cn

5. Xinyi Wang<sup>c</sup> E-mail: wangxinyi17@lzu.edu.cn

6. Anchen Shi<sup>d</sup> E-mail: 3120115202@stu.xjtu.edu.cn

7. Junxian Zhao<sup>a</sup> E-mail: zhaojx2017@lzu.edu.cn

8. Yunxu Liu<sup>a</sup> E-mail: yxliu17@lzu.edu.cn

9. Yafei Liu<sup>a</sup> E-mail: isak-even@qq.com

10. Jing Tang<sup>a</sup> E-mail: tangj19@lzu.edu.cn

11. Xiayang Li<sup>a</sup> E-mail: lixiayang 18@lzu.edu.cn

10. Xiaoling Zhang<sup>b</sup> E-mail: xlzhang@ium.cn

11. Yong Guo<sup>e</sup> E-mail: gycau@qq.com

12. Shigong Wang<sup>b</sup> E-mail: wangsg@lzu.edu.cn

<sup>&</sup>lt;sup>a</sup> School of Public Health, Lanzhou University, Lanzhou 730000, China;

<sup>&</sup>lt;sup>b</sup> College of Atmospheric Sciences, Chengdu University of Information Technology,

Chengdu 610000, China;

<sup>c</sup> Second Clinical College, Lanzhou University, Lanzhou 730000, China;

<sup>d</sup> Department of General Surgery, The First Affiliated Hospital of Xi'an Jiao Tong

University, Shaanxi 710061, China;

<sup>e</sup> Department of Civil Affairs in Guizhou Province, Guiyang 550004, China.

# **Corresponding author 1:**

Name: Xiaoling Zhang

Postal Address: College of Atmospheric Sciences, Chengdu University of Information

Technology, Chengdu 610000, Sichuan, China

E-mail address: xlzhang@ium.cn

Fax: 028-85966502

#### **Corresponding author 2:**

Name: Shigong Wang

Postal Address: College of Atmospheric Sciences, Chengdu University of Information

Technology, Chengdu 610000, Sichuan, China

E-mail address: wangsg@cuit.edu.cn

Fax: 028-85966502

#### **Abstract**

**Objective** Adverse health effects of fine particles ( $PM_{2.5}$ ) have been well documented by a series of studies. However, evidences on the impacts of black carbon (BC) or elemental carbon (EC) on health are limited. The objectives were (i) to explored the effects of BC and EC on cardiovascular and respiratory morbidity and mortality; (ii) to verified the reliability of the meta-analysis by drawing p-value plots.

**Design** The systematic review and meta-analysis using adapted Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach and p-value plots approach.

**Data sources** PubMed, Embase and Web of Science were searched from inception to July 19<sup>th</sup>, 2021.

**Eligibility criteria for selecting studies** Time series, case crossover and cohort studies that evaluated the associations between BC/EC on cardiovascular or respiratory morbidity or mortality were included.

**Data extraction and synthesis** Two reviewers independently selected studies, extracted data, and assessed risk of bias. Outcomes were analyzed via a random effects model and reported as relative risk (RR) with 95% confidence interval (CI). The certainty of evidences were assessed by adapted GRADE. The reliabilities of meta-analyses were analyzed by p-value plots.

**Results** Seventy studies met our inclusion criteria. (i) Short-term exposure to BC/EC was associated with 1.6% (95% CI: 0.4%-2.8%) increase in cardiovascular diseases per 1  $\mu$ g/m³ in the elderly; (ii) Long-term exposure to BC/EC was associated with

6.8% (95% CI: 0.4%-13.5%) increase in cardiovascular diseases; (iii) The p-value plot indicated that the association between BC/EC and respiratory diseases was consistent with randomness.

**Conclusions** Both short-term and long-term exposures to BC/EC were related with cardiovascular diseases. However, the impact of BC/EC on respiratory diseases did not present consistent evidence and further investigations are required.

PROSPERO registration number CRD42020186244.

### Strengths and limitations of this study

- 1. Adapted GRADE (Grading of Recommendations assessment, Development and Evaluation), formulated by the WHO global air quality guidelines working group, was used to evaluate the certainty of evidence.
- 2. This study incorporated a detailed search strategy, explicit literature screening and risk of bias assessment.

- 3. The p-value plots were used to evaluate the reliabilities of meta-analyses.
- 4. Limitation on searching grey literature should be noted.

#### 1. Background

Black carbon (BC), a ubiquitous component of air particulate matter, is usually measured through optical absorption. Elemental carbon (EC), another carbonaceous material with a graphitic structure, is commonly measured by thermal or thermo-optical method.<sup>1, 2</sup> Although the measurement methods are different, BC and EC are often considered interchangeable. BC is mainly emitted from traffic and combustion-related sources and is a measured component of the particulate matter (PM). The adverse health effects of PM, especially PM<sub>2.5</sub>, are well documented. In 2017, a total of 2.94 million deaths resulted from ambient PM worldwide.<sup>3-5</sup> PM<sub>2.5</sub> is composed of various constituents, in which some of them are more toxic and hypothesized as the main cause of the adverse effects of PM2.5. A growing body of studies indicates a potential role of BC among these more toxic constituents.<sup>6, 7</sup> In addition, some reviews demonstrated that BC is a better indicator of adverse effects of PM from combustion sources according to robust associations from epidemiological studies.<sup>8, 9</sup> The underlying pathological mechanisms of BC include oxidative stress, inflammation and gene mutations. 10-12

Due to its association with adverse health, the number of studies exploring the effects of BC on cardiorespiratory diseases has rapidly increased in recent years. Cardiovascular and respiratory diseases are common diseases worldwide, with a heavy disease burden and major implications for clinical practice and public health. The global burden of disease study 2017 indicated that cardiovascular and respiratory-related death ranked first and third respectively among non-communicable

diseases.<sup>4</sup> Health effects of acute and chronic exposure to BC have been widely reported. Despite that there is some epidemiological evidence that BC was associated with cardiorespiratory diseases, in other studies, no statistically effects were observed.

The reliability of air quality epidemiological studies is often poor, with a serious lack of reproducibility of published findings.<sup>13</sup>

A lack of reproducibility in epidemiological studies can be attributed to many factors, but p-hacking are most common issue. If researchers run a regression with and without outliers, with and without a covariate, with one and then another dependent variable, then false positive results are much more likely to be reported. There can be a selective reporting problem (compute many tests and selectively report small p-values), which is referred to p-hacking.<sup>14</sup> When a study examines many questions, tests numerous statistical models and does not perform multiple testing statistical corrections, P-hacking is referred to as multiple testing and multiple modelling (MTMM).<sup>15, 16</sup> Since the uncorrected statistical estimates are likely not unbiased, the results of meta-analysis may unreliable. Therefore, it is essential to exploring the p-values in meta-analysis.

Some systematic reviews analyzed the impact of BC on health. Nevertheless, quantitative associations between BC exposure and cardiovascular and respiratory diseases have not been well-characterized due to different objectives of the reviews.<sup>17,</sup>

18 A series of eligible studies published recently have not been considered. In addition, the GRADE (Grading of Recommendations assessment, Development and Evaluation) framework was not adopted in previous systematic reviews. Compared

with Yang et al. 2019<sup>19</sup>, this study included recently published eligible studies. Furthermore, meta-analysis of BC effects on vulnerable populations and geographical regions were conducted. Moreover, based on a p-value plot, the reliability of meta-analysis was performed. Therefore, a systematic review and meta-analysis was performed to further elucidate the health effects of BC/EC in this study. The objectives were (1) to investigate the association of short-term and long-term exposure to BC/EC with the respiratory and cardiovascular morbidity and mortality; (2) to verify the reliability of the meta-analysis using p-value plots.

#### 2. Methods

The protocol was published online at the PROSPERO (registration number: CRD42020186244).

#### 2.1 Patient and public involvement

Patients or the public were not involved in this study.

#### 2.2 Database

PubMed, Web of Science and Embase databases were systematically searched using the following terms: (black carbon\* or elemental carbon\*) AND (respiratory\* or cardiovascular\*) AND (morbidit\* or hospitalization\* or death\* or mortalit\* or outpatien\*) AND (time series\* or case cross\* or cohort\*)". We limited our search to studies from inception to July 19th, 2021. In addition, the reference lists of the included studies and related reviews were manually evaluated to identify additional relevant studies. The details of the search strategy in PubMed were shown in Table S1.

#### 2.3 Inclusion and exclusion criteria

A time series study, case crossover study or cohort study that evaluated the impact of BC/EC on cardiovascular or respiratory diseases was included in this systematic review and meta-analysis. Studies were considered eligible for inclusion if they fulfilled the inclusion criteria as follows: (1) study types restricted to time series, case crossover or cohort studies; (2) studies considering BC/EC as air pollutants; (3) based on the International Classification of Diseases (ICD) 9th or 10th revision, diseases included respiratory diseases, wheeze, other respiratory distress insufficiency or respiratory cancer (ICD-9 codes 460–519, 786.07, 786.09 or 162; ICD-10 codes J00–J99, R06.251, R06.001 or C34) or cardiovascular diseases (ICD-9 codes 390–459, ICD-10 codes I00–I99); (4) studies considering morbidity or mortality as outcome; (5) estimates were odds ratio (OR), relative risk (RR) or hazard ratio (HR) with 95% confidence interval (CI) or enough information for their calculation; (6) publication language was restricted to English.

The exclusion criteria were as follows: (1) studies on soot or black smoke were excluded, because the definition of such components usually lacked precision; (2) studies assessing the disease progression exposure to pollutants in individuals with cardiovascular or respiratory diseases (for example chronic obstructive pulmonary disease and asthma); (3) studies focusing on particular populations (for example pregnant women and miners) or population living in specific environments with high pollution concentration (for example residential area near industrial complexes, population exposed to sugar cane burning and neighborhoods that expose many

streets); (4) studies focusing on seasonality; (5) conference abstracts; (6) study period less than 1 year.

#### 2.4 Selection of articles and extraction of data

To identify eligible studies, two investigators independently screened titles and abstracts. Studies whose relevance could not be determined by titles and abstracts were subjected to full text screening. Any disagreement was resolved by discussion. A third investigator was involved in the discussion when a consensus could not be reached.

Two reviewers independently extracted the following items from each included study. Study characteristics were extracted using a standardized form that included but was not limited to the following items: first author, publication year, country, study design, diagnosis standard, time period, population age, statistical models, air pollutants, outcomes and number of events. If the reported data of the included studies were unclear or missing, the first author or corresponding author was contacted by e-mail. Any conflicts were resolved by the involvement of a third investigator if the controversy was not solved after the discussion.

#### 2.5 Data synthesis

Regarding the meta-analysis, the RR was used as an effect estimate, and the OR in case crossover study and HR in cohort study were considered equivalent to RR. Estimates from the maximally adjusted model in the cohort study were extracted when multiple estimates were present in the original study to reduce the risk of potential unmeasured confounding.<sup>20</sup> In addition, the estimate was converted to a

standardized increment (1  $\mu$ g/m³) of RR. The following formula was used to calculate standardized risk estimates:

 $RR_{(standardized)} = RR_{(original)}^{Increment(1)/Increment(original)}$ 

Two studies did not show the overall risk, while stratified risk estimates by age and location were reported.<sup>21, 22</sup> In this case, the stratified estimates were pooled. One study presented the estimates of both morbidity and mortality, which were combined in the overall analysis.<sup>23</sup> In addition, if the same cohort data were analyzed in different studies and the latest study was included.<sup>24-26</sup>

#### 2.6 Risk of bias assessment

The risk of bias was assessed for each study according to the Office of Health Assessment and Translation (OHAT) tool and the Navigation Guide tool. 17, 27, 28 Risk of bias evaluation was conducted as follows: exposure assessment, outcome assessment, confounding bias, selection bias, incomplete outcome data, selective reporting, conflict of interest and other bias. Each domain was considered as "low", "probably low", "probably high", "high", or "not applicable" criteria. Two investigators conducted the risk of bias evaluation. Any inconsistency between the investigators was discussed and a third researcher was involved to resolve any disagreement.

#### 2.7 Evaluation of certainty of evidence

An adaptation of the GRADE (Grading of Recommendations assessment, Development and Evaluation) framework, formulated by the WHO (World Health Organization) global air quality guidelines working group, was used to evaluate the

certainty of evidence.<sup>29</sup> The rating process on the certainty of evidence started at moderate. The certainty was graded into four levels: "high", "moderate", "low" and "very low". Five reasons were used to downgrade the certainty of evidence: limitations in studies, indirectness, inconsistency, imprecision, and publication bias; 3 reasons were used to upgrade: large magnitude of effect size, all plausible confounding shifts the relative risk towards the null and concentration-response gradient. To evaluate the magnitude of the effect size, the E-value was calculated using the following formula:

 $E - value = RR + sqrt\{RR * (RR - 1)\}$ 

#### 2.8 Statistical analysis

Statistical analysis was performed using STATA (version12.0, Stata Corp, College Station, TX, USA). In this meta-analysis, the random-effects model was conducted for anticipating significant heterogeneity among studies. Heterogeneity among trials was assessed by the Chi-square test and the extent of inconsistency was evaluated by the  $I^2$ . An 80% prediction interval (PI) of meta-estimate was calculated to assess the inconsistency. To assess potential sources of heterogeneity, subgroup analyses were performed on outcomes (morbidity and mortality), single lag days (0, 1 and 2 days), study areas (Europe, America, and Asia) and seasons (warm and cold). The estimates from BC and EC were combined, since both of them are indicators of carbon-rich combustion sources, and are usually considered interchangeable in medical research.

Estimates were pooled separately where more than three estimates were

available. Most studies presented estimates for single lags and the estimate of shortest lag was used to combine the estimates (RRs) of shortest lag in meta-analysis. However, only a few studies presented cumulative lags, and the estimates of shortest cumulative lags were used in the meta-analysis. In addition, Mostofsky et al. indicated that PM<sub>2.5</sub> is a potential confounder in assessing the health effects of PM<sub>2.5</sub> constituents.<sup>7</sup> For overall and outcome analysis, PM<sub>2.5</sub>-adjusted estimates and PM<sub>2.5</sub>-unadjusted estimates in the models were combined, respectively where more three estimates were available. Regarding the subgroup PM<sub>2.5</sub>-unadjusted estimates were analyzed, while PM<sub>2.5</sub>-adjusted estimates were not presented due to the limited number of included studies. Moreover, primary data of the included studies could not be obtained, hence it was impossible to evaluate whether the same patients were repeatedly included across multiple studies. Therefore, the sensitivity analysis was performed on all age populations to investigate the robustness of the aggregation results by the removal of studies with partial temporal overlap from the same geographical location. Most of the included studies analyzed and presented results of cardiovascular or respiratory diseases, hence systematic diseases were analyzed in the acute effect analysis, except for the chronic effect analysis. Publication bias was assessed by Egger's regression test when the outcome included more than 10 studies. Trim and fill method was used to correct on asymmetry for the outcome with publication bias. p < 0.05 was considered statistically significant.

Non-traditional methods were used to assess the reliability of basic studies,

which is different from mainstream environmental epidemiology. Studies with large analysis search spaces suggest the use of a large number of statistical models and statistical tests for an effect, thereby allowing greater flexibility of researchers to selectively search through and only report results showing positive effects. 15 studies included in the meta-analysis were randomly selected. Number of outcomes, predictors, and covariates were counted. We computed the search spaces as follows: Space1 is outcome times predictor times lags. Space2 is 2<sup>covariate</sup>. Space3 is Space1 times Space2. Space3 is the total analysis search space. Search spaces were computed by the method introduced in Young et al, 2019.<sup>30</sup>

The p-value plot was used to inspect the distribution condition of the p-values.<sup>31</sup> Regardless of sample size, the p-value is distributed uniformly between 0 to 1 under the null hypothesis. If the shape of p-value plot is a straight line, the p-values are in a distribution of true null hypothesis.<sup>31</sup> If the shape follows an approximate 45-degree line, the p-values are assumed to be random. If the shape is approximately a hockey stick, the p-values on the blade are unlikely due to chance. Therefore, p-value plot was used to assess the validity and reliability of included studies.

P-values of included studies were computed using RR, low CI and high CI.

Then, the p-values were ranked from smallest to largest using 1, 2, 3... and the plots were constructed. The following formulas were used to calculate p-value:

$$SE = (lnCI high - lnCI low)/2/1.96$$

$$Z = lnRR/SE$$

$$p - value = \{1 - NORMSDIST[ABS(Z)]\} * 2$$

#### 3. Results

A total of 1694 studies were initially identified and 129 were reviewed in depth. We excluded the studies which study period less than 1 year or same data were analyzed in different studies.<sup>32, 33</sup> Of these, 70 fulfilled the inclusion criteria (Figure 1).<sup>7,21-26,34-96</sup> Of the 70 included studies, 56 estimated the short-term effects of BC/EC using a time series design or case crossover design, while 14 studies explored the long-term effects of BC/EC using a cohort design. Thirty-seven of the 70 studies reported morbidity as the outcome variable, 25 studies reported mortality, and 8 studies reported both morbidity and mortality. Thirty-five studies analyzed both cardiovascular and respiratory diseases, 18 studies merely investigated cardiovascular diseases, and 17 studies assessed respiratory diseases. Thirty-seven studies were conducted in the United States, 14 in China, 4 in Canada, 2 in the United Kingdom, Sweden, Korea and Serbia, 1 in Denmark, Iran, Germany and the Netherlands. The remaining 3 studies collected data from two different countries: Spain and Greece, Spain and Italy, Sweden and Denmark. Twenty-seven studies classified the diseases using the ICD-9 codes, 26 used the ICD-10 codes, and 10 used both the ICD-9 and ICD-10 codes. However, the remaining 7 studies did not employ the ICD standards (Table S2). In addition, the authors of 33 studies were contacted, but only 19 answered our request (response rate: 57.6%).

#### 3.1 Short-term effect of BC/EC on cardiovascular and respiratory diseases

Overall, short-term exposure to BC/EC was associated with an increased risk of cardiovascular diseases (RR=1.007 per 1  $\mu$ g/m³, 95% CI: 1.002–1.011) (adjusted by

trim and fill method) in overall analyses (Table 1 and Figure 2). Cardiovascular diseases (RR=1.016 per 1  $\mu$ g/m³, 95% CI: 1.004–1.028) were associated with BC/EC in the elderly (65+ years). (Figure 2)

Impact of BC/EC on cardiovascular diseases was related to the exposure lag. The estimates of the association were strongest on the day of the event (lag 0) (RR=1.011 per 1  $\mu$ g/m<sup>3</sup>, 95% CI: 1.006–1.016), and then diminished on lag 1 (RR=1.005 per 1  $\mu g/m^3$ , 95% CI: 1.002–1.008) and lag 2 (RR=1.002 per 1  $\mu g/m^3$ , 95% CI: 0.999– 1.005) (Table S3). Subgroup analyses on geographical location was performed for morbidity and mortality, respectively. Significant association between BC/EC and cardiovascular mortality was observed in Asia (RR=1.003, 95% CI: 1.001-1.005). However, no association was found in America (RR=1.017, 95% CI: 0.998–1.037) and Europe (RR=0.990, 95% CI: 0.979-1.001) (Figure S1). On the other hand, an increased risk of cardiovascular morbidity was observed in America (RR=1.022, 95%) CI: 1.016–1.029) with short-term exposure to BC/EC, while only one study performed in Europe (RR=1.026, 95% CI: 1.006–1.047) investigated the short-term effect of BC/EC on cardiovascular morbidity.<sup>23</sup> In addition, just one study in Asia performed the short-term effects of BC/EC on stroke morbidity (Figure S2).<sup>66</sup>

No association was observed between short-term exposure of BC/EC and respiratory morbidity (RR=1.012, 95% CI: 0.993–1.031) and mortality (RR=1.013, 95% CI: 0.997–1.030) (Table 1).

Table 1 Short-term impacts of BC/EC on cardiovascular and respiratory diseases in different models

	PM <sub>2.5</sub> -unadjusted model					ω PM <sub>2.5</sub> -adjusted model			
Subgroup Analysis	No. of Studies	No. of Estimates	Relative Risk (95%CI)	I <sup>2</sup>	Egger regression test (p value)	No. of Studies	No. of Estimates	Relative Risk (95%CI)	I <sup>2</sup>
Cardiovascular Diseases						22. [			
Age						Jown			
All population	20	22	1.008 (1.004, 1.012)	64.40%	0.007	6 ac	7	1.014 (1.001, 1.027)	51.00%
Relative risk adjusted for publication bias with trim and fill method	24	26	1.007 (1.002, 1.011)	_	_	ed fro	_	_	_
Sensitive analysis on study of partial temporal overlap from the same geographical location	16	16	1.006 (1.002, 1.010)	60.00%	0.020	Downloaded from http://bmjopen.bmj.com/ on	_	_	
≥65 years	5	6	1.016 (1.004, 1.028)	87.40%	_	- //bn	_	_	_
Outcome						njope			
Morbidity	12	12	1.022 (1.016, 1.029)	37.20%	0.163	4 en.b	5	1.018 (1.006, 1.031)	39.50%
Mortality	14	15	1.003 (1.001, 1.006)	29.70%	0.266	4 <u>a</u> j. g	4	1.006 (0.993, 1.019)	42.90%
Respiratory Diseases						om/ c			
Age						on A			
All population	16	18	1.010 (0.996, 1.025)	87.20%	0.627	April 1	8	1.002 (0.990, 1.014)	43.80%
Sensitive analysis on study of partial temporal overlap from the same geographical location	12	12	1.008 (0.992, 1.023)	90.30%	0.449	9, 2024	_	_	_
≥65	3	4	1.038 (1.006, 1.071)	82.90%	_	– 14 by	_	_	_
Outcome						guest.			
Morbidity	10	10	1.012 (0.993, 1.031)	91.80%	0.671	3 St. P	5	0.996 (0.987, 1.004)	0
Mortality	10	11	1.013 (0.997, 1.030)	66.40%	0.328	3 P	3	1.017 (0.985, 1.050)	48.30%
						cted by o			

# 3.2 P-value plots of short-term exposure to BC/EC on cardiovascular and respiratory diseases in the $PM_{2.5}$ -unadjusted model

We chose at random 15 studies included in the meta-analysis. Then, we extracted analysis items (outcomes, predictors, covariates, and lags) and calculated the search spaces. Table 2 listed the counts of outcomes, predictors, covariates and lags for the 15 studies. There were many thousands of possible analysis options in each of the randomly selected studies and summary statistics of the numbers of options are given in Table S4. Across the studies, the median number of possible analyses was 12,000 (interquartile range 2,688–15,360) for Space3, which took all the factors into account.

In Figure 3, the plot of cardiovascular studies showed a shape of hockey stick. There were nine p-values less than 0.05 and thirteen larger than 0.05 (Table S8). The smallest p-value in cardiovascular group was 0.000087 and the largest was 0.921904, which was of a wide range. The association between BC and cardiovascular diseases were consistent with a mixture based on p-values and p-value plot. We did not find a consistent effect so there is no proof of a causal effect. The shape of the plot on the impact of BC on respiratory diseases was close to 45-degree line. Four calculated p-values were less than 0.05, while fourteen were larger than 0.05 and fell on an approximate 45-degree line (Table S8). In addition, the smallest p-value was 3.2036\*10<sup>-45</sup> and the largest was 0.836403. The smallest p-value was so small that p-hacking (or even data fabrication) may exist. As the p-value plot's shape approached a 45-degree line, the impact of short-term exposure to BC/EC on respiratory diseases was likely to be random.

Table 2 Variable counts, and analysis search spaces for the 15 studies chosen from the meta-analysis.

Number	Study	Outcome	Predictor	Covariate	Lag	Space1	Space2	Space3
1	Atkinson,2016	3	7	6	2	42	64	2688
2	Geng,2013	3	1	5	3	9	32	288
3	Sarnat,2015	8	22	5	4	704	32	22528
4	Kim,2012	3	5	6	15	225	64	14400
5	Maynard,2007	4	2	5	1	8	32	256
6	Winquist,2015	4	8	6	3	96	64	6144
7	Gong,2019	1	2	7	9	18	128	2304
8	Huang,2012	3	13	6	7	273	64	17472
9	Basagana,2015	5	16	6	3	240	64	15360
10	Son,2012	3	11	5	7	231	32	7392
11	Heo,2014	3	9	7	4	108	128	13824
12	Kim,2015	5	5	5	15	375	32	12000
13	Tolbert,2007	2	13	7	3	78	128	9984
14	Wang,2019a	3	6	6	11	198	64	12672
15	Metzger,2004	6	14	5	8	672	32	21504

#### 3.3 Long-term impact of BC/EC on cardiovascular and respiratory diseases

Five studies assessed the long-term exposure to BC/EC and cardiovascular diseases, and a positive association was observed (RR=1.068, 95% CI: 1.004-1.135) (Figure S3). Three studies assessed the long-term exposure to BC/EC and ischemic heart disease (IHD), and a positive association was observed (RR=1.066, 95% CI: 1.009-1.127). On the other hand, 4 studies assessed the long-term exposure to BC/EC and respiratory mortality. Meta-analysis was not performed due to limited included studies and no association was observed among the include studies.<sup>25, 60, 68, 75</sup> However, one study analyzed COPD. It indicated that long-term exposure to BC/EC was associated with an increased risk of chronic obstructive pulmonary disease (COPD) morbidity (RR=1.060, 95% CI: 1.020-1.100), while no impact was observed for COPD mortality (RR=1.070, 95% CI: 1.000-1.140).<sup>24</sup>

#### 3.4 Results from the PM<sub>2.5</sub>-adjusted model

In the  $PM_{2.5}$ -adjusted model, six studies were included in the meta-analysis of

short-term exposure to BC/EC and cardiovascular diseases (RR=1.014 per 1  $\mu$ g/m³, 95% CI: 1.001-1.027) (Figure S4). The meta-analysis indicated that the association was robust compared to the results of the PM<sub>2.5</sub>-unadjusted model. In addition, the impact of BC/EC on cardiovascular morbidity in the PM<sub>2.5</sub>-adjusted model (RR=1.018 per 1  $\mu$ g/m³, 95% CI: 1.006-1.031) was consistent with the results in the PM<sub>2.5</sub>-unadjusted model (RR=1.022 per 1  $\mu$ g/m³, 95% CI: 1.016-1.029). However, an increased risk was found between BC/EC and cardiovascular mortality in the PM<sub>2.5</sub>-unadjusted model (RR=1.003 per 1  $\mu$ g/m³, 95% CI: 1.001-1.006), while no association was observed in the PM<sub>2.5</sub>-adjusted model (RR=1.006 per 1  $\mu$ g/m³, 95% CI: 0.993-1.019) (Table 1).

#### 3.5 Sensitive analysis

In the sensitive analysis, similar results were observed from the overall analysis of all age populations. Increased risk of cardiovascular diseases after exposure to BC/EC was found (RR=1.006 per 1  $\mu$ g/m³, 95% CI: 1.002-1.010) by eliminating studies with partial overlap from the same geographical location.<sup>21, 23, 38, 80</sup> In addition, no statistical significance was observed (RR=1.008 per 1  $\mu$ g/m³, 95% CI: 0.992-1.023) between respiratory diseases and BC/EC after eliminating overlapped studies (Table 1).<sup>21, 23, 88, 94</sup>

#### 3.6 Risk of bias and certainty of evidence

The risk of bias assessment of the included studies is shown in Table S5 and more analytically in Table S6. In general, the majority of the included studies were rated as "low risk" in the items of outcome assessment, selection bias, incomplete

outcome data, conflict of interest and other bias. The confounding bias and selective reporting were mostly rated as "probably low". However, 7 studies were rated as "probably high" risk because not all critical potential confounders were adjusted in the analysis. 7, 24, 26, 46, 55, 74, 91 In addition, the majority of the included studies on the exposure assessment were assessed as "probably low" and "probably high", and in some cases studies were rated as "high" risk. Three studies were rated as "high risk" on exposure assessment mainly because pollutants were measured with a single monitoring over a large geographical area, and not measured at least daily. 53, 85, 92

The certainty of evidence on the acute effects of BC/EC on cardiovascular diseases in the  $PM_{2.5}$ -adjusted model was rated as "moderate" and in the  $PM_{2.5}$ -unadjusted model was rated as "low". The evidence on the chronic effects of BC/EC on cardiovascular diseases was evaluated as "moderate" certainty (Table S7).

#### 4. Discussion

A comprehensive search of three electronic databases was performed using a well-defined search strategy. Finally, 70 studies assessing the short-term and long-term impacts of BC/EC on cardiovascular and respiratory morbidity and mortality were included. Using a random effects model, the pooled effect estimates indicated that the short-term exposure to BC/EC was associated with an increased risk of cardiovascular diseases, but not on respiratory diseases in all populations. BC/EC was associated with cardiovascular diseases in the elderly (65+ years). In addition, association between short-term exposure to BC/EC and cardiovascular diseases differ across continents.

# 4.1 Short-term exposure to BC/EC was related with cardiovascular diseases in the elderly

Overall, the meta-analysis results indicated that short-term exposure to BC/EC was associated with an increased risk of cardiovascular diseases, but not on respiratory diseases in all populations. In general, the PM<sub>2.5</sub>-adjusted model and the PM<sub>2.5</sub>-unadjusted model and sensitivity analysis showed that the associations were consistent. In contrast to the meta-analysis calculations, p-value plots indicated mixed results for cardiovascular. Some studies indicated an effect while others appeared to be random. For respiratory effects, the p-value plot was consistent with randomness, no effect. Our counting results, Table 2 and Table S4 indicated that small p-values could be the result of multiple testing/multiple modeling.

However, the association between BC/EC and cardiovascular mortality should be further explored by further studies, which should pay more attention to the PM<sub>2.5</sub>-adjusted model. Subgroup analysis indicated that the effects of BC/EC on cardiovascular diseases were the most significant on the current day and the impacts were decreased with lag days. In addition, the association between BC/EC and cardiovascular mortality in the cold season was stronger than that in the warm season. A potential reason could be that the concentration of BC/EC in the cold season was higher than that in the warm season. 97-99 Subgroup analysis on pollutant (BC and EC) indicated that the results from the PM<sub>2.5</sub>-unadjusted model and PM<sub>2.5</sub>-adjusted model were not consistent. Furthermore, the sensitivity analysis on omitting a single study showed that the results were not robust (data not shown). An essential reason could be

that BC and EC were considered interchangeable. Three included studies simultaneously assessed the effects of BC/EC on cardiovascular diseases. 22, 63, 93 However, in the PM<sub>2.5</sub>-adjusted model, no statistically significant difference was observed between EC (RR=1.039, 95% CI: 0.993–1.083) and cardiovascular morbidity. In addition, Samoli et al illustrated that the impact of BC/EC on cardiovascular morbidity differed in the elderly and other age groups, while Atkinson et al indicated no statistically significant difference between BC/EC and cardiovascular mortality in both the PM<sub>2.5</sub>-adjusted model and PM<sub>2.5</sub>-unadjusted model. 22, 85 On the other hand, increased risk of long-term exposure to BC/EC and cardiovascular diseases was observed. However, in this meta-analysis, due to the limited number of included studies, only short-term exposure to asthma morbidity was evaluated. In addition, a subgroup analysis on the chronic effects of BC/EC on cardiovascular and respiratory diseases was not performed because of the limited number of included studies.

The overall quality of acute effects of BC/EC on cardiovascular diseases in all populations in the PM<sub>2.5</sub>-unadjusted model was evaluated as "moderate". We downgraded one level for publication bias, hence the estimate was adjusted using the trim and fill method.<sup>29</sup> In addition, inconsistency was not downgraded because 80% PI does not included unity, or it included unity but less than twice the 95% CI.

#### 4.2 Vulnerable populations

This meta-analysis revealed that BC/EC may have acute effects on cardiovascular diseases in the elderly. 100 In addition, lung function and mucociliary

clearance decline with long-term exposure to pollutants and increasing age.<sup>5, 101</sup> These factors might contribute to making the elderly more vulnerable to BC. On the other hand, this meta-analysis indicated that an increased risk was observed between BC/EC and asthma morbidity in children of 0-18 years. Asthma, a chronic airway disorder, is a serious health disease and previous studies indicated that children have higher  $PM_{2.5}$  deposition rather than the adults, and BC is an essential constituent of  $PM_{2.5}$ .<sup>102</sup>

#### 4.3 Underlying pathological mechanism

In our study, the pooled effect estimate indicated that short-term and long-term exposure to BC/EC was associated with an increased risk of cardiovascular diseases. There are considerable speculative literatures on possible underlying mechanisms. An animal study conducted by Niwa et al revealed that BC accelerated atherosclerotic plaque formation. Furthermore, a human panel study was performed to assess whether the patients with IHD experience change in the repolarization parameters exposure to rising concentration of pollutants. He results indicated that the variability of the T-wave complexity increased with increasing EC during periods of 0-5 hours, 12-17 hours and 0-2 hours before ECG measurement. He of the other hand, a p-value plot analysis did not support a consistent effect of BC/EC on cardiovascular disease. The original meta-analysis examined heart attacks and claim effects for PM<sub>10</sub> and PM<sub>2.5</sub>, which performed by Mustafic et al, 2012. A critique was given in Young et al, 2019, who used p-value plots to call those claims into question. So

#### 4.4 Suggestions for further research

First, critical potential confounders (temperature, seasonality, day of the week, and long-term trends) and other potential confounders (holidays and influenza epidemics) should be considered in time series and case crossover studies, especially for influenza epidemics. Influenza epidemics are factors usually neglected in short-term studies. Second, studies should adjust PM<sub>2.5</sub> when assessing the health effect of PM<sub>2.5</sub> constituents. Mostofsky et al. proved that PM<sub>2.5</sub> may be associated with both health and its constituents. Constituent having closer association with PM<sub>2.5</sub> may illustrate a stronger association with diseases. Therefore, the results of PM<sub>2.5</sub>-unadjusted model could introduce bias.<sup>7</sup> Third, further studies are suggested to evaluate the health effects of long-term exposure to BC, especially for morbidity. An essential difficulty that needs to be acknowledged is the availability of the disease data. Emergency department visits and outpatients are more time-sensitive data than mortality, hence these indicators are more representative to some extent in investigating the health effects of environmental factors. However, the data of emergency department visits and outpatients generally from medical institutions are more difficult to obtain than data on mortality, with a large portion of mortality data arriving from departments of disease control institutions in China. Forth, the present evidence on the health effects of BC was mainly from America and Asia. Studies assessing the association in other geographical locations are suggested, which might contribute to the evaluation of the potentially different effects of BC in different continents. Fifth, more studies need to provide evidence to prove the association between BC/EC and respiratory diseases in vulnerable populations.

#### 4.5 Strength and limitation

This systematic review and meta-analysis provided a comprehensive and current evidence for the short-term and long-term exposure to BC/EC on cardiorespiratory morbidity and mortality. Adapted GRADE framework was used to assess the certainty of the evidence. Multiple testing/multiple modeling was not considered in current GRADE theory, which should be further explored in the future. Potential limitations in our study are as follows. A significant heterogeneity for the pooled estimates was noticed in the meta-analysis, which might be due to the high variability in the study population, outcomes, and geographical locations. Therefore, subgroup analyses on age of the population (all and older than 65 years old), outcomes (morbidity and mortality), geological locations (Europe, America and Asia) and lag days (0, 1, 2 days) were conducted for a further investigation of the potential sources in conditions more than 3 estimates. Most of the included papers used in our study were from the US or China, which affected the pooled estimates, although it is an inherent and inevitable selection bias. We have extracted and calculated the regional distribution of BC concentration of included studies. It showed that the mean BC concentration is highest in Asia, which maybe an essential reason of the results. In addition, consistent results of cardiovascular and respiratory diseases exposure to BC/EC were observed by eliminating studies with partial overlap from the same geographical locations.

Reliability of meta-analysis is an essential challenge existed in environmental epidemiology researches, which should be improved in the future. The reliability of meta-analysis was analyzed by combining p-value plots and heterogeneity. Our

findings indicated that the impact of BC on cardiovascular diseases was more reliable. However, the impact of BC on respiratory diseases was random and some reported small p-values may exist p-hacking. It is not appropriate to do meta-analysis blindly when researchers do not understand the limitations in the basic studies. Therefore, it is essential for authors to understand the causes of limitations and draw objective conclusions.

#### 5. Conclusions

Both short-term and long-term exposures to BC/EC were related with cardiovascular diseases. However, the impacts of BC/EC on respiratory diseases did not present consistent evidence and further investigations were required.

# Acknowledgements

We would like to thank the authors of the original studies for their contributions to our systematic review and meta-analysis, especially authors who provided their raw data for the analysis. We are grateful to Professor S. Stanley Young and all reviewers for their helpful comments and suggestions on this manuscript.



#### **Contributorship statement**

SW, XZ and XS developed the research design. XS, YH, YM and LJ analyzed the data and interpreted the results. XS, YH, YM, XW and JZ drafted manuscript. AS, YuL, YaL, JT, XL and YG did literature screening and data extraction. All of the authors contributed to drafting the manuscript. The final manuscript was approved by TO CORRECTION ONLY all authors.

# **Funding**

The work was supported by the National Key Research and Development Program of China (No.2016YFA0602004) and Innovation Fund Project on Public Meteorological Service Center of China Meteorological Administration in 2020 (Grant numbers: K2020010).



# **Competing interests**

We declare that all authors have no competing interests.



# Data sharing statement

All data relevant to the study are included in the article or uploaded as supplementary information.



#### Reference

- 1. Bond TC, Doherty SJ, Fahey DW. Bounding the role of black carbon in the climate system: A scientific assessment. *Journal of geophysical research: Atmospheres*. 2013;118(11):5380-552.
- 2. Zencak Z, Elmquist M, Gustafsson Ö. Quantification and radiocarbon source apportionment of black carbon in atmospheric aerosols using the CTO-375 method. *Atmospheric Environment*. 2007;41(36):7895-906.
- 3. Atkinson RW, Kang S, Anderson HR, et al. Epidemiological time series studies of PM2.5 and daily mortality and hospital admissions: a systematic review and meta-analysis. *Thorax*. 2014;69(7):660-5.
- 4. Global, regional, and national comparative risk assessment of 84 behavioural, environmental and occupational, and metabolic risks or clusters of risks for 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet*. 2018;392(10159):1923-94.
- 5. Ross MA. Integrated science assessment for particulate matter. *US Environmental Protection Agency: Washington DC, USA*. 2009:61-161.
- 6. Bell ML, Dominici F, Ebisu K, et al. Spatial and temporal variation in PM(2.5) chemical composition in the United States for health effects studies. *Environ Health Perspect*. 2007;115(7):989-95.
- 7. Mostofsky E, Schwartz J, Coull BA, et al. Modeling the association between particle constituents of air pollution and health outcomes. *Am J Epidemiol*. 2012;176(4):317-26.
- 8. Janssen N, Gerlofs NM, Lanki T. Health effects of black carbon, The WHO European Centre for Environment and Health, Bonn, Germany. *World Health Organisation Regional Office for Europe, Copenhagen, Denmark.* 2012.
- 9. Grahame TJ, Klemm R, Schlesinger RB. Public health and components of particulate matter: the changing assessment of black carbon. *J Air Waste Manag Assoc*. 2014;64(6):620-60.
- 10. Husain M, Kyjovska ZO, Bourdon-Lacombe J, et al. Carbon black nanoparticles induce biphasic gene expression changes associated with inflammatory responses in the lungs of C57BL/6 mice following a single intratracheal instillation. *Toxicol Appl Pharmacol*. 2015;289(3):573-88.
- 11. Colicino E, Giuliano G, Power MC, et al. Long-term exposure to black carbon, cognition and single nucleotide polymorphisms in microRNA processing genes in older men. *Environ Int.* 2016;88:86-93.
- 12. Büchner N, Ale-Agha N, Jakob S, et al. Unhealthy diet and ultrafine carbon black particles induce senescence and disease associated phenotypic changes. *Exp Gerontol*. 2013;48(1).
- 13. Young SS. Air quality environmental epidemiology studies are unreliable. *REGULATORY TOXICOLOGY AND PHARMACOLOGY*. 2017;86:177-80.
- 14. Simonsohn U, Nelson LD, Simmons JP. p-Curve and Effect Size: Correcting for Publication Bias Using Only Significant Results. *PERSPECTIVES ON PSYCHOLOGICAL SCIENCE*. 2014;9(6):666-81.
- 15. Spellman BA. The Seven Deadly Sins of Psychology: A Manifesto for Reforming the Culture of Scientific Practice. *NATURE*. 2017;544(7651):414-5.
- 16. Munafo M. Rigor Mortis: How Sloppy Science Creates Worthless Cures, Crushes Hope, and Wastes Billions. *NATURE*. 2017;543(7647):619-20.
- 17. Achilleos S, Kioumourtzoglou M-A, Wu C-D, et al. Acute effects of fine particulate matter constituents on mortality: A systematic review and meta-regression analysis. *Environ Int.* 2017;109.

- 18. Luben TJ, Nichols JL, Dutton SJ, et al. A systematic review of cardiovascular emergency department visits, hospital admissions and mortality associated with ambient black carbon. *Environ Int.* 2017;107:154-62.
- 19. Yang Y, Ruan Z, Wang X, et al. Short-term and long-term exposures to fine particulate matter constituents and health: A systematic review and meta-analysis. *ENVIRONMENTAL POLLUTION*. 2019;247:874-82.
- 20. Cumberbatch MG, Rota M, Catto JWF, et al. The Role of Tobacco Smoke in Bladder and Kidney Carcinogenesis: A Comparison of Exposures and Meta-analysis of Incidence and Mortality Risks. *Eur Urol*. 2016;70(3):458-66.
- 21. Ostro B, Hu J, Goldberg D, et al. Associations of mortality with long-term exposures to fine and ultrafine particles, species and sources: results from the California Teachers Study Cohort. *Environ Health Perspect*. 2015;123(6):549-56.
- 22. Samoli E, Atkinson RW, Analitis A, et al. Associations of short-term exposure to traffic-related air pollution with cardiovascular and respiratory hospital admissions in London, UK. *Occup Environ Med.* 2016;73(5):300-7.
- 23. Basagaña X, Jacquemin B, Karanasiou A, et al. Short-term effects of particulate matter constituents on daily hospitalizations and mortality in five South-European cities: results from the MED-PARTICLES project. *Environ Int.* 2015;75:151-8.
- 24. Gan WQ, FitzGerald JM, Carlsten C, et al. Associations of ambient air pollution with chronic obstructive pulmonary disease hospitalization and mortality. *Am J Respir Crit Care Med*. 2013;187(7):721-7.
- 25. Ostro B, Tobias A, Karanasiou A, et al. The risks of acute exposure to black carbon in Southern Europe: results from the MED-PARTICLES project. *Occup Environ Med.* 2015;72(2):123-9.
- 26. Thurston GD, Burnett RT, Turner MC, et al. Ischemic Heart Disease Mortality and Long-Term Exposure to Source-Related Components of U.S. Fine Particle Air Pollution. *Environ Health Perspect*. 2016;124(6):785-94.
- 27. National Toxicology Program. Handbook for conducting a literature-based health assessment using OHAT approach for systematic review and evidence integration. Office of Health Assessment and Translation (OHAT), Division of the National Toxicology Program, National Institute of Environmental Health Sciences https://ntpniehsnihgov/ntp/ohat/ pubs/handbookjan2015 508pdf 2015.
- 28. Lam J, Sutton P, Kalkbrenner A, et al. A Systematic Review and Meta-Analysis of Multiple Airborne Pollutants and Autism Spectrum Disorder. *PLoS One*. 2016;11(9):e0161851.
- 29. Morgan RL, Thayer KA, Santesso N, et al. A risk of bias instrument for non-randomized studies of exposures: A users' guide to its application in the context of GRADE. *Environ Int.* 2019;122:168-84.
- 30. Stanley Young S, Kindzierski WB. Evaluation of a meta-analysis of air quality and heart attacks, a case study. *Critical reviews in toxicology*. 2019;49(1):85-94.
- 31. Schweder T, Spjotvoll E. PLOTS OF P-VALUES TO EVALUATE MANY TESTS SIMULTANEOUSLY. *BIOMETRIKA*. 1982;69(3):493-502.
- 32. Strickland MJ, Darrow LA, Mulholland JA, et al. Implications of different approaches for characterizing ambient air pollutant concentrations within the urban airshed for time-series studies and health benefits analyses. *Environ Health*. 2011;10:36.
- 33. Nayebare SR, Aburizaiza OS, Siddique A, et al. Association of fine particulate air pollution with cardiopulmonary morbidity in Western Coast of Saudi Arabia. *Saudi Med J.* 2017;38(9):905-12.

- 34. Cai J, Zhao A, Zhao J, et al. Acute effects of air pollution on asthma hospitalization in Shanghai, China. *Environ Pollut*. 2014;191:139-44.
- 35. Hua J, Yin Y, Peng L, et al. Acute effects of black carbon and PM<sub>2.5</sub> on children asthma admissions: a time-series study in a Chinese city. *Sci Total Environ*. 2014;481:433-8.
- 36. Darrow LA, Klein M, Flanders WD, et al. Air pollution and acute respiratory infections among children 0-4 years of age: an 18-year time-series study. *Am J Epidemiol*. 2014;180(10):968-77.
- 37. Zanobetti A, Schwartz J. Air pollution and emergency admissions in Boston, MA. *J Epidemiol Community Health*. 2006;60(10):890-5.
- 38. Metzger KB, Tolbert PE, Klein M, et al. Ambient air pollution and cardiovascular emergency department visits. *Epidemiology*. 2004;15(1):46-56.
- 39. O'Lenick CR, Winquist A, Mulholland JA, et al. Assessment of neighbourhood-level socioeconomic status as a modifier of air pollution-asthma associations among children in Atlanta. *J Epidemiol Community Health*. 2017;71(2):129-36.
- 40. Mar TF, Norris GA, Koenig JQ, et al. Associations between air pollution and mortality in Phoenix, 1995-1997. *Environ Health Perspect*. 2000;108(4):347-53.
- 41. Krall JR, Mulholland JA, Russell AG, et al. Associations between Source-Specific Fine Particulate Matter and Emergency Department Visits for Respiratory Disease in Four U.S. Cities. *Environ Health Perspect*. 2017;125(1).
- 42. Gong T, Sun Z, Zhang X, et al. Associations of black carbon and PM2.5 with daily cardiovascular mortality in Beijing, China. *Atmospheric Environment*. 2019;214:116876.
- 43. Wang Y, Shi Z, Shen F, et al. Associations of daily mortality with short-term exposure to PM and its constituents in Shanghai, China. *Chemosphere*. 2019;233:879-87.
- 44. Dai L, Zanobetti A, Koutrakis P, et al. Associations of fine particulate matter species with mortality in the United States: a multicity time-series analysis. *Environ Health Perspect*. 2014;122(8):837-42.
- 45. Bell ML, Ebisu K, Leaderer BP, et al. Associations of  $PM_{2.5}$  constituents and sources with hospital admissions: analysis of four counties in Connecticut and Massachusetts (USA) for persons  $\geq$  65 years of age. *Environ Health Perspect*. 2014;122(2):138-44.
- 46. Wang M, Hopke PK, Masiol M, et al. Changes in triggering of ST-elevation myocardial infarction by particulate air pollution in Monroe County, New York over time: a case-crossover study. *Environmental Health*. 2019;18(1).
- 47. Son J-Y, Lee J-T, Kim K-H, et al. Characterization of fine particulate matter and associations between particulate chemical constituents and mortality in Seoul, Korea. *Environ Health Perspect*. 2012;120(6):872-8.
- 48. Cakmak S, Dales RE, Gultekin T, et al. Components of particulate air pollution and emergency department visits in Chile. *Arch Environ Occup Health*. 2009;64(3):148-55.
- 49. Geng F, Hua J, Mu Z, et al. Differentiating the associations of black carbon and fine particle with daily mortality in a Chinese city. *Environ Res.* 2013;120:27-32.
- 50. Lin H, Tao J, Du Y, et al. Differentiating the effects of characteristics of PM pollution on mortality from ischemic and hemorrhagic strokes. *Int J Hyg Environ Health*. 2016;219(2):204-11.
- 51. Lall R, Ito K, Thurston GD. Distributed lag analyses of daily hospital admissions and source-apportioned fine particle air pollution. *Environ Health Perspect*. 2011;119(4):455-60.
- 52. Ostro B, Feng W-Y, Broadwin R, et al. The effects of components of fine particulate air pollution on mortality in california: results from CALFINE. *Environ Health Perspect*. 2007;115(1):13-9.

- 53. Ostro B, Roth L, Malig B, et al. The effects of fine particle components on respiratory hospital admissions in children. *Environ Health Perspect*. 2009;117(3):475-80.
- 54. Peng RD, Bell ML, Geyh AS, et al. Emergency admissions for cardiovascular and respiratory diseases and the chemical composition of fine particle air pollution. *Environ Health Perspect*. 2009;117(6):957-63.
- 55. Tomić-Spirić V, Kovačević G, Marinković J, et al. Evaluation of the Impact of Black Carbon on the Worsening of Allergic Respiratory Diseases in the Region of Western Serbia: A Time-Stratified Case-Crossover Study. *Medicina (Kaunas)*. 2019;55(6).
- 56. Pearce JL, Waller LA, Mulholland JA, et al. Exploring associations between multipollutant day types and asthma morbidity: epidemiologic applications of self-organizing map ambient air quality classifications. *Environ Health*. 2015;14:55.
- 57. Heo J, Schauer JJ, Yi O, et al. Fine particle air pollution and mortality: importance of specific sources and chemical species. *Epidemiology*. 2014;25(3):379-88.
- 58. Liu S, Ganduglia CM, Li X, et al. Fine particulate matter components and emergency department visits among a privately insured population in Greater Houston. *Sci Total Environ*. 2016;566-567:521-7.
- 59. Sarnat SE, Winquist A, Schauer JJ, et al. Fine particulate matter components and emergency department visits for cardiovascular and respiratory diseases in the St. Louis, Missouri-Illinois, metropolitan area. *Environ Health Perspect*. 2015;123(5):437-44.
- 60. Lavigne É, Talarico R, van Donkelaar A, et al. Fine particulate matter concentration and composition and the incidence of childhood asthma. *Environ Int*. 2021;152:106486.
- 61. Cao J, Xu H, Xu Q, et al. Fine particulate matter constituents and cardiopulmonary mortality in a heavily polluted Chinese city. *Environ Health Perspect*. 2012;120(3):373-8.
- 62. Ito K, Mathes R, Ross Z, et al. Fine particulate matter constituents associated with cardiovascular hospitalizations and mortality in New York City. *Environ Health Perspect*. 2011;119(4):467-73.
- 63. Winquist A, Schauer JJ, Turner JR, et al. Impact of ambient fine particulate matter carbon measurement methods on observed associations with acute cardiorespiratory morbidity. *J Expo Sci Environ Epidemiol*. 2015;25(2):215-21.
- 64. Ostro BD, Feng WY, Broadwin R, et al. The impact of components of fine particulate matter on cardiovascular mortality in susceptible subpopulations. *Occup Environ Med.* 2008;65(11):750-6.
- 65. Klemm RJ, Thomas EL, Wyzga RE. The impact of frequency and duration of air quality monitoring: Atlanta, GA, data modeling of air pollution and mortality. *J Air Waste Manag Assoc.* 2011;61(11):1281-91.
- 66. Chen S-Y, Lin Y-L, Chang W-T, et al. Increasing emergency room visits for stroke by elevated levels of fine particulate constituents. *Sci Total Environ*. 2014;473-474:446-50.
- 67. Tolbert PE, Klein M, Metzger KB, et al. Interim results of the study of particulates and health in Atlanta (SOPHIA). *J Expo Anal Environ Epidemiol*. 2000;10(5):446-60.
- 68. Yang Y, Tang R, Qiu H, et al. Long term exposure to air pollution and mortality in an elderly cohort in Hong Kong. *Environ Int.* 2018;117.
- 69. Hasslöf H, Molnár P, Andersson EM, et al. Long-term exposure to air pollution and atherosclerosis in the carotid arteries in the Malmö diet and cancer cohort. *Environ Res.* 2020;191:110095.
- 70. Rodins V, Lucht S, Ohlwein S, et al. Long-term exposure to ambient source-specific particulate matter and its components and incidence of cardiovascular events The Heinz Nixdorf Recall study.

Environ Int. 2020;142.

- 71. Liu L, Zhang Y, Yang Z, et al. Long-term exposure to fine particulate constituents and cardiovascular diseases in Chinese adults. *Journal of Hazardous Materials*. 2021;416.
- 72. Liu S, Jorgensen JT, Ljungman P, et al. Long-term exposure to low-level air pollution and incidence of chronic obstructive pulmonary disease: The ELAPSE project. *Environ Int.* 2021;146.
- 73. Ljungman PLS, Andersson N, Stockfelt L, et al. Long-Term Exposure to Particulate Air Pollution, Black Carbon, and Their Source Components in Relation to Ischemic Heart Disease and Stroke. *Environ Health Perspect*. 2019;127(10):107012.
- 74. Gan WQ, Koehoorn M, Davies HW, et al. Long-term exposure to traffic-related air pollution and the risk of coronary heart disease hospitalization and mortality. *Environ Health Perspect*. 2011;119(4):501-7.
- 75. Hvidtfeldt UA, Sørensen M, Geels C, et al. Long-term residential exposure to PM2.5, PM10, black carbon, NO2, and ozone and mortality in a Danish cohort. *Environ Int.* 2019;123:265-72.
- 76. Levy JI, Diez D, Dou Y, et al. A meta-analysis and multisite time-series analysis of the differential toxicity of major fine particulate matter constituents. *Am J Epidemiol*. 2012;175(11):1091-9.
- 77. Strickland MJ, Klein M, Flanders WD, et al. Modification of the effect of ambient air pollution on pediatric asthma emergency visits: susceptible subpopulations. *Epidemiology*. 2014;25(6):843-50.
- 78. Wang Y-C, Lin Y-K. Mortality and emergency room visits associated with ambient particulate matter constituents in metropolitan Taipei. *Sci Total Environ*. 2016;569-570:1427-34.
- 79. Maynard D, Coull BA, Gryparis A, et al. Mortality risk associated with short-term exposure to traffic particles and sulfates. *Environ Health Perspect*. 2007;115(5):751-5.
- 80. Tolbert PE, Klein M, Peel JL, et al. Multipollutant modeling issues in a study of ambient air quality and emergency department visits in Atlanta. *J Expo Sci Environ Epidemiol*. 2007;17 Suppl 2:S29-S35.
- 81. Vedal S, Campen MJ, McDonald JD, et al. National Particle Component Toxicity (NPACT) initiative report on cardiovascular effects. *Res Rep Health Eff Inst.* 2013(178):5-8.
- 82. Ito K, Ross Z, Zhou J, et al. NPACT Study 3. Time-Series Analysis of Mortality, Hospitalizations, and Ambient PM2.5 and Its Components. In: National Particle Component Toxicity (NPACT) Initiative: Integrated Epidemiologic and Toxicologic Studies of the Health Effects of Particulate Matter Components. Research Report 177. Health Effects Institute, Boston, MA. *Res Rep Health Eff Inst.* 2013.
- 83. Lin H, Tao J, Du Y, et al. Particle size and chemical constituents of ambient particulate pollution associated with cardiovascular mortality in Guangzhou, China. *Environ Pollut*. 2016;208(Pt B):758-66.
- 84. Jung C-R, Young L-H, Hsu H-T, et al. PM components and outpatient visits for asthma: A time-stratified case-crossover study in a suburban area. *Environ Pollut*. 2017;231(Pt 1):1085-92.
- 85. Rahmatinia M, Hadei M, Hopke PK, et al. Relationship between ambient black carbon and daily mortality in Tehran, Iran: a distributed lag nonlinear time series analysis. *Journal of environmental health science & engineering*. 2021;19(1):907-16.
- 86. de Kluizenaar Y, van Lenthe FJ, Visschedijk AJH, et al. Road traffic noise, air pollution components and cardiovascular events. *Noise Health*. 2013;15(67):388-97.
- 87. Huang W, Cao J, Tao Y, et al. Seasonal variation of chemical species associated with short-term mortality effects of PM(2.5) in Xi'an, a Central City in China. *Am J Epidemiol*. 2012;175(6):556-66.
- 88. Kim S-Y, Dutton SJ, Sheppard L, et al. The short-term association of selected components of fine

particulate matter and mortality in the Denver Aerosol Sources and Health (DASH) study. *Environ Health*. 2015;14:49.

- 89. Strickland MJ, Darrow LA, Klein M, et al. Short-term associations between ambient air pollutants and pediatric asthma emergency department visits. *Am J Respir Crit Care Med*. 2010;182(3):307-16.
- 90. Liu S, Ganduglia CM, Li X, et al. Short-term associations of fine particulate matter components and emergency hospital admissions among a privately insured population in Greater Houston. *Atmospheric Environment*. 2016;147:369-75.
- 91. Kovacevic G, Spiric VT, Marinkovic J, et al. Short-Term effects of air pollution on exacerbations of allergic asthma in uzice region, serbia. *Postepy Dermatologii i Alergologii*. 2020;37(3):377-83.
- 92. Krall JR, Anderson GB, Dominici F, et al. Short-term exposure to particulate matter constituents and mortality in a national study of U.S. urban communities. *Environ Health Perspect*. 2013;121(10):1148-53.
- 93. Atkinson RW, Analitis A, Samoli E, et al. Short-term exposure to traffic-related air pollution and daily mortality in London, UK. *J Expo Sci Environ Epidemiol*. 2016;26(2):125-32.
- 94. Kim S-Y, Peel JL, Hannigan MP, et al. The temporal lag structure of short-term associations of fine particulate matter chemical constituents and cardiovascular and respiratory hospitalizations. *Environ Health Perspect*. 2012;120(8):1094-9.
- 95. Zhou J, Ito K, Lall R, et al. Time-series analysis of mortality effects of fine particulate matter components in Detroit and Seattle. *Environ Health Perspect*. 2011;119(4):461-6.
- 96. Sinclair AH, Edgerton ES, Wyzga R, et al. A two-time-period comparison of the effects of ambient air pollution on outpatient visits for acute respiratory illnesses. *J Air Waste Manag Assoc*. 2010;60(2):163-75.
- 97. Anand A, Phuleria HC. Spatial and seasonal variation of outdoor BC and PM 2.5 in densely populated urban slums. *Environ Sci Pollut Res Int.* 2021;28(2):1397-408.
- 98. Chen P, Kang S, Gul C, et al. Seasonality of carbonaceous aerosol composition and light absorption properties in Karachi, Pakistan. *J Environ Sci (China)*. 2020;90:286-96.
- 99. Yang Y, Xu X, Zhang Y, et al. Seasonal size distribution and mixing state of black carbon aerosols in a polluted urban environment of the Yangtze River Delta region, China. *Sci Total Environ*. 2019;654:300-10.
- 100. Bell ML, Zanobetti A, Dominici F. Evidence on vulnerability and susceptibility to health risks associated with short-term exposure to particulate matter: a systematic review and meta-analysis. *Am J Epidemiol*. 2013;178(6):865-76.
- 101. Sinharay R, Gong J, Barratt B, et al. Respiratory and cardiovascular responses to walking down a traffic-polluted road compared with walking in a traffic-free area in participants aged 60 years and older with chronic lung or heart disease and age-matched healthy controls: a randomised, crossover study. *Lancet*. 2018;391(10118):339-49.
- 102. Phalen RF, Oldham MJ, Kleinman MT, et al. TRACHEOBRONCHIAL DEPOSITION PREDICTIONS FOR INFANTS, CHILDREN AND ADOLESCENTS. In: Dodgson J, McCallum RI, Bailey MR, Fisher DR, editors. Inhaled Particles VI: Pergamon; 1988. p. 11-21.
- 103. Niwa Y, Hiura Y, Murayama T, et al. Nano-sized carbon black exposure exacerbates atherosclerosis in LDL-receptor knockout mice. *Circ J.* 2007;71(7):1157-61.
- 104. Henneberger A, Zareba W, Ibald-Mulli A, et al. Repolarization changes induced by air pollution in ischemic heart disease patients. *Environ Health Perspect*. 2005;113(4):440-6.
- 105. Mustafic H, Jabre P, Caussin C, et al. Main air pollutants and myocardial infarction: a systematic

review and meta-analysis. Jama. 2012;307(7):713-21.

#### **Table captions**

**Table 1** Short-term impact of BC/EC on cardiovascular and respiratory diseases in different models.

**Table 2** Variable counts, and analysis search spaces for the 15 studies chosen from the meta-analysis.

# Figure captions

Figure 1 Flow diagram of literature screening process.

**Figure 2** Impact of short-term exposure to BC/EC on cardiovascular diseases in the PM<sub>2.5</sub>-unadjusted model.

Figure 3 P-value plots of short-term exposure to BC/EC on cardiovascular diseases (A) and respiratory diseases (B) in the  $PM_{2.5}$ -unadjusted model.

#### Appendix A. Supplementary data

 Table S1 Search strategy in PubMed.

**Table S2** Characteristics of the included studies in the systematic review and meta-analysis.

**Table S3** Subgroup analysis on short-term effects of BC/EC on cardiovascular and respiratory diseases.

**Table S4** Summary statistics for the number of possible analyses using the three search spaces.

**Table S5** Results of risk of bias assessment.

Table S6 Details of risk of bias assessment.

**Table S7** Assessment of certainty of evidence for the outcomes.

**Table S8** The p-value calculation process for each study using RR, CI low and CI high.

**Figure S1** Impact of short-term exposure to BC/EC on cardiovascular mortality stratified by geographical locations.

**Figure S2** Impact of short-term exposure to BC/EC on cardiovascular morbidity stratified by geographical locations.

**Figure S3** Impact of long-term exposure to BC/EC on cardiovascular diseases.

**Figure S4** Impact of short-term exposure to BC/EC on cardiovascular diseases in the PM<sub>2.5</sub>-adjusted model.

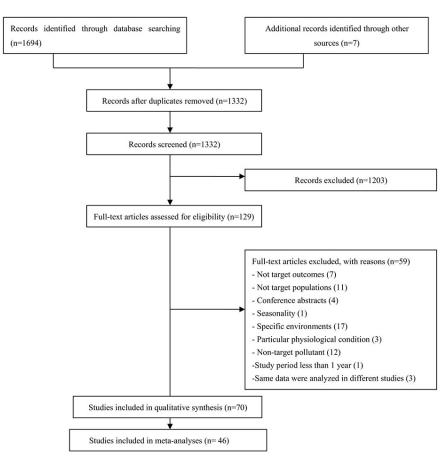


Fig. 1. Flow diagram of literature screening process

Figure 1 Flow diagram of literature screening process.

90x90mm (300 x 300 DPI)

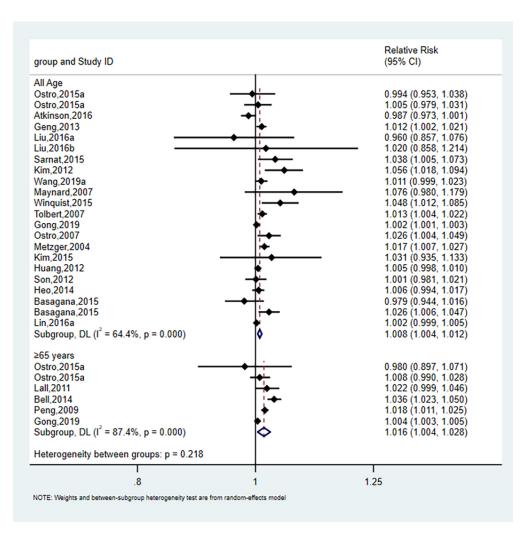


Figure 2 Impact of short-term exposure to BC/EC on cardiovascular diseases in the PM2.5-unadjusted model.

90x90mm (300 x 300 DPI)

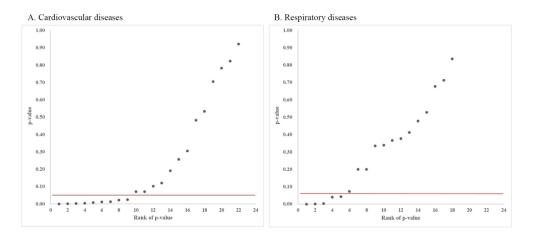


Figure 3 P-value plots of short-term exposure to BC/EC on cardiovascular diseases (A) and respiratory diseases (B) in the PM2.5-unadjusted model.

160x71mm (300 x 300 DPI)

#### SUPPLEMENTARY APPENDIX

# Is Short-term and Long-term Exposure to Black Carbon Associated with Cardiovascular and Respiratory Diseases? A Systematic Review and Meta-Analysis based on Evidence Reliability

Xuping Song<sup>a</sup>, Yue Hu<sup>a</sup>, Yan Ma<sup>a</sup>, Liangzhen Jiang<sup>a</sup>, Xinyi Wang<sup>c</sup>, Anchen Shi<sup>d</sup>, Junxian Zhao<sup>a</sup>, Yunxu Liu<sup>a</sup>, Yafei Liu<sup>a</sup>, Jing Tang<sup>a</sup>, Xiayang Li<sup>a</sup>, Xiaoling Zhang\*<sup>b</sup>, Yong Guo<sup>e</sup>, Shigong Wang\*<sup>b</sup>

#### **Corresponding author 1:**

Name: Xiaoling Zhang

Postal Address: College of Atmospheric Sciences, Chengdu University of Information

Technology, Chengdu 610000, Sichuan, China

E-mail address: xlzhang@ium.cn

Fax: 028-85966502 Corresponding author 2: Name: Shigong Wang

Postal Address: College of Atmospheric Sciences, Chengdu University of Information

Technology, Chengdu 610000, Sichuan, China

E-mail address: wangsg@cuit.edu.cn

Fax: 028-85966502

<sup>&</sup>lt;sup>a</sup> School of Public Health, Lanzhou University, Lanzhou 730000, China;

<sup>&</sup>lt;sup>b</sup> College of Atmospheric Sciences, Chengdu University of Information Technology, Chengdu 610000, China;

<sup>&</sup>lt;sup>c</sup> Second Clinical College, Lanzhou University, Lanzhou 730000, China;

<sup>&</sup>lt;sup>d</sup> Department of General Surgery, The First Affiliated Hospital of Xi'an Jiao Tong University, Shaanxi 710061, China;

<sup>&</sup>lt;sup>e</sup> Department of Civil Affairs in Guizhou Province, Guiyang 550004, China.

#### Supplementary data

- Table S1 Search strategy in PubMed.
- **Table S2** Characteristics of the included studies in the systematic review and meta-analysis.
- **Table S3** Subgroup analysis on short-term effects of BC/EC on cardiovascular and respiratory diseases.
- **Table S4** Summary statistics for the number of possible analyses using the three search spaces.
- Table S5 Results of risk of bias assessment.
- Table S6 Details of risk of bias assessment.
- **Table S7** Assessment of certainty of evidence for the outcomes.
- **Table S8** The p-value calculation process for each study using RR, CI low and CI high.
- **Figure S1** Impact of short-term exposure to BC/EC on cardiovascular mortality stratified by geographical locations.
- **Figure S2** Impact of short-term exposure to BC/EC on cardiovascular morbidity stratified by geographical locations.
- Figure S3 Impact of long-term exposure to BC/EC on cardiovascular diseases.
- **Figure S4** Impact of short-term exposure to BC/EC on cardiovascular diseases in the PM<sub>2.5</sub>-adjusted model.

36/bmjopen-2021-04951

Table	e S1 Search Strategy for PubMed.
No.	Search Strategy $\omega$
#1	particulate matter/or aerosols.sh.
#2	particulate matter*/or "PM10"/or "PM2.5"/or fine particle*/or thoracic particle*/or ultrafine/or aerosol*/or carbon*/or soot*.ti,ab.
#3	particulate matter/or aerosols.sh.  particulate matter*/or "PM10"/or "PM2.5"/or fine particle*/or thoracic particle*/or ultrafine/or aerosol*/or carbon*/or soot*.ti,ab.  "PM".tw.
#4	
#5	or/1,2,3 "EC" /or "BC".tw. and/4,5 black carbon*/or elemental carbon*.ti,ab.
#6	and/4,5
#7	
#8	or/6,7
#9	respiratory tract disease.sh.
#10	respirat*/or pulmonary disease*/or lung/or chest infection*/or airway/or asthma*/or pneumonia*/or "chronic obstructive pulmonary disease"/or COPD.ti,ab.
#11	cardiovascular diseases.sh.
#12	cardio*/or cardiop*/or cardior*/or heart/or coronary/or vascular/or blood/or cardiac.ti,ab.
#13	or/9,10,11,12
#14	morbidity/or hospitalization/or death/or mortality/or outpatient.sh
#15	morbidit*/or hospitalisation*/or hospitalization*/or death*/or mortalit*/or outpatien*/or emergency room*/or emergency department*/og emergency admi*/or hospital
1113	admission*.ti,ab.
#16	or/14,15
#17	epidemiologic studies/or cross over study.sh.
#18	time series*/or timeseries*/or case cross*/or casecross*.tw.
	generalized additive model/or generalised additive model/or generalized linear model/or generalised linear model/or distributed lag non-
#19	model/or distributed lag model/or quasipoisson*/or poisson*/or generalized estimating equation/or generalised estimating equation/or @AM/or GLM/or DLNM/or GEE/or DLM/or
	ARIMA.tw.
#20	cohort*/or follow up*/or observational/or longitudinal/or case control*/or epidemiologic/or population
1120	stud*/or prospective*/or retrospective*.tw.
#21	or/17,18,19,20 and/8,13,16,21
#22	and/8,13,16,21 gg
	<b>Ş</b>
	by соругі
	ýri.

Table S2 Characteristics of included studies in the systematic review and meta-analysis.

Study	Study	Country	Study	Outcome	Age	Pollutant	ICD	Siseases
Atkinson et al. 2016	<b>Design</b> TS	UK	2011-2012	Montality	All	BC,EC	code ICD-10	CVD(ICD-10:100-I99),RES(ICD-10:J00-J99) 8
Atkinson et al. 2010	15	UK	2011-2012	Mortality	All	BC,EC	ICD-10	Ŋ.
								RES[COPD(ICD-9-CM:490-492,RTI(ICD-9-CM:46\footnote{A66}, 480-487)];CVD[HF(ICD-9-CM:428),Heart Rhythm
Bell et al. 2014	TS	USA	2000-2004	Morbidity	≥65	ВС	ICD-9	Disturbances(ICD-9-CM:426-427), Cerebrovascular vents(ICD-9-CM:430-438),IHD(ICD-9-CM:410-414,
					<u> </u>			429),PVD(ICD-9-CM:440–448)]
Cai et al. 2014	TS	China	2005-2011	Morbidity	≥18	ВС	ICD-10	
Geng et al. 2013	TS	China	2007-2008	Mortality	All	BC	ICD-10	CVD(ICD-10:I00-I99),RES(ICD-10:J00-J98)
Hua et al. 2014	TS	China	2007-2012	Morbidity	0-14	BC	ICD-10	Asthma(ICD-10:J45)
Ostro et al. 2015a	CS	Spain, Greece	2008-2009 (Athens), 2009-2010(Barc elona)	Mortality	All	ВС	ICD-10	CVD(ICD-10:100-I99),RES(ICD-10:J00-J98)  Asthma(ICD-10:J45)  CVD(ICD-10:I00-I99),RES(ICD-10:J00-J99)  CVD(ICD-10:I00-I99),RES(ICD-10:J00-J99)
Samoli et al. 2016	TS	UK	2011-2012	Morbidity	≥15(CVD), all (RES)	BC,EC	ICD-10	CVD(ICD-10:I00-I99),RES(ICD-10:J00-J99)
Zanobetti and Schwartz 2006	CS	USA	1995-1999	Morbidity	≥65	ВС	ICD-9	MI(ICD-9:410),Pneumonia (ICD-9: 480–487)
V 1 2016	ma	110.4	2000 2012			F.C.	ICD 0	CVD(ICD-9:390-429),Stroke(ICD-9:430-438),RES(ICD-9:460-519),COPD(ICD-9:490-492,494,496),Pneumonia(I
Liu et al. 2016a	TS	USA	2008-2013	Morbidity	All	EC	ICD-9	CD-9:480-486),Asthma(ICD-9:493),SSID(ICD-9:78
		***				700		CVD(ICD-9:390-429),Stroke(ICD-9:430-438),RESRECD-9:460-519),COPD(ICD-9:490-492,494,496),Pneumonia
Liu et al. 2016b	TS	USA	2008-2013	Morbidity	All	EC	ICD-9	(ICD-9:480-486),Asthma(ICD-9:493)
								CVD[IHD(ICD9:410–414),Cardiac Dysrhythmias(ICD9:427),CHF(ICD9:428),Other CVD
Sarnat et al. 2015	TS	USA	2001-2003	Morbidity	All	EC	ICD9	(ICD9:433-437,440,443-445,451-453)],RES[Pneumæ]aa(ICD9:480-486),COPD
								(ICD:491,492,496),Asthma/Wheeze (ICD9:493,786. 76),Other RES(ICD9:460-466,477)]
Kim et al. 2012	TS	USA	2003-2007	Morbidity	All	EC	ICD-9	CVD(ICD-9:390-459),RES(ICD-9:460-519)
								copyright.

49 of 133						В	MJ Opei	36/bmjope
Table S2 Chara	cteristics (	of included s	studies in the	systematic re	eview and n	neta-analysi	s.	36/bmjopen-2021-049516 on
Study	Study Design	Country	Study Period	Outcome	Age	Pollutant	ICD code	သ ယ Discases ဩ
Ostro et al. 2009	TS	USA	2000-2003	Morbidity	<19	EC	ICD9	RES(ICD-9:460-519),Asthma(ICD-9:493),Acute bro hitis(ICD-9:466),Pneumonia(ICD-9:480-486)
Kim et al. 2015	TS	USA	2003-2007	Mortality	All	EC	ICD-10	CVD,RES
Huang et al. 2012	TS	China	2004-2008	Mortality	All	EC	ICD-10	RES(ICD-10:100-198),CVD(ICD-10:100-199 )
								CVD[Cardiac Dysrhythmias(ICD-9:428),Heart Rhytton Disturbances(ICD-9:426-427),Cerebrovascular Events
Peng et al. 2009	TS	USA	2000-2006	Morbidity	≥65	EC	ICD-9	(ICD-9:430-438),IHD (ICD-9:410-414,
								429),PVD(ICD-9:440-448)],RES[COPD(ICD-9:490
Levy et al. 2012	TS	USA	2000-2008	Morbidity	≥65	EC	ICD-9	CVD(ICD-9:390-459),RES(ICD-9:464-466 and 480-487).
Son et al. 2012	TS	Korea	2008-2009	Mortality	All	EC	ICD-10	CVD(ICD-10:100-I99),RES(ICD-10:J00-J99)
Heo et al. 2014	TS	Korea	2003-2007	Mortality	All	EC	ICD-10	CVD(ICD-10:100-I99),RES(ICD-10:J00-J99)  CVD(ICD-10:100-I99),RES(ICD-10:J00-J98)
Basagaña et al. 2015	CS	Spain, Italy	2003-2013	Morbidity,  Mortality	All	EC	ICD-9, ICD-10	CVD(ICD-9:390-459,ICD-10:100-199),RES(ICD-9:469-519,ICD-10:J00-J99)
Dai et al. 2014	TS	USA	2000-2006	Mortality	All	EC	ICD-10	CVD(ICD-10:I01-I59),RES(ICD-10:J00-J99),MI(ICD-10:I21-I22),Stroke(ICD-10:I60-I69)
Lin et al. 2016a	TS	China	2007-2011	Mortality	All	EC	ICD-10	CVD(ICD-10:I00-I99)
Cao et al. 2012	TS	China	2004-2008	Mortality	All	EC	ICD-10	
Klemm et al. 2011	TS	USA	1998-2007	Mortality	≥65	EC	ICD-10	CVD(ICD-10:100-I99),RES(ICD-10:J00-J98)  CVD(ICD-10:100-I99),RES(ICD-10:J00-J99)
Zhou et al. 2011	TS	USA	2002-2004	Mortality	All	EC	ICD-10	CVD(ICD-10:I01-I99),RES(ICD-10:J00-J99)
Winquist et al. 2015	TS	USA	2001-2003	Morbidity	All	BC,EC	ICD-9	CVD(ICD-10:I01-I99),RES(ICD-10:J00-J99)  RES(ICD-9:460-465,466.0,466.1,466.11,466.19,477, 80-486,491,492,493,496,786.07),CVD(ICD-9:410-414,427, 428,433-437,440,443-445,451-453)
Ostro et al. 2007	TS	USA	2000-2003	Mortality	All	EC	ICD-10	428,433-437,440,443-445,451-453)  CVD(ICD-10:I00-I99),RES(ICD-10:J00-J98)
Tolbert et al. 2000	TS	USA	1998-2000	Morbidity	All	EC	ICD-9	CVD(ICD-9:402,410-414,427,428,433-437,440,444,491-453),RES(ICD-9:460-466,477,480-486,491,492,493,496,
								786.09)  Red by copyright.

**Table S2** Characteristics of included studies in the systematic review and meta-analysis.

Study	Study Design	Country	Study Period	Outcome	Age	Pollutant	ICD code	On Wiscases Way
Wang and Lin 2016	TS	China	2004-2010	Morbidity, Mortality	≥65(mortality), all(morbidity)	EC	ICD-9	CVD(ICD-9-CM:390-459),RES(ICD-9-CM:460-519)
Darrow et al. 2014	TS	USA	1993-2010	Morbidity	0–4	EC	ICD-9	Acute Bronchitis or Bronchiolitis(ICD-9:466),Pneumonia(ICD-9:480-486),URI(ICD-9:460-465)
Metzger et al. 2004	TS	USA	1993-2000	Morbidity	All	EC	ICD-9	CVD[IHD(ICD-9:410-414),AMI(ICD-9:410),cardiacoddysrhythmias(ICD-9:427),CA(ICD-9:427.5),CHF(ICD-9:428),PVD and cerebrovascular events(ICD-9:433-437,440,443-444,451-453),CHD(IGD-9:440),Stroke(ICD-9:436)]
Mar et al. 2000	TS	USA	1995-1997	Mortality	All	EC	ICD-9	CVD(ICD-9:390-448.9)
Wang et al. 2019a	TS	China	2013-2015	Mortality	All	EC	ICD-10	CVD(ICD-9:390-448.9)  CVD(ICD-10:I00-I99),RES(ICD-10:J00-J99)  Stroke(ICD-10:I60-I66)
Lin et al. 2016b	TS	China	2007-2011	Mortality	All	EC	ICD-10	Stroke(ICD-10:I60-I66)
Ostro et al. 2008	TS	USA	2000-2003	Mortality	All	EC	ICD-10	CVD(ICD-10:100-199)
Ito et al. 2011	TS	USA	2000-2006	Morbidity, Mortality	≥40	EC	ICD-9, ICD-10	CVD[Hypertensive Diseases(ICD-9:402,ICD-10:I11] MI(ICD-9:410;ICD-10:I21-I22),IHD  (ICD-9:414,ICD-10:I25),Dysrhythmias(ICD-9:427,IO)-10:I48),HF(ICD-9:428,ICD-10:I50),Stroke(ICD-9:430-43-43-43-43-43-43-43-43-43-43-43-43-43-
Chen et al. 2014	TS	China	2004-2008	Morbidity	All	EC	ICD-9	Stroke[Ischemic Stroke(ICD-9:433-434),Hemorrhagie Stroke(ICD-9:430-432)]
Tomic'-Spiric' et al. 2019	CS	Serbia	2012-2014	Morbidity	≥18	ВС	ICD-10	Allergic RES[AR(ICD-10:J.30.4),AA(ICD-10:J.45.0
Maynard et al. 2007	CS	USA	1995-1997, 1999-2002	Mortality	All	BC	ICD-9, ICD-10	CVD(ICD-9:390-429,ICD-10:101-152),Stroke(ICD-9-330-438,ICD-10:160-169),RES(ICD-9:460-519,ICD-10:J00-J
Sinclair et al. 2010	TS	USA	1998-2002	Morbidity	All	EC	NR	Asthma,URII,LRII
Krall et al. 2013	TS	USA	2000-2005	Mortality	All	EC	NR	CVD and RES(NR)  RES(ICD-9:460-519)
Cakmak et al. 2009	TS	Canada	2001-2006	Morbidity	All	EC	ICD-9	RES(ICD-9:460-519)
								by co

Table S2 Characteristics of included studies in the systematic review and meta-analysis.

Study	Study	Country	Study	Outcome	Age	Pollutant	ICD	O D W Nisangan
Study	Design	Country	Period	Outcome	Age	ronutant	code	Suscases Discases
								CVD[IHD(ICD-9:410-414),Cardiac Dysrhythmias(ICD-9:427),CHF(ICD-9:428),PVD and Cerebrovascular
Tolbert et al. 2007	TS	USA	1993-2004	Morbidity	All	EC	ICD-9	Events(ICD-9:433-437,440,443-445,451-453)],
Tolbert et al. 2007	13	USA	1993-2004	Morbialty	All	EC	ICD-9	RES[Asthma(ICD-9:493,786.07,786.09),COPD(ICD 2:491,492,496),URTI(ICD-9:460-465,460.0,477),Pneumoni
								(ICD-9:480-486),Bronchiolitis(ICD-9:466.1,466.11,466.19)]
								RES[Pneumonia(ICD-9:480-486),COPD(ICD-9:490
Lall et al. 2011	TS	USA	2001-2002	Morbidity	≥65	EC	ICD-9	Bronchiolitis(ICD-9:466),Asthma(ICD-9:493)],CVD (ICD-9:427),IHD(ICD-9:410-414),HF(ICD-9:493)
								28),Stroke(ICD-9:431-437)]
Jung and Lin 2017	CS	China	2000-2010	Morbidity	0-20	BC	ICD-9	Asthma(ICD-9-CM:493)
Gong et al. 2019	TS	China	2006-2011	Mortality	All	ВС		Asthma(ICD-9-CM:493)  CVD(ICD-10:100-199)  Acute Ischemic Stroke
							ICD-10	Gen.
Mostofsky et al. 2012	CS	USA	2003-2008	Morbidity	≥21	ВС	NO	Acute Ischemic Stroke
			1999-2009(Atlan					.con
			ta,Georgia),					√ or
			2004-010(Birmi					Ap
Krall et al. 2017	TS	USA	ngham,Alabama,	Morbidity	All	EC	ICD-9	RES[Pneumonia(ICD-9:480-486),COPD(ICD-9:491, \$\frac{1}{29}2,496),URTI(ICD-9:460-465,466.0,477),Asthma and/or
			2001-2007(St.Lo					Wheeze(ICD-9:493,786.07)]
			uis, Missouri ),					92 4
			2006-2009(Dalla					Wheeze(ICD-9:493,786.07)]  20 24  by 90  85  Asthma(ICD-9:493.0-493.9),Wheeze(ICD-9:786.07);
			s,Texas)					ues
O'Lenick et al. 2017	CS	USA	2001-2008	Morbidity	5–18	EC	ICD-9	
Pearce et al. 2015	TS	USA	1999-2008	Morbidity	5–17	EC	ICD-9	Asthma(ICD-9:493.0-493.9),Wheeze(ICD-9:786.07)
Strickland et al. 2010	CS	USA	1993-2004	Morbidity	5-17	EC	ICD-9	Asthma(ICD-9:493.0-493.9),Wheeze(ICD-9:786.09)

Table S2 Characteristics of included studies in the systematic review and meta-analysis.

Table 52 Charac	Study		Study				ICD	9
Study	·	Country	·	Outcome	Age	Pollutant		₩iseases D
	Design		Period				code	<u> </u>
Strickland et al. 2014	TS	USA	2000-2010	Morbidity	2-16	EC	ICD-9	Asthma(codes beginning with 493),Wheeze (ICD-9:78).07)
Ito et al. 2013	TS	USA	2001-2006	Morbidity,	all (mortality),	EC	ICD-9,	.N CVD(ICD-10:I01-I79),RES(ICD-10:J00-J99) □
110 et al. 2015	15	OBN	2001-2000	Mortality	≥65(morbidity)	LC	ICD-10	CVD(ICD-10:I01-I79),RES(ICD-10:J00-J99)
Ostro et al. 2015b	Co	USA	2001-2007	Mortality	≥30	EC	ICD-10	CVD(ICD-10:I00-I99),IHD(ICD-10:I20-I25),Pulmortary(ICD-10:C34,J00-J98)
G 1 2012			1000 2002	Morbidity,	45.05	D.C.	ICD-9,	Q @ Q
Gan et al. 2013	Со	Canada	1999-2002	Mortality	45-85	ВС	ICD-10	COPD(ICD-9:490-492,496,ICD10:J40-J44)
Hvidtfeldt et al. 2019	Co	Denmark	1993-2015	Mortality	50 -64	BC	ICD-10	CVD(ICD-10:I00-I99),RES(ICD-10:J00-J99,C34)
TI 1 2016		TIG A	1000 2004	Mark	> 20	FC	ICD-9,	HID/ICD 0 410 414 ICD 10 100 100
Thurston et al. 2016	Со	USA	1988-2004	Mortality	≥30	EC	ICD-10	IHD(ICD-9:410-414,ICD-10:120-125)
Yang et al. 2018	Co	China	1998-2011	Mortality	≥65	BC	ICD-10	CVD(ICD-10:100-199),RES(ICD-10:J00-J99,C34)  IHD(ICD-9:410-414,ICD-10:I20-I25)  CVD(ICD-10:I00-I99),RES(ICD-10:J00-J47,J80-J999
			4000 4004	Morbidity,			ICD-9,	
Gan et al. 2011	Со	Canada	1999-2002	Mortality	45–85	BC	ICD-10	CHD(ICD-9:410-414,429.2),(ICD-10:120-125)  IHD(ICD-9:410-414),CHD(ICD-9:430-438)  CVD (ICD-9:CM 410-452)  On Appli
De Kluizenaar et al.								3
2013	Со	Netherlands	1991-2003	Morbidity	15-74	EC	ICD-9	IHD(ICD-9:410-414),CHD(ICD-9:430-438)
				Morbidity,				pril
Vedal et al. 2013	Со	USA	1994-2005	Mortality	50-79	EC	ICD-9	
Rahmatinia et al. 2021	TS	Iran	2014-2017	Mortality	All	ВС	ICD-10	RES(ICD10:J00- J99),CVD(ICD10:I00-I99),IHD(ICW)10:I20-I25)
Liu et al. 2021b	Co	China	2010–2017	Morbidity	All	ВС	NR	CVD(including but not limited to hypertension and stocke)
Lavigne et al. 2021	Co	Canada	2006-2014	Morbidity	€6	BC	ICD-10	Asthma(ICD-10:J45)
Rodins et al. 2020	Co	Germany	2000-2015	Morbidity	All	EC	NR	
Kovačević et al. 2020	CS	Serbia	2012-2014	Morbidity	≥18	BC	ICD-10	AA(ICD-10:J45.0) or asthma with coexisting AR  Atherosclerosis in the carotid arteries
Hasslöf et al. 2020	Co	Sweden	1991-1994	Morbidity	All	BC	NR	
								δ

**Table S2** Characteristics of included studies in the systematic review and meta-analysis.

								<u>0</u>
Study	Study	Country	Study	Outcome	Age	Pollutant	ICD	 ↓ ↓iseases
Study	Design	Country	Period	Outcome	Age	1 onutant	code	a)
Wang et al. 2019b	CS	USA	2005-2016	Morbidity	All	BC	NR	STEMI 20
1		Sweden	1000 2011	Morbidity,	4.11	ВС	ICD-9,	NO THE PROPERTY OF THE PROPERT
Ljungman et al. 2019	Co		1990-2011	Mortality	All		ICD-10	IHD(ICD-9:410–414 and ICD-10:120-25);stroke(ICD 3:431–436 and ICD-10:161–165)
Time at al. 2021a	C-	Sweden,	1002 2004	M. J. 1414	A 11	D.C.	ICD-9,	CONDUCTO 0.400, 402, and 404, 405, and ICD 10.1400440
Liu et al. 2021a	Со	Denmark	1992-2004	Morbidity	All	ВС	ICD-10	COPD(ICD-9:490–492, and 494–496, or ICD-10:J40)

Abbreviations: NR: Not Reported; TS: Time-Series; CS: Case-Crossover; Co: Cohort; ICD: International Classification of Diseases; MI: Myocardial infarction; CHD: Coronary heart disease; CVD are all content of the composition of the compositio

Table S3 Subgroup analysis on short-term effects of BC/EC on cardiovascular and respiratory diseases.

Subgroup Analysis	No. of	No. of	Relative Risk	$\mathbf{I}^2$	Egger Regression Test
Subgroup Analysis	Studies	Estimates	(95%CI)	1	(p value)
Cardiovascular Diseases					
Lag Days					
Lag 0d	15	18	1.013 (1.006, 1.020)*	77.30%	0.024
Lag 1d	12	15	1.005 (1.002, 1.008)	32.70%	0.299
Lag 2d	11	14	1.002 (0.999, 1.005)	73.80%	0.969
Geographical Location (Mortality)					
Asia	8	8	1.004 (1.002, 1.006)*	70.00%	_
Europe	4	5	0.991 (0.983, 0.999)	0	_
America	4	4	1.017 (0.998, 1.037)	20.80%	_
Geographical Location (Morbidity)					
Asia	_	_	_	_	_
Europe	_	_	_	_	_
America	12	12	1.023 (1.016, 1.030)	46.00%	0.078
Disease					
Congestive heart failure (Morbidity)	3	3	1.076 (1.021, 1.134)*	64.70%	_
Season (Mortality)					
Warm season	3	3	1.002 (0.995, 1.010)	0	_
Cold season	3	3	1.014 (1.008, 1.019)*	0	_
Respiratory Diseases					
Asthma (Morbidity)					
Asthma 0-18	5	6	1.021 (1.006, 1.035)*	69.10%	
Asthma ≥18	4	5	1.011 (1.000, 1.021)	0	_

Annotation: "\*" means the data were statistically significant, p < 0.05.

Table S4 Summary statistics for the number of possible analyses using the three search spaces.

Statistic	Space1	Space2	Space3
maximum	704	128	22528
quartile	273	64	15360
median	198	64	12000
quartile	42	32	2688
minimum	8	32	256

Table S5 Results of risk of bias assessment.

			Key criteria	I		Other criteria					
No.	Study	Exposure	Outcome	Confounding	Selection	Incomplete	Selective	Conflict of	Otho		
		assessment	assessment	bias	bias	outcome data	reporting	interest	Othe		
1	Atkinson et al. 2016										
2	Bell et al. 2014										
3	Cai et al. 2014										
4	Geng et al. 2013										
5	Hua et al. 2014										
6	Ostro et al. 2015a										
7	Samoli et al. 2016										
0	Zanobetti and Schwartz										
8	2006										
9	Liu et al. 2016a										
10	Liu et al. 2016b										
11	Sarnat et al. 2015										
12	Kim et al. 2012										
13	Ostro et al. 2009										
14	Kim et al. 2015										
15	Huang et al. 2012										
16	Peng et al. 2009										
17	Levy et al. 2012										
18	Son et al. 2012										
19	Heo et al. 2014										
20	Basagaña et al. 2015										
21	Dai et al. 2014										
22	Lin et al. 2016a										
23	Cao et al. 2012										
24	Klemm et al. 2011										
25	Zhou et al. 2011										
26	Winquist et al. 2015										
27	Ostro et al. 2007										
28	Tolbert et al. 2000										
29	Wang and Lin 2016										
30	Darrow et al. 2014										
31	Metzger et al. 2004										
32	Mar et al. 2000										
33	Wang et al. 2019a										
34	Lin et al. 2016b										
35	Ostro et al. 2008										

Table S5 Results of risk of bias assessment. (continued)

			Key criteria	1		Otl	her criteria		
No.	Study	Exposure	Outcome	Confounding	Selection	Incomplete	Selective	Conflict	O.I.
		assessment	assessment	bias	bias	outcome data	reporting	of interest	Other
36	Ito et al. 2011								
37	Chen et al. 2014								
38	Tomic'-Spiric' et al. 2019								
39	Maynard et al. 2007								
40	Sinclair et al. 2010								
41	Krall et al. 2013								
42	Cakmak et al. 2009								
43	Tolbert et al. 2007								
44	Lall et al. 2011								
45	Jung and Lin 2017								
46	Gong et al. 2019								
47	Mostofsky et al. 2012								
48	Krall et al. 2017								
49	O'Lenick et al. 2017								
50	Pearce et al. 2015								
51	Strickland et al. 2010								
52	Strickland et al. 2014								
53	Ito et al. 2013								
54	Ostro et al. 2015b								
55	Gan et al. 2013								
56	Hvidtfeldt et al. 2019								
57	Thurston et al. 2016								
58	Yang et al. 2018								
59	Gan et al. 2011								
60	De Kluizenaar et al. 2013								
61	Vedal et al. 2013								
62	Rahmatinia et al. 2021								
63	Liu et al. 2021b								
64	Lavigne et al. 2021								
65	Rodins et al. 2020								
66	Kovačević et al. 2020								
67	Hasslöf et al. 2020								
68	Wang et al. 2019b								
69	Ljungman et al. 2019								
70	Liu et al. 2021a								
	Risk of bias rating:	Low		Probably Low		Probably High		High	

Table S6 Details of risk of bias assessment.

e 57 of	f 133			BMJ Oper	١	36/bmJoper			
						7-2021-04951			
	Table S	6 Details of risk of bias asses	ssment.						
No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias			Conflict of interest	Other
1	Atkinson	Probably Low	Low	Probably Low	Low	Low	Probably Low	Low	Low
	et al. 2016	All of the pollutants were measured at the central London background monitoring site at North Kensington. All measurements were 24-h averages except for CO. The number of all observations was 621-693 (<25% missing data).	Death data for the period 1 January 2011 to 31 December 2012 were obtained from the Office for National Statistics. Daily counts of deaths in London, United Kingdom were classified as all disease-related causes, cardiovascular (International Classification of Diseases,10th revision-ICD10: I00-I99) and respiratory (ICD10: J00-J99) diseases.	Adjusted for time (seasonality, long-term trend), temperature, humidity, day of week and public holidays.	Study included daily counts of deaths in London, United Kingdom for the period 1 January 2011 to 31 December 2012.	Daily counts for death were obtained, so likely have all outcome data. However, any potential errors or missing dataged did not depend on air pollution levels.	There was insufficient information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of selective report.	The authors declare no conflict of interest.	No other potential sources of bias identified.
		No. Study  1 Atkinson	Table S6 Details of risk of bias asses  No. Study Exposure assessment  1 Atkinson et al. 2016 All of the pollutants were measured at the central London background monitoring site at North Kensington. All measurements were 24-h averages except for CO. The number of all observations was 621-693 (<25% missing	Table S6 Details of risk of bias assessment.  No. Study Exposure assessment Outcome assessment  1 Atkinson et al. 2016 All of the pollutants were measured at the central London background monitoring site at North Kensington. All measurements were 24-h averages except for CO. The number of all observations was 621-693 (<25% missing data).  Classification of Diseases,10th revision-ICD10: 100-199) and respiratory (ICD10:	Table S6 Details of risk of bias assessment  No. Study  Exposure assessment  Outcome assessment  Confounding bias  Atkinson et al. 2016  All of the pollutants were measured at the central London background monitoring site at North Kensington. All measurements were 24-h averages except for CO. The number of all observations was 621-693 (<25% missing data).  Confounding bias  Death data for the period 1 January 2011 to 31 December 2012 were obtained from the Office for National Statistics. Daily counts of deaths in London, United Kingdom were classified as all disease-related causes, cardiovascular (International Classification of Diseases, 10th revision-ICD10: 100-199) and respiratory (ICD10:	Table S6 Details of risk of bias assessment.  No. Study Exposure assessment Outcome assessment Confounding bias Selection bias  Atkinson et al. 2016 All of the pollutants were measured at the central London background monitoring site at North Kensington. All measurements were 24-h averages except for CO. The number of all observations was 621-693 (<25% missing data).  Confounding bias Selection bias  Confounding bias Selection bias  Study included Adjusted for time (seasonality, long-term trend), temperature, humidity, day of week and public period 1 January 2011 to 31 December 2012 were obtained from the Office for National Statistics. Daily counts of deaths in unwidity, day of week and public holidays.  Classification of Diseases, 10th revision-ICD10: 100-199) and respiratory (ICD10:	No. Study    Probably Low	Table S6 Details of risk of bias assessment.  No. Study  Exposure assessment  Outcome assessment  Confounding bias  Selection bias  Atkinson et al. 2016  Atkinson et al. 2016  All of the pollutants were measured at the central London background monitoring site at North Kensington. All measurements were 24-h averages except for CO. The number of all observations was 621-693 (<25% missing data).  Classification of Diseases, 10th revision-ICD10: 100-199) and respiratory (ICD10:	No. Study    Exposure assessment   Outcome assessment   Confounding bias   Selection bias   Incomplete outcome data   Selective reporting   Conflict of interest

No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data S		Conflict of interest	Other
2	Bell et al.	Probably High	Low	Probably Low	Low	Low	Probably Low	Low	Low
	2014	BC measured from filters	The study used the	Models adjusted	Data obtained	Daily counts	There was	The authors	No other
		collected daily using	Medicare beneficiary	for time	from records of	for hospital	insufficient	declare no	potential
		optical reflectance.	denominator file from the	(seasonality,	individuals ≥65	admissions \( \frac{\blue{2}}{2} \)	information	conflict of	sources of
		Monitors from 5 sites	Centers for Medicare and	long-term trend),	years of age	were obtained,	about	interest.	bias
		across 4 counties were	Medicaid Services. Cause	day of week,	enrolled in the	so likely have	selective		identified.
		used. Sampling occurred	of admission was	temperature, and	Medicare	all outcome	outcome to		
		daily, with some missing	determined by principal	dew point.	fee-for-service	data. However,	judge for low		
		periods, for Hartford,	discharge diagnosis code		plan during	any potential	risk, but		
		New Haven, and	according to International	1/6	August 2000 to	errors or	indirect		
		Springfield, and every	Classification of	' (2)	February 2004.	missing data	evidence that		
		third day for Bridgeport	Diseases, Ninth Revision,			did not depend	suggests study		
		and Danbury. Days with	Clinical Modification			on air pollution	was free of		
		missing data were	(ICD-9-CM; National			levels.	selective		
		omitted from analysis	Center for Health			Api	report.		
		(the number of missing	Statistics 2006).						
		data was not reported).				9, 20			
						)24			
						by g			
						lues			
						April 19, 2024 by guest. Protected by			
						) Stec			

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data		Conflict of interest	Other
8	3	Cai et al.	Probably Low	Low	Probably Low	Low	Low	Probably Low	Low	Low
10		2014	Daily concentrations of	Asthmatic hospitalization	Adjusted for time	Study included	Daily counts	There was	Authors	No other
11			BC were measured at a	data was obtained from	(seasonality,	all asthmatic	for asthmatic	insufficient	declared no	potential
12			fixed-site station. Daily	the Shanghai Health	long-term trend),	hospitalization	hospitalization 💆	information	competing	sources of
13 14			data was available and no	Insurance Bureau	temperature,	for adult	were obtained,	about	financial	bias
15			missing data was	(SHIB). The causes of	relative humidity	residents living	so likely have	selective	interests.	identified.
16			reported.	hospital admission were	and day of the	in the nine urban	all outcome	outcome to		
17 18				coded according to	week.	districts between	data. However,	judge for low		
19				International		January 1, 2005	any potential	risk, but		
20				Classification of	' /	and December	errors or	indirect		
21				Diseases, Revision 10	' (2)	31, 2011(2922	missing data	evidence that		
22 23				(ICD-10): Asthma (J45).		days) from the	did not depend.	suggests study		
24						Shanghai Health	on air pollution	was free of		
25						Insurance	levels.	selective		
26 27						Bureau.	Ap	report.		
28								:		
29							9, 20			
30							2024 by			
31 32							by g	•		
33							' guest.			
34										
35							rote			
36 37							Protected			
38							<u>b</u>			

4 5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data ≤	Selective reporting	Conflict of interest	Other
8 9			Probably High	Low	Probably Low	Low	Low $\overset{\mathbf{a}}{\overset{\mathbf{b}}{\overset{\mathbf{c}}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}}{\overset{\mathbf{c}}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{c}}{\overset{c}}{\overset{\mathbf{c}}}}{\overset{\mathbf{c}}}{\overset{\mathbf{c}}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}}{\overset{c}}}{\overset{c}}}{\overset{\mathbf{c}}{\overset{c}}}{\overset{c}}{\overset{c}}{\overset{c}}{\overset{c}}}{\overset{c}}{\overset{c}}{\overset{c}}{\overset{c}}{\overset{c}}}}{\overset{c}}}{\overset{c}}{\overset{c}}{\overset{c}}}{\overset{c}}}{\overset{c}}}{\overset{c}}}{\overset{c}}{\overset{c}}{\overset{c}}}{\overset{c}}}{\overset{c}}}{\overset{c}}}{\overset{c}}}{\overset{c}}{\overset{c}}}{\overset{c}}}{\overset{c}}}{\overset{c}}}{\overset{c}}}{\overset{c}}{\overset{c}}}{\overset{c}}}{\overset{c}}}{\overset{c}}}}{\overset{c}}{\overset{c}}{\overset{c}}}{\overset{c}}}{\overset{c}}}{\overset{c}}}{\overset{c}}}{\overset{c}}{\overset{c}}}{\overset{c}}}{\overset{c}}}}{\overset{c}}}{\overset{c}}{\overset{c}}}{\overset{c}}}{\overset{c}}{\overset{c}}}{\overset{c}}}{\overset{c}}}{\overset{c}$	Probably Low	Low	Low
10	4	Geng et	Single, central-site	Health data were	Models included	Data consisted of	Daily counts	There was	The authors	No other
11		al. 2013	monitor. Daily BC and	obtained from Shanghai	time (seasonality,	all causes	for death were	insufficient	declare no	potential
12			PM <sub>2.5</sub> were measured	Municipal Center of	long-term trend),	(excluding	obtained, so	information	conflict of	sources of
13 14			continuously and 24hr	Disease Control and	temperature,	accidents or	likely have all	about	interest.	bias
15			averaged was estimated	Prevention database. The	humidity and day	injuries) deaths	outcome data.	selective		identified.
16			if >75% of the 1hr values	causes of death were	of week.	during over the	However, any	outcome to		
17 18			was available for that	coded according to the		course of the	potential errors	judge for low		
19			day. Missing data was not	International		study.	or missing data	risk, but		
20			replaced by other values.	Classification of	' /		did not depend	indirect		
21				Diseases, Revision 10	' (2)	•	on air pollution	evidence that		
22 23				(ICD 10).			levels.	suggests study		
24						<b>101.</b>	com	was free of		
25						1eh	on	selective		
26 27							Αp	report.		
28								_		
29							9, 2			
30							024			
31							by (			
33							gue			
34							St. Ti			
35							rote			
36 37							ecte			
37 38							on April 19, 2024 by guest. Protected by			

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data		Conflict of interest	Other
3			Probably High	Low	Probably Low	Low	Low	Probably Low	Low	Low
10	5	Hua et al.	Daily 24h average PM <sub>2.5</sub>	Daily asthma hospital	Adjusted for	Study included	Daily counts	There was	Authors	No other
11		2014	and BC data was	admission data was	long-term and	all asthma	for asthma	insufficient	declared no	potential
12			obtained from a fixed-site	obtained from Shanghai	seasonal trend, day	hospital	hospital <u>§</u>	information	competing	sources of
13 14			station. The study only	Children's Medical	of week,	admissions of	admissions of	about	financial	bias
15			used the actual collected	Center. Dates of	temperature and	children ≤ 14	children were	selective	interests.	identified.
16			data and did not fill in the	admission and discharge,	relative humidity.	years of age from	obtained, so	outcome to		
17 18			missing data for PM <sub>2.5</sub>	and diagnoses using the	<b>'</b> O.	Shanghai	likely have all	judge for low		
19			and black carbon.	International		Children's	outcome data.	risk, but		
20				Classification of	' /	Medical Center	However, any	indirect		
21				Diseases, Revision 10.	. 01	between1	potential errors	evidence that		
22   23						January 2007 and	or missing data	suggests study		
24						31 July 2012 in	did not depend			
25						nine urban	on air pollution			
26   27						districts of				
28						Shanghai.	April 19, 2024 by guest. Protected b	1		
29							9, 2			
30							024			
31							by			
32 33							gue			
34							st.			
35							Prot			
36							ecte			
37   38										

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data ≤	Selective reporting	Conflict of interest	Other
8 9			Probably Low	Low	Low	Low	Low	Probably Low	Low	Low
10	6	Ostro et	Daily 24hr average BC	For both cities daily	Adjusted for long	Study population	Daily counts	There was	Authors	No other
11		al. 2015a	concentrations were	counts of all-cause	term and seasonal	consisted of daily	for death were	insufficient	declared no	potential
12			obtained from one station	mortality for all ages	(year, month, day	counts of	obtained, so	information	competing	sources of
13 14			in Barcelona and Athens.	were collected (excluding	of week) trends,	all-cause	likely have all	about	interests.	bias
15			Daily data was available	deaths from external	temperature,	mortality for all	outcome data.	selective		identified.
16			and no missing data was	causes, International	holidays, summer	ages and daily	However, any	outcome to		
17 18			reported.	Classification of	vacations and	counts of	potential errors	judge for low		
19				Disease-ICD9: 001799,	influenza.	cardiovascular,	or missing data	risk, but		
20				ICD10 A00R99), as well	' /	respiratory and	did not depend	indirect		
21				as daily counts of	' (2)	all-cause	on air pollution	evidence that		
22 23				cardiovascular (ICD9:		mortality for	levels.	suggests study		
24				390459, ICD10: I00I99),		those greater than	com	was free of		
25				respiratory		age 65.	on	selective		
26 27				(ICD9:460519,			Αp	report.		
28				ICD10:J00J99) and			April 19, 2024 by guest.			
29				all-cause mortality for			9, 20			
30				those greater than age 65.			)24			
31 32							by ç			
33							Jues			
34							; <u>;</u> 			
35							rote			
36 37							Protected by			
38							by c			

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete Soutcome data		Conflict of interest	Other
8 9			Low	Low	Probably Low	Low	Low	Probably Low	Low	Low
10	7	Samoli et	Daily concentrations of	Based on the primary	Adjusted for long	Study included	Daily counts	There was	Authors	No other
11		al. 2016	BC and EC were	discharge diagnosis, daily	term and seasonal	all cardiovascular	for all	insufficient	declared no	potential
12			collected from the	numbers of admissions	trends,	and respiratory	emergency §	information	competing	sources of
13 14			ClearfLo project,	for cardiovascular disease	temperature,	hospital	hospital 8	about	interests.	bias
15			supplemented by local	(International	relative humidity,	admissions in	admissions 🛱	selective		identified.
16			measurements made at	Classification of	regulated	London, UK	were obtained,	outcome to		
17 18			the North Kensington	Diseases, 10th	pollutants (PM <sub>10</sub> ,	between 2011	so likely have	judge for low		
19			urban background site.	revision-ICD-10:	PM <sub>2.5</sub> , NO <sub>2</sub> , SO <sub>2</sub>	and 2012.	all outcome	risk, but		
20			Number of days of	I00-I99) for those aged	and O <sub>3</sub> ), day of the		data. However,	indirect		
21			observation for BC: 629	15-64 (adult) and 65+	week and public		any potential	evidence that		
22 23			(BC urban in PM <sub>2.5</sub> ) and	years (elderly), and	holidays.		errors or	suggests study		
24			702 (BC in PM <sub>2.5</sub> )	respiratory diseases		'01.	missing data	was free of		
25			between 2011 and 2012	(ICD-10: J00-J99) for			did not depend 9	selective		
26 27			(<25% missing data).	those aged 0-14 years			on air pollution €	report.		
28				(paediatric), adult and the			levels.			
29				elderly were calculated.			9, 20			
30							2024 by			
31 32							оу д			
33							guest.			
34							τ	1		
35 36							rote			
37							rotected			
38							9	-		

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data		Conflict of interest	Other
8 9			Probably High	Low	Probably Low	Low	Low <sup>ay</sup>	Probably Low	Low	Low
9 10	8	Zanobetti	Ambient BC from one	The study extracted data	Adjusted for	Data consisted of	Daily counts	There was	Authors	No other
11		and	monitor. The hourly	on all hospital admissions	temperature, day	all U.S. Medicare	for hospital	insufficient	declared no	potential
12		Schwartz	measurements for BC and	for residents of the	of the week,	hospital	admissions 💆	information	competing	sources of
13 14		2006	PM <sub>2.5</sub> were not complete.	Boston Metropolitan area	seasonality,	admissions in the	were obtained,	about	interests.	bias
15			Missing values were	who were admitted to the	long-term trends,	Boston	so likely have	selective		identified.
16			replaced with the	hospital (in the Boston	humidity,	Metropolitan	all outcome	outcome to		
17 18			predicted values.	area) with a primary	barometric	area for	data. However,	judge for low		
19			Additionally BC data was	diagnosis of MI	pressure, and the	myocardial	any potential	risk, but		
20			missing from March 1997	(International	extinction	infarction during	errors or	indirect		
21 22			to March 1999 and was	Classification of	coefficient.	the study	missing data	evidence that		
22			not included in the study.	Diseases, 9th		duration.	did not depend	suggests study		
24				revision-ICD-9:410), and		<b>'</b> 0/.	on air pollution	was free of		
25				pneumonia (ICD-9:			levels.	selective		
26 27				480–487), from Medicare			Apr	report.		
28				billing records for the			19,			
29				years 1995-1999.			9, 20			
30 31							2024 by			
32							оу <u>д</u>			
33							' guest.			
34										
35 36							Protected			
37							Sted			
38 <sup>l</sup>							\$	1		

5 No	0.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data		Conflict of interest	Other
3			Probably High	Low	Probably Low	Low	Low $\stackrel{\text{ad}}{\sim}$	Probably Low	Low	Low
9		Liu et al.	EC were collected from a	Emergency department	Adjusted for time	Study included	Daily counts	There was	Authors	No other
1		2016a	single monitor on a	visit data was obtained	(long-term and	daily counts of	for emergency	insufficient	declared no	potential
12			one-in-three or one-in-six	from the Blue Cross Blue	seasonal trend),	emergency	department \( \)	information	potential	sources of
3  4			day schedule. EC were	Shield Texa. International	day of week,	department visits	visits were	about	competing	bias
5			measured for 566 days	Classification of Diseases	temperature, dew	for Greater	obtained, so	selective	financial	identified.
6			from April 02, 2009, to	9th Revision (ICD-9)	point and	Houston from	likely have all	outcome to	interests.	
7  8			December 30, 2013,	diagnosis codes were	population growth.	claims data	outcome data.	judge for low		
19			<25% missing for the	used to classify outcome	C/	insured from	However, any	risk, but		
20			frequency of sampling.	groups.	1 /	January 1, 2008	potential errors	indirect		
21					' (%)	through	or missing data			
22   23						December 31,	did not depend			
24						2013.	on air pollution			
25							levels.	selective		
26							ieveis.	report.		
27										
28 29							ي ا			
30							2024 by			
31							4			
32							y 9			
33							, guest.			
34							i ii	<u> </u>		
35							Protected			
36							ecte			
37 38							Ď			

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on the outcome data		Conflict of interest	Other
8 9			Probably High	Low	Probably Low	Low	Low	Probably Low	Low	Low
10	10	Liu et al.	EC were collected from a	Hospital admission data	Adjusted for time,	Study included	Daily counts	There was	Authors	No other
11		2016b	single monitor on a	was obtained from the	day of week,	all hospital	for HA were	insufficient	declared no	potential
12			one-in-three or one-in-six	Blue Cross Blue Shield	temperature,	admissions	obtained, so	information	competing	sources of
13 14			day schedule. EC were	Texa. International	seasonaility,	obtained from	likely have all	about	financial	bias
15			measured for 566 days	Classification of Diseases	humidity and	billing claims of	outcome data.	selective	interests.	identified.
16			from April 02, 2009, to	9th Revision (ICD-9)	population growth.	Blue Cross Blue	However, any	outcome to		
17			December 30, 2013,	diagnosis codes were		Shield Texa	potential errors	judge for low		
18 19			<25% missing for the	used to classify outcome		enrollees for	or missing data	risk, but		
20			frequency of sampling.	groups.	'/	Greater Houston	did not depend	indirect		
21					(0)	from January 1,	on air pollution	evidence that		
22 23						2008 to	levels.	suggests study		
24						December 31,	.con	was free of		
25						2013.	or or	selective		
26							Α̈́			
27 28							April 19,	. 1		
29							, ç			
30							, 2024 by			
31							by	-		
32 33							gue			
34							st.			
35							Protected			
36							ecte			
37   38							<u> </u>	-		

36/bmjopen-2021-0495<mark>1</mark>

2	
3	
4	
5	
6	
7	
8	_
9	
10	
11	
12	
13	
14	
15	
16	
16 17	
18	
19	
20	
21	
22	
23	
24	
25	
26	
27	
28	
29	
30	
31	
32	
33	
34	
35	
36	
38	
20	

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on the outcome data of the outcome data on the outcome data of the outcome data on the outcome data outcome data on the outcome data on the outcome data on the outcome data on the outcome data of the outcome data on the outcome data of the outcome data of the outcome data of the outcome data o		Conflict of interest	Other
8 9			Probably Low	Low	Probably Low	Low	Probably Low N	Probably Low	Low	Low
10	11	Sarnat et	24hr average	Computerized billing	Models adjusted	Data consisted of	Daily counts 8	There was	The authors	No other
11		al. 2015	concentration of PM <sub>2.5</sub>	records were obtained	for season, day of	all emergency	for emergency	insufficient	declare they	potential
12			were obtained from a	from the Missouri	week, holidays,	department visits	department \frac{\delta}{2}	information	have no	sources of
13 14			Supersite (single, central	Hospital Association	time trends (using	during the study	visits were	about	actual or	bias
15			site monitoring location).	(MHA) for emergency	cubic splines for	period for	obtained, ⊕	selective	potential	identified.
16			The observations of EC	department visits. The	day of visit with	cardiovascular	hence one	outcome to	competing	
17 18			was 666 days during 1	outcome groups were	monthly knots),	disease	hospital not	judge for low	financial	
19			June 2001-30 April 2003	identified using primary	and temperature.	outcomes.	providing data	risk, but	interests.	
20			(missing data <25%).	International	1/6		after 26 April	indirect		
21				Classification of Diseases	. 01		2002.	evidence that		
22 23				9th Revision (ICD9)			However, any	suggests study		
24				codes.		(0)	potential errors	was free of		
25							or missing data	selective		
26 27							did not depend €	report.		
28							on air pollution	_		
29										
30							)24			
31 32							by ç			
33							Jues			
34							: 			
35 36							rote			
37							cted			
38 <sup>l</sup>							2024 by guest. Protected by copyright.	·		
39 40							copy			
40 41							yrigh			
42										

4 5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data	Selective reporting	Conflict of interest	Other
8 9			Probably Low	Low	Probably Low	Low	Low	Probably Low	Low	Low
10	12	Kim et al.	PM <sub>2.5</sub> mass and chemical	All individual hospital	Model adjusted for	Data consisted of	Daily counts	There was	The authors	No other
11		2012	constituents were	admission records during	days from the start	all cardiovascular	for hospital	insufficient	declare they	potential
12			measured daily at one	the study period were	of the study, day of	hospital	admission were≝	information	have no	sources of
13 14			residential monitoring	extracted from	week, seasonality,	admissions over	obtained, so	about	actual or	bias
15			station located on the	nonelective hospital	long-term trends,	the course of the	likely have all ≟	selective	potential	identified.
16			roof of an elementary	admission discharge data	daily average	study.	outcome data.	outcome to	competing	
17			school building in	obtained from the	temperature and		However, any	judge for low	financial	
18 19			Denver. The observations	Colorado Hospital	relative humidity.		potential errors	risk, but	interests.	
20			of EC was 1809 days	Association. The	1/6		or missing data	indirect		
21			during 2003-2007	International	' (2)	•	did not depend	evidence that		
22 23			(missing data <25%).	Classification of			on air pollution			
24				Diseases, Ninth		<b>10</b> <sub>1</sub>	levels.	was free of		
25				Revision(ICD-9) codes			v or	selective		
26 27				were used to define			ı Ap	report.		
27 28				cardiovascular hospital			April 19, 2024 by			
29				admissions (codes			9, 2			
30				390–459) and respiratory			024			
31 32				hospital admissions			by (	•		
33				(codes 460–519).			' guest.			
34				(55355 100 517).						
35							Protected			
36 37							) 			
38   38							<del>0</del>	:		

36/bmjopen-2021-0495

2	
3	
4	
5	
6	
7	
8	_
9	
10	
11	
12	
13	
14	
14 15	
16	
17	
16 17 18	
19	
20	
21 22 23	
22	
23	
24	
25	
26	
27	
28	
29	
30	
31	
32 33	
33	
34	
35	
36	
37	
34 35 36 37 38	

No. Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data S		Conflict of interest	Other
	High	Low	Probably Low	Low	Low <sup>ay</sup>	Probably Low	Low	Low
O 13 Ostro et al. 2009	EC were generally recorded every 3 days from two co-located monitors or one monitor	Data for hospitalizations were obtained from the Office of Statewide Health Planning and	Adjusted for time, day of the week, temperature, seasonality,	Study included all hospitalizations for children < 19	Daily counts Not be provided by the counts of the counts o	about	Authors declared no competing financial	No other potential sources of bias
5 5 6 7 7 8 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9	in 6 counties. The number of available days of data over the 4-year period ranged from 227 to 381 (some counties had >25% missing for the frequency of sampling).	Development, Healthcare Quality and Analysis Division. Hospital admissions for children <19 years of age were classified into one or more categories: all respiratory disease (International Classification of Diseases, Ninth Revision-ICD-9 codes 460–519), asthma (ICD-9 code 493), acute bronchitis (ICD-9 code 466), and pneumonia (ICD-9 codes 480–486).	relative humidity and pollutant.	and < 5 years of age for total respiratory diseases and several subcategories including pneumonia, acute bronchitis, and asthma for six California counties from 2000 through 2003.	were obtained, so likely have all outcome data. However, any potential errors or missing data did not depend on air pollutions levels.  Protected by copyright.	outcome to judge for low risk, but indirect evidence that suggests study was free of selective	interests.	identified.

1 2				BMJ Oper	BMJ Open					
No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data a	Selective reporting	Conflict of interest	Other	
9 10 14	Kim et al.	Probably Low Daily 24-hour composite	Low Daily mortality counts for	Probably Low  Models adjusted	Low Data consisted of	Low Solution Daily counts Solution		None of the	Low No other	
11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37	2015	PM <sub>2.5</sub> samples were collected from single, central-site monitor. The observations of EC was 1809 days from 2003 through 2007 (missing data <25%).	metropolitan Denver were computed from the Colorado Health Information Dataset compiled by the Colorado Department of Public Health and Environment. Data included cause of death by the International Classification of Diseases 10th Revision (ICD-10) code.	for longer-term temporal trend, as time since the study began, day of week, and daily temperature and humidity.	all deaths over the course of the study in a defined geographical area.	for death were obtained, so likely have all outcome data. However, any potential errors or missing data did not depend on air pollution levels.  Protected by	information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of	authors has any actual or potential competing interests.	potential sources of bias identified.	

2	
3	
4	
5	
6	
7	
8	
9	
10	
11	
12	
13	
14	
14 15	
16	
16 17	
18	
19	
20	
21 22 23 24 25	
22	
23	
24	
25	
26	
26 27	
28	
29	
30	
31	
33	
34	
32 33 34 35 36	
36	
3/	
38	

Page 7	1 of 13	33			BMJ Oper	า	36/bmjop			
1 2 3 4							Incomplete			
5 6 <b>N</b> 7	0.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data	Selective reporting	Conflict of interest	Other
8			Probably Low	Low	Probably Low	Probably Low	Low	Probably Low	Low	Low
9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37		fuang et 1. 2012	Daily average concentrations of PM <sub>2.5</sub> were obtained from a single, central-site monitor. Daily average concentrations of EC in PM <sub>2.5</sub> samples were further analyzed. Daily data was available and no missing data was reported.	Daily mortality data were obtained from the Xi'an Center for Disease Control and Prevention. The International Classification of Diseases, Tenth Revision (ICD-10), codes of mortality were as follows: all natural causes (ICD-10 codes A00–R99), respiratory diseases (ICD-10 codes I00–I98), and cardiovascular diseases (ICD-10 codes I00–I99).	Models adjusted for calendar time (seasonality, long-term trends), weather(temperatu re, relative humidity), year, day of week.	The author removed the death counts on December 31 and January 1 of each year.	Daily counts for death were obtained, so likely have all outcome data. However, any potential errors or missing data did not depend on air pollution levels.  Protected by copyright.	There was insufficient information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of selective report.	No competing financial interests.	No other potential sources of bias identified.
38 — 39 40 41 42							y copyrignt.			

					BMJ Oper	1	36/bmjope			Page 72
1 2 3 4 5							36/bmjopen-2021-049516 o Incomplete		Conflict of	
6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	outcome data⇔		interest	Other
8 9			Probably High	Low	Probably Low	Low	Low 2	Probably Low	Low	Low
10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34	16	Peng et al. 2009	Ambient EC obtained from Speciation Trends Network monitors and either from central site or averaged over a county. Air pollution concentrations were measured on a 1-in-3-day schedule in the national air monitoring stations and on a 1-in-6-day schedule in the state and local air monitoring stations. Study removed suspect data and extreme values from the original monitor records; monitors with very little data were omitted altogether. Missing data	Daily counts of hospital admissions were obtained from billing claims of enrollees in the U.S.  Medicare system. Each billing claim contains the date of service, disease classification using International Classification of Diseases, 9th Revision (ICD-9) codes (Centers for Disease Control and Prevention 2008).	Model adjusted for weather (i.e., temperature, dew point temperature), day of week, unobserved seasonal factors, and long-term trends.	Data consisted of all cardiovascular hospital admissions during over the course of the study.	Daily counts for hospital admission were obtained, so likely have all outcome data. However, any potential errors or missing dataged did not depend on air pollution levels.	information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of	The authors declare they have no competing financial interests.	No other potential sources of bias identified.
35 36 37 38			was not replaced by other values.				rotected by c			

2	
3	
4	
5	
6	
7	
8	
9	
10	
11	
12	
13	
14	
15	
16 17	
17	
18	
19	
20	
21	
22	
23	
24	
25	
26 27	
27	
28	
29	
30	
31	
32	
33	
34	
35 36	
36	
37 38	
38	

'age	e 73 of	<sup>-</sup> 133			BMJ Oper	า	36/bmjopen-2021-049516 on Incomplete			
	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data	Selective reporting	Conflict of interest	Other
,			Probably High	Low	Probably Low	Low	Low Y	Probably Low	Low	Low
) 10 11 12 13 14 15 16 17 18 19 19 19 19 19 19 19 19 19 19	17	Levy et al. 2012	The U.S. Environmental Protection Agency established the PM Speciation Trends Network (STN) to measure more than 50 PM <sub>2.5</sub> chemical components, in addition to total mass. The STN includes > 50 national air monitoring stations (NAMS) and > 200 state and local air monitoring stations (SLAMS). Air pollution concentrations were typically measured on a 1-in-3-day schedule in the NAMS and on a 1-in-6-day schedule in the SLAMS. There was no information about	Hospital admissions data were obtained from billing claims information for US Medicare enrollees in 119 counties for the years 2000–2008. The Medicare billing claims data were classified into disease categories according to their International Classification of Diseases, Ninth Revision (ICD-9), codes.	Adjusted for time (seasonality, long-term trends), seasonality, day of the week and dew-point temperature.	Study included people who died any day between 2000 and 2008 in 119 US counties.	Daily counts of hospital admissions were obtained from billing claims information, so likely have all outcome data. However, any potential errors or missing data did not depend on air pollution on air pollution levels.	There was insufficient information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of selective report.	No competing financial interests.	No other potential sources of bias identified.
37   88			missing data.				ted X			

7	[o.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data		Conflict of interest	Other
8			Probably Low	Low	Probably Low	Low	Low <sup>ay</sup>	Probably Low	Low	Low
10 18	8	Son et al.	Hourly air samples were	Daily death counts were	Models adjusted	Data consisted of	Daily counts	There was	The authors	No other
11		2012	obtained from a single,	obtained from the	for time (long-term	all cardiovascular	for death were	insufficient	declare they	potential
12			central-site monitor. The	National Statistical	trends and	deaths over the	obtained, so ≤	information	have no	sources of
13 14			monitoring system	Office. The study	seasonality), day	course of the	likely have all	about	actual or	bias
15			produces hourly	classified mortality data	of week,	study.	outcome data.	selective	potential	identified.
16			estimates of PM <sub>2.5</sub> total	into all causes of death	temperature and		However, any	outcome to	competing	
17			mass, and PM <sub>2.5</sub> levels of	[International	relative humidity.		potential errors	judge for low	financial	
18 19			EC. Daily data was	Classification of			or missing data	risk, but	interests.	
20			available and no missing	Diseases, 10th Revision	'/_		did not depend	indirect		
21			data was reported.	(ICD-10; codes	(0)		on air pollution	evidence that		
22 23			_	A00–R99),			levels.	suggests study		
24				cardiovascular causes			com	was free of		
25				(codes I00–I99), and			n∕ or	selective		
26				respiratory causes (codes			ар г	report.		
27 28				J00–J99)] (World Health			April 19,	1		
29				Organization 2007).			9, 2			
30				8			2024 by guest.			
31							by			
32 33							gue			
34										
35							Protected			
36							ecte			
37 38							<u> </u>			

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data S		Conflict of interest	Other
8 9			Probably High	Low	Low	Low	Low ay 2	Probably Low	Low	Low
10	19	Heo et al.	Ambient air samples	Seoul daily mortality data	Adjusted for	Study included	Daily counts 2	There was	Authors	No other
11		2014	were collected over a	were obtained from the	long-term trends,	all death for	for death were	insufficient	declared no	potential
12			24-hour period at 3-day	Korea National Statistical	seasonality,	all-cause,	obtained, so	information	competing	sources of
13 14			intervals from a single	Office. Using the	temperature and	cardiovascular,	likely have all	about	financial	bias
15			monitor. Missing data	International	humidity, day of	and respiratory in	outcome data. 🚊	selective	interests.	identified.
16			<25% for the frequency	Classification of Disease,	the week, holiday	Seoul during	However, any	outcome to		
17 18			of EC samples.	10th Revision (ICD-10;	and influenza	2003–2007.	potential errors	judge for low		
19				World Health	epidemics.		or missing data	risk, but		
20				Organization 1993), the	' /		did not depend	indirect		
21				mortality data were	' (2)	•	on air pollution	evidence that		
22 23				classified as all			levels.	suggests study		
24				nonaccidental causes		ich	com	was free of		
25				(codes A00-R99),			on on	selective		
26 27				cardiovascular disease			Apı	report.		
28				(codes I00-I99),			11 10			
29				respiratory disease (codes			9, 20			
30 31				J00-J98), and injury			)24			
32				(S00-T98).			р д			
33							ues			
34							April 19, 2024 by guest. Protected b			
35 36							rotec			
37							cted			
38							by			

4 5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data S	Selective	Conflict of interest	Other
8 9			Probably High	Low	Probably Low	Low	Low	Probably Low	Low	Low
10	20	Basagaña	Single central-site	Daily mortality counts for	Models adjusted	Data consisted of	Daily counts	There was	The authors	No other
11		et al. 2015	monitor in each city. For	all non-external causes	for holidays,	all deaths over	for death and	insufficient	have no	potential
12			each city, PM	[International	summer	the course of the	emergency §	information	conflicts of	sources of
13 14			constituents with >20%	Classification of	population	study in a	hospital a	about	interest to	bias
15			of the values below the	Diseases, 9th Revision	decrease, influenza	defined	admissions 3	selective	disclose.	identified.
16			detection limit or missing	(ICD9) codes 001–799;	epidemics,	geographical	were obtained,	outcome to		
17 18			were excluded.	10th revision (ICD10)	seasonality,	area.	so likely have	judge for low		
19			Otherwise,	codes A00-R99],	long-term trends		all outcome	risk, but		
20			non-detectable were	cardiovascular (ICD9	and temperature.		data. However,	indirect		
21 22			replaced by half the limit	codes 390–459, ICD-10	. 01		any potential	evidence that		
23			of detection. Air pollution	codes I00-I99) and			errors or	suggests study		
24			data was collected daily	respiratory (ICD9 codes		Ch	missing data	was free of		
25			in Bologna (n=472),	460-519, ICD10 codes			did not depend 9	selective		
26 27			twice a week in	J00-J99) were collected.			on air pollution	report.		
28			Barcelona (n=736) and	Cardiovascular and			levels.			
29			Madrid (n=104), and	respiratory						
30 31			once a week in Huelva	hospitalizations were			24 5			
32			(n=406). There was no	defined on the basis of			у д			
33			information about	the primary discharge			uest			
34 35			missing data.	diagnosis using the same			ָּי דַ			
35 36				ICD codes defined above.			2024 by guest. Protected by			
37							ted			
38 39							by cop			

2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 31 33 33 34 35 36 36 37 37 37 37 37 37 37 37 37 37 37 37 37	
5	
6	
7	
8	
9	
10	
11	
12	
13	
14 15	
16	
17	
18	
19	
20	
21	
22	
23	
24	
25	
26	
27	
28	
29	
30 21	
31 31	
32 32	
34	
35	
36	
37	
38	
20	

12   2014   1-in-3 or 1-in-6 day schedule. Most of the cities had a single monitor. For every species, the study calculated the monthly average species-to-PM2.5 proportions for each month as a solution to the missing speciation data problem due to the 1-in-6 or 1-in-3 day sampling   2007).   1-in-3 or 1-in-6 day schedule. Most of the center for Health   Center for Health   Center for Health   Statistical temperature, day of the week, and season.   all death for all causes, cardiovascular disease, outcome data.   Good the week, and season.   all death for all causes, cardiovascular disease, outcome data.   However, any potential errors selective potential outcome to judge for low financial interests.   interests	Page 7	7 of	133			BMJ Oper	1	36/bmjope			
Probably High Low Probably Low Low Daily counts Schedule. Most of the cities had a single monitor. For every examined nonaccidental species, the study calculated the monthly average species-to-PM <sub>2.5</sub> proportions for each month as a solution to the missing speciation data problem due to the 1-in-6 or 1-in-3 day sampling 2007).  Probably Low Low Daily counts Schudy included all death for all counts of the week, and season.  Study included all death for all for death were obtained, so obtained, s	1 2 3 4							en-2021-0495			
Dai et al. 21 Dai et al. 2014  Daily mortality data were obtained from National schedule. Most of the cities had a single monitor. For every examined nonaccidental species, the study average species-to-PM25 proportions for each month as a solution to the missing speciation data problem due to the 1-in-6 or 1-in-3 day sampling  Daily counts for death were obtained, so blained for time, temperature, day of the week, and season.  Adjusted for time, temperature, day of the week, and season.  Adjusted for time, temperature, day obtained, so blained, so blain	5 5 N	0.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data	Selective reporting		Other
11	3			Probably High	Low	Probably Low	Low	Low	Probably Low	Low	Low
34 35 36 36 37	11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 36 37 38 38 38 38 38 38 38 38 38 38			1-in-3 or 1-in-6 day schedule. Most of the cities had a single monitor. For every species, the study calculated the monthly average species-to-PM <sub>2.5</sub> proportions for each month as a solution to the missing speciation data problem due to the 1-in-6 or 1-in-3 day sampling frequency. There was no information of missing data for that sampling	obtained from National Center for Health Statistics. The study examined nonaccidental deaths due to all causes and specific diseases, derived from the International Statistical Classification of Disease, 10th Revision (World Health Organization	temperature, day of the week, and	all death for all causes, cardiovascular disease, myocardial infarction, stroke, and respiratory diseases from National Center for Health Statistics in 75 U.S. cities between 2000	for death were obtained, so likely have all outcome data. However, any potential errors or missing data did not depend on air pollution	insufficient information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of selective	declare they have no actual or potential competing financial	No other potential sources of bias identified.

1					ВМЈ Орег	n	36/bmJopen-2021-0495			Page 78
3 4 5 7 8	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on the control outcome data	Selective reporting	Conflict of interest	Other Low
910 111 112 113 114 115 116 117 118 119 120 21 222 223 224 225 226 227 228 229 330 331 332 333 334 335	22	Lin et al. 2016a	Probably Low  The concentrations of different particle size fractions and PM <sub>2.5</sub> chemical constituents were measured at two air monitoring stations. EC were measured for four months of each year from 2007 through 2010.  During the period 2009-2011, the proportion of missing data was very low (ranging from 1% to 2%). There were about 20 days without chemical constituents records and were treated as missing observations.	Daily mortality data from 1 January 2007 to 31 December 2011 were obtained from Guangdong Provincial Center for Disease Control and Prevention. The cause of death was coded using the International Classification of Diseases, Tenth Revision (ICD-10). Mortality from cardiovascular diseases (ICD-10:I00-I99) were extracted to construct the time series.	Adjusted for public holidays, day of the week, influenza outbreaks, seasonal patterns and long-term trends, temperature and relative humidity.	Study included daily cardiovascular mortality data from 1 January 2007 to 31 December 2011 in Guangzhou.	Daily counts for death were obtained, so likely have all outcome data. However, any potential errors or missing data did not depend on air pollution levels.  Protected by	insufficient information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of	Low The authors declare they have no actual or potential competing financial interests.	No other potential sources of bias identified.
35 36 37 38							Protected by			

36/bmjopen-2021-0495

2	
4	
5	
6	
7	
8	L
9	
10	
11	
12	
13	
14	
15	
16	
17	
18	
19	
20	
21	
22	
23	
24	
25	
26	
27	
28	
29	
30	
31	
32	
33	
34	
35	
36	
37	
38	
39	

5 5 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data ≤		Conflict of interest	Other
3			Probably Low	Low	Probably Low	Low	Low $\overset{\mathfrak{B}}{\searrow}$	Probably Low	Low	Low
10	23	Cao et al.	Daily concentrations of	The study obtained	Model adjusted for	Data consisted of	Daily counts	There was	The authors	No other
1		2012	EC was obtained from a	numbers of deaths in	long-term and	all nonaccidental	for death were	insufficient	declare they	potential
2			single monitoring site.	Xi'an for each day from	seasonal trends,	causes deaths	obtained, so	information	have no	sources of
3			The observations of EC	the Shanxi Provincial	day of week,	during over the	likely have all	about	actual or	bias
5			was 1749 in 1827 days	Center for Disease	temperature,	course of the	outcome data.	selective	potential	identified.
6			(missing data <25%).	Control and Prevention	humidity, and SO <sub>2</sub>	study.	However, any		competing	
7			,	(SPCDCP). SPCDCP	and NO <sub>2</sub>		potential errors		financial	
8  9				staff then classify the	concentrations.		or missing data		interests.	
20				cause of death according			did not depend			
21				to the International	(0)		on air pollution			
22				Classification of			levels.	suggests study		
23 24				Diseases, 10th Revision		10,	.cor	was free of		
25				[ICD-10; World Health			n/ o	selective		
26				Organization (WHO)			n A			
27				1992] as due to total				тероп.		
28				nonaccidental causes			19, 2			
80				(ICD-10 codes			202			
31				`			4 by			
32				A00–R99),			gue			
33 34				cardiovascular diseases			est.			
35				(I00–I99), respiratory			April 19, 2024 by guest. Protected			
36				diseases(J00–J98), or			tect			
37 <u> </u>				injury (S00–T98).			ed .			

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data S		Conflict of interest	Other
8 9			Probably Low	Low	Probably Low	Low	Low ay 2	Probably Low	Low	Low
10	24	Klemm et	Daily 24-hr average EC	Records of individual	Adjusted for time	Study included	Daily counts 2	There was	Authors	No other
11		al. 2011	measurements are	deaths were provided by	(seasonality,	all nonaccidental	for death were	insufficient	declared no	potential
12			available for Atlanta	the Georgia Department	long-term trends),	deaths during	obtained, so	information	competing	sources of
13 14			during the study period.	of Human Resources.	temperature, and	over the course	likely have all	about	financial	bias
15			The observations of EC	Cause of death is	day of the week.	of the study.	outcome data. 🚊	selective	interests.	identified.
16			was 3317 days from	categorized using the			However, any	outcome to		
17 18			August 1998 to	International			potential errors	judge for low		
19			December 31, 2007.	Classification of	errel		or missing data	risk, but		
20			Missing data <25%.	Diseases, 10th edition	' /		did not depend	indirect		
21			There was no information	(ICD-10), including	. 01	•	on air pollution	evidence that		
22 23			for monitor stations.	circulatory conditions			levels.	suggests study		
24				(I00–I99), respiratory		<b>'</b> 01.	com	was free of		
25				conditions (J00–J99),			/ on	selective		
26 27				malignant neoplasm			Apr	report.		
28				(cancer; C00–D48), or			ii 19			
29				other nonaccidental			), 20			
30 31				causes (A00-R99,			1 124			
32				excluding cardiovascular,			ру д			
33				respiratory, or cancer			ues			
34				causes).			t. Pr			
35 36							otec			
37							on April 19, 2024 by guest. Protected by			
38								I		
39							сор			

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data		Conflict of interest	Other
8 9			Probably Low	Low	Probably Low	Low	Low	Probably Low	Low	Low
9 10	25	Zhou et al.	24hr PM <sub>2.5</sub> samples were	Using codes from the	Models adjusted	Data consisted of	Daily counts	There was	The authors	No other
11		2011	obtained from a single,	International	for time,	all cardiovascular	for death were	insufficient	declare they	potential
12			central-site monitor.	Classification of	seasonality and	deaths over the	obtained, so	information	have no	sources of
13   14			Daily data was available	Diseases, version 10	long-term trends,	course of the	likely have all	about	actual or	bias
15			and no missing data was	(ICD10; World Health	day of week,	study.	outcome data.	selective	potential	identified.
16			reported.	Organization 2007), daily	temperature, and		However, any	outcome to	competing	
17				death counts were	humidity.		potential errors	judge for low	financial	
18   19				aggregated to			or missing data	risk, but	interests.	
20				nonaccidental allcause	1/6		did not depend			
21				deaths (ICD10, codes	(0)		on air pollution	evidence that		
22   23				A00 through R99),		ion	levels.	suggests study		
24				cardiovascular deaths		101	com	was free of		
25				(ICD10, codes I01			n∕ or	selective		
26				through I99), and			Ap	report.		
27   28				respiratory deaths			April 19, 2024 by	1		
29				(ICD10, codes J00			9, 2			
30				through J99).			024			
31				unough 377).			by			
32   33							, guest.			
34										
35							Protected			
36							tect			
37   38							ed			

				BMJ Oper	1	36/bmJopen-2021-0495			Pa
						Incomplete o		Conflict of	
No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	outcome data		interest	Other
		Probably Low	Low	Probably Low	Low	Low	Probably Low	Low	Low
26	Winquist	Daily EC and BC were	Individual-level data	Adjusted for time	Study included	Daily counts	There was	Authors	No other
	et al. 2015	from a single monitor	were obtained from the	trends, day of	emergency	for emergency	insufficient	declared no	potential
		site. All species of	Missouri Hospital	week, holidays,	department visits	department $\frac{5}{5}$	information	competing	sources o
		pollutant statistics are	Association for all	season,	in St Louis	visit were	about	financial	bias
		missing less than 5%.	emergency department	temperature and	metropolitan	obtained, so	selective	interests.	identifie
			visits to 36 of 43	dew point.	statistical area	likely have all	•		
			acute-care non-federal	104	during 1 June	outcome data.	judge for low		
			hospitals with emergency	- / h	2001 through 30	However, any	risk, but		
			department visits in the		April 2003.	potential errors			
			16-county St Louis		· ·	or missing data			
			metropolitan statistical area during 1 June 2001		10.	did not depend			
			through 30 April 2003.				selective		
			Cardiorespiratory			_			
			outcomes of interest were				icport.		
			defined based on the			, g			
			primary ICD-9			024			
			(International			by	•		
			Classification of			Jues			
			Diseases, version 9)			April 19, 2024 by guest. Protected by cop	)		
			diagnosis code for the			rotec			
			visit.			Cled			

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data		Conflict of interest	Other
8 9			Probably High	Low	Probably Low	Low	Low	Probably Low	Low	Low
10	27	Ostro et	Each of the six counties	Daily mortality data were	Adjusted for time	Data consisted of	Daily counts	There was	The authors	No other
11		al. 2007	had two monitors	obtained from the	trend, day of week,	all cardiovascular	for death were	insufficient	declare they	potential
12			measuring PM <sub>2.5</sub>	California Department of	seasonality,	deaths over the	obtained, so	information	have no	sources of
13 14			components and mass.	Health Services, Center	long-term trends,	course of the	likely have all	about	competing	bias
15			Fresno, Kern, Riverside,	for Health Statistics. The	temperature and	study.	outcome data.	selective	financial	identified.
16			and Sacramento Counties	study determined daily	humidity.		However, any	outcome to	interests.	
17 18			reported data every third	total mortality counts for			potential errors	judge for low		
19			day, whereas San Diego	those > 65 years of age			or missing data	risk, but		
20			and Santa Clara Counties	and for deaths from	' /		did not depend	indirect		
21 22			reported data every sixth	respiratory disease	' (2)		on air pollution	evidence that		
22			day. For the speciation	[International			levels.	suggests study		
24			analyses, the number of	Classification of		<b>'</b> 0/.	com	was free of		
25			observation days	Diseases, 10th Revision			on on	selective		
26 27			available ranged from	(ICD10; World Health			Apr	report.		
28			243 (San Diego County)	Organization 1993) codes						
29			to 395 (Sacramento	J00–J98] and			9, 20			
30 31			County) from 2000 to	cardiovascular disease			124			
32			2003. There was no	(codes I00–I99).			у <u>ө</u>			
33			specific information				19, 2024 by guest.			
34			about missing data.							
35 36							Protected			
37							Sted			
38 <sup>l</sup>								1		

4 5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data		Conflict of interest	Other
8 9			Probably Low	Low	Probably Low	Low	Low S	Probably Low	Low	Low
9 10	28	Tolbert et	Daily 24h EC from a	Computerized billing	Adjusted for time	Study included	Daily count for	There was	Authors	No other
11		al. 2000	single monitor site. The	record data are being	(seasonality,	emergency	emergency	insufficient	declared no	potential
12			observation of EC was	obtained from the	long-term trends),	department visits	department \(\frac{8}{2}\)	information	competing	sources of
13 14			356 in 365 days, missing	emergency department	temperature, dew	of the	visits were	about	financial	bias
15			data <25%.	visits participating in the	point, and day of	participating	obtained, so	selective	interests.	identified.
16				study. Several case	week.	hospitals in the	likely have all	outcome to		
17 18				groups are being defined		Atlanta	outcome data.	judge for low		
19				using the primary ICD-9	( ) ·	Metropolitan	However, any	risk, but		
20				(International	' /	Statistical Area,	potential errors	indirect		
21				Classification of	. 61	including 33	or missing data	evidence that		
22 23				Diseases, 9th Revision)		hospitals	did not depend	suggests study		
24				diagnostic code.		between January	on air pollution			
25						1 1993-August	levels.	selective		
26 27						31 2000, 4	ı Ap	report.		
27 28						hospitals	rii 19,	:		
29						between January	9, 2			
30						1 1993-February	2024 by guest.			
31 32						30 2000.	by (	•		
33							gues			
34										
35							Protected			
36 37							 			
38							9			

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data		Conflict of interest	Other
8 9			Low	Low	Probably Low	Low	Low	Probably Low	Low	Low
10	29	Wang and	The hourly data were	This study obtained	Adjusted for	Study included	Daily counts	There was	Authors	No other
11		Lin 2016	simply averaged to	universal health insurance	temperature,	-1.11 (>(5	for elderly	insufficient	declared no	potential
12			calculate the daily	claims from the National	relative humidity,	elderly (≧65	mortality and	information	competing	sources of
13 14			average data for PM <sub>10</sub> ,	Health Research Institute	wind speed,	years) mortality	all population	about	financial	bias
15			PM <sub>2.5</sub> monitored at 13	(NHRI) and vital	barometric	from 2004 to	emergency $\stackrel{\omega}{=}$	selective	interests.	identified.
16			general air quality	statistics from the	pressure, holidays,	2008 and all	room visits	outcome to		
17 18			monitoring stations	Ministry of Health and	day of the week,	population EVR	were obtained,	judge for low		
19			located in a densely	Welfare from 2004 to	pneumonia and	from 2004 to	so likely have	risk, but		
20			populated area in Taipei.	2008. Death causes were	influenza.	2010 in Taipei,	all outcome	indirect		
21			Hourly concentrations of	coded according to the		Taiwan.	data. However,	evidence that		
22   23			EC were detected by	diagnoses of the 9th			any potential	suggests study		
24			series 5400 Monitor. Very	revision of International			errors or	was free of		
25			few missing values in the	Classification of Diseases			missing data	selective		
26   27			database were omitted as	(ICD-9). Disease			did not depend ≧	report.		
28			the daily average was	diagnoses were based on			on air pollution			
29			calculated.	the International						
30				Classification of Diseases			levels.			
32				with Clinical			оу 9			
33				Modification, Ninth			guest.			
34				Revision (ICD-9 CM).						
35 36							Protected			
36 37							Ctec			
38 L							<u> </u>			

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data S		Conflict of interest	Other
8 9			Low	Low	Low	Low	Probably Low	Probably Low	Low	Low
10	30	Darrow et	Daily 24-hour average	Health data were	Adjusted for dew	Study included	Daily counts	There was	Authors	No other
11		al. 2014	EC was from ambient	obtained from 41	point, temperature,	daily emergency	for emergency	insufficient	declared no	potential
12			monitoring networks.	metropolitan Atlanta	seasonality,	department visit	department $\frac{8}{2}$	information	competing	sources of
13 14			Missing data <1%.	hospitals and the Georgia	long-term trends,	data from 41	visit were	about	financial	bias
15				Hospital Association. The	day of week,	metropolitan	obtained. In the	selective	interests.	identified.
16				diagnoses of respiratory	holiday and	Atlanta hospitals	earliest years	outcome to		
17 18				infection were based on	influenza	for the period	of the study,	judge for low		
19				International	epidemics.	January 1, 1993,	not all	risk, but		
20				Classification of	' /	to December 31,	hospitals were	indirect		
21 22				Diseases, 9th Revision	(0)	2004 (not all	participating.	evidence that		
23				(ICD-9), diagnosis codes:		hospitals	However, any	suggests study		
24				acute bronchitis or		contributed the	potential errors	was free of		
25				bronchiolitis (code 466);		full period), and	or missing data9	selective		
26 27				pneumonia (codes		from the Georgia	did not depend ਨੂੰ	report.		
28				480–486); and upper		Hospital	on air pollution			
29				respiratory infection		Association for	levels.			
30 31				(codes 460–465).		the period	24 b			
32						January 1, 2005,	y gi			
33						to June 30, 2010.	uest			
34 35							2024 by guest. Protected by			
36							otec			
37							l ted			
38				1	l	l	\$	1		

2	
3	
4	
5	
6 7	
8	Т
9	,
10 11 12	,
11	
12	
10	
14	
15	
16	
17	
18	
19	
20	
21	
22	
23	
24	
25	
26	
27	
28	
29	
30	
31	
32	
33	
34	
35	
36 37	
37	
38	

Page 87	of 133			BMJ Oper	า	so/amjope			
<u>!</u> }						Incomplete			
No	. Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data	Selective reporting	Conflict of interest	Other
<i>'</i>		Probably High	Low	Probably Low	Low	Low	Probably Low	Low	Low
31 1 2 3 3 4 4 5 5 6 6 7 8 8 9 9 9 9 9 9 9 9 1 1 1 1 2 2 3 3 4 4 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9	Metzger et al. 2004	Ambient 24hr average EC were obtained from one monitor. On days when measurements were missing at the central site, data for the pollutant were imputed using an algorithm that modeled measurements. The observations of EC was 714 days during the period August 1, 1998–August 31, 2000 (missing data >25%).	The study asked 41 hospitals with emergency departments that serve the 20-county Atlanta metropolitan statistical area (MSA) to provide computerized billing data for all emergency department visits between January 1, 1993, and August 31, 2000. Using the primary International Classification of Diseases, 9th Revision (ICD-9) diagnosis code, the study defined several cardiovascular disease (cardiovascular disease) groups based largely on ICD-9 diagnosis codes.	Model adjusted for temporal trends, meteorological conditions (i.e., temperature, dew point temperature), day of week, hospital entry and exit, and federally observed holidays.	Data consisted of all cardiovascular hospital admissions over the course of the study.	Daily counts for emergency department visits were obtained, so likely have all outcome data. However, any potential errors or missing data did not depend on air pollution levels.	There was insufficient information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of selective report.	No competing financial interests.	No other potential sources of bias identified.
39 10 11 12						сорупдпг	<u>.</u>		

No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete o	Selective reporting	Conflict of interest	Other
		Probably Low	Low	Probably Low	Low	Low $\overset{a}{\checkmark}$	Probably Low	Low	Low
0 32	Mar et al.	Hourly PM <sub>2.5</sub> chemical	Mortality data for all of	Adjusted for time	Data consisted of	Daily counts	There was	No	No other
1	2000	composition data from a	Maricopa County from	trend, seasonality,	all cardiovascular	for death were	insufficient	competing	potential
2		single, central-site	1995 to 1997 were	day of week,	deaths during	obtained, so	information	financial	sources of
3 4		monitor. Daily data was	obtained from the	temperature and	over the course	likely have all	about	interests.	bias
5		available and no missing	Arizona Center for	relative humidity.	of the study.	outcome data.	selective		identified.
6		data was reported.	Health Statistics in			However, any	outcome to		
7			Phoenix. Death certificate			potential errors	judge for low		
8 9			data included residence	er rel		or missing data	risk, but		
o			zip code and the primary			did not depend			
1			cause of death as	(0)		on air pollution			
2			identified by the			levels.	suggests study		
3 4			International			8	was free of		
5			Classification of			n/ o	selective		
6			Diseases, Ninth Revision			n Ag			
7 8			(ICD-9, World Health			April 19, 2024 by guest.	Eport.		
9			Organization, Geneva).			9,			
0			Organization, Geneva).			20.22			
1						l by			
2						gue			
3 4									
5						Protected	)		
6						l tect			
7						ea <del>-</del>			
8 —— 9			1			·	1		1

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data		Conflict of interest	Other
8 9			Low	Low	Probably Low	Low	Low ay	Probably Low	Low	Low
9 10	33	Wang et	Hourly data of PM <sub>2.5</sub>	The daily mortality data	Adjusted for long	Study included	Daily counts	There was	No	No other
11		al. 2019a	were collected at 10	were obtained from the	term trends,	daily mortality	for death were	insufficient	competing	potential
12			Chinese air quality	system of Disease	seasonal influence,	data in Huangpu	obtained, so	information	financial	sources of
13 14			monitoring sites in	Monitoring Point	day of the week,	district from	likely have all	about	interests.	bias
15			Shanghai. Hourly mass	belonged to the Chinese	holidays,	January 1, 2013	outcome data. ⊖	selective		identified.
16			concentrations of PM <sub>2.5</sub>	Center for Disease	temperature and	to December 31,	However, any	outcome to		
17 18			and EC were predicted in	Control and Prevention	relative humidity.	2015.	potential errors	judge for low		
19			Shanghai by using a	(China CDC). Deaths			or missing data	risk, but		
20			Community Multiscale	were classified according	' /		did not depend	indirect		
21			Air Quality model. The	to the 10th revised	' (2)	•	on air pollution	evidence that		
22 23			study included	International Statistical			levels.	suggests study		
24			continuous daily data	Classification of Disease		<b>'</b> 01.	com	was free of		
25			from 2013 to 2015 (1095	(ICD-10), all-cause			/ on	selective		
26 27			days). Daily data was	mortality (A00-R99),			Apr	report.		
28			available and no missing	circulatory disease						
29			data was reported.	mortality (I00-I99, the			19, 2024 by guest.			
30 31				circulatory disease is also			)24			
32				known as cardiovascular			оу д			
33				disease) and respiratory			ues			
34				disease mortality						
35 36				(J00-J99).			ote			
37							Protected			
38 <sup>L</sup>							ृ			

monitor site for four months of each year from 2007 to 2010. Missing data for the particle concentration was very low (ranging from 1% to 2%).  Classification of Diseases, Fenth Revision (ICD-10:160-166), and sub-categories, including ischemic stroke (ICD-10:163-166), and hemorrhagic stroke (ICD-10:160-162) were extracted to construct the time series.	5 No. 7	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data		Conflict of interest	Other
Line et al.   EC was from a single monitor site for four monits of each year from 2007 to 2010. Missing data for the particle concentration was very low (ranging from 1% to 20%).   Classification of 20%.   Classific			Probably High	Low	Probably Low	Low	Low s	Probably Low	Low	Low
monitor site for four months of each year from 2007 to 2010. Missing data for the particle concentration was very low (ranging from 1% to 19 2%).  Classification of Diseases, Tenth Revision (ICD-10:160-166), and sub-categories, including ischemic stroke (ICD-10:163-166), and hemorrhagic stroke (ICD-10:160-162) were extracted to construct the time series.	121	Lin et al.	EC was from a single	Daily mortality data were	Adjusted for	Study included	Daily counts	There was	Authors	No other
2007 to 2010. Missing data for the particle concentration was very low (ranging from 1% to 22%).  Classification of Diseases, Tenth Revision (ICD-10:160–166), and sub-categories, including ischemic stroke (ICD-10:163–166), and hemorrhagic stroke (ICD-10:160–162) were extracted to construct the time series.  Classification of Diseases, Tenth Revision (ICD-10:160–166), and hemorrhagic stroke (ICD-10:160–162) were extracted to construct the time series.  Cause of death was coded tumidity, day of week and public holidays.  Classification of Diseases, Tenth Revision (ICD-10:160–166), and districts of Guangzhou between 2007 and 2011.  Classification of Diseases, Tenth Revision (ICD-10:160–166), and hemorrhagic stroke (ICD-10:160–166), and hemorrhagic stroke (ICD-10:160–162) were extracted to construct the time series.		2016b	monitor site for four	obtained from the death	long-term trends,	the residents who	for death were	insufficient	declared no	potential
data for the particle concentration was very low (ranging from 1% to 2%).  Classification of Diseases, Tenth Revision (ICD-10). Mortality from stroke (ICD-10:160–166), and sub-categories, including ischemic stroke (ICD-10:160–162) were extracted to construct the time series.  Lemperature, or hemorrhagic stroke in urban week and public districts of Guangzhou between 2007 or missing datage of very extracted to construct the time series.  Lemperature, or hemorrhagic stroke in urban week and public districts of Guangzhou between 2007 or missing datage of very evidence that suggests study was free of selective report.			months of each year from	registry system. The	seasonality,	died of ischemic	obtained, so ₹	information	conflict of	sources of
data for the particle concentration was very low (ranging from 1% to 2%).  Classification of Diseases, Tenth Revision (ICD-10). Mortality from stroke (ICD-10:160-166), and sub-categories, including ischemic stroke (ICD-10:163-166), and hemorrhagic stroke (ICD-10:160-162) were extracted to construct the time series.  data for the particle concentration was very low (ranging from 1% to 2%).  Lassification of week and public holidays.  Diseases, Tenth Revision (ICD-10). Mortality from stroke (ICD-10:160-166), and sub-categories, including ischemic stroke (ICD-10:163-166), and hemorrhagic stroke (ICD-10:160-162) were extracted to construct the time series.  Diseases, Tenth Revision (ICD-10:160-166), and hemorrhagic ischemic stroke (ICD-10:163-166), and hemorrhagic stroke (ICD-10:160-162) were extracted to construct the time series.			2007 to 2010. Missing	cause of death was coded	temperature,	or hemorrhagic	likely have all	about	interest.	bias
low (ranging from 1% to 2%).  Diseases, Tenth Revision (ICD-10). Mortality from stroke (ICD-10:160–166), and sub-categories, including ischemic stroke (ICD-10:163–166), and hemorrhagic stroke (ICD-10:160–162) were extracted to construct the time series.  Diseases, Tenth Revision (ICD-10:160–166), and sub-categories, including ischemic stroke (ICD-10:160–166), and hemorrhagic stroke (ICD-10:160–162) were extracted to construct the time series.  Diseases, Tenth Revision holidays.  Guangzhou between 2007 and 2011.  Guangzhou potential errors jujudge for low risk, but indirect evidence that suggests study was free of selective report.			data for the particle	using the International	humidity, day of	strokes in urban	outcome data.	selective		identified.
Diseases, Tehth Revision (ICD-10). Mortality from stroke (ICD-10:160–166), and sub-categories, including ischemic stroke (ICD-10:163–166), and hemorrhagic stroke (ICD-10:160–162) were extracted to construct the time series.	16		concentration was very	Classification of	week and public	districts of	However, any	outcome to		
10   2%). (ICD-10: Mortality from stroke (ICD-10:160–166), and sub-categories, including ischemic stroke (ICD-10:163–166), and hemorrhagic stroke (ICD-10:160–162) were extracted to construct the time series.			low (ranging from 1% to	Diseases, Tenth Revision	holidays.	Guangzhou	potential errors	judge for low		
stroke (ICD-10:160–166), and sub-categories, including ischemic stroke (ICD-10:163–166), and hemorrhagic stroke (ICD-10:160–162) were extracted to construct the time series.    Stroke (ICD-10:160–166), and sub-categories, including ischemic stroke (ICD-10:163–166), and hemorrhagic stroke (ICD-10:160–162) were extracted to construct the time series.			2%).	(ICD-10). Mortality from		between 2007	D			
and sub-categories, including ischemic stroke (ICD-10:163–166), and hemorrhagic stroke (ICD-10: 160–162) were extracted to construct the time series.				stroke (ICD-10:I60–I66),	' /_	and 2011.	did not depend	indirect		
including ischemic stroke (ICD-10:I63–I66), and hemorrhagic stroke (ICD-10: I60–I62) were extracted to construct the time series.				and sub-categories,	(0)		×			
(ICD-10:I63–I66), and hemorrhagic stroke (ICD-10: I60–I62) were extracted to construct the time series.				including ischemic stroke			· ·			
(ICD-10: 160–162) were extracted to construct the time series.						10,	.cor	00		
(ICD-10: 160–162) were extracted to construct the time series.				`		\ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \				
time series.  2024 by guest. 32 as				=			n A			
time series.  2024 by guest.  2033 334 34 35 36				` ′				Top or a		
30										
74 35 36				time series.			024			
74 35 36							by			
74 35 36							gue			
35   70   70   70   70   70   70   70   7										
36							Prot			
							ect			
37	37						<u>ea</u> b			

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data ≤		Conflict of interest	Other
8			Probably High	Low	Probably Low	Low	Low ay 2	Probably Low	Low	Low
10	35	Lin et al.	Each of the six counties	Daily mortality for all	Adjusted for time,	Study included	Daily counts 8	There was	Authors	No other
11		2016b	had two monitors	California residents were	temperature,	daily	for death were	insufficient	declared no	potential
12			measuring components of	obtained from the	humidity and day	cardiovascular	obtained, so	information	competing	sources of
13 14			PM <sub>2.5</sub> . Fresno, Kern,	California Department of	of the week.	mortality for all	likely have all	about	interests.	bias
15			Riverside and	Health Services, Center		California	outcome data.	selective		identified.
16			Sacramento counties	for Health Statistics.		residents from 1	However, any	outcome to		
17 18			reported 24-hour average	Daily counts of deaths		January 2000 to	potential errors	judge for low		
19			EC in PM <sub>2.5</sub> every third	from cardiovascular		31 December	or missing data	risk, but		
20			day; San Diego and Santa	disease (International	' /	2003.	did not depend	indirect		
21 22			Clara counties reported	Classification of	(0)		on air pollution	evidence that		
23			data every sixth day. The	Diseases, Tenth Revision			levels.	suggests study		
24			study included only	(ICD10) =I00–I99) were		'01.	com	was free of		
25			species for which at least	calculated.			on /	selective		
26 27			50% of the observations				Apr	report.		
28			were above the level of				ii 19			
29			detection.				, 20			
30 31							24 b			
32							y gi			
33							uest			
34 35							April 19, 2024 by guest. Protected by			
36							otec			
37							ted			
38 <sup>l</sup>			<u> </u>	<u> </u>			by by	l		

BMJ Open

Page 92 of 133

4 5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data		Conflict of interest	Other
8 9			Probably Low	Low	Probably Low	Low	Low	Probably Low	Low	Low
10	36	Ito et al.	Ambient EC obtained	Hospitalizations and	Model adjusted for	Data consisted of	Daily counts	There was	The authors	No other
11		2011	from multiple monitors	mortality data were	temporal trends	all cardiovascular	for death and	insufficient	declare they	potential
12			and the average of data	available at the New York	and seasonal	hospital	hospitalization \( \frac{8}{2} \)	information	have no	sources of
13 14			from multiple monitors	City Department of	cycles, immediate	admissions over	were obtained,	about	actual or	bias
15			was computed using the	Health and Mental	and delayed	the course of the	so likely have	selective	potential	identified.
16			24hr average values. The	Hygiene. The relevant	temperature	study.	all outcome	outcome to	competing	
17			sampling frequency of	variables available in the	effects, and day of		data. However,	judge for low	financial	
18 19			the chemical speciation	electronic discharge	the week.		any potential	risk, but	interests.	
20			data was every third day.	abstract for each patient	' /_		errors or	indirect		
21			Daily data was available	included date of	(0)		missing data	evidence that		
22			and no missing data was	admission and			did not depend	suggests study		
24			reported.	International			on air pollution			
25				Classification of			levels.	selective		
26				Diseases, Nine Revision			April	report.		
27 28				(ICD9) discharge			19,			
29				diagnosis code. The						
30				International			024			
31				Classification of			by	•		
32 33				Diseases, Tenth Revision			2024 by guest.			
34				(ICD10) codes for			S: +			
35				determining cause of			Protected			
36 37				death.			 			
37 <sub>L</sub> 38			I	ucani.			9	1		

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data ≤	Selective reporting	Conflict of interest	Other
8 9			Probably Low	Low	Probably Low	Low	Low $\overset{\mathbf{a}}{\searrow}$	Probably Low	Low	Low
10	37	Chen et al.	Hourly mass	The counts of daily	Models adjusted	Data consisted of	Daily counts	There was	No	No other
11		2014	concentrations of PM <sub>2.5</sub>	emergency room visits	for time, day of	all emergency	for emergency	insufficient	competing	potential
12			and the four PM <sub>2.5</sub>	were obtained from the	week, temperature,	department visits	room visit	information	financial	sources of
13 14			constituents obtained	National Taiwan	seasonality and	during the study	were obtained, a	about	interests.	bias
15			from a Supersite (single,	University Hospital. The	relative humidity.	period for	so likely have	selective		identified.
16			central site monitoring	emergency room visit		ischemic and	all outcome	outcome to		
17 18			location). The	data were coded		hemorrhagic	data. However,	judge for low		
19			observations of EC was	regarding the discharge		stroke.	any potential	risk, but		
20			1599 in 1705 days	diagnosis using the	' /		errors or	indirect		
21			(missing data <25%).	International	. 01		missing data	evidence that		
22 23				Classification of Disease,			did not depend.	suggests study		
24				9th revision (ICD-9).		<b>101.</b>	on air pollution	was free of		
25							levels.	selective		
26 27								report.		
28							11 12			
29							9, 20			
30							)24			
31 32							by g			
33							ues			
34							April 19, 2024 by guest. Protected			
35 36							rote			
37							cted			
38							by			

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data		Conflict of interest	Other
8 9			Low	Low	Probably High	Low	Low 2	Probably Low	Low	Low
9 10	38	Tomic'-Sp	Average daily	Emergency department	Adjusted for	Study included	All counts for	There was	Authors	No other
11		iric' et al.	concentrations of BC in	visits data were obtained	temperature,	emergency	emergency 5	insufficient	declared no	potential
12		2019	micrograms per cubic	from the Health Center	humidity, and air	department visit	department <u>\frac{8}{2}</u>	information	competing	sources of
13 14			meter were measured by	Užice, either from the	pressure.	for allergic	visits were	about	financial	bias
15			three automatic ambient	emergency department		rhinitis and	obtained, so	selective	interests.	identified.
16			air quality monitoring	visits in Užice, Sevojno,		allergic asthma	likely have all	outcome to		
17 18			stations. There was no	and Kosjeri' c, or from a		from 1 July 2012	outcome data.	judge for low		
19			information about	general hospital in Užice.		to 30 June 2014	However, any	risk, but		
20			missing data.	The inclusion criteria	' /	in the Zlatibor	potential errors	indirect		
21				were adults aged 18 years	' (2)	District, Western	or missing data	evidence that		
22 23				and older with the		Serbia.	did not depend.	suggests study		
24				diagnosis of allergic		(0).	on air pollution	was free of		
25				rhinitis (International			levels.	selective		
26 27				Classification of			Api	report.		
28				Diseases, 10th revision,			11 19			
29				code J.30.4), allergic						
30				asthma (International			2024 by			
31 32				Classification of			by g			
33				Diseases, 10th revision,			' guest.			
34				code J.45.0), or asthma						
35 36				with coexisting allergic			Protected			
37 37				rhinitis.			) 			
38 <sup>¹</sup>			I			I	9		I	

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on the outcome data		Conflict of interest	Other
8 9			Probably Low	Low	Probably Low	Low	Low s	Probably Low	Low	Low
9 10	39	Maynard	Daily measurements of	Individual mortality	Adjusted for	Study included	Daily counts	There was	Authors	No other
11		et al. 2007	BC were obtained from a	records were obtained	season and long	all death for all	for individual	insufficient	declared no	potential
12			single monitor site. In	from the Massachusetts	term trend,	causes,	mortality <u>§</u>	information	competing	sources of
13 14			order to predict local BC	Department of Public	temperature, dew	cardiovascular,	records were	about	financial	bias
15			level, the study used a	Health, for the years	point and day of	respirator, stroke,	obtained, so	selective	interests.	identified.
16			validated	1995–2002. Specific	week.	and diabetes	likely have all	outcome to		
17 18			spatial-temporal land use	cause mortality was		diseases in	outcome data.	judge for low		
19			regression model to	derived from the		Boston	However, any	risk, but		
20			predict 24-hr measures of	International	' /	metropolitan area	potential errors	indirect		
21			traffic exposure data	Classification of Diseases	. 61	from the	or missing data	evidence that		
22 23			(BC) at $> 80$ locations in	(ICD) codes [9th		Massachusetts	did not depend.	suggests study		
24			the Boston area.	Revision before 1999		Department of	on air pollution	was free of		
25				(World Health		Public Health	levels.	selective		
26 27				Organization 1975) and		between	April	report.		
28				10th Revision 1999 to		1995–1997 and	rii 19,			
29				2002 World Health		1999–2002.	9, 20			
30				Organization 1993)].			2024 by			
31 32				,,,			by g			
33							, guest.			
34										
35							Protected			
36 37							) 			
37   38							<u> </u>			

5 5	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data ≤		Conflict of interest	Other
3			Probably Low	Probably Low	Probably Low	Low	Low S	Probably Low	Low	Low
0	40	Sinclair et	Daily 24-hr averages EC	Daily outpatient visits	Adjusted for	Study included	Daily counts	There was	No	No other
1		al. 2010	was from a single	were obtained from the	season, day of	daily outpatient	for outpatient	insufficient	competing	potential
2			monitor site. The total	electronic patient data	week, federal	visits for acute	visits were	information	financial	sources of
3 4			observed rate of EC was	warehouse of a	holidays, study	respiratory	obtained, so	about	interests.	bias
5			95.2%.	not-for-profit,	month, time,	diseases from the	likely have all	selective		identified.
6				group-model managed	temperature and	electronic patient	outcome data.	outcome to		
7  8				care organization (MCO)	dew point.	data warehouse	However, any	judge for low		
9				in the metropolitan		of a	potential errors	risk, but		
20				Atlanta area between	' /	not-for-profit,	or missing data	indirect		
21				August 1, 1998 and	. 01	group-model	did not depend	evidence that		
22				December 31, 2002.		managed care	on air pollution.	suggests study		
24				Visits that met acute visit		organization	levels.	was free of		
25				definition and that had a		(MCO) in the	v on	selective		
26 27				visit diagnosis code of		metropolitan	Ap	report.		
28				asthma, upper respiratory		Atlanta area				
9				infection (URI), or lower		between August	9, 20			
30				respiratory infection		1, 1998 and	)24			
31 32				(LRI) were included in		December 31,	by g			
33				the study.		2002.	Jues			
34							April 19, 2024 by guest. Protected b			
35 36							rote			
37							ctec			
88							by by			

36/bmjopen-2021-0495

2	
3	
4	
5	
6	
7	
8	ŀ
8 9	
10	
11	
12	
14	
15	
16	
17 18	
18	
19	
20	
21	
22	
23	
24	
25	
26	
27	
28 29	
30	
31	
32	
33	
34	
35	
37	
36 37 38	
39	

5   5   7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data		Conflict of interest	Other
3			High	Probably Low	Probably Low	Low	Low ay	Probably Low	Low	Low
0	41	Krall et al.	Monitors typically	All-cause mortality data	Adjusted for	Study included	Daily counts	There was	The authors	No other
11		2013	measure PM <sub>2.5</sub>	(excluding accidental	temperature, day	all death	for death were	insufficient	declare they	potential
12			constituent	deaths) were aggregated	of week, long-term	(excluding	obtained, so	information	have no	sources of
13 14			concentrations every	from death certificate	and seasonal	accidental	likely have all	about	actual or	bias
15			third or sixth day. Some	data obtained from the	trends.	deaths) for 108	outcome data. $\stackrel{ω}{=}$	selective	potential	identified.
6			communities with a	National Center for		urban	However, any	outcome to	competing	
17 18			single monitor. The	Health Statistics for 2000		communities	potential errors	judge for low	financial	
19			observation of EC was	to 2005.		from 2000 to	or missing data	risk, but	interests.	
20			58-921 days,some		' /	2005.	did not depend	indirect		
21			communities had >25%		. 01		on air pollution	evidence that		
22			missing data.				levels.	suggests study		
24							com	was free of		
25							v on	selective		
26 27										
28								1		
29							9, 2			
30							024			
31							by	•		
32							gue			
34							st. F			
35							April 19, 2024 by guest. Protected			
36							ecte			
7 8							ä.			

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data		Conflict of interest	Other
8 9			Probably High	Low	Probably Low	Low	Low ay	Probably Low	Low	Low
10	42	Cakmak et	Daily PM <sub>2.5</sub> aerosol	Diseases were coded	Adjusted for	Study included	Daily counts	There was	No	No other
11		al. 2009	samples approximately 1	using the WHO	temperature and	all emergency	for emergency	insufficient	competing	potential
12			of every 4 days from a	International	humidity, day of	department visits	department 💆	information	financial	sources of
13 14			single monitor site.	Classification of Disease,	week, long-term	obtained from the	visit were	about	interests.	bias
15			Sampling occurred daily	9th Revision (ICD-9).	and seasonal	Departamento de	obtained, so	selective		identified.
16			during the cold season	The daily number of	trends.	Es-tad' isticas e	likely have all	outcome to		
17 18			(April through	emergency department	<b>'</b> O.	InformaciónenSa	outcome data.	judge for low		
19			September) and alternate	visits for all		lud (DEIS) of the	However, any	risk, but		
20			days during the warm	nonaccidental (ICD-9 <	' /	Ministry of	potential errors	indirect		
21 22			season (October through	800) and respiratory	' 01	Health from	or missing data	evidence that		
23			March). Missing data	(ICD-9 460–519) causes		April 2001	did not depend	suggests study		
24			<25% for that frequency.	in Santiago Centro,		through August	on air pollution	was free of		
25				Cerrillos, and Pudahuel		2006.	levels.	selective		
26 27				were obtained from the			Apr	report.		
28				Departamento de Estad'			19,			
29				ısticas e			, 20			
30   31				InformaciónenSalud			2024 by			
32				(DEIS) of the Ministry of			у д Э			
33				Health from April 2001			' guest.			
34				through August 2006.						
35 36							Protected			
37							ted			
38 <sup>l</sup>							\$	1		

36/bmjopen-2021-0495

2	
3	
4	
5	
6	
7	
8	_
9	
10 11	
11	
12	
13	
1/	
14 15	
16	
17	
15 16 17 18	
19	
20	
20	
21 22 23	
22	
23	
23 24 25 26 27	
25	
26	
2/	
28	
29	
30	
31	
32	
33	
34	
35	
36	
37 38	
38	

5 5 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data		Conflict of interest	Other
3			Low	Low	Probably Low	Low	Low ay	Probably Low	Low	Low
0	43	Tolbert et	Daily ambient EC	Computerized billing	Model adjusted for	Data consisted of	Daily counts	There was	No	No other
11		al. 2007	obtained from multiple	records for all emergency	long-term and	all cardiovascular	for emergency	insufficient	competing	potential
12			monitors and a single	department visits between	seasonal trends,	disease and	department <u>§</u>	information	financial	sources of
13 14			concentration obtained by	January 1, 1993 and	daily average	respiratory	visit were	about	interests.	bias
5			averaging across	December 31, 2004 were	temperature, dew	disease hospital	obtained, so	selective		identified.
6			monitors. The	collected, including the	point, day of week,	admissions	likely have all	outcome to		
17 18			observations of EC was	following data for each	federal holiday,	during the period	outcome data.			
19			2258 during the period	visit: primary	and hospital entry	1993 to 2004	However, any	risk, but		
20			August 1, 1998 to	International	and exit.	over the course	potential errors	indirect		
21			December 31, 2004	Classification of Diseases		of the study.	or missing data	evidence that		
22			(missing data <25%).	9th Revision (ICD-9)			did not depend.	suggests study		
24				diagnostic code,		<b>101.</b>	on air pollution	was free of		
25				secondary ICD-9			levels.	selective		
26 27				diagnosis codes.			_	report.		
28										
29							9, 20			
30							)24			
31 32							by g			
33							Jues			
34							April 19, 2024 by guest. Protected			
35 36							rote			
37							cted			
8 L							<u> </u>			

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data ∞		Conflict of interest	Other
8 9			Low	Low	Probably Low	Low	Low by	Probably Low	Low	Low
10	44	Lall et al.	Daily EC data were	The categorization of the	Model adjusted for	Data consisted of	Daily counts 8	There was	The authors	No other
11		2011	obtained from two	admissions data was	season, wintertime	all cardiovascular	for hospital	insufficient	declare they	potential
12			monitors. Daily data was	based on codes from the	influenza episode,	hospital	admission were	information	have no	sources of
13 14			available and no missing	International	weather, day of	admissions over	obtained, so	about	actual or	bias
15			data was reported.	Classification of	week, and other	the course of the	likely have all 🚊	selective	potential	identified.
16				Diseases, revision 9	possible	study.	outcome data.	outcome to	competing	
17 18				(ICD-9).	confounders (e.g.,		However, any	judge for low	financial	
19					federal holidays).		potential errors	risk, but	interests.	
20					'/		or missing data	indirect		
21					. 01		did not depend	evidence that		
22 23							on air pollution.	suggests study		
24						<b>'</b> 0/.	levels.	was free of		
25							on /	selective		
26 27						Teh (	Apr	report.		
28							110			
29							9, 20			
30 31							1924			
32							эу <u>ө</u>			
33							ues			
34							t. Pr			
35 36							otec			
37							on April 19, 2024 by guest. Protected by			
38			<u> </u>	I	l			I		
39							сор			

36/bmjopen-2021-0495

2	
2	
4	
5	
5	
6 7	
7 8	
9	
9 10	
10 11	
12	
13	
14	
15	
17	
16 17 18	
19	
19 20	
21	
22	
23	
25 26	
26	
28	
29 30	
31	
32 33	
34	
35	
36 37	
38	
38	_

N	0.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data o		Conflict of interest	Other
			Probably High	Low	Probably Low	Low	Low ay	Probably Low	Low	Low
0 45	5	Jung and	A total of 153 daily	The health data used in	Adjusted for	Study included	Daily counts	There was	No	No other
1		Lin 2017	samples (approximately 4	the study were sourced	seasonal trend, day	all asthma	for asthma	insufficient	competing	potential
2			weeks per season) from a	from Longitudinal Health	of week,	outpatient visits	outpatient \(\frac{\tilde{8}}{2}\)	information	financial	sources of
3 4			single monitor site were	Insurance Database 2000.	temperature,	(0-20 years old)	visits (0-20	about	interests.	bias
5			collected. Multiple linear	Daily outpatient visits for	precipitation and	in Shalu district	years old) data	selective		identified.
6			regression models were	asthma (International	wind vectors.	from	were obtained,	outcome to		
7			used to back extrapolate	Classification of	<b>'</b> O.	Longitudinal	so likely have	judge for low		
8			the historic concentration	Diseases, Ninth Revision,	C/	Health Insurance	all outcome	risk, but		
20			of individual components	Clinical Modification,	1	Database 2000	data. However,	indirect		
1			of PM <sub>2.5</sub> from 2000	ICD-9-CM code 493)	(0)	during January 1,	any potential	evidence that		
22   23			through to 2010,	data was obtained from		2000 to	errors or	suggests study		
24			including BC.	Longitudinal Health		December 31,	missing data	was free of		
25			C	Insurance Database 2000.		2010.	did not depend 9	selective		
6							on air pollution			
.7 .8							112	_		
9							9, 2			
0							024			
1							by			
3							gue			
34							19, 2024 by guest. Protected			
5							Prot			
6							ecte			
37 <u> </u>							<u></u>			

4 5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data S	Selective reporting	Conflict of interest	Other
8 9			Probably Low	Low	Probably Low	Low	Low $\overset{\mathbf{a}}{\searrow}$	Probably Low	Low	Low
10	46	Gong et	The 24-h mean BC	The disease data used in	Adjusted for	Study included	Daily counts	There was	Authors	No other
11		al. 2019	concentrations data were	this study were collected	calendar effects,	all cardiovascular	for all deaths	insufficient	declared no	potential
12			obtained from a single	from the Chinese Center	long-term trends,	mortality in	were obtained, ≦	information	conflict of	sources of
13 14			monitor site. During the	for Disease Control and	temperature,	Beijing obtained	so likely have $\frac{8}{2}$	about	interest.	bias
15			study period (2091 days),	Prevention, and included	humidity, day of	from the Chinese	all outcome	selective		identified.
16			missing rate of BC was	all deaths in Beijing from	week, NO2 and	Center for	data. However,∃	outcome to		
17 18			0.68%.	January 1, 2006 to	SO <sub>2</sub> .	Disease Control	any potential	judge for low		
19				December 31, 2011.		and Prevention	errors or	risk, but		
20				Causes of death were	'/	during January 1,	missing data	indirect		
21				classified according to	' 01	2006 to	did not depend	evidence that		
22 23				the International		December 31,	on air pollution.	suggests study		
24				Classification of		2011.	levels.	was free of		
25				Diseases, 10th Edition			v on	selective		
26 27				(ICD-10) and data on				report.		
28				cardiovascular diseases				_		
29				(ICD-10 code: I00–I99)			9, 20			
30				were obtained.			024			
31 32							by (			
33							gue			
34							St. F			
35							rote			
36 37							April 19, 2024 by guest. Protected			
38							d by			

36/bmjopen-2021-0495<mark>1</mark>

2 3	
4	
5	
7	
8	_
9	
10	
11	
12	
13	
14	
15	
16 17	
18	
19	
20	
21	
22	
23	
24	
25	
26	
27	
28	
29	
30	
31	
32	
33	
34 35	
36 37	
38	
20	

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data		Conflict of interest	Other
8 9			Probably Low	Probably Low	Probably High	Low	Low 2	Probably Low	Low	Low
9 10	47	Mostofsky	Ambient EC obtained	Patients potentially	Model adjusted for	Population	Daily counts 8	There was	No	No other
11		et al. 2012	from one monitor. BC	eligible for this study	seasonality,	consisted of	for emergency $\bigcirc$	insufficient	competing	potential
12			concentrations were	were identified by	time-trends,	patients ≥21	department 💆	information	financial	sources of
13 14			measured continuously.	reviewing daily	temperature, dew	years of age	admission were	about	interests.	bias
15			Daily data was available	emergency department	point temperature,	admitted to the	obtained, so	selective		identified.
16			and no missing data was	admission logs, stroke	barometric	hospital with	likely have all	outcome to		
17			reported.	service admission logs,	pressure and	neurologist-confi	outcome data.			
18 19			•	stroke service consult	chronic and	rmed ischemic	However, any			
20				logs, and hospital	slowly-varying	stroke and	potential errors	indirect		
21				electronic discharge	potential	residing in the	or missing data			
22 23				records.	confounders.	Boston	did not depend.			
23 24						metropolitan	on air pollution			
25						region. Also	levels.	selective		
26						patients had to				
27 28						reside within 40	J h	тероге.		
20 29						km of the air	9, 2			
30						pollution	2022			
31						monitor.	l by			
32 33						momor.	gue			
34							st.			
35							Prot			
36							ecte			
37							90			
38 39							April 19, 2024 by guest. Protected by copyright.			
40							рупі			
41 42							ight.			

Page 104 of 133

4 5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data ≅	Selective reporting	Conflict of interest	Other
8 9			Probably High	Low	Probably Low	Low	Low	Probably Low	Low	Low
10	48	Krall et al.	PM <sub>2.5</sub> constituents from	The study obtained	Adjusted for	Study included	Daily counts	There was	The authors	No other
11		2017	one urban, ambient	electronic billing data for	holidays,	all emergency	for emergency	insufficient	declare they	potential
12			monitor located in each	respiratory disease	long-term trends,	department visits	department 💆	information	have no	sources of
13 14			city. Daily pollution data	emergency department	day of the week,	for respiratory	visits of	about	actual or	bias
15			were available in Atlanta;	visits for all ages at acute	season,	disease at acute	respiratory	selective	potential	identified.
16			however, data were only	care hospitals. Using	hospitalsreporting	care hospitals in	disease were	outcome to	competing	
17 18			available approximately	diagnosis codes from the	data, temperature	the 20-county	obtained, so	judge for low	financial	
19			every third day in the	International	and dew point.	Atlanta	likely have all	risk, but	interests.	
20			remaining three cities.	Classification of		metropolitan	outcome data.	indirect		
21			There was no information	Diseases, 9th Revision		area, the	However, any	evidence that		
22 23			about missing data.	(ICD-9), the study		7-county	potential errors	suggests study		
24				considered subcategories		Birmingham	or missing data	was free of		
25				of respiratory diseases		metropolitan	did not depend 9	selective		
26 27				including pneumonia		area, the 8	on air pollution €	report.		
28				(ICD-9 codes 480–486),		Missouri and 8	levels.			
29				chronic obstructive		Illinois counties	9, 20			
30 31				pulmonary disease		in the St. Louis	)24			
32				(491,492,496), upper		metropolitan	by g			
33				respiratory infection		area, and the	lues			
34				(URI) (460–465, 466.0,		12-county Dallas	t. <u>P</u>			
35 36				477), and asthma and/or		metropolitan	19, 2024 by guest. Protected			
37				wheeze (493, 786.07).		area.	) 			
38 39			1	,			by cop	,		

36/bmjopen-2021-0495<mark>1</mark>

•	
2	
3	
4	
5	
6	
7	
8	-
9	
10	
11	
12	
13	
14	
15	
16	
17	
18	
19	
20	
21	
22	
23	
24	
25	
26	
27	
28	
29	
30	
31	
32	
33	
34	
35	
36	
37	
38	

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data		Conflict of interest	Other
8			Probably Low	Low	Probably Low	Low	Low	Probably Low	Low	Low
9 10	49	O'Lenick	The 24-hour average	Patient-level emergency	Adjusted for	Study included	Daily counts	There was	Competing	No other
11		et al. 2017	concentration of EC was	department visit data	season, periods of	all emergency	for emergency	insufficient	interests:	potential
12			evaluated. Pollutant	from 1 January 2002 to	hospital	department visit	department \frac{\frac{3}{2}}{2}	information	None	sources of
13 14			concentration estimates	31 December 2008 were	participation and	data acquired	visit were	about	declared.	bias
15			were obtained by fusing	acquired from hospitals	holidays,	directly from	obtained, so	selective		identified.
16			observational data from	located within the	temperature and	hospitals	likely have all	outcome to		
17 18			available network	20-county metropolitan	mean dew point,	(2002–2004	outcome data.	judge for low		
19			monitors with pollutant	area of Atlanta; Relevant	interaction terms	period) and the	However, any	risk, but		
20			concentration simulations	data elements included	between season	Georgia Hospital	potential errors	indirect		
21 22			from the Community	admission date,	and maximum	Association	or missing data	evidence that		
23			Multi-Scale Air Quality	International	temperature and	(2005–2008	did not depend	suggests study		
24			emissions-based chemical	Classification of Diseases	day of year.	period) located	on air pollution	was free of		
25 26			transport model at	Ninth Revision (ICD-9)		within the	levels.	selective		
26 27			12×12km grids over	diagnosis codes, age and		20-county	Apr	report.		
28			Atlanta. 24-hour average	ZIP code of patient		metropolitan area	19			
29			EC were evaluated. Daily	residence.		of Atlanta.	, 20			
30 31			data was available and no				24 b			
32			missing data was				y gi			
33			reported.				Jest			
34 35							P 7			
36							otec			
37							ted_			
38 39			ı	ı	1		by c	ı	1	
39 40							April 19, 2024 by guest. Protected by copyright			
41							ight			
42							• *			

Page 106 of 133

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data		Conflict of interest	Other
8 9			Probably Low	Low	Probably Low	Low	Low	Probably Low	Low	Low
10	50	Pearce et	Daily EC data were	The study obtained	Adjusted for year,	Study included	Daily counts	There was	The authors	No other
11		al. 2015	obtained from a central	aggregate daily counts for	season, month, day	all emergency	for pediatric	insufficient	declare that	potential
12			monitoring location in	pediatric asthma related	of the week,	department visits	asthma related \( \frac{8}{2} \)	information	they have	sources of
13 14			Atlanta. Daily data was	emergency department	hospital, holidays,	for pediatric	emergency a	about	no	bias
15			available and no missing	visits for children ages 5	temperature and	asthma of	department department	selective	competing	identified.
16			data was reported.	to 18 years from 41	dew point.	children ages 5 to	visits were	outcome to	interests.	
17 18				hospitals within	<b>'</b> O.	18 years from 41	obtained, so	judge for low		
19				metropolitan Atlanta; and		hospitals within	likely have all	risk, but		
20				defined emergency	' /	metropolitan	outcome data.	indirect		
21				department visits for	. 01	Atlanta for study	However, any	evidence that		
22 23				pediatric asthma as all		period.	potential errors	suggests study		
24				visits with a code for		<b>101.</b>	or missing data	was free of		
25				asthma (493.0-493.9) or			did not depend 9	selective		
26 27				wheeze (786.07) using			on air pollution ≧	report.		
28				the International			levels.			
29				Classification of			9, 20			
30				Diseases, 9th Revision.			)24			
31 32							by g			
33							Jues			
34							9, 2024 by guest. Protected			
35 36							rote			
37							ctec			
38							<u> </u>			

2	
4	
4 5 6	
6	
7	
7 8 9	_
9	
10	
11	
12	
12 13	
14	
15	
16	
15 16 17 18	
18	
19	
20	
21	
22	
23	
23 24 25	
25	
25 26	
27	
27 28	
29	
30	
31	
32	
33	
34	
34 35 36 37 38	
36	
37	
38	

age	e 107 of 133 BMJ Open									
							36/bmjopen-2021-049516 on Incomplete			
	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on on ontcome data on ontcome data on ontcome data on one one	Selective reporting	Conflict of interest	Other
<u>;</u> [			Low	Low	Probably Low	Low	Low ay	Probably Low	Low	Low
50 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5	1	Strickland et al. 2010	24-hour average EC were obtained from 6 monitors. Missing data <1%.	Daily counts of emergency department visits for asthma or wheeze among children were collected from 41 Metropolitan Atlanta hospitals during 1993-2004. Using the International Classification of Diseases, 9th Revision, the study defined emergency department visits for pediatric asthma as all visits with a code for asthma (493.0–493.9) or wheeze (786.09 before October 1, 1998; 786.07 after October 1, 1998).	Adjusted for season, dew point, temperature, year, month, day of week, hospital, upper respiratory infections (the logarithm of the daily count of upper respiratory infections) and pollen concentrations (various lags of ambient ragweed, pine, oak, juniper, grass and birch concentrations).	Study included all emergency department visits for asthma or wheeze among children aged 5 to 17 years from metropolitan Atlanta hospitals during 1993–2004.	Daily counts for emergency room visits of asthma or wheeze disease were obtained, and so likely have all outcome data. However, any potential errors or missing data did not depend on air pollution levels.  Protected by	There was insufficient information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of selective report.	No conflict of interests.	No other potential sources of bias identified.

5 5 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data S	Selective reporting	Conflict of interest	Other
3			Low	Low	Probably Low	Low	Low $\overset{\mathbf{a}}{\searrow}$	Probably Low	Low	Low
0	52	Strickland	24-hour average EC were	Daily counts of	Adjusted for	Study included	Daily counts 2	There was	No conflict	No other
1		et al. 2014	obtained from 6	emergency department	season, dew point,	all emergency	for emergency $\bigcirc$	insufficient	of interests.	potential
2			monitors. Missing data	visits for asthma or	temperature, day	department visits	room visits of	information		sources of
3  4			was 1%.	wheeze among children	of week, and	for asthma or	asthma or	about		bias
5				aged 2 to 16 years were	holiday.	wheeze among	wheeze disease	selective		identified.
6				collected from the		children 2 to 16	were obtained,	outcome to		
7  8				Georgia Hospital		years of age from	so likely have	judge for low		
9				Association from 1		the Georgia	all outcome	risk, but		
20				January 2002 through 30	' /	Hospital	data. However,	indirect		
21				June 2010. The study	' (2)	Association.	any potential	evidence that		
22				identified all emergency			errors or	suggests study		
24				department visits with an		<b>'</b> 01.	missing data	was free of		
25				International			did not depend?	selective		
26 27				Classification of			on air pollution	report.		
28				Diseases, 9th revision			levels.			
29				(ICD-9) code for asthma			), 20			
30   31				(codes beginning with			24 k			
32				493) or wheeze (code			у д			
33				786.07) present in any			uest			
34 35				diagnosis field.			19, 2024 by guest. Protected b			
36							otec			
37							ted			
88 <sup>L</sup>							\$			

2 3	
4	
5	
6	
0	
8	
9	
10	
11	
12	
13	
14	
15	
16	
17	
18	
19	
20	
21	
22	
23	
24	
25	
26	
27	
28	
29	
30	
31	
32	
33	
34	
35	
36	
37	
38	

Page 10	ge 109 of 133 BMJ Open								
1 2 3 4						Incomplete			
5 6 <b>No</b> 7	. Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data	Selective reporting	Conflict of interest	Other
8		Probably High	Low	Probably Low	Low	Low	Probably Low	Low	Low
9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37	Ito et al. 2013	The study chose 150 U.S. metropolitan statistical areas where the data from at least one Chemical Species Network monitor were available. The Chemical Species Network data for PM <sub>2.5</sub> components were available either every third day or every sixth day. There was no information about missing data.	Using International Classification of Diseases, 10th Revision (ICD-10) codes, the study aggregated daily death counts for the nonaccidental all-cause, cardiovascular disease and respiratory deaths. Using International Classification of Diseases, 9th Revision (ICD-9) codes, emergency hospitalizations for the elderly (those 65 and older) data were divided into cardiovascular disease and respiratory categories.	Adjusted for modeling of confounding temporal trends (annual cycles and influenza epidemics), day-of-week patterns and temperature.	Study included all nonaccidental all-cause, cardiovascular disease and respiratory deaths and emergency hospitalizations for the elderly (those 65 and older) of cardiovascular disease and respiratory diseases.	Daily counts for death and emergency hospitalization were obtained, so likely have all outcome data. However, any potential errors or missing data did not depend on air pollution levels.	There was insufficient information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of selective report.	No conflict of interests.	No other potential sources of bias identified.
38 5 39 40 41 42						Protected by copyright.			

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on the outcome data of the outcome data on the outcome data of the outcome data on the outcome data outcome data on the outcome data o	Selective reporting	Conflict of interest	Other
8 9			Probably Low	Low	Probably Low	Low	Probably Low	Probably Low	Low	Low
9 10	54	Ostro et	The model calculations	Deaths were assigned	ge, race, marital	Data obtained for	There was no	There was	The authors	No other
11		al. 2015b	track the mass and	codes based on the	status, smoking	a cohort of	information on	insufficient	declare they	potential
12			concentrations of the PM	International	status, pack-years	female teachers	the rate of lost $\frac{8}{2}$	information	have no	sources of
13 14			constituents in particle	Classification of	of smoking,	≥30 years old.	follow up.	about	actual or	bias
15			diameters ranging from	Diseases, 10th Revision	secondhand smoke		ed fr	selective	potential	identified.
16			0.01 to 10μm through	(ICD-10) for the	exposure, body		om.	outcome to	competing	
17 18			calculations that describe	following outcomes:	mass index,		http	judge for low	financial	
19			emissions, transport,	all-cause deaths	lifetime physical		://br	risk, but	interests.	
20			diffusion, deposition,	excluding those with an	activity, alcohol		njop	indirect		
21			coagulation, gas- and	external cause	consumption,		en.t	evidence that		
22 23			particle-phase chemistry,	(A00–R99),	average daily		) ji	suggests study		
24			and gas-to-particle	cardiovascular deaths	dietary intake of	<b>'</b> 01.	com	was free of		
25			conversion. The	(I00-I99), Ischemic heart	fat, calories,		on on	selective		
26 27			University of California	disease deaths (I20-I25),	menopausal status,		Apr	report.		
28			Davis/California Institute	and pulmonary deaths	family history of		111111111111111111111111111111111111111			
29			of Technology model was	(C34, J00–J98).	myocardial		9, 20			
30 31			used to estimate		infarction, stroke,		1924			
32			ground-level		use of blood		эу <u>д</u>			
33			concentrations of 50 PM		pressure		April 19, 2024 by guest. Protected			
34			constituents over the		medication,		l. Pr			
35 36			major population regions		aspirin; living		otec			
37			in California.		conditions					
38 ˈ							y			

3 4
5
-
6
/
8
-
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39

age 111	of 133			BMJ Oper	BMJ Open  BMJ Open  Incomplete				
No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete coutcome data	Selective reporting	Conflict of interest	Other
0 1 2 3 4 5 6			COMPOS	(income, income inequality, education, population size, racial composition, unemployment).		outcome data			
8 9 0 55 1 2 3 4 5 6 7 8 9 0 1 2 3 4 5 6	Gan et al. 2013	Probably Low Using high spatial resolution land use regression models to estimate residential exposure to traffic-related air pollutants including black carbon. During the 5-year exposure period, individual exposures to ambient air pollutants were estimated at each person's residential postal code centroid using land	Low The study used International Statistical Classification of Diseases, 9th Revision (ICD-9) codes 490–492 and 496 or 10th Revision (ICD-10) codes J40–J44 to identify COPD cases during the 4-year follow-up period.	Probably High Individual-level covariates: age, sex, preexisting comorbid conditions; and neighborhood socioeconomic status (SES).	Low Data obtained for a cohort of people (45-85 years old) registered with the provincial health insurance plan. Study provided total number of subjects along with those lost during the	During the 4-year follow-up period, 38,377 (8%) subjects were lost to follow-up because of moving out of the province or dying from other diseases.	Probably Low There was insufficient information about selective outcome to judge for low risk, but indirect evidence that suggests study	Low The authors declare they have no actual or potential competing financial interests.	Low No other potential sources of bias identified.

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data ≤	Selective reporting	Conflict of interest	Other
8 9			Probably Low	Low	Probably Low	Low	Probably Low	Probably Low	Low	Low
10	56	Hvidtfeldt	The PM, NO <sub>2</sub> , BC, and	Participants who died	Age, sex,	Data obtained for	There was no 8	There was	The authors	No other
11		et al. 2019	O <sub>3</sub> concentrations at	from external causes such	educational	a cohort of men	information on	insufficient	declare they	potential
12			residential addresses of	as injuries, accidents and	attainment,	and women aged	the rate of lost	information	have no	sources of
13 14			the cohort members were	suicides (International	occupational	50–64 years	follow up.	about	competing	bias
15			derived by a	Classification of	status, marital	residing in the	led fr	selective	financial	identified.
16			high-resolution	Diseases, 10th	status, smoking	areas of	mo	outcome to	interests.	
17 18			dispersion modelling	Revision-ICD-10 codes	(status, intensity,	Copenhagen and	http	judge for low		
19			system which	S–Z) were censored at	and duration),	Aarhus.	://br	risk, but		
20			incorporates	date of death. In addition,	environmental		njop	indirect		
21 22			contributions from local,	the study investigated	tobacco smoke		en.k	evidence that		
23			urban, and regional	cardiovascular (ICD10	(ETS), alcohol		) mj.	suggests study		
24			sources of precursors to	codes I00–I99) and	consumption, body	<b>101.</b>	com	was free of		
25			PM, NO <sub>2</sub> , BC, and O <sub>3</sub> .	respiratory (ICD10 codes	mass index, waist		on	selective		
26 27				J00–J99 and C34)	circumference,		Apr	report.		
28				subgroups of mortality.	fruit consumption,		119			
29					vegetable		), 20			
30 31					consumption,		1 124			
32					physical activity;		April 19, 2024 by guest.			
33					neighborhood		uesi			
34					level		t. Pr			
35 36					socioeconomic		Protected by			
37					status (SES).		ted			
38 ˈ							Ş			

36/bmjopen-2021-0495

2	
3	
4	
5	
6	
6 7 8	
8	
9	
10	
11	
12	
13	
14 15 16 17	
15	
16	
17	
10	
19	
20	
21	
22	
23	
24	
25	
26	
27	
20 21 22 23 24 25 26 27 28 29	
29	
30	
31	
32	
33	
34	
35	
36	
32 33 34 35 36 37 38	
38	

No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data		Conflict of interest	Other
		Probably Low	Probably Low	Probably High	Low	Probably High	Probably Low	Low	Low
0 57	Thurston	The mean concentrations	More than 99% of known	Active smoking	Data obtained for	The analytic	There was	No	No other
1	et al. 2016	of PM <sub>2.5</sub> mass and trace	deaths were assigned a	and former	a cohort of	cohort included	insufficient	competing	potential
2		constituents were	cause using the	smoking, passive	persons at least	445,860	information	financial	sources of
3 4		obtained from U.S.	International	smoke exposure,	30 years of age,	participants,	about	interests.	bias
5		Environmental Protection	Classification of	possible workplace	in households	with 34,408	selective		identified.
6		Agency Air Quality	Diseases, 9th and 10th	exposure to PM,	including	Ischemic heart	outcome to		
7 8		System. These PM <sub>2.5</sub>	Revision (ICD-9 codes	occupational	someone at least	disease deaths	judge for low		
9		constituent data were	410–414; ICD-10 codes	dirtiness index,	45 years of age	(of a total of	risk, but		
)		analyzed to derive	I20–I25).	marital status,	and resided in all	157,572 deaths	indirect		
1		estimates of source		education, BMI	50 states, the	from all	evidence that		
2   3		apportioned PM <sub>2.5</sub> mass		and BMI <sup>2</sup> ,	District of	causes)	suggests study		
4		exposure concentrations		consumption of	Columbia, and	occurring	was free of		
5		using the absolute		beer, wine, and	Puerto Rico.	during	selective		
5 7		principal component		other alcohol,		follow-up. ₹	report.		
8		analysis (APCA) PM <sub>2.5</sub>		quintile of dietary			=		
9		source apportionment		fat consumption,		9, 20			
0		method.		quintile of		)24			
1 2				combined dietary		by g			
3				vegetable, fruit,		lues			
4				fiber consumption;		; <u>7</u>	)		
5				Six ecologic		rote			
7				covariates.		April 19, 2024 by guest. Protected by			
8									
9						copyrignt			
0 1						yrigi	<u>.</u>		
2						7.	•		

4 5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data	Selective reporting	Conflict of interest	Other
8 9			Probably Low	Low	Probably Low	Low	Probably Low	Probably Low	Low	Low
10	58	Yang et al.	Land use regression	Deaths were coded	Age at entry,	Data obtained for	There was no 22	There was	The authors	No other
11		2018	models were derived	according to the	gender, individual	a cohort of	information on	insufficient	declare they	potential
12			from street level	International	smoking status,	people who were	the rate of lost	information	have no	sources of
13 14			measurements collected	classification of Diseases,	body mass index	older than or	follow up.	about	actual or	bias
15			during two sampling	10th Revision (ICD-10;	(BMI), physical	equal to 65 years	ed fr	selective	potential	identified.
16			campaigns conducted in	WHO 2010) including	activity, education	old.	mo	outcome to	competing	
17 18			2014 and 2015.	natural cause mortality	level and monthly		http	judge for low	financial	
19				(A00–R99), overall	expenses;		://br	risk, but	interests.	
20				cardiovascular disease	percentage of		njop	indirect		
21				(I00–I99) and overall	participants who	•	en.k	evidence that		
22 23				respiratory disease	were equal to or		) mj.	suggests study		
24				(J00–J47 and J80–J99).	older than 65 years	'01.	com	was free of		
25				Subcategories included	old, percentage of		/ on	selective		
26 27				Ischemic heart disease	participants whose		Apr	report.		
28				(IHD) (I20–I25),	educational level		119			
29				cerebrovascular disease	was higher than		), 20			
30 31				(I60–I69), Pneumonia	secondary school,		)24			
32				(J12–J18) and chronic	average income		р д			
33				obstructive pulmonary	per month and		ues			
34				disease (COPD) (J40–I44	percentage of		April 19, 2024 by guest. Protected			
35 36				and I47).	smokers.		oter.			
37				,			cted			
38 <sup>[</sup>							by			

36/bmjopen-2021-0495

2	
3	
4	
5	
7	
8	_
9	
10	
11	
12	
13	
14	
15	
16	
17	
18	
19	
20	
21	
22	
23	
24	
25 26	
26 27	
28	
26 29	
30	
31	
32	
33	
34	
35	
36	
37 38	
38	
39	
40	

No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data		Conflict of interest	Other
		Probably Low	Low	Probably High	Low	Probably Low	Probably Low	Low	Low
0 59	Gan et al.	Land use regression to	A coronary heart disease	Model adjusted for	Study provided	During the	There was	The authors	No other
1	2011	estimate air pollution	hospitalization case is a	age, sex,	total number of	4-year	insufficient	declare they	potential
2		concentrations and	record of hospitalization	preexisting	subjects along	follow-up	information	have no	sources of
3   4		exposure assigned to	with the following	comorbidity, and	with those lost	period, 17,542 a	about	actual or	bias
5		residential centroid.	International Statistical	neighborhood	during the	(3.9%) moved ⊕	selective	potential	identified.
6			Classification of	socioeconomic	follow-up period.	out of the	outcome to	competing	
7 8			Diseases, 9th Revision	status. No		province and	judge for low	financial	
9			codes, ICD-9, 410-414	individual data on		16,367 (3.6%)	risk, but	interests.	
.0			and 429.2or 10th	behavioral risk		died from other	indirect		
11			Revision (ICD-10),	factors.	•	diseases,	evidence that		
2			I20–I25, as the principal			leaving	suggests study		
4			diagnosis (the most		<b>10</b> 1.	418,826	was free of		
.5			responsible diagnosis) for			(9 <sub>2.5</sub> %) 9	selective		
.6 .7			a hospital admission in			subjects at the \(\frac{\beta}{2}\)	report.		
.7			the hospitalization			end of			
9			database. A coronary						
0			heart disease death is a			1 024			
1 2			death record with			by g			
3			coronary heart disease as			Jues			
4			the cause of death in the			; <del>;</del>			
5			provincial death			rote			
6 7			registration database.			follow-up. 2024 by guest. Protected			

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data		Conflict of interest	Other
8 9			Probably High	Low	Probably Low	Low	Probably Low	Probably Low	Low	Low
9 10	60	De	Used black smoke (BS)	The study obtained	Individual-level	Data obtained for	There was no	There was	No	No other
11		Kluizenaa	as an indicator of EC	information on the	covariates: age,	a cohort of	information on	insufficient	competing	potential
12		r et al.	concentrations. Derived	incidence of	gender, marital	27,070	the rate of lost	information	financial	sources of
13 14		2013	background EC	hospital-based Ischemic	status, education,	non-institutionali	follow up.	about	interests.	bias
15			concentrations from BS	heart disease	smoking, alcohol	zed subjects.	ean	selective		identified.
16			measured at two regional	(International	use, physical		Om	outcome to		
17 18			monitoring sites. Local	Classification of Diseases	activity, body mass		nup	judge for low		
19			traffic-related EC	[ICD9] 410-414) and	index, living		.//br	risk, but		
20			emission contributions	cerebrovascular disease	conditions		njob	indirect		
21			were estimated based on	(ICD9 430-438) in the	(employment		en.	evidence that		
22 23			fuel-specific EC content	study population.	status, financial		]	suggests study		
24			of exhaust PM <sub>10</sub>		problems).		Com	was free of		
25			emission. Used the				on	selective		
26 27			traffic-related EC				Ap	report.		
28			emissions as input to				April 19, 2024 by			
29			calculate local EC				9, 2			
30			concentrations, assuming				)24	5		
31 32			absence of other local EC				by g			
33			sources. Also assumed				guest.			
34			that dispersion dynamics							
35 36			of EC are identical to				Protected			
30 37			those of $PM_{10}$ .				Cted			
38							9			

36/bmjopen-2021-0495<mark>1</mark>

2	
3	
4	
6	
7	
8	_
9	
10	
11	
12	
13	
14	
15	
16	
17	
18	
19	
20	
21	
22 23	
24	
25	
26	
27	
28	
29	
30	
31	
32	
33	
34	
35	
36	
37	
38	
39	

5 5 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data		Conflict of interest	Other
3			Probably Low	Probably Low	Probably Low	Low	Probably Low	Probably Low	Low	Low
10	61	Vedal et	The exposure estimation	All outcomes were	Individual-level	Data obtained for	There was no	There was	No financial	No other
11		al. 2013	were used the national	reported via questionnaire	covariates: age,	a cohort of	information on	insufficient	interests.	potential
12			spatial model predictions	and assessed via	body mass index,	postmenopausal	the rate of lost $\frac{8}{2}$	information		sources of
13 14			and secondary exposure	physician-adjudicator	smoking status,	women.	follow up.	about		bias
15			measures of citywide	review of medical records	cigarettes smoked		ed ±	selective		identified.
16			average exposures and	following established	per day and years		rom	outcome to		
17			distance to major	protocols.	of smoking,		h#p	judge for low		
18 19			roadways.		systolic blood		)://bi	risk, but		
20			-		pressure, history of		//bmjop	indirect		
21					hypertension,		oen.	evidence that		
22					hypercholesterole		bmj	suggests study		
24					mia, history of	(0)	.con	was free of		
25					diabetes,	h	U/ 0I	selective		
26					education,		η Ap			
27 28					household income			<b>F</b>		
29					level, and race.		9, 2			
30					ievei, una rucc.		024			
31							by			
32 33							April 19, 2024 by guest. Protected by			
34							st.			
35							Prot			
36							ecte			
37 38							 			
88   80							S S			

4,							ज्			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data ≤	Selective reporting	Conflict of interest	Other
8 9			High	Low	Probably Low	Low	Low ay	Probably Low	Low	Low
10	62	Rahmatini	BC were collected from	Daily non-accidental	Models adjusted	Study included	Daily counts 8	There was	The authors	No other
11		a et al.	two monitors (Sharif and	deaths were obtained	for time,	all daily	for death were	insufficient	of this	potential
12		2021	Setad) with data recorded	from Ministry of Health	temperature,	non-accidental	obtained, so	information	article	sources of
13 14			at 5 min intervals. BC	and Medical Education	relative humidity,	deaths from	likely have all	about	declare that	bias
15			measurements began	database. The causes of	atmospheric	Ministry of	outcome data.	selective	they have	identified.
16			from March 2017 to	death were coded	pressure, PM2.5	Health and	However, any	outcome to	no conflict	
17 18			August 2017. But the	according to the	data, Day of week	Medical	potential errors	judge for low	of interests.	
19			gaseous pollutant at the	International	(DOW) and public	Education	or missing data	risk, but		
20			Setad site were unreliable	Classification of Disease	holidays.	database from	did not depend	indirect		
21 22			and models utilizing the	(10th revision—ICD-10).	. 01	March 2017 to	on air pollution	evidence that		
23			2-site data were			August 2017.	levels.	suggests		
24			unsatisfactory. So, only			'01.	com	study was		
25			the Sharif data were used.				/ on	free of		
26 27							Apr	selective		
28							ii 19,	report.		
29							9, 20			
30 31							, 2024 by			
31 32							by g			
33							' guest.			
34										
35 36							Protected			
30 37							cted			
38							by			

36/bmjopen-2021-0495

1 2 3 4	
5	
6	
7 8	
8	
9	
10	
11	
12	
13	
14 15	
15	
16 17	
18	
19	
20	
21	
22	
23	
24	
25	
26	
27	
28	
29	
30	
31	
32	
33	
34	
35	
36	
37 38	
38	

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on the outcome data		Conflict of interest	Other
8 9			Probably Low	Probably Low	Probably Low	Low	Low 20	Probably Low	Low	Low
10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38	63	Liu et al. 2021b	Annual county-level exposures of PM2.5 and its constituents for each participant were assessed by aggregating satellite-derived estimates at a monthly time-scale and 1 km-resolution.	The three cardiovascular events as health outcomes: 1) total cardiovascular disease, including but not limited to hypertension and stroke; 2) hypertension; 3) stroke were defined according to the Disease Classification Codebook for Chinese Family Panel Studies.	Model adjusted for age, gender, education level (illiteracy, primary to middle school, and high school or above), household income (RMB, strata of ≤ 15,000, 15,000 − 40,000, and 40,000 +, grouped according to the upper and lower quartiles), urbanicity (urban/rural, defined by CFPS participants' home addresses).	All of participants were drawn from the China Family Panel Studies (CFPS) launched by Peking University Institute of Social Science Survey (ISSS) in 2010, an ongoing national longitudinal survey of social-demograp hy in China.	The cohort included 14,331 adults who completed three waves of follow-up.	insufficient information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of selective report.	The authors declare that they have no known competing financial interests or personal relationship s that could have appeared to influence the work reported in this paper.	No other potential sources of bias identified.
39 40 41 42							copyright.			

					BMJ Oper	1	36/bmjope			Page 120 c
1 2 3 4							36/bmjopen-2021-049516 o Incomplete			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on the outcome data S		Conflict of interest	Other
8			Probably Low	Low	Probably Low	Low	Probably Low	Probably Low	Low	Low
9 10	64	Lavigne et	A spatial PM2.5 surface	Incident childhood	Model adjusted for	The study used	There was no	There was	The authors	No other
11		al. 2021	gridded at a resolution of	asthma cases were	parity, child sex,	data on singleton	information on		declared	potential
12			approximately 1-km2	identified according to	breastfeeding	live births that	the rate of lost $\frac{8}{2}$	information	that there is	sources of
13 14			was derived using	International	status at the time	occurred	the rate of lost of follow up.	about	no conflict	bias
15			multiple satellite-based	Classification of Diseases	of discharge,	between April 1st	d fr	selective	of interest.	identified.
16			retrievals of aerosol	[ICD]-10: J45.	maternal smoking	2006 and March	from h	outcome to		
17 18			optical depth in		during pregnancy,	31st 2014 in the	http://bmjopen.bmj.com/	judge for low		
19			combination with a		maternal atopy,	Province of	//bm	risk, but		
20			chemical transport model,		gestational age and	Ontario, Canada.	jope	indirect		
21 22			and enhanced through		birth weight.	Mother-infant	en.b	evidence that		
23			statistical incorporation			pair data were	mj.c	suggests		
24			of ground- based			obtained from		study was		
25 26			observations (including			the Better	S S	free of		
27			BC).			Outcomes	Apri	selective		
28						Registry &	April 19, 2024 by guest	report.		
29 30						Network	202			
31						(BORN) Ontario,	24 b			
32						a province wide	y gu			
33						birth registry that	est.			
34 35						captures	Pro			
36						perinatal health	tect			
37						information.	ed b			
38   39							Protected by copyright.			
40							ругі			
41 42							ght.			

36/bmjopen-2021-0495<mark>1</mark>

'	
2	
3	
4	
5	
6	
7	
8	ŀ
9	
10	
11	
12	
13	
14	
15	
16	
17	
18	
19	
20	
21	
22	
23	
24	
25	
26	
27	
28	
29	
30	
31	
32	
33	
34	
35	
36	
37	
36 37 38	
39	

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on the second of t		Conflict of interest	Other
8 9			Probably Low	Probably Low	Probably Low	Low	Probably Low	Probably Low	Low	Low
10	65	Rodins et	The study used the	Cardiovascular outcomes	Model adjusted for	The study used	There was no	There was	The authors	No other
11		al. 2020	validated,	in the HNR Study were	age, sex,	baseline	information on	insufficient	declare that	potential
12			time-dependent,	determined by an	individual and	(2000–2003) and	the rate of lost	information	they have	sources of
13 14			three-dimensional	independent endpoint	neighborhood	14 years	follow up.	about	no known	bias
15			European Air Pollution	committee based on	SES, BMI,	follow-up data	ed fr	selective	competing	identified.
16			Dispersion chemistry	self-reports, physician	nighttime traffic	from the German	m	outcome to	financial	
17 18			transport model	and next-of-kin	noise exposure and	HNR Study, an	http	judge for low	interests or	
19			(EURAD) to estimate the	interviews, and medical	lifestyle factors:	ongoing	://br	risk, but	personal	
20			exposure to EC.	records.	smoking, alcohol	population-based	mjope	indirect	relationship	
21					consumption,	prospective	en.k	evidence that	s that could	
22 23					physical activity	cohort study.	) Jį	suggests	have	
24					and nutritional	101.	com	study was	appeared to	
25					pattern.		on /	free of	influence	
26 27							Apr	selective	the work	
28								report.	reported in	
29							19, 2024 by		this paper.	
30 31							124			
32							эу <u>ө</u>			
33							, guest.			
34										
35 36							Protected			
37							cted			
38 <sup>[</sup>							9			

Page 122 of 133

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data		Conflict of interest	Other
8 9			Probably Low	Low	Probably High	Low	Low ay 2	Probably Low	Low	Low
10	66	Kovačević	The daily average	The data of emergency	Model adjusted for	Study included	Daily counts	There was	The authors	No other
11		et al. 2020	concentration of BC were	department (ED) visits	seasonality,	all the data of	for emergency	insufficient	declare no	potential
12			collected from three	for allergic asthma were	long-term trends,	emergency	department \frac{8}{2}	information	conflict of	sources of
13 14			automatic ambient air	collected from the Užice	temperature,	department (ED)	(ED) visits	about	interest.	bias
15			quality monitoring	Health Centre, either	humidity, air	visits for allergic	were obtained,	selective		identified.
16			stations located in Užice,	from the EDs	pressure, air	asthma were	so likely have	outcome to		
17 18			Sevojno, and Kosjerić.	(ambulances or home	pollutants and	collected from	all outcome	judge for low		
19			BC were measured	care) in Užice, Sevojno,	pollens.	the Užice Health	data. However,	risk, but		
20			between 1st July 2012	and Kosjerić or from a	' /	Centre, either	any potential	indirect		
21 22			and 30th June 2014.	general hospital in Užice.	. 01	from the EDs	errors or	evidence that		
23			There was no information	International		(ambulances or	missing data	suggests		
24			about missing data.	Classification of		home care) in	did not depend	study was		
25				Diseases, 10th revision,		Užice, Sevojno,	on air pollutiong	free of		
26 27				codes were used in the		and Kosjerić or	levels. ਨੂੰ	selective		
28				diagnosis of allergic		from a general	ii 19,	report.		
29				asthma or asthma with		hospital in Užice				
30 31				coexisting allergic rhinitis		during 1st July	2024 by guest.			
32				(AR).		2012 to 30th	эу <u>ө</u>			
33						June 2014.	uesi			
34										
35 36							Protected			
37							l Xed			
38 <sup>l</sup>							<u> </u>			

36/bmjopen-2021-0495

2 3	
4	
5 6	
7	
8	L
9	
10	
11	
12	
13	
14	
15	
16	
16 17	
18	
19	
20	
21	
22	
23	
24	
25	
26	
27	
28	
29	
30	
31	
32	
33 34	
34 35	
35 36	
37	
38	
50	

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data se		Conflict of interest	Other
3			Probably Low	Probably Low	Probably Low	Low	Probably Low	Probably Low	Low	Low
9 10	67	Hasslöf et	BC levels were modelled	The outcomes were	Model adjusted for	In the	Of these, 224	There was	The authors	No other
11		al. 2020	using EnviMan (Opsis	plaque presence and	age, sex, air	cardiovascular	were missing		declare that	potential
2			AB, Sweden) by the	CIMT of the right carotid	pollutant,	subcohort of the	data on plaque	information	they have	sources of
3  4			Environmental	artery, which were	education level,	MDCS cohort,	and 20 on	about	no known	bias
5			Department of Malm"o.	assessed by ultrasound	smoke score,	6031 participants	CIMT,	selective	competing	identified.
6			The program uses a	examination B-mode	apoB/apoA1 ratio,	who had a	respectively.	outcome to	financial	
7			Gaussian dispersion	ultrasonography,	use of lipid	residential	Hence, the	judge for low	interests or	
8			model (AERMOD)	conducted by trained and	lowering drugs,	address within	Hence, the number of participants	risk, but	personal	
20			combined with an	certified sonographers.	living alone,	the air pollution	participants $\frac{3}{9}$	indirect	relationship	
21			emission database for the		cardiovascular	modelling area.	included in the	evidence that	s that could	
22			county of Scania in		heredity, diabetes	Of these, 224	plaque analyses.		have	
24			Sweden.		mellitus, waist hip	were missing	were 5807 and	study was	appeared to	
25					ratio, physical	data on plaque	in the CIMT 9	free of	influence	
26 27					activity, alcohol	and 20 on CIMT,	analyses 6011. ⋛	selective	the work	
28					consumption,	respectively. The	<b>//</b>		reported in	
29					median income	number of	9, 2		this paper.	
0					level in residential	participants	024		1 1	
1 2					area, systolic blood	included in the	by (			
3					pressure and being	plaque analyses	yues			
4					born outside of	were 5807 and in	; <del>:</del>   ''			
35					Sweden.	the CIMT	rote			
36 37						analyses 6011.	ctec			
88 <sup> </sup>							19, 2024 by guest. Protected by copyright.			
39							сор			
₩ 11							yrigl			
12							)ť.			

Page 124 of 133

			BMJ Oper	1	3/bmjopen-			Pag
					Incomplete	Selective	Conflict of	
No. Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	outcome data⇔		interest	Other
	Probably High	Probably Low	Probably High	Low	Low	Probably Low	Low	Low
Wang et al. 2019b	BC were collected from a routine air quality monitoring site operated by the New York State Department of Environmental Conservation continuously throughout the study period (2005–2016). There was no information about missing data.	All patients treated at the Cardiac Catheterization Laboratory (Cath Lab) at URMC in Rochester, NY for STEMI, who resided within 15 miles of the pollution monitoring station in Rochester were included. American College of Cardiology (ACC)/American Heart Association (AHA) guidelines were used at the time of Cath Lab admission to diagnose STEMI.	Model adjusted for seasonality, long-term trends, temperature and relative humidity.	Study included all patients treated at the Cardiac Catheterization Laboratory (Cath Lab) at URMC in Rochester, NY for STEMI throughout the study period (2005–2016).	Daily counts for all patients were obtained, so likely have all outcome data. However, any potential errors or missing data did not depend on air pollution levels.  Protected by cop	information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of selective report.	The authors declare that they have no competing interests.	No other potential sources of bias identified

36/bmjopen-2021-0495

2 3 4	
5	
6	
7	L
8 9	
10	
11	
12	
13	
14	
15	
16 17	
18	
19	
20	
21	
22	
23 24	
25	
26	
27	
28	
29	
30	
31	
32	
33	
34	
35	
36	
37	
38	

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data ≤	Selective reporting	Conflict of interest	Other
8 9			Probably Low	Low	Probably Low	Low	Probably Low	Probably Low	Low	Low
10	69	Ljungman	Based on detailed	The International	Model adjusted for	The study	The study used	There was	The authors	No other
11		et al. 2019	emission databases,	Classification of	sex, calendar year,	included	high-quality	insufficient	declare they	potential
12			monitoring data, and	Diseases, Ninth Revision	subcohort,	individuals in	and $\frac{8}{2}$	information	have no	sources of
13 14			high-resolution	(ICD-9) codes 410–414	smoking status,	two cohorts from	comprehensive	about	actual or	bias
15			dispersion models, the	and ICD-10 I20-25 codes	alcohol	Gothenburg, four	national patien		potential	identified.
6			study calculated source	were used to define IHD	consumption in	pooled cohorts	and death	outcome to	competing	
17			contributions to black	and ICD-9 codes	Stockholm and	from Stockholm,	registries,	judge for low	financial	
18 19			carbon (BC) from road	431–436 and ICD-10	Umeå, physical	and one cohort	minimizing	risk, but	interests.	
20			wear, traffic exhaust,	codes I61– I65 were used	activity, marital	from Umeå. In	minimizing loss to	indirect		
21			residential heating, and	to define stroke.	status,	total, 114,758	follow-up for	evidence that		
22 23			other sources in		socioeconomic	individuals were	our outcomes $\stackrel{\circ}{=}$ .	suggests		
24			Gothenburg, Stockholm,		index by	included from all	our outcomes of interest.  Missing	study was		
25			and Umeå.		occupation,	study areas.	Missing 9	free of		
26 27					education level,			selective		
28					occupation status,		information for on the variables ≤ 100 control of the variabl	report.		
29					and mean		5% not			
30					neighborhood		specified.			
31 32					individual income		by (			
33					in persons of		jues			
34					working age by		; <del>;</del>			
35					Small Areas for		rote			
36 37					Market Statistics.		cted			
38 <sup> </sup>							5% not specified. Protected by copyright.			
39							сор			
40 41							yrigl			
42							.÷			

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data ≤	Selective reporting	Conflict of interest	Other
8 9			Probably Low	Low	Probably Low	Low	Probably Low	Probably Low	Low	Low
10	70	Liu et al.	Annual mean	COPD was defined by	Model adjusted for	The study used	From a total of	There was	The authors	No other
11		2021a	concentrations of BC for	following the principal	age, sex, smoking	data from three	106,727	insufficient	declare that	potential
12			2010 were estimated at	diagnosis of International	status, smoking	cohorts within	participants \$	information	they have	sources of
13 14			the study participants'	Classification of	duration, smoking	the ELAPSE	with complete a	about	no known	bias
15			baseline residential	Diseases, 9th Revision	intensity,	project with	air pollution	selective	competing	identified.
16			addresses, using	(ICD-9) codes 490–492,	body-mass index,	available	exposure data,	outcome to	financial	
17 18			standardized	and 494–496, or ICD-10	marital status,	information on	the study	judge for low	interests or	
19			Europe-wide hybrid land	codes J40–44.	employment	COPD hospital	excluded 633 participants	risk, but	personal	
20			use regression (LUR)		status, educational	discharge		indirect	relationship	
21   22			models. The LUR model		level and	diagnoses. Mean	with COPD at	evidence that	s that could	
23			utilized routine		area-level annual	follow-up time is	baseline and	suggests	have	
24			monitoring data from the		year income.	16.6 years.	7,586	study was	appeared to	
25			European Environment				participants 9	free of	influence	
26   27			Agency (EEA) AirBase				with missing 출	selective	the work	
28			for PM2.5, NO2, and O3,				information on $\frac{=}{6}$	report.	reported in	
29			and ESCAPE monitoring				confounders.		this paper.	
30   31			data for BC as the				24 b			
32			dependent variable. BC				y gu			
33			was measured by the				uest			
34 35			reflectance of PM2.5				2024 by guest. Protected			
36			filters and expressed in				otec			
37   38			absorbance units.				ted by			

45

7Table S7 Assessment of certainty of evidence for the outcomes.

8 9 Evidence					Reaso	ons for downgrading						2	ນ <reasons for="" upgrading<br="">ຽ</reasons>				Final
Evidence 10	A1	Rationale	A2	Rationale	A3	Rationale	A4	Rationale	A5	Rationale	B1		Rationale	В3	Rationale	Overall	certainty assessment
12 1/3 ute effects of 1/4 / EC on CVD in 15 / EC / EC on CVD in 15 / EC / E	0	Little influence on the overall effect	0	All included studies were consistent with our prespecified PECOS	0	80% PI 1.005 (95%CI: 1.001, 1.009) does not include unity	0	Risk estimates reported by the studies are sufficiently precise	-1	publication bias exised, RR adjusted for publication bias with trim and fill.	0	Insufficient basis for upgrading	Confounders would shift the RR in both directions	0	Evidence of increase in risk with increasing exposure	-1	Low
18 12 Acute effects of BC 20 BC/EC on CVD in 21 22 M2.5-adjusted 23 del 24	0	Little influence on the overall effect	0	All included studies were consistent with our prespecified PECOS	0	80% PI 1.011(95%CI: 1.002, 1.020) does not include unity	0	Risk estimates reported by the studies are sufficiently precise	0	No evidence of publication bias	0	Insufficient basis for upgrading	Confounders would shift the RR in both directions	0	Evidence of increase in risk with increasing exposure	0	Moderate
25 26ronic effects of 24C/EC on CVD in 28 15N <sub>2.5</sub> -unadjusted 29 30odel	0	Little influence on the overall effect	0	All included studies were consistent with our prespecified PECOS	0	80% PI 1.068 (95%CI: 0.965, 1.181) include unity but no larger than twice the 95%CI	0	Risk estimates reported by the studies are sufficiently precise	0	No evidence of publication bias	0	upgrading G	Confounders would Shift the RR in both directions	0	No evidence of a clear increasing risk with exposure	0	Moderate

31
32 Abbreviations: BC: Black carbon; EC: Elemental carbon; CVD: cardiovascular diseases; RES: respiratory diseases; IHD: ischemic heart diseases; PI: prediction interval; CI: confidence interval; A1 = limitations in studies (risk of bias); A2 = 33 indirectness; A3 = inconsistency; A4 = imprecision; A5 = publication bias; B1 = large RR; B2 = all confounding decreases observed RR; B3 = concentration-response gradient.

Protect

The second response gradient and the second response gradient a

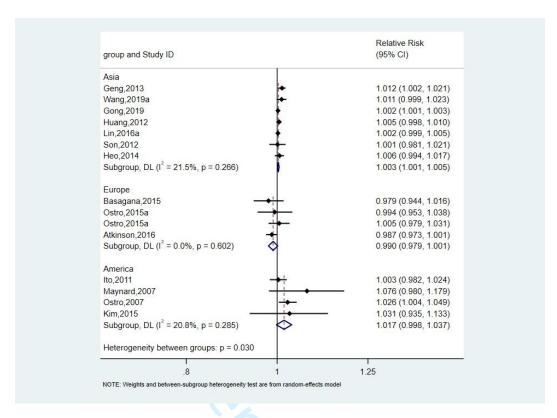
36/bmjopen-2021-049516 on 3 Ma

Table S8 The p-value calculation process for each study using RR, CI low and CI high.

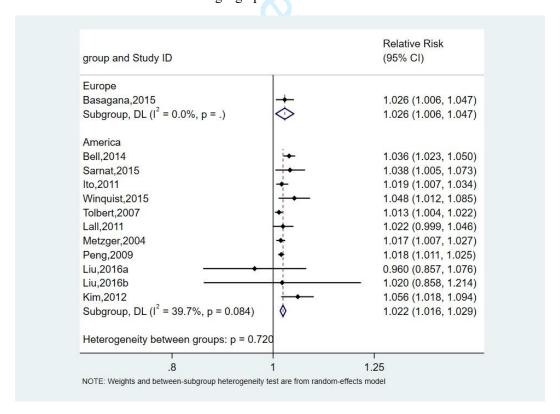
										ັນ 3		
	Number	Study ID	RR	CI low	CI high	InRR	InCI low	lnCI high	SE ag	Z	p-values	
	1	Ostro,2015a	0.994000	0.953000	1.038000	0.006018	0.048140	0.037296	<b>№</b> 0.021795	0.276122	0.782454	
	2	Ostro,2015a	1.005000	0.979000	1.031000	0.004988	0.021224	0.030529	$\stackrel{\mathbf{N}}{\sim}_{0.013202}$	0.377780	0.705594	
	3	Atkinson,2016	0.987000	0.973000	1.001000	0.013085	0.027371	0.001000	Q 0.007237	1.807997	0.070607	
	4	Geng,2013	1.012000	1.002000	1.021000	0.011929	0.001998	0.020783	<u>5</u> 0.004792	2.489281	0.012800	
	5	Liu,2016a	0.960000	0.857000	1.076000	0.040822	0.154317	0.073250	0.058053	0.703185	0.481941	
	6	Liu,2016b	1.020000	0.858000	1.214000	0.019803	0.153151	0.193921	ਰੋ 0.088539	0.223661	0.823021	
	7	Sarnat,2015	1.038000	1.005000	1.073000	0.037296	0.004988	0.070458	30.016702	2.233044	0.025546	
	8	Kim,2012	1.056000	1.018000	1.094000	0.054488	0.017840	0.089841	0.018368	2.966547	0.003012	
	9	Wang,2019a	1.011000	0.999000	1.023000	0.010940	0.001001	0.022739	0.006056	1.806427	0.070852	
	10	Maynard,2007	1.076000	0.980000	1.179000	0.073250	0.020203	0.164667	0.047161	1.553215	0.120372	
Cardiovascular Diseases	11	Winquist,2015	1.048000	1.012000	1.085000	0.046884	0.011929	0.081580	0.017768	2.638621	0.008324	
aruiovascular Diseases	12	Tolbert,2007	1.013000	1.004000	1.022000	0.012916	0.003992	0.021761	0.004533	2.849359	0.004381	
	13	Gong,2019	1.002000	1.001000	1.003000	0.001998	0.001000	0.002996	0.000509	3.923916	0.000087	
	14	Ostro,2007	1.026000	1.004000	1.049000	0.025668	0.003992	0.047837	9 0.011185	2.294831	0.021743	
	15	Metzger,2004	1.017000	1.007000	1.027000	0.016857	0.006976	0.026642	<u>=</u> .0.005017	3.360055	0.000779	
	16	Kim,2015	1.031000	0.935000	1.133000	0.030529	0.067209	0.124869	0.048999	0.623052	0.533250	
	17	Huang,2012	1.005000	0.998000	1.010000	0.004988	0.002002	0.009950	0.003049	1.635761	0.101890	
	18	Son,2012	1.001000	0.981000	1.021000	0.001000	0.019183	0.020783	\$ 0.010195	0.098036	0.921904	
	19	Heo,2014	1.006000	0.994000	1.017000	0.005982	0.006018	0.016857	G 0.005836	1.025116	0.305308	
	20	Basagana,2015	0.979000	0.944000	1.016000	0.021224	0.057629	0.015873	o.018751	1.131889	0.257681	
	21	Basagana,2015	1.026000	1.006000	1.047000	0.025668	0.005982	0.045929	면 0.010191	2.518785	0.011776	
	22	Lin,2016a	1.002000	0.999000	1.005000	0.001998	0.001001	0.004988	ဂ္ဂ ဂ္ဂ 0.001528	1.307969	0.190884	

Table S8 The p-value calculation process for each study using RR, CI low and CI high. (continued)

									_ <u>5</u>		
	Number	Study ID	RR	CI low	CI high	InRR	lnCI low	lnCI high	ω ≤se ay	z	p-values
	1	Atkinson,2016	1.013000	0.993000	1.033000	0.012916	0.007025	0.032467	80.010074	1.282079	0.199815
	2	Geng,2013	1.002000	0.983000	1.021000	0.001998	0.017146	0.020783	N 0.009676	0.206497	0.836403
	3	Ostro,2015a	1.090000	1.004000	1.183000	0.086178	0.003992	0.168054	0.041852	2.059084	0.039486
	4	Ostro,2015a	1.064000	1.020000	1.110000	0.062035	0.019803	0.104360	0.021571	2.875902	0.004029
	5	Sarnat,2015	0.995000	0.969000	1.022000	0.005013	0.031491	0.021761	0.013585	0.368983	0.712140
	6	Huang,2012	1.005000	0.993000	1.017000	0.004988	0.007025	0.016857	ਰੋ 0.006092	0.818666	0.412977
	7	Son,2012	0.989000	0.956000	1.024000	0.011061	0.044997	0.023717	∃ <sub>0.017529</sub>	0.631007	0.528036
	8	Kim,2015	1.081000	0.920000	1.266000	0.077887	0.083382	0.235862	0.081440	0.956370	0.338885
Description Discourse	9	Heo,2014	0.988000	0.962000	1.015000	0.012073	0.038741	0.014889	0.013681	0.882435	0.377541
Respiratory Diseases	10	Basagana,2015	0.986000	0.949000	1.026000	0.014099	0.052346	0.025668	0.019902	0.708432	0.478677
	11	Basagana,2015	0.940000	0.879000	1.006000	0.061875	0.128970	0.005982	0.034427	1.797311	0.072286
	12	Maynard,2007	1.196000	1.005000	1.421000	0.178983	0.004988	0.351361	0.088361	2.025595	0.042806
	13	Liu,2016a	0.964000	0.895000	1.039000	0.036664	0.110932	0.038259	0.038059	0.963352	0.335371
	14	Liu,2016b	0.963000	0.806000	1.150000	0.037702	0.215672	0.139762	9 0.090672	0.415806	0.677552
	15	Kim,2012	1.100000	0.949000	1.270000	0.095310	0.052346	0.239017	<u>=</u> .0.074327	1.282302	0.199737
	16	Cakmak,2009	1.036000	1.031000	1.041000	0.035367	0.030529	0.040182	0.002462	14.36291	3.2036*10-45
	17	Wang,2019a	1.038000	1.017000	1.059000	0.037296	0.016857	0.057325	0.010323	3.612723	0.000303
	18	Tolbert,2007	0.997000	0.990000	1.003000	0.003005	0.010050	0.002996	\$ 0.003328	0.902791	0.366637



**Figure S1** Impact of short-term exposure to BC/EC on cardiovascular mortality stratified by geographical locations.



**Figure S2** Impact of short-term exposure to BC/EC on cardiovascular morbidity stratified by geographical locations.

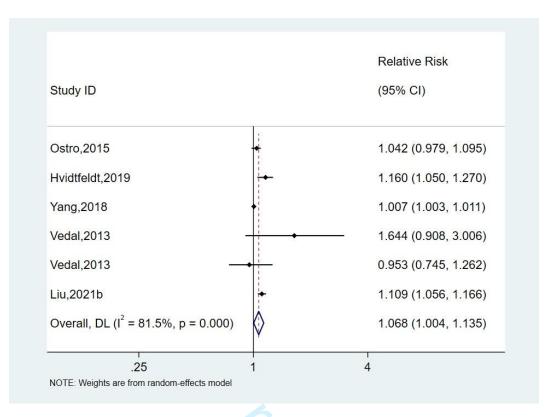
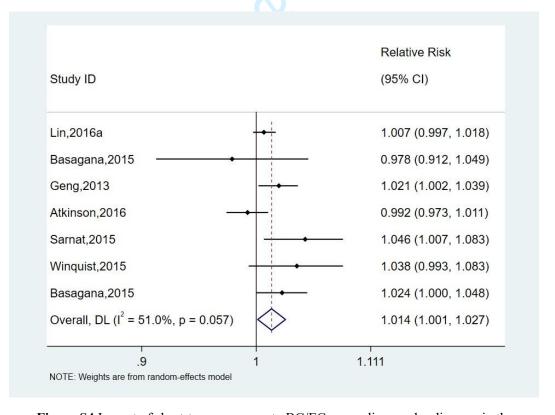


Figure S3 Impact of long-term exposure to BC/EC on cardiovascular diseases.



**Figure S4** Impact of short-term exposure to BC/EC on cardiovascular diseases in the PM<sub>2.5</sub>-adjusted model.



46 47

## PRISMA 2020 Checklist

		-2C	
Section and Topic	Item #	Checklist item 04 95	Location where item is reported
TITLE		6	
Title	1	Identify the report as a systematic review.	#1
ABSTRACT		<u>~</u> <u>~</u>	
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	#3-4
INTRODUCTION		ŶŶŎ	
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	#6-8
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	#8
METHODS		olr color	
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	#9
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to Hentify studies. Specify the date when each source was last searched or consulted.	#8-9
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	#8-9
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	#10
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	#10-11
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each gutcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	#10-11
, \$	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	#10-11
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	#11-12
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	#11
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intergention characteristics and comparing against the planned groups for each synthesis (item #5)).	#11
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summer statistics, or data conversions.	#11, 14-15
7	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	#11
] 3 9	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	#11-12
<b>)</b>	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysig, meta-regression).	#11-12
1	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	#11-12
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases.	#12
Certainty	15	Describe any methods use to topassess/isertainty (ortconfidence) in the body of evidence for iale butsonnem	#11



## PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
assessment		316	
RESULTS	,	) A	
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	#15
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	#15
Study characteristics	17	Cite each included study and present its characteristics.	#15
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	#22
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	#15-18
Results of	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	#23-24
syntheses	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	#18
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	#19-21
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	#21
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	#22-24
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	#22
DISCUSSION		5	
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	#25-29
	23b	Discuss any limitations of the evidence included in the review.	#29-30
	23c	Discuss any limitations of the review processes used.	#29-30
	23d	Discuss implications of the results for practice, policy, and future research.	#28-29
OTHER INFORMA	TION	<u>Q</u>	
Registration and	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	#8
protocol	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	#8
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	#8
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the region.	#34
Competing interests	26	Declare any competing interests of review authors.	#35
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	#36

# **BMJ Open**

### Is Short-term and Long-term Exposure to Black Carbon Associated with Cardiovascular and Respiratory Diseases? A Systematic Review and Meta-Analysis based on Evidence Reliability

Journal:	BMJ Open
Manuscript ID	bmjopen-2021-049516.R4
Article Type:	Original research
Date Submitted by the Author:	29-Mar-2022
Complete List of Authors:	Song, Xuping; Lanzhou University, School of Public Health Hu, Yue; Lanzhou University, School of Public Health Ma, Yan; Lanzhou University, School of Public Health Jiang, Liangzhen; Lanzhou University, School of Public Health Wang, Xinyi; Lanzhou University, Second Clinical College Shi, Anchen; Xi'an Jiaotong University Medical College First Affiliated Hospital, Department of General Surgery Zhao, Junxian; Lanzhou University, School of Public Health Liu, Yunxu; Lanzhou University, School of Public Health Tang, Jing; Lanzhou University, School of Public Health Li, Xiayang; Lanzhou University, School of Public Health Li, Xiayang; Lanzhou University, School of Public Health Zhang, Xiaoling; Chengdu University of Information Technology, College of Atmospheric Sciences Guo, Yong; Guizhou Province Wang, Shigong; Chengdu University of Information Technology, College of Atmospheric Sciences
<b>Primary Subject Heading</b> :	Public health
Secondary Subject Heading:	Cardiovascular medicine, Respiratory medicine
Keywords:	PUBLIC HEALTH, RESPIRATORY MEDICINE (see Thoracic Medicine), CARDIOLOGY

SCHOLARONE™ Manuscripts



I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

## **Title Page**

#### Title:

Is Short-term and Long-term Exposure to Black Carbon Associated with

Cardiovascular and Respiratory Diseases? A Systematic Review and Meta-Analysis

based on Evidence Reliability

### **Author names and affiliations:**

1. Xuping Song<sup>a</sup> E-mail: songxp@lzu.edu.cn

2. Yue Hu<sup>a</sup> E-mail: huy20@lzu.edu.cn

3. Yan Ma<sup>a</sup> E-mail: may2020@lzu.edu.cn

4. Liangzhen Jiang<sup>a</sup> E-mail: jianglzh19@lzu.edu.cn

5. Xinyi Wang<sup>c</sup> E-mail: wangxinyi17@lzu.edu.cn

6. Anchen Shi<sup>d</sup> E-mail: 3120115202@stu.xjtu.edu.cn

7. Junxian Zhao<sup>a</sup> E-mail: zhaojx2017@lzu.edu.cn

8. Yunxu Liu<sup>a</sup> E-mail: yxliu17@lzu.edu.cn

9. Yafei Liu<sup>a</sup> E-mail: isak-even@qq.com

10. Jing Tang<sup>a</sup> E-mail: tangj19@lzu.edu.cn

11. Xiayang Li<sup>a</sup> E-mail: lixiayang 18@lzu.edu.cn

10. Xiaoling Zhang<sup>b</sup> E-mail: xlzhang@ium.cn

11. Yong Guo<sup>e</sup> E-mail: gycau@qq.com

12. Shigong Wang<sup>b</sup> E-mail: wangsg@lzu.edu.cn

<sup>&</sup>lt;sup>a</sup> School of Public Health, Lanzhou University, Lanzhou 730000, China;

<sup>&</sup>lt;sup>b</sup> College of Atmospheric Sciences, Chengdu University of Information Technology,

Chengdu 610000, China;

<sup>c</sup> Second Clinical College, Lanzhou University, Lanzhou 730000, China;

<sup>d</sup> Department of General Surgery, The First Affiliated Hospital of Xi'an Jiao Tong

University, Shaanxi 710061, China;

<sup>e</sup> Department of Civil Affairs in Guizhou Province, Guiyang 550004, China.

## **Corresponding author 1:**

Name: Xiaoling Zhang

Postal Address: College of Atmospheric Sciences, Chengdu University of Information

Technology, Chengdu 610000, Sichuan, China

E-mail address: xlzhang@ium.cn

Fax: 028-85966502

#### **Corresponding author 2:**

Name: Shigong Wang

Postal Address: College of Atmospheric Sciences, Chengdu University of Information

Technology, Chengdu 610000, Sichuan, China

E-mail address: wangsg@cuit.edu.cn

Fax: 028-85966502

## **Abstract**

**Objective** Adverse health effects of fine particles ( $PM_{2.5}$ ) have been well documented by a series of studies. However, evidences on the impacts of black carbon (BC) or elemental carbon (EC) on health are limited. The objectives were (i) to explored the effects of BC and EC on cardiovascular and respiratory morbidity and mortality; (ii) to verified the reliability of the meta-analysis by drawing p-value plots.

**Design** The systematic review and meta-analysis using adapted Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach and p-value plots approach.

**Data sources** PubMed, Embase and Web of Science were searched from inception to July 19<sup>th</sup>, 2021.

**Eligibility criteria for selecting studies** Time series, case crossover and cohort studies that evaluated the associations between BC/EC on cardiovascular or respiratory morbidity or mortality were included.

**Data extraction and synthesis** Two reviewers independently selected studies, extracted data, and assessed risk of bias. Outcomes were analyzed via a random effects model and reported as relative risk (RR) with 95% confidence interval (CI). The certainty of evidences were assessed by adapted GRADE. The reliabilities of meta-analyses were analyzed by p-value plots.

**Results** Seventy studies met our inclusion criteria. (i) Short-term exposure to BC/EC was associated with 1.6% (95% CI: 0.4%-2.8%) increase in cardiovascular diseases per 1  $\mu$ g/m³ in the elderly; (ii) Long-term exposure to BC/EC was associated with

6.8% (95% CI: 0.4%-13.5%) increase in cardiovascular diseases; (iii) The p-value plot indicated that the association between BC/EC and respiratory diseases was consistent with randomness.

**Conclusions** Both short-term and long-term exposures to BC/EC were related with cardiovascular diseases. However, the impact of BC/EC on respiratory diseases did not present consistent evidence and further investigations are required.

PROSPERO registration number CRD42020186244.

# Strengths and limitations of this study

- 1. Adapted GRADE (Grading of Recommendations assessment, Development and Evaluation), formulated by the WHO global air quality guidelines working group, was used to evaluate the certainty of evidence.
- 2. This study incorporated a detailed search strategy, explicit literature screening and risk of bias assessment.

- 3. The p-value plots were used to evaluate the reliabilities of meta-analyses.
- 4. Limitation on searching grey literature should be noted.

## 1. Background

Black carbon (BC), a ubiquitous component of air particulate matter, is usually measured through optical absorption. Elemental carbon (EC), another carbonaceous material with a graphitic structure, is commonly measured by thermal or thermo-optical method.<sup>1, 2</sup> Although the measurement methods are different, BC and EC are often considered interchangeable. BC is mainly emitted from traffic and combustion-related sources and is a measured component of the particulate matter (PM). The adverse health effects of PM, especially PM<sub>2.5</sub>, are well documented. In 2017, a total of 2.94 million deaths resulted from ambient PM worldwide.<sup>3-5</sup> PM<sub>2.5</sub> is composed of various constituents, in which some of them are more toxic and hypothesized as the main cause of the adverse effects of PM2.5. A growing body of studies indicates a potential role of BC among these more toxic constituents.<sup>6, 7</sup> In addition, some reviews demonstrated that BC is a better indicator of adverse effects of PM from combustion sources according to robust associations from epidemiological studies.<sup>8, 9</sup> The underlying pathological mechanisms of BC include oxidative stress, inflammation and gene mutations. 10-12

Due to its association with adverse health, the number of studies exploring the effects of BC on cardiorespiratory diseases has rapidly increased in recent years. Cardiovascular and respiratory diseases are common diseases worldwide, with a heavy disease burden and major implications for clinical practice and public health. The global burden of disease study 2017 indicated that cardiovascular and respiratory-related death ranked first and third respectively among non-communicable

diseases.<sup>4</sup> Health effects of acute and chronic exposure to BC have been widely reported. Despite that there is some epidemiological evidence that BC was associated with cardiorespiratory diseases, in other studies, no statistically effects were observed.

The reliability of air quality epidemiological studies is often poor, with a serious lack of reproducibility of published findings.<sup>13</sup>

A lack of reproducibility in epidemiological studies can be attributed to many factors, but p-hacking is a common issue. If researchers run a regression with and without outliers, with and without a covariate, with one and then another dependent variable, then false positive results are much more likely to be reported. There can be a selective reporting problem (compute many tests and selectively report small p-values), which is referred to p-hacking.<sup>14</sup> When a study examines many questions, tests numerous statistical models and does not perform multiple testing statistical corrections, p-hacking is referred to as multiple testing and multiple modelling (MTMM).<sup>15, 16</sup> Since the uncorrected statistical estimates are likely not unbiased, the results of meta-analysis may unreliable. Therefore, it is essential to exploring the p-values in a meta-analysis.

Some systematic reviews analyzed the impact of BC on health. Nevertheless, quantitative associations between BC exposure and cardiovascular and respiratory diseases have not been well-characterized due to different objectives of the reviews. 17, 18 A series of eligible studies published recently have not been considered. In addition, the GRADE (Grading of Recommendations assessment, Development and Evaluation) framework was not adopted in previous systematic reviews. Compared

with Yang et al. 2019<sup>19</sup>, this study included recently published eligible studies. Furthermore, meta-analysis of BC effects on vulnerable populations and geographical regions were conducted. Moreover, based on a p-value plot, the reliability of meta-analysis was examined. Therefore, a systematic review and meta-analysis was performed to further elucidate the health effects of BC/EC in this study. The objectives were (1) to investigate the association of short-term and long-term exposure to BC/EC with the respiratory and cardiovascular morbidity and mortality; (2) to verify the reliability of the meta-analysis using p-value plots.

#### 2. Methods

The protocol was published online at the PROSPERO (registration number: CRD42020186244).

#### 2.1 Patient and public involvement

Patients or the public were not involved in this study.

#### 2.2 Database

PubMed, Web of Science and Embase databases were systematically searched using the following terms: (black carbon\* or elemental carbon\*) AND (respiratory\* or cardiovascular\*) AND (morbidit\* or hospitalization\* or death\* or mortalit\* or outpatien\*) AND (time series\* or case cross\* or cohort\*)". We limited our search to studies from inception to July 19th, 2021. In addition, the reference lists of the included studies and related reviews were manually evaluated to identify additional relevant studies. The details of the search strategy in PubMed were shown in Table S1.

#### 2.3 Inclusion and exclusion criteria

A time series study, case crossover study or cohort study that evaluated the impact of BC/EC on cardiovascular or respiratory diseases was included in this systematic review and meta-analysis. Studies were considered eligible for inclusion if they fulfilled the inclusion criteria as follows: (1) study types restricted to time series, case crossover or cohort studies; (2) studies considering BC/EC as air pollutants; (3) based on the International Classification of Diseases (ICD) 9th or 10th revision, diseases included respiratory diseases, wheeze, other respiratory distress insufficiency or respiratory cancer (ICD-9 codes 460–519, 786.07, 786.09 or 162; ICD-10 codes J00–J99, R06.251, R06.001 or C34) or cardiovascular diseases (ICD-9 codes 390–459, ICD-10 codes I00–I99); (4) studies considering morbidity or mortality as outcome; (5) estimates were odds ratio (OR), relative risk (RR) or hazard ratio (HR) with 95% confidence interval (CI) or enough information for their calculation; (6) publication language was restricted to English.

The exclusion criteria were as follows: (1) studies on soot or black smoke were excluded, because the definition of such components usually lacked precision; (2) studies assessing the disease progression exposure to pollutants in individuals with cardiovascular or respiratory diseases (for example chronic obstructive pulmonary disease and asthma); (3) studies focusing on particular populations (for example pregnant women and miners) or population living in specific environments with high pollution concentration (for example residential area near industrial complexes, population exposed to sugar cane burning and neighborhoods that expose many

streets); (4) studies focusing on seasonality; (5) conference abstracts; (6) study period less than 1 year.

#### 2.4 Selection of articles and extraction of data

To identify eligible studies, two investigators independently screened titles and abstracts. Studies whose relevance could not be determined by titles and abstracts were subjected to full text screening. Any disagreement was resolved by discussion. A third investigator was involved in the discussion when a consensus could not be reached.

Two reviewers independently extracted the following items from each included study. Study characteristics were extracted using a standardized form that included but was not limited to the following items: first author, publication year, country, study design, diagnosis standard, time period, population age, statistical models, air pollutants, outcomes and number of events. If the reported data of the included studies were unclear or missing, the first author or corresponding author was contacted by e-mail. Any conflicts were resolved by the involvement of a third investigator if the controversy was not solved after the discussion.

## 2.5 Data synthesis

Regarding the meta-analysis, the RR was used as an effect estimate, and the OR in case crossover study and HR in cohort study were considered equivalent to RR. Estimates from the maximally adjusted model in the cohort study were extracted when multiple estimates were present in the original study to reduce the risk of potential unmeasured confounding.<sup>20</sup> In addition, the estimate was converted to a

standardized increment (1  $\mu$ g/m³) of RR. The following formula was used to calculate standardized risk estimates:

 $RR_{(standardized)} = RR_{(original)}^{Increment(1)/Increment(original)}$ 

Two studies did not show the overall risk, while stratified risk estimates by age and location were reported.<sup>21, 22</sup> In this case, the stratified estimates were pooled. One study presented the estimates of both morbidity and mortality, which were combined in the overall analysis.<sup>23</sup> In addition, if the same cohort data were analyzed in different studies and the latest study was included.<sup>24-26</sup>

#### 2.6 Risk of bias assessment

The risk of bias was assessed for each study according to the Office of Health Assessment and Translation (OHAT) tool and the Navigation Guide tool. 17, 27, 28 Risk of bias evaluation was conducted as follows: exposure assessment, outcome assessment, confounding bias, selection bias, incomplete outcome data, selective reporting, conflict of interest and other bias. Each domain was considered as "low", "probably low", "probably high", "high", or "not applicable" criteria. Two investigators conducted the risk of bias evaluation. Any inconsistency between the investigators was discussed and a third researcher was involved to resolve any disagreement.

## 2.7 Evaluation of certainty of evidence

An adaptation of the GRADE (Grading of Recommendations assessment, Development and Evaluation) framework, formulated by the WHO (World Health Organization) global air quality guidelines working group, was used to evaluate the

certainty of evidence.<sup>29</sup> The rating process on the certainty of evidence started at moderate. The certainty was graded into four levels: "high", "moderate", "low" and "very low". Five reasons were used to downgrade the certainty of evidence: limitations in studies, indirectness, inconsistency, imprecision, and publication bias; 3 reasons were used to upgrade: large magnitude of effect size, all plausible confounding shifts the relative risk towards the null and concentration-response gradient. To evaluate the magnitude of the effect size, the E-value was calculated using the following formula:

 $E - value = RR + sqrt\{RR * (RR - 1)\}$ 

#### 2.8 Statistical analysis

Statistical analysis was performed using STATA (version12.0, Stata Corp, College Station, TX, USA). In this meta-analysis, the random-effects model was conducted for anticipating significant heterogeneity among studies. Heterogeneity among trials was assessed by the Chi-square test and the extent of inconsistency was evaluated by the  $I^2$ . An 80% prediction interval (PI) of meta-estimate was calculated to assess the inconsistency. To assess potential sources of heterogeneity, subgroup analyses were performed on outcomes (morbidity and mortality), single lag days (0, 1 and 2 days), study areas (Europe, America, and Asia) and seasons (warm and cold). The estimates from BC and EC were combined, since both of them are indicators of carbon-rich combustion sources, and are usually considered interchangeable in medical research.

Estimates were pooled separately where more than three estimates were

available. Most studies presented estimates for single lags and the estimate of shortest lag was used to combine the estimates (RRs) of shortest lag in meta-analysis. However, only a few studies presented cumulative lags, and the estimates of shortest cumulative lags were used in the meta-analysis. In addition, Mostofsky et al. indicated that PM<sub>2.5</sub> is a potential confounder in assessing the health effects of PM<sub>2.5</sub> constituents.<sup>7</sup> For overall and outcome analysis, PM<sub>2.5</sub>-adjusted estimates and PM<sub>2.5</sub>-unadjusted estimates in the models were combined, respectively where more three estimates were available. Regarding the subgroup PM<sub>2.5</sub>-unadjusted estimates were analyzed, while PM<sub>2.5</sub>-adjusted estimates were not presented due to the limited number of included studies. Moreover, primary data of the included studies could not be obtained, hence it was impossible to evaluate whether the same patients were repeatedly included across multiple studies. Therefore, the sensitivity analysis was performed on all age populations to investigate the robustness of the aggregation results by the removal of studies with partial temporal overlap from the same geographical location. Most of the included studies analyzed and presented results of cardiovascular or respiratory diseases, hence systematic diseases were analyzed in the acute effect analysis, except for the chronic effect analysis. Publication bias was assessed by Egger's regression test when the outcome included more than 10 studies. Trim and fill method was used to correct on asymmetry for the outcome with publication bias. p < 0.05 was considered statistically significant.

Non-traditional methods were used to assess the reliability of basic studies,

which is different from mainstream environmental epidemiology. Studies with large analysis search spaces suggest the use of a large number of statistical models and statistical tests for an effect, thereby allowing greater flexibility of researchers to selectively search through and only report results showing positive effects. 15 studies included in the meta-analysis were randomly selected. The number of outcomes, predictors, and covariates were counted. We computed the search spaces as follows: Space1 is outcome times predictor times lags. Space2 is 2<sup>covariate</sup>. Space3 is Space1 times Space2. Space3 is the total analysis search space. Search spaces were computed by the method introduced in Young et al, 2019.<sup>30</sup>

The p-value plot was used to inspect the distribution condition of the p-values.<sup>31</sup> Regardless of sample size, the p-value is distributed uniformly between 0 to 1 under the null hypothesis. If the shape of p-value plot is a straight line and follows an approximate 45-degree line, then the p-values are consistent with a distribution of true null hypothesis; the p-values are assumed to be random.<sup>31</sup> If the shape is approximately a hockey stick, the p-values on the blade are not consistent with chance, whereas those on the arm are consistent with chance, the results are ambiguous. Therefore, p-value plot was used to assess the validity and reliability of included studies.

P-values of included studies were computed using RR, low CI and high CI.

Then, the p-values were ranked from smallest to largest using 1, 2, 3... and the plots were constructed. The following formulas were used to calculate p-value:

$$SE = (lnCI high - lnCI low)/2/1.96$$

Z = lnRR/SE

 $p - value = \{1 - NORMSDIST[ABS(Z)]\} * 2$ 

#### 3. Results

A total of 1694 studies were initially identified and 129 were reviewed in depth. We excluded the studies which study period less than 1 year or same data were analyzed in different studies.<sup>32, 33</sup> Of these, 70 fulfilled the inclusion criteria (Figure 1).<sup>7,21-26, 34-96</sup> Of the 70 included studies, 56 estimated the short-term effects of BC/EC using a time series design or case crossover design, while 14 studies explored the long-term effects of BC/EC using a cohort design. Thirty-seven of the 70 studies reported morbidity as the outcome variable, 25 studies reported mortality, and 8 studies reported both morbidity and mortality. Thirty-five studies analyzed both cardiovascular and respiratory diseases, 18 studies merely investigated cardiovascular diseases, and 17 studies assessed respiratory diseases. Thirty-seven studies were conducted in the United States, 14 in China, 4 in Canada, 2 in the United Kingdom, Sweden, Korea and Serbia, 1 in Denmark, Iran, Germany and the Netherlands. The remaining 3 studies collected data from two different countries: Spain and Greece, Spain and Italy, Sweden and Denmark. Twenty-seven studies classified the diseases using the ICD-9 codes, 26 used the ICD-10 codes, and 10 used both the ICD-9 and ICD-10 codes. However, the remaining 7 studies did not employ the ICD standards (Table S2). In addition, the authors of 33 studies were contacted, but only 19 answered our request (response rate: 57.6%).

#### 3.1 Short-term effect of BC/EC on cardiovascular and respiratory diseases

Overall, short-term exposure to BC/EC was associated with an increased risk of cardiovascular diseases (RR=1.007 per 1  $\mu$ g/m³, 95% CI: 1.002–1.011) (adjusted by trim and fill method) in overall analyses (Table 1 and Figure 2). Cardiovascular diseases (RR=1.016 per 1  $\mu$ g/m³, 95% CI: 1.004–1.028) were associated with BC/EC in the elderly (65+ years). (Figure 2)

Impact of BC/EC on cardiovascular diseases was related to the exposure lag. The estimates of the association were strongest on the day of the event (lag 0) (RR=1.011 per 1  $\mu$ g/m<sup>3</sup>, 95% CI: 1.006–1.016), and then diminished on lag 1 (RR=1.005 per 1  $\mu g/m^3$ , 95% CI: 1.002–1.008) and lag 2 (RR=1.002 per 1  $\mu g/m^3$ , 95% CI: 0.999– 1.005) (Table S3). Subgroup analyses on geographical location was performed for morbidity and mortality, respectively. Significant association between BC/EC and cardiovascular mortality was observed in Asia (RR=1.003, 95% CI: 1.001-1.005). However, no association was found in America (RR=1.017, 95% CI: 0.998–1.037) and Europe (RR=0.990, 95% CI: 0.979-1.001) (Figure S1). On the other hand, an increased risk of cardiovascular morbidity was observed in America (RR=1.022, 95%) CI: 1.016–1.029) with short-term exposure to BC/EC, while only one study performed in Europe (RR=1.026, 95% CI: 1.006-1.047) investigated the short-term effect of BC/EC on cardiovascular morbidity.<sup>23</sup> In addition, just one study in Asia performed the short-term effects of BC/EC on stroke morbidity (Figure S2).<sup>66</sup>

No association was observed between short-term exposure of BC/EC and respiratory morbidity (RR=1.012, 95% CI: 0.993–1.031) and mortality (RR=1.013, 95% CI: 0.997–1.030) (Table 1).

Table 1 Short-term impacts of BC/EC on cardiovascular and respiratory diseases in different models

	PM <sub>2.5</sub> -unadjusted model					ω PM <sub>2.5</sub> -adjusted model			
Subgroup Analysis	No. of Studies	No. of Estimates	Relative Risk (95%CI)	I <sup>2</sup>	Egger regression test (p value)	No. of Studies	No. of Estimates	Relative Risk (95%CI)	I <sup>2</sup>
Cardiovascular Diseases						22. [			
Age						Jown			
All population	20	22	1.008 (1.004, 1.012)	64.40%	0.007	6 ac	7	1.014 (1.001, 1.027)	51.00%
Relative risk adjusted for publication bias with trim and fill method	24	26	1.007 (1.002, 1.011)	_	_	ed fro	_	_	_
Sensitive analysis on study of partial temporal overlap from the same geographical location	16	16	1.006 (1.002, 1.010)	60.00%	0.020	Downloaded from http://bmjopen.bmj.com/ on	_	_	
≥65 years	5	6	1.016 (1.004, 1.028)	87.40%	_	- //bn	_	_	_
Outcome						njope			
Morbidity	12	12	1.022 (1.016, 1.029)	37.20%	0.163	4 en.b	5	1.018 (1.006, 1.031)	39.50%
Mortality	14	15	1.003 (1.001, 1.006)	29.70%	0.266	4 <u>a</u> j. g	4	1.006 (0.993, 1.019)	42.90%
Respiratory Diseases						om/ c			
Age						on A			
All population	16	18	1.010 (0.996, 1.025)	87.20%	0.627	April 1	8	1.002 (0.990, 1.014)	43.80%
Sensitive analysis on study of partial temporal overlap from the same geographical location	12	12	1.008 (0.992, 1.023)	90.30%	0.449	9, 2024	_	_	_
≥65	3	4	1.038 (1.006, 1.071)	82.90%	_	– 14 by	_	_	_
Outcome						guest.			
Morbidity	10	10	1.012 (0.993, 1.031)	91.80%	0.671	3 St. P	5	0.996 (0.987, 1.004)	0
Mortality	10	11	1.013 (0.997, 1.030)	66.40%	0.328	3 P	3	1.017 (0.985, 1.050)	48.30%
						cted by o			

# 3.2 P-value plots of short-term exposure to BC/EC on cardiovascular and respiratory diseases in the $PM_{2.5}$ -unadjusted model

We chose at random 15 studies included in the meta-analysis. Then, we extracted analysis items (outcomes, predictors, covariates, and lags) and calculated the search spaces. Table 2 listed the counts of outcomes, predictors, covariates and lags for the 15 studies. There were many thousands of possible analysis options in each of the randomly selected studies and summary statistics of the numbers of options are given in Table S4. Across the studies, the median number of possible analyses was 12,000 (interquartile range 2,688–15,360) for Space3, which took all the factors into account.

In Figure 3, the plot of cardiovascular studies showed a shape of hockey stick. There were nine p-values less than 0.05 and thirteen larger than 0.05 (Table S5). The smallest p-value in cardiovascular group was 0.000087 and the largest was 0.921904, which was of a wide range. The association between BC and cardiovascular diseases were consistent with a mixture based on p-values and p-value plot. We did not find a consistent effect so there is no proof of a causal effect. The shape of the plot on the impact of BC on respiratory diseases was close to 45-degree line. Four calculated p-values were less than 0.05, while fourteen were larger than 0.05 and fell on an approximate 45-degree line (Table S5). In addition, the smallest p-value was 3.2036\*10<sup>-45</sup> and the largest was 0.836403. The smallest p-value was so small that p-hacking (or even data fabrication) may exist. As the p-value plot's shape approached a 45-degree line, the impact of short-term exposure to BC/EC on respiratory diseases was likely to be random.

Table 2 Variable counts, and analysis search spaces for the 15 studies chosen from the meta-analysis.

Number	Study	Outcome	Predictor	Covariate	Lag	Space1	Space2	Space3
1	Atkinson,2016	3	7	6	2	42	64	2688
2	Geng,2013	3	1	5	3	9	32	288
3	Sarnat,2015	8	22	5	4	704	32	22528
4	Kim,2012	3	5	6	15	225	64	14400
5	Maynard,2007	4	2	5	1	8	32	256
6	Winquist,2015	4	8	6	3	96	64	6144
7	Gong,2019	1	2	7	9	18	128	2304
8	Huang,2012	3	13	6	7	273	64	17472
9	Basagana,2015	5	16	6	3	240	64	15360
10	Son,2012	3	11	5	7	231	32	7392
11	Heo,2014	3	9	7	4	108	128	13824
12	Kim,2015	5	5	5	15	375	32	12000
13	Tolbert,2007	2	13	7	3	78	128	9984
14	Wang,2019a	3	6	6	11	198	64	12672
15	Metzger,2004	6	14	5	8	672	32	21504

## 3.3 Long-term impact of BC/EC on cardiovascular and respiratory diseases

Five studies assessed the long-term exposure to BC/EC and cardiovascular diseases, and a positive association was observed (RR=1.068, 95% CI: 1.004-1.135) (Figure S3). Three studies assessed the long-term exposure to BC/EC and ischemic heart disease (IHD), and a positive association was observed (RR=1.066, 95% CI: 1.009-1.127). On the other hand, 4 studies assessed the long-term exposure to BC/EC and respiratory mortality. Meta-analysis was not performed due to limited included studies and no association was observed among the include studies.<sup>25, 60, 68, 75</sup> However, one study analyzed COPD. It indicated that long-term exposure to BC/EC was associated with an increased risk of chronic obstructive pulmonary disease (COPD) morbidity (RR=1.060, 95% CI: 1.020-1.100), while no impact was observed for COPD mortality (RR=1.070, 95% CI: 1.000-1.140).<sup>24</sup>

#### 3.4 Results from the PM<sub>2.5</sub>-adjusted model

In the  $PM_{2.5}$ -adjusted model, six studies were included in the meta-analysis of

short-term exposure to BC/EC and cardiovascular diseases (RR=1.014 per 1  $\mu$ g/m³, 95% CI: 1.001-1.027) (Figure S4). The meta-analysis indicated that the association was robust compared to the results of the PM<sub>2.5</sub>-unadjusted model. In addition, the impact of BC/EC on cardiovascular morbidity in the PM<sub>2.5</sub>-adjusted model (RR=1.018 per 1  $\mu$ g/m³, 95% CI: 1.006-1.031) was consistent with the results in the PM<sub>2.5</sub>-unadjusted model (RR=1.022 per 1  $\mu$ g/m³, 95% CI: 1.016-1.029). However, an increased risk was found between BC/EC and cardiovascular mortality in the PM<sub>2.5</sub>-unadjusted model (RR=1.003 per 1  $\mu$ g/m³, 95% CI: 1.001-1.006), while no association was observed in the PM<sub>2.5</sub>-adjusted model (RR=1.006 per 1  $\mu$ g/m³, 95% CI: 0.993-1.019) (Table 1).

### 3.5 Sensitive analysis

In the sensitive analysis, similar results were observed from the overall analysis of all age populations. Increased risk of cardiovascular diseases after exposure to BC/EC was found (RR=1.006 per 1  $\mu$ g/m³, 95% CI: 1.002-1.010) by eliminating studies with partial overlap from the same geographical location.<sup>21, 23, 38, 80</sup> In addition, no statistical significance was observed (RR=1.008 per 1  $\mu$ g/m³, 95% CI: 0.992-1.023) between respiratory diseases and BC/EC after eliminating overlapped studies (Table 1).<sup>21, 23, 88, 94</sup>

## 3.6 Risk of bias and certainty of evidence

The risk of bias assessment of the included studies is shown in Table S6 and more analytically in Table S7. In general, the majority of the included studies were rated as "low risk" in the items of outcome assessment, selection bias, incomplete

outcome data, conflict of interest and other bias. The confounding bias and selective reporting were mostly rated as "probably low". However, 7 studies were rated as "probably high" risk because not all critical potential confounders were adjusted in the analysis. 7, 24, 26, 46, 55, 74, 91 In addition, the majority of the included studies on the exposure assessment were assessed as "probably low" and "probably high", and in some cases studies were rated as "high" risk. Three studies were rated as "high risk" on exposure assessment mainly because pollutants were measured with a single monitoring over a large geographical area, and not measured at least daily. 53, 85, 92

The certainty of evidence on the acute effects of BC/EC on cardiovascular diseases in the  $PM_{2.5}$ -adjusted model was rated as "moderate" and in the  $PM_{2.5}$ -unadjusted model was rated as "low". The evidence on the chronic effects of BC/EC on cardiovascular diseases was evaluated as "moderate" certainty (Table S8).

#### 4. Discussion

A comprehensive search of three electronic databases was performed using a well-defined search strategy. Finally, 70 studies assessing the short-term and long-term impacts of BC/EC on cardiovascular and respiratory morbidity and mortality were included. Using a random effects model, the pooled effect estimates indicated that the short-term exposure to BC/EC was associated with an increased risk of cardiovascular diseases, but not on respiratory diseases in all populations. BC/EC was associated with cardiovascular diseases in the elderly (65+ years). In addition, association between short-term exposure to BC/EC and cardiovascular diseases differ across continents.

# 4.1 Short-term exposure to BC/EC was related with cardiovascular diseases in the elderly

Overall, the meta-analysis results indicated that short-term exposure to BC/EC was associated with an increased risk of cardiovascular diseases, but not on respiratory diseases in all populations. In general, the PM<sub>2.5</sub>-adjusted model and the PM<sub>2.5</sub>-unadjusted model and sensitivity analysis showed that the associations were consistent. In contrast to the meta-analysis calculations, p-value plots indicated mixed results for cardiovascular. Some studies indicated an effect while others appeared to be random. For respiratory effects, the p-value plot was consistent with randomness, no effect. Our counting results, Table 2 and Table S4 indicated that small p-values could be the result of multiple testing/multiple modeling.

However, the association between BC/EC and cardiovascular mortality should be further explored by further studies, which should pay more attention to the PM<sub>2.5</sub>-adjusted model. Subgroup analysis indicated that the effects of BC/EC on cardiovascular diseases were the most significant on the current day and the impacts were decreased with lag days. In addition, the association between BC/EC and cardiovascular mortality in the cold season was stronger than that in the warm season. A potential reason could be that the concentration of BC/EC in the cold season was higher than that in the warm season. 97-99 Subgroup analysis on pollutant (BC and EC) indicated that the results from the PM<sub>2.5</sub>-unadjusted model and PM<sub>2.5</sub>-adjusted model were not consistent. Furthermore, the sensitivity analysis on omitting a single study showed that the results were not robust (data not shown). An essential reason could be

that BC and EC were considered interchangeable. Three included studies simultaneously assessed the effects of BC/EC on cardiovascular diseases. 22, 63, 93 However, in the PM<sub>2.5</sub>-adjusted model, no statistically significant difference was observed between EC (RR=1.039, 95% CI: 0.993–1.083) and cardiovascular morbidity. In addition, Samoli et al illustrated that the impact of BC/EC on cardiovascular morbidity differed in the elderly and other age groups, while Atkinson et al indicated no statistically significant difference between BC/EC and cardiovascular mortality in both the PM<sub>2.5</sub>-adjusted model and PM<sub>2.5</sub>-unadjusted model. 22, 85 On the other hand, increased risk of long-term exposure to BC/EC and cardiovascular diseases was observed. However, in this meta-analysis, due to the limited number of included studies, only short-term exposure to asthma morbidity was evaluated. In addition, a subgroup analysis on the chronic effects of BC/EC on cardiovascular and respiratory diseases was not performed because of the limited number of included studies.

The overall quality of acute effects of BC/EC on cardiovascular diseases in all populations in the PM<sub>2.5</sub>-unadjusted model was evaluated as "moderate". We downgraded one level for publication bias, hence the estimate was adjusted using the trim and fill method.<sup>29</sup> In addition, inconsistency was not downgraded because 80% PI does not included unity, or it included unity but less than twice the 95% CI.

#### 4.2 Vulnerable populations

This meta-analysis revealed that BC/EC may have acute effects on cardiovascular diseases in the elderly. 100 In addition, lung function and mucociliary

clearance decline with long-term exposure to pollutants and increasing age.<sup>5, 101</sup> These factors might contribute to making the elderly more vulnerable to BC. On the other hand, this meta-analysis indicated that an increased risk was observed between BC/EC and asthma morbidity in children of 0-18 years. Asthma, a chronic airway disorder, is a serious health disease and previous studies indicated that children have higher  $PM_{2.5}$  deposition rather than the adults, and BC is an essential constituent of  $PM_{2.5}$ .<sup>102</sup>

### 4.3 Underlying pathological mechanism

In our study, the pooled effect estimate indicated that short-term and long-term exposure to BC/EC was associated with an increased risk of cardiovascular diseases. There are considerable speculative literatures on possible underlying mechanisms. An animal study conducted by Niwa et al revealed that BC accelerated atherosclerotic plaque formation. Furthermore, a human panel study was performed to assess whether the patients with IHD experience change in the repolarization parameters exposure to rising concentration of pollutants. He results indicated that the variability of the T-wave complexity increased with increasing EC during periods of 0-5 hours, 12-17 hours and 0-2 hours before ECG measurement. He of the other hand, a p-value plot analysis did not support a consistent effect of BC/EC on cardiovascular disease. The original meta-analysis examined heart attacks and claim effects for PM<sub>10</sub> and PM<sub>2.5</sub>, which performed by Mustafic et al, 2012. A critique was given in Young et al, 2019, who used p-value plots to call those claims into question. So

#### 4.4 Suggestions for further research

First, critical potential confounders (temperature, seasonality, day of the week, and long-term trends) and other potential confounders (holidays and influenza epidemics) should be considered in time series and case crossover studies, especially for influenza epidemics. Influenza epidemics are factors usually neglected in short-term studies. Second, studies should adjust PM<sub>2.5</sub> when assessing the health effect of PM<sub>2.5</sub> constituents. Mostofsky et al. showed that PM<sub>2.5</sub> may be associated with both health and its constituents. Constituents having closer association with PM<sub>2.5</sub> may illustrate a stronger association with diseases. Therefore, the results of PM<sub>2.5</sub>-unadjusted model could introduce bias.<sup>7</sup> Third, further studies are suggested to evaluate the health effects of long-term exposure to BC, especially for morbidity. An essential difficulty that needs to be acknowledged is the availability of the disease data. Emergency department visits and outpatients are more time-sensitive data than mortality, hence these indicators are more representative to some extent in investigating the health effects of environmental factors. However, the data of emergency department visits and outpatients generally from medical institutions are more difficult to obtain than data on mortality, with a large portion of mortality data arriving from departments of disease control institutions in China. Forth, the present evidence on the health effects of BC was mainly from America and Asia. Studies assessing the association in other geographical locations are suggested, which might contribute to the evaluation of the potentially different effects of BC in different continents. Fifth, more studies need to provide evidence to prove the association between BC/EC and respiratory diseases in vulnerable populations.

#### 4.5 Strength and limitation

This systematic review and meta-analysis provided a comprehensive and current evidence for the short-term and long-term exposure to BC/EC on cardiorespiratory morbidity and mortality. Adapted GRADE framework was used to assess the certainty of the evidence. Multiple testing/multiple modeling was not considered in current GRADE theory, which should be further explored in the future. Potential limitations in our study are as follows. A significant heterogeneity for the pooled estimates was noticed in the meta-analysis, which might be due to the high variability in the study population, outcomes, and geographical locations. Therefore, subgroup analyses on age of the population (all and older than 65 years old), outcomes (morbidity and mortality), geological locations (Europe, America and Asia) and lag days (0, 1, 2 days) were conducted for a further investigation of the potential sources in conditions more than 3 estimates. Most of the included papers used in our study were from the US or China, which affected the pooled estimates, although it is an inherent and inevitable selection bias. We have extracted and calculated the regional distribution of BC concentration of included studies. It showed that the mean BC concentration is highest in Asia, which maybe an essential reason of the results. In addition, consistent results of cardiovascular and respiratory diseases exposure to BC/EC were observed by eliminating studies with partial overlap from the same geographical locations.

The reliability of meta-analysis is an essential challenge for environmental epidemiology research, which should be improved in the future. The reliability of meta-analysis was analyzed by combining p-value plots and heterogeneity. Our

findings indicated that the impact of BC on cardiovascular diseases was more reliable. However, the impact of BC on respiratory diseases was random and some reported small p-values may exist p-hacking. It is not appropriate to do meta-analysis blindly when researchers do not understand the limitations in the basic studies. Therefore, it is essential for authors to understand the causes of limitations and draw objective conclusions.

## 5. Conclusions

Both short-term and long-term exposures to BC/EC were related with cardiovascular diseases. However, the impacts of BC/EC on respiratory diseases did not present consistent evidence and further investigations were required.

# Acknowledgements

We would like to thank the authors of the original studies for their contributions to our systematic review and meta-analysis, especially authors who provided their raw data for the analysis. We are grateful to Professor S. Stanley Young and all reviewers for their helpful comments and suggestions on this manuscript. We would like to thank MogoEdit company for helping us in the language editing of our article. Tipu.,

# **Contributorship statement**

SW, XZ and XS developed the research design. XS, YH, YM and LJ analyzed the data and interpreted the results. XS, YH, YM, XW and JZ drafted manuscript. AS, YuL, YaL, JT, XL and YG did literature screening and data extraction. All of the authors contributed to drafting the manuscript. The final manuscript was approved by TO CORRECTION ONLY all authors.

# **Funding**

The work was supported by the National Key Research and Development Program of China (No.2016YFA0602004) and Innovation Fund Project on Public Meteorological Service Center of China Meteorological Administration in 2020 (Grant numbers: K2020010).



# **Competing interests**

We declare that all authors have no competing interests.



# Data sharing statement

All data relevant to the study are included in the article or uploaded as supplementary information.



#### Reference

- 1. Bond TC, Doherty SJ, Fahey DW. Bounding the role of black carbon in the climate system: A scientific assessment. *Journal of geophysical research: Atmospheres*. 2013;118(11):5380-552.
- 2. Zencak Z, Elmquist M, Gustafsson Ö. Quantification and radiocarbon source apportionment of black carbon in atmospheric aerosols using the CTO-375 method. *Atmospheric Environment*. 2007;41(36):7895-906.
- 3. Atkinson RW, Kang S, Anderson HR, et al. Epidemiological time series studies of PM2.5 and daily mortality and hospital admissions: a systematic review and meta-analysis. *Thorax*. 2014;69(7):660-5.
- 4. Global, regional, and national comparative risk assessment of 84 behavioural, environmental and occupational, and metabolic risks or clusters of risks for 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet*. 2018;392(10159):1923-94.
- 5. Ross MA. Integrated science assessment for particulate matter. *US Environmental Protection Agency: Washington DC, USA*. 2009:61-161.
- 6. Bell ML, Dominici F, Ebisu K, et al. Spatial and temporal variation in PM(2.5) chemical composition in the United States for health effects studies. *Environ Health Perspect*. 2007;115(7):989-95.
- 7. Mostofsky E, Schwartz J, Coull BA, et al. Modeling the association between particle constituents of air pollution and health outcomes. *Am J Epidemiol*. 2012;176(4):317-26.
- 8. Janssen N, Gerlofs NM, Lanki T. Health effects of black carbon, The WHO European Centre for Environment and Health, Bonn, Germany. *World Health Organisation Regional Office for Europe, Copenhagen, Denmark.* 2012.
- 9. Grahame TJ, Klemm R, Schlesinger RB. Public health and components of particulate matter: the changing assessment of black carbon. *J Air Waste Manag Assoc*. 2014;64(6):620-60.
- 10. Husain M, Kyjovska ZO, Bourdon-Lacombe J, et al. Carbon black nanoparticles induce biphasic gene expression changes associated with inflammatory responses in the lungs of C57BL/6 mice following a single intratracheal instillation. *Toxicol Appl Pharmacol*. 2015;289(3):573-88.
- 11. Colicino E, Giuliano G, Power MC, et al. Long-term exposure to black carbon, cognition and single nucleotide polymorphisms in microRNA processing genes in older men. *Environ Int.* 2016;88:86-93.
- 12. Büchner N, Ale-Agha N, Jakob S, et al. Unhealthy diet and ultrafine carbon black particles induce senescence and disease associated phenotypic changes. *Exp Gerontol*. 2013;48(1).
- 13. Young SS. Air quality environmental epidemiology studies are unreliable. *REGULATORY TOXICOLOGY AND PHARMACOLOGY*. 2017;86:177-80.
- 14. Simonsohn U, Nelson LD, Simmons JP. p-Curve and Effect Size: Correcting for Publication Bias Using Only Significant Results. *PERSPECTIVES ON PSYCHOLOGICAL SCIENCE*. 2014;9(6):666-81.
- 15. Spellman BA. The Seven Deadly Sins of Psychology: A Manifesto for Reforming the Culture of Scientific Practice. *NATURE*. 2017;544(7651):414-5.
- 16. Munafo M. Rigor Mortis: How Sloppy Science Creates Worthless Cures, Crushes Hope, and Wastes Billions. *NATURE*. 2017;543(7647):619-20.
- 17. Achilleos S, Kioumourtzoglou M-A, Wu C-D, et al. Acute effects of fine particulate matter constituents on mortality: A systematic review and meta-regression analysis. *Environ Int.* 2017;109.

- 18. Luben TJ, Nichols JL, Dutton SJ, et al. A systematic review of cardiovascular emergency department visits, hospital admissions and mortality associated with ambient black carbon. *Environ Int.* 2017;107:154-62.
- 19. Yang Y, Ruan Z, Wang X, et al. Short-term and long-term exposures to fine particulate matter constituents and health: A systematic review and meta-analysis. *ENVIRONMENTAL POLLUTION*. 2019;247:874-82.
- 20. Cumberbatch MG, Rota M, Catto JWF, et al. The Role of Tobacco Smoke in Bladder and Kidney Carcinogenesis: A Comparison of Exposures and Meta-analysis of Incidence and Mortality Risks. *Eur Urol*. 2016;70(3):458-66.
- 21. Ostro B, Hu J, Goldberg D, et al. Associations of mortality with long-term exposures to fine and ultrafine particles, species and sources: results from the California Teachers Study Cohort. *Environ Health Perspect*. 2015;123(6):549-56.
- 22. Samoli E, Atkinson RW, Analitis A, et al. Associations of short-term exposure to traffic-related air pollution with cardiovascular and respiratory hospital admissions in London, UK. *Occup Environ Med.* 2016;73(5):300-7.
- 23. Basagaña X, Jacquemin B, Karanasiou A, et al. Short-term effects of particulate matter constituents on daily hospitalizations and mortality in five South-European cities: results from the MED-PARTICLES project. *Environ Int.* 2015;75:151-8.
- 24. Gan WQ, FitzGerald JM, Carlsten C, et al. Associations of ambient air pollution with chronic obstructive pulmonary disease hospitalization and mortality. *Am J Respir Crit Care Med*. 2013;187(7):721-7.
- 25. Ostro B, Tobias A, Karanasiou A, et al. The risks of acute exposure to black carbon in Southern Europe: results from the MED-PARTICLES project. *Occup Environ Med.* 2015;72(2):123-9.
- 26. Thurston GD, Burnett RT, Turner MC, et al. Ischemic Heart Disease Mortality and Long-Term Exposure to Source-Related Components of U.S. Fine Particle Air Pollution. *Environ Health Perspect*. 2016;124(6):785-94.
- 27. National Toxicology Program. Handbook for conducting a literature-based health assessment using OHAT approach for systematic review and evidence integration. Office of Health Assessment and Translation (OHAT), Division of the National Toxicology Program, National Institute of Environmental Health Sciences https://ntpniehsnihgov/ntp/ohat/ pubs/handbookjan2015 508pdf 2015.
- 28. Lam J, Sutton P, Kalkbrenner A, et al. A Systematic Review and Meta-Analysis of Multiple Airborne Pollutants and Autism Spectrum Disorder. *PLoS One*. 2016;11(9):e0161851.
- 29. Morgan RL, Thayer KA, Santesso N, et al. A risk of bias instrument for non-randomized studies of exposures: A users' guide to its application in the context of GRADE. *Environ Int.* 2019;122:168-84.
- 30. Stanley Young S, Kindzierski WB. Evaluation of a meta-analysis of air quality and heart attacks, a case study. *Critical reviews in toxicology*. 2019;49(1):85-94.
- 31. Schweder T, Spjotvoll E. PLOTS OF P-VALUES TO EVALUATE MANY TESTS SIMULTANEOUSLY. *BIOMETRIKA*. 1982;69(3):493-502.
- 32. Strickland MJ, Darrow LA, Mulholland JA, et al. Implications of different approaches for characterizing ambient air pollutant concentrations within the urban airshed for time-series studies and health benefits analyses. *Environ Health*. 2011;10:36.
- 33. Nayebare SR, Aburizaiza OS, Siddique A, et al. Association of fine particulate air pollution with cardiopulmonary morbidity in Western Coast of Saudi Arabia. *Saudi Med J.* 2017;38(9):905-12.

- 34. Cai J, Zhao A, Zhao J, et al. Acute effects of air pollution on asthma hospitalization in Shanghai, China. *Environ Pollut*. 2014;191:139-44.
- 35. Hua J, Yin Y, Peng L, et al. Acute effects of black carbon and PM<sub>2.5</sub> on children asthma admissions: a time-series study in a Chinese city. *Sci Total Environ*. 2014;481:433-8.
- 36. Darrow LA, Klein M, Flanders WD, et al. Air pollution and acute respiratory infections among children 0-4 years of age: an 18-year time-series study. *Am J Epidemiol*. 2014;180(10):968-77.
- 37. Zanobetti A, Schwartz J. Air pollution and emergency admissions in Boston, MA. *J Epidemiol Community Health*. 2006;60(10):890-5.
- 38. Metzger KB, Tolbert PE, Klein M, et al. Ambient air pollution and cardiovascular emergency department visits. *Epidemiology*. 2004;15(1):46-56.
- 39. O'Lenick CR, Winquist A, Mulholland JA, et al. Assessment of neighbourhood-level socioeconomic status as a modifier of air pollution-asthma associations among children in Atlanta. *J Epidemiol Community Health*. 2017;71(2):129-36.
- 40. Mar TF, Norris GA, Koenig JQ, et al. Associations between air pollution and mortality in Phoenix, 1995-1997. *Environ Health Perspect*. 2000;108(4):347-53.
- 41. Krall JR, Mulholland JA, Russell AG, et al. Associations between Source-Specific Fine Particulate Matter and Emergency Department Visits for Respiratory Disease in Four U.S. Cities. *Environ Health Perspect*. 2017;125(1).
- 42. Gong T, Sun Z, Zhang X, et al. Associations of black carbon and PM2.5 with daily cardiovascular mortality in Beijing, China. *Atmospheric Environment*. 2019;214:116876.
- 43. Wang Y, Shi Z, Shen F, et al. Associations of daily mortality with short-term exposure to PM and its constituents in Shanghai, China. *Chemosphere*. 2019;233:879-87.
- 44. Dai L, Zanobetti A, Koutrakis P, et al. Associations of fine particulate matter species with mortality in the United States: a multicity time-series analysis. *Environ Health Perspect*. 2014;122(8):837-42.
- 45. Bell ML, Ebisu K, Leaderer BP, et al. Associations of  $PM_{2.5}$  constituents and sources with hospital admissions: analysis of four counties in Connecticut and Massachusetts (USA) for persons  $\geq$  65 years of age. *Environ Health Perspect*. 2014;122(2):138-44.
- 46. Wang M, Hopke PK, Masiol M, et al. Changes in triggering of ST-elevation myocardial infarction by particulate air pollution in Monroe County, New York over time: a case-crossover study. *Environmental Health*. 2019;18(1).
- 47. Son J-Y, Lee J-T, Kim K-H, et al. Characterization of fine particulate matter and associations between particulate chemical constituents and mortality in Seoul, Korea. *Environ Health Perspect*. 2012;120(6):872-8.
- 48. Cakmak S, Dales RE, Gultekin T, et al. Components of particulate air pollution and emergency department visits in Chile. *Arch Environ Occup Health*. 2009;64(3):148-55.
- 49. Geng F, Hua J, Mu Z, et al. Differentiating the associations of black carbon and fine particle with daily mortality in a Chinese city. *Environ Res.* 2013;120:27-32.
- 50. Lin H, Tao J, Du Y, et al. Differentiating the effects of characteristics of PM pollution on mortality from ischemic and hemorrhagic strokes. *Int J Hyg Environ Health*. 2016;219(2):204-11.
- 51. Lall R, Ito K, Thurston GD. Distributed lag analyses of daily hospital admissions and source-apportioned fine particle air pollution. *Environ Health Perspect*. 2011;119(4):455-60.
- 52. Ostro B, Feng W-Y, Broadwin R, et al. The effects of components of fine particulate air pollution on mortality in california: results from CALFINE. *Environ Health Perspect*. 2007;115(1):13-9.

- 53. Ostro B, Roth L, Malig B, et al. The effects of fine particle components on respiratory hospital admissions in children. *Environ Health Perspect*. 2009;117(3):475-80.
- 54. Peng RD, Bell ML, Geyh AS, et al. Emergency admissions for cardiovascular and respiratory diseases and the chemical composition of fine particle air pollution. *Environ Health Perspect*. 2009;117(6):957-63.
- 55. Tomić-Spirić V, Kovačević G, Marinković J, et al. Evaluation of the Impact of Black Carbon on the Worsening of Allergic Respiratory Diseases in the Region of Western Serbia: A Time-Stratified Case-Crossover Study. *Medicina (Kaunas)*. 2019;55(6).
- 56. Pearce JL, Waller LA, Mulholland JA, et al. Exploring associations between multipollutant day types and asthma morbidity: epidemiologic applications of self-organizing map ambient air quality classifications. *Environ Health*. 2015;14:55.
- 57. Heo J, Schauer JJ, Yi O, et al. Fine particle air pollution and mortality: importance of specific sources and chemical species. *Epidemiology*. 2014;25(3):379-88.
- 58. Liu S, Ganduglia CM, Li X, et al. Fine particulate matter components and emergency department visits among a privately insured population in Greater Houston. *Sci Total Environ*. 2016;566-567:521-7.
- 59. Sarnat SE, Winquist A, Schauer JJ, et al. Fine particulate matter components and emergency department visits for cardiovascular and respiratory diseases in the St. Louis, Missouri-Illinois, metropolitan area. *Environ Health Perspect*. 2015;123(5):437-44.
- 60. Lavigne É, Talarico R, van Donkelaar A, et al. Fine particulate matter concentration and composition and the incidence of childhood asthma. *Environ Int*. 2021;152:106486.
- 61. Cao J, Xu H, Xu Q, et al. Fine particulate matter constituents and cardiopulmonary mortality in a heavily polluted Chinese city. *Environ Health Perspect*. 2012;120(3):373-8.
- 62. Ito K, Mathes R, Ross Z, et al. Fine particulate matter constituents associated with cardiovascular hospitalizations and mortality in New York City. *Environ Health Perspect*. 2011;119(4):467-73.
- 63. Winquist A, Schauer JJ, Turner JR, et al. Impact of ambient fine particulate matter carbon measurement methods on observed associations with acute cardiorespiratory morbidity. *J Expo Sci Environ Epidemiol*. 2015;25(2):215-21.
- 64. Ostro BD, Feng WY, Broadwin R, et al. The impact of components of fine particulate matter on cardiovascular mortality in susceptible subpopulations. *Occup Environ Med.* 2008;65(11):750-6.
- 65. Klemm RJ, Thomas EL, Wyzga RE. The impact of frequency and duration of air quality monitoring: Atlanta, GA, data modeling of air pollution and mortality. *J Air Waste Manag Assoc.* 2011;61(11):1281-91.
- 66. Chen S-Y, Lin Y-L, Chang W-T, et al. Increasing emergency room visits for stroke by elevated levels of fine particulate constituents. *Sci Total Environ*. 2014;473-474:446-50.
- 67. Tolbert PE, Klein M, Metzger KB, et al. Interim results of the study of particulates and health in Atlanta (SOPHIA). *J Expo Anal Environ Epidemiol*. 2000;10(5):446-60.
- 68. Yang Y, Tang R, Qiu H, et al. Long term exposure to air pollution and mortality in an elderly cohort in Hong Kong. *Environ Int.* 2018;117.
- 69. Hasslöf H, Molnár P, Andersson EM, et al. Long-term exposure to air pollution and atherosclerosis in the carotid arteries in the Malmö diet and cancer cohort. *Environ Res.* 2020;191:110095.
- 70. Rodins V, Lucht S, Ohlwein S, et al. Long-term exposure to ambient source-specific particulate matter and its components and incidence of cardiovascular events The Heinz Nixdorf Recall study.

Environ Int. 2020;142.

- 71. Liu L, Zhang Y, Yang Z, et al. Long-term exposure to fine particulate constituents and cardiovascular diseases in Chinese adults. *Journal of Hazardous Materials*. 2021;416.
- 72. Liu S, Jorgensen JT, Ljungman P, et al. Long-term exposure to low-level air pollution and incidence of chronic obstructive pulmonary disease: The ELAPSE project. *Environ Int.* 2021;146.
- 73. Ljungman PLS, Andersson N, Stockfelt L, et al. Long-Term Exposure to Particulate Air Pollution, Black Carbon, and Their Source Components in Relation to Ischemic Heart Disease and Stroke. *Environ Health Perspect*. 2019;127(10):107012.
- 74. Gan WQ, Koehoorn M, Davies HW, et al. Long-term exposure to traffic-related air pollution and the risk of coronary heart disease hospitalization and mortality. *Environ Health Perspect*. 2011;119(4):501-7.
- 75. Hvidtfeldt UA, Sørensen M, Geels C, et al. Long-term residential exposure to PM2.5, PM10, black carbon, NO2, and ozone and mortality in a Danish cohort. *Environ Int.* 2019;123:265-72.
- 76. Levy JI, Diez D, Dou Y, et al. A meta-analysis and multisite time-series analysis of the differential toxicity of major fine particulate matter constituents. *Am J Epidemiol*. 2012;175(11):1091-9.
- 77. Strickland MJ, Klein M, Flanders WD, et al. Modification of the effect of ambient air pollution on pediatric asthma emergency visits: susceptible subpopulations. *Epidemiology*. 2014;25(6):843-50.
- 78. Wang Y-C, Lin Y-K. Mortality and emergency room visits associated with ambient particulate matter constituents in metropolitan Taipei. *Sci Total Environ*. 2016;569-570:1427-34.
- 79. Maynard D, Coull BA, Gryparis A, et al. Mortality risk associated with short-term exposure to traffic particles and sulfates. *Environ Health Perspect*. 2007;115(5):751-5.
- 80. Tolbert PE, Klein M, Peel JL, et al. Multipollutant modeling issues in a study of ambient air quality and emergency department visits in Atlanta. *J Expo Sci Environ Epidemiol*. 2007;17 Suppl 2:S29-S35.
- 81. Vedal S, Campen MJ, McDonald JD, et al. National Particle Component Toxicity (NPACT) initiative report on cardiovascular effects. *Res Rep Health Eff Inst.* 2013(178):5-8.
- 82. Ito K, Ross Z, Zhou J, et al. NPACT Study 3. Time-Series Analysis of Mortality, Hospitalizations, and Ambient PM2.5 and Its Components. In: National Particle Component Toxicity (NPACT) Initiative: Integrated Epidemiologic and Toxicologic Studies of the Health Effects of Particulate Matter Components. Research Report 177. Health Effects Institute, Boston, MA. *Res Rep Health Eff Inst.* 2013.
- 83. Lin H, Tao J, Du Y, et al. Particle size and chemical constituents of ambient particulate pollution associated with cardiovascular mortality in Guangzhou, China. *Environ Pollut*. 2016;208(Pt B):758-66.
- 84. Jung C-R, Young L-H, Hsu H-T, et al. PM components and outpatient visits for asthma: A time-stratified case-crossover study in a suburban area. *Environ Pollut*. 2017;231(Pt 1):1085-92.
- 85. Rahmatinia M, Hadei M, Hopke PK, et al. Relationship between ambient black carbon and daily mortality in Tehran, Iran: a distributed lag nonlinear time series analysis. *Journal of environmental health science & engineering*. 2021;19(1):907-16.
- 86. de Kluizenaar Y, van Lenthe FJ, Visschedijk AJH, et al. Road traffic noise, air pollution components and cardiovascular events. *Noise Health*. 2013;15(67):388-97.
- 87. Huang W, Cao J, Tao Y, et al. Seasonal variation of chemical species associated with short-term mortality effects of PM(2.5) in Xi'an, a Central City in China. *Am J Epidemiol*. 2012;175(6):556-66.
- 88. Kim S-Y, Dutton SJ, Sheppard L, et al. The short-term association of selected components of fine

particulate matter and mortality in the Denver Aerosol Sources and Health (DASH) study. *Environ Health*. 2015;14:49.

- 89. Strickland MJ, Darrow LA, Klein M, et al. Short-term associations between ambient air pollutants and pediatric asthma emergency department visits. *Am J Respir Crit Care Med*. 2010;182(3):307-16.
- 90. Liu S, Ganduglia CM, Li X, et al. Short-term associations of fine particulate matter components and emergency hospital admissions among a privately insured population in Greater Houston. *Atmospheric Environment*. 2016;147:369-75.
- 91. Kovacevic G, Spiric VT, Marinkovic J, et al. Short-Term effects of air pollution on exacerbations of allergic asthma in uzice region, serbia. *Postepy Dermatologii i Alergologii*. 2020;37(3):377-83.
- 92. Krall JR, Anderson GB, Dominici F, et al. Short-term exposure to particulate matter constituents and mortality in a national study of U.S. urban communities. *Environ Health Perspect*. 2013;121(10):1148-53.
- 93. Atkinson RW, Analitis A, Samoli E, et al. Short-term exposure to traffic-related air pollution and daily mortality in London, UK. *J Expo Sci Environ Epidemiol*. 2016;26(2):125-32.
- 94. Kim S-Y, Peel JL, Hannigan MP, et al. The temporal lag structure of short-term associations of fine particulate matter chemical constituents and cardiovascular and respiratory hospitalizations. *Environ Health Perspect*. 2012;120(8):1094-9.
- 95. Zhou J, Ito K, Lall R, et al. Time-series analysis of mortality effects of fine particulate matter components in Detroit and Seattle. *Environ Health Perspect*. 2011;119(4):461-6.
- 96. Sinclair AH, Edgerton ES, Wyzga R, et al. A two-time-period comparison of the effects of ambient air pollution on outpatient visits for acute respiratory illnesses. *J Air Waste Manag Assoc*. 2010;60(2):163-75.
- 97. Anand A, Phuleria HC. Spatial and seasonal variation of outdoor BC and PM 2.5 in densely populated urban slums. *Environ Sci Pollut Res Int.* 2021;28(2):1397-408.
- 98. Chen P, Kang S, Gul C, et al. Seasonality of carbonaceous aerosol composition and light absorption properties in Karachi, Pakistan. *J Environ Sci (China)*. 2020;90:286-96.
- 99. Yang Y, Xu X, Zhang Y, et al. Seasonal size distribution and mixing state of black carbon aerosols in a polluted urban environment of the Yangtze River Delta region, China. *Sci Total Environ*. 2019;654:300-10.
- 100. Bell ML, Zanobetti A, Dominici F. Evidence on vulnerability and susceptibility to health risks associated with short-term exposure to particulate matter: a systematic review and meta-analysis. *Am J Epidemiol*. 2013;178(6):865-76.
- 101. Sinharay R, Gong J, Barratt B, et al. Respiratory and cardiovascular responses to walking down a traffic-polluted road compared with walking in a traffic-free area in participants aged 60 years and older with chronic lung or heart disease and age-matched healthy controls: a randomised, crossover study. *Lancet*. 2018;391(10118):339-49.
- 102. Phalen RF, Oldham MJ, Kleinman MT, et al. TRACHEOBRONCHIAL DEPOSITION PREDICTIONS FOR INFANTS, CHILDREN AND ADOLESCENTS. In: Dodgson J, McCallum RI, Bailey MR, Fisher DR, editors. Inhaled Particles VI: Pergamon; 1988. p. 11-21.
- 103. Niwa Y, Hiura Y, Murayama T, et al. Nano-sized carbon black exposure exacerbates atherosclerosis in LDL-receptor knockout mice. *Circ J.* 2007;71(7):1157-61.
- 104. Henneberger A, Zareba W, Ibald-Mulli A, et al. Repolarization changes induced by air pollution in ischemic heart disease patients. *Environ Health Perspect*. 2005;113(4):440-6.
- 105. Mustafic H, Jabre P, Caussin C, et al. Main air pollutants and myocardial infarction: a systematic

review and meta-analysis. Jama. 2012;307(7):713-21.

## **Table captions**

**Table 1** Short-term impact of BC/EC on cardiovascular and respiratory diseases in different models.

**Table 2** Variable counts, and analysis search spaces for the 15 studies chosen from the meta-analysis.

## Figure captions

Figure 1 Flow diagram of literature screening process.

**Figure 2** Impact of short-term exposure to BC/EC on cardiovascular diseases in the PM<sub>2.5</sub>-unadjusted model.

Figure 3 P-value plots of short-term exposure to BC/EC on cardiovascular diseases (A) and respiratory diseases (B) in the  $PM_{2.5}$ -unadjusted model.

## Appendix A. Supplementary data

**Table S1** Search strategy in PubMed.

**Table S2** Characteristics of the included studies in the systematic review and meta-analysis.

**Table S3** Subgroup analysis on short-term effects of BC/EC on cardiovascular and respiratory diseases.

**Table S4** Summary statistics for the number of possible analyses using the three search spaces.

**Table S5** The p-value calculation process for each study using RR, CI low and CI high.

**Table S6** Results of risk of bias assessment.

**Table S7** Details of risk of bias assessment.

**Table S8** Assessment of certainty of evidence for the outcomes.

**Figure S1** Impact of short-term exposure to BC/EC on cardiovascular mortality stratified by geographical locations.

**Figure S2** Impact of short-term exposure to BC/EC on cardiovascular morbidity stratified by geographical locations.

**Figure S3** Impact of long-term exposure to BC/EC on cardiovascular diseases.

**Figure S4** Impact of short-term exposure to BC/EC on cardiovascular diseases in the PM<sub>2.5</sub>-adjusted model.

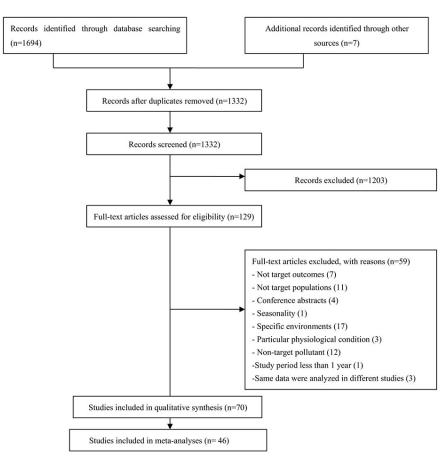


Fig. 1. Flow diagram of literature screening process

Figure 1 Flow diagram of literature screening process.

90x90mm (300 x 300 DPI)

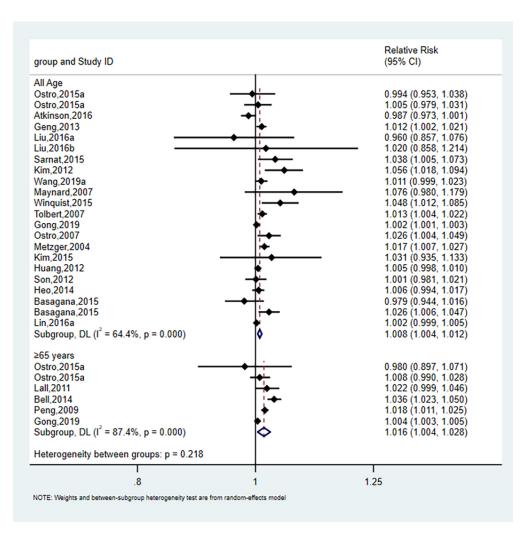


Figure 2 Impact of short-term exposure to BC/EC on cardiovascular diseases in the PM2.5-unadjusted model.

90x90mm (300 x 300 DPI)

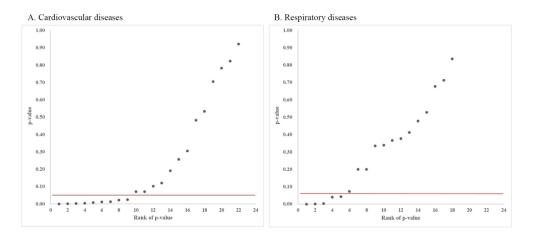


Figure 3 P-value plots of short-term exposure to BC/EC on cardiovascular diseases (A) and respiratory diseases (B) in the PM2.5-unadjusted model.

160x71mm (300 x 300 DPI)

#### SUPPLEMENTARY APPENDIX

# Is Short-term and Long-term Exposure to Black Carbon Associated with Cardiovascular and Respiratory Diseases? A Systematic Review and Meta-Analysis based on Evidence Reliability

Xuping Song<sup>a</sup>, Yue Hu<sup>a</sup>, Yan Ma<sup>a</sup>, Liangzhen Jiang<sup>a</sup>, Xinyi Wang<sup>c</sup>, Anchen Shi<sup>d</sup>, Junxian Zhao<sup>a</sup>, Yunxu Liu<sup>a</sup>, Yafei Liu<sup>a</sup>, Jing Tang<sup>a</sup>, Xiayang Li<sup>a</sup>, Xiaoling Zhang<sup>\*b</sup>, Yong Guo<sup>e</sup>, Shigong Wang<sup>\*b</sup>

### **Corresponding author 1:**

Name: Xiaoling Zhang

Postal Address: College of Atmospheric Sciences, Chengdu University of Information

Technology, Chengdu 610000, Sichuan, China

E-mail address: xlzhang@ium.cn

Fax: 028-85966502 Corresponding author 2: Name: Shigong Wang

Postal Address: College of Atmospheric Sciences, Chengdu University of Information

Technology, Chengdu 610000, Sichuan, China

E-mail address: wangsg@cuit.edu.cn

Fax: 028-85966502

<sup>&</sup>lt;sup>a</sup> School of Public Health, Lanzhou University, Lanzhou 730000, China;

<sup>&</sup>lt;sup>b</sup> College of Atmospheric Sciences, Chengdu University of Information Technology, Chengdu 610000, China;

<sup>&</sup>lt;sup>c</sup> Second Clinical College, Lanzhou University, Lanzhou 730000, China;

<sup>&</sup>lt;sup>d</sup> Department of General Surgery, The First Affiliated Hospital of Xi'an Jiao Tong University, Shaanxi 710061, China;

<sup>&</sup>lt;sup>e</sup> Department of Civil Affairs in Guizhou Province, Guiyang 550004, China.

## Supplementary data

- Table S1 Search strategy in PubMed.
- **Table S2** Characteristics of the included studies in the systematic review and meta-analysis.
- **Table S3** Subgroup analysis on short-term effects of BC/EC on cardiovascular and respiratory diseases.
- **Table S4** Summary statistics for the number of possible analyses using the three search spaces.
- **Table S5** The p-value calculation process for each study using RR, CI low and CI high.
- Table S6 Results of risk of bias assessment.
- Table S7 Details of risk of bias assessment.
- **Table S8** Assessment of certainty of evidence for the outcomes.
- **Figure S1** Impact of short-term exposure to BC/EC on cardiovascular mortality stratified by geographical locations.
- **Figure S2** Impact of short-term exposure to BC/EC on cardiovascular morbidity stratified by geographical locations.
- Figure S3 Impact of long-term exposure to BC/EC on cardiovascular diseases.
- **Figure S4** Impact of short-term exposure to BC/EC on cardiovascular diseases in the PM<sub>2.5</sub>-adjusted model.

Table S1	Search	Strategy	for	PubMed
I able 51	Scarcii	Suawgy	101	i ubivicu.

	BMJ Open	36/bmjopen-2021-049516
		pen-
		202
		1-02
		195
Table	e S1 Search Strategy for PubMed.	б 0
No.	Search Strategy	ω
#1	particulate matter/or aerosols.sh.	May 2022.
#2	particulate matter*/or "PM10"/or "PM2.5"/or fine particle*/or thoracic particle*/or ultrafine/or aerosol*/or carbon*/or soot*.ti,ab.	y 20
#3	"PM".tw.	022.
#4	or/1,2,3	Do
#5	"EC" /or "BC".tw.	Downloaded
#6	and/4,5	oad
#7	black carbon*/or elemental carbon*/or element carbon*.ti,ab.	<u>e</u> d
#8	or/6,7	from
#9	respiratory tract disease.sh.	<u></u>
#10	respirat*/or pulmonary disease*/or lung/or chest infection*/or airway/or asthma*/or pneumonia*/or "chronic obstructive pulmonary disease"	iscase"/or COPD.ti,ab.
#11	cardiovascular diseases.sh.	ъ Э
#12	cardio*/or cardiop*/or cardior*/or heart/or coronary/or vascular/or blood/or cardiac.ti,ab.	mjopen
#13	or/9,10,11,12	э .ь
#14	morbidity/or hospitalization/or death/or mortality/or outpatient.sh	<u>ā</u> .
#15	morbidit*/or hospitalisation*/or hospitalization*/or death*/or mortalit*/or outpatien*/or emergency room*/or emergency department*	/
1113	admission*.ti,ab.	0
#16	or/14,15	AK
#17	epidemiologic studies/or cross over study.sh.	April 1
#18	time series*/or timeseries*/or case cross*/or casecross*.tw.	9,
	generalized additive model/or generalised additive model/or generalized linear model/or generalised linear model/or distributed lag no	
#19	model/or distributed lag model/or quasipoisson*/or poisson*/or generalized estimating equation/or generalised estimating equation/or	AM/or GLM/or DLNM/or GEE/or DLM/or
	ARIMA.tw.	٥
#20	cohort*/or follow up*/or observational/or longitudinal/or case control*/or epidemiologic/or population	guest.
π20	stud*/or prospective*/or retrospective*.tw.	
#21	or/17,18,19,20	oteo
#22	and/8,13,16,21	Protected
		ьу
		by cop

Table S2 Characteristics of included studies in the systematic review and meta-analysis.

Study	Study	Country	Study	Outcome	Age	Pollutant	ICD	Siseases
Atkinson et al. 2016	<b>Design</b> TS	UK	2011-2012	Montality	All	BC,EC	code ICD-10	CVD(ICD-10:100-I99),RES(ICD-10:J00-J99) 8
Atkinson et al. 2010	15	UK	2011-2012	Mortality	All	BC,EC	ICD-10	Ŋ.
								RES[COPD(ICD-9-CM:490-492,RTI(ICD-9-CM:46\footnote{A66}, 480-487)];CVD[HF(ICD-9-CM:428),Heart Rhythm
Bell et al. 2014	TS	USA	2000-2004	Morbidity	≥65	ВС	ICD-9	Disturbances(ICD-9-CM:426-427), Cerebrovascular vents(ICD-9-CM:430-438),IHD(ICD-9-CM:410-414,
					<u> </u>			429),PVD(ICD-9-CM:440–448)]
Cai et al. 2014	TS	China	2005-2011	Morbidity	≥18	ВС	ICD-10	
Geng et al. 2013	TS	China	2007-2008	Mortality	All	BC	ICD-10	CVD(ICD-10:I00-I99),RES(ICD-10:J00-J98)
Hua et al. 2014	TS	China	2007-2012	Morbidity	0-14	BC	ICD-10	Asthma(ICD-10:J45)
Ostro et al. 2015a	CS	Spain, Greece	2008-2009 (Athens), 2009-2010(Barc elona)	Mortality	All	ВС	ICD-10	CVD(ICD-10:100-I99),RES(ICD-10:J00-J98)  Asthma(ICD-10:J45)  CVD(ICD-10:I00-I99),RES(ICD-10:J00-J99)  CVD(ICD-10:I00-I99),RES(ICD-10:J00-J99)
Samoli et al. 2016	TS	UK	2011-2012	Morbidity	≥15(CVD), all (RES)	BC,EC	ICD-10	CVD(ICD-10:I00-I99),RES(ICD-10:J00-J99)
Zanobetti and Schwartz 2006	CS	USA	1995-1999	Morbidity	≥65	ВС	ICD-9	MI(ICD-9:410),Pneumonia (ICD-9: 480–487)
V 1 2016	ma	110.4	2000 2012			F.C.	ICD 0	CVD(ICD-9:390-429),Stroke(ICD-9:430-438),RES(ICD-9:460-519),COPD(ICD-9:490-492,494,496),Pneumonia(I
Liu et al. 2016a	TS	USA	2008-2013	Morbidity	All	EC	ICD-9	CD-9:480-486),Asthma(ICD-9:493),SSID(ICD-9:78
		***				700		CVD(ICD-9:390-429),Stroke(ICD-9:430-438),RESRECD-9:460-519),COPD(ICD-9:490-492,494,496),Pneumonia
Liu et al. 2016b	TS	USA	2008-2013	Morbidity	All	EC	ICD-9	(ICD-9:480-486),Asthma(ICD-9:493)
								CVD[IHD(ICD9:410–414),Cardiac Dysrhythmias(ICD9:427),CHF(ICD9:428),Other CVD
Sarnat et al. 2015	TS	USA	2001-2003	Morbidity	All	EC	ICD9	(ICD9:433-437,440,443-445,451-453)],RES[Pneumæ]aa(ICD9:480-486),COPD
								(ICD:491,492,496),Asthma/Wheeze (ICD9:493,786. 76),Other RES(ICD9:460-466,477)]
Kim et al. 2012	TS	USA	2003-2007	Morbidity	All	EC	ICD-9	CVD(ICD-9:390-459),RES(ICD-9:460-519)
								copyright.

49 of 133						В	MJ Opei	36/bmjope
Table S2 Chara	cteristics (	of included s	studies in the	systematic re	eview and n	neta-analysi	s.	36/bmjopen-2021-049516 on
Study	Study Design	Country	Study Period	Outcome	Age	Pollutant	ICD code	သ ယ Discases ဩ
Ostro et al. 2009	TS	USA	2000-2003	Morbidity	<19	EC	ICD9	RES(ICD-9:460-519),Asthma(ICD-9:493),Acute bro hitis(ICD-9:466),Pneumonia(ICD-9:480-486)
Kim et al. 2015	TS	USA	2003-2007	Mortality	All	EC	ICD-10	CVD,RES
Huang et al. 2012	TS	China	2004-2008	Mortality	All	EC	ICD-10	RES(ICD-10:100-198),CVD(ICD-10:100-199 )
								CVD[Cardiac Dysrhythmias(ICD-9:428),Heart Rhytton Disturbances(ICD-9:426-427),Cerebrovascular Events
Peng et al. 2009	TS	USA	2000-2006	Morbidity	≥65	EC	ICD-9	(ICD-9:430-438),IHD (ICD-9:410-414,
								429),PVD(ICD-9:440-448)],RES[COPD(ICD-9:490
Levy et al. 2012	TS	USA	2000-2008	Morbidity	≥65	EC	ICD-9	CVD(ICD-9:390-459),RES(ICD-9:464-466 and 480-487).
Son et al. 2012	TS	Korea	2008-2009	Mortality	All	EC	ICD-10	CVD(ICD-10:100-I99),RES(ICD-10:J00-J99)
Heo et al. 2014	TS	Korea	2003-2007	Mortality	All	EC	ICD-10	CVD(ICD-10:100-I99),RES(ICD-10:J00-J99)  CVD(ICD-10:100-I99),RES(ICD-10:J00-J98)
Basagaña et al. 2015	CS	Spain, Italy	2003-2013	Morbidity,  Mortality	All	EC	ICD-9, ICD-10	CVD(ICD-9:390-459,ICD-10:100-199),RES(ICD-9:469-519,ICD-10:J00-J99)
Dai et al. 2014	TS	USA	2000-2006	Mortality	All	EC	ICD-10	CVD(ICD-10:I01-I59),RES(ICD-10:J00-J99),MI(ICD-10:I21-I22),Stroke(ICD-10:I60-I69)
Lin et al. 2016a	TS	China	2007-2011	Mortality	All	EC	ICD-10	CVD(ICD-10:I00-I99)
Cao et al. 2012	TS	China	2004-2008	Mortality	All	EC	ICD-10	
Klemm et al. 2011	TS	USA	1998-2007	Mortality	≥65	EC	ICD-10	CVD(ICD-10:100-199),RES(ICD-10:J00-J98)  CVD(ICD-10:100-199),RES(ICD-10:J00-J99)
Zhou et al. 2011	TS	USA	2002-2004	Mortality	All	EC	ICD-10	CVD(ICD-10:I01-I99),RES(ICD-10:J00-J99)
Winquist et al. 2015	TS	USA	2001-2003	Morbidity	All	BC,EC	ICD-9	CVD(ICD-10:I01-I99),RES(ICD-10:J00-J99)  RES(ICD-9:460-465,466.0,466.1,466.11,466.19,477, 80-486,491,492,493,496,786.07),CVD(ICD-9:410-414,427, 428,433-437,440,443-445,451-453)
Ostro et al. 2007	TS	USA	2000-2003	Mortality	All	EC	ICD-10	428,433-437,440,443-445,451-453)  CVD(ICD-10:I00-I99),RES(ICD-10:J00-J98)
Tolbert et al. 2000	TS	USA	1998-2000	Morbidity	All	EC	ICD-9	CVD(ICD-9:402,410-414,427,428,433-437,440,444,491-453),RES(ICD-9:460-466,477,480-486,491,492,493,496,
								786.09)  Red by copyright.

**Table S2** Characteristics of included studies in the systematic review and meta-analysis.

Study	Study Design	Country	Study Period	Outcome	Age	Pollutant	ICD code	On Wiscases Way
Wang and Lin 2016	TS	China	2004-2010	Morbidity, Mortality	≥65(mortality), all(morbidity)	EC	ICD-9	CVD(ICD-9-CM:390-459),RES(ICD-9-CM:460-519)
Darrow et al. 2014	TS	USA	1993-2010	Morbidity	0–4	EC	ICD-9	Acute Bronchitis or Bronchiolitis(ICD-9:466),Pneumonia(ICD-9:480-486),URI(ICD-9:460-465)
Metzger et al. 2004	TS	USA	1993-2000	Morbidity	All	EC	ICD-9	CVD[IHD(ICD-9:410-414),AMI(ICD-9:410),cardiacoddysrhythmias(ICD-9:427),CA(ICD-9:427.5),CHF(ICD-9:428),PVD and cerebrovascular events(ICD-9:433-437,440,443-444,451-453),CHD(IGD-9:440),Stroke(ICD-9:436)]
Mar et al. 2000	TS	USA	1995-1997	Mortality	All	EC	ICD-9	CVD(ICD-9:390-448.9)
Wang et al. 2019a	TS	China	2013-2015	Mortality	All	EC	ICD-10	CVD(ICD-9:390-448.9)  CVD(ICD-10:I00-I99),RES(ICD-10:J00-J99)  Stroke(ICD-10:I60-I66)
Lin et al. 2016b	TS	China	2007-2011	Mortality	All	EC	ICD-10	Stroke(ICD-10:I60-I66)
Ostro et al. 2008	TS	USA	2000-2003	Mortality	All	EC	ICD-10	CVD(ICD-10:100-199)
Ito et al. 2011	TS	USA	2000-2006	Morbidity, Mortality	≥40	EC	ICD-9, ICD-10	CVD[Hypertensive Diseases(ICD-9:402,ICD-10:I11] MI(ICD-9:410;ICD-10:I21-I22),IHD  (ICD-9:414,ICD-10:I25),Dysrhythmias(ICD-9:427,IO)-10:I48),HF(ICD-9:428,ICD-10:I50),Stroke(ICD-9:430-43-43-43-43-43-43-43-43-43-43-43-43-43-
Chen et al. 2014	TS	China	2004-2008	Morbidity	All	EC	ICD-9	Stroke[Ischemic Stroke(ICD-9:433-434),Hemorrhagie Stroke(ICD-9:430-432)]
Tomic'-Spiric' et al. 2019	CS	Serbia	2012-2014	Morbidity	≥18	ВС	ICD-10	Allergic RES[AR(ICD-10:J.30.4),AA(ICD-10:J.45.0
Maynard et al. 2007	CS	USA	1995-1997, 1999-2002	Mortality	All	BC	ICD-9, ICD-10	CVD(ICD-9:390-429,ICD-10:101-152),Stroke(ICD-9-330-438,ICD-10:160-169),RES(ICD-9:460-519,ICD-10:J00-J
Sinclair et al. 2010	TS	USA	1998-2002	Morbidity	All	EC	NR	Asthma,URII,LRII
Krall et al. 2013	TS	USA	2000-2005	Mortality	All	EC	NR	CVD and RES(NR)  RES(ICD-9:460-519)
Cakmak et al. 2009	TS	Canada	2001-2006	Morbidity	All	EC	ICD-9	RES(ICD-9:460-519)
								by co

Table S2 Characteristics of included studies in the systematic review and meta-analysis.

Study	Study	Country	Study	Outcome	Age	Pollutant	ICD	O D W Nisangan
Study	Design	Country	Period	Outcome	Age	ronutant	code	Suscases Discases
								CVD[IHD(ICD-9:410-414),Cardiac Dysrhythmias(ICD-9:427),CHF(ICD-9:428),PVD and Cerebrovascular
Tolbert et al. 2007	TS	USA	1993-2004	Morbidity	All	EC	ICD-9	Events(ICD-9:433-437,440,443-445,451-453)],
Tolbert et al. 2007	13	USA	1993-2004	Morbialty	All	EC	ICD-9	RES[Asthma(ICD-9:493,786.07,786.09),COPD(ICD 2:491,492,496),URTI(ICD-9:460-465,460.0,477),Pneumoni
								(ICD-9:480-486),Bronchiolitis(ICD-9:466.1,466.11,466.19)]
								RES[Pneumonia(ICD-9:480-486),COPD(ICD-9:490
Lall et al. 2011	TS	USA	2001-2002	Morbidity	≥65	EC	ICD-9	Bronchiolitis(ICD-9:466),Asthma(ICD-9:493)],CVD (ICD-9:427),IHD(ICD-9:410-414),HF(ICD-9:493)
								28),Stroke(ICD-9:431-437)]
Jung and Lin 2017	CS	China	2000-2010	Morbidity	0-20	BC	ICD-9	Asthma(ICD-9-CM:493)
Gong et al. 2019	TS	China	2006-2011	Mortality	All	ВС		Asthma(ICD-9-CM:493)  CVD(ICD-10:100-199)  Acute Ischemic Stroke
							ICD-10	Gen.
Mostofsky et al. 2012	CS	USA	2003-2008	Morbidity	≥21	ВС	NO	Acute Ischemic Stroke
			1999-2009(Atlan					.con
			ta,Georgia),					√ or
			2004-010(Birmi			EC	ICD-9	Ap
Krall et al. 2017	TS	USA	ngham,Alabama,	Morbidity	All			RES[Pneumonia(ICD-9:480-486),COPD(ICD-9:491, \$\frac{1}{2}\)2,496),URTI(ICD-9:460-465,466.0,477),Asthma and/or
			2001-2007(St.Lo					Wheeze(ICD-9:493,786.07)]
			uis, Missouri ),					92 4
			2006-2009(Dalla					Wheeze(ICD-9:493,786.07)]  20 24  by 90  85  Asthma(ICD-9:493.0-493.9),Wheeze(ICD-9:786.07);
			s,Texas)					ues
O'Lenick et al. 2017	CS	USA	2001-2008	Morbidity	5–18	EC	ICD-9	
Pearce et al. 2015	TS	USA	1999-2008	Morbidity	5–17	EC	ICD-9	Asthma(ICD-9:493.0-493.9),Wheeze(ICD-9:786.07)
Strickland et al. 2010	CS	USA	1993-2004	Morbidity	5-17	EC	ICD-9	Asthma(ICD-9:493.0-493.9),Wheeze(ICD-9:786.09)

Table S2 Characteristics of included studies in the systematic review and meta-analysis.

Table 52 Charac	Study		Study				ICD	9
Study	·	Country	·	Outcome	Age	Pollutant		₩iseases D
	Design		Period				code	<u> </u>
Strickland et al. 2014	TS	USA	2000-2010	Morbidity	2-16	EC	ICD-9	Asthma(codes beginning with 493),Wheeze (ICD-9:78).07)
Ito et al. 2013	TS	USA	2001-2006	Morbidity,	all (mortality),	EC	ICD-9,	.N CVD(ICD-10:I01-I79),RES(ICD-10:J00-J99) □
110 et al. 2015	15	OBN	2001-2000	Mortality	≥65(morbidity)	LC	ICD-10	CVD(ICD-10:I01-I79),RES(ICD-10:J00-J99)
Ostro et al. 2015b	Co	USA	2001-2007	Mortality	≥30	EC	ICD-10	CVD(ICD-10:I00-I99),IHD(ICD-10:I20-I25),Pulmortary(ICD-10:C34,J00-J98)
G 1 2012			1000 2002	Morbidity,	45.05	D.C.	ICD-9,	Q @ Q
Gan et al. 2013	Со	Canada	1999-2002	Mortality	45-85	ВС	ICD-10	COPD(ICD-9:490-492,496,ICD10:J40-J44)
Hvidtfeldt et al. 2019	Co	Denmark	1993-2015	Mortality	50 -64	BC	ICD-10	CVD(ICD-10:I00-I99),RES(ICD-10:J00-J99,C34)
TI 1 2016		TIG A	1000 2004	Mark	> 20	FC	ICD-9,	HID/ICD 0 410 414 ICD 10 100 100
Thurston et al. 2016	Со	USA	1988-2004	Mortality	≥30	EC	ICD-10	IHD(ICD-9:410-414,ICD-10:120-125)
Yang et al. 2018	Co	China	1998-2011	Mortality	≥65	BC	ICD-10	CVD(ICD-10:100-199),RES(ICD-10:J00-J99,C34)  IHD(ICD-9:410-414,ICD-10:I20-I25)  CVD(ICD-10:I00-I99),RES(ICD-10:J00-J47,J80-J999
			4000 0000	Morbidity,			ICD-9,	
Gan et al. 2011	Со	Canada	1999-2002	Mortality	45–85	BC	ICD-10	CHD(ICD-9:410-414,429.2),(ICD-10:120-125)  IHD(ICD-9:410-414),CHD(ICD-9:430-438)  CVD (ICD-9:CM 410-452)  On Appli
De Kluizenaar et al.								3
2013	Со	Netherlands	1991-2003	Morbidity	15-74	EC	ICD-9	IHD(ICD-9:410-414),CHD(ICD-9:430-438)
				Morbidity,				pri
Vedal et al. 2013	Со	USA	1994-2005	Mortality	50-79	EC	ICD-9	
Rahmatinia et al. 2021	TS	Iran	2014-2017	Mortality	All	ВС	ICD-10	RES(ICD10:J00- J99),CVD(ICD10:I00-I99),IHD(ICW)10:I20-I25)
Liu et al. 2021b	Co	China	2010–2017	Morbidity	All	ВС	NR	CVD(including but not limited to hypertension and stocke)
Lavigne et al. 2021	Co	Canada	2006-2014	Morbidity	€6	BC	ICD-10	Asthma(ICD-10:J45)
Rodins et al. 2020	Co	Germany	2000-2015	Morbidity	All	EC	NR	
Kovačević et al. 2020	CS	Serbia	2012-2014	Morbidity	≥18	BC	ICD-10	AA(ICD-10:J45.0) or asthma with coexisting AR  Atherosclerosis in the carotid arteries
Hasslöf et al. 2020	Co	Sweden	1991-1994	Morbidity	All	BC	NR	
								δ

**Table S2** Characteristics of included studies in the systematic review and meta-analysis.

								<u>0</u>
Study	Study	Country	Study	Outcome	Age	Pollutant	ICD	 ↓ ↓iseases
Study	Design	Country	Period	Outcome	Age	1 onutant	code	a)
Wang et al. 2019b	CS	USA	2005-2016	Morbidity	All	BC	NR	STEMI 20
1		G 1	1000 2011	Morbidity,	4.11	D.C.	ICD-9,	NO THE PROPERTY OF THE PROPERT
Ljungman et al. 2019	Co	Sweden	1990-2011	Mortality	All	BC	ICD-10	IHD(ICD-9:410–414 and ICD-10:120-25);stroke(ICD 3:431–436 and ICD-10:161–165)
Time at al. 2021a	C-	Sweden,	1002 2004	M. J. 1414	A 11	D.C.	ICD-9,	CONDUCTO 0.400, 402, and 404, 405, and ICD 10.1400440
Liu et al. 2021a	Со	Denmark	1992-2004	Morbidity	Morbidity All BC	вс	ICD-10	COPD(ICD-9:490–492, and 494–496, or ICD-10:J40)

Abbreviations: NR: Not Reported; TS: Time-Series; CS: Case-Crossover; Co: Cohort; ICD: International Classification of Diseases; MI: Myocardial infarction; CHD: Coronary heart disease; CVD are all content of the cont

Table S3 Subgroup analysis on short-term effects of BC/EC on cardiovascular and respiratory diseases.

Subgroup Analysis	No. of	No. of	Relative Risk	$\mathbf{I}^2$	Egger Regression Test
Subgroup Analysis	Studies	Estimates	(95%CI)	1	(p value)
Cardiovascular Diseases					
Lag Days					
Lag 0d	15	18	1.013 (1.006, 1.020)*	77.30%	0.024
Lag 1d	12	15	1.005 (1.002, 1.008)	32.70%	0.299
Lag 2d	11	14	1.002 (0.999, 1.005)	73.80%	0.969
Geographical Location (Mortality)					
Asia	8	8	1.004 (1.002, 1.006)*	70.00%	_
Europe	4	5	0.991 (0.983, 0.999)	0	_
America	4	4	1.017 (0.998, 1.037)	20.80%	_
Geographical Location (Morbidity)					
Asia	_	_	_	_	_
Europe	_	_	_	_	_
America	12	12	1.023 (1.016, 1.030)	46.00%	0.078
Disease					
Congestive heart failure (Morbidity)	3	3	1.076 (1.021, 1.134)*	64.70%	_
Season (Mortality)					
Warm season	3	3	1.002 (0.995, 1.010)	0	_
Cold season	3	3	1.014 (1.008, 1.019)*	0	_
Respiratory Diseases					
Asthma (Morbidity)					
Asthma 0-18	5	6	1.021 (1.006, 1.035)*	69.10%	
Asthma ≥18	4	5	1.011 (1.000, 1.021)	0	_

Annotation: "\*" means the data were statistically significant, p < 0.05.

Table S4 Summary statistics for the number of possible analyses using the three search spaces.

Statistic	Space1	Space2	Space3
maximum	704	128	22528
quartile	273	64	15360
median	198	64	12000
quartile	42	32	2688
minimum	8	32	256

Table S5 The p-value calculation process for each study using RR, CI low and CI high.

	Number	Study ID	RR	CI low	CI high	InRR	lnCI low	lnCI high	ω ≤SE ag	Z	p-values
	1	Ostro,2015a	0.994000	0.953000	1.038000	0.006018	0.048140	0.037296	80.021795	0.276122	0.782454
	2	Ostro,2015a	1.005000	0.979000	1.031000	0.004988	0.021224	0.030529	$\stackrel{\textstyle \sim}{\!$	0.377780	0.705594
	3	Atkinson,2016	0.987000	0.973000	1.001000	0.013085	0.027371	0.001000	Q 0.007237	1.807997	0.070607
	4	Geng,2013	1.012000	1.002000	1.021000	0.011929	0.001998	0.020783	0.004792	2.489281	0.012800
	5	Liu,2016a	0.960000	0.857000	1.076000	0.040822	0.154317	0.073250	0.058053	0.703185	0.481941
	6	Liu,2016b	1.020000	0.858000	1.214000	0.019803	0.153151	0.193921	ਰੋ 0.088539	0.223661	0.823021
	7	Sarnat,2015	1.038000	1.005000	1.073000	0.037296	0.004988	0.070458	₹ <sub>0.016702</sub>	2.233044	0.025546
	8	Kim,2012	1.056000	1.018000	1.094000	0.054488	0.017840	0.089841	0.018368	2.966547	0.003012
	9	Wang,2019a	1.011000	0.999000	1.023000	0.010940	0.001001	0.022739	0.006056	1.806427	0.070852
	10	Maynard,2007	1.076000	0.980000	1.179000	0.073250	0.020203	0.164667	0.047161	1.553215	0.120372
. P Is Discour	11	Winquist,2015	1.048000	1.012000	1.085000	0.046884	0.011929	0.081580	0.017768	2.638621	0.008324
ardiovascular Diseases	12	Tolbert,2007	1.013000	1.004000	1.022000	0.012916	0.003992	0.021761	0.004533	2.849359	0.004381
	13	Gong,2019	1.002000	1.001000	1.003000	0.001998	0.001000	0.002996	0.000509	3.923916	0.000087
	14	Ostro,2007	1.026000	1.004000	1.049000	0.025668	0.003992	0.047837	9 0.011185	2.294831	0.021743
	15	Metzger,2004	1.017000	1.007000	1.027000	0.016857	0.006976	0.026642	<u>5</u> .0.005017	3.360055	0.000779
	16	Kim,2015	1.031000	0.935000	1.133000	0.030529	0.067209	0.124869	0.048999	0.623052	0.533250
	17	Huang,2012	1.005000	0.998000	1.010000	0.004988	0.002002	0.009950	0.003049	1.635761	0.101890
	18	Son,2012	1.001000	0.981000	1.021000	0.001000	0.019183	0.020783	<b>5</b> 0.010195	0.098036	0.921904
	19	Heo,2014	1.006000	0.994000	1.017000	0.005982	0.006018	0.016857	Q 0.005836	1.025116	0.305308
	20	Basagana,2015	0.979000	0.944000	1.016000	0.021224	0.057629	0.015873	© 0.018751	1.131889	0.257681
	21	Basagana,2015	1.026000	1.006000	1.047000	0.025668	0.005982	0.045929	O.010191	2.518785	0.011776
	22	Lin,2016a	1.002000	0.999000	1.005000	0.001998	0.001001	0.004988	0.001528	1.307969	0.190884

Table S5 The p-value calculation process for each study using RR, CI low and CI high. (continued)

									<u> </u>		
	Number	Study ID	RR	CI low	CI high	InRR	lnCI low	lnCI high	ω ≤SE ag	Z	p-values
	1	Atkinson,2016	1.013000	0.993000	1.033000	0.012916	0.007025	0.032467	≥0.010074	1.282079	0.199815
	2	Geng,2013	1.002000	0.983000	1.021000	0.001998	0.017146	0.020783	$\stackrel{\text{N}}{\sim} 0.009676$	0.206497	0.836403
	3	Ostro,2015a	1.090000	1.004000	1.183000	0.086178	0.003992	0.168054	Q 0.041852	2.059084	0.039486
	4	Ostro,2015a	1.064000	1.020000	1.110000	0.062035	0.019803	0.104360	0.021571	2.875902	0.004029
	5	Sarnat,2015	0.995000	0.969000	1.022000	0.005013	0.031491	0.021761	0.013585	0.368983	0.712140
	6	Huang,2012	1.005000	0.993000	1.017000	0.004988	0.007025	0.016857	ਰੋ 0.006092	0.818666	0.412977
	7	Son,2012	0.989000	0.956000	1.024000	0.011061	0.044997	0.023717	3 <sub>0.017529</sub>	0.631007	0.528036
	8	Kim,2015	1.081000	0.920000	1.266000	0.077887	0.083382	0.235862	0.081440	0.956370	0.338885
Daminatana Diagona	9	Heo,2014	0.988000	0.962000	1.015000	0.012073	0.038741	0.014889	0.013681	0.882435	0.377541
Respiratory Diseases	10	Basagana,2015	0.986000	0.949000	1.026000	0.014099	0.052346	0.025668	0.019902	0.708432	0.478677
	11	Basagana,2015	0.940000	0.879000	1.006000	0.061875	0.128970	0.005982	0.034427	1.797311	0.072286
	12	Maynard,2007	1.196000	1.005000	1.421000	0.178983	0.004988	0.351361	0.088361	2.025595	0.042806
	13	Liu,2016a	0.964000	0.895000	1.039000	0.036664	0.110932	0.038259	0.038059	0.963352	0.335371
	14	Liu,2016b	0.963000	0.806000	1.150000	0.037702	0.215672	0.139762	9 0.090672	0.415806	0.677552
	15	Kim,2012	1.100000	0.949000	1.270000	0.095310	0.052346	0.239017	<u>5</u> .0.074327	1.282302	0.199737
	16	Cakmak,2009	1.036000	1.031000	1.041000	0.035367	0.030529	0.040182	0.002462	14.36291	3.2036*10-45
	17	Wang,2019a	1.038000	1.017000	1.059000	0.037296	0.016857	0.057325	0.010323	3.612723	0.000303
	18	Tolbert,2007	0.997000	0.990000	1.003000	0.003005	0.010050	0.002996	<del>\$</del> 0.003328	0.902791	0.366637

Table S6 Results of risk of bias assessment.

			Key criteria	I		Otl	ner criteria		
No.	Study	Exposure	Outcome	Confounding	Selection	Incomplete	Selective	Conflict of	Other
		assessment	assessment	bias	bias	outcome data	reporting	interest	Otner
1	Atkinson et al. 2016								
2	Bell et al. 2014								
3	Cai et al. 2014								
4	Geng et al. 2013								
5	Hua et al. 2014								
6	Ostro et al. 2015a								
7	Samoli et al. 2016								
8	Zanobetti and Schwartz 2006								
9	Liu et al. 2016a								
10	Liu et al. 2016b								
11	Sarnat et al. 2015								
12	Kim et al. 2012								
13	Ostro et al. 2009								
14	Kim et al. 2015								
15	Huang et al. 2012								
16	Peng et al. 2009								
17	Levy et al. 2012								
18	Son et al. 2012								
19	Heo et al. 2014								
20	Basagaña et al. 2015								
21	Dai et al. 2014								
22	Lin et al. 2016a								
23	Cao et al. 2012								
24	Klemm et al. 2011								
25	Zhou et al. 2011								
26	Winquist et al. 2015								
27	Ostro et al. 2007								
28	Tolbert et al. 2000								
29	Wang and Lin 2016								
30	Darrow et al. 2014								
31	Metzger et al. 2004								
32	Mar et al. 2000								
33	Wang et al. 2019a								
34	Lin et al. 2016b								
35	Ostro et al. 2008								

**Table S6** Results of risk of bias assessment. (continued)

			Key criteria	ı		Otl	her criteria		
No.	Study	Exposure	Outcome	Confounding	Selection	Incomplete	Selective	Conflict	Other
		assessment	assessment	bias	bias	outcome data	reporting	of interest	Otner
36	Ito et al. 2011								
37	Chen et al. 2014								
38	Tomic'-Spiric' et al. 2019								
39	Maynard et al. 2007								
40	Sinclair et al. 2010								
41	Krall et al. 2013								
42	Cakmak et al. 2009								
43	Tolbert et al. 2007								
44	Lall et al. 2011								
45	Jung and Lin 2017								
46	Gong et al. 2019								
47	Mostofsky et al. 2012								
48	Krall et al. 2017								
49	O'Lenick et al. 2017								
50	Pearce et al. 2015								
51	Strickland et al. 2010								
52	Strickland et al. 2014								
53	Ito et al. 2013								
54	Ostro et al. 2015b								
55	Gan et al. 2013								
56	Hvidtfeldt et al. 2019								
57	Thurston et al. 2016	·							
58	Yang et al. 2018								
59	Gan et al. 2011								
60	De Kluizenaar et al. 2013								
61	Vedal et al. 2013								
62	Rahmatinia et al. 2021								
63	Liu et al. 2021b								
64	Lavigne et al. 2021								
65	Rodins et al. 2020	·							
66	Kovačević et al. 2020								
67	Hasslöf et al. 2020								
68	Wang et al. 2019b								
69	Ljungman et al. 2019								
70	Liu et al. 2021a								
	Risk of bias rating:	Low		Probably Low		Probably High		High	

36/bmjopen-2021-049516

**Table S7** Details of risk of bias assessment.

6 7 8	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete Soutcome datas		Conflict of interest	Other
9 10	1	Atkinson	Probably Low	Low	Probably Low	Low	Low 8	Probably Low	Low	Low
11		et al. 2016	All of the pollutants were	Death data for the period	Adjusted for time	Study included	Daily counts	There was	The authors	No other
12			measured at the central	1 January 2011 to 31	(seasonality,	daily counts of	for death were \( \frac{8}{2} \)	insufficient	declare no	potential
13 14			London background	December 2012 were	long-term trend),	deaths in	obtained, so	information	conflict of	sources of
15			monitoring site at North	obtained from the Office	temperature,	London, United	likely have all 🚊	about	interest.	bias
16			Kensington. All	for National Statistics.	humidity, day of	Kingdom for the	outcome data.	selective		identified.
17 18			measurements were 24-h	Daily counts of deaths in	week and public	period 1 January	However, any	outcome to		
19			averages except for CO.	London, United Kingdom	holidays.	2011 to 31	potential errors	judge for low		
20			The number of all	were classified as all		December 2012.	or missing data	risk, but		
21			observations was	disease-related causes,	(0)		did not depend			
22 23			621-693 (<25% missing	cardiovascular			on air pollution	evidence that		
24			data).	(International		101	levels.	suggests study		
25				Classification of			on	was free of		
26 27				Diseases,10th			Ap	selective		
28				revision-ICD10: I00-I99)				report.		
29				and respiratory (ICD10:			9, 20	_		
30				J00-J99) diseases.			024			
31 32							by ç			
33							jues			
34							; <del>;</del> 'T			
35							rote			
36 37							April 19, 2024 by guest. Protected by			
38							<u> </u>			

8   2   2014   BC measured from filters collected daily using optical reflectance. Monitors from 5 sites across 4 counties were used. Sampling occurred daily, with some missing periods, for Hartford, New Haven, and Springfield, and every third day for Bridgeport and Danbury. Days with missing data were omitted from analysis (the number of missing data was not reported).  Bell et al. 2014  BC measured from filters collected daily using optical reflectance. Medicare beneficiary denominator file from the Centers for Medicare and Medicaid Services. Cause of admission was determined by principal determined by principal determined by principal determined by principal discharge diagnosis code according to International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CR; National Center for Health Statistics 2006).  Selective all outcome of missing data was not reported).  BC measured from filters collected daily using optical reflectance. Medicare and Medicare hencicary denominator file from the (seasonality, long-term trend), deseasonality, long-term trend), day of week, temperature, and developint.  Garage from records of from records of from records of geasonality, long-term trend), day of week, temperature, and developint.  Garage from records of from records of selective and mission against from solicition of plan during any potential graph and principal developint.  Garage from records of from records of from records of selective and mission against from records of declare no individuals ≥ 65.  Garage from records of from records of selective and missions against from records of admissions against from records of selective and missions against from records of from records of for mercords of for mercords of from records of for mercords of for	Other
BC measured from filters collected daily using optical reflectance.  Monitors from 5 sites across 4 counties were used. Sampling occurred daily, with some missing periods, for Hartford, New Haven, and Springfield, and every third day for Bridgeport and Danbury. Days with missing data were  BC measured from filters collected daily using optical reflectance.  Medicare beneficiary denominator file from the Centers for Medicare and Medicare and Medicare and Medicare and determined by principal determined by principal discharge diagnosis code according to International Classification of Diseases, Ninth Revision, and Danbury. Days with missing data were  BC measured from filters or the study used the Medicare for time (seasonality, long-term trend), day of week, temperature, and dew point.  Models adjusted from records of individuals ≥65 years of age enrolled in the so likely have selective outcome to judge for low plan during any potential suggests study on air pollution glevels.  BC measured from filters for time (seasonality, long-term trend), day of week, temperature, and dew point.  Medicare beneficiary denominator file from the (seasonality, long-term trend), day of week, temperature, and dew point.  Medicare beneficiary denominator file from the (seasonality, long-term trend), day of week, temperature, and dew point.  Medicare beneficiary denominator file from the (seasonality, long-term trend), day of week, temperature, and dew point.  Medicare and Medicare all outcome all outcome any potential suggests study on air pollution on air pollutio	Low
collected daily using optical reflectance.  Monitors from 5 sites across 4 counties were used. Sampling occurred daily, with some missing periods, for Hartford, New Haven, and Springfield, and every third day for Bridgeport and Danbury. Days with missing data were  collected daily using optical reflectance.  Medicare beneficiary denominator file from the (seasonality, long-term trend), day of week, temperature, and devery third day for Bridgeport and Danbury. Days with missing data were  collected daily using optical reflectance.  Medicare beneficiary denominator file from the (seasonality, long-term trend), day of week, temperature, and devery third day for Bridgeport and Danbury. Days with missing data were  collected daily using optical reflectance.  Monitors from 5 sites Centers for Medicare and long-term trend), day of week, temperature, and devery classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM; National for time (seasonality, long-term trend), day of week, temperature, and devery plan during any potential suggests study was free of selective  admissions were obtained, about selective outcome to data. However, and data. However, sisk, but indirect evidence that suggests study was free of selective.  Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM; National selective)  Conflict of individuals ≥65 prindividuals ≥65	No other
Monitors from 5 sites across 4 counties were used. Sampling occurred daily, with some missing periods, for Hartford, New Haven, and Springfield, and every third day for Bridgeport and Danbury. Days with missing data were (ICD-9-CM; National)  Nonitors from 5 sites across 4 counties were used. Sampling occurred daily, with some missing across 4 counties were used. Sampling occurred daily, with some missing data were (ICD-9-CM; National)  Nonitors from 5 sites across 4 counties were determinated interior used. Sampling occurred day of week, temperature, and devery determined by principal dew point.  Springfield, and every third day for Bridgeport and Danbury. Days with missing data were (ICD-9-CM; National)  Centers for Medicare and long-term trend), day of week, temperature, and dew point.  Medicare all outcome all outcome all outcome all outcome and pount of the principal dew point.  Springfield, and every third day for Bridgeport and Danbury. Days with missing data were detail outcome all outcome and pount outcome and out	potential
Monitors from 5 sites across 4 counties were used. Sampling occurred daily, with some missing periods, for Hartford, New Haven, and Springfield, and every third day for Bridgeport and Danbury. Days with missing data were (ICD-9-CM; National)  Medicaid Services. Cause day of week, temperature, and dew point.  Medicare fee-for-service plan during August 2000 to February 2004.  Medicaid Services. Cause of age enrolled in the Medicare all outcome to judge for low risk, but indirect evidence that suggests study was free of selective.	sources of
across 4 counties were used. Sampling occurred daily, with some missing periods, for Hartford, New Haven, and Springfield, and every third day for Bridgeport and Danbury. Days with missing data were  Medicaid Services. Cause of admission was determined by principal discharge diagnosis code according to International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM; National)  Medicare day of week, temperature, and dew point.  Medicare fee-for-service plan during August 2000 to February 2004.  February 2004.  Medicare all outcome to data. However, plan during August 2000 to February 2004.  Medicare all outcome to judge for low risk, but indirect evidence that suggests study on air pollutione was free of selective	bias
daily, with some missing periods, for Hartford, New Haven, and Springfield, and every third day for Bridgeport and Danbury. Days with missing data were  determined by principal determined by principal determined by principal dew point.  dew point.  dew point.  fee-for-service plan during any potential grisk, but indirect evidence that suggests study on air pollution on air poll	identified.
daily, with some missing periods, for Hartford, periods, for Hartford, New Haven, and Springfield, and every third day for Bridgeport and Danbury. Days with missing data were determined by principal dew point. The fee-for-service plan during any potential pludge for low risk, but errors or plan during any potential pludge for low any potential pludge for low risk, but errors or plan during any potential pludge for low any potential pludge for low risk, but errors or pludge for low any potential pludge for low risk, but errors or pludge for low any potential pludge for low any potential pludge for low risk, but errors or pludge for low any potential pludge for low any potential pludge for low any potential pludge for low risk, but errors or pludge for low any potential pludge for low any p	
periods, for Hartford, New Haven, and Springfield, and every third day for Bridgeport and Danbury. Days with missing data were  plan during August 2000 to February 2004.  plan during August 2000 to February 2004.  plan during August 2000 to February 2004.  Classification of Diseases, Ninth Revision, and Danbury. Days with missing data were  (ICD-9-CM; National  plan during August 2000 to February 2004.  Suggests study on air pollutions was free of levels.  Selective	
Springfield, and every third day for Bridgeport and Danbury. Days with missing data were  Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM; National Closested and Danbury Days with missing data were Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM; National Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM; National Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM; National Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM; National Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM; National Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM; National Classification of Diseases) (ICD-9-CM; National Classifi	
third day for Bridgeport and Danbury. Days with missing data were  Classification of Diseases, Ninth Revision, and Danbury. Days with missing data were  Classification of Diseases, Ninth Revision, and Danbury. Days with missing data were  Classification of Diseases, Ninth Revision, on air pollution was free of levels.	
third day for Bridgeport and Danbury. Days with missing data were  Diseases, Ninth Revision, Clinical Modification (ICD-9-CM; National levels.  Diseases, Ninth Revision, Clinical Modification levels.	
and Danbury. Days with missing data were  Clinical Modification (ICD-9-CM; National levels.  Glinical Modification on air pollution was free of levels.  Selective	
26 Inissing data were (ICD-)-Civi, National	
omitted from analysis (the number of missing data was not reported).  Center for Health Statistics 2006).	
(the number of missing data was not reported).  Statistics 2006).	
data was not reported).  data was not reported).	
30 31	
32 \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \	
33 6 6 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7	
34 P P O	
35 Otto Otto Otto Otto Otto Otto Otto Ott	
37	
38 39 8	

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data		Conflict of interest	Other
8 9	3	Cai et al.	Probably Low	Low	Probably Low	Low	Low	Probably Low	Low	Low
10		2014	Daily concentrations of	Asthmatic hospitalization	Adjusted for time	Study included	Daily counts	There was	Authors	No other
11			BC were measured at a	data was obtained from	(seasonality,	all asthmatic	for asthmatic	insufficient	declared no	potential
12			fixed-site station. Daily	the Shanghai Health	long-term trend),	hospitalization	hospitalization ≦	information	competing	sources of
13 14			data was available and no	Insurance Bureau	temperature,	for adult	were obtained,	about	financial	bias
15			missing data was	(SHIB). The causes of	relative humidity	residents living	so likely have	selective	interests.	identified.
16			reported.	hospital admission were	and day of the	in the nine urban	all outcome	outcome to		
17 18				coded according to	week.	districts between	data. However,	judge for low		
19				International		January 1, 2005	any potential	risk, but		
20				Classification of	' /	and December	errors or	indirect		
21				Diseases, Revision 10	' (2)	31, 2011(2922	missing data	evidence that		
22 23				(ICD-10): Asthma (J45).		days) from the	did not depend	suggests study		
24						Shanghai Health	on air pollution			
25						Insurance	levels.	selective		
26						Bureau.	λ ξ	report.		
27   28						Zursuu.		_		
20 29							19,			
30							, 2024 by			
31							4 by			
32							n. gu			
33   34							guest.			
34   35										
36							Protected			
37							ted			
38 <sup>L</sup>			I	I			\$	1	<u> </u>	

4 5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data ≤	Selective reporting	Conflict of interest	Other
8 9			Probably High	Low	Probably Low	Low	Low $\overset{\mathbf{a}}{\searrow}$	Probably Low	Low	Low
9 10	4	Geng et	Single, central-site	Health data were	Models included	Data consisted of	Daily counts	There was	The authors	No other
11		al. 2013	monitor. Daily BC and	obtained from Shanghai	time (seasonality,	all causes	for death were	insufficient	declare no	potential
12			PM <sub>2.5</sub> were measured	Municipal Center of	long-term trend),	(excluding	obtained, so	information	conflict of	sources of
13 14			continuously and 24hr	Disease Control and	temperature,	accidents or	likely have all	about	interest.	bias
15			averaged was estimated	Prevention database. The	humidity and day	injuries) deaths	outcome data.	selective		identified.
16			if >75% of the 1hr values	causes of death were	of week.	during over the	However, any	outcome to		
17 18			was available for that	coded according to the		course of the	potential errors	judge for low		
19			day. Missing data was not	International		study.	or missing data	risk, but		
20			replaced by other values.	Classification of	' /		did not depend	indirect		
21				Diseases, Revision 10	' (2)		on air pollution	evidence that		
22 23				(ICD 10).			levels.	suggests study		
24						<b>10</b> 1.	com	was free of		
25						1eh	on	selective		
26 27							Αp	report.		
28								_		
29							9, 20			
30							024			
31 32							by ç			
33							Jues			
34							on April 19, 2024 by guest. Protected by			
35							rote			
36 37							ctec			
38							by by			

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data		Conflict of interest	Other
8 9			Probably High	Low	Probably Low	Low	Low ay	Probably Low	Low	Low
10	5	Hua et al.	Daily 24h average PM <sub>2.5</sub>	Daily asthma hospital	Adjusted for	Study included	Daily counts	There was	Authors	No other
11		2014	and BC data was	admission data was	long-term and	all asthma	for asthma	insufficient	declared no	potential
12			obtained from a fixed-site	obtained from Shanghai	seasonal trend, day	hospital	hospital 💆	information	competing	sources of
13 14			station. The study only	Children's Medical	of week,	admissions of	admissions of	about	financial	bias
15			used the actual collected	Center. Dates of	temperature and	children ≤ 14	children were	selective	interests.	identified.
16			data and did not fill in the	admission and discharge,	relative humidity.	years of age from	obtained, so	outcome to		
17 18			missing data for PM <sub>2.5</sub>	and diagnoses using the	<b>'</b> O.	Shanghai	likely have all	judge for low		
19			and black carbon.	International		Children's	outcome data.	risk, but		
20				Classification of	' /	Medical Center	However, any	indirect		
21				Diseases, Revision 10.	' 01	between1	potential errors	evidence that		
22 23						January 2007 and	or missing data	suggests study		
24						31 July 2012 in	did not depend	was free of		
25						nine urban	on air pollution	selective		
26 27						districts of	levels.	report.		
28						Shanghai.	11 19,			
29							9, 20			
30							2024 by			
31 32							by g			
33							guest.			
34										
35							rote			
36 37							Protected			
38							9	1		

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data		Conflict of interest	Other
8 9			Probably Low	Low	Low	Low	Low S	Probably Low	Low	Low
10	6	Ostro et	Daily 24hr average BC	For both cities daily	Adjusted for long	Study population	Daily counts	There was	Authors	No other
11		al. 2015a	concentrations were	counts of all-cause	term and seasonal	consisted of daily	for death were	insufficient	declared no	potential
12			obtained from one station	mortality for all ages	(year, month, day	counts of	obtained, so	information	competing	sources of
13 14			in Barcelona and Athens.	were collected (excluding	of week) trends,	all-cause	likely have all	about	interests.	bias
15			Daily data was available	deaths from external	temperature,	mortality for all	outcome data.	selective		identified.
16			and no missing data was	causes, International	holidays, summer	ages and daily	However, any	outcome to		
17 18			reported.	Classification of	vacations and	counts of	potential errors	judge for low		
19				Disease-ICD9: 001799,	influenza.	cardiovascular,	or missing data	risk, but		
20				ICD10 A00R99), as well	' /	respiratory and	did not depend	indirect		
21				as daily counts of	' (2)	all-cause	on air pollution	evidence that		
22 23				cardiovascular (ICD9:		mortality for	levels.	suggests study		
24				390459, ICD10: I00I99),		those greater than	com	was free of		
25				respiratory		age 65.	or or	selective		
26				(ICD9:460519,			1 Ap	report.		
27 28				ICD10:J00J99) and			April 19,	1		
29				all-cause mortality for			9, 2			
30				those greater than age 65.			2024 by guest.			
31							by			
32 33							gue			
34										
35							rot			
36							Protected			
37   38							9			

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data		Conflict of interest	Other
8 9			Low	Low	Probably Low	Low	Low <sup>ay</sup>	Probably Low	Low	Low
10	7	Samoli et	Daily concentrations of	Based on the primary	Adjusted for long	Study included	Daily counts	There was	Authors	No other
11		al. 2016	BC and EC were	discharge diagnosis, daily	term and seasonal	all cardiovascular	for all	insufficient	declared no	potential
12			collected from the	numbers of admissions	trends,	and respiratory	emergency §	information	competing	sources of
13 14			ClearfLo project,	for cardiovascular disease	temperature,	hospital	hospital	about	interests.	bias
15			supplemented by local	(International	relative humidity,	admissions in	admissions 3	selective		identified.
16			measurements made at	Classification of	regulated	London, UK	were obtained,	outcome to		
17 18			the North Kensington	Diseases, 10th	pollutants (PM <sub>10</sub> ,	between 2011	so likely have	judge for low		
19			urban background site.	revision-ICD-10:	PM <sub>2.5</sub> , NO <sub>2</sub> , SO <sub>2</sub>	and 2012.	all outcome	risk, but		
20			Number of days of	I00-I99) for those aged	and O <sub>3</sub> ), day of the		data. However,	indirect		
21 22			observation for BC: 629	15-64 (adult) and 65+	week and public	•	any potential	evidence that		
23			(BC urban in PM <sub>2.5</sub> ) and	years (elderly), and	holidays.		errors or	suggests study		
24			702 (BC in PM <sub>2.5</sub> )	respiratory diseases		'61.	missing data	was free of		
25			between 2011 and 2012	(ICD-10: J00-J99) for			did not depend 9	selective		
26 27			(<25% missing data).	those aged 0-14 years			on air pollution₫	report.		
28				(paediatric), adult and the			levels.	<u>-</u>		
29				elderly were calculated.						
30 31							24 5			
32							) 9 <u>9</u>			
33							2024 by guest.			
34 35										
35 36							Protected			
37							ed Sted			
38 <sup>l</sup>			I	I	<u> </u>		\$	1		

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on the outcome data		Conflict of interest	Other
8 9			Probably High	Low	Probably Low	Low	Low	Probably Low	Low	Low
10	8	Zanobetti	Ambient BC from one	The study extracted data	Adjusted for	Data consisted of	Daily counts	There was	Authors	No other
11		and	monitor. The hourly	on all hospital admissions	temperature, day	all U.S. Medicare	for hospital	insufficient	declared no	potential
12		Schwartz	measurements for BC and	for residents of the	of the week,	hospital	admissions 💆	information	competing	sources of
13 14		2006	PM <sub>2.5</sub> were not complete.	Boston Metropolitan area	seasonality,	admissions in the	were obtained,	about	interests.	bias
15			Missing values were	who were admitted to the	long-term trends,	Boston	so likely have	selective		identified.
16			replaced with the	hospital (in the Boston	humidity,	Metropolitan	all outcome	outcome to		
17 18			predicted values.	area) with a primary	barometric	area for	data. However,	judge for low		
19			Additionally BC data was	diagnosis of MI	pressure, and the	myocardial	any potential	risk, but		
20			missing from March 1997	(International	extinction	infarction during	errors or	indirect		
21			to March 1999 and was	Classification of	coefficient.	the study	missing data	evidence that		
22			not included in the study.	Diseases, 9th		duration.	did not depend.	suggests study		
24				revision-ICD-9:410), and		<b>101</b>	on air pollution	was free of		
25				pneumonia (ICD-9:			levels.	selective		
26 27				480–487), from Medicare			April	report.		
28				billing records for the			11 19,			
29				years 1995–1999.						
30							2024 by guest.			
31							by g			
33							Jues			
34										
35							rote			
36 37							Protected			
38							by			

36/bmjopen-2021-0495

2	
3	
4	
5	
6	
7 8	_
9	
10 11	
11	
12	
13	
14	
15	
16	
17	
14 15 16 17 18 19 20 21 22 23	
19	
20	
21	
22	
23	
24	
25	
26	
27	
26 27 28	
29	
30	
31	
31 32	
33	
3 V	
34 35 36 37 38	
33 36	
30	
3/	
38	

7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data ≤		Conflict of interest	Other
3			Probably High	Low	Probably Low	Low	Low <sup>ay</sup>	Probably Low	Low	Low
10	9	Liu et al.	EC were collected from a	Emergency department	Adjusted for time	Study included	Daily counts 8	There was	Authors	No other
11		2016a	single monitor on a	visit data was obtained	(long-term and	daily counts of	for emergency 💆	insufficient	declared no	potential
12			one-in-three or one-in-six	from the Blue Cross Blue	seasonal trend),	emergency	department <u>§</u>	information	potential	sources of
3  4			day schedule. EC were	Shield Texa. International	day of week,	department visits	visits were	about	competing	bias
5			measured for 566 days	Classification of Diseases	temperature, dew	for Greater	obtained, so	selective	financial	identified.
6			from April 02, 2009, to	9th Revision (ICD-9)	point and	Houston from	likely have all	outcome to	interests.	
7  8			December 30, 2013,	diagnosis codes were	population growth.	claims data	outcome data.			
19			<25% missing for the	used to classify outcome	C/	insured from	However, any	risk, but		
20			frequency of sampling.	groups.	1 /	January 1, 2008	potential errors	indirect		
21					(0)	through	or missing data			
22						December 31,	did not depend			
24						2013.	on air pollution			
25						\ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \	levels.	selective		
26							Ap			
27 28							April 19,	1		
29							9, 2			
30							.024			
31							by			
32							gue			
34							2024 by guest. Protected			
35							Prot			
36							lecte			
37 38							ed b			

			BMJ Oper	ו	36/bmJopen-2021-0495			Page
							~ ~ ~	
No. Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete 9		Conflict of interest	Other
	Probably High	Low	Probably Low	Low	Low	Probably Low	Low	Low
10 Liu et al. 2016b	EC were collected from a single monitor on a one-in-three or one-in-six day schedule. EC were measured for 566 days from April 02, 2009, to December 30, 2013, <25% missing for the frequency of sampling.	Hospital admission data was obtained from the Blue Cross Blue Shield Texa. International Classification of Diseases 9th Revision (ICD-9) diagnosis codes were used to classify outcome groups.	Adjusted for time, day of week, temperature, seasonaility, humidity and population growth.	Study included all hospital admissions obtained from billing claims of Blue Cross Blue Shield Texa enrollees for Greater Houston from January 1, 2008 to December 31, 2013.	Daily counts for HA were obtained, so likely have all outcome data. However, any potential errors or missing data did not depend on air pollution levels.	selective outcome to judge for low risk, but indirect evidence that suggests study was free of selective	Authors declared no competing financial interests.	No other potential sources of bias identified.

2	
3	
4	
5	
6	]
6 7	
	_
8 9	
10	]
11	
12	
13	
14	
15	
16	
17	
13 14 15 16 17 18	
19	
19 20	
21	
21 22 23 24 25	
23	
24	
25	
26	
26 27	
20	
29 30 31	
30	
31	
32	
33	
34	
35	
36	
37	
20	

Pag	e 69 of	<sup>:</sup> 133			BMJ Oper	า	36/bmJop			
1 2 3 4							36/bmJopen-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data	Selective	Conflict of interest	Other
8 9			Probably Low	Low	Probably Low	Low	Probably Low	Probably Low	Low	Low
10	11	Sarnat et	24hr average	Computerized billing	Models adjusted	Data consisted of	Daily counts		The authors	No other
11 12		al. 2015	concentration of PM <sub>2.5</sub>	records were obtained	for season, day of	all emergency	for emergency		declare they	potential
13			were obtained from a	from the Missouri	week, holidays,	department visits	department Solution visits were	information about	have no actual or	sources of bias
14 15			Supersite (single, central site monitoring location).	Hospital Association (MHA) for emergency	time trends (using cubic splines for	during the study period for	department visits were obtained, hence one	selective	potential	identified.
16			The observations of EC	department visits. The	day of visit with	cardiovascular	hence one	outcome to	competing	identified.
17			was 666 days during 1	outcome groups were	monthly knots),	disease	hospital not	judge for low	financial	
18 19			June 2001-30 April 2003	identified using primary	and temperature.	outcomes.	providing data	risk, but	interests.	
20			(missing data <25%).	International			after 26 April	indirect		
21 22				Classification of Diseases	. 61		2002.	evidence that		
23				9th Revision (ICD9)			However, any			
24				codes.		.617	potential errors			
25 26						Teh,	or missing data			
27							did not depend ≥			
28 29							on air pollution			
30							levels. 2024 by guest			
31							Lby			
32 33							gues			
34										
35 36							otec			
37							Protected by copyright.			
38 <sup>1</sup> 39				1	1	1	, do	ı	ı	
40							оруп			
41 42							ght.			

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data		Conflict of interest	Other
8 9			Probably Low	Low	Probably Low	Low	Low 2	Probably Low	Low	Low
9 10	12	Kim et al.	PM <sub>2.5</sub> mass and chemical	All individual hospital	Model adjusted for	Data consisted of	Daily counts	There was	The authors	No other
11		2012	constituents were	admission records during	days from the start	all cardiovascular	for hospital	insufficient	declare they	potential
12			measured daily at one	the study period were	of the study, day of	hospital	admission wer	information	have no	sources of
13 14			residential monitoring	extracted from	week, seasonality,	admissions over	obtained, so	about	actual or	bias
15			station located on the	nonelective hospital	long-term trends,	the course of the	likely have all	selective	potential	identified.
16			roof of an elementary	admission discharge data	daily average	study.	outcome data.	outcome to	competing	
17 18			school building in	obtained from the	temperature and		However, any	judge for low	financial	
19			Denver. The observations	Colorado Hospital	relative humidity.		potential errors	risk, but	interests.	
20			of EC was 1809 days	Association. The	' /		or missing data	indirect		
21 22			during 2003-2007	International	' (2)		did not depend	evidence that		
23			(missing data <25%).	Classification of			on air pollution	suggests study		
24				Diseases, Ninth		'01.	levels.	was free of		
25				Revision(ICD-9) codes			/ on	selective		
26 27				were used to define			Apr	report.		
28				cardiovascular hospital			11 19,			
29				admissions (codes			9, 20			
30				390–459) and respiratory			2024 by guest.			
31 32				hospital admissions			by g			
33				(codes 460–519).			lues			
34				,						
35							Protected			
36 37							ctec			
38							<u> </u>			

36/bmjopen-2021-0495

2	
3	
4	
5	
6	
7	
8	_
9	
10	
11	
12	
13	
14	
14 15	
16	
17	
16 17 18	
19	
20	
21 22 23	
22	
23	
24	
25	
26	
27	
28	
29	
30	
31	
32 33	
33	
34	
35	
36	
37	
34 35 36 37 38	

5 5 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data o		Conflict of interest	Other
3			High	Low	Probably Low	Low	Low <sup>ay</sup>	Probably Low	Low	Low
0	13	Ostro et	EC were generally	Data for hospitalizations	Adjusted for time,	Study included	Daily counts 8	There was	Authors	No other
1		al. 2009	recorded every 3 days	were obtained from the	day of the week,	all	for	insufficient	declared no	potential
2			from two co-located	Office of Statewide	temperature,	hospitalizations	hospitalization \( \frac{\zeta}{2} \)	information	competing	sources of
3  4			monitors or one monitor	Health Planning and	seasonality,	for children < 19	s of children	about	financial	bias
5			in 6 counties. The	Development, Healthcare	relative humidity	and < 5 years of	were obtained, =	selective	interests.	identified.
6			number of available days	Quality and Analysis	and pollutant.	age for total	so likely have	outcome to		
7			of data over the 4-year	Division. Hospital		respiratory	all outcome	judge for low		
9			period ranged from 227	admissions for children		diseases and	data. However,	risk, but		
20			to 381 (some counties	<19 years of age were	' /	several	any potential	indirect		
21			had >25% missing for the	classified into one or	' (2)	subcategories	errors or	evidence that		
22			frequency of sampling).	more categories: all		including	missing data	suggests study		
24				respiratory disease		pneumonia, acute	did not depend	was free of		
25				(International		bronchitis, and	on air pollution	selective		
26 27				Classification of		asthma for six	levels. $\frac{1}{2}$	report.		
28				Diseases, Ninth		California		_		
29				Revision-ICD-9 codes		counties from	9, 20			
30				460–519), asthma (ICD-9		2000 through	024			
31 32				code 493), acute		2003.	by ç			
33				bronchitis (ICD-9 code			Jues			
34				466), and pneumonia			19, 2024 by guest. Protected			
35				(ICD-9 codes 480–486).			rote			
36 37				, , , , , , , , , , , , , , , , , , ,			ctec			
38 L							\$			

5 5 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data ≤	Selective reporting	Conflict of interest	Other
3			Probably Low	Low	Probably Low	Low	Low <sup>ay</sup>	Probably Low	Low	Low
10	14	Kim et al.	Daily 24-hour composite	Daily mortality counts for	Models adjusted	Data consisted of	Daily counts	There was	None of the	No other
11		2015	PM <sub>2.5</sub> samples were	metropolitan Denver	for longer-term	all deaths over	for death were	insufficient	authors has	potential
12			collected from single,	were computed from the	temporal trend, as	the course of the	obtained, so	information	any actual	sources of
13 14			central-site monitor. The	Colorado Health	time since the	study in a	likely have all	about	or potential	bias
15			observations of EC was	Information Dataset	study began, day	defined	outcome data.	selective	competing	identified.
16			1809 days from 2003	compiled by the Colorado	of week, and daily	geographical	However, any	outcome to	interests.	
17 18			through 2007 (missing	Department of Public	temperature and	area.	potential errors	judge for low		
19			data <25%).	Health and Environment.	humidity.		or missing data	risk, but		
20				Data included cause of	' /		did not depend	indirect		
21				death by the International	' (2)	•	on air pollution	evidence that		
22				Classification of Diseases			levels.	suggests study		
24				10th Revision (ICD-10)		Teh (	com	was free of		
25				code.			v or	selective		
26 27							Αp	report.		
28								-		
29							9, 2			
30							024			
31 32							by			
33							April 19, 2024 by guest. Protected			
34							St. 17			
35							rote			
36   37							 			
38   38										

36/bmjopen-2021-0495

2	
3	
4	
5	
6	
7	
8	
9	
10	
11	
12	
13	
14	
15	
16	
17	
18	
19	
20	
21	
22	
23	
24	
25	
26	
27	
28	
29	
30	
31	
32	
33	
34	
35	
36	
37	
38	
39	

5 5 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data o		Conflict of interest	Other
3			Probably Low	Low	Probably Low	Probably Low	Low $\overset{\text{as}}{\searrow}$	Probably Low	Low	Low
0	15	Huang et	Daily average	Daily mortality data were	Models adjusted	The author	Daily counts	There was	No	No other
11		al. 2012	concentrations of PM <sub>2.5</sub>	obtained from the Xi'an	for calendar time	removed the	for death were	insufficient	competing	potential
2			were obtained from a	Center for Disease	(seasonality,	death counts on	obtained, so	information	financial	sources of
3			single, central-site	Control and Prevention.	long-term trends),	December 31 and	likely have all	about	interests.	bias
5			monitor. Daily average	The International	weather(temperatu	January 1 of each	outcome data.	selective		identified.
6			concentrations of EC in	Classification of	re, relative	year.	However, any	outcome to		
7			PM <sub>2.5</sub> samples were	Diseases, Tenth Revision	humidity), year,		potential errors	judge for low		
8			further analyzed. Daily	(ICD-10), codes of	day of week.		or missing data	risk, but		
20			data was available and no	mortality were as			did not depend	indirect		
21			missing data was	follows: all natural causes	(0)		on air pollution			
22			reported.	(ICD-10 codes			levels.	suggests study		
23 24				A00–R99), respiratory		10,	.cor	was free of		
25				diseases (ICD-10 codes			n/ o	selective		
26				I00–I98), and			n Aş			
27 28				cardiovascular diseases				тероги.		
29				(ICD-10 codes I00–I99).			9, 2			
30				(ICD-10 codes 100–199).			2022			
31							1 by			
32							gue			
33							April 19, 2024 by guest. Protected by			
35							Pro			
36							tect			
37							ed R			
88 <sup>L</sup>										

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data		Conflict of interest	Other
8 9			Probably High	Low	Probably Low	Low	Low	Probably Low	Low	Low
10	16	Peng et al.	Ambient EC obtained	Daily counts of hospital	Model adjusted for	Data consisted of	Daily counts	There was	The authors	No other
11		2009	from Speciation Trends	admissions were obtained	weather (i.e.,	all cardiovascular	for hospital	insufficient	declare they	potential
12 13			Network monitors and	from billing claims of	temperature, dew	hospital	admission wer 🛓	information	have no	sources of
14			either from central site or	enrollees in the U.S.	point temperature),	admissions	obtained, so	about	competing	bias
15			averaged over a county.	Medicare system. Each	day of week,	during over the	likely have all	selective	financial	identified.
16			Air pollution	billing claim contains the	unobserved	course of the	outcome data.	outcome to	interests.	
17 18			concentrations were	date of service, disease	seasonal factors,	study.	However, any	judge for low		
19			measured on a 1-in-3-day	classification using	and long-term		potential errors	risk, but		
20			schedule in the national	International	trends.		or missing data	indirect		
21 22			air monitoring stations	Classification of	. 01		did not depend	evidence that		
23			and on a 1-in-6-day	Diseases, 9th Revision			on air pollution	suggests study		
24			schedule in the state and	(ICD-9) codes (Centers		'Ch	levels.	was free of		
25 26			local air monitoring	for Disease Control and			on	selective		
27			stations. Study removed	Prevention 2008).			Apri	report.		
28			suspect data and extreme				19			
29			values from the original				, 20			
30 31			monitor records;				24 b			
32			monitors with very little				יץ פונ			
33			data were omitted				Jest			
34 35			altogether. Missing data					ı		
36			was not replaced by other				otec:			
37			values.				April 19, 2024 by guest. Protected by			
38 <sup>1</sup> 39					1	ı			1	
39							сор			

36/bmjopen-2021-0495

2	
3	
4	
5	
6	
7	
8	H
9	
10	
11	
12	
13	
14	
15	
16 17	
17	
18	
10	
20	
21	
22	
23	
24	
25	
26	
27	
28	
29	
30	
31	
32	
33	
34	
35	
36	
36 37	
38	
-	

5 5	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data		Conflict of interest	Other
3			Probably High	Low	Probably Low	Low	Low ay	Probably Low	Low	Low
0	17	Levy et al.	The U.S. Environmental	Hospital admissions data	Adjusted for time	Study included	Daily counts of	There was	No	No other
1		2012	Protection Agency	were obtained from	(seasonality,	people who died	hospital 💆	insufficient	competing	potential
2			established the PM	billing claims information	long-term trends),	any day between	admissions 💆	information	financial	sources of
3			Speciation Trends	for US Medicare	seasonality, day of	2000 and 2008 in	were obtained a	about	interests.	bias
5			Network (STN) to	enrollees in 119 counties	the week and	119 US counties.	from billing	selective		identified.
6			measure more than 50	for the years 2000–2008.	dew-point		claims 3	outcome to		
7			PM <sub>2.5</sub> chemical	The Medicare billing	temperature.		information, so	judge for low		
8			components, in addition	claims data were	G/		likely have all			
20			to total mass. The STN	classified into disease	' /_		outcome data.	indirect		
21			includes > 50 national air	categories according to	(0)		However, any	evidence that		
22			monitoring stations	their International			potential errors	suggests study		
24			(NAMS) and > 200 state	Classification of		101	or missing data			
25			and local air monitoring	Diseases, Ninth Revision			did not depend			
26			stations (SLAMS). Air	(ICD-9), codes.			on air pollution €			
27 28			pollution concentrations	//			levels =			
29			were typically measured				9,			
80			on a 1-in-3-day schedule				024			
31   32			in the NAMS and on a				by (			
3			1-in-6-day schedule in				2024 by guest. Protected			
34			the SLAMS. There was							
35			no information about				rote			
36 37			missing data.				cte			
'' [ 88			imssing data.				by	1		

7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data		Conflict of interest	Other
8 9			Probably Low	Low	Probably Low	Low	Low 2	Probably Low	Low	Low
10	18	Son et al.	Hourly air samples were	Daily death counts were	Models adjusted	Data consisted of	Daily counts	There was	The authors	No other
11		2012	obtained from a single,	obtained from the	for time (long-term	all cardiovascular	for death were	insufficient	declare they	potential
12			central-site monitor. The	National Statistical	trends and	deaths over the	obtained, so	information	have no	sources of
13 14			monitoring system	Office. The study	seasonality), day	course of the	likely have all	about	actual or	bias
15			produces hourly	classified mortality data	of week,	study.	outcome data.	selective	potential	identified.
16			estimates of PM <sub>2.5</sub> total	into all causes of death	temperature and		However, any	outcome to	competing	
17 18			mass, and PM <sub>2.5</sub> levels of	[International	relative humidity.		potential errors	judge for low	financial	
19			EC. Daily data was	Classification of			or missing data	risk, but	interests.	
20			available and no missing	Diseases, 10th Revision	1/6		did not depend	indirect		
21			data was reported.	(ICD-10; codes	(0)		on air pollution	evidence that		
22 23			_	A00–R99),			levels.	suggests study		
24				cardiovascular causes			com	was free of		
25				(codes I00–I99), and			) or	selective		
26 27				respiratory causes (codes			1 Ар	report.		
28				J00–J99)] (World Health			April 19, 2024 by			
29				Organization 2007).			9, 2			
30				,			024			
31							by	•		
32 33							guest.			
34										
35							Prof			
36							Protected			
37 38							ed c			

2	
3	
4	
5	
6	
7	L
8	
9	
10 11	
12	
13	
14	
15	
16	
17	
18	
19	
20	
21	
22	
23	
24	
25	
26	
27 28	
28 29	
30	
31	
32	
33	
34	
35	
36	
37 38	
39	
40	

ge 77 of 133 BMJ Open								
					en-2021-0495			
. Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete 9 outcome data	Selective reporting	Conflict of interest	Other
	Probably High	Low	Low	Low	Low	Probably Low	Low	Low
Heo et al. 2014	Ambient air samples were collected over a 24-hour period at 3-day intervals from a single monitor. Missing data <25% for the frequency of EC samples.	Seoul daily mortality data were obtained from the Korea National Statistical Office. Using the International Classification of Disease, 10th Revision (ICD-10; World Health Organization 1993), the mortality data were classified as all nonaccidental causes (codes A00-R99), cardiovascular disease (codes I00-I99), respiratory disease (codes J00-J98), and injury (S00-T98).	Adjusted for long-term trends, seasonality, temperature and humidity, day of the week, holiday and influenza epidemics.	Study included all death for all-cause, cardiovascular, and respiratory in Seoul during 2003–2007.	for death were obtained, so likely have all outcome data. However, any potential errors or missing data did not depend on air pollution levels.	insufficient information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of selective report.	Authors declared no competing financial interests.	No other potential sources of bias identified.
	. Study  Heo et al.	Probably High Heo et al. 2014  Probably High Ambient air samples were collected over a 24-hour period at 3-day intervals from a single monitor. Missing data <25% for the frequency	Probably High Heo et al. 2014  Probably High Ambient air samples were collected over a 24-hour period at 3-day intervals from a single monitor. Missing data <25% for the frequency of EC samples.  Seoul daily mortality data were obtained from the Korea National Statistical Office. Using the International Classification of Disease, 10th Revision (ICD-10; World Health Organization 1993), the mortality data were classified as all nonaccidental causes (codes A00-R99), cardiovascular disease (codes I00-I99), respiratory disease (codes J00-J98), and injury	Probably High Low Low Ambient air samples were collected over a 24-hour period at 3-day intervals from a single monitor. Missing data <25% for the frequency of EC samples.  Outcome assessment Confounding bias  Exposure assessment Confounding bias  Seoul daily mortality data were obtained from the Korea National Statistical Office. Using the International Classification of Disease, 10th Revision (ICD-10; World Health Organization 1993), the mortality data were classified as all nonaccidental causes (codes A00-R99), cardiovascular disease (codes 100-199), respiratory disease (codes J00-J98), and injury	Probably High Low Low Ambient air samples were collected over a 24-hour period at 3-day intervals from a single monitor. Missing data <25% for the frequency of EC samples.  Cardiovascular, World Health Organization 1993), the mortality data were classified as all nonaccidental causes (codes A00-R99), cardiovascular disease (codes 100-199), respiratory disease (codes J00-J98), and injury  Canfounding bias  Selection bias  Study included all death for all-cause, cardiovascular, and respiratory in Seoul during 2003-2007.	Probably High Heo et al. 2014  Probably High Ambient air samples were collected over a 24-hour period at 3-day intervals from a single monitor. Missing data 25% for the frequency of EC samples. PEC samples.  Seoul daily mortality data were obtained from the Korea National Statistical Office. Using the International Classification of Disease, 10th Revision (ICD-10; World Health Organization 1993), the mortality data were classified as all nonaccidental causes (codes A00-R99), cardiovascular disease (codes I00-199), respiratory disease (codes J00-J98), and injury (S00-T98).  Probably High Low Low Adjusted for long-term trends, seasonality, temperature and humidity, day of the weck, holiday and respiratory in Seoul during all-cause, cardiovascular, ind respiratory in Seoul during 2003-2007. However, any potential errors or missing data did not depended on air pollution levels.  Probably High Adjusted for seasonality, temperature and humidity, day of the weck, holiday and influenza epidemics.  Office. Using the lumidity, day of the weck, holiday and influenza epidemics.  Office death were cardiovascular, ind respiratory in Seoul during 2003-2007. However, any potential errors or missing data did not depended on air pollution levels.  Probably High Adjusted for searchivascular, and respiratory in Seoul dail death for solventer and humidity, day of the weck, holiday and influenza epidemics.  Office. Using the lumidity, day of the weck, holiday and influenza epidemics.  Office death were cardiovascular, id office. Using the lumidity, day of the weck, holiday and influenza epidemics.  Office. Using the lumidity, day of the weck, holiday and influenza epidemics.  Office. Using the lumidity, day of the weck, holiday and influenza epidemics.  Office. Using the lumidity, day of the weck, holiday or missing data did not depended on air pollution levels.  Probably High Adjusted for searchive all death for solved the weck, holiday or missing data did not depended on air pollution or missing data did not depended on air	Study   Exposure assessment   Outcome assessment   Confounding bias   Selection bias   Incomplete outcome data   Selective reporting	Probably High  Heo et al. 2014  Mere collected over a 24-hour period at 3-day intervals from a single monitor. Missing data <25% for the frequency of EC samples.  Probably High  Low  Low  Low  Study included  John Daily counts of roteath were obtained from the Korea National Statistical International  International  Classification of Disease, 10th Revision (ICD-10; World Health Organization 1993), the mortality data were classified as all nonaccidental causes (codes A00-R99), cardiovascular disease (codes J00-J998), and injury (S00-T98).  Probably High  Low  Low  Study included  all death for all ceause, scardiovascular, and respiratory in Seoul during and influenza epidemics.  Study included  all death for obtained, so for death were obtained from the korea National Statistical obtained, seasonality, temperature and humidity, day of the week, holiday and influenza epidemics.  Scoul daily mortality data were obtained from the korea National Statistical interents.  Normal Heavision (ICD-10; World Health Organization 1993), the mortality data were classified as all nonaccidental causes (codes J00-J999), respiratory disease (codes J00-J998), and injury (S00-T98).  Probably Low  Low  Low  There was declared no obtained, so likely have all death for all-cause, cardiovascular, and respiratory in Seoul during and influenza epidemics.  Study included all leath for all-cause, cardiovascular, and respiratory in Seoul during potential errors in the week, holiday outcome to obtained, so likely have all death for all-cause, cardiovascular, and respiratory in Seoul during and influenza epidemics.  Study included all leath for all-cause, cardiovascular, and respiratory in Seoul during to outcome to obtained, so likely have all death for all-cause, cardiovascular, and respiratory in Seoul during and influenza epidemics.  Secoul daily metal for all-cause, cardiovascular, and respiratory in Seoul during to the week, holiday outcome to obtained, so likely have all death for all-cause, cardiovascular, and respiratory in Seoul duri

Basagaña et al. 2015	rting interest	Other
Basagaña et al. 2015   Basagaña et al. 2015   Single central-site monitor in each city. For each city, PM constituents with >20%   Classification of of the values below the detection limit or missing   CICD9) codes 001–799;   CICD9) codes 001–799	ly Low Low	Low
et al. 2015 monitor in each city. For each city, PM constituents with >20% of the values below the detection limit or missing linear and linear population detection limit or missing linear population all deaths over the course of the study in a defined geographical geographical geographical for holidays, all deaths over the course of the study in a defined geographical geographical outcomes.	vas The authors	No other
constituents with >20% Classification of population decrease, influenza defined detection limit or missing (ICD9) codes 001–799; epidemics, geographical decrease, influenza defined geographical were obtained, summer the codes of the content of the codes of the code	eient have no	potential
of the values below the detection limit or missing (ICD9) codes 001–799; descrease, influenza epidemics, population decrease, influenza epidemics, geographical were obtained, study in a hospital admissions outcomes defined geographical were obtained, study in a hospital admissions outcomes outcomes.	ation   conflicts of	sources of
of the values below the detection limit or missing (ICD9) codes 001–799; decrease, influenza epidemics, defined geographical were obtained, selection decrease, influenza epidemics, decrease, decrease, influenza epidemics, decrease, influenza epidemics, decrease, dec	interest to	bias
17 geographical were obtained, 5 outcomes,	disclose.	identified.
1/	ie to	
were excluded. 10th revision (ICD10) seasonality, area. so likely have judge	or low	
Otherwise, codes A00–R99], long-term trends all outcome risk, b	ıt	
20 non-detectable were cardiovascular (ICD9 and temperature. data. However, indire	t	
replaced by half the limit codes 390–459, ICD-10 any potential eviden	ce that	
	ts study	
data was collected daily respiratory (ICD9 codes missing data was from the missing data was from	e of	
in Bologna (n=472), 460–519, ICD10 codes did not depend selection	re	
twice a week in  J00–J99) were collected.  on air pollution report		
Barcelona (n=736) and Cardiovascular and levels.		
once a week in Huelva hospitalizations were		
(n=406). There was no defined on the basis of		
information about the primary discharge		
missing data. diagnosis using the same		
Madrid (n=104), and once a week in Huelva (n=406). There was no information about missing data.  Madrid (n=104), and respiratory hospitalizations were defined on the basis of the primary discharge diagnosis using the same ICD codes defined above.		
37 8		
38 <u>契</u> 39		

2	
3	
4	
5	
6	
7	
8	
9	
10	
11	
12	
13	
14	
15	
16	
17	
18	
19	
20	
21	
22	
23	
24	
25	
26	
27	
28	
29	
30	
31	
32	
33	
34	
35	
36	
37	
38	

Pag	e 79 of	f 133			BMJ Oper	ı	86/bmJop			
) <u>)</u> }							36/bmJopen-2021-0495			
5	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data		Conflict of interest	Other
}			Probably High	Low	Probably Low	Low	Low	Probably Low	Low	Low
9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 31 31 31 31 31 31 31 31 31 31 31 31	21	Dai et al. 2014	EC were measured on a 1-in-3 or 1-in-6 day schedule. Most of the cities had a single monitor. For every species, the study calculated the monthly average species-to-PM <sub>2.5</sub> proportions for each month as a solution to the missing speciation data problem due to the 1-in-6 or 1-in-3 day sampling frequency. There was no information of missing data for that sampling frequency.	Daily mortality data were obtained from National Center for Health Statistics. The study examined nonaccidental deaths due to all causes and specific diseases, derived from the International Statistical Classification of Disease, 10th Revision (World Health Organization 2007).	Adjusted for time, temperature, day of the week, and season.	Study included all death for all causes, cardiovascular disease, myocardial infarction, stroke, and respiratory diseases from National Center for Health Statistics in 75 U.S. cities between 2000 and 2006.	Daily counts for death were obtained, so likely have all outcome data. However, any potential errors or missing data did not depend on air pollution levels.	information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of selective	The authors declare they have no actual or potential competing financial interests.	No other potential sources of bias identified.
36 37 38							icted b)			

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data S		Conflict of interest	Other
8			Probably Low	Low	Low	Low	Low	Probably Low	Low	Low
9 10	22	Lin et al.	The concentrations of	Daily mortality data from	Adjusted for	Study included	Daily counts	There was	The authors	No other
11		2016a	different particle size	1 January 2007 to 31	public holidays,	daily	for death were	insufficient	declare they	potential
12			fractions and PM <sub>2.5</sub>	December 2011 were	day of the week,	cardiovascular	obtained, so	information	have no	sources of
13 14			chemical constituents	obtained from	influenza	mortality data	likely have all	about	actual or	bias
15			were measured at two air	Guangdong Provincial	outbreaks,	from 1 January	outcome data.	selective	potential	identified.
16			monitoring stations. EC	Center for Disease	seasonal patterns	2007 to 31	However, any	outcome to	competing	
17 18			were measured for four	Control and Prevention.	and long-term	December 2011	potential errors	judge for low	financial	
19			months of each year from	The cause of death was	trends, temperature	in Guangzhou.	or missing data	risk, but	interests.	
20			2007 through 2010.	coded using the	and relative		did not depend	indirect		
21			During the period	International	humidity.		on air pollution	evidence that		
22 23			2009-2011, the	Classification of			levels.	suggests study		
24			proportion of missing	Diseases, Tenth Revision		Ch,	com	was free of		
25			data was very low	(ICD-10). Mortality from			on	selective		
26 27			(ranging from 1% to 2%).	cardiovascular diseases			Apr	report.		
28			There were about 20 days	(ICD-10:I00-I99) were						
29			without chemical	extracted to construct the			9, 20			
30 31			constituents records and	time series.			)24			
32			were treated as missing				оу g			
33			observations.				ues			
34							t. P			
35 36							on April 19, 2024 by guest. Protected by			
37							) Sted			
38								I	1	
39							сор			

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data S		Conflict of interest	Other
8 9			Probably Low	Low	Probably Low	Low	Low	Probably Low	Low	Low
9 10	23	Cao et al.	Daily concentrations of	The study obtained	Model adjusted for	Data consisted of	Daily counts	There was	The authors	No other
11		2012	EC was obtained from a	numbers of deaths in	long-term and	all nonaccidental	for death were	insufficient	declare they	potential
12			single monitoring site.	Xi'an for each day from	seasonal trends,	causes deaths	obtained, so	information	have no	sources of
13 14			The observations of EC	the Shanxi Provincial	day of week,	during over the	likely have all	about	actual or	bias
15			was 1749 in 1827 days	Center for Disease	temperature,	course of the	outcome data.	selective	potential	identified.
16			(missing data <25%).	Control and Prevention	humidity, and SO <sub>2</sub>	study.	However, any	outcome to	competing	
17 18				(SPCDCP). SPCDCP	and NO <sub>2</sub>		potential errors	judge for low	financial	
19				staff then classify the	concentrations.		or missing data	risk, but	interests.	
20				cause of death according	'/		did not depend	indirect		
21				to the International	. 01	•	on air pollution	evidence that		
22 23				Classification of			levels.	suggests study		
24				Diseases, 10th Revision		(0).	com	was free of		
25				[ICD-10; World Health			on	selective		
26 27				Organization (WHO)			Api	report.		
28				1992] as due to total			April 19,			
29				nonaccidental causes			9, 20			
30				(ICD-10 codes			)24			
31 32				A00–R99),			by g			
33				cardiovascular diseases			2024 by guest.			
34				(I00–I99), respiratory						
35 36				diseases(J00–J98), or			Protected			
30 37				injury (S00–T98).			cted			
38 <sup>1</sup>				/	l		9			

BMJ Open

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data o	Selective reporting	Conflict of interest	Other
8 9			Probably Low	Low	Probably Low	Low	Low $\overset{\mathbf{a}}{\overset{\mathbf{b}}{\overset{\mathbf{c}}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}}{\overset{\mathbf{c}}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}}{\overset{\mathbf{c}}}{\overset{\mathbf{c}}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}}{\overset{\mathbf{c}}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{c}}}{\overset{\mathbf{c}}{\overset{c}}}{\overset{\mathbf{c}}{\overset{c}}}{\overset{c}}{\overset{c}}{\overset{c}}{\overset{c}}{\overset{c}}{\overset{c}}{\overset{c}}{\overset{c}}{\overset{c}}{\overset{c}}{\overset{c}}{\overset{c}}}{\overset{c}}{\overset{c}}{\overset{c}}{\overset{c}}}{\overset{c}}{\overset{c}}{\overset{c}}{\overset{c}}{\overset{c}}}{\overset{c}}{\overset{c}}}{\overset{c}}{\overset{c}}}{\overset{c}}}}{\overset{c}}}{\overset{c}}{\overset{c}}{\overset{c}}{\overset{c}}{\overset{c}}}{\overset{c}}}{\overset{c}}}{\overset{c}}{\overset{c}}}{\overset{c}}}{\overset{c}}}{\overset{c}}}{\overset{c}}}{\overset{c}}}{\overset{c}}}{\overset{c}}{\overset{c}}}{\overset{c}}}{\overset{c}}}{\overset{c}}}{\overset{c}}}{\overset{c}}}{\overset{c}}}{\overset{c}}{\overset{c}}}{\overset{c}}}{\overset{c}}}{\overset{c}}}{\overset{c}}{\overset{c}}{\overset{c}}}{\overset{c}}}}{\overset{c}}}{\overset{c}}}{\overset{c}}}{\overset{c}}{\overset{c}}{\overset{c}}}{\overset{c}}}{\overset{c}}}{\overset{c}}}{\overset{c}}}{\overset{c}}}{\overset{c}}}{\overset{c}}}{\overset{c}}}}{\overset{c}}}{\overset{c}}}}{\overset{c}}}{\overset{c}}{\overset{c}}}{\overset{c}}}{\overset{c}}{\overset{c}}}}{\overset{c}}}{\overset{c}}{\overset{c}$	Probably Low	Low	Low
10	24	Klemm et	Daily 24-hr average EC	Records of individual	Adjusted for time	Study included	Daily counts	There was	Authors	No other
11		al. 2011	measurements are	deaths were provided by	(seasonality,	all nonaccidental	for death were	insufficient	declared no	potential
12			available for Atlanta	the Georgia Department	long-term trends),	deaths during	obtained, so	information	competing	sources of
13 14			during the study period.	of Human Resources.	temperature, and	over the course	likely have all	about	financial	bias
15			The observations of EC	Cause of death is	day of the week.	of the study.	outcome data.	selective	interests.	identified.
16			was 3317 days from	categorized using the			However, any	outcome to		
17 18			August 1998 to	International	<b>'</b> O.		potential errors	judge for low		
19			December 31, 2007.	Classification of	er tel		or missing data	risk, but		
20			Missing data <25%.	Diseases, 10th edition	' /		did not depend	indirect		
21 22			There was no information	(ICD-10), including			on air pollution	evidence that		
23			for monitor stations.	circulatory conditions			levels.	suggests study		
24				(I00–I99), respiratory		'01.	om	was free of		
25				conditions (J00–J99),			on	selective		
26 27				malignant neoplasm			Apr	report.		
28				(cancer; C00–D48), or			10			
29				other nonaccidental			, 20			
30 31				causes (A00-R99,			24 1			
32				excluding cardiovascular,			у д			
33				respiratory, or cancer			ues			
34				causes).			t. P			
35 36							on April 19, 2024 by guest. Protected			
37							Sted			
38 <sup>l</sup>							<u> </u>			

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data		Conflict of interest	Other
8 9			Probably Low	Low	Probably Low	Low	Low	Probably Low	Low	Low
10	25	Zhou et al.	24hr PM <sub>2.5</sub> samples were	Using codes from the	Models adjusted	Data consisted of	Daily counts	There was	The authors	No other
11		2011	obtained from a single,	International	for time,	all cardiovascular	for death were	insufficient	declare they	potential
12			central-site monitor.	Classification of	seasonality and	deaths over the	obtained, so	information	have no	sources of
13 14			Daily data was available	Diseases, version 10	long-term trends,	course of the	likely have all	about	actual or	bias
15			and no missing data was	(ICD10; World Health	day of week,	study.	outcome data.	selective	potential	identified.
16			reported.	Organization 2007), daily	temperature, and		However, any	outcome to	competing	
17 18				death counts were	humidity.		potential errors	judge for low	financial	
19				aggregated to			or missing data	risk, but	interests.	
20				nonaccidental allcause	' /		did not depend	indirect		
21				deaths (ICD10, codes	. 01		on air pollution	evidence that		
22 23				A00 through R99),		ien	levels.	suggests study		
24				cardiovascular deaths		(0)	com	was free of		
25				(ICD10, codes I01			vor	selective		
26 27				through I99), and			1 Ap	report.		
28				respiratory deaths			April 19, 2024 by guest.			
29				(ICD10, codes J00			9, 2			
30				through J99).			024			
31							by	•		
32 33							gue			
34										
35							Protected			
36							ecte			
37 38							<u></u>			

No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on the second of t		Conflict of interest	Other
		Probably Low	Low	Probably Low	Low	Low	Probably Low	Low	Low
26	Winquist	Daily EC and BC were	Individual-level data	Adjusted for time	Study included	Daily counts	There was	Authors	No other
	et al. 2015	from a single monitor	were obtained from the	trends, day of	emergency	for emergency	insufficient	declared no	potential
		site. All species of	Missouri Hospital	week, holidays,	department visits	department \frac{8}{2}	information	competing	sources of
		pollutant statistics are	Association for all	season,	in St Louis	visit were	about	financial	bias
		missing less than 5%.	emergency department	temperature and	metropolitan	obtained, so	selective	interests.	identified.
			visits to 36 of 43	dew point.	statistical area	likely have all	outcome to		
			acute-care non-federal	<b>'</b> O.	during 1 June	outcome data.	judge for low		
			hospitals with emergency		2001 through 30	However, any	risk, but		
			department visits in the	' /	April 2003.	potential errors	indirect		
			16-county St Louis	. 01		or missing data	evidence that		
			metropolitan statistical			did not depend	suggests study		
			area during 1 June 2001		'01.	on air pollution	was free of		
			through 30 April 2003.			levels.	selective		
			Cardiorespiratory				report.		
			outcomes of interest were			100			
			defined based on the			), 20			
			primary ICD-9			24 k			
			(International			у g			
			Classification of			uest			
			Diseases, version 9)						
			diagnosis code for the			otec			
			visit.			April 19, 2024 by guest. Protected by			

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data ≤	Selective reporting	Conflict of interest	Other
8 9			Probably High	Low	Probably Low	Low	Low $\overset{\mathbf{a}}{\searrow}$	Probably Low	Low	Low
9 10	27	Ostro et	Each of the six counties	Daily mortality data were	Adjusted for time	Data consisted of	Daily counts	There was	The authors	No other
11		al. 2007	had two monitors	obtained from the	trend, day of week,	all cardiovascular	for death were	insufficient	declare they	potential
12			measuring PM <sub>2.5</sub>	California Department of	seasonality,	deaths over the	obtained, so	information	have no	sources of
13 14			components and mass.	Health Services, Center	long-term trends,	course of the	likely have all	about	competing	bias
15			Fresno, Kern, Riverside,	for Health Statistics. The	temperature and	study.	outcome data.	selective	financial	identified.
16			and Sacramento Counties	study determined daily	humidity.		However, any	outcome to	interests.	
17 18			reported data every third	total mortality counts for	<b>'</b> O.		potential errors	judge for low		
19			day, whereas San Diego	those > 65 years of age			or missing data	risk, but		
20			and Santa Clara Counties	and for deaths from	' /		did not depend	indirect		
21 22			reported data every sixth	respiratory disease	. 01		on air pollution	evidence that		
23			day. For the speciation	[International			levels.	suggests study		
24			analyses, the number of	Classification of		'01.	com	was free of		
25			observation days	Diseases, 10th Revision			on	selective		
26 27			available ranged from	(ICD10; World Health			Apr	report.		
28			243 (San Diego County)	Organization 1993) codes			11 19			
29			to 395 (Sacramento	J00–J98] and			), 20			
30 31			County) from 2000 to	cardiovascular disease			)24			
32			2003. There was no	(codes I00–I99).			)			
33			specific information				uesi			
34			about missing data.				on April 19, 2024 by guest. Protected by			
35 36							otec			
37							ted			
38 <sup>L</sup>							\$			

5 5 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data	Selective reporting	Conflict of interest	Other
3			Probably Low	Low	Probably Low	Low	Low	Probably Low	Low	Low
10	28	Tolbert et	Daily 24h EC from a	Computerized billing	Adjusted for time	Study included	Daily count for	There was	Authors	No other
11		al. 2000	single monitor site. The	record data are being	(seasonality,	emergency	emergency	insufficient	declared no	potential
12			observation of EC was	obtained from the	long-term trends),	department visits	department ≦	information	competing	sources of
13 14			356 in 365 days, missing	emergency department	temperature, dew	of the	visits were	about	financial	bias
15			data <25%.	visits participating in the	point, and day of	participating	obtained, so	selective	interests.	identified.
16				study. Several case	week.	hospitals in the	likely have all	outcome to		
17				groups are being defined	<b>'</b> O	Atlanta	outcome data.	judge for low		
18 19				using the primary ICD-9	C/	Metropolitan	However, any	risk, but		
20				(International	' /_	Statistical Area,	potential errors	indirect		
21				Classification of	(0)	including 33	or missing data			
22				Diseases, 9th Revision)		hospitals	did not depend			
24				diagnostic code.		between January	on air pollution	""		
25						1 1993-August	levels.	selective		
26						31 2000, 4	n April			
27 28						hospitals				
29						between January	19, 2			
30						1 1993-February	2024 by guest.			
31						30 2000.	by			
32 33						30 2000.	gue			
34										
35							Protected			
36							ecte			
37   38							<u>_</u>			

2	
3	
4	
5	
6	
7	
4 5 6 7 8 9	
9	
10 11	
11	
12	
13	
14	
13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30	
16	
17	
18	
19	
20	
21	
22	
23	
24	
25	
20	
2/	
20	
30	
31	
32	
33	
34	
31 32 33 34 35 36 37 38	
36	
37	
38	

'age	e 87 of	BMJ Open								
:							36/bmjopen-2021-049516 on Incomplete			
; ;	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data o	Selective reporting	Conflict of interest	Other
			Low	Low	Probably Low	Low	Low 2	Probably Low	Low	Low
0	29	Wang and	The hourly data were	This study obtained	Adjusted for	Study included	Daily counts 8	There was	Authors	No other
1		Lin 2016	simply averaged to	universal health insurance	temperature,	elderly (≧65	for elderly Down mortality and all population	insufficient	declared no	potential
2   3			calculate the daily	claims from the National	relative humidity,		mortality and $\frac{3}{5}$	information	competing	sources of
4			average data for PM <sub>10</sub> ,	Health Research Institute	wind speed,	years) mortality			financial	bias
5			PM <sub>2.5</sub> monitored at 13	(NHRI) and vital	barometric	from 2004 to	emergency	selective	interests.	identified.
6 7			general air quality	statistics from the	pressure, holidays,	2008 and all	room visits	outcome to		
8			monitoring stations	Ministry of Health and	day of the week,	population EVR	were obtained,			
9			located in a densely	Welfare from 2004 to	pneumonia and	from 2004 to	so likely have	· ·		
20			populated area in Taipei.	2008. Death causes were	influenza.	2010 in Taipei,	all outcome	indirect		
2			Hourly concentrations of	coded according to the		Taiwan.	data. However,			
3			EC were detected by series 5400 Monitor. Very	diagnoses of the 9th revision of International		10.	any potential	suggests study was free of		
25			few missing values in the	Classification of Diseases			errors or missing data 9	selective		
6			database were omitted as	(ICD-9). Disease			did not depend ∂			
.7 .8			the daily average was	diagnoses were based on			on air pollution			
9			calculated.	the International						
0			ourouruteu.	Classification of Diseases			024			
1				with Clinical			by (			
3				Modification, Ninth			gues			
4				Revision (ICD-9 CM).			; <del>t</del>   <u>P</u>			
5							roteo			
7							2024 by guest. Protected by			
8 <sup>L</sup>							<u></u>	1		

			ВМЈ Ореі	1	vomjopen-			Paç
		I			36/bmJopen-z0z1-04951			I
No. Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data		Conflict of interest	Other
	Low	Low	Low	Low	Probably Low	Probably Low	Low	Low
Darrow et al. 2014	Daily 24-hour average EC was from ambient monitoring networks. Missing data <1%.	Health data were obtained from 41 metropolitan Atlanta hospitals and the Georgia Hospital Association. The diagnoses of respiratory infection were based on International Classification of Diseases, 9th Revision (ICD-9), diagnosis codes: acute bronchitis or bronchiolitis (code 466); pneumonia (codes 480–486); and upper respiratory infection (codes 460–465).	Adjusted for dew point, temperature, seasonality, long-term trends, day of week, holiday and influenza epidemics.	Study included daily emergency department visit data from 41 metropolitan Atlanta hospitals for the period January 1, 1993, to December 31, 2004 (not all hospitals contributed the full period), and from the Georgia Hospital Association for the period January 1, 2005, to June 30, 2010.	Daily counts for emergency department visit were obtained. In the earliest years of the study, not all hospitals were participating. However, any potential errors or missing datas did not depend on air pollution levels.	information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of selective report.	Authors declared no competing financial interests.	No other potential sources of bias identified

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data S		Conflict of interest	Other
8 9			Probably High	Low	Probably Low	Low	Low 2	Probably Low	Low	Low
10	31	Metzger et	Ambient 24hr average	The study asked 41	Model adjusted for	Data consisted of	Daily counts 8	There was	No	No other
11		al. 2004	EC were obtained from	hospitals with emergency	temporal trends,	all cardiovascular	for emergency	insufficient	competing	potential
12			one monitor. On days	departments that serve	meteorological	hospital	department \frac{8}{2}	information	financial	sources of
13 14			when measurements were	the 20-county Atlanta	conditions (i.e.,	admissions over	visits were	about	interests.	bias
15			missing at the central site,	metropolitan statistical	temperature, dew	the course of the	obtained, so	selective		identified.
16			data for the pollutant	area (MSA) to provide	point temperature),	study.	likely have all	outcome to		
17 18			were imputed using an	computerized billing data	day of week,		outcome data.	judge for low		
19			algorithm that modeled	for all emergency	hospital entry and		However, any	risk, but		
20			measurements. The	department visits between	exit, and federally		potential errors	indirect		
21			observations of EC was	January 1, 1993, and	observed holidays.	•	or missing data	evidence that		
22 23			714 days during the	August 31, 2000. Using			did not depend.	suggests study		
24			period August 1,	the primary International		<b>101</b>	on air pollution	was free of		
25			1998–August 31, 2000	Classification of			levels.	selective		
26 27			(missing data >25%).	Diseases, 9th Revision			Api	report.		
28				(ICD-9) diagnosis code,						
29				the study defined several			9, 20			
30				cardiovascular disease			)24			
31 32				(cardiovascular disease)			by g			
33				groups based largely on			Jues			
34				ICD-9 diagnosis codes.			April 19, 2024 by guest. Protected by			
35 36							rote			
37							ctec			
38							<u> </u>			

BMJ Open

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data ≤	Selective reporting	Conflict of interest	Other
8 9			Probably Low	Low	Probably Low	Low	Low ay	Probably Low	Low	Low
10	32	Mar et al.	Hourly PM <sub>2.5</sub> chemical	Mortality data for all of	Adjusted for time	Data consisted of	Daily counts 2	There was	No	No other
11		2000	composition data from a	Maricopa County from	trend, seasonality,	all cardiovascular	for death were	insufficient	competing	potential
12			single, central-site	1995 to 1997 were	day of week,	deaths during	obtained, so	information	financial	sources of
13 14			monitor. Daily data was	obtained from the	temperature and	over the course	likely have all	about	interests.	bias
15			available and no missing	Arizona Center for	relative humidity.	of the study.	outcome data.	selective		identified.
16			data was reported.	Health Statistics in			However, any	outcome to		
17 18				Phoenix. Death certificate	er rei		potential errors	judge for low		
19				data included residence			or missing data	risk, but		
20				zip code and the primary	' /		did not depend	indirect		
21				cause of death as	. 01		on air pollution	evidence that		
22 23				identified by the			levels.	suggests study		
24				International			com	was free of		
25				Classification of			on on	selective		
26 27				Diseases, Ninth Revision			Apr	report.		
28				(ICD-9, World Health			11 18			
29				Organization, Geneva).			9, 20			
30 31							)24			
32							by g			
33							ues			
34							on April 19, 2024 by guest. Protected by			
35 36							rote			
37							cted			
38 <sup> </sup>							<u> </u>			

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data		Conflict of interest	Other
8 9			Low	Low	Probably Low	Low	Low ay	Probably Low	Low	Low
10	33	Wang et	Hourly data of PM <sub>2.5</sub>	The daily mortality data	Adjusted for long	Study included	Daily counts	There was	No	No other
11		al. 2019a	were collected at 10	were obtained from the	term trends,	daily mortality	for death were	insufficient	competing	potential
12			Chinese air quality	system of Disease	seasonal influence,	data in Huangpu	obtained, so 💆	information	financial	sources of
13 14			monitoring sites in	Monitoring Point	day of the week,	district from	likely have all	about	interests.	bias
15			Shanghai. Hourly mass	belonged to the Chinese	holidays,	January 1, 2013	outcome data. $\frac{α}{3}$	selective		identified.
16			concentrations of PM <sub>2.5</sub>	Center for Disease	temperature and	to December 31,	However, any	outcome to		
17 18			and EC were predicted in	Control and Prevention	relative humidity.	2015.	potential errors	judge for low		
19			Shanghai by using a	(China CDC). Deaths			or missing datag	risk, but		
20			Community Multiscale	were classified according	' /		did not depend	indirect		
21 22			Air Quality model. The	to the 10th revised	. 01	•	on air pollution	evidence that		
23			study included	International Statistical			levels.	suggests study		
24			continuous daily data	Classification of Disease		'61.	com	was free of		
25			from 2013 to 2015 (1095	(ICD-10), all-cause			on	selective		
26 27			days). Daily data was	mortality (A00-R99),			Apr	report.		
28			available and no missing	circulatory disease			April 19,			
29			data was reported.	mortality (I00-I99, the			, 20			
30 31				circulatory disease is also			24 b			
32				known as cardiovascular			y gi			
33				disease) and respiratory			2024 by guest.			
34 35				disease mortality						
36				(J00-J99).			Protected			
37							l ted			
38 <sup>l</sup>			I	I	<u> </u>		\$	1		

BMJ Open

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data		Conflict of interest	Other
8 9			Probably High	Low	Probably Low	Low	Low ay	Probably Low	Low	Low
10	34	Lin et al.	EC was from a single	Daily mortality data were	Adjusted for	Study included	Daily counts	There was	Authors	No other
11		2016b	monitor site for four	obtained from the death	long-term trends,	the residents who	for death were	insufficient	declared no	potential
12			months of each year from	registry system. The	seasonality,	died of ischemic	obtained, so	information	conflict of	sources of
13 14			2007 to 2010. Missing	cause of death was coded	temperature,	or hemorrhagic	likely have all	about	interest.	bias
15			data for the particle	using the International	humidity, day of	strokes in urban	outcome data.	selective		identified.
16			concentration was very	Classification of	week and public	districts of	However, any	outcome to		
17			low (ranging from 1% to	Diseases, Tenth Revision	holidays.	Guangzhou	potential errors	judge for low		
18 19			2%).	(ICD-10). Mortality from		between 2007	or missing data	risk, but		
20				stroke (ICD-10:I60–I66),	1/6	and 2011.	did not depend	indirect		
21				and sub-categories,	(0)		on air pollution	evidence that		
22 23				including ischemic stroke			levels.	suggests study		
24				(ICD-10:I63–I66), and			con	was free of		
25				hemorrhagic stroke			or or	selective		
26				(ICD-10: I60–I62) were			Ap	report.		
27 28				extracted to construct the			April 19, 2024 by	1		
29				time series.			9, 2			
30				<b>11110</b> 5 <b>0110</b> 5.			024			
31							by			
32 33							guest.			
34										
35							Pro			
36							Protected			
37 38							<u>a</u>			

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on the outcome data of the outcome		Conflict of interest	Other
8			Probably High	Low	Probably Low	Low	Low 2	Probably Low	Low	Low
9	35	Lin et al.	Each of the six counties	Daily mortality for all	Adjusted for time,	Study included	Daily counts 8	There was	Authors	No other
11		2016b	had two monitors	California residents were	temperature,	daily	for death were	insufficient	declared no	potential
12			measuring components of	obtained from the	humidity and day	cardiovascular	obtained, so	information	competing	sources of
13 14			PM <sub>2.5</sub> . Fresno, Kern,	California Department of	of the week.	mortality for all	likely have all	about	interests.	bias
15			Riverside and	Health Services, Center		California	outcome data.	selective		identified.
16			Sacramento counties	for Health Statistics.		residents from 1	However, any	outcome to		
17 18			reported 24-hour average	Daily counts of deaths		January 2000 to	potential errors	judge for low		
19			EC in PM <sub>2.5</sub> every third	from cardiovascular		31 December	or missing data	risk, but		
20			day; San Diego and Santa	disease (International	' /	2003.	did not depend	indirect		
21			Clara counties reported	Classification of	. 01		on air pollution 🖺	evidence that		
22 23			data every sixth day. The	Diseases, Tenth Revision			levels.	suggests study		
24			study included only	(ICD10) =I00–I99) were		(0)	com	was free of		
25			species for which at least	calculated.			v on	selective		
26 27			50% of the observations				Apı	report.		
28			were above the level of							
29			detection.				9, 20			
30							)24			
31 32							by ç			
33							Jues			
34										
35							rote			
36 37							April 19, 2024 by guest. Protected			
38							<u> </u>			

BMJ Open

Page 94 of 133

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data		Conflict of interest	Other
8 9			Probably Low	Low	Probably Low	Low	Low S	Probably Low	Low	Low
10	36	Ito et al.	Ambient EC obtained	Hospitalizations and	Model adjusted for	Data consisted of	Daily counts	There was	The authors	No other
11		2011	from multiple monitors	mortality data were	temporal trends	all cardiovascular	for death and	insufficient	declare they	potential
12			and the average of data	available at the New York	and seasonal	hospital	hospitalization \( \frac{5}{2} \)	information	have no	sources of
13 14			from multiple monitors	City Department of	cycles, immediate	admissions over	were obtained,	about	actual or	bias
15			was computed using the	Health and Mental	and delayed	the course of the	so likely have	selective	potential	identified.
16			24hr average values. The	Hygiene. The relevant	temperature	study.	all outcome	outcome to	competing	
17 18			sampling frequency of	variables available in the	effects, and day of		data. However,	judge for low	financial	
19			the chemical speciation	electronic discharge	the week.		any potential	risk, but	interests.	
20			data was every third day.	abstract for each patient	' /		errors or	indirect		
21 22			Daily data was available	included date of	' (2)		missing data	evidence that		
23			and no missing data was	admission and			did not depend	suggests study		
24			reported.	International		'01.	on air pollution	was free of		
25				Classification of			levels.	selective		
26 27				Diseases, Nine Revision			Apr	report.		
28				(ICD9) discharge			19,			
29				diagnosis code. The						
30 31				International			24 5			
32				Classification of			2024 by guest.			
33				Diseases, Tenth Revision			uest			
34 35				(ICD10) codes for						
36				determining cause of			Protected			
37				death.			ted			
38 ໍ							ру			

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data		Conflict of interest	Other
8 9			Probably Low	Low	Probably Low	Low	Low 2	Probably Low	Low	Low
9 10	37	Chen et al.	Hourly mass	The counts of daily	Models adjusted	Data consisted of	Daily counts	There was	No	No other
11		2014	concentrations of PM <sub>2.5</sub>	emergency room visits	for time, day of	all emergency	for emergency	insufficient	competing	potential
12			and the four PM <sub>2.5</sub>	were obtained from the	week, temperature,	department visits	room visit	information	financial	sources of
13 14			constituents obtained	National Taiwan	seasonality and	during the study	were obtained,	about	interests.	bias
15			from a Supersite (single,	University Hospital. The	relative humidity.	period for	so likely have	selective		identified.
16			central site monitoring	emergency room visit		ischemic and	all outcome	outcome to		
17			location). The	data were coded	<b>'</b> O.	hemorrhagic	data. However,	judge for low		
18 19			observations of EC was	regarding the discharge	C/	stroke.	any potential	risk, but		
20			1599 in 1705 days	diagnosis using the	' / <sub>~</sub>		errors or	indirect		
21			(missing data <25%).	International	'(0)		missing data	evidence that		
22 23				Classification of Disease,			did not depend	suggests study		
24				9th revision (ICD-9).		10,	on air pollution			
25						\ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \	levels.	selective		
26							Ap r	report.		
27 28							April 19,			
29							9, 2			
30							024			
31 32							by (	•		
32 33							2024 by guest.			
34										
35							rote			
36 37							Protected			
38							d by	:		
20							0			

4 5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data	Selective reporting	Conflict of interest	Other
8 9			Low	Low	Probably High	Low	Low	Probably Low	Low	Low
10	38	Tomic'-Sp	Average daily	Emergency department	Adjusted for	Study included	All counts for 8	There was	Authors	No other
11		iric' et al.	concentrations of BC in	visits data were obtained	temperature,	emergency	emergency $\bigcirc$	insufficient	declared no	potential
12		2019	micrograms per cubic	from the Health Center	humidity, and air	department visit	department	information	competing	sources of
13 14			meter were measured by	Užice, either from the	pressure.	for allergic	visits were	about	financial	bias
15			three automatic ambient	emergency department		rhinitis and	obtained, so 🚊	selective	interests.	identified.
16			air quality monitoring	visits in Užice, Sevojno,		allergic asthma	likely have all	outcome to		
17 18			stations. There was no	and Kosjeri' c, or from a	<b>'</b> O.	from 1 July 2012	outcome data.	judge for low		
19			information about	general hospital in Užice.		to 30 June 2014	However, any	risk, but		
20			missing data.	The inclusion criteria	'/	in the Zlatibor	potential errors	indirect		
21				were adults aged 18 years	. 01	District, Western	or missing data	evidence that		
22 23				and older with the		Serbia.	did not depend.	suggests study		
24				diagnosis of allergic		<b>101.</b>	on air pollution	was free of		
25				rhinitis (International			levels.	selective		
26 27				Classification of				report.		
28				Diseases, 10th revision,			11 10			
29				code J.30.4), allergic			9, 20			
30 31				asthma (International			)24			
31 32				Classification of			by g			
33				Diseases, 10th revision,			April 19, 2024 by guest. Protected			
34				code J.45.0), or asthma			t. Pr			
35 36				with coexisting allergic			otec			
37				rhinitis.			cted			
38 <sup>1</sup>							9			

•	
2	
3	
4	
5	
6	
7	
7 8	Н
9	
10	
11	
12	
13	
14	
15	
16	
17	
16 17 18	
19	
20	
21 22 23	
22	
23	
24	
25	
26	
27	
/X	
29	
30	
30 31	
32	
33	
34	
35	
26	
37	
38	

Page 97	ge 97 of 133 BMJ Open								
1 2 3 4									
5 No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data		Conflict of interest	Other
3		Probably Low	Low	Probably Low	Low	Low	Probably Low	Low	Low
9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38	Maynard et al. 2007	Daily measurements of BC were obtained from a single monitor site. In order to predict local BC level, the study used a validated spatial—temporal land use regression model to predict 24-hr measures of traffic exposure data (BC) at > 80 locations in the Boston area.	Individual mortality records were obtained from the Massachusetts Department of Public Health, for the years 1995–2002. Specific cause mortality was derived from the International Classification of Diseases (ICD) codes [9th Revision before 1999 (World Health Organization 1975) and 10th Revision 1999 to 2002 World Health Organization 1993)].	Adjusted for season and long term trend, temperature, dew point and day of week.	Study included all death for all causes, cardiovascular, respirator, stroke, and diabetes diseases in Boston metropolitan area from the Massachusetts Department of Public Health between 1995–1997 and 1999–2002.	Daily counts for individual mortality records were obtained, so likely have all outcome data. However, any potential errorspor missing data did not depend on air pollutions levels.  April 19, 2024 by guest. Protected by	information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of selective report.	Authors declared no competing financial interests.	No other potential sources of bias identified.

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on the outcome data S		Conflict of interest	Other
8 9			Probably Low	Probably Low	Probably Low	Low	Low by	Probably Low	Low	Low
10	40	Sinclair et	Daily 24-hr averages EC	Daily outpatient visits	Adjusted for	Study included	Daily counts	There was	No	No other
11		al. 2010	was from a single	were obtained from the	season, day of	daily outpatient	for outpatient	insufficient	competing	potential
12			monitor site. The total	electronic patient data	week, federal	visits for acute	visits were	information	financial	sources of
13 14			observed rate of EC was	warehouse of a	holidays, study	respiratory	obtained, so	about	interests.	bias
15			95.2%.	not-for-profit,	month, time,	diseases from the	likely have all 🚉	selective		identified.
16				group-model managed	temperature and	electronic patient	outcome data.	outcome to		
17 18				care organization (MCO)	dew point.	data warehouse	However, any	judge for low		
19				in the metropolitan	C/	of a	potential errors	risk, but		
20				Atlanta area between	1/6	not-for-profit,	or missing data	indirect		
21				August 1, 1998 and	. 01	group-model	did not depend	evidence that		
22 23				December 31, 2002.		managed care	on air pollution	suggests study		
24				Visits that met acute visit		organization	levels.	was free of		
25				definition and that had a		(MCO) in the	on	selective		
26 27				visit diagnosis code of		metropolitan		report.		
28				asthma, upper respiratory		Atlanta area				
29				infection (URI), or lower		between August	9, 20			
30				respiratory infection		1, 1998 and	)24			
31 32				(LRI) were included in		December 31,	by g			
33				the study.		2002.	Jues			
34							:t 			
35 36							April 19, 2024 by guest. Protected by			
37							cted			
38 <sup>l</sup>							1 8			
39							сор			

36/bmjopen-2021-0495

3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 36 37 37 37 37 37 37 37 37 37 37 37 37 37	2	
5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 33 34 34 35 36 36 37 37 38 37 38 37 38 37 38 38 38 38 38 38 38 38 38 38 38 38 38	3	
6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34		
7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34	5	
9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34	6	
9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34	7	
10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34		
12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34	9	
12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34	10	
12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34	11	
13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34	12	
14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34	13	
15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34	1/	
16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33	15	
19 20 21 22 23 24 25 26 27 28 29 30 31 32 33	16	
19 20 21 22 23 24 25 26 27 28 29 30 31 32 33	17	
19 20 21 22 23 24 25 26 27 28 29 30 31 32 33	18	
20 21 22 23 24 25 26 27 28 29 30 31 32 33	19	
21 22 23 24 25 26 27 28 29 30 31 32 33	20	
24 25 26 27 28 29 30 31 32 33	21	
24 25 26 27 28 29 30 31 32 33	22	
24 25 26 27 28 29 30 31 32 33	23	
28 29 30 31 32 33 34	24	
28 29 30 31 32 33 34	25	
28 29 30 31 32 33 34	26	
28 29 30 31 32 33 34	27	
29 30 31 32 33 34	28	
30 31 32 33 34	29	
32 33 34		
32 33 34		
33	32	
34	33	
35	34	
	35	
36	36	
37	37	
37 38	38	

5 5 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data ≤		Conflict of interest	Other
3			High	Probably Low	Probably Low	Low	Low $\overset{\mathbf{a}}{\checkmark}$	Probably Low	Low	Low
0	41	Krall et al.	Monitors typically	All-cause mortality data	Adjusted for	Study included	Daily counts 8	There was	The authors	No other
11		2013	measure PM <sub>2.5</sub>	(excluding accidental	temperature, day	all death	for death were	insufficient	declare they	potential
12			constituent	deaths) were aggregated	of week, long-term	(excluding	obtained, so		have no	sources of
13 14			concentrations every	from death certificate	and seasonal	accidental	likely have all	about	actual or	bias
15			third or sixth day. Some	data obtained from the	trends.	deaths) for 108	outcome data.	selective	potential	identified.
16			communities with a	National Center for		urban	However, any	outcome to	competing	
17 18			single monitor. The	Health Statistics for 2000		communities	potential errors	judge for low	financial	
19			observation of EC was	to 2005.		from 2000 to	or missing data	risk, but	interests.	
20			58-921 days,some		' /	2005.	did not depend	indirect		
21			communities had >25%		' (2)		on air pollution			
22			missing data.				levels.	suggests study		
24			_			(0)	con	was free of		
25							n/ or	selective		
26							1 Ap	report.		
27 28								•		
29							9, 2			
30							024			
31							by			
32							gue			
34							on April 19, 2024 by guest. Protected			
35							Prot			
36							ecte			
37   38							<u>ä</u>			

1 2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37 38
38

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on the outcome data	Selective reporting	Conflict of interest	Other
8 9			Probably High	Low	Probably Low	Low	Low ay	Probably Low	Low	Low
10	42	Cakmak et	Daily PM <sub>2.5</sub> aerosol	Diseases were coded	Adjusted for	Study included	Daily counts	There was	No	No other
11		al. 2009	samples approximately 1	using the WHO	temperature and	all emergency	for emergency	insufficient	competing	potential
12			of every 4 days from a	International	humidity, day of	department visits	department <u>\frac{8}{2}</u>	information	financial	sources of
13 14			single monitor site.	Classification of Disease,	week, long-term	obtained from the	visit were	about	interests.	bias
15			Sampling occurred daily	9th Revision (ICD-9).	and seasonal	Departamento de	obtained, so ⊖	selective		identified.
16			during the cold season	The daily number of	trends.	Es-tad' isticas e	likely have all	outcome to		
17 18			(April through	emergency department		InformaciónenSa	outcome data.	judge for low		
19			September) and alternate	visits for all		lud (DEIS) of the	However, any	risk, but		
20			days during the warm	nonaccidental (ICD-9 <	' /	Ministry of	potential errors	indirect		
21			season (October through	800) and respiratory	' (2)	Health from	or missing data	evidence that		
22			March). Missing data	(ICD-9 460–519) causes		April 2001	did not depend.	suggests study		
24			<25% for that frequency.	in Santiago Centro,		through August	on air pollution	was free of		
25				Cerrillos, and Pudahuel		2006.	levels.	selective		
26   27				were obtained from the			1 Ap	report.		
28				Departamento de Estad'			April 19,	_		
29				ısticas e			9, 20			
30				InformaciónenSalud			2024 by			
31 32				(DEIS) of the Ministry of			by g			
33				Health from April 2001			guest.			
34				through August 2006.						
35				<i></i>			Protected			
36   37							Ctex			
38							<u> </u>			

36/bmjopen-2021-0495<mark>1</mark>

2	
4	
5 6	
6	
7	
7 8 9	
9	
10	
11	
12	
13	
14	
15	
13 14 15 16 17 18	
10	
10 10	
19 20	
21	
22	
23	
24	
26	
27	
25 26 27 28 29	
29	
30	
31	
31 32	
33	
34	
34 35 36 37 38	
36	
37	
38	

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete of outcome data o		Conflict of interest	Other
3			Low	Low	Probably Low	Low	Low S	Probably Low	Low	Low
10	43	Tolbert et	Daily ambient EC	Computerized billing	Model adjusted for	Data consisted of	Daily counts	There was	No	No other
11		al. 2007	obtained from multiple	records for all emergency	long-term and	all cardiovascular	for emergency	insufficient	competing	potential
12			monitors and a single	department visits between	seasonal trends,	disease and	department 💆	information	financial	sources of
13 14			concentration obtained by	January 1, 1993 and	daily average	respiratory	visit were	about	interests.	bias
15			averaging across	December 31, 2004 were	temperature, dew	disease hospital	obtained, so	selective		identified.
16			monitors. The	collected, including the	point, day of week,	admissions	likely have all	outcome to		
17 18			observations of EC was	following data for each	federal holiday,	during the period	outcome data.	judge for low		
10			2258 during the period	visit: primary	and hospital entry	1993 to 2004	However, any			
20			August 1, 1998 to	International	and exit.	over the course	potential errors	indirect		
21			December 31, 2004	Classification of Diseases	(0)	of the study.	or missing data			
22			(missing data <25%).	9th Revision (ICD-9)			did not depend	suggests study		
24			,	diagnostic code,		(0)	on air pollution			
25				secondary ICD-9			levels.	selective		
26				diagnosis codes.			ı Ap	report.		
27 28								1		
29							9, 2			
30							024			
31							by			
32   33							April 19, 2024 by guest. Protected			
34							st. F			
35							rote			
36 37							ecte			
87   88							<u>s</u>			

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data ∞	Selective reporting	Conflict of interest	Other
8 9			Low	Low	Probably Low	Low	Low $\overset{\mathbf{a}}{\overset{\mathbf{b}}{\overset{\mathbf{c}}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}}{\overset{\mathbf{c}}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{}}{\overset{\mathbf{c}}}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{}}}{}}{}{$	Probably Low	Low	Low
9 10	44	Lall et al.	Daily EC data were	The categorization of the	Model adjusted for	Data consisted of	Daily counts	There was	The authors	No other
11		2011	obtained from two	admissions data was	season, wintertime	all cardiovascular	for hospital	insufficient	declare they	potential
12			monitors. Daily data was	based on codes from the	influenza episode,	hospital	admission wer	information	have no	sources of
13 14			available and no missing	International	weather, day of	admissions over	obtained, so	about	actual or	bias
15			data was reported.	Classification of	week, and other	the course of the	likely have all	selective	potential	identified.
16				Diseases, revision 9	possible	study.	outcome data.	outcome to	competing	
17 18				(ICD-9).	confounders (e.g.,		However, any	judge for low	financial	
19					federal holidays).		potential errors	risk, but	interests.	
20					' /	ich	or missing data	indirect		
21					. 01		did not depend	evidence that		
22 23							on air pollution.	suggests study		
24						<b>101</b>	levels.	was free of		
25							on	selective		
26 27							on April 19, 2024 by guest.	report.		
28										
29							9, 20			
30							024			
31 32							by g			
33							Jues			
34							St.			
35							rote			
36 37							Protected by			
38							9			
20							C			

2	
3	
4	
6	
5 6 7	
8	_
9	
10	
11	
12	
13	
14	
15	
16	
17	
14 15 16 17 18	
19	
20	
21	
22	
22 23	
24	
25	
26	
26 27	
28	
29	
30	
31	
32 33	
34	
35	
35 36	
$\sim$ $-$	
3 <i>/</i> 38	
20	

Page	103 (	of 133			ВМЈ Орег	า	36/amjop			
1 2 3							Incomplete			
7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data	Selective reporting	Conflict of interest	Other
8			Probably High	Low	Probably Low	Low	Low	Probably Low	Low	Low
9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38	45	Jung and Lin 2017	A total of 153 daily samples (approximately 4 weeks per season) from a single monitor site were collected. Multiple linear regression models were used to back extrapolate the historic concentration of individual components of PM <sub>2.5</sub> from 2000 through to 2010, including BC.	The health data used in the study were sourced from Longitudinal Health Insurance Database 2000. Daily outpatient visits for asthma (International Classification of Diseases, Ninth Revision, Clinical Modification, ICD-9-CM code 493) data was obtained from Longitudinal Health Insurance Database 2000.	Adjusted for seasonal trend, day of week, temperature, precipitation and wind vectors.	Study included all asthma outpatient visits (0-20 years old) in Shalu district from Longitudinal Health Insurance Database 2000 during January 1, 2000 to December 31, 2010.	Daily counts for asthma outpatient visits (0-20 years old) data were obtained, so likely have all outcome data. However, population any potential errors or missing data did not depend on air pollution levels.	There was insufficient information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of selective report.	No competing financial interests.	No other potential sources of bias identified.
39 40 41 42							у сорупдпт.			

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data ≤	Selective reporting	Conflict of interest	Other
8 9			Probably Low	Low	Probably Low	Low	Low $\overset{\mathbf{a}}{\searrow}$	Probably Low	Low	Low
10	46	Gong et	The 24-h mean BC	The disease data used in	Adjusted for	Study included	Daily counts	There was	Authors	No other
11		al. 2019	concentrations data were	this study were collected	calendar effects,	all cardiovascular	for all deaths	insufficient	declared no	potential
12			obtained from a single	from the Chinese Center	long-term trends,	mortality in	were obtained, \subseteq	information	conflict of	sources of
13 14			monitor site. During the	for Disease Control and	temperature,	Beijing obtained	so likely have	about	interest.	bias
15			study period (2091 days),	Prevention, and included	humidity, day of	from the Chinese	all outcome	selective		identified.
16			missing rate of BC was	all deaths in Beijing from	week, NO2 and	Center for	data. However,	outcome to		
17 18			0.68%.	January 1, 2006 to	$SO_2$ .	Disease Control	any potential	judge for low		
19				December 31, 2011.		and Prevention	errors or	risk, but		
20				Causes of death were	' /	during January 1,	missing data	indirect		
21   22				classified according to	' (2)	2006 to	did not depend	evidence that		
23				the International		December 31,	on air pollution.	suggests study		
24				Classification of		2011.	levels.	was free of		
25				Diseases, 10th Edition			on /	selective		
26 27				(ICD-10) and data on				report.		
28				cardiovascular diseases			April 19, 2024 by			
29				(ICD-10 code: I00–I99)			9, 20			
30				were obtained.			)24			
31   32							by ç			
33							gues			
34							St. 17			
35							rote			
36 37							guest. Protected b			
38							d by			

36/bmjopen-2021-0495<mark>1</mark>

2	
3	
4	
5	
6	
7	
8	
9	
10	
11	
12	
13	
14	
15	
16	
17	
18	
19	
20	
21	
22	
23	
24	
25	
26	
27	
28	
29	
30	
31	
32	
33	
34	
35	
36	
37	
38	
39	
• •	

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data ≤	Selective reporting	Conflict of interest	Other
8 9			Probably Low	Probably Low	Probably High	Low	Low ay	Probably Low	Low	Low
10	47	Mostofsky	Ambient EC obtained	Patients potentially	Model adjusted for	Population	Daily counts 2	There was	No	No other
11		et al. 2012	from one monitor. BC	eligible for this study	seasonality,	consisted of	for emergency $\bigcirc$	insufficient	competing	potential
12			concentrations were	were identified by	time-trends,	patients ≥21	department \(\frac{8}{2}\)	information	financial	sources of
13   14			measured continuously.	reviewing daily	temperature, dew	years of age	admission were	about	interests.	bias
15			Daily data was available	emergency department	point temperature,	admitted to the	obtained, so	selective		identified.
16			and no missing data was	admission logs, stroke	barometric	hospital with	likely have all	outcome to		
17 18			reported.	service admission logs,	pressure and	neurologist-confi	outcome data.	judge for low		
19				stroke service consult	chronic and	rmed ischemic	However, any	risk, but		
20				logs, and hospital	slowly-varying	stroke and	potential errors	indirect		
21				electronic discharge	potential	residing in the	or missing data	evidence that		
22				records.	confounders.	Boston	did not depend.	suggests study		
24						metropolitan	on air pollution	was free of		
25						region. Also	levels.	selective		
26   27						patients had to	April	report.		
28						reside within 40				
29						km of the air	9, 20			
30						pollution	)24			
31 32						monitor.	by g			
33							lues			
34							19, 2024 by guest. Protected			
35 36							rote			
37							cted			
38 L							b			

Page 106 of 133

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data		Conflict of interest	Other
8			Probably High	Low	Probably Low	Low	Low	Probably Low	Low	Low
10	48	Krall et al.	PM <sub>2.5</sub> constituents from	The study obtained	Adjusted for	Study included	Daily counts	There was	The authors	No other
11		2017	one urban, ambient	electronic billing data for	holidays,	all emergency	for emergency	insufficient	declare they	potential
12			monitor located in each	respiratory disease	long-term trends,	department visits	department \frac{\frac{3}{2}}{2}	information	have no	sources of
13 14			city. Daily pollution data	emergency department	day of the week,	for respiratory	visits of	about	actual or	bias
15			were available in Atlanta;	visits for all ages at acute	season,	disease at acute	respiratory	selective	potential	identified.
16			however, data were only	care hospitals. Using	hospitalsreporting	care hospitals in	disease were	outcome to	competing	
17 18			available approximately	diagnosis codes from the	data, temperature	the 20-county	obtained, so	judge for low	financial	
19			every third day in the	International	and dew point.	Atlanta	likely have all	risk, but	interests.	
20			remaining three cities.	Classification of	' /	metropolitan	outcome data.	indirect		
21 22			There was no information	Diseases, 9th Revision	. 01	area, the	However, any	evidence that		
23			about missing data.	(ICD-9), the study		7-county	potential errors	suggests study		
24				considered subcategories		Birmingham	or missing data	was free of		
25				of respiratory diseases		metropolitan	did not depend 9	selective		
26 27				including pneumonia		area, the 8	on air pollution	report.		
28				(ICD-9 codes 480–486),		Missouri and 8	levels.			
29				chronic obstructive		Illinois counties	, 20			
30 31				pulmonary disease		in the St. Louis	24 b			
32				(491,492,496), upper		metropolitan	y gi			
33				respiratory infection		area, and the	uest			
34 35				(URI) (460–465, 466.0,		12-county Dallas	 P			
36				477), and asthma and/or		metropolitan	19, 2024 by guest. Protected			
37				wheeze (493, 786.07).		area.	ted.			
38						•	by c			
39							сор			

36/bmjopen-2021-0495

2	
4	
5 6	
6	
7	
7 8 9	
9	
10	
11	
12	
13	
14	
15	
13 14 15 16 17 18	
10	
10 10	
19 20	
21	
22	
23	
24	
26	
27	
25 26 27 28 29	
29	
30	
31	
31 32	
33	
34	
34 35 36 37 38	
36	
37	
38	

5 5 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data		Conflict of interest	Other
3			Probably Low	Low	Probably Low	Low	Low	Probably Low	Low	Low
0	49	O'Lenick	The 24-hour average	Patient-level emergency	Adjusted for	Study included	Daily counts	There was	Competing	No other
1		et al. 2017	concentration of EC was	department visit data	season, periods of	all emergency	for emergency	insufficient	interests:	potential
2			evaluated. Pollutant	from 1 January 2002 to	hospital	department visit	department §	information	None	sources of
3			concentration estimates	31 December 2008 were	participation and	data acquired	visit were	about	declared.	bias
5			were obtained by fusing	acquired from hospitals	holidays,	directly from	obtained, so	selective		identified.
16			observational data from	located within the	temperature and	hospitals	likely have all	outcome to		
7  8			available network	20-county metropolitan	mean dew point,	(2002–2004	outcome data.			
19			monitors with pollutant	area of Atlanta; Relevant	interaction terms	period) and the	However, any	risk, but		
20			concentration simulations	data elements included	between season	Georgia Hospital	potential errors	indirect		
21			from the Community	admission date,	and maximum	Association	or missing data	evidence that		
22			Multi-Scale Air Quality	International	temperature and	(2005–2008	did not depend	suggests study		
24			emissions-based chemical	Classification of Diseases	day of year.	period) located	on air pollution			
25			transport model at	Ninth Revision (ICD-9)		within the	levels.	selective		
26 27			12×12km grids over	diagnosis codes, age and		20-county	Api	report.		
28			Atlanta. 24-hour average	ZIP code of patient		metropolitan area				
29			EC were evaluated. Daily	residence.		of Atlanta.	9, 20			
30			data was available and no				)24			
31			missing data was				by g			
33			reported.				Jues			
34			•				April 19, 2024 by guest. Protected			
35   36							rote			
37							ctec			
38 L							<u>\$</u>			

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data ≤	Selective reporting	Conflict of interest	Other
8 9			Probably Low	Low	Probably Low	Low	Low $\overset{\mathbf{a}}{\overset{\mathbf{b}}{\overset{\mathbf{c}}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}}{\overset{\mathbf{c}}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}{\overset{\mathbf{c}}}{}}{}}{}{$	Probably Low	Low	Low
10	50	Pearce et	Daily EC data were	The study obtained	Adjusted for year,	Study included	Daily counts	There was	The authors	No other
11		al. 2015	obtained from a central	aggregate daily counts for	season, month, day	all emergency	for pediatric	insufficient	declare that	potential
12			monitoring location in	pediatric asthma related	of the week,	department visits	asthma related	information	they have	sources of
13 14			Atlanta. Daily data was	emergency department	hospital, holidays,	for pediatric	emergency a	about	no	bias
15			available and no missing	visits for children ages 5	temperature and	asthma of	department department	selective	competing	identified.
16			data was reported.	to 18 years from 41	dew point.	children ages 5 to	visits were	outcome to	interests.	
17 18				hospitals within		18 years from 41	obtained, so	judge for low		
19				metropolitan Atlanta; and		hospitals within	likely have all	risk, but		
20				defined emergency	' /	metropolitan	outcome data.	indirect		
21				department visits for	' (2)	Atlanta for study	However, any	evidence that		
22 23				pediatric asthma as all		period.	potential errors.	suggests study		
24				visits with a code for		701	or missing data			
25				asthma (493.0–493.9) or			did not depend 9	selective		
26 27				wheeze (786.07) using			on air pollution ≥			
28				the International			lavala ≟	•		
29				Classification of			9, 20			
30				Diseases, 9th Revision.			024			
31 32				,			by			
33							gues			
34							S: T			
35							19, 2024 by guest. Protected b			
36 37							ecte			
38										

36/bmjopen-2021-0495

2 3 4	
5	
6	
7	L
8	
9	
10	
11 12	
13	
14	
15	
16 17	
18	
19	
20	
21	
22	
23	
24	
25	
26	
27	
28	
29	
30 31	
32	
33	
34	
35	
36	
37	
38	

5 5 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data		Conflict of interest	Other
3			Low	Low	Probably Low	Low	Low 2	Probably Low	Low	Low
10	51	Strickland	24-hour average EC were	Daily counts of	Adjusted for	Study included	Daily counts 🕺	There was	No conflict	No other
11		et al. 2010	obtained from 6	emergency department	season, dew point,	all emergency	for emergency	insufficient	of interests.	potential
12			monitors. Missing data	visits for asthma or	temperature, year,	department visits	room visits of	information		sources of
13   14			<1%.	wheeze among children	month, day of	for asthma or	asthma or	about		bias
15				were collected from 41	week, hospital,	wheeze among	wheeze disease	selective		identified.
16				Metropolitan Atlanta	upper respiratory	children aged 5	were obtained,	outcome to		
17 18				hospitals during	infections (the	to 17 years from	so likely have	judge for low		
19				1993-2004. Using the	logarithm of the	metropolitan	all outcome	risk, but		
20				International	daily count of	Atlanta hospitals	data. However,	indirect		
21				Classification of	upper respiratory	during	any potential	evidence that		
22				Diseases, 9th Revision,	infections) and	1993–2004.	errors or	suggests study		
24				the study defined	pollen	<b>'</b> 01.	missing data	was free of		
25				emergency department	concentrations		did not depend 9	selective		
26   27				visits for pediatric asthma	(various lags of		on air pollution ≧	report.		
28				as all visits with a code	ambient ragweed,		levels.			
29				for asthma (493.0–493.9)	pine, oak, juniper,		9, 20			
30				or wheeze (786.09 before	grass and birch		)24			
31   32				October 1, 1998; 786.07	concentrations).		by g			
33				after October 1, 1998).	,		Jues			
34				, ,			; <del>;</del> 			
35   36							9, 2024 by guest. Protected			
37							ctec			
38 L							<u> </u>			

5 5	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data ≤	Selective reporting	Conflict of interest	Other
3			Low	Low	Probably Low	Low	Low <sup>ay</sup>	Probably Low	Low	Low
0	52	Strickland	24-hour average EC were	Daily counts of	Adjusted for	Study included	Daily counts	There was	No conflict	No other
1		et al. 2014	obtained from 6	emergency department	season, dew point,	all emergency	for emergency 💆	insufficient	of interests.	potential
2			monitors. Missing data	visits for asthma or	temperature, day	department visits	room visits of 💆	information		sources of
3 4			was 1%.	wheeze among children	of week, and	for asthma or	asthma or	about		bias
5				aged 2 to 16 years were	holiday.	wheeze among	wheeze disease	selective		identified.
6				collected from the		children 2 to 16	were obtained,	outcome to		
7				Georgia Hospital		years of age from	so likely have	judge for low		
9				Association from 1		the Georgia	all outcome	risk, but		
20				January 2002 through 30	' /	Hospital	data. However,	indirect		
21				June 2010. The study	' (2)	Association.	any potential	evidence that		
22				identified all emergency			errors or	suggests study		
24				department visits with an		'01.	missing data	was free of		
25				International			did not depend 9	selective		
26 27				Classification of			on air pollution≧	report.		
28				Diseases, 9th revision			levels.			
9				(ICD-9) code for asthma			), 20			
30 31				(codes beginning with			124 k			
				493) or wheeze (code			) 9 9			
32 33				786.07) present in any			uesi			
34				diagnosis field.			19, 2024 by guest. Protected			
35 36							otec			
37							l ted			
88 <sup>L</sup>							<u> </u>		l	

36/bmjopen-2021-0495<mark>1</mark>

2	
2	
3	
4	
5	
6	
7	
8	
9	
10	
11	
12	
13	
14	
15	
16	
17	
18	
19	
20	
21	
22	
23	
24	
25	
26	
26 27	
28	
29	
30	
31	
32	
33	
34	
35	
36 37	
38	
50	

7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on the outcome data		Conflict of interest	Other
3			Probably High	Low	Probably Low	Low	Low ay	Probably Low	Low	Low
10	53	Ito et al.	The study chose 150 U.S.	Using International	Adjusted for	Study included	Daily counts	There was	No conflict	No other
11		2013	metropolitan statistical	Classification of	modeling of	all nonaccidental	for death and	insufficient	of interests.	potential
12			areas where the data from	Diseases, 10th Revision	confounding	all-cause,	emergency §	information		sources of
13 14			at least one Chemical	(ICD-10) codes, the study	temporal trends	cardiovascular	hospitalization	about		bias
5			Species Network monitor	aggregated daily death	(annual cycles and	disease and	were obtained,	selective		identified.
6			were available. The	counts for the	influenza	respiratory	so likely have	outcome to		
17 18			Chemical Species	nonaccidental all-cause,	epidemics),	deaths and	all outcome	judge for low		
19			Network data for PM <sub>2.5</sub>	cardiovascular disease	day-of-week	emergency	data. However,	risk, but		
20			components were	and respiratory deaths.	patterns and	hospitalizations	any potential	indirect		
21			available either every	Using International	temperature.	for the elderly	errors or	evidence that		
22			third day or every sixth	Classification of		(those 65 and	missing data	suggests study		
24			day. There was no	Diseases, 9th Revision		older) of	did not depend	was free of		
25			information about	(ICD-9) codes,		cardiovascular	on air pollution	selective		
26 27			missing data.	emergency		disease and	levels. ਰ੍ਰੇ	report.		
28				hospitalizations for the		respiratory	19,	1		
29				elderly (those 65 and		diseases.	9, 20			
30				older) data were divided			)24			
31				into cardiovascular			by g			
33				disease and respiratory			2024 by guest.			
34				categories.						
35 36				_			Protected			
37							Cted			
8 L							<u> </u>	•		

No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data		Conflict of interest	Other
		Probably Low	Low	Probably Low	Low	Probably Low	Probably Low	Low	Low
54	Ostro et	The model calculations	Deaths were assigned	ge, race, marital	Data obtained for	There was no	There was	The authors	No other
	al. 2015b	track the mass and	codes based on the	status, smoking	a cohort of	information on	insufficient	declare they	potential
		concentrations of the PM	International	status, pack-years	female teachers	the rate of lost	information	have no	sources of
		constituents in particle	Classification of	of smoking,	≥30 years old.	follow up.	about	actual or	bias
		diameters ranging from	Diseases, 10th Revision	secondhand smoke		ed #	selective	potential	identified.
		0.01 to 10μm through	(ICD-10) for the	exposure, body		Ö	outcome to	competing	
		calculations that describe	following outcomes:	mass index,		http	judge for low	financial	
		emissions, transport,	all-cause deaths	lifetime physical		://br	risk, but	interests.	
		diffusion, deposition,	excluding those with an	activity, alcohol		njop	indirect		
		coagulation, gas- and	external cause	consumption,		en.l	evidence that		
		particle-phase chemistry,	(A00–R99),	average daily		<u>) j</u> .	suggests study		
		and gas-to-particle	cardiovascular deaths	dietary intake of	'eh,	com	was free of		
		conversion. The	(I00–I99), Ischemic heart	fat, calories,		on	selective		
		University of California	disease deaths (I20–I25),	menopausal status,		Api	report.		
		Davis/California Institute	and pulmonary deaths	family history of					
		of Technology model was	(C34, J00–J98).	myocardial		9, 20			
		used to estimate		infarction, stroke,		)24			
		ground-level		use of blood		by g			
		concentrations of 50 PM		pressure		lues			
		constituents over the		medication,		:: 			
		major population regions		aspirin; living		April 19, 2024 by guest. Protected			
		in California.		conditions		cted by cop			

2	
4	
5	
6	
7	
8	
9	
10	
11	
12	
13	
14	
15 16	
16	
17	
18	
19	
20	
21	
22	
23	
24	
25 26	
26	
27	
27 28	
29	
30	
31	
32	
33	
34	
35 36	
36	
37 38	
38	

age 113	of 133			BMJ Opei	BMJ Open  BMJ Open  Incomplete				
No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete coutcome data	Selective reporting	Conflict of interest	Other
0 1 2 3 4 5 6 7			COMPOS	(income, income inequality, education, population size, racial composition, unemployment).		outcome data			
8 9 0 55 1 2 3 4 5 6 7 8 9 0 1 2 3 4 5 6	Gan et al. 2013	Probably Low  Using high spatial resolution land use regression models to estimate residential exposure to traffic-related air pollutants including black carbon. During the 5-year exposure period, individual exposures to ambient air pollutants were estimated at each person's residential postal code centroid using land	Low The study used International Statistical Classification of Diseases, 9th Revision (ICD-9) codes 490–492 and 496 or 10th Revision (ICD-10) codes J40–J44 to identify COPD cases during the 4-year follow-up period.	Probably High Individual-level covariates: age, sex, preexisting comorbid conditions; and neighborhood socioeconomic status (SES).	Low Data obtained for a cohort of people (45-85 years old) registered with the provincial health insurance plan. Study provided total number of subjects along with those lost during the	Probably Low During the 4-year follow-up period, 38,377 (8%) subjects were lost to follow-up because of moving out of the province or dying from other diseases.	Probably Low There was insufficient information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of	Low The authors declare they have no actual or potential competing financial interests.	Low No other potential sources of bias identified.

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data		Conflict of interest	Other
8 9			Probably Low	Low	Probably Low	Low	Probably Low	Probably Low	Low	Low
9 10	56	Hvidtfeldt	The PM, NO <sub>2</sub> , BC, and	Participants who died	Age, sex,	Data obtained for	There was no	There was	The authors	No other
11		et al. 2019	O <sub>3</sub> concentrations at	from external causes such	educational	a cohort of men	information on	insufficient	declare they	potential
12			residential addresses of	as injuries, accidents and	attainment,	and women aged	the rate of lost	information	have no	sources of
13 14			the cohort members were	suicides (International	occupational	50–64 years	follow up.	about	competing	bias
15			derived by a	Classification of	status, marital	residing in the	e	selective	financial	identified.
16			high-resolution	Diseases, 10th	status, smoking	areas of	) Mo	outcome to	interests.	
17 18			dispersion modelling	Revision-ICD-10 codes	(status, intensity,	Copenhagen and	nttp	judge for low		
19			system which	S–Z) were censored at	and duration),	Aarhus.	://br	risk, but		
20			incorporates	date of death. In addition,	environmental		njop	indirect		
21			contributions from local,	the study investigated	tobacco smoke		en.r	evidence that		
22 23			urban, and regional	cardiovascular (ICD10	(ETS), alcohol		) J	suggests study		
24			sources of precursors to	codes I00–I99) and	consumption, body		COM	was free of		
25			PM, NO <sub>2</sub> , BC, and O <sub>3</sub> .	respiratory (ICD10 codes	mass index, waist		on	selective		
26 27				J00–J99 and C34)	circumference,		Api	report.		
28				subgroups of mortality.	fruit consumption,					
29					vegetable		9, 20			
30 31					consumption,		April 19, 2024 by			
32					physical activity;		oy g			
33					neighborhood		guest.			
34					level					
35 36					socioeconomic		Protected			
37					status (SES).		) 			
38 <sup>ˈ</sup>			1	1	` ′		9			

2 3 4	
5	
6	
7	
8	
9	
10	
11	
12	
13	
14	
15	
16 17	
17	
18 19	
20	
21	
22	
23	
24	
25	
26	
27	
28	
29	
30	
31	
32	
33	
34	
35	
36 37	
38	
39	

Page	e 115 d	115 of 133 BMJ Open 96 bm 96 b									
 <u> </u>  }							Incomplete				
5 5	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data	Selective reporting	Conflict of interest	Other	
}			Probably Low	Probably Low	Probably High	Low	Probably High	Probably Low	Low	Low	
111 112 113 114 115 116 117 118 119 120 121 122 122 122 122 122 122 123 124 125 126 127 128 129 131 131 131 131 131 131 131 131 131 13	57	Thurston et al. 2016	The mean concentrations of PM <sub>2.5</sub> mass and trace constituents were obtained from U.S.  Environmental Protection Agency Air Quality System. These PM <sub>2.5</sub> constituent data were analyzed to derive estimates of source apportioned PM <sub>2.5</sub> mass exposure concentrations using the absolute principal component analysis (APCA) PM <sub>2.5</sub> source apportionment method.	More than 99% of known deaths were assigned a cause using the International Classification of Diseases, 9th and 10th Revision (ICD-9 codes 410–414; ICD-10 codes I20–I25).	Active smoking and former smoking, passive smoke exposure, possible workplace exposure to PM, occupational dirtiness index, marital status, education, BMI and BMI <sup>2</sup> , consumption of beer, wine, and other alcohol, quintile of dietary fat consumption, quintile of combined dietary vegetable, fruit, fiber consumption; Six ecologic	Data obtained for a cohort of persons at least 30 years of age, in households including someone at least 45 years of age and resided in all 50 states, the District of Columbia, and Puerto Rico.	The analytic cohort included 445,860 participants, with 34,408 Ischemic heart disease deaths (of a total of 157,572 deaths from all causes) occurring during follow-up.	There was insufficient information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of selective report.	No competing financial interests.	No other potential sources of bias identified.	
37   38   39 40 41					covariates.		Protected by copyright.	:			

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on the outcome data of the outcome data on the outcome data of the outcome data on the outcome		Conflict of interest	Other
8 9			Probably Low	Low	Probably Low	Low	Probably Low	Probably Low	Low	Low
10	58	Yang et al.	Land use regression	Deaths were coded	Age at entry,	Data obtained for	There was no	There was	The authors	No other
11		2018	models were derived	according to the	gender, individual	a cohort of	information on	insufficient	declare they	potential
12			from street level	International	smoking status,	people who were	the rate of lost $\frac{5}{2}$	information	have no	sources of
13 14			measurements collected	classification of Diseases,	body mass index	older than or	follow up.	about	actual or	bias
15			during two sampling	10th Revision (ICD-10;	(BMI), physical	equal to 65 years	ed fr	selective	potential	identified.
16			campaigns conducted in	WHO 2010) including	activity, education	old.	om om	outcome to	competing	
17 18			2014 and 2015.	natural cause mortality	level and monthly		http	judge for low	financial	
19				(A00–R99), overall	expenses;		://br	risk, but	interests.	
20				cardiovascular disease	percentage of		mjop	indirect		
21 22				(I00–I99) and overall	participants who		en.k	evidence that		
23				respiratory disease	were equal to or		<u> </u>	suggests study		
24				(J00–J47 and J80–J99).	older than 65 years	(0).	com	was free of		
25				Subcategories included	old, percentage of	"eh	on /	selective		
26 27				Ischemic heart disease	participants whose			report.		
28				(IHD) (I20–I25),	educational level		119			
29				cerebrovascular disease	was higher than		9, 20			
30 31				(I60–I69), Pneumonia	secondary school,		124			
32				(J12–J18) and chronic	average income		ру д			
33				obstructive pulmonary	per month and		ues			
34				disease (COPD) (J40–I44	percentage of		 			
35 36				and I47).	smokers.		April 19, 2024 by guest. Protected by			
37							Xed			
38									I.	
39							сор			

2 3 4	
5	
6	
7	
8	L
9	
10	
11	
12	
13	
14	
15	
16	
17	
18	
19	
20	
21	
22	
23	
24	
25	
26	
27	
28	
29	
30	
31	
32	
33	
34	
35	
36 37 38	
37	
39	
40	

5 5 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on the outcome data of the outcome		Conflict of interest	Other
3			Probably Low	Low	Probably High	Low	Probably Low	Probably Low	Low	Low
10	59	Gan et al.	Land use regression to	A coronary heart disease	Model adjusted for	Study provided	During the	There was	The authors	No other
11		2011	estimate air pollution	hospitalization case is a	age, sex,	total number of	4-year	insufficient	declare they	potential
12			concentrations and	record of hospitalization	preexisting	subjects along	follow-up	information	have no	sources of
3  4			exposure assigned to	with the following	comorbidity, and	with those lost	period, 17,542	about	actual or	bias
5			residential centroid.	International Statistical	neighborhood	during the	(3.9%) moved ⊕	selective	potential	identified.
6				Classification of	socioeconomic	follow-up period.	out of the	outcome to	competing	
7  8				Diseases, 9th Revision	status. No		province and	judge for low	financial	
9				codes, ICD-9, 410–414	individual data on		16,367 (3.6%)	risk, but	interests.	
20				and 429.2or 10th	behavioral risk		died from others	indirect		
21				Revision (ICD-10),	factors.	•	diseases,	evidence that		
22				I20–I25, as the principal			leaving 3	suggests study		
24				diagnosis (the most		<b>10</b> 1.	418,826	was free of		
25				responsible diagnosis) for			$(9_{2.5}\%)$ 9	selective		
26 27				a hospital admission in			subjects at the \rightarrow{\	report.		
28				the hospitalization			end of			
9				database. A coronary			follow-up.			
30				heart disease death is a			)24			
31 32				death record with			by g			
33				coronary heart disease as			Jues			
34				the cause of death in the			2024 by guest. Protected			
35   36				provincial death			rotec			
37				registration database.			cted			
88							9	I	1	1

5 5	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data ≤		Conflict of interest	Other
3			Probably High	Low	Probably Low	Low	Probably Low	Probably Low	Low	Low
0	60	De	Used black smoke (BS)	The study obtained	Individual-level	Data obtained for	There was no 22	There was	No	No other
1		Kluizenaa	as an indicator of EC	information on the	covariates: age,	a cohort of	information on	insufficient	competing	potential
2		r et al.	concentrations. Derived	incidence of	gender, marital	27,070	the rate of lost	information	financial	sources of
3		2013	background EC	hospital-based Ischemic	status, education,	non-institutionali	follow up.	about	interests.	bias
5			concentrations from BS	heart disease	smoking, alcohol	zed subjects.	ed fr	selective		identified.
6			measured at two regional	(International	use, physical		om.	outcome to		
7 8			monitoring sites. Local	Classification of Diseases	activity, body mass		http	judge for low		
9			traffic-related EC	[ICD9] 410-414) and	index, living		://br	risk, but		
20			emission contributions	cerebrovascular disease	conditions		njop	indirect		
11			were estimated based on	(ICD9 430-438) in the	(employment		en.t	evidence that		
22			fuel-specific EC content	study population.	status, financial		omj.	suggests study		
4			of exhaust PM <sub>10</sub>		problems).	<b>101</b>	com	was free of		
25			emission. Used the			Teh,	on on	selective		
6			traffic-related EC				Apı	report.		
8			emissions as input to				11 10			
9			calculate local EC				9, 20			
0			concentrations, assuming				)24			
2			absence of other local EC				by g			
3			sources. Also assumed				April 19, 2024 by guest. Protected			
4			that dispersion dynamics				t. Pr			
5 6			of EC are identical to				ote:			
37			those of PM <sub>10</sub> .				cted			
8 -							9		<u> </u>	

2	
3	
4	
5	
6	
7	
8	-
9	
10	
11	
12	
13	
14	
15	
16	
16 17 18	
18	
19	
20	
21	
20 21 22 23	
23	
24	
25	
26	
26 27	
28 29	
29	
30	
31	
32	
33	
34	
35	
36 37	
38	
50	Ш

Pag	Page 119 of 133 BMJ Open						36/bmJop			
1 2 3 4							Incomplete			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data		Conflict of interest	Other
8			Probably Low	Probably Low	Probably Low	Low	Probably Low	Probably Low	Low	Low
9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37	61	Vedal et al. 2013	The exposure estimation were used the national spatial model predictions and secondary exposure measures of citywide average exposures and distance to major roadways.	All outcomes were reported via questionnaire and assessed via physician-adjudicator review of medical records following established protocols.	Individual-level covariates: age, body mass index, smoking status, cigarettes smoked per day and years of smoking, systolic blood pressure, history of hypertension, hypercholesterole mia, history of diabetes, education, household income level, and race.	Data obtained for a cohort of postmenopausal women.	y guest.	insufficient information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of selective report.	No financial interests.	No other potential sources of bias identified.
38   39 40 41 42				1	1	<u> </u>	Protected by copyright.		<u> </u>	

4 5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on to outcome data	Selective reporting	Conflict of interest	Other
3			High	Low	Probably Low	Low	Low $^{\text{ay}}_{\text{N}}$	Probably Low	Low	Low
10	62	Rahmatini	BC were collected from	Daily non-accidental	Models adjusted	Study included	Daily counts	There was	The authors	No other
11		a et al.	two monitors (Sharif and	deaths were obtained	for time,	all daily	for death were	insufficient	of this	potential
12		2021	Setad) with data recorded	from Ministry of Health	temperature,	non-accidental	obtained, so	information	article	sources of
13   14			at 5 min intervals. BC	and Medical Education	relative humidity,	deaths from	likely have all	about	declare that	bias
15			measurements began	database. The causes of	atmospheric	Ministry of	outcome data.	selective	they have	identified.
16			from March 2017 to	death were coded	pressure, PM2.5	Health and	However, any	outcome to	no conflict	
17   18			August 2017. But the	according to the	data, Day of week	Medical	potential errors	judge for low	of interests.	
19			gaseous pollutant at the	International	(DOW) and public	Education	or missing data	risk, but		
20			Setad site were unreliable	Classification of Disease	holidays.	database from	did not depend	indirect		
21			and models utilizing the	(10th revision—ICD-10).	. 01	March 2017 to	on air pollution	evidence that		
22			2-site data were			August 2017.	levels.	suggests		
24			unsatisfactory. So, only			(0)	com	study was		
25			the Sharif data were used.				or	free of		
26   27							ı Ap	selective		
28							April 19, 2024 by	report.		
29							9, 20			
30							024			
31   32							by g			
33							' guest.			
34										
35							rote			
36 37							Protected			
38 38			ı	I	1	ı	by			

1	
2	
3	
4	
5	
6	
7	
8	
9	
10	
11	
12	
13	
14	
15	
16	
17	
18	
19	
20	
21	
22	
23	
24	
25	
26	
27	
28	
29	
30 31	
≺ I	
32	
32 33	
32 33 34	
32 33 34 35	
32 33 34 35 36	
32 33 34 35	

5 5	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data S		Conflict of interest	Other
3			Probably Low	Probably Low	Probably Low	Low	Low 20	Probably Low	Low	Low
111 112 113 114 115 116 117 118 119 120 121 122 122 122 123 124 125 126 127 128 129 130 131 131 131 131 131 131 131 131 131	63	Liu et al. 2021b	Annual county-level exposures of PM2.5 and its constituents for each participant were assessed by aggregating satellite-derived estimates at a monthly time-scale and 1 km-resolution.	The three cardiovascular events as health outcomes: 1) total cardiovascular disease, including but not limited to hypertension and stroke; 2) hypertension; 3) stroke were defined according to the Disease Classification Codebook for Chinese Family Panel Studies.	Model adjusted for age, gender, education level (illiteracy, primary to middle school, and high school or above), household income (RMB, strata of ≤ 15,000, 15,000 − 40,000, and 40,000 +, grouped according to the upper and lower quartiles), urbanicity (urban/rural, defined by CFPS participants' home addresses).	All of participants were drawn from the China Family Panel Studies (CFPS) launched by Peking University Institute of Social Science Survey (ISSS) in 2010, an ongoing national longitudinal survey of social-demograp hy in China.	The cohort included 14,331 adults who completed three waves of follow-up.  The cohort included 14,331 adults who completed three waves of follow-up.	insufficient information about selective	The authors declare that they have no known competing financial interests or personal relationship s that could have appeared to influence the work reported in this paper.	No other potential sources of bias identified.
39 40 41 42							copyright.			

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data		Conflict of interest	Other
8 9			Probably Low	Low	Probably Low	Low	Probably Low	Probably Low	Low	Low
9 10	64	Lavigne et	A spatial PM2.5 surface	Incident childhood	Model adjusted for	The study used	There was no	There was	The authors	No other
11		al. 2021	gridded at a resolution of	asthma cases were	parity, child sex,	data on singleton	information on	insufficient	declared	potential
12			approximately 1-km2	identified according to	breastfeeding	live births that	the rate of lost $\frac{8}{2}$	information	that there is	sources of
13 14			was derived using	International	status at the time	occurred	follow up.	about	no conflict	bias
15			multiple satellite-based	Classification of Diseases	of discharge,	between April 1st	ed <del>i</del>	selective	of interest.	identified.
16			retrievals of aerosol	[ICD]-10: J45.	maternal smoking	2006 and March	rom	outcome to		
17			optical depth in		during pregnancy,	31st 2014 in the	h#p	judge for low		
18 19			combination with a		maternal atopy,	Province of	)://b	risk, but		
20			chemical transport model,		gestational age and	Ontario, Canada.	njop	indirect		
21			and enhanced through		birth weight.	Mother-infant	oen.	evidence that		
22 23			statistical incorporation			pair data were	bmj.	suggests		
24			of ground- based			obtained from	com	study was		
25			observations (including			the Better	) on	free of		
26			BC).			Outcomes	n April			
27 28			,			Registry &		report		
29						Network	9, 2	_		
30						(BORN) Ontario,	2024 by guest.			
31						a province wide	by			
32 33						birth registry that	gue			
34						captures				
35						perinatal health	Protected			
36						1	ecte			
37 38						information.	d by			
39 39							8	1		

2	
3	
4	
5	
6	
7	
8	
9	
10	
11 12	
13	
14	
15	
16	
17	
18	
19	
20	
21	
22	
23	
24	
25	
26 27	
27	
28	
29	
30	
31	
32	
27	
3 <del>4</del>	
36	
37	
38	

No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data S		Conflict of interest	Other
		Probably Low	Probably Low	Probably Low	Low	Probably Low	Probably Low	Low	Low
0 65	Rodins et	The study used the	Cardiovascular outcomes	Model adjusted for	The study used	There was no	There was	The authors	No other
1	al. 2020	validated,	in the HNR Study were	age, sex,	baseline	information on		declare that	potential
2		time-dependent,	determined by an	individual and	(2000–2003) and	the rate of lost $\frac{8}{2}$	information	they have	sources of
3 4		three-dimensional	independent endpoint	neighborhood	14 years	the rate of lost of follow up.	about	no known	bias
5		European Air Pollution	committee based on	SES, BMI,	follow-up data	ed f	selective	competing	identified.
6		Dispersion chemistry	self-reports, physician	nighttime traffic	from the German	rom	outcome to	financial	
7		transport model	and next-of-kin	noise exposure and	HNR Study, an	http	judge for low	interests or	
8 9		(EURAD) to estimate the	interviews, and medical	lifestyle factors:	ongoing	o://bi	risk, but	personal	
0		exposure to EC.	records.	smoking, alcohol	population-based	njop	indirect	relationship	
1				consumption,	prospective	oen.	evidence that	s that could	
2   3				physical activity	cohort study.	bmj	suggests	have	
4				and nutritional	10,	.con	study was	appeared to	
5				pattern.	\ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \	n/ oi	free of	influence	
6				Panerin		n Ar	selective	the work	
7 8							report.	reported in	
9						9, 2	o lepoit.	this paper.	
0						2024		uns paper.	
1						l by	-		
2   3						gue			
4						ist.			
5						Prot	[		
6						 			
7 8						<u> </u>	:		
o 9						from http://bmjopen.bmj.com/ on April 19, 2024 by guest. Protected by copyright.			
0						руп			
1 2						ight.			

Page 124 of 133

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data see	Selective reporting	Conflict of interest	Other
8 9			Probably Low	Low	Probably High	Low	Low $\stackrel{\mathbf{a}}{\checkmark}$	Probably Low	Low	Low
10	66	Kovačević	The daily average	The data of emergency	Model adjusted for	Study included	Daily counts	There was	The authors	No other
11		et al. 2020	concentration of BC were	department (ED) visits	seasonality,	all the data of	for emergency 🖯	insufficient	declare no	potential
12			collected from three	for allergic asthma were	long-term trends,	emergency	department \frac{8}{2}	information	conflict of	sources of
13 14			automatic ambient air	collected from the Užice	temperature,	department (ED)	(ED) visits	about	interest.	bias
15			quality monitoring	Health Centre, either	humidity, air	visits for allergic	were obtained,	selective		identified.
16			stations located in Užice,	from the EDs	pressure, air	asthma were	so likely have	outcome to		
17 18			Sevojno, and Kosjerić.	(ambulances or home	pollutants and	collected from	all outcome	judge for low		
19			BC were measured	care) in Užice, Sevojno,	pollens.	the Užice Health	data. However,	risk, but		
20			between 1st July 2012	and Kosjerić or from a	1/6	Centre, either	any potential	indirect		
21			and 30th June 2014.	general hospital in Užice.	' (2)	from the EDs	errors or	evidence that		
22			There was no information	International		(ambulances or	missing data	suggests		
24			about missing data.	Classification of		home care) in	did not depend	study was		
25				Diseases, 10th revision,		Užice, Sevojno,	on air pollution	free of		
26 27				codes were used in the		and Kosjerić or	levels.	selective		
28				diagnosis of allergic		from a general		report.		
29				asthma or asthma with		hospital in Užice	9, 2			
30				coexisting allergic rhinitis		during 1st July	2024 by			
31				(AR).		2012 to 30th	by g			
33						June 2014.	guest.			
34							l 7			
35							rote			
36 37							rotected			
38							9			

2 3	
5 [	
6	
7	
8	_
9	
10	
11	
12	
13	
14	
15	
16	
17	
18	
19	
20	
21	
22	
23	
24	
25	
26	
27 28	
28	
30	
31	
32	
33	
34	
35	
36	
37	
38 <sup>L</sup>	

7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data ≤		Conflict of interest	Other
3			Probably Low	Probably Low	Probably Low	Low	Probably Low	Probably Low	Low	Low
0 6	57	Hasslöf et	BC levels were modelled	The outcomes were	Model adjusted for	In the	Of these, 224 🕺	There was	The authors	No other
11		al. 2020	using EnviMan (Opsis	plaque presence and	age, sex, air	cardiovascular	were missing		declare that	potential
12			AB, Sweden) by the	CIMT of the right carotid	pollutant,	subcohort of the	data on plaque	information	they have	sources of
13 14			Environmental	artery, which were	education level,	MDCS cohort,	and 20 on	about	no known	bias
15			Department of Malm"o.	assessed by ultrasound	smoke score,	6031 participants	CIMT,	selective	competing	identified.
16			The program uses a	examination B-mode	apoB/apoA1 ratio,	who had a	respectively.	outcome to	financial	
17 18			Gaussian dispersion	ultrasonography,	use of lipid	residential	Hence, the	judge for low	interests or	
19			model (AERMOD)	conducted by trained and	lowering drugs,	address within	number of	risk, but	personal	
20			combined with an	certified sonographers.	living alone,	the air pollution	participants	indirect	relationship	
21			emission database for the		cardiovascular	modelling area.	included in the	evidence that	s that could	
22			county of Scania in		heredity, diabetes	Of these, 224	plaque analyses.	suggests	have	
24			Sweden.		mellitus, waist hip	were missing	were 5807 and	study was	appeared to	
25					ratio, physical	data on plaque	in the CIMT	free of	influence	
26 27					activity, alcohol	and 20 on CIMT,	analyses 6011. ⋛	selective	the work	
28					consumption,	respectively. The	il 19,	report.	reported in	
29					median income	number of	9, 20		this paper.	
30 31					level in residential	participants	)24			
32					area, systolic blood	included in the	by g			
33					pressure and being	plaque analyses	lues			
34					born outside of	were 5807 and in	t. Pr			
35 36					Sweden.	the CIMT	roter			
37						analyses 6011.	2024 by guest. Protected by			

Page 126 of 133

5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data ≤	Selective reporting	Conflict of interest	Other
8 9			Probably High	Probably Low	Probably High	Low	Low ex	Probably Low	Low	Low
9 10	68	Wang et	BC were collected from a	All patients treated at the	Model adjusted for	Study included	Daily counts	There was	The authors	No other
11		al. 2019b	routine air quality	Cardiac Catheterization	seasonality,	all patients	for all patients	insufficient	declare that	potential
12			monitoring site operated	Laboratory (Cath Lab) at	long-term trends,	treated at the	were obtained,	information	they have	sources of
13 14			by the New York State	URMC in Rochester, NY	temperature and	Cardiac	so likely have	about	no	bias
15			Department of	for STEMI, who resided	relative humidity.	Catheterization	all outcome	selective	competing	identified.
16			Environmental	within 15 miles of the		Laboratory (Cath	data. However, $\stackrel{\circ}{\exists}$	outcome to	interests.	
17 18			Conservation	pollution monitoring	<b>'</b> O.	Lab) at URMC	any potential	judge for low		
19			continuously throughout	station in Rochester were		in Rochester, NY	errors or	risk, but		
20			the study period	included. American	' /	for STEMI	missing data	indirect		
21			(2005–2016). There was	College of Cardiology	' (2)	throughout the	did not depend	evidence that		
22 23			no information about	(ACC)/American Heart		study period	on air pollution.	suggests		
24			missing data.	Association (AHA)		(2005–2016).	levels.	study was		
25				guidelines were used at			/ on	free of		
26 27				the time of Cath Lab				selective		
28				admission to diagnose				report.		
29				STEMI.			9, 20	•		
30							024			
31 32							by (			
33							gues			
34							st. F			
35							rote			
36 37							April 19, 2024 by guest. Protected			
37 38							d by			

2	
3	
4	
5	
7	
8	L
9	
10	
11	
12	
13	
14	
15	
16	
17	
18	
19	
20	
21	
22 23	
24	
25	
26	
27	
28	
29	
30	
31	
32	
33	
34	
35	
36	
37 38	
38 39	
39	

No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data ≤	Selective reporting	Conflict of interest	Other
		Probably Low	Low	Probably Low	Low	Probably Low		Low	Low
0 69	Ljungman	Based on detailed	The International	Model adjusted for	The study	The study used	There was	The authors	No other
1	et al. 2019	emission databases,	Classification of	sex, calendar year,	included	high-quality	insufficient	declare they	potential
2		monitoring data, and	Diseases, Ninth Revision	subcohort,	individuals in	,		have no	sources of
3 4		high-resolution	(ICD-9) codes 410–414	smoking status,	two cohorts from	and 500 comprehensive 200	about	actual or	bias
5		dispersion models, the	and ICD-10 I20-25 codes	alcohol	Gothenburg, four	national patien	selective	potential	identified.
6		study calculated source	were used to define IHD	consumption in	pooled cohorts	and death	outcome to	competing	
7		contributions to black	and ICD-9 codes	Stockholm and	from Stockholm,	registries,	judge for low	financial	
8 9		carbon (BC) from road	431–436 and ICD-10	Umeå, physical	and one cohort	and death registries, minimizing loss to	risk, but	interests.	
0		wear, traffic exhaust,	codes I61– I65 were used	activity, marital	from Umeå. In	loss to	indirect		
1		residential heating, and	to define stroke.	status,	total, 114,758	follow-up for	evidence that		
2   3		other sources in		socioeconomic	individuals were		suggests		
4		Gothenburg, Stockholm,		index by	included from all	our outcomes of interest.  Missing	study was		
5		and Umeå.		occupation,	study areas.	Missing 9	free of		
5 7				education level,		information for	selective		
8				occupation status,		information for Portion variables ≤ 1.00	report.		
9				and mean		5% not	1		
0				neighborhood		specified.			
1 2				individual income		by (			
3				in persons of		Jues			
4				working age by					
5				Small Areas for		rote			
6 7				Market Statistics.		ctec			
, 8				Market Statistics.		<u> </u>			
9						5% not specified. Protected by copyright.			
0						yrig			
1 2						ht.			

Probably Low Liu et al.  2021a  Probably Low Low Probably Low Annual mean COPD was defined by concentrations of BC for diagnosis of International the study participants' Classification of  Probably Low Low Probably Low Probably Low Probably Low The study used data from three cohorts within the ELAPSE With complete about	The authors Non declare that properties they have	Low No other potential
10   70   Liu et al.   Annual mean   COPD was defined by   Model adjusted for   The study used   From a total of No.	nt declare that point they have so	ootential
	on they have so	
2010 were estimated at the study participants'   Classification of the study participants   Classification of the study participants'   Classification of the ELAPSE   with complete   about		
the study participants' Classification of duration, smoking the ELAPSE with complete about	no known b	sources of
14 duration, smoking the ELAFSE with complete a about	1	oias
baseline residential Diseases, 9th Revision intensity, project with air pollution $\stackrel{\Omega}{=}$ selective	competing	dentified.
addresses, using (ICD-9) codes 490–492, body-mass index, available exposure data, outcome	o financial	
standardized and 494–496, or ICD-10 marital status, information on the study judge fo	low interests or	
Europe-wide hybrid land use regression (LUR)  Europe-wide hybrid land use regression (LUR)  Europe-wide hybrid land codes J40–44.  employment codes J40–44.  employment discharge excluded 633 prisk, but discharge indirect	personal	
	relationship	
models. The LUR model level and diagnoses. Mean with COPD at evidence evidence	that s that could	
utilized routine area-level annual follow-up time is baseline and suggests	have	
monitoring data from the year income. 16.6 years. 7,586 g study was	appeared to	
European Environment participants 9 free of	influence	
Agency (EEA) AirBase with missing $\frac{26}{9}$ selective	the work	
for PM2.5, NO2, and O3, information on control report.	reported in	
and ESCAPE monitoring confounders.	this paper.	
data for BC as the		
dependent variable. BC		
was measured by the		
reflectance of PM2.5		
filters and expressed in		
and ESCAPE monitoring data for BC as the dependent variable. BC was measured by the reflectance of PM2.5 filters and expressed in absorbance units.		

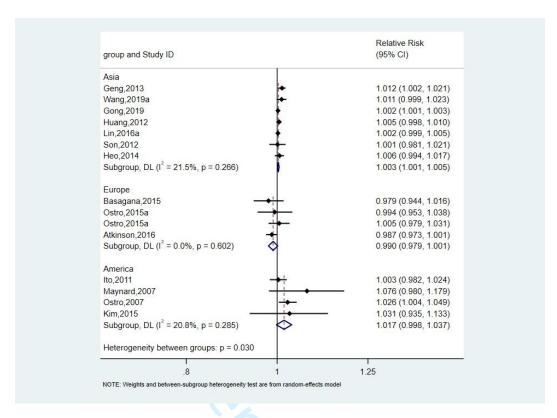
45

7Table S8 Assessment of certainty of evidence for the outcomes.

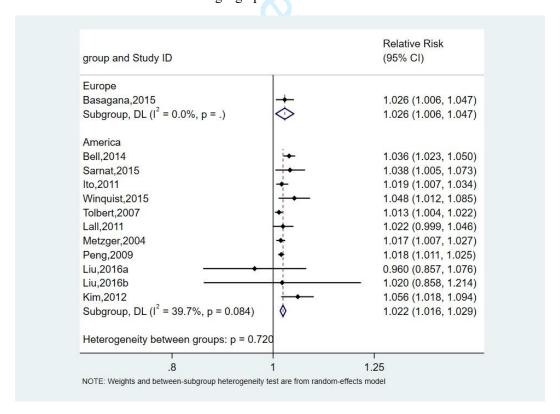
8 9 Fridance					Reaso	ons for downgrading						ı	N	ons for upgrading				Final
Evidence 10	A1	Rationale	A2	Rationale	A3	Rationale	A4	Rationale	A5	Rationale	B1	Rationale	0 2 2	Rationale	В3	Rationale	Overall	certainty
11 12  *Soute effects of  IF#:/EC on CVD in  15  PM2.5-unadjusted  16  1**Podel	0	Little influence on the overall effect	0	All included studies were consistent with our prespecified PECOS	0	80% PI 1.005 (95%CI: 1.001, 1.009) does not include unity	0	Risk estimates reported by the studies are sufficiently precise	-1	publication bias exised, RR adjusted for publication bias with trim and fill.	0	Insufficient basis for upgrading	Downloaded from http	Confounders would shift the RR in both directions	0	Evidence of increase in risk with increasing exposure	-1	Low
18 1Acute effects of BC 20 BC/EC on CVD in 21 22/12.5-adjusted 2336del 24	0	Little influence on the overall effect	0	All included studies were consistent with our prespecified PECOS	0	80% PI 1.011(95%CI: 1.002, 1.020) does not include unity	0	Risk estimates reported by the studies are sufficiently precise	0	No evidence of publication bias	0	Insufficient basis for upgrading	o://bmiopea.bmi.com	Confounders would shift the RR in both directions	0	Evidence of increase in risk with increasing exposure	0	Moderate
25 26 ronic effects of 27 /EC on CVD in 28 / <sub>M2.5</sub> -unadjusted 29 30 del 31	0	Little influence on the overall effect	0	All included studies were consistent with our prespecified PECOS	0	80% PI 1.068 (95%CI: 0.965, 1.181) include unity but no larger than twice the 95%CI	0	Risk estimates reported by the studies are sufficiently precise	0	No evidence of publication bias	0	Insufficient basis for upgrading	/ on April∽l9, 2024 t	Confounders would shift the RR in both directions	0	No evidence of a clear increasing risk with exposure	0	Moderate
32 Abbreviations:						diseases; RES: respirate						-	A A ⊃¥auest. Protected by copyright.	= limitations in studie	s (risk	of bias); A2 =		

**BMJ** Open

36/bmjopen-2021-049516 on 3 M



**Figure S1** Impact of short-term exposure to BC/EC on cardiovascular mortality stratified by geographical locations.



**Figure S2** Impact of short-term exposure to BC/EC on cardiovascular morbidity stratified by geographical locations.

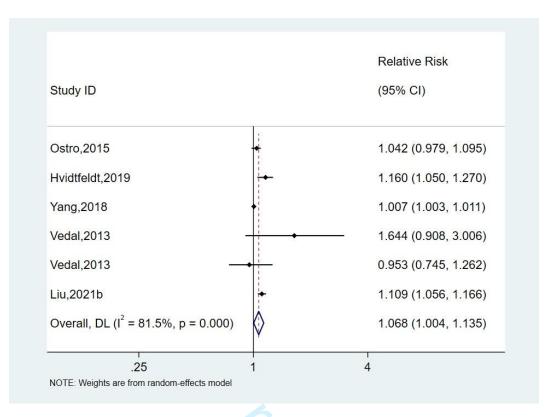
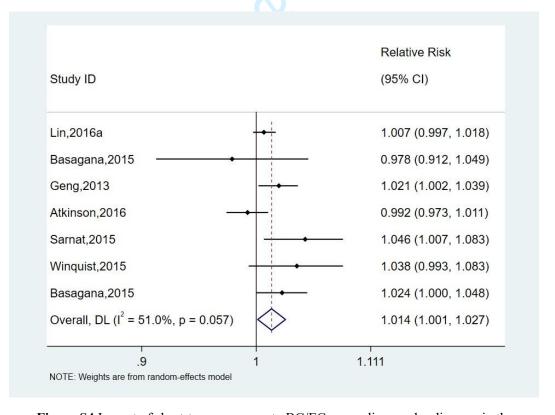


Figure S3 Impact of long-term exposure to BC/EC on cardiovascular diseases.



**Figure S4** Impact of short-term exposure to BC/EC on cardiovascular diseases in the PM<sub>2.5</sub>-adjusted model.



46 47

## PRISMA 2020 Checklist

		-2C	
Section and Topic	Item #	Checklist item 04 95	Location where item is reported
TITLE		6	
Title	1	Identify the report as a systematic review.	#1
ABSTRACT		<u>~</u> <u>~</u>	
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	#3-4
INTRODUCTION		ŶŶŎ	
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	#6-8
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	#8
METHODS		olr color	
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	#9
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to Hentify studies. Specify the date when each source was last searched or consulted.	#8-9
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	#8-9
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	#10
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	#10-11
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each gutcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	#10-11
, \$	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	#10-11
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	#11-12
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	#11
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intergention characteristics and comparing against the planned groups for each synthesis (item #5)).	#11
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summer statistics, or data conversions.	#11, 14-15
7	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	#11
] 3 9	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	#11-12
<b>)</b>	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysig, meta-regression).	#11-12
1	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	#11-12
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases.	#12
Certainty	15	Describe any methods use to topassess/icertainty (ortconfidence) in the body of evidence for iale butsonnem	#11



## PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
assessment		316	
RESULTS	,	) A	
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	#15
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	#15
Study characteristics	17	Cite each included study and present its characteristics.	#15
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	#22
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	#15-18
Results of	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	#23-24
syntheses	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	#18
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	#19-21
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	#21
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	#22-24
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	#22
DISCUSSION		5	
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	#25-29
	23b	Discuss any limitations of the evidence included in the review.	#29-30
	23c	Discuss any limitations of the review processes used.	#29-30
	23d	Discuss implications of the results for practice, policy, and future research.	#28-29
OTHER INFORMA	TION	<u>Q</u>	
Registration and	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	#8
protocol	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	#8
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	#8
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the region.	#34
Competing interests	26	Declare any competing interests of review authors.	#35
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	#36