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

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Title Page

Title:

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

Respiratory Diseases: A Systematic Review and Meta-Analysis

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Abstract

Background: Adverse health effects of fine particles ($PM_{2.5}$) 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 μ g/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.^[1] 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_{2.5}, are well documented. In 2017, a total of 2.94 million deaths resulted from ambient PM worldwide.^[3-5] PM_{2.5} 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_{2.5}. 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.^[8, 9] 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.^[4] 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.^[13, 14] 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 6th, 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) 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 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

Page 11 of 122

BMJ Open

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 μ 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.^[16, 17] 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.^[18] In addition, the same cohort data were analyzed in different studies and the latest studies were included in the systematic review and meta-analysis.^[19-21]

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.^[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 $PM_{2.5}$ is a potential confounder in assessing the health effects of $PM_{2.5}$ constituents.^[7] For overall and outcome analysis, PM_{2.5}-adjusted estimates and PM_{2.5}-unadjusted estimates in the models were combined, respectively where more Regarding than three estimates were available. the subgroup analysis. PM2.5-unadjusted estimates were analyzed, while PM2.5-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

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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 μ 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 μ g/m³, 95% CI: 0.996–1.025) in overall analyses (Table 1). However, both cardiovascular (RR = 1.016 per 1 μ g/m³, 95% CI: 1.004–1.029) and respiratory diseases (RR = 1.038 per 1 μ 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 μ g/m³, 95% CI: 1.016–1.029) were higher compared to their effect on mortality (RR = 1.003 per 1 μ 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 μ g/m³, 95% CI: 1.006–1.016), and then diminished on lag 1 (RR = 1.005 per 1 μ g/m³, 95% CI: 1.002–1.008) and lag 2 (RR = 1.002 per 1 μ 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.^[18] In addition, just one study in Asia was performed assessing the short-term effects of BC or EC on stroke morbidity^[25] (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).

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	PM _{2.5} -unadjusted model						C PM _{2.5} -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)	\mathbf{I}^2	
Cardiovascular Diseases						22. [
Age						Downloaded 6				
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)	_	_	 	—	_	—	
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, 1.029)	87.80%	_	/br	<u> </u>	—	—	
Outcome						http://bmjopen.bu				
Morbidity	12	12	1.022 (1.016, 1.029)	37.20%	0.163	4 <mark>en.b</mark>	5	1.018 (1.006, 1.031)	39.50%	
Mortality	14	15	1.003 (1.001, 1.006)	29.70%	0.266	4 .com	4	1.006 (0.993, 1.019)	42.90%	
Respiratory Diseases						om/				
Age						on A				
All population	16	18	1.010 (0.996, 1.025)	86.80%	0.627	April 1	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	<u></u> ,		—	_	
≥65	3	4	1.038 (1.006, 1.071)	83.30%	—	2024 by 	_	—	—	
Outcome						, gue				
Morbidity	10	10	1.012 (0.993, 1.031)	91.80%	0.671	guest. P	5	0.996 (0.987, 1.004)	0	
Mortality	10	11	1.013 (0.997, 1.030)	66.40%	0.328	₃ Tote	3	1.017 (0.985, 1.050)	48.30	
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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.^[20, 26, 27] 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: 1.020-1.140).^[19]

3.3 Results from the PM_{2.5}-adjusted model

In the PM_{2.5}-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 μ 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_{2.5}-unadjusted model. In addition, the impact of BC or EC on cardiovascular morbidity in the PM_{2.5}-adjusted model (RR = 1.018 per 1 μ g/m³, 95% CI: 1.006-1.031) was consistent with the results in the PM_{2.5}-unadjusted model (RR = 1.022 per 1 μ 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 μ g/m³, 95% CI: 1.001-1.006), while no association was observed in the PM_{2.5}-adjusted model (RR = 1.006 per 1 μ g/m³, 95% CI: 0.993-1.019) (Table 1). On the other hand, consistent

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 results (RR = 1.002 per 1 μ g/m³, 95% CI: 0.990-1.014) were observed in the meta-analysis of the PM_{2.5}-adjusted models for respiratory diseases (Supplementary Figure S6). 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 μ g/m³, 95% CI: 1.002-1.010) by eliminating studies with partial overlap from the same geographical location.^[16, 18, 28, 29] In addition, no statistical significance was observed (RR = 1.008 per 1 μ g/m³, 95% CI: 0.992-1.023) between respiratory diseases and BC or EC after eliminating overlapped studies^[16, 18, 30, 31] (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.^[7, 19, 21, 32, 33] 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.^[34, 35]

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 "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).

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Table 2. Results of risk of bias assessment

			Key criteria	l	Other criteria				
No.	Study	Exposure	Outcome	Confounding	Selection	Incomplete	Selective	Conflict of	0.1
		assessment	assessment	bias	bias	outcome data	reporting	interest	Ot
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. 2019								
34	Lin et al. 2016b								
35	Ostro et al. 2008								

			Key criteria	a	Other criteria				
No.	Study	Exposure	Outcome	Confounding	Selection	Incomplete	Selective	Conflict	0
		assessment	assessment	bias	bias	outcome data	reporting	of interest	U
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	

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

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 $PM_{2.5}$ -adjusted model were obtained in the $PM_{2.5}$ -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 $PM_{2.5}$ -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.[36-38] Subgroup analysis on pollutant (BC and EC) indicated that the results from the PM2.5-unadjusted model and PM_{2.5}-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_{2.5}-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^[17] illustrated that the impact of BC and EC on cardiovascular morbidity differed in the elderly and other age groups, while Atkinson et al^[39] indicated no statistically significant difference between BC or EC and cardiovascular mortality in both the PM_{2.5}-adjusted model and PM_{2.5}-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

Page 25 of 122

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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 $PM_{2.5}$ -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 $PM_{2.5}$ -unadjusted/adjusted model and chronic effects of BC or EC on cardiovascular diseases in $PM_{2.5}$ -unadjusted model) upgrade one level on concentration-response gradient for an increase in risk with increasing BC or EC.^[24] 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.^[41] In addition, lung function and mucociliary clearance decline with long-term exposure to pollutants and increasing age.^[5, 42] 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_{2.5} deposition rather than the adults, and BC is an essential constituent of PM_{2.5}. In addition, BC activates macrophages from the lung cells, which release pro-inflammatory mediators, finally leading to an accumulation of inflammatory cells.^[43] Persistent airway inflammation is a pathological feature of asthma.^[44]

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.^[45] Yamawaki et al found that BC directly impacts the vascular endothelium, causing inflammatory responses, cytotoxic injury, and inhibition of cell growth.^[46] These responses contribute to the progression of atherosclerosis, leading to cardiovascular disease.^[46] 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.^[47] 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.^[47]

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

Page 27 of 122

BMJ Open

for influenza epidemics. Influenza epidemics are factors usually neglected in short-term studies. Second, studies should adjust PM2.5 when assessing the health effect of PM_{2.5} constituents. Mostofsky et al. proved that PM_{2.5} may be associated with both health and its constituents. Constituent having closer association with PM_{2.5} may illustrate a stronger association with diseases. Therefore, the results of PM_{2.5}-unadjusted model could introduce bias.^[7] 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.

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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.

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Competing interests

We declare that all authors have no competing interests.

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Data sharing statement

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

information.

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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

BMJ Open

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 <u>https://ntpniehsnihgov/ntp/ohat/</u> 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 35

BMJ Open

(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.

BMJ Open

[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.

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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_{2.5}-unadjusted model.

Fig. 3. Impact of short-term exposure to BC or EC on respiratory diseases in the

PM_{2.5}-unadjusted model.

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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.

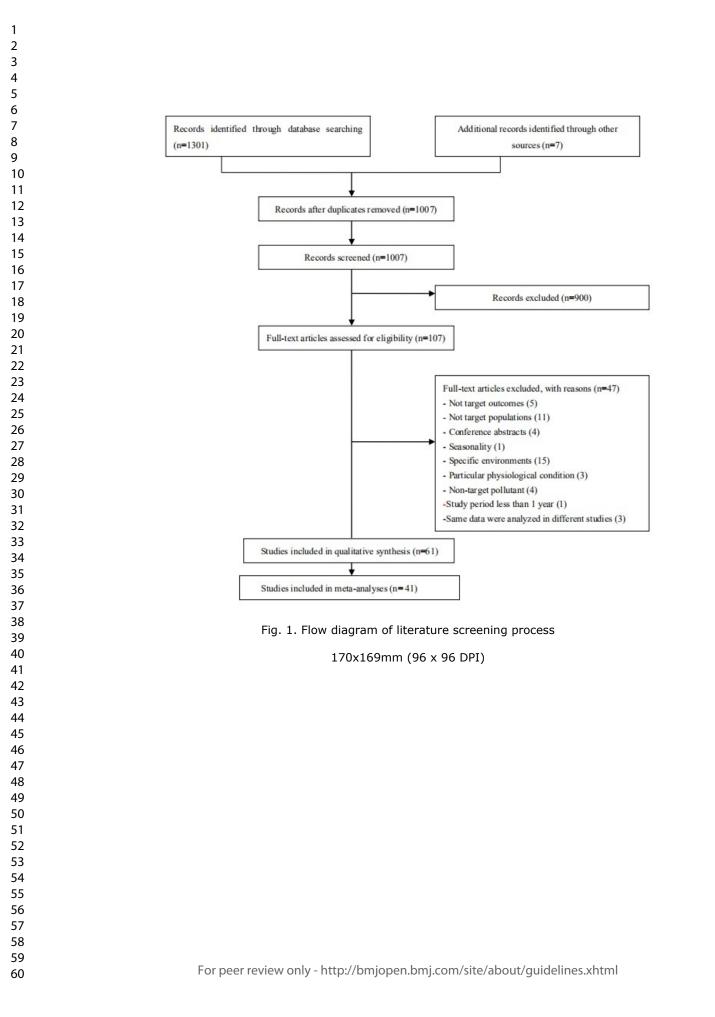
Fig. S2. Impact of short-term exposure to BC or EC on cardiovascular morbidity stratified by geographical locations.

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

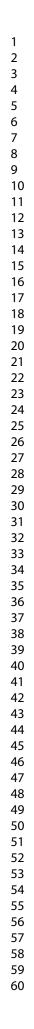
Fig. S4. Impact of long-term exposure to BC or EC on cardiovascular diseases.

Fig. S5. Impact of short-term exposure to BC or EC on cardiovascular diseases in the PM_{2.5}-adjusted model.

Fig. S6. Impact of short-term exposure to BC or EC on respiratory diseases in the PM_{2.5}-adjusted model.



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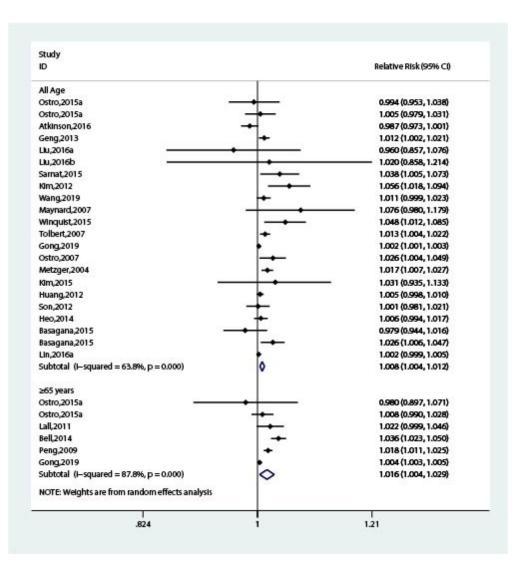


Fig. 2. Impact of short-term exposure to BC or EC on cardiovascular diseases in the PM2.5-unadjusted model.

176x188mm (72 x 72 DPI)

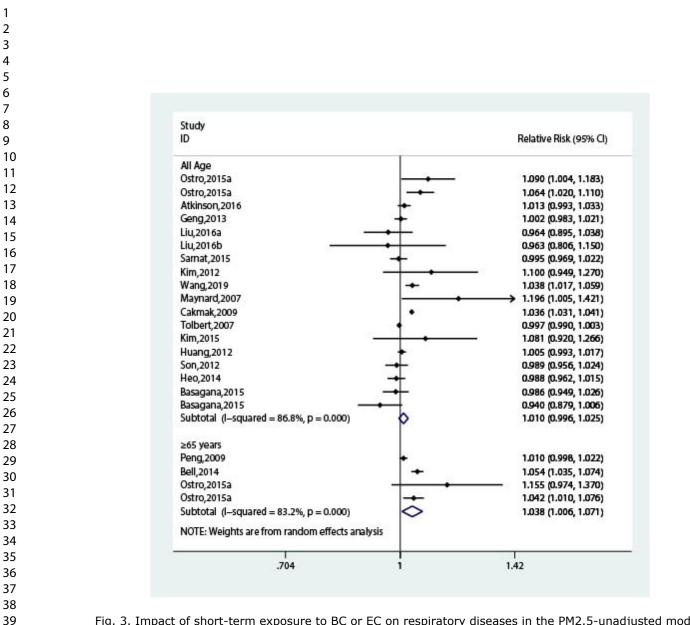


Fig. 3. Impact of short-term exposure to BC or EC on respiratory diseases in the PM2.5-unadjusted model.

176x178mm (72 x 72 DPI)

SUPPLEMENTARY APPENDIX

Short-term and Long-term Exposure to Black Carbon

and Cardiovascular and Respiratory Diseases: A

Systematic Review and Meta-Analysis

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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_{2.5}-adjusted model.

Fig. S6. Impact of short-term exposure to BC or EC on respiratory diseases in the PM_{2.5}-adjusted model.

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Table	
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#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.
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#5	or/1,2,3 "EC" /or "BC".tw. and/4,5 black carbon*/or element 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	cardioVascular diseases.sii. 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*/or emergency admi*/or hospital admission*.ti,ab.
#16	
#17	or/14,15 epidemiologic studies/or cross over study.sh.
#18	time series*/or timeseries*/or case cross*/or casecross*.tw.
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#21	or/17,18,19,20
#22	stud*/or prospective*/or retrospective*.tw. or/17,18,19,20 or/17,18,19,20 and/8,13,16,21 by copyright
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Table S2. Characteristics of included studies in the systematic review and meta analysis

Ctra Jan	Study	Growten	Study	0		Dellester (ICD	5
Study	Design	Country	Period	Outcome	Age	Pollutant	code	Siseases
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, 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)] Oo Asthma(ICD-10:J45) Oo O O O O O O O O O O O O O
Geng et al. 2013	TS	China	2007-2008	Mortality	All	BC	ICD-10	
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	BC	ICD-10	CVD(ICD-10:100-199),RES(ICD-10:J00-J98) for Asthma(ICD-10:J45) for CVD(ICD-10:100-199),RES(ICD-10:J00-J99) for CVD(ICD-10:100-199),RES(ICD-10:J00-J99) for
Samoli et al. 2016	TS	UK	2011-2012	Morbidity	≥15(CVD), all (RES)	BC,EC	ICD-10	CVD(ICD-10:100-199),RES(ICD-10:J00-J99)
Zanobetti and Schwartz 2006	CS	USA	1995-1999	Morbidity	≥65	BC	ICD-9	MI(ICD-9:410),Pneumonia (ICD-9: 480–487)
1 1 2016	TO	110.4	2000 2012	N. 111.	4.11	FC	ICD-9	CVD(ICD-9:390-429),Stroke(ICD-9:430-438),RES(100-9:460-519),COPD(ICD-9:490-492,494,496),Pneumonia
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)
Liu et al. 2016b	TS	USA	2008-2013	Morbidity	All	EC	ICD-9	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. 20100	15	USA	2008-2013	Worblandy	All	EC	ICD-9	(ICD-9:480-486),Asthma(ICD-9:493)
								CVD[IHD(ICD9:410–414),Cardiac Dysrhythmias(ICD):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(1209:480-486),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)
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Table S2. Characteris	stics of inclu	ded studies in th	e systematic revi Study	ew and meta anal	lysis		ICD	36/bmjopen-2021-049516 dn :
Study	Design	Country	Period	Outcome	Age	Pollutant	code	
Ostro et al. 2009	TS	USA	2000-2003	Morbidity	<19	EC	ICD9	RES(ICD-9:460-519),Asthma(ICD-9:493),Acute brochitis(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:I00-I98),CVD(ICD-10:I00-I99)
								CVD[Cardiac Dysrhythmias(ICD-9:428),Heart Rhyton 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 2),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 480-27).
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-J99)
Basagaña et al. 2015	CS	Spain, Italy	2003-2013	Morbidity, Mortality	All	EC	ICD-9, ICD-10	CVD(ICD-9:390-459,ICD-10:I00-I99),RES(ICD-9:400-519,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) 10
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, +0486,491,492,493,496,786.07),CVD(ICD-9:410-414,42
Ostro et al. 2007	TS	USA	2000-2003	Mortality	All	EC	ICD-10	428,433-437,440,443-445,451-453) CVD(ICD-10:100-199),RES(ICD-10:J00-J98)
Folbert et al. 2000	TS	USA	1998-2000	Morbidity	All	EC	ICD-9	CVD(ICD-9:402,410-414,427,428,433-437,440,444,44,44,44,44,44,44,44,44,44,44,4
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Table S2. Characteristics of included studies in the systematic review and meta analysis	
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Study	Study Design	Country	Study Period	Outcome	Age	Pollutant	ICD code	S Hiseases D
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),Pneuromia(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),cardiace dysrhythmias(ICD-9:427),CA(ICD-9:427.5),CHF(ICe 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) Difference CVD(ICD-10:100-199),RES(ICD-10:J00-J99) Difference Stroke(ICD-10:I60-I66) Difference
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-10:111) MI(ICD-9:410;ICD-10:121-122),IHD (ICD-9:414,ICD-10:125),Dysrhythmias(ICD-9:427,ICD-10:148),HF(ICD-9:428,ICD-10:150),Stroke(ICD-9:430-43 9,ICD-10:I60-I69)]
Chen et al. 2014	TS	China	2004-2008	Morbidity	All	EC	ICD-9	Stroke[Ischemic Stroke(ICD-9:433-434),Hemorrhag
Tomic´-Spiric´ et al. 2019	CS	Serbia	2012-2014	Morbidity	≥18	BC	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:I01-I52),Stroke(ICD-9:430-438,ICD-10:I60-I69),RES(ICD-9:460-519,ICD-10:J00-J 99)
Sinclair et al. 2010	TS	USA	1998-2002	Morbidity	All	EC	NR	
Krall et al. 2013	TS	USA	2000-2005	Mortality	All	EC	NR	Asinma, URTI, LRTI Poperturbation CVD and RES(NR) Operation RES(ICD-9:460-519) Operation
Cakmak et al. 2009	TS	Canada	2001-2006	Morbidity	All	EC	ICD-9	
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Table S2. Characteristics of included studies in the systematic review and meta analysis

Period 1993-2004 2001-2002 2000-2010 2000-2011 2003-2008 1999-2009(Atlan 1099-2009(Atlan 10, Georgia), 2004-010(Birmi ngham,Alabama,	Outcome Morbidity Morbidity Morbidity Mortality Morbidity	Age All ≥65 0-20 All ≥21	Pollutant EC EC BC BC BC	code ICD-9 ICD-9 ICD-10 NO	Events(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-9:491,492,496),URTI(ICD-9:460-465,460.0,477),Pneumon (ICD-9:480-486),Bronchiolitis(ICD-9:466.1,466.11,465.19)] RES[Pneumonia(ICD-9:480-486),COPD(ICD-9:490, 22,496),Acute Bronchitis and Bronchiolitis(ICD-9:460,Asthma(ICD-9:493)],CVD Bysrhythmia(ICD-9:461,466.11,465.19)] CVD(ICD-9:430-486),Asthma(ICD-9:493)],CVD Bysrhythmia(ICD-9:460,Asthma(ICD-9:490,Acute Bronchitis and Bronchiolitis(ICD-9:460,Asthma(ICD-9:493)],CVD Bysrhythmia(ICD-9:410-414),HF(ICD-9:410-414),HF(ICD-9:48),Stroke(ICD-9:410-414),HF(ICD-9:400,Acute Bronchitis and Asthma(ICD-9-CM:493) CVD(ICD-10:100-199) Acute Ischemic Stroke RES[Pneumonia(ICD-9:480-486),COPD(ICD-9:491, 422,496),URTI(ICD-9:460-465,466.0,477),Asthma and/or
2001-2002 2000-2010 2006-2011 2003-2008 1999-2009(Atlan ta,Georgia), 2004-010(Birmi	Morbidity Morbidity Mortality	≥65 0-20 All	EC BC BC	ICD-9	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),Pneumo (ICD-9:480-486),Bronchiolitis(ICD-9:466.1,466.11,466.11,465.19)] RES[Pneumonia(ICD-9:480-486),COPD(ICD-9:490,2496),Acute Bronchitis and Bronchiolitis(ICD-9:466),Asthma(ICD-9:493)],CVDBysrhythmia(ICD-9:427),IHD(ICD-9:410-414),HF(ICD-9
2001-2002 2000-2010 2006-2011 2003-2008 1999-2009(Atlan ta,Georgia), 2004-010(Birmi	Morbidity Morbidity Mortality	≥65 0-20 All	EC BC BC	ICD-9	RES[Pneumonia(ICD-9:480-486),COPD(ICD-9:490,Acute Bronchiolitis(ICD-9:480-486),Acute Bronchiolitis(ICD-9:480-486),COPD(ICD-9:490,Acute Bronchiolitis(ICD-9:480-486),COPD(ICD-9:490,Acute Bronchiolitis(ICD-9:410-414),HF(ICD-1))
2001-2002 2000-2010 2006-2011 2003-2008 1999-2009(Atlan ta,Georgia), 2004-010(Birmi	Morbidity Morbidity Mortality	≥65 0-20 All	EC BC BC	ICD-9	(ICD-9:480-486),Bronchiolitis(ICD-9:466.1,466.11,466.11,466.19)] RES[Pneumonia(ICD-9:480-486),COPD(ICD-9:490,2496),Acute Bronchitis and Bronchiolitis(ICD-9:466),Asthma(ICD-9:493)],CVDBysrhythmia(ICD-9:427),IHD(ICD-9:410-414),HF(ICD-9
2000-2010 2006-2011 2003-2008 1999-2009(Atlan ta,Georgia), 2004-010(Birmi	Morbidity	0-20 All	BC BC		RES[Pneumonia(ICD-9:480-486),COPD(ICD-9:490, 490, Acute Bronchitis and Bronchiolitis(ICD-9:466),Asthma(ICD-9:493)],CVDBysrhythmia(ICD-9:427),IHD(ICD-9:410-414),HF(ICD-9:493)
2000-2010 2006-2011 2003-2008 1999-2009(Atlan ta,Georgia), 2004-010(Birmi	Morbidity	0-20 All	BC BC		Bronchiolitis(ICD-9:466),Asthma(ICD-9:493)],CVDBysrhythmia(ICD-9:427),IHD(ICD-9:410-414),HF(ICD-9:493)
2000-2010 2006-2011 2003-2008 1999-2009(Atlan ta,Georgia), 2004-010(Birmi	Morbidity	0-20 All	BC BC		
2006-2011 2003-2008 1999-2009(Atlan ta,Georgia), 2004-010(Birmi	Mortality	All	BC	ICD-10 NO	28),Stroke(ICD-9:431-437)] Dip Asthma(ICD-9-CM:493) Dip CVD(ICD-10:100-199) Dip Acute Ischemic Stroke Dip
2006-2011 2003-2008 1999-2009(Atlan ta,Georgia), 2004-010(Birmi	Mortality	All	BC	ICD-9 ICD-10 NO	Asthma(ICD-9-CM:493) Image: CVD(ICD-10:100-199) Acute Ischemic Stroke Image: CVD(ICD-10:100-199)
2003-2008 1999-2009(Atlan ta,Georgia), 2004-010(Birmi				ICD-10 NO	CVD(ICD-10:100-199) Acute Ischemic Stroke
1999-2009(Atlan ta,Georgia), 2004-010(Birmi	Morbidity	≥21	BC	NO	Acute Ischemic Stroke
ta,Georgia), 2004-010(Birmi					nj.com/
2001-2007(St.Lo uis, Missouri), 2006-2009(Dalla s,Texas)	Morbidity	All	EC	ICD-9	RES[Pneumonia(ICD-9:480-486),COPD(ICD-9:491 #92,496),URTI(ICD-9:460-465,466.0,477),Asthma and/or Wheeze(ICD-9:493,786.07)] ,0 2024 by guest Asthma(ICD-9:493.0-493.9),Wheeze(ICD-9:786.07);
2001-2008	Morbidity	5-18	EC	ICD-9	Asthma(ICD-9:493.0-493.9),Wheeze(ICD-9:786.07).
1999-2008	Morbidity	5-17	EC	ICD-9	Asthma(ICD-9:493.0-493.9),Wheeze(ICD-9:786.07)
1993-2004	Morbidity	5-17	EC	ICD-9	Asthma(ICD-9:493.0-493.9),Wheeze(ICD-9:786.09)
	s,Texas) 2001-2008 1999-2008	s,Texas) 2001-2008 Morbidity 1999-2008 Morbidity	s,Texas) 2001-2008 Morbidity 5–18 1999-2008 Morbidity 5–17	s,Texas) 2001-2008 Morbidity 5–18 EC 1999-2008 Morbidity 5–17 EC	s,Texas) 2001-2008 Morbidity 5–18 EC ICD-9 1999-2008 Morbidity 5–17 EC ICD-9

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

3 of 122 Table S2. Characteris	tics of inclu	ided studies in th	e systematic revi	ew and meta ar	nalysis	E	BMJ Oper	36/bmjopen-2021-049516 c
Study	Study	Country	Study	Outcome	Age	Pollutant	ICD	G Hiseases D
	Design		Period				code	y y
Strickland et al. 2014	TS	USA	2000-2010	Morbidity	2-16	EC	ICD-9	Asthma(codes beginning with 493),Wheeze (ICD-9:726.07)
Ito et al. 2013	TS	USA	2001-2006	Morbidity,	all (mortality),	EC	ICD-9,	
				Mortality	$\geq 65(morbidity)$		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	BC	ICD-9,	COPD(ICD-9:490-492,496,ICD10:J40-J44)
		Cuntuu	1777 2002	Mortality	10 00	20	ICD-10	Tron on the second s
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)
	G		1000 0004		. 20	50	ICD-9,	
Thurston et al. 2016	Co	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-I99),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
				Morbidity,			ICD-9,	
Gan et al. 2011	Co	Canada	1999-2002	Mortality	45-85	BC	ICD-10	CHD(ICD-9:410-414,429.2),(ICD-10:I20-I25)
De Kluizenaar et al.								M.
2013	Co	Netherlands	1991-2003	Morbidity	15-74	EC	ICD-9	IHD(ICD-9:410-414),CHD(ICD-9:430-438)
				Morbidity				April
Vedal et al. 2013	Co	USA	1994-2005	-	50-79	EC	ICD-9	CVD (ICD-9:CM 410-452)
Vedal et al. 2013		USA	1994-2005	Morbidity, Mortality	50-79	EC	ICD-9	

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: Stardiovascular 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 mgcardial infarction; CA: cardiac arrest; RTI: respiratory tract infection; URTI: Upper Respiratory Infection; LRTI: Lower Respiratory Infection; ARTI: Acute respiratory infections. guest. Protected by copyright.

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
	Studies	Estimates	(95%CI)		(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%	
Asthma ≥18	3	4	1.011 (0.998, 1.025)	14.20%	_



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 Table S4. Details of risk of bias assessment

No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	⊐ ۵۵ Incomplete ۵۷ outcome data		Conflict of interest	Other
1	Atkinson	Probably Low	Low	Probably Low	Low	Low 022	Probably Low	Low	Low
	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
		measured at the central	1 January 2011 to 31	(seasonality,	daily counts of	for death were $\frac{5}{2}$	insufficient	declare no	potential
		London background	December 2012 were	long-term trend),	deaths in	obtained, so	information	conflict of	sources of
		monitoring site at North	obtained from the Office	temperature,	London, United	likely have all ≞	about	interest.	bias
		Kensington. All	for National Statistics.	humidity, day of	Kingdom for the	outcome data.	selective		identified.
		measurements were 24-h	Daily counts of deaths in	week and public	period 1 January	However, any	outcome to		
		averages except for CO.	London, United Kingdom	holidays.	2011 to 31	potential errors			
		The number of all	were classified as all		December 2012.	or missing datag	risk, but		
		observations was 621-693	disease-related causes,			did not depend	indirect		
		(<25% missing data).	cardiovascular	l l		on air pollution	evidence that		
			(International		· ()	levels.	suggests study		
			Classification of			on	was free of		
			Diseases,10th			Apri	selective		
			revision-ICD10: I00-I99)			1 19,	report.		
			and respiratory (ICD10:			202			
			J00-J99) diseases.			<u>1</u> 4 b			
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2 3 4 5							21-049516			
6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete S outcome data∝ ≤	Selective reporting	Conflict of interest	Other
8	2	Bell et al.	Probably High	Low	Probably Low	Low	Low X	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		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).	The study used the Medicare beneficiary denominator file from the Centers 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).	Models adjusted for time (seasonality, long-term trend), day of week, temperature, and dew point.	Data obtained from records of individuals ≥65 years of age enrolled in the Medicare fee-for-service plan during August 2000 to February 2004.	Daily counts for hospital admissions 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.
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Pag	e 57 of	122			BMJ Oper	1	36/bmjop			
1 2 3 4							36/bmjopen-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete \int_{Ω}^{10} outcome data \cong	Selective reporting	Conflict of interest	Other
8 0	3	Cai et al.	Probably Low	Low	Probably Low	Low	Low y	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		2014	Daily concentrations of BC were measured at a fixed-site station. Daily data was available and no missing data was reported.	Asthmatic hospitalization data was obtained from the Shanghai Health Insurance Bureau (SHIB). The causes of hospital admission were coded according to International Classification of Diseases, Revision 10 (ICD-10): Asthma (J45).	Adjusted for time (seasonality, long-term trend), temperature, relative humidity and day of the week.	Study included all asthmatic hospitalization for adult residents living in the nine urban districts between January 1, 2005 and December 31, 2011(2922 days) from the Shanghai Health Insurance Bureau.	Daily counts for asthmatic 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.	Authors declared no competing financial interests.	No other potential sources of bias identified.
38 39 40 41 42 43			1	For peer review only	r - http://bmjopen.bmj.	.com/site/about/quid	L By copyright opyright delines.xhtml		1	

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1 2 3 4							36/bmjopen-2021-049516 on Incomplete			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	Selective reporting	Conflict of interest	Other
8 9			Probably High	Low	Probably Low	Low	Low X	Probably Low	Low	Low
10 11 12	4	Geng et al. 2013	Single, central-site monitor. Daily BC and PM _{2.5} were measured	Health data were obtained from Shanghai Municipal Center of	Models included time (seasonality, long-term trend),	Data consisted of all causes (excluding	Daily counts for death were obtained, so		The authors declare no conflict of	No other potential sources of
13			continuously and 24hr	Disease Control and	temperature,	accidents or	likely have all	about	interest.	bias
14 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	0.	course of the	potential errors			
19			day. Missing data was not	International		study.	or missing data			
20 21			replaced by other values.	Classification of			did not depend			
22				Diseases, Revision 10			on air pollution			
23 24				(ICD 10).		10.	levels.	suggests study was free of		
24 25							levels. April 19, 2024 by guest	selective		
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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 High	Low	Probably Low	Low	Low 2	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	5	Hua et al. 2014	Daily 24h average PM _{2.5} and BC data was obtained from a fixed-site station. The study only used the actual collected data and did not fill in the missing data for PM _{2.5} and black carbon.	Daily asthma hospital admission data was obtained from Shanghai Children's Medical Center. Dates of admission and discharge, and diagnoses using the International Classification of Diseases, Revision 10.	Adjusted for long-term and seasonal trend, day of week, temperature and relative humidity.	Study included all asthma hospital admissions of children ≤ 14 years of age from Shanghai Children's Medical Center between1 January 2007 and 31 July 2012 in nine urban districts of Shanghai.	Daily counts for asthma hospital admissions of children 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 report.	Authors declared no competing financial interests.	No other potential sources of bias identified.
37 38 39 40 41 42 43				For peer review only	- http://bmjopen.bmj.	.com/site/about/quic	by copyright.			

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1 2 3 4							-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete og outcome data∞	Selective	Conflict of interest	Other
8			Probably Low	Low	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 26	6	Ostro et al. 2015a	Daily 24hr average BC concentrations were obtained from one station in Barcelona and Athens. Daily data was available and no missing data was reported.	For both cities daily counts of all-cause mortality for all ages were collected (excluding deaths from external causes, International Classification of Disease-ICD9: 001799, ICD10 A00R99), as well as daily counts of cardiovascular (ICD9: 390459, ICD10: I00I99), respiratory (ICD9:460519, ICD10:J00J99) and all-cause mortality for those greater than age 65.	Adjusted for long term and seasonal (year, month, day of week) trends, temperature, holidays, summer vacations and influenza.	Study population consisted of daily counts of all-cause mortality for all ages and daily counts of cardiovascular, respiratory and all-cause mortality for those greater than age 65.	Daily counts for death were obtained, so likely have all death outcome data. However, any potential errors or missing data did not depended on air pollution levels.	There was insufficient information about selective outcome to judge for low risk, but indirect evidence that	Authors declared no competing interests.	No other potential sources of bias identified.
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1 2 3 4							36/bmjopen-2021-0498			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete \int_{Ω}^{Ω} outcome data ω	Selective reporting	Conflict of interest	Other
8			Low	Low	Probably Low	Low	Low X	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	7	Samoli et al. 2016	Daily concentrations of 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 (BC urban in PM _{2.5}) and 702 (BC in PM _{2.5}) between 2011 and 2012 (<25% missing data).	Based on the primary discharge diagnosis, daily numbers of admissions for cardiovascular disease (International Classification of Diseases, 10th revision-ICD-10: I00-I99) for those aged 15-64 (adult) and 65+ years (elderly), and respiratory diseases (ICD-10: J00-J99) for those aged 0-14 years (paediatric), adult and the elderly were calculated.	Adjusted for long term and seasonal trends, temperature, relative humidity, regulated pollutants (PM ₁₀ , PM _{2.5} , NO ₂ , SO ₂ and O ₃), day of the week and public holidays.	Study included all cardiovascular and respiratory hospital admissions in London, UK between 2011 and 2012.	Daily counts for all emergency hospital admissions 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 report.	Authors declared no competing interests.	No other potential sources of bias identified.
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					BMJ Oper	1	36/bmjopen-2021-0495			Page 62 of
1 2 3 4							2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete og 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	8	Zanobetti and Schwartz 2006	Ambient BC from one monitor. The hourly measurements for BC and PM _{2.5} 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.	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 revision-ICD-9:410), and pneumonia (ICD-9: 480–487), from Medicare billing records for the years 1995–1999.	Adjusted for temperature, day of the week, seasonality, long-term trends, humidity, barometric pressure, and the extinction coefficient.	Data consisted of all U.S. Medicare hospital admissions in the Boston Metropolitan area for myocardial infarction during the study duration.	Daily counts for hospital admissions 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 interests.	No other potential sources of bias identified.
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1 2 3 4							36/bmjopen-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	ີດ Incomplete ິ outcome dataຜ ຊ	Selective reporting	Conflict of interest	Other
8 9			Probably High	Low	Probably Low	Low	Low ay 2	Probably Low	Low	Low
10 11	9	Liu et al. 2016a	EC were collected from a single monitor on a	Emergency department visit data was obtained	Adjusted for time (long-term and	Study included daily counts of	Daily counts		Authors declared no	No other potential
12			one-in-three or one-in-six	from the Blue Cross Blue	seasonal trend),	emergency	department	information	potential	sources of
13 14			day schedule. EC were	Shield Texa. International	day of week,	department visits	visits were	about	competing	bias
14			measured for 566 days	Classification of Diseases	temperature, dew	for Greater	obtained, so	selective	financial	identified.
16			from April 02, 2009, to	9th Revision (ICD-9)	point and	Houston from	likely have all ∃	outcome to	interests.	
17 18			December 30, 2013,	diagnosis codes were	population growth.	claims data	outcome data.	judge for low		
19			<25% missing for the	used to classify outcome		insured from	However, any	risk, but		
20			frequency of sampling.	groups.		January 1, 2008	potential errors			
21 22						through	or missing data	evidence that		
23						December 31,	did not depend			
24 25						2013.	on air pollution			
26							levels. 9	selective		
27							, pril	report.		
28 29							April 19, 2024 by gues			
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1 2 3 4							36/bmjopen-2021-049516 on Incomplete			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete of the second secon	Selective reporting	Conflict of interest	Other
8 9			Probably High	Low	Probably Low	Low	Low X	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 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.
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1 2 3 4							36/bmjopen-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete g outcome data ω	Selective reporting	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	11	Sarnat et al. 2015	24hr average concentration of PM _{2.5} 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 Download department visits were obtained, hence one hospital not providing data after 26 April 2002. 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.
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete og outcome data∞		Conflict of interest	Other
8			Probably Low	Low	Probably Low	Low	Low 2	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	12	Kim et al. 2012	PM _{2.5} 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	The authors declare they have no actual or potential competing financial interests.	No other potential sources of bias identified.
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Page 67 of 122				BMJ Open	I	36/bmjop				
1 2 3 4			_				36/bmjopen-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete $\frac{16}{9}$ outcome data $\omega \leq$	Selective reporting	Conflict of interest	Other
8 9			High	Low	Probably Low	Low	ay 2 Low	Probably Low	Low	Low
9 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 13			from two co-located	Office of Statewide	temperature,	hospitalizations	hospitalization	information	competing	sources of
13			monitors or one monitor	Health Planning and	seasonality,	for children < 19	of children $\frac{\omega}{\omega}$	about	financial	bias
15			in 6 counties. The number	Development, Healthcare	relative humidity	and < 5 years of	were obtained, $\frac{d}{d}$	selective	interests.	identified.
16 17			of available days of data	Quality and Analysis	and pollutant.	age for total	so likely have \exists	outcome to		
17			over the 4-year period	Division. Hospital	0.	respiratory	all outcome	judge for low		
19			ranged from 227 to 381	admissions for children		diseases and	data. However,	risk, but		
20			(some counties had >25%	<19 years of age were		several	any potential	indirect		
21 22			missing for the frequency	classified into one or	C	subcategories	errors or	evidence that		
23			of sampling).	more categories: all	L.	including	missing data \exists	suggests study		
24				respiratory disease		pneumonia, acute	did not depend	was free of		
25 26				(International		bronchitis, and	on air pollutiong	selective		
27				Classification of		asthma for six	levels. April	report.		
28				Diseases, Ninth		California	1 19,			
29 30				Revision-ICD-9 codes		counties from	2024			
31				460–519), asthma (ICD-9		2000 through	24 b			
32				code 493), acute		2003.	by gues			
33				bronchitis (ICD-9 code			lest.			
34 35				466), and pneumonia			Pro			
36				(ICD-9 codes 480–486).			Protected			
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1 2 3 4							-2021-0496			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	Selective reporting	Conflict of interest	Other
8 9			Probably Low	Low	Probably Low	Low	Low X	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	14	Kim et al. 2015	Daily 24-hour composite PM _{2.5} samples were collected from single, central-site monitor. The observations of EC was 1809 days from 2003 through 2007 (missing data <25%).	Daily mortality counts for 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.	Models adjusted for longer-term temporal trend, as time since the study began, day of week, and daily temperature and humidity.	Data consisted of all deaths over the course of the study in a defined geographical area.	Daily counts for death were obtained, so likely have all outcome data. However, any potential errors or missing data	There was insufficient information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of selective report.	None of the authors has any actual or potential competing interests.	No other potential sources of bias identified.
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1 2 3 4							36/bmjopen-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete g	Selective	Conflict of interest	Other
8			Probably Low	Low	Probably Low	Probably Low	Low S	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	15	Huang et al. 2012	Daily average concentrations of PM _{2.5} were obtained from a single, central-site monitor. Daily average concentrations of EC in PM _{2.5} 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 Downloaded for death were all 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 report.	No competing financial interests.	No other potential sources of bias identified.
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1 2 3 4							-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete \int_{Ω}^{Ω} outcome data \cong		Conflict of interest	Other
8			Probably High	Low	Probably Low	Low	Low 2	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	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 was not replaced by other values.	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 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 competing financial interests.	No other potential sources of bias identified.
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete \int_{Ω}^{0} outcome data $\omega \leq$	Selective reporting	Conflict of interest	Other
8			Probably High	Low	Probably Low	Low	ay 2 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 4 35 36 37	17	Levy et al. 2012	The U.S. Environmental Protection Agency established the PM Speciation Trends Network (STN) to measure more than 50 PM _{2.5} 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 missing data.	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 22 hospital damissions were obtained from http://bmjopen.bmjop	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.
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1 2 3 4							36/bmJopen-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete og outcome data⇔	Selective	Conflict of interest	Other
8			Probably Low	Low	Probably Low	Low	Low X	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	18	Son et al. 2012	Hourly air samples were obtained from a single, central-site monitor. The monitoring system produces hourly estimates of PM _{2.5} total mass, and PM _{2.5} levels of EC. Daily data was available and no missing data was reported.	Daily death counts were obtained from the National Statistical Office. The study classified mortality data into all causes of death [International Classification of Diseases, 10th Revision (ICD-10; codes A00–R99), cardiovascular causes (codes I00–I99), and respiratory causes (codes J00–J99)] (World Health Organization 2007).	Models adjusted for time (long-term trends and seasonality), day of week, temperature and relative 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.	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.
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Pag	e 73 of	f 122			BMJ Oper	1	36/bmjopen-2021			
1 2 3 4							en-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete \int_{Ω}^{10} outcome data ω	Selective reporting	Conflict of interest	Other
8			Probably High	Low	Low	Low	Low ay 2	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	19	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.	19, 2024 by guest. Protected	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.
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1 2 3 4							36/bmJopen-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete og outcome data⇔	Selective	Conflict of interest	Other
8			Probably High	Low	Probably Low	Low	Low X	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	20	Basagaña et al. 2015	Single central-site monitor in each city. For each city, PM constituents with >20% of the values below the detection limit or missing were excluded. Otherwise, non-detectable were replaced by half the limit of detection. Air pollution data was collected daily in Bologna (n=472), twice a week in Barcelona (n=736) and Madrid (n=104), and once a week in Huelva (n=406). There was no information about missing data.	Daily mortality counts for all non-external causes [International Classification of Diseases, 9th Revision (ICD9) codes 001–799; 10th revision (ICD10) codes A00–R99], cardiovascular (ICD9 codes 390–459, ICD-10 codes 390–459, ICD-10 codes 100–I99) and respiratory (ICD9 codes 460–519, ICD10 codes J00–J99) were collected. Cardiovascular and respiratory hospitalizations were defined on the basis of the primary discharge diagnosis using the same ICD codes defined above.	Models adjusted for holidays, summer population decrease, influenza epidemics, seasonality, long-term trends and temperature.	Data consisted of all deaths over the course of the study in a defined geographical area.	Daily counts for death and emergency hospital admissions 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 report.	The authors have no conflicts of interest to disclose.	No other potential sources of bias identified.
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete \int_{Ω}^{0} outcome data ω	Selective reporting	Conflict of interest	Other
8			Probably High	Low	Probably Low	Low	Low 2	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	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 _{2.5} 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 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 ded outcome data. However, any potential errors or missing data did not dependoon levels.	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 interests.	No other potential sources of bias identified.
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1 2 3 4							6/bmjopen-2021-049516 on Incomplete			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete of outcome data	Selective reporting	Conflict of interest	Other
8			Probably Low	Low	Low	Low	Low X	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	22	Lin et al. 2016a	The concentrations of different particle size fractions and PM _{2.5} 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-10:100-199) 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.	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.
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1 2 3 4			-				36/bmjopen-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete \int_{Ω}^{10} outcome data $\omega \leq$	Selective reporting	Conflict of interest	Other
8			Probably Low	Low	Probably Low	Low	ay 2 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	23	Cao et al. 2012	Daily concentrations of EC was obtained from a single monitoring site. The observations of EC was 1749 in 1827 days (missing data <25%).	The study obtained numbers of deaths in Xi'an for each day from the Shanxi Provincial Center for Disease Control and Prevention (SPCDCP). SPCDCP staff then classify the cause of death according to the International Classification of Diseases, 10th Revision [ICD-10; World Health Organization (WHO) 1992] as due to total nonaccidental causes (ICD-10 codes A00–R99), cardiovascular diseases (I00–I99), respiratory diseases(J00–J98), or injury (S00–T98).	Model adjusted for long-term and seasonal trends, day of week, temperature, humidity, and SO ₂ and NO ₂ concentrations.	Data consisted of all nonaccidental causes deaths during over the course of the study.	Daily counts for death were Downloaded 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 report.	The authors declare they have no actual or potential competing financial interests.	No other potential sources of bias identified.
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1 2 3 4							36/bmjopen-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete og outcome data∞	Selective	Conflict of interest	Other
8			Probably Low	Low	Probably Low	Low	Low 2	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	24	Klemm et al. 2011	Daily 24-hr average EC measurements are available for Atlanta during the study period. The observations of EC was 3317 days from August 1998 to December 31, 2007. Missing data <25%. There was no information for monitor stations.	Records of individual deaths were provided by the Georgia Department of Human Resources. Cause of death is	Adjusted for time (seasonality, long-term trends), temperature, and day of the week.	Study included all nonaccidental deaths during 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.	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.
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1 2 3 4							36/bmjopen-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	ດ Incomplete ິ outcome dataຜ ≤	Selective	Conflict of interest	Other
8			Probably Low	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	25	Zhou et al. 2011	24hr PM _{2.5} 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.	19, 2024 by guest.	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.
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete og outcome data∞	Selective	Conflict of interest	Other
8			Probably Low	Low	Probably Low	Low	Low 2	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	26	Winquist et al. 2015	Daily EC and BC were from a single monitor site. All species of pollutant statistics are missing less than 5%.	Individual-level data were obtained from the Missouri Hospital Association for all emergency department visits to 36 of 43 acute-care non-federal hospitals with emergency department visits in the 16-county St Louis metropolitan statistical area during 1 June 2001 through 30 April 2003. Cardiorespiratory outcomes of interest were defined based on the primary ICD-9 (International Classification of Diseases, version 9) diagnosis code for the visit.	Adjusted for time trends, day of week, holidays, season, temperature and dew point.	Study included emergency department visits in St Louis metropolitan statistical area during 1 June 2001 through 30 April 2003.	Daily counts for emergency Downloaded for emergency Downloaded department visit 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.
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete \int_{Ω}^{10} outcome data $\omega \leq$	Selective reporting	Conflict of interest	Other
8			Probably High	Low	Probably Low	Low	Low ay 2	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	27	Ostro et al. 2007	Each of the six counties had two monitors measuring PM _{2.5} components and mass. Fresno, Kern, Riverside, and Sacramento Counties reported data every third day, whereas San Diego and Santa Clara Counties reported data every sixth day. For the speciation analyses, the number of observation days available ranged from 243 (San Diego County) to 395 (Sacramento County) from 2000 to 2003. There was no specific information about missing data.	Daily mortality data were obtained from the California Department of Health Services, Center for Health Statistics. The study determined daily total mortality counts for those > 65 years of age and for deaths from respiratory disease [International Classification of Diseases, 10th Revision (ICD10; World Health Organization 1993) codes J00–J98] and cardiovascular disease (codes I00–I99).	Adjusted for time trend, day of week, seasonality, long-term trends, temperature and humidity.	Data consisted of all cardiovascular deaths over the course of the study.	Daily counts for death were Downloaded obtained, so likely have all death outcome data. However, any potential errors or missing data did not depended 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	The authors declare they have no competing financial interests.	No other potential sources of bias identified.
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No. Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete og outcome data⇔	Selective	Conflict of interest	Other
28 Tolbert et al. 2000	Probably Low Daily 24h EC from a single monitor site. The observation of EC was 356 in 365 days, missing data <25%.	Low Computerized billing record data are being obtained from the emergency department visits participating in the study. Several case groups are being defined using the primary ICD-9 (International Classification of Diseases, 9th Revision) diagnostic code.	Probably Low Adjusted for time (seasonality, long-term trends), temperature, dew point, and day of week.	Low Study included emergency department visits of the participating hospitals in the Atlanta Metropolitan Statistical Area, including 33 hospitals between January 1 1993-August 31 2000, 4 hospitals between January 1 1993-February 30 2000.	Low Daily count for Protected by copyright.	insufficient information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of selective report.	Low Authors declared no competing financial interests.	Low No other potential sources of bias identified.

Pag	e 83 of	122			BMJ Oper	1	36/bmjop			
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete $\begin{bmatrix} 0 \\ 0 \\ 0 \end{bmatrix}$ outcome data ω	Selective reporting	Conflict of interest	Other
8			Low	Low	Probably Low	Low	Low 2	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	29	Wang and Lin 2016	The hourly data were simply averaged to calculate the daily average data for PM ₁₀ , PM _{2.5} 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.	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 Revision (ICD-9 CM).	Adjusted for temperature, relative humidity, wind speed, barometric pressure, holidays, day of the week, pneumonia and influenza.	Study included elderly (≧65 years) mortality from 2004 to 2008 and all population EVR from 2004 to 2010 in Taipei, Taiwan.	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 depend on air pollution levels.	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.
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4 5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data⇔	Selective	Conflict of interest	Other
8			Low	Low	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	30	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 Development department visit were obtained. In the earliest years of the study, not all hospitals were participating. 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.
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1 2 3 4							36/bmjopen-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete $\frac{16}{9}$ outcome data ω	Selective reporting	Conflict of interest	Other
8 9			Probably High	Low	Probably Low	Low	Low $\stackrel{\mathfrak{A}}{\prec}$	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	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 12. for emergency Downloaded from http://onidecommonstatic solution of the second secon	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.
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1 2 3 4							36/bmjopen-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete \int_{Ω}^{0} outcome data ω	Selective	Conflict of interest	Other
8 9			Probably Low	Low	Probably Low	Low	Low ay	Probably Low	Low	Low
9 10	32	Mar et al.	Hourly PM _{2.5} 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	for death were	insufficient	competing	potential
12 13			single, central-site	1995 to 1997 were	day of week,	cardiovascular	obtained, so $\frac{3}{0}$	information	financial	sources of
14			monitor. Daily data was	obtained from the	temperature and	deaths during	likely have all		interests.	bias
15 16			available and no missing	Arizona Center for	relative humidity.	over the course	outcome data.			identified.
17			data was reported.	Health Statistics in	er rei	of the study.	However, any			
18				Phoenix. Death certificate data included residence	04		potential errors			
19 20				zip code and the primary	The second secon		did not depend			
21				cause of death as			on air pollution			
22 23				identified by the			levels.	suggests study		
23 24				International			levels.	was free of		
25				Classification of			l on	selective		
26 27				Diseases, Ninth Revision			Apr	report.		
28				(ICD-9, World Health						
29				Organization, Geneva).			, 20			
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data∞	Selective reporting	Conflict of interest	Other
8			Low	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 38	33	Wang et al. 2019	Hourly data of PM _{2.5} were collected at 10 Chinese air quality monitoring sites in Shanghai. Hourly mass concentrations of PM _{2.5} 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 Downloaded for death were death obtained, so likely have all outcome data. However, any potential errors or missing data did not dependoon 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.
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1 2 3 4							So/bmjopen-2021-049516 on Incomplete			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete of the second secon	Selective reporting	Conflict of interest	Other
8 0			Probably High	Low	Probably Low	Low	Low X	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	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:I60–I66), and sub-categories, including ischemic stroke (ICD-10:I63–I66), and hemorrhagic stroke (ICD-10: I60–I62) 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.	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 conflict of interest.	No other potential sources of bias identified.
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Pag	e 89 of	122			BMJ Oper	I	36/bmjop			
1 2 3 4							66/bmjopen-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete g outcome data ω	Selective reporting	Conflict of interest	Other
8			Probably High	Low	Probably Low	Low	Low $\overset{a}{\overset{\vee}{\overset{\vee}}}$	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	35	Lin et al. 2016b	Each of the six counties had two monitors measuring components of PM _{2.5} . Fresno, Kern, Riverside and Sacramento counties reported 24-hour average EC in PM _{2.5} 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.	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 calculated.	Adjusted for time, temperature, humidity and day of the week.	Study included daily cardiovascular mortality for all California residents from 1 January 2000 to 31 December 2003.	Daily counts for death were obtained, so likely have all death were all obtained, so likely have all death outcome data. However, any potential errors or missing data did not depended 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 interests.	No other potential sources of bias identified.
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1 2 3 4							36/bmJopen-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	Selective	Conflict of interest	Other
8			Probably Low	Low	Probably Low	Low	Low X	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	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 death.	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.	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.
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Pag	e 91 of	⁻ 122			BMJ Oper	1	36/bmjop			
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete \int_{Ω}^{Ω} outcome data ω	Selective reporting	Conflict of interest	Other
8 9			Probably Low	Low	Probably Low	Low	Low y	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 _{2.5}	emergency room visits	for time, day of	all emergency	for emergency	insufficient	competing	potential
12 13			and the four PM _{2.5}	were obtained from the	week, temperature,	department visits	room visit wer		financial	sources of
14			constituents obtained	National Taiwan	seasonality and	during the study	obtained, so	about	interests.	bias
15 16			from a Supersite (single,	University Hospital. The	relative humidity.	period for	likely have all $\frac{d}{d}$			identified.
17			central site monitoring	emergency room visit		ischemic and	outcome data.			
18			location). The observations of EC was	data were coded	0	hemorrhagic	However, any			
19 20			1599 in 1705 days	regarding the discharge diagnosis using the		stroke.	potential errors			
21			(missing data <25%).	International			did not depend	evidence that		
22			(missing data <25%).	Classification of Disease,			on air pollution			
23 24				9th revision (ICD-9).	·	10	levels.	was free of		
25							n/ on	selective		
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete og outcome data∝	Selective reporting	Conflict of interest	Other
8			Low	Low	Probably High	Low	Low X	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 28	38	Tomic´-Sp iric´ et al. 2019	Average daily concentrations of BC in micrograms per cubic meter were measured by three automatic ambient air quality monitoring stations. There was no information about missing data.	Emergency department visits data were obtained from the Health Center Užice, either from the emergency department visits in Užice, Sevojno, and Kosjeri´c, or from a general hospital in Užice. The inclusion criteria were adults aged 18 years and older with the diagnosis of allergic rhinitis (International Classification of Diseases, 10th revision, code J.30.4), allergic asthma (International Classification of Diseases, 10th revision, code J.45.0), or asthma with coexisting allergic rhinitis.	Adjusted for temperature, humidity, and air pressure.	Study included emergency department visit for allergic rhinitis and allergic asthma from 1 July 2012 to 30 June 2014 in the Zlatibor District, Western Serbia.	All 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.	 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.
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete \int_{Ω}^{0} outcome data ω	Selective reporting	Conflict of interest	Other
8			Probably Low	Low	Probably Low	Low	Low ay 2	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	39	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 Downloaded for individual Downloaded mortality records were obtained, so likely have all more 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.
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete og outcome data∞	Selective	Conflict of interest	Other
8 9			Probably Low	Probably Low	Probably Low	Low	Low ay 2	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 13			monitor site. The total	electronic patient data	week, federal	visits for acute	visits were	information	financial	sources of
14			observed rate of EC was	warehouse of a	holidays, study	respiratory	obtained, so $\frac{\overline{0}}{0}$	about	interests.	bias
15			95.2%.	not-for-profit,	month, time,	diseases from the	likely have all	selective		identified.
16 17				group-model managed	temperature and	electronic patient	outcome data. ∃	outcome to		
17				care organization (MCO)	dew point.	data warehouse	However, any	judge for low		
19				in the metropolitan		of a	potential errors			
20 21				Atlanta area between		not-for-profit,	or missing data			
21 22				August 1, 1998 and		group-model	did not depend	evidence that		
23				December 31, 2002.		managed care	on air pollution			
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	April	report.		
28				asthma, upper respiratory		Atlanta area	19,			
29 30				infection (URI), or lower		between August	202			
31				respiratory infection		1, 1998 and	j4 bj			
32				(LRI) were included in		December 31,	n6 /			
33 34				the study.		2002.	est.			
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete $\frac{1}{9}$ outcome data ω	Selective reporting	Conflict of interest	Other
8 9			High	Probably Low	Probably Low	Low	Low Y	Probably Low	Low	Low
9 10	41	Krall et al.	Monitors typically	All-cause mortality data	Adjusted for	Study included	Daily counts N	There was	The authors	No other
11		2013	measure PM _{2.5}	(excluding accidental	temperature, day	all death	for death were \bigtriangledown	insufficient	declare they	potential
12 13			constituent	deaths) were aggregated	of week, long-term	(excluding	obtained, so $\frac{S}{2}$	information	have no	sources of
14			concentrations every third	from death certificate	and seasonal	accidental	likely have all $\frac{20}{6}$	about	actual or	bias
15			or sixth day. Some	data obtained from the	trends.	deaths) for 108	outcome data. $\frac{\dot{\alpha}}{\dot{z}}$		potential	identified.
16 17			communities with a	National Center for		urban	However, any B		competing	
18			single monitor. The	Health Statistics for 2000		communities	potential errors		financial	
19			observation of EC was	to 2005.		from 2000 to	or missing data		interests.	
20 21			58-921 days,some			2005.	did not depende			
22			communities had >25%		C C		on air pollution			
23			missing data.				levels.	suggests study		
24 25							/mc	was free of		
25							on A	selective		
27						(April April	report.		
28 29							19,			
30							202			
31							4 by			
32 33							April 19, 2024 by gues			
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1 2 3 4							202 2040-1 202			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	Selective	Conflict of interest	Other
8 9			Probably High	Low	Probably Low	Low	Low	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 	42	Cakmak et al. 2009	Daily PM _{2.5} aerosol samples approximately 1 of every 4 days from a single monitor site. Sampling occurred daily during the cold season (April through September) and alternate days during the warm season (October through March). Missing data <25% for that frequency.	Diseases were coded using the WHO International Classification of Disease, 9th Revision (ICD-9). The daily number of emergency department visits for all nonaccidental (ICD-9 < 800) and respiratory (ICD-9 460–519) causes in Santiago Centro, Cerrillos, and Pudahuel were obtained from the Departamento de Estad´ isticas e InformaciónenSalud (DEIS) of the Ministry of Health from April 2001 through August 2006.	Adjusted for temperature and humidity, day of week, long-term and seasonal trends.	Study included all emergency department visits obtained from the Departamento de Es-tad´ 1sticas e InformaciónenSa lud (DEIS) of the Ministry of Health from April 2001 through August 2006.	Daily counts for emergency department visit 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 report.	No competing financial interests.	No other potential sources of bias identified.
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete g outcome data ω	Selective reporting	Conflict of interest	Other
8			Low	Low	Probably Low	Low	Low ay 2	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	43	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 Downloaded for emergency Downloaded department visit were obtained, so likely have all outcome data. However, any potential errors or missing data did not depending 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.
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4 5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	outcome data	Selective reporting	Conflict of interest	Other
8 9			Low	Low	Probably Low	Low	Low	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	44	Lall et al. 2011	Daily EC data were obtained from two monitors. Daily data was available and no missing data was reported.	The categorization of the admissions data was based on codes from the International Classification of Diseases, revision 9 (ICD-9).	Model adjusted for season, wintertime influenza episode, weather, day of week, and other possible confounders (e.g., federal holidays).	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.
38 39 40 41 42 43 44				For peer review only	- http://bmjopen.bmj	.com/site/about/guid	-			

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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	Selective reporting	Conflict of interest	Other
8 0			Probably High	Low	Probably Low	Low	Low X	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 _{2.5} 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, 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.	No competing financial interests.	No other potential sources of bias identified.
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1 2 3 4							9n-2021-0499			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete og outcome data∞	Selective reporting	Conflict of interest	Other
8			Probably Low	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 38	46	Gong et al. 2019	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 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) were obtained.	Adjusted for calendar effects, long-term trends, temperature, humidity, day of week, NO ₂ and SO ₂ .	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.	Daily counts for all deaths 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 conflict of interest.	No other potential sources of bias identified.
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1 2 3 4							36/bmjopen-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete \int_{Ω}^{Ω} outcome data ω		Conflict of interest	Other
8			Probably Low	Probably Low	Probably High	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	47	Mostofsky et al. 2012	Ambient EC obtained from one monitor. BC concentrations were measured continuously. Daily data was available and no missing data was reported.	Patients potentially eligible for this study were identified by reviewing daily emergency department admission logs, stroke service admission logs, stroke service consult logs, and hospital electronic discharge records.	Model adjusted for seasonality, time-trends, temperature, dew point temperature, barometric pressure and chronic and slowly-varying potential confounders.	Population consisted of patients ≥21 years of age admitted to the hospital with neurologist-confi rmed ischemic stroke and residing in the Boston metropolitan region. Also patients had to reside within 40 km of the air pollution monitor.	Daily counts for emergency Down department admission 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 report.	No competing financial interests.	No other potential sources of bias identified.
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1 2 3 4							36/bmjopen-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete \int_{Ω}^{Ω} outcome data ω	Selective	Conflict of interest	Other
8			Probably 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	48	Krall et al. 2017	PM _{2.5} constituents from one urban, ambient monitor located in each city. Daily pollution data were available in Atlanta; however, data were only available approximately every third day in the remaining three cities. There was no information about missing data.	The study obtained electronic billing data for respiratory disease emergency department visits for all ages at acute care hospitals. Using diagnosis codes from the International Classification of Diseases, 9th Revision (ICD-9), the study considered subcategories of respiratory diseases including pneumonia (ICD-9 codes 480–486), chronic obstructive pulmonary disease (491,492,496), upper respiratory infection (URI) (460–465, 466.0, 477), and asthma and/or	Adjusted for holidays, long-term trends, day of the week, season, hospitalsreporting data, temperature and dew point.	Study included all emergency department visits for respiratory disease at acute care hospitals in the 20-county Atlanta metropolitan area, the 7-county Birmingham metropolitan area, the 8 Missouri and 8 Illinois counties in the St. Louis metropolitan area, and the 12-county Dallas metropolitan	Daily counts for emergency Downloaded for emergency Downloaded respiratory disease 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 report.	The authors declare they have no actual or potential competing financial interests.	No other potential sources of bias identified.
37 38 39 40 41 42				wheeze (493, 786.07).		area.	d by copyright.		<u> </u>	

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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete $\frac{6}{9}$ outcome data $^{\omega}$	Selective reporting	Conflict of interest	Other
8			Probably Low	Low	Probably Low	Low	Low ay 2	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	49	O'Lenick et al. 2017	The 24-hour average concentration of EC was evaluated. Pollutant concentration estimates were obtained by fusing observational data from available network monitors with pollutant concentration simulations from the Community Multi-Scale Air Quality emissions-based chemical transport model at 12×12km grids over Atlanta. 24-hour average EC were evaluated. Daily data was available and no missing data was reported.	Patient-level emergency department visit data from 1 January 2002 to 31 December 2008 were acquired from hospitals located within the 20-county metropolitan area of Atlanta; Relevant data elements included admission date, International Classification of Diseases Ninth Revision (ICD-9) diagnosis codes, age and ZIP code of patient residence.	Adjusted for season, periods of hospital participation and holidays, temperature and mean dew point, interaction terms between season and maximum temperature and day of year.	Study included all emergency department visit data acquired directly from hospitals (2002–2004 period) and the Georgia Hospital Association (2005–2008 period) located within the 20-county metropolitan area of Atlanta.	Daily counts for emergency Downloaded for emergency Downloaded department visit 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.	Competing interests: None declared.	No other potential sources of bias identified.
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1 2 3 4							36/bmjopen-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete \int_{Ω}^{Ω} outcome data \cong		Conflict of interest	Other
8 9			Probably Low	Low	Probably Low	Low	Low ay	Probably Low	Low	Low
9 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 13			monitoring location in	pediatric asthma related	of the week,	department visits	asthma related	information	they have	sources of
14			Atlanta. Daily data was	emergency department	hospital, holidays,	for pediatric	emergency	about	no	bias
15			available and no missing	visits for children ages 5	temperature and	asthma of	department d	selective	competing	identified.
16 17			data was reported.	to 18 years from 41	dew point.	children ages 5	visits were	outcome to	interests.	
18				hospitals within		to 18 years from	obtained, so	judge for low		
19				metropolitan Atlanta; and		41 hospitals	likely have all			
20 21				defined emergency		within	outcome data.			
22				department visits for		metropolitan	However, any	evidence that		
23				pediatric asthma as all	-	Atlanta for study	potential errors			
24 25				visits with a code for asthma (493.0–493.9) or		period.	or missing data			
26				wheeze (786.07) using			did not dependg on air pollution			
27 28				the International						
20 29				Classification of			, , ,			
30				Diseases, 9th Revision.			024			
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete \bigcup_{Ω}^{O} outcome data ω	Selective reporting	Conflict of interest	Other
8			Low	Low	Probably Low	Low	Low 2	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	51	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 Down 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.
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1 2 3 4							36/bmjopen-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete \int_{Ω}^{Ω} outcome data ω	Selective	Conflict of interest	Other
8			Low	Low	Probably Low	Low	Low 2	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	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 of 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.
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete g outcome data ω	Selective reporting	Conflict of interest	Other
8 9			Probably High	Low	Probably Low	Low	Low S	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 	53	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 _{2.5} 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 P22 for death and emergency hospitalization were obtained, from http://bmjopen.bmj. so likely have all outcome data. However, bmjopen.bmj. com of the provided from http://bmjopen.bmj. any potential errors or missing data did not depend on air pollution levels. 90 19, 2024 by guest.	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.
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1 2 3 4							36/bmjopen-2021-0499			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete og outcome data∞	Selective reporting	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	54	Ostro et al. 2015b	The model calculations track the mass and concentrations of the PM constituents in particle diameters ranging from 0.01 to 10µm through calculations that describe emissions, transport, diffusion, deposition, coagulation, gas- and particle-phase chemistry, and gas-to-particle conversion. The University of California Davis/California Institute of Technology model was used to estimate ground-level concentrations of 50 PM constituents over the major population regions in California.	Deaths were assigned codes based on the International Classification of Diseases, 10th Revision (ICD-10) for the following outcomes: all-cause deaths excluding those with an external cause (A00–R99), cardiovascular deaths (I00–I99), Ischemic heart disease deaths (I20–I25), and pulmonary deaths (C34, J00–J98).	ge, race, marital status, smoking status, pack-years of smoking, secondhand smoke exposure, body mass index, lifetime physical activity, alcohol consumption, average daily dietary intake of fat, calories, menopausal status, family history of myocardial infarction, stroke, use of blood pressure medication, aspirin; living conditions	Data obtained for a cohort of female teachers ≥30 years old.	There was no 222. Downloaded from http://bmjopen.bmj.com/ on April 19, 2024 by guest. Protected	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.
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1 2 3 4							36/bmjopen-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete \int_{Ω}^{16} outcome data \Im	Selective reporting	Conflict of interest	Other
8 9 10 11 12 13 14 15 16 17 18				KOrpe	(income, income inequality, education, population size, racial composition, unemployment).		ay 2022. Downloaded from http://www.com/com/com/com/com/com/com/com/com/com/			
19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37	55	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 use regression models.	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 follow-up period.	Probably Low During the 4-year follow-up period, 38,377 (8%) subjects (8%) subjects (8%) subjects follow-up because of moving out of the province or dying from other diseases. Protected	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.
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1 2 3 4							36/bmjopen-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete \int_{Ω}^{0} outcome data ω		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	56	Hvidtfeldt et al. 2019	The PM, NO ₂ , BC, and O ₃ 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 ₂ , BC, and O ₃ .	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 consumption, physical activity; neighborhood level socioeconomic status (SES).	Data obtained for a cohort of men and women aged 50–64 years residing in the areas of Copenhagen and Aarhus.	There was no 222 information on Downloaded from http://bmjopen.bmj.com/ on April 19, 2024 by guest. Protected	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.
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Pag	je 111 d	of 122			BMJ Oper	1	36/bmjop			
1 2 3 4							36/bmjopen-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete \int_{2}^{20} outcome data \simeq	Selective reporting	Conflict of interest	Other
8			Probably Low	Probably Low	Probably High	Low	Probably High	Probably Low	Low	Low
9 10	57	Thurston	The mean concentrations	More than 99% of known	Active smoking	Data obtained for	The analytic N	There was	No	No other
11		et al. 2016	of PM _{2.5} 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			Agency Air Quality	Diseases, 9th and 10th	exposure to PM,	including	Ischemic heart	outcome to		
17 18			System. These PM _{2.5}	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 _{2.5} mass		and BMI^2 ,	District of	causes)	suggests study		
24			exposure concentrations		consumption of	Columbia, and	occurring	was free of		
25 26			using the absolute		beer, wine, and	Puerto Rico.	during 9	selective		
27			principal component		other alcohol,		follow-up.	report.		
28			analysis (APCA) PM _{2.5}		quintile of dietary		19,			
29 30			source apportionment		fat consumption,		2024			
31			method.		quintile of		24 by			
32					combined dietary		by gues			
33 34					vegetable, fruit,					
35					fiber consumption;		Pro			
36					Six ecologic		tect			
37 38					covariates.		Protected by	:		
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41 42							ght.			
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1 2 3 4							36/bmJopen-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete og outcome data∝ ≤	Selective	Conflict of interest	Other
8 9			Probably Low	Low	Probably Low	Low	Probably Low	Probably Low	Low	Low
9 10	58	Yang et al.	Land use regression	Deaths were coded	Age at entry,	Data obtained for	There was no N	There was	The authors	No other
11		2018	models were derived	according to the	gender, individual	a cohort of	information on		declare they	potential
12 13			from street level	International	smoking status,	people who were	the rate of lost	information	have no	sources of
14			measurements collected	classification of Diseases,	body mass index	older than or	the rate of lost	about	actual or	bias
15			during two sampling	10th Revision (ICD-10;	(BMI), physical	equal to 65 years		selective	potential	identified.
16 17			campaigns conducted in	WHO 2010) including	activity, education	old.		-	competing	
18			2014 and 2015.	natural cause mortality	level and monthly		mp:/	judge for low	financial	
19				(A00–R99), overall	expenses;		i mjope	risk, but	interests.	
20 21				cardiovascular disease	percentage of		ope	indirect		
22				(I00–I99) and overall	participants who		n.on	evidence that		
23				respiratory disease	were equal to or	10.		suggests study		
24 25				(J00–J47 and J80–J99).	older than 65 years	en a		was free of		
26				Subcategories included	old, percentage of		on A	selective		
27				Ischemic heart disease	participants whose			report.		
28 29				(IHD) (I20–I25), cerebrovascular disease	educational level was higher than		19, 2			
30				(I60–I69), Pneumonia	secondary school,		2024			
31				(J12–J18) and chronic	average income		on April 19, 2024 by guest	-		
32 33				obstructive pulmonary	per month and		gue			
34				disease (COPD) (J40–I44	percentage of		•			
35				and I47).	smokers.		rote			
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1 2 3 4							36/bmjopen-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete \int_{2}^{2} outcome data ω	Selective reporting	Conflict of interest	Other
8			Probably Low	Low	Probably High	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	59	Gan et al. 2011	Land use regression to estimate air pollution concentrations and exposure assigned to residential centroid.	A coronary heart disease hospitalization case is a record of hospitalization with the following International Statistical Classification of Diseases, 9th Revision codes, ICD-9, 410–414 and 429.2or 10th Revision (ICD-10), I20–I25, as the principal diagnosis (the most responsible diagnosis) for a hospital admission in the hospitalization database. A coronary heart disease death is a death record with coronary heart disease as the cause of death in the provincial death registration database.	Model adjusted for age, sex, preexisting comorbidity, and neighborhood socioeconomic status. No individual data on behavioral risk factors.	Study provided total number of subjects along with those lost during the follow-up period.	During the 4-year follow-up period, 17,542 (3.9%) moved from out of the province and 16,367 (3.6%) died from other diseases, leaving 418,826 (9 _{2.5} %) subject at the end of 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 actual or potential competing financial interests.	No other potential sources of bias identified.
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1 2 3 4							2021-0495 			
4 5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	outcome data ≤ ≤	Selective	Conflict of interest	Other
8 9			Probably High	Low	Probably Low	Low	Probably Low	Probably Low	Low	Low
10 11 12 13 14 15 16 17 18 19 20 21 22 23 24		Kluizenaa r et al. 2013	as an indicator of EC concentrations. Derived background EC concentrations from BS measured at two regional monitoring sites. Local traffic-related EC emission contributions were estimated based on fuel-specific EC content of exhaust PM ₁₀	information on the incidence of hospital-based Ischemic heart disease (International Classification of Diseases [ICD9] 410-414) and cerebrovascular disease (ICD9 430-438) in the study population.	covariates: age, gender, marital status, education, smoking, alcohol use, physical activity, body mass index, living conditions (employment status, financial problems).	a cohort of 27,070 non-institutionali zed subjects.	information on bottom on the rate of lost follow up.		competing financial interests.	potential sources of bias identified.
25 26 27 28 29 30 31 32 33 34 35 36 37 37 38			emission. Used the traffic-related EC emissions as input to calculate local EC concentrations, assuming absence of other local EC sources. Also assumed that dispersion dynamics of EC are identical to those of PM_{10} .			en o	3, 2024 by guest. Protected by			
39 40 41 42							copyright.			

Pag	je 115 d	of 122			BMJ Oper	1	36/bmjo			
1 2 3 4							36/bmjopen-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete og outcome data∞	Selective	Conflict of interest	Other
8 9			Probably Low	Probably Low	Probably Low	Low	Probably Low	Probably Low	Low	Low
10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29	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.	There was no 22. Downloaded information on Optimized from http://bmjopen.bmj.com/ on April 19, 20	information about selective outcome to	No financial interests.	No other potential sources of bias identified.
30 31 32 33 34 35 36 37 38 39 40 41 42 43 44				For peer review only	r - http://bmjopen.bmj	.com/site/about/guic	24 by guest. Protected by copyright.			

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	ment (of certainty of eviden	nce for	r outcome									36/bmiopen-2021-049516 on					
6 7					Reaso	ons for downgrading						c	Reasons for	upgrading				Final
8 9	A1	Rationale	A2	Rationale	A3	Rationale	A4	Rationale	A5	Rationale	B1	Rationale 1	uate2022.	Rationale	B3	Rationale	Overall	certainty assessment
10 Performed and the set of the	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			founders would t the RR in both directions	+1	Evidence of increase in risk with increasing exposure	0	Moderate
16 17 Acute effects of BC 18 19 or EC on CVD 20 PM _{2.5} -adjusted 2 model 22	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	shift i	founders would t the RR in both directions	+1	Evidence of increase in risk with increasing exposure	+1	High
23 24pute effects of BC 25pt or EC on RES 26 11 PM25-unadjusted 27 28pdel	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			founders would t the RR in both directions	0	No evidence of a clear increasing risk with exposure	0	Moderate
29 30 30 31 32 EC on RES in 32 33 34 2-5-adjusted 34 35	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	Conception of the shift of the	founders would t the RR in both directions	0	No evidence of a clear increasing risk with exposure	0	Moderate
36 37 38 39 40 41 42 43 44	-				_	For peer review o	only	- http://bmjoŗ	əen.b	vmj.com/site/ał	oout/g	-	Protected by copyright.		-			

Page 117 of 122		BMJ Open	36/bmjoj
1 2 3 4 5Table S5. Assessment	certainty of evidence for outcome		36/bmjopen-2021-049516
б		for downgrading	S GReasons for upgrading Final
7 Evidence A1 9 A1	Rationale A2 Rationale A3	Rationale A4 Rationale A5 Rationale B1	Rationale B3 Rationale assessment
10 Performing effects of 122: or EC on CVD 13 ¹⁰ PM _{2.5} -unadjusted 14 16 16 16 16 16 16 16 16 16 16	Little influence on were consistent with	Risk estimates 30% PI 1.052 (95%CI: reported by the 1.001, 1.104) does not 0 studies are 0 publication bias include unity precise	Insufficient basis for upgrading fo by Confounders would Solution Solutio
	nsistency; A4 = imprecision; A5 = publication bias; B1 = lar	eases; RES: respiratory diseases; IHD: ischemic heart diseases; PI: prediction interval; C rge RR; B2 = all confounding decreases observed RR; B3= concentration-response grad	; C1: confidence interval A1 = limitations in studies (risk of bias); A2 = adient.

Study ID Asia Geng,2013 Wang,2019 Gong,2019 Huang,2012 Lin,2016a Son,2012 Heo,2014 Subtotal (I-squared = 11.8%, p = 0.340) Europe Basagana,2015 Ostro,2015a Atkinson,2016 Subtotal (I-squared = 0.0%, p = 0.608) America Ito,2011 Maynard,2007 Ostro,2007 Kim,2015 Subtotal (I-squared = 21.3%, p = 0.283) NOTE: Weights are from random effects analysis	Relative Risk (95% Cl) 1.012 (1.002, 1.021) 1.011 (0.999, 1.023) 1.002 (1.001, 1.003) 1.005 (0.998, 1.010) 1.002 (0.999, 1.005) 1.001 (0.981, 1.021) 1.006 (0.994, 1.017) 1.003 (1.001, 1.004) 0.979 (0.944, 1.016) 0.994 (0.953, 1.038) 1.005 (0.979, 1.031) 0.987 (0.973, 1.001) 0.990 (0.979, 1.002) 1.003 (0.982, 1.024) 1.076 (0.980, 1.179) 1.026 (1.004, 1.049) 1.031 (0.935, 1.133) 1.017 (0.998, 1.037)
ID Asia Geng,2013 Wang,2019 Gong,2019 Huang,2012 Lin,2016a Son,2012 Heo,2014 Subtotal (I–squared = 11.8%, p = 0.340) Europe Basagana,2015 Ostro,2015a Ostro,2015a Ostro,2015a Atkinson,2016 Subtotal (I–squared = 0.0%, p = 0.608) America Ito,2011 Maynard,2007 Ostro,2007 Kim,2015 Subtotal (I–squared = 21.3%, p = 0.283)	1.012 (1.002, 1.021) 1.011 (0.999, 1.023) 1.002 (1.001, 1.003) 1.005 (0.998, 1.010) 1.002 (0.999, 1.005) 1.001 (0.981, 1.021) 1.006 (0.994, 1.017) 1.003 (1.001, 1.004) 0.979 (0.944, 1.016) 0.994 (0.953, 1.038) 1.005 (0.979, 1.031) 0.987 (0.973, 1.001) 0.990 (0.979, 1.002) 1.003 (0.982, 1.024) 1.076 (0.980, 1.179) 1.026 (1.004, 1.049) 1.031 (0.935, 1.133)
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Geng,2013 Wang,2019 Gong,2019 Huang,2012 Lin,2016a Son,2012 Heo,2014 Subtotal (I-squared = 11.8%, p = 0.340) Europe Basagana,2015 Ostro,2015a Ostro,2015a Ostro,2015a Atkinson,2016 Subtotal (I-squared = 0.0%, p = 0.608) America Ito,2011 Maynard,2007 Ostro,2007 Kim,2015 Subtotal (I-squared = 21.3%, p = 0.283)	1.011 (0.999, 1.023) 1.002 (1.001, 1.003) 1.005 (0.998, 1.010) 1.002 (0.999, 1.005) 1.001 (0.981, 1.021) 1.006 (0.994, 1.017) 1.003 (1.001, 1.004) 0.979 (0.944, 1.016) 0.994 (0.953, 1.038) 1.005 (0.979, 1.031) 0.987 (0.973, 1.001) 0.990 (0.979, 1.002) 1.003 (0.982, 1.024) 1.076 (0.980, 1.179) 1.026 (1.004, 1.049) 1.031 (0.935, 1.133)
Wang,2019 Gong,2019 Huang,2012 Lin,2016a Son,2012 Heo,2014 Subtotal (I-squared = 11.8%, p = 0.340) Europe Basagana,2015 Ostro,2015a Ostro,2015a Ostro,2015a Atkinson,2016 Subtotal (I-squared = 0.0%, p = 0.608) America Ito,2011 Maynard,2007 Ostro,2007 Kim,2015 Subtotal (I-squared = 21.3%, p = 0.283)	1.011 (0.999, 1.023) 1.002 (1.001, 1.003) 1.005 (0.998, 1.010) 1.002 (0.999, 1.005) 1.001 (0.981, 1.021) 1.006 (0.994, 1.017) 1.003 (1.001, 1.004) 0.979 (0.944, 1.016) 0.994 (0.953, 1.038) 1.005 (0.979, 1.031) 0.987 (0.973, 1.001) 0.990 (0.979, 1.002) 1.003 (0.982, 1.024) 1.076 (0.980, 1.179) 1.026 (1.004, 1.049) 1.031 (0.935, 1.133)
Gong,2019 Huang,2012 Lin,2016a Son,2012 Heo,2014 Subtotal (I-squared = 11.8%, p = 0.340) Europe Basagana,2015 Ostro,2015a Ostro,2015a Atkinson,2016 Subtotal (I-squared = 0.0%, p = 0.608) America Ito,2011 Maynard,2007 Ostro,2007 Kim,2015 Subtotal (I-squared = 21.3%, p = 0.283)	1.002 (1.001, 1.003) 1.005 (0.998, 1.010) 1.002 (0.999, 1.005) 1.001 (0.981, 1.021) 1.006 (0.994, 1.017) 1.003 (1.001, 1.004) 0.979 (0.944, 1.016) 0.994 (0.953, 1.038) 1.005 (0.979, 1.031) 0.987 (0.973, 1.001) 0.990 (0.979, 1.002) 1.003 (0.982, 1.024) 1.076 (0.980, 1.179) 1.026 (1.004, 1.049) 1.031 (0.935, 1.133)
Huang,2012 Lin,2016a Son,2012 Heo,2014 Subtotal (I–squared = 11.8%, p = 0.340) Europe Basagana,2015 Ostro,2015a Atkinson,2016 Subtotal (I–squared = 0.0%, p = 0.608) America Ito,2011 Maynard,2007 Ostro,2007 Kim,2015 Subtotal (I–squared = 21.3%, p = 0.283)	1.005 (0.998, 1.010) 1.002 (0.999, 1.005) 1.001 (0.981, 1.021) 1.006 (0.994, 1.017) 1.003 (1.001, 1.004) 0.979 (0.944, 1.016) 0.994 (0.953, 1.038) 1.005 (0.979, 1.031) 0.987 (0.973, 1.001) 0.990 (0.979, 1.002) 1.003 (0.982, 1.024) 1.076 (0.980, 1.179) 1.026 (1.004, 1.049) 1.031 (0.935, 1.133)
Lin,2016a Son,2012 Heo,2014 Subtotal (I–squared = 11.8%, p = 0.340) Europe Basagana,2015 Ostro,2015a Atkinson,2016 Subtotal (I–squared = 0.0%, p = 0.608) America Ito,2011 Maynard,2007 Ostro,2007 Kim,2015 Subtotal (I–squared = 21.3%, p = 0.283)	1.002 (0.999, 1.005) 1.001 (0.981, 1.021) 1.006 (0.994, 1.017) 1.003 (1.001, 1.004) 0.979 (0.944, 1.016) 0.994 (0.953, 1.038) 1.005 (0.979, 1.031) 0.987 (0.973, 1.001) 0.990 (0.979, 1.002) 1.003 (0.982, 1.024) 1.076 (0.980, 1.179) 1.026 (1.004, 1.049) 1.031 (0.935, 1.133)
Heo,2014 Subtotal (I-squared = 11.8%, p = 0.340) Europe Basagana,2015 Ostro,2015a Atkinson,2016 Subtotal (I-squared = 0.0%, p = 0.608) America Ito,2011 Maynard,2007 Ostro,2007 Kim,2015 Subtotal (I-squared = 21.3%, p = 0.283)	1.006 (0.994, 1.017) 1.003 (1.001, 1.004) 0.979 (0.944, 1.016) 0.994 (0.953, 1.038) 1.005 (0.979, 1.031) 0.987 (0.973, 1.001) 0.990 (0.979, 1.002) 1.003 (0.982, 1.024) 1.076 (0.980, 1.179) 1.026 (1.004, 1.049) 1.031 (0.935, 1.133)
Subtotal (I–squared = 11.8%, p = 0.340)	1.003 (1.001, 1.004) 0.979 (0.944, 1.016) 0.994 (0.953, 1.038) 1.005 (0.979, 1.031) 0.987 (0.973, 1.001) 0.990 (0.979, 1.002) 1.003 (0.982, 1.024) 1.076 (0.980, 1.179) 1.026 (1.004, 1.049) 1.031 (0.935, 1.133)
Subtotal (I–squared = 11.8%, p = 0.340)	0.979 (0.944, 1.016) 0.994 (0.953, 1.038) 1.005 (0.979, 1.031) 0.987 (0.973, 1.001) 0.990 (0.979, 1.002) 1.003 (0.982, 1.024) 1.076 (0.980, 1.179) 1.026 (1.004, 1.049) 1.031 (0.935, 1.133)
Basagana,2015 Ostro,2015a Ostro,2015a Atkinson,2016 Subtotal (I–squared = 0.0%, p = 0.608) America Ito,2011 Maynard,2007 Ostro,2007 Kim,2015 Subtotal (I–squared = 21.3%, p = 0.283)	0.994 (0.953, 1.038) 1.005 (0.979, 1.031) 0.987 (0.973, 1.001) 0.990 (0.979, 1.002) 1.003 (0.982, 1.024) 1.076 (0.980, 1.179) 1.026 (1.004, 1.049) 1.031 (0.935, 1.133)
Basagana,2015 Ostro,2015a Ostro,2015a Atkinson,2016 Subtotal (I–squared = 0.0%, p = 0.608) America Ito,2011 Maynard,2007 Ostro,2007 Kim,2015 Subtotal (I–squared = 21.3%, p = 0.283)	0.994 (0.953, 1.038) 1.005 (0.979, 1.031) 0.987 (0.973, 1.001) 0.990 (0.979, 1.002) 1.003 (0.982, 1.024) 1.076 (0.980, 1.179) 1.026 (1.004, 1.049) 1.031 (0.935, 1.133)
Ostro,2015a Ostro,2015a Atkinson,2016 Subtotal (I-squared = 0.0%, p = 0.608) America Ito,2011 Maynard,2007 Ostro,2007 Kim,2015 Subtotal (I-squared = 21.3%, p = 0.283)	1.005 (0.979, 1.031) 0.987 (0.973, 1.001) 0.990 (0.979, 1.002) 1.003 (0.982, 1.024) 1.076 (0.980, 1.179) 1.026 (1.004, 1.049) 1.031 (0.935, 1.133)
Atkinson,2016 Subtotal (I-squared = 0.0%, p = 0.608) America Ito,2011 Maynard,2007 Ostro,2007 Kim,2015 Subtotal (I-squared = 21.3%, p = 0.283)	0.987 (0.973, 1.001) 0.990 (0.979, 1.002) 1.003 (0.982, 1.024) 1.076 (0.980, 1.179) 1.026 (1.004, 1.049) 1.031 (0.935, 1.133)
Subtotal (I-squared = 0.0%, p = 0.608)	0.990 (0.979, 1.002) 1.003 (0.982, 1.024) 1.076 (0.980, 1.179) 1.026 (1.004, 1.049) 1.031 (0.935, 1.133)
America Ito,2011 Maynard,2007 Ostro,2007 Kim,2015 Subtotal (I–squared = 21.3%, p = 0.283)	0.990 (0.979, 1.002) 1.003 (0.982, 1.024) 1.076 (0.980, 1.179) 1.026 (1.004, 1.049) 1.031 (0.935, 1.133)
Ito,2011 Maynard,2007 Ostro,2007 Kim,2015 Subtotal (I-squared = 21.3%, p = 0.283)	1.076 (0.980, 1.179) 1.026 (1.004, 1.049) 1.031 (0.935, 1.133)
Ito,2011 Maynard,2007 Ostro,2007 Kim,2015 Subtotal (I-squared = 21.3%, p = 0.283)	1.076 (0.980, 1.179) 1.026 (1.004, 1.049) 1.031 (0.935, 1.133)
Maynard,2007 Ostro,2007 Kim,2015 Subtotal (I–squared = 21.3%, p = 0.283)	1.076 (0.980, 1.179) 1.026 (1.004, 1.049) 1.031 (0.935, 1.133)
Ostro,2007 Kim,2015 Subtotal (I–squared = 21.3%, p = 0.283)	1.026 (1.004, 1.049) 1.031 (0.935, 1.133)
Kim,2015 Subtotal (I–squared = 21.3%, p = 0.283)	1.031 (0.935, 1.133)
Subtotal (I–squared = 21.3%, p = 0.283)	
	1.017 (0.998, 1.037)
NOTE: Weights are from random effects analysis	
1	
.848 1	1.18
.010	1.10
1. Impact of short-term exposure to BC or EC on cardiovascular mortality	stratified by geographical loc

ID		Relative Risk (95%CI)
Europe		
Basagana,2015	-	1.026 (1.006, 1.047)
America		
Bell,2014	-	1.036 (1.023, 1.050)
Sarnat,2015	— •—	1.038 (1.005, 1.073)
to,2011	-	1.019 (1.007, 1.034)
Winquist,2015		1.048 (1.012, 1.085)
Tolbert,2007	+	1.013 (1.004, 1.022)
Lall,2011		1.022 (0.999, 1.046)
Metzger,2004	+	1.017 (1.007, 1.027)
Peng,2009	+	1.018 (1.011, 1.025)
Liu,2016a	•	0.960 (0.857, 1.076)
Liu,2016b		1.020 (0.858, 1.214)
Kim,2012		1.056 (1.018, 1.094)
Subtotal (I-squared = 41.7%, p = 0.071)	\diamond	1.022 (1.016, 1.029)
NOTE: Weights are from random effects analy:	sis	

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

itudy	
D	Relative Risk (95%CI)
-18	
0'Lenick, 2017	1.026 (1.010, 1.044)
trickland,2014	+ 1.045 (1.018, 1.073)
trickland,2010	1.021 (0.996, 1.047)
lua,2014	+ 1.028 (1.020, 1.031)
inclair,2010 +	1.019 (0.981, 1.060)
inclair,2010 +	0.974 (0.948, 1.002)
ubtotal (I–squared = 68.4%, p = 0.007)	> 1.020 (1.006, 1.035)
18 years	
inclair,2010	0.993 (0.963, 1.023)
inclair,2010	1.021 (0.978, 1.065)
ai,2014 +	1.009 (0.995, 1.022)
omic-Spiri,2019	+ 1.033 (1.001, 1.066)
ubtotal (I–squared = 14.2%, p = 0.321)	1.011 (0.998, 1.025)
IOTE: Weights are from random effects analysis	
.932 1	1.07

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

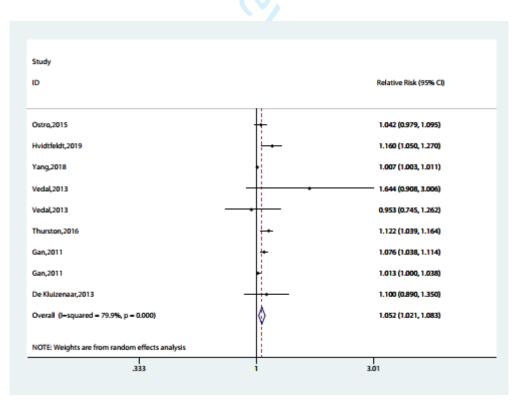


Fig. S4. Impact of long-term exposure to BC or EC on cardiovascular diseases.

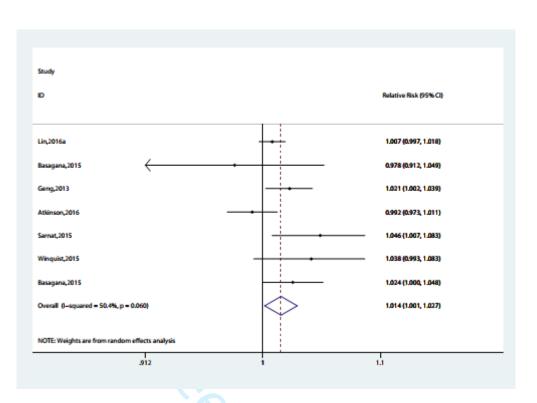


Fig. S5. Impact of short-term exposure to BC or EC on cardiovascular diseases in the PM2.5-adjusted model.

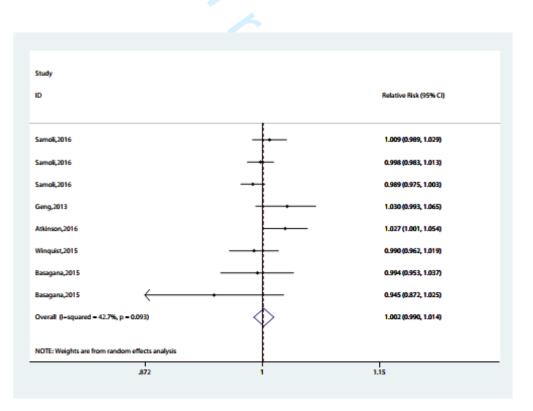


Fig. S6. Impact of short-term exposure to BC or EC on respiratory diseases in the PM_{2.5}-adjusted model.



PRISMA 2009 Checklist

		BMJ Open 30	Page 122 of 122
PRISMA 20)09 (BMJ Open 136/bmj Checklist 202	
Section/topic	#	Checklist item	Reported on page #
TITLE		9 9	
Title	1	Identify the report as a systematic review, meta-analysis, or both. α	#1
ABSTRACT		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; conclusions and implications of key findings; systematic review registration number.	#3-4
INTRODUCTION			
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 study 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 ate) and any processes for obtaining 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 any assumptions 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., I ²) for each meta-analysis. For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml	#11

Page 123 of 122



PRISMA 2009 Checklist

Page 1 of 2

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		Page 1 of 2						
Section/topic	#	Checklist item						
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	bescribe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating #						
RESULTS								
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with be asons 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, PIC S, 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 tee 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-regession [see Item 16]).	#18					
DISCUSSION	<u> </u>							
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider 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., incomplete retrieval of 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.						
FUNDING	<u> </u>							
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	#30					
	1	8	1					

41 *From:* Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097.
 43 For more information, visit: www.prisma-statement.org.

Page 2 of 2 For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

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

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Title Page

Title:

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

Respiratory Diseases: A Systematic Review and Meta-Analysis

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Abstract

Background Adverse health effects of fine particles (PM_{2.5}) 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 μ g/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%

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4	(95% CI: 0.4%-13.5%) increase in cardiovascular diseases.
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6	Conclusions Both short-term and long-term exposure to BC or EC were related with
7	Conclusions both short-term and long-term exposure to be of he were related with
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9	cardiovascular diseases and the association differs across continents. There is still not
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11	
12	enough evidence on respiratory diseases in vulnerable groups, which requires further
13	
14	investigation.
15	investigation.
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17	Keywords Black carbon, Cardiovascular disease, Respiratory disease, Systematic
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20	review
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22	PROSPERO registration number CRD42020186244.
23	PROSPERO registration number CRD42020186244.
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Strengths and limitations of this study

 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.¹ 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_{2.5}, are well documented. In 2017, a total of 2.94 million deaths resulted from ambient PM worldwide.³⁻⁵ PM_{2.5} 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.^{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.8,9 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.⁴ 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.^{13, 14} 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) 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 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 Page 11 of 136

BMJ Open

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 μ 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.^{16, 17} 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.¹⁸ In addition, the same cohort data were analyzed in different studies and the latest studies were included in the systematic review and meta-analysis.¹⁹⁻²¹

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.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 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 $PM_{2.5}$ is a potential confounder in assessing the health effects of $PM_{2.5}$ constituents.⁷ For overall and outcome analysis, PM_{2.5}-adjusted estimates and PM_{2.5}-unadjusted estimates in the models were combined, respectively where more Regarding than three estimates were available. the subgroup analysis. PM2.5-unadjusted estimates were analyzed, while PM2.5-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.^{25, 26} Of these, 70 fulfilled the inclusion criteria (Figure 1).^{7, 16-21, 27-89} 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 μ 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 μ 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 μ 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 μ g/m³, 95% CI: 1.016–1.029) were higher compared to their effect on mortality (RR=1.003 per 1 μ 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 μ g/m³, 95% CI: 1.006–1.016), and then diminished on lag 1 (RR=1.005 per 1 μ g/m³, 95% CI: 1.002–1.008) and lag 2 (RR=1.002 per 1 μ 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.¹⁸ 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).

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	PM _{2.5} -unadjusted model					ے۔ س PM _{2.5} -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. L			
Age						Dowr			
All population	20	22	1.008 (1.004, 1.012)	64.40%	0.007	6 6	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)	_	_	6 –	_	_	_
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%	—	— br	_	—	—
Outcome						http://bmjopen.bi			
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 mj.com/	4	1.006 (0.993, 1.019)	42.90
Respiratory Diseases), /mc			
Age						on A			
All population	16	18	1.010 (0.996, 1.025)	87.20%	0.627	5 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	Ģ,		_	_
≥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	3 ^{išt} . 7	5	0.996 (0.987, 1.004)	0
Mortality	10	11	1.013 (0.997, 1.030)	66.40%	0.328	3 Tote	3	1.017 (0.985, 1.050)	48.30
			16			cted by copyright.			

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.^{20, 53, 61, 68} 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).¹⁹

3.3 Results from the PM_{2.5}-adjusted model

In the PM_{2.5}-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 μ 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_{2.5}-unadjusted model. In addition, the impact of BC or EC on cardiovascular morbidity in the PM_{2.5}-adjusted model (RR=1.018 per 1 μ g/m³, 95% CI: 1.006-1.031) was consistent with the results in the PM_{2.5}-unadjusted model (RR=1.022 per 1 μ 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 µg/m³, 95% CI: 1.001-1.006), while no association was observed in the $PM_{2.5}$ -adjusted model (RR=1.006 per 1 µg/m³, 95% CI: 0.993-1.019) (Table 1). On the other hand, consistent results (RR=1.002 per 1 µg/m³, 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 μ g/m³, 95% CI: 1.002-1.010) by eliminating studies with partial overlap from the same geographical location.^{16, 18, 31, 73} In addition, no statistical significance was observed (RR=1.008 per 1 μ g/m³, 95% CI: 0.992-1.023) between respiratory diseases and BC or EC after eliminating overlapped studies (Table 1).^{16, 18, 81, 87}

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.^{7, 19, 21, 39, 48, 67, 84} 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.^{46, 78, 85}

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 "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).

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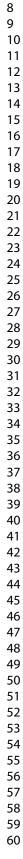
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Table 2 Results of risk of bias assessment

			Key criteria			Oth	ner criteria		
No.	Study	Exposure	Outcome	Confounding	Selection	Incomplete	Selective	Conflict of	
		assessment	assessment	bias	bias	outcome data	reporting	interest	
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								

			Key criteria	a		Ot	her criteria		
No.	Study	Exposure	Outcome	Confounding	Selection	Incomplete	Selective	Conflict	0
		assessment	assessment	bias	bias	outcome data	reporting	of interest	Ŭ
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 2 Results of risk of bias assessment (continued)



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 $PM_{2.5}$ -adjusted model were obtained in the $PM_{2.5}$ -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 $PM_{2.5}$ -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_{2.5}-unadjusted model and PM_{2.5}-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_{2.5}-unadjusted model.⁵⁶ However, in the PM_{2.5}-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 PM25-adjusted model and PM_{2.5}-unadjusted model.^{17, 78} 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

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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 $PM_{2.5}$ -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 $PM_{2.5}$ -unadjusted/adjusted model and chronic effects of BC or EC on cardiovascular diseases in $PM_{2.5}$ -unadjusted model) upgrade one level on concentration-response gradient for an increase in risk with increasing BC or EC.²⁴ 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.⁹³ In addition, lung function and mucociliary clearance decline with long-term exposure to pollutants and increasing age.^{5, 94} 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_{2.5}.⁹⁵ In addition, BC activates macrophages from the

lung cells, which release pro-inflammatory mediators, finally leading to an accumulation of inflammatory cells.⁹⁶ 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.⁹⁸ Yamawaki et al found that BC directly impacts the vascular endothelium, causing inflammatory responses, cytotoxic injury, and inhibition of cell growth.⁹⁹ These responses contribute to the progression of atherosclerosis, leading to cardiovascular disease.⁹⁹ 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.¹⁰⁰ 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.¹¹⁰

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 $PM_{2.5}$ when assessing the health Page 27 of 136

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effect of PM_{2.5} constituents. Mostofsky et al. proved that PM_{2.5} may be associated with both health and its constituents. Constituent having closer association with PM_{2.5} may illustrate a stronger association with diseases. Therefore, the results of PM₂ 5-unadjusted model could introduce bias.⁷ 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.

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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 all authors.

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Competing interests

We declare that all authors have no competing interests.

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Data sharing statement

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

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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.

 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.

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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).

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 <u>https://ntpniehsnihgov/ntp/ohat/</u> 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_{2.5} 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

BMJ Open

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 ≥ 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 36

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.

BMJ Open

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* 39

BMJ Open

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 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.

Λ exp.. Figure 3 Impact of short-term exposure to BC or EC on respiratory diseases 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 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_{2.5}-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.

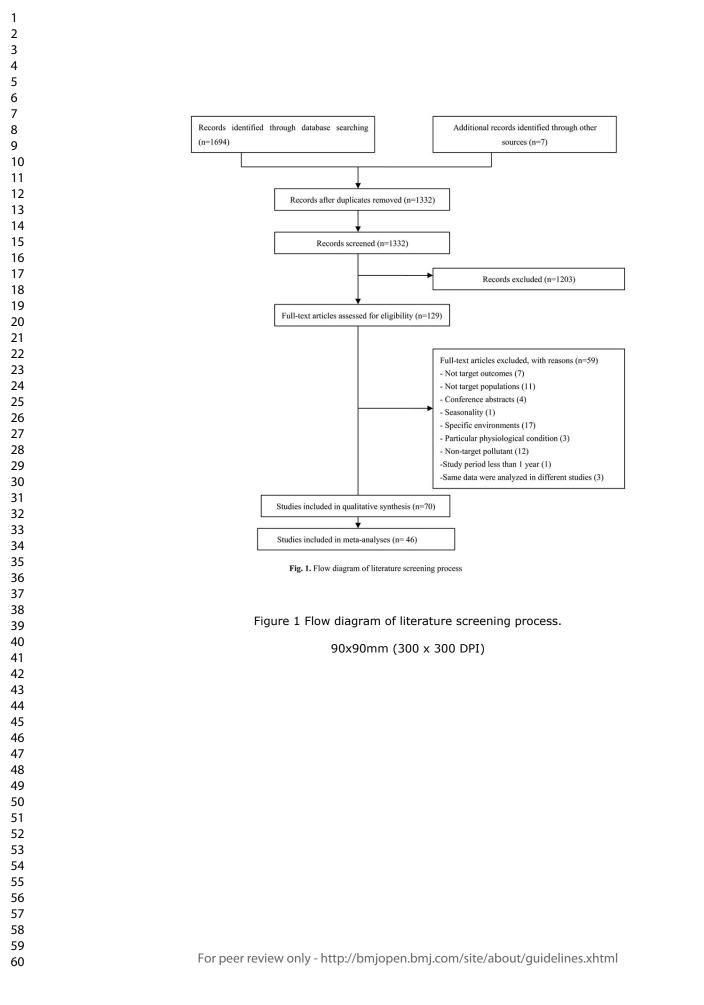
Figure S4 Impact of short-term exposure to BC or EC on asthma morbidity in

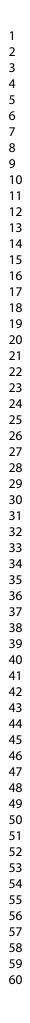
different age groups.

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_{2.5}-adjusted model.





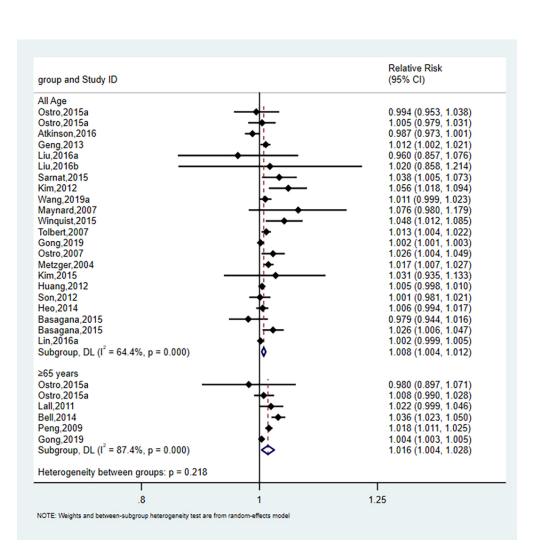


Figure 2 Impact of short-term exposure to BC or EC on cardiovascular diseases in the PM2.5-unadjusted model.

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	Relative Risk
Study ID	(95% CI)
Atkinson,2016	1.013 (0.993, 1.033)
Geng,2013	1.002 (0.983, 1.021)
Ostro,2015a	- 1.090 (1.004, 1.183)
Ostro,2015a	1.064 (1.020, 1.110)
Sarnat,2015	0.995 (0.969, 1.022)
Huang,2012	1.005 (0.993, 1.017)
Son,2012 -	0.989 (0.956, 1.024)
Kim,2015	1.081 (0.920, 1.266)
Heo,2014 -	0.988 (0.962, 1.015)
Basagana,2015 -	0.986 (0.949, 1.026)
Basagana,2015	0.940 (0.879, 1.006)
Maynard,2007	
Liu,2016a	0.964 (0.895, 1.039)
Liu,2016b	0.963 (0.806, 1.150)
Kim,2012	1.100 (0.949, 1.270)
Cakmak,2009	1.036 (1.031, 1.041)
Wang,2019a	1.038 (1.017, 1.059)
Tolbert,2007	0.997 (0.990, 1.003)
Overall, DL (l ² = 87.2%, p = 0.000)	1.010 (0.996, 1.025)
.667 1	1.5

Figure 3 Impact of short-term exposure to BC or EC on respiratory diseases in the PM2.5-unadjusted model.

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SUPPLEMENTARY APPENDIX

Short-term and Long-term Exposure to Black

Carbon and Cardiovascular and Respiratory

Diseases: A Systematic Review and Meta-Analysis

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Supplementary data

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Figure S1 Impact of short-term exposure to BC or EC on respiratory diseases in 65+ years age group in the PM_{2.5}-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_{2.5}-adjusted model.

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No.	Search Strategy ω
#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	"PM".tw.
#4	
#5	or/1,2,3 "EC" /or "BC".tw. and/4,5 black carbon*/or element arbon*.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.
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Table S2 Charact	teristics o	of included	studies in the s	systematic 1	review and m	eta-analys	iis	36/bmjopen-2021-049516 c
Study	Study Design	Country	Study Period	Outcome	Age	Pollutant	ICD code	G G Seases So
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
Bell et al. 2014	TS	USA	2000-2004	Morbidity	≥65	BC	ICD-9	RES[COPD(ICD-9-CM:490-492,RTI(ICD-9-CM:464466, 480-487)];CVD[HF(ICD-9-CM:428),Heart Rhy Disturbances(ICD-9-CM:426-427), Cerebrovascular events(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) e
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	BC	ICD-10	Asthma(ICD-10:J45) CVD(ICD-10:I00-I99),RES(ICD-10:J00-J99) Pbb//
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	BC	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(CD-9:460-519),COPD(ICD-9:490-492,494,496),Pneum CD-9:480-486),Asthma(ICD-9:493),SSID(ICD-9:78
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),Pneu (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(IED9:480-486),COPD (ICD:491,492,496),Asthma/Whe (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)

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Table S2 Charad	cteristics	of included s	studies in the	systematic re	eview and 1	meta-analys	is	36/bmjopen-2021-049516	
Study	Study Design	Country	Study Period	Outcome	Age	Pollutant	ICD code	⊖ ₩ ₩ ₩ ₩	
Ostro et al. 2009	TS	USA	2000-2003	Morbidity	<19	EC	ICD9	ی	
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 Rhythen 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 2),RES(ICD-9:464-466,480-487)]	
Levy et al. 2012	TS	USA	2000-2008	Morbidity	≥65	EC	ICD-9	러 CVD(ICD-9:390-459),RES(ICD-9:464-466 and 480-뾾7).	
on et al. 2012	TS	Korea	2008-2009	Mortality	All	EC	ICD-10	CVD(ICD-10:I00-I99),RES(ICD-10:J00-J99)	
Ieo 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-9:460-519,ICD-10:J00-J99)	
Dai et al. 2014	TS	USA	2000-2006	Mortality	All	EC	ICD-10	CVD(ICD-10:101-I59),RES(ICD-10:J00-J99),MI(IC	
Lin et al. 2016a	TS	China	2007-2011	Mortality	All	EC	ICD-10	CVD(ICD-10:100-199) 9	
Cao et al. 2012	TS	China	2004-2008	Mortality	All	EC	ICD-10	CVD(ICD-10:100-199),RES(ICD-10:J00-J98)	
Klemm et al. 2011	TS	USA	1998-2007	Mortality	≥65	EC	ICD-10	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:I01-I99),RES(ICD-10:J00-J99)	
Vinquist 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,	1,
Ostro et al. 2007	TS	USA	2000-2003	Mortality	All	EC	ICD-10	428,433-437,440,443-445,451-453) CVD(ICD-10:100-199),RES(ICD-10:100-198)	
Folbert et al. 2000	TS	USA	1998-2000	Morbidity	All	EC	ICD-9	CVD(ICD-9:402,410-414,427,428,433-437,440,444, 49 1-453),RES(ICD-9:460-466,477,480-486,491,492,493,49 786.09)	6,
								786.09) ec ed by copyright.	
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1 2 3 4 5	Table S2 Charac	cteristics c	of included	studies in the	systematic	review and me	eta-analys	iis	36/bmjopen-2021-049516 on
6 7 8	Study	Study Design	Country	Study Period	Outcome	Age	Pollutant	ICD code	⊐ Biseases
9 10 11 12	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)
13	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)
14									CVD[IHD(ICD-9:410-414),AMI(ICD-9:410),cardiaco
15 16	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
17									events(ICD-9:433-437,440,443-444,451-453),CHD(IgD-9:440),Stroke(ICD-9:436)]
18	Mar et al. 2000	TS	USA	1995-1997	Mortality	All	EC	ICD-9	CVD(ICD-9:390-448.9)
19 20	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)
21	Lin et al. 2016b	TS	China	2007-2011	Mortality	All	EC	ICD-10	Stroke(ICD-10:I60-I66)
22	Ostro et al. 2008	TS	USA	2000-2003	Mortality	All	EC	ICD-10	CVD(ICD-10:100-199)
23 24 25 26	Ito et al. 2011	TS	USA	2000-2006	Morbidity, Mortality	≥40	EC	ICD-9, ICD-10	CVD[Hypertensive Diseases(ICD-9:402,ICD-10:11116/11(ICD-9:410;ICD-10:121-122),IHD (ICD-9:414,ICD-10:125),Dysrhythmias(ICD-9:427,ICD-10:148),HF(ICD-9:428,ICD-10:150),Stroke(ICD-9:430-43 9,ICD-10:I60-169)]
27 28	Chen et al. 2014	TS	China	2004-2008	Morbidity	All	EC	ICD-9	Stroke[Ischemic Stroke(ICD-9:433-434),Hemorrhagi Stroke(ICD-9:430-432)]
29 30	Tomic'-Spiric' et al. 2019	CS	Serbia	2012-2014	Morbidity	≥18	BC	ICD-10	Allergic RES[AR(ICD-10:J.30.4),AA(ICD-10:J.45.0)
31 32 33	Maynard et al. 2007	CS	USA	1995-1997, 1999-2002	Mortality	All	BC	ICD-9, ICD-10	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 99)
34	Sinclair et al. 2010	TS	USA	1998-2002	Morbidity	All	EC	NR	
35 36	Krall et al. 2013	TS	USA	2000-2005	Mortality	All	EC	NR	CVD and RES(NR)
37	Cakmak et al. 2009	TS	Canada	2001-2006	Morbidity	All	EC	ICD-9	RES(ICD-9:460-519)
38 39 40 41 42									Asthma, UK II, LK II CVD and RES(NR) RES(ICD-9:460-519) Sy copyright.

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Table S2 Charact	teristics of Study Design	of included Country	studies in the s Study Period	ystematic re Outcome	eview and r Age	neta-analys Pollutant	iS ICD code	21 -04 99 51 60 57 56 57 56 57 56 57 56 57 57 57 57 57 57 57 57 57 57 57 57 57	
Folbert et al. 2007	TS	USA	1993-2004	Morbidity	All	EC	ICD-9	Bit 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),Pneumo (ICD-9:480-486),Bronchiolitis(ICD-9:466.1,466.11,466.19)]	nia
.all et al. 2011	TS	USA	2001-2002	Morbidity	≥65	EC	ICD-9	RES[Pneumonia(ICD-9:480-486),COPD(ICD-9:490 2,496),Acute Bronchitis and Bronchiolitis(ICD-9:466),Asthma(ICD-9:493)],CVDB ysrhythmia(ICD-9:427),IHD(ICD-9:410-414),HF(ICD-9 28),Stroke(ICD-9:431-437)]	9:4
Jung and Lin 2017 Gong et al. 2019	CS TS	China China	2000-2010 2006-2011	Morbidity Mortality	0-20 All	BC BC	ICD-9 ICD-10	Asthma(ICD-9-CM:493) CVD(ICD-10:100-199)	
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	26);3t0Ke(ICD-9:491437)] Asthma(ICD-9-CM:493) CVD(ICD-10:100-199) CVD(ICD-10:100-199) Acute Ischemic Stroke Diminion of the stroke RES[Pneumonia(ICD-9:480-486),COPD(ICD-9:491,E2,496),URTI(ICD-9:460-465,466.0,477),Asthma and/or Wheeze(ICD-9:493,786.07)] URTI(ICD-9:460-465,466.0,477),Asthma and/or	
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)	

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5 of 136					В	n "b mjope			
Table S2 Charac	eteristics	of included s	studies in the	systematic	review and m	eta-analysi	is	36/bmjopen-2021-049516 (
Study	Study Design	Country	Study Period	Outcome	Age	Pollutant	ICD code	C D D Seases D Seases	
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, Mortality	all (mortality), ≥65(morbidity)	EC	ICD-9, 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),Pulmor@ry(ICD-10:C34,J00-J98)	
Gan et al. 2013	Со	Canada	1999-2002	Morbidity, Mortality	45-85	BC	ICD-9, 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	Со	USA	1988-2004	Mortality	≥30	EC	ICD-9, ICD-10	COPD(ICD-9:490-492,496,ICD10:J40-J44) CVD(ICD-10:100-I99),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-J99	
Yang et al. 2018	Co	China	1998-2011	Mortality	≥65	BC	ICD-10	CVD(ICD-10:100-199),RES(ICD-10:J00-J47,J80-J992	
Gan et al. 2011	Со	Canada	1999-2002	Morbidity, Mortality	45-85	BC	ICD-9, ICD-10	CHD(ICD-9:410-414,429.2),(ICD-10:120-125)	
De Kluizenaar et al. 2013	Со	Netherlands	1991-2003	Morbidity	15-74	EC	ICD-9	CHD(ICD-9:410-414,429.2),(ICD-10:120-125) 00 IHD(ICD-9:410-414),CHD(ICD-9:430-438) 00 Pril 01 CVD (ICD-9:CM 410-452) 10	
Vedal et al. 2013	Со	USA	1994-2005	Morbidity, 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(IC2010:120-I25)	
Liu et al. 2021b	Со	China	2010-2017	Morbidity	All	BC	NR	CVD(including but not limited to hypertension and stocke)	
Lavigne et al. 2021	Со	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		
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Table S2 Chara	acteristics of includ	ed studies in th	e systematic re	view and meta-analy	sis

Study	Study	Country	Study	Ontron	A ma	Pollutant	ICD	S Wiseases
Study	Design	Country	Period	Outcome	Age	Pollutant	code	a a a a a a a a a a a a a a a a a a a
Wang et al. 2019b	CS	USA	2005-2016	Morbidity	All	BC	NR	STEMI DO
Ljungman et al. 2019	Со	Sweden	1990-2011	Morbidity,	All	BC	ICD-9,	IHD(ICD-9:410–414 and ICD-10:120-25);stroke(ICD C9 :431–436 and ICD-10:I61–I65)
Ljungman et al. 2019	0		1990-2011	Mortality	All	БС	ICD-10	RD(1CD-9.410-414 and 1CD-10.120-25), Stroke(1CD 3 ,451-456 and 1CD-10.101-105)
Liu et al. 2021a	Со	Sweden,	1992-2004	Morbidity	All	BC	ICD-9,	COPD(ICD-9:490–492, and 494–496, or ICD-10:J40244)
Liu et al. 2021a	0	Denmark	1992-2004	woroldity	All	DC	ICD-10	COFD(ICD-9.490-492, and 494-490, or ICD-10.34(At4) 0 0

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; and the contract 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 medication; 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. http://bmjopen.bmj.com/ on April 19, 2024 by guest. Protected by copyright

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Table S3 Subgroup analysis on short-term effects of BC or EC on cardiovascular and respiratory diseases
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Subgroup Analysis	No. of	No. of	Relative Risk	I ²	Egger Regression Test
Subgroup Analysis	Studies	Estimates	(95%CI)	I	(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.

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Table S4 Details of risk of bias assessment

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	Table S	4 Details of risk of bias asses	ssment			36/bmjopen-2021-049516 c			
No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete Solution		Conflict of interest	Other
1	Atkinson	Probably Low	Low	Probably Low	Low	Low 22	5	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: 100-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 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 no conflict of interest.	No other potential sources of bias identified.
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1 2 3 4							36/bm)open-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete S outcome data	Selective reporting	Conflict of interest	Other
8	2	Bell et al.	Probably High	Low	Probably Low	Low	Low X	Probably Low	Low	Low
9 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 $\overleftarrow{\nabla}$	insufficient	declare no	potential
12 13			optical reflectance.	denominator file from the	(seasonality,	individuals ≥ 65	admissions	information	conflict of	sources of
14			Monitors from 5 sites	Centers for Medicare and	long-term trend),	years of age	were obtained,		interest.	bias
15			across 4 counties were	Medicaid Services. Cause	day of week,	enrolled in the	so likely have			identified.
16 17			used. Sampling occurred	of admission was	temperature, and	Medicare	all outcome	outcome to		
18			daily, with some missing	determined by principal	dew point.	fee-for-service	data. However,			
19 20			periods, for Hartford, New Haven, and	discharge diagnosis code		plan during	any potential	risk, but indirect		
20			Springfield, and every	according to International Classification of		August 2000 to February 2004.	errors or generation missing data	evidence that		
22			third day for Bridgeport	Diseases, Ninth Revision,		reordary 2004.	did not depend	•		
23 24			and Danbury. Days with	Clinical Modification			on air pollution			
25			missing data were	(ICD-9-CM; National			levels.			
26 27			omitted from analysis	Center for Health						
27			(the number of missing	Statistics 2006).			April 19,			
29			data was not reported).				9, 20			
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1 2 3 4							Incomplete			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	incomplete g outcome data	Selective reporting	Conflict of interest	Other
8 9	3	Cai et al.	Probably Low	Low	Probably Low	Low	Low X	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		declared no	potential
12 13			fixed-site station. Daily	the Shanghai Health	long-term trend),	hospitalization	hospitalization		competing	sources of
14			data was available and no	Insurance Bureau	temperature,	for adult	were obtained,		financial	bias
15 16			missing data was	(SHIB). The causes of	relative humidity	residents living	so likely have all outcome		interests.	identified.
17			reported.	hospital admission were	and day of the	in the nine urban		e are entre re		
18				coded according to	week.	districts between January 1, 2005	data. However,			
19 20				Classification of		and December	any potential errors or	risk, but indirect		
21				Diseases, Revision 10		31, 2011(2922	missing data	evidence that		
22				(ICD-10): Asthma (J45).		days) from the	did not depend	-		
23 24						Shanghai Health	on air pollution			
25						Insurance	levels.	-		
26 27						Bureau.				
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete		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 39	4	Geng et al. 2013	Single, central-site monitor. Daily BC and PM _{2.5} were measured continuously and 24hr averaged was estimated if >75% of the 1hr values was available for that day. Missing data was not replaced by other values.	Health data were obtained from Shanghai Municipal Center of Disease Control and Prevention database. The	Models included time (seasonality, long-term trend), temperature, humidity and day of week.	Data consisted of all causes (excluding accidents or injuries) deaths	Daily counts for death were obtained, so likely have all outcome data.	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.
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete of the second seco		Conflict of interest	Other
8			Probably High	Low	Probably Low	Low	Low X	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	5	Hua et al. 2014	Daily 24h average PM _{2.5} and BC data was obtained from a fixed-site station. The study only used the actual collected data and did not fill in the missing data for PM _{2.5} and black carbon.	Daily asthma hospital admission data was obtained from Shanghai Children's Medical Center. Dates of admission and discharge, and diagnoses using the International Classification of Diseases, Revision 10.	Adjusted for long-term and seasonal trend, day of week, temperature and relative humidity.	Study included all asthma hospital admissions of children ≤ 14 years of age from Shanghai Children's Medical Center between1 January 2007 and 31 July 2012 in nine urban districts of Shanghai.	Daily counts for asthma hospital admissions of children 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.
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete ్ల outcome dataచ		Conflict of interest	Other
8			Probably Low	Low	Low	Low	Low A	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	6	Ostro et al. 2015a	Daily 24hr average BC concentrations were obtained from one station in Barcelona and Athens. Daily data was available and no missing data was reported.	For both cities daily counts of all-cause mortality for all ages were collected (excluding deaths from external causes, International Classification of Disease-ICD9: 001799, ICD10 A00R99), as well as daily counts of cardiovascular (ICD9: 390459, ICD10: I00I99), respiratory (ICD9:460519, ICD10:J00J99) and all-cause mortality for those greater than age 65.	Adjusted for long term and seasonal (year, month, day of week) trends, temperature, holidays, summer vacations and influenza.	Study population consisted of daily counts of all-cause mortality for all ages and daily counts of cardiovascular, respiratory and all-cause mortality for those greater than age 65.	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 interests.	No other potential sources of bias identified.
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1 2 3							-2021-04			
4 5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on 3 outcome data		Conflict of interest	Other
8 9			Low	Low	Probably Low	Low	Low X	Probably Low	Low	Low
10 11 12 13 14 15 16 17 18 19		al. 2016	BC and EC were collected from the ClearfLo project, supplemented by local measurements made at the North Kensington urban background site.	discharge diagnosis, daily numbers of admissions for cardiovascular disease (International Classification of Diseases, 10th revision-ICD-10:	term and seasonal trends, temperature, relative humidity, regulated pollutants (PM ₁₀ , PM _{2.5} , NO ₂ , SO ₂	all cardiovascular and respiratory hospital admissions in London, UK between 2011 and 2012.	for all Download emergency hospital admissions were obtained, so likely have all outcome	information about selective outcome to judge for low risk, but	declared no competing interests.	potential sources of bias identified.
20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38			Number of days of observation for BC: 629 (BC urban in PM _{2.5}) and 702 (BC in PM _{2.5}) between 2011 and 2012 (<25% missing data).	I00-I99) for those aged 15-64 (adult) and 65+ years (elderly), and respiratory diseases (ICD-10: J00-J99) for those aged 0-14 years (paediatric), adult and the elderly were calculated.	and O ₃), day of the week and public holidays.	ien	data. However, any potential errors or missing data did not depend on on air pollution levels.	evidence that suggests study was free of selective report.		
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	incomplete of outcome data	j j	Conflict of interest	Other
8			Probably High	Low	Probably Low	Low	Low X	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	8	Zanobetti and Schwartz 2006	Ambient BC from one monitor. The hourly measurements for BC and PM _{2.5} 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.	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 revision-ICD-9:410), and pneumonia (ICD-9: 480–487), from Medicare billing records for the years 1995–1999.	Adjusted for temperature, day of the week, seasonality, long-term trends, humidity, barometric pressure, and the extinction coefficient.	Data consisted of all U.S. Medicare hospital admissions in the Boston Metropolitan area for myocardial infarction during the study duration.	Daily counts for hospital admissions 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 interests.	No other potential sources of bias identified.
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1 2 3 4							Incomplete			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data	5	Conflict of interest	Other
8 9			Probably High	Low	Probably Low	Low	Low 2	Probably Low	Low	Low
9 10	9	Liu et al.	EC were collected from a	Emergency department	Adjusted for time	Study included	Daily counts	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 13			one-in-three or one-in-six	from the Blue Cross Blue	seasonal trend),	emergency	department	information	potential	sources of
14			day schedule. EC were	Shield Texa. International	day of week,	department visits	visits were	about	competing	bias
15			measured for 566 days	Classification of Diseases	temperature, dew	for Greater	obtained, so	selective	financial	identified.
16 17			from April 02, 2009, to	9th Revision (ICD-9)	point and	Houston from	likely have all	-	interests.	
18			December 30, 2013,	diagnosis codes were	population growth.	claims data	outcome data.	•		
19			<25% missing for the	used to classify outcome		insured from	However, any			
20 21			frequency of sampling.	groups.		January 1, 2008	potential errors			
22						through	or missing data			
23						December 31,	did not depend			
24 25						2013.	on air pollution	1		
26							levels.	selective		
27								report.		
28 29										
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31							Aprill 19, 2024 by gues			
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete \int_{Ω}^{16} outcome data ω	Selective reporting	Conflict of interest	Other
8			Probably High	Low	Probably Low	Low	Low 2	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	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.	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.
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1 2 3 4							Incomplete			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	5	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 _{2.5}	records were obtained	for season, day of	all emergency	for emergency		declare they	potential
12 13			were obtained from a	from the Missouri	week, holidays,	department visits	department	information	have no	sources of
14			Supersite (single, central	Hospital Association	time trends (using	during the study	department visits were obtained, hence one	about	actual or	bias
15			site monitoring location).	(MHA) for emergency	cubic splines for	period for	obtained,	selective	potential	identified.
16 17			The observations of EC	department visits. The	day of visit with	cardiovascular			competing	
18			was 666 days during 1	outcome groups were	monthly knots),	disease	hospital not		financial	
19 20			June 2001-30 April 2003	identified using primary International	and temperature.	outcomes.	providing data		interests.	
20			(missing data <25%).	Classification of Diseases			after 26 April 2002.	evidence that		
22				9th Revision (ICD9)		· · ·	However, any	-		
23 24				codes.		10,	potential errors			
25						en.	or missing data			
26							did not depend			
27 28							on air pollution			
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete		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	12	Kim et al. 2012	PM _{2.5} 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.	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.
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1 2 3 4							36/bm)open-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias		Selective	Conflict of interest	Other
8			High	Low	Probably Low	Low	Low X	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	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 hospitalization s of children 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.
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	incomplete og outcome dataຜ క		Conflict of interest	Other
8			Probably Low	Low	Probably Low	Low	Low X	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	14	Kim et al. 2015	Daily 24-hour composite PM _{2.5} samples were collected from single, central-site monitor. The observations of EC was 1809 days from 2003 through 2007 (missing data <25%).	Daily mortality counts for 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.	Models adjusted for longer-term temporal trend, as time since the study began, day of week, and daily temperature and humidity.	Data consisted of all deaths over the course of the study in a defined geographical area.	Daily counts for death were obtained, so likely have all outcome data. However, any potential errors or missing data	There was insufficient information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of selective report.	None of the authors has any actual or potential competing interests.	No other potential sources of bias identified.
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1 2 3 4							36/bmjopen-2021-049516 o Incomplete			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete \int_{Ω}^{Ω} outcome data ω		Conflict of interest	Other
8 9			Probably Low	Low	Probably Low	Probably Low	Low ay	Probably Low	Low	Low
9 10	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 _{2.5}	obtained from the Xi'an	for calendar time	removed the	for death were	insufficient	competing	potential
12 13			were obtained from a	Center for Disease	(seasonality,	death counts on	obtained, so	information	financial	sources of
14			single, central-site	Control and Prevention.	long-term trends),	December 31 and	likely have all		interests.	bias
15			monitor. Daily average	The International	weather(temperatu	January 1 of each	outcome data.			identified.
16 17			concentrations of EC in	Classification of	re, relative	year.	However, any	•		
18			PM _{2.5} samples were	Diseases, Tenth Revision	humidity), year,		potential errors			
19			further analyzed. Daily	(ICD-10), codes of	day of week.		or missing data			
20 21			data was available and no	mortality were as			did not depend			
22			missing data was	follows: all natural causes		1.	on air pollution			
23			reported.	(ICD-10 codes			levels.	suggests study		
24 25				A00–R99), respiratory		ien		was free of		
26				diseases (ICD-10 codes			on A	selective		
27				I00–I98), and cardiovascular diseases			pri	report.		
28 29				(ICD-10 codes I00–I99).			on April 19, 2024 by guest			
30				(ICD-10 codes 100–199).			2022			
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	incomplete of outcome data		Conflict of interest	Other
8			Probably High	Low	Probably Low	Low	Low 2	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 9	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 was not replaced by other values.	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 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 they have no competing financial interests.	No other potential sources of bias identified.
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1 2 3 4							36/bm)open-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	Selective	Conflict of interest	Other
8			Probably High	Low	Probably Low	Low	Low X	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	17	Levy et al. 2012	The U.S. Environmental Protection Agency established the PM Speciation Trends Network (STN) to measure more than 50 PM _{2.5} 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 missing data.	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 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.
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4 5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	Selective	Conflict of interest	Other
8			Probably Low	Low	Probably Low	Low	Low y	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	18	Son et al. 2012	Hourly air samples were obtained from a single, central-site monitor. The monitoring system produces hourly estimates of PM _{2.5} total mass, and PM _{2.5} levels of EC. Daily data was available and no missing data was reported.	Daily death counts were obtained from the National Statistical Office. The study classified mortality data into all causes of death [International Classification of Diseases, 10th Revision (ICD-10; codes A00–R99), cardiovascular causes (codes I00–I99), and respiratory causes (codes J00–J99)] (World Health Organization 2007).	Models adjusted for time (long-term trends and seasonality), day of week, temperature and relative 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.
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1 2 3 4							2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	Selective reporting	Conflict of interest	Other
8 0			Probably High	Low	Low	Low	Low X	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	19	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.	19, 2024 by guest.	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.
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1 2 3 4							en-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	incomplete of outcome data	Selective reporting	Conflict of interest	Other
8			Probably High	Low	Probably Low	Low	Low X	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	20	Basagaña et al. 2015	Single central-site monitor in each city. For each city, PM constituents with >20% of the values below the detection limit or missing were excluded. Otherwise, non-detectable were replaced by half the limit of detection. Air pollution data was collected daily in Bologna (n=472), twice a week in Barcelona (n=736) and Madrid (n=104), and once a week in Huelva (n=406). There was no information about missing data.	Daily mortality counts for all non-external causes [International Classification of Diseases, 9th Revision (ICD9) codes 001–799; 10th revision (ICD10) codes A00–R99], cardiovascular (ICD9 codes 390–459, ICD-10 codes 100–199) and respiratory (ICD9 codes 460–519, ICD10 codes J00–J99) were collected. Cardiovascular and respiratory hospitalizations were defined on the basis of the primary discharge diagnosis using the same ICD codes defined above.	Models adjusted for holidays, summer population decrease, influenza epidemics, seasonality, long-term trends and temperature.	Data consisted of all deaths over the course of the study in a defined geographical area.	Daily counts for death and emergency hospital admissions 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 have no conflicts of interest to disclose.	No other potential sources of bias identified.
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3 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			Probably High	Low	Probably Low	Low	Low X	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	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 _{2.5} 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 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.	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.
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Pag	je 79 of	f 136			BMJ Oper	1	36/bmjop			
1 2 3 4							36/bmJopen-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete of the second secon	Selective reporting	Conflict of interest	Other
8 0			Probably Low	Low	Low	Low	Low Y	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	22	Lin et al. 2016a	The concentrations of different particle size fractions and PM _{2.5} 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-10:100-199) 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.	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.
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1 2 3 4							Incomplete			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias		Selective reporting	Conflict of interest	Other
8 9			Probably Low	Low	Probably Low	Low	Low X	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 13			single monitoring site.	Xi'an for each day from	seasonal trends,	causes deaths	obtained, so		have no	sources of
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.		potential	identified.
16 17			(missing data <25%).	Control and Prevention	humidity, and SO ₂	study.	However, any		competing	
18				(SPCDCP). SPCDCP	and NO ₂		potential errors		financial	
19				staff then classify the	concentrations.		or missing data		interests.	
20 21				cause of death according			did not depend			
22				to the International		- ,°	on air pollution			
23				Classification of			levels.	suggests study was free of		
24 25				Diseases, 10th Revision [ICD-10; World Health		ien	.com/ on April 19, 2024 by guest	selective		
26				Organization (WHO)			on A	report.		
27 28				1992] as due to total						
28 29				nonaccidental causes			,,			
30				(ICD-10 codes			024			
31 32				A00–R99),			by (
33				cardiovascular diseases			Jues			
34				(I00–I99), respiratory						
35 36				diseases(J00–J98), or			Protected			
37				injury (S00–T98).						
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Pag	je 81 of	f 136			BMJ Oper	1	36/bmjopen-2021			
1 2 3 4							9n-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete		Conflict of interest	Other
8			Probably Low	Low	Probably Low	Low	Low X	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	24	Klemm et al. 2011	Daily 24-hr average EC measurements are available for Atlanta during the study period. The observations of EC was 3317 days from August 1998 to December 31, 2007. Missing data <25%. There was no information for monitor stations.	Records of individual deaths were provided by the Georgia Department of Human Resources. Cause of death is	Adjusted for time (seasonality, long-term trends), temperature, and day of the week.	Study included all nonaccidental deaths during over the course of the study.	Daily counts for death were obtained, so likely have all outcome data.	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.
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1					BMJ Oper	1	Incomplete			Page 82 o
2 3 4 5							Lncomplete	Selective	Conflict of	
6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	outcome data	reporting	interest	Other
8 9			Probably Low	Low	Probably Low	Low	Low X	Probably Low	Low	Low
9 10	25	Zhou et al.	24hr PM _{2.5} 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		declare they	potential
12 13			central-site monitor.	Classification of	seasonality and	deaths over the	obtained, so	information	have no	sources of
14			Daily data was available	Diseases, version 10	long-term trends,	course of the	likely have all		actual or	bias
15			and no missing data was	(ICD10; World Health	day of week,	study.	outcome data.		potential	identified.
16 17			reported.	Organization 2007), daily	temperature, and		However, any	-	competing	
18				death counts were	humidity.		potential errors		financial	
19				aggregated to			or missing data		interests.	
20 21				nonaccidental allcause			did not depend			
22				deaths (ICD10, codes			on air pollution			
23				A00 through R99), cardiovascular deaths		10.	levels.	suggests study was free of		
24 25				(ICD10, codes I01		ien (selective		
26				through I99), and				report.		
27 28				respiratory deaths (ICD-						
20 29				10, codes J00 through			, y			
30				J99).			024			
31 32							levels.	-		
33							Jues			
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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 4	Probably Low	Low	Low
11 12 13 14 15 16 17 18 19 20 21 22		et al. 2015	from a single monitor site. All species of pollutant statistics are missing less than 5%.	were obtained from the Missouri Hospital Association for all emergency department visits to 36 of 43 acute-care non-federal hospitals with emergency department visits in the 16-county St Louis	trends, day of week, holidays, season, temperature and dew point.	emergency department visits in St Louis metropolitan statistical area during 1 June 2001 through 30 April 2003.	for emergency control of the emergence control	information about selective outcome to judge for low risk, but indirect	declared no competing financial interests.	potential sources of bias identified.
22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38				metropolitan statistical area during 1 June 2001 through 30 April 2003. Cardiorespiratory outcomes of interest were defined based on the primary ICD-9 (International Classification of Diseases, version 9) diagnosis code for the visit.		en o	did not depend on air pollution levels.	was free of selective report.		
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1 2 3 4							36/bm)open-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	Selective	Conflict of interest	Other
8			Probably High	Low	Probably Low	Low	Low X	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	27	Ostro et al. 2007	Each of the six counties had two monitors measuring PM _{2.5} components and mass. Fresno, Kern, Riverside, and Sacramento Counties reported data every third day, whereas San Diego and Santa Clara Counties reported data every sixth day. For the speciation analyses, the number of observation days available ranged from 243 (San Diego County) to 395 (Sacramento County) from 2000 to 2003. There was no specific information about missing data.	Daily mortality data were obtained from the California Department of Health Services, Center for Health Statistics. The study determined daily total mortality counts for those > 65 years of age and for deaths from respiratory disease [International Classification of Diseases, 10th Revision (ICD10; World Health Organization 1993) codes J00–J98] and cardiovascular disease (codes I00–I99).	Adjusted for time trend, day of week, seasonality, long-term trends, 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	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.
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1 2 3 4							36/bmJopen-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete 0 outcome data⇔		Conflict of interest	Other
8			Probably Low	Low	Probably Low	Low	Low X	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	28	Tolbert et al. 2000	Daily 24h EC from a single monitor site. The observation of EC was 356 in 365 days, missing data <25%.	Computerized billing record data are being obtained from the emergency department visits participating in the study. Several case groups are being defined using the primary ICD-9 (International Classification of Diseases, 9th Revision) diagnostic code.	Adjusted for time (seasonality, long-term trends), temperature, dew point, and day of week.	Study included emergency department visits of the participating hospitals in the Atlanta Metropolitan Statistical Area, including 33 hospitals between January 1 1993-August 31 2000, 4 hospitals between January 1 1993-February 30 2000.	Daily count 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.	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.
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1 2 3							-2021-049516			
4 5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data	Selective	Conflict of interest	Other
8			Low	Low	Probably Low	Low	Low X	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	29	Wang and Lin 2016	The hourly data were simply averaged to calculate the daily average data for PM ₁₀ , PM _{2.5} 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.	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 Revision (ICD-9 CM).	Adjusted for temperature, relative humidity, wind speed, barometric pressure, holidays, day of the week, pneumonia and influenza.	Study included elderly (≧65 years) mortality from 2004 to 2008 and all population EVR from 2004 to 2010 in Taipei, Taiwan.	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 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.
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Page 87 of 136					BMJ Open 20221-					
1 2 3 4							en-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete og outcome data⇔	Selective	Conflict of interest	Other
8			Low	Low	Low	Low	Probably Low	Probably Low	Low	Low
9 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	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 17				diagnoses of respiratory	holiday and	Atlanta hospitals	earliest years ∃	outcome to		
17				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 21				Classification of		to December 31,	hospitals were			
21				Diseases, 9th Revision		2004 (not all	participating.	evidence that		
23				(ICD-9), diagnosis codes:	L L	hospitals	However, any			
24 25				acute bronchitis or		contributed the	potential errors			
25 26				bronchiolitis (code 466);		full period), and	or missing datag			
27				pneumonia (codes		from the Georgia	did not depend	report.		
28 29				480–486); and upper		Hospital	فے on air pollution			
30				respiratory infection		Association for	levels. 2024 by guest			
31				(codes 460–465).		the period	4 by			
32 33						January 1, 2005,	gue			
33 34						to June 30, 2010.	ist. F			
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No. Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data	Selective	Conflict of interest	Other		
	Probably High	Low	Probably Low	Low	Low y	Probably Low	Low	Low		
0 31 Metzger et al. 2004 1 2 3 4 5 6 6 7 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 8 9 0 1 2 3 4 5 6 7 8 9 0 1 2 3 4 5 6 7 8 8 9 0 1 2 3 4 5 6 7 8 9 9 9	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 Downloaded department visits 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 report.	No competing financial interests.	No other potential sources of bias identified.		

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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete of outcome data	Selective	Conflict of interest	Other
8			Probably Low	Low	Probably Low	Low	Low A	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	32	Mar et al. 2000	Hourly PM _{2.5} chemical composition data from a single, central-site monitor. Daily data was available and no missing data was reported.	Mortality data for all of Maricopa County from 1995 to 1997 were obtained from the Arizona Center for	Adjusted for time trend, seasonality, day of week, temperature and relative humidity.	Data consisted of all cardiovascular deaths during over the course of the study.	Daily counts for death were obtained, so likely have all outcome data.	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.
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1 2 3 4							Incomplete o			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete		Conflict of interest	Other
8			Low	Low	Probably Low	Low	Low X	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	33	Wang et al. 2019a	Hourly data of PM _{2.5} were collected at 10 Chinese air quality monitoring sites in Shanghai. Hourly mass concentrations of PM _{2.5} 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.	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.
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete		Conflict of interest	Other
8			Probably High	Low	Probably Low	Low	Low 2	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	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:I60–I66), and sub-categories, including ischemic stroke (ICD-10:I63–I66), and hemorrhagic stroke (ICD-10: I60–I62) 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.	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 conflict of interest.	No other potential sources of bias identified.
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1 2 3							-2021-0495			
4 5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete of outcome data	Selective	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	35	Lin et al. 2016b	Each of the six counties had two monitors measuring components of PM _{2.5} . Fresno, Kern, Riverside and Sacramento counties reported 24-hour average EC in PM _{2.5} 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.	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 calculated.	Adjusted for time, temperature, humidity and day of the week.	Study included daily cardiovascular mortality for all California residents from 1 January 2000 to 31 December 2003.	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	Authors declared no competing interests.	No other potential sources of bias identified.
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	Selective reporting	Conflict of interest	Other
8			Probably Low	Low	Probably Low	Low	Low X	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	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 death.	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.	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.
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on the second seco	Selective	Conflict of interest	Other
8 9			Probably Low	Low	Probably Low	Low	Low X	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 _{2.5}	emergency room visits	for time, day of	all emergency	for emergency	insufficient	competing	potential
12 13			and the four PM _{2.5}	were obtained from the	week, temperature,	department visits	room visit	information	financial	sources of
14			constituents obtained	National Taiwan	seasonality and	during the study	were obtained,		interests.	bias
15			from a Supersite (single,	University Hospital. The	relative humidity.	period for	so likely have and all outcome			identified.
16 17			central site monitoring	emergency room visit		ischemic and				
18			location). The observations of EC was	data were coded		hemorrhagic	data. However,			
19 20			1599 in 1705 days	regarding the discharge diagnosis using the		stroke.	any potential errors or			
21			(missing data <25%).	International			missing data	evidence that		
22			(initioning data	Classification of Disease,			did not depend	-		
23 24				9th revision (ICD-9).		10	on air pollution			
25							levels.	-		
26 27							Ap	report.		
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	incomplete ဝ outcome dataယ	Selective	Conflict of interest	Other
8			Low	Low	Probably High	Low	Low 2	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	Tomic'-Sp iric' et al. 2019	Average daily concentrations of BC in micrograms per cubic meter were measured by three automatic ambient air quality monitoring stations. There was no information about missing data.	Emergency department visits data were obtained from the Health Center Užice, either from the emergency department visits in Užice, Sevojno, and Kosjeri' c, or from a general hospital in Užice. The inclusion criteria were adults aged 18 years and older with the diagnosis of allergic rhinitis (International Classification of Diseases, 10th revision, code J.30.4), allergic asthma (International Classification of Diseases, 10th revision, code J.45.0), or asthma with coexisting allergic rhinitis.	Adjusted for temperature, humidity, and air pressure.	Study included emergency department visit for allergic rhinitis and allergic asthma from 1 July 2012 to 30 June 2014 in the Zlatibor District, Western Serbia.	All 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.	Authors declared no competing financial interests.	No other potential sources of bias identified.
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1 2 3 4					36/bmjopen-2021-0495			
5 No. Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete og outcome data⇔	Selective	Conflict of interest	Other
3	Probably Low	Low	Probably Low	Low	Low a	Probably Low	Low	Low
39 39 Maynard 11 et al. 2007 12 et al. 2007 13 et al. 2007 14 et al. 2007 15 et al. 2007 16 et al. 2007 17 et al. 2007 18 et al. 2007 19 et al. 2007 20 et al. 2007 21 et al. 2007 22 et al. 2007 23 et al. 2007 24 et al. 2007 25 et al. 2007 26 et al. 2007 27 et al. 2007 28 et al. 2007 29 et al. 2007 30 et al. 2007 31 et al. 2007 32 et al. 2007 33 et al. 2007 34 et al. 2007 35 et al. 2007 36 et al. 2007 37 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. 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.

Pag	e 97 of	f 136		doluua/og	-					
1 2 3 4							30/bm)open-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	incomplete of outcome data		Conflict of interest	Other
8			Probably Low	Probably Low	Probably Low	Low	Low X	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	40	Sinclair et al. 2010	Daily 24-hr averages EC was from a single monitor site. The total observed rate of EC was 95.2%.	Daily outpatient visits were obtained from the electronic patient data warehouse of a not-for-profit, group-model managed care organization (MCO) in the metropolitan Atlanta area between August 1, 1998 and December 31, 2002. Visits that met acute visit definition and that had a visit diagnosis code of asthma, upper respiratory infection (URI), or lower respiratory infection (LRI) were included in the study.	Adjusted for season, day of week, federal holidays, study month, time, temperature and dew point.	Study included daily outpatient visits for acute respiratory diseases from the electronic patient data warehouse of a not-for-profit, group-model managed care organization (MCO) in the metropolitan Atlanta area between August 1, 1998 and December 31, 2002.	Daily counts for outpatient 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.
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1 2 3 4							Incomplete			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	Selective reporting	Conflict of interest	Other
8 9			High	Probably Low	Probably Low	Low	Low	Probably Low	Low	Low
9 10	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 _{2.5}	(excluding accidental	temperature, day	all death	for death were		declare they	potential
12 13			constituent	deaths) were aggregated	of week, long-term	(excluding	obtained, so	information	have no	sources of
14			concentrations every	from death certificate	and seasonal	accidental	likely have all		actual or	bias
15 16			third or sixth day. Some	data obtained from the	trends.	deaths) for 108	outcome data.		potential	identified.
17			communities with a	National Center for Health Statistics for 2000		urban communities	However, any		competing financial	
18			single monitor. The observation of EC was	to 2005.		from 2000 to	or missing data		interests.	
19 20			58-921 days,some	10 2005.		2005.	did not depend		Interests.	
21			communities had >25%			2003.	on air pollution			
22 23			missing data.				C	F		
24						101		was free of		
25							On	selective		
26 27							Арп	report.		
28										
29 30										
31							levels.			
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete of outcome data∝	Selective reporting	Conflict of interest	Other
8			Probably High	Low	Probably Low	Low	Low A	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	42	Cakmak et al. 2009	Daily PM _{2.5} aerosol samples approximately 1 of every 4 days from a single monitor site. Sampling occurred daily during the cold season (April through September) and alternate days during the warm season (October through March). Missing data <25% for that frequency.	Diseases were coded using the WHO International Classification of Disease, 9th Revision (ICD-9). The daily number of emergency department visits for all nonaccidental (ICD-9 < 800) and respiratory (ICD-9 460–519) causes in Santiago Centro, Cerrillos, and Pudahuel were obtained from the Departamento de Estad' isticas e InformaciónenSalud (DEIS) of the Ministry of Health from April 2001 through August 2006.	Adjusted for temperature and humidity, day of week, long-term and seasonal trends.	Study included all emergency department visits obtained from the Departamento de Es-tad´ isticas e InformaciónenSa lud (DEIS) of the Ministry of Health from April 2001 through August 2006.	Daily counts for emergency department visit 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.
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1 2 3 4							36/bm)open-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	Selective	Conflict of interest	Other
8			Low	Low	Probably Low	Low	Low X	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	43	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 Do department visit 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.
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete og outcome data∝	Selective	Conflict of interest	Other
8 9			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	44	Lall et al. 2011	Daily EC data were obtained from two monitors. Daily data was available and no missing data was reported.	The categorization of the admissions data was based on codes from the International Classification of Diseases, revision 9 (ICD-9).	Model adjusted for season, wintertime influenza episode, weather, day of week, and other possible confounders (e.g., federal holidays).	Data consisted of all cardiovascular hospital admissions over the course of the study.	19, 2024 by guest. Protected	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.
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1 2 3 4							36/bm)open-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete og outcome data∝ ≤	Selective	Conflict of interest	Other
8			Probably High	Low	Probably Low	Low	Low X	Probably Low	Low	Low
9 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 13			weeks per season) from a	from Longitudinal Health	of week,	outpatient visits	outpatient	information	financial	sources of
14			single monitor site were	Insurance Database 2000.	temperature,	(0-20 years old)	visits (0-20		interests.	bias
15			collected. Multiple linear	Daily outpatient visits for	precipitation and	in Shalu district	years old) data			identified.
16 17			regression models were	asthma (International	wind vectors.	from	were obtained,			
18			used to back extrapolate	Classification of		Longitudinal	so likely have			
19			the historic concentration	Diseases, Ninth Revision,		Health Insurance	all outcome	risk, but		
20 21			of individual components	Clinical Modification,		Database 2000	data. However,			
21			of PM _{2.5} from 2000	ICD-9-CM code 493)		during January 1,	any potential	evidence that		
23			through to 2010,	data was obtained from		2000 to	errors or	suggests study		
24 25			including BC.	Longitudinal Health		December 31,	missing data	was free of		
25				Insurance Database 2000.		2010.	did not depend			
27							on air pollution \mathbf{E}	report.		
28 29							ا levels.			
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	Selective	Conflict of interest	Other
8			Probably Low	Low	Probably Low	Low	Low g	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	46	Gong et al. 2019	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 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) were obtained.	Adjusted for calendar effects, long-term trends, temperature, humidity, day of week, NO ₂ and SO ₂ .	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.	Daily counts for all deaths 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 conflict of interest.	No other potential sources of bias identified.
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	Selective reporting	Conflict of interest	Other
8			Probably Low	Probably Low	Probably High	Low	Low X	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	47	Mostofsky et al. 2012	Ambient EC obtained from one monitor. BC concentrations were measured continuously. Daily data was available and no missing data was reported.	Patients potentially eligible for this study were identified by reviewing daily emergency department admission logs, stroke service admission logs, stroke service consult logs, and hospital electronic discharge records.	Model adjusted for seasonality, time-trends, temperature, dew point temperature, barometric pressure and chronic and slowly-varying potential confounders.	Population consisted of patients ≥21 years of age admitted to the hospital with neurologist-confi rmed ischemic stroke and residing in the Boston metropolitan region. Also patients had to reside within 40 km of the air pollution monitor.	Daily counts for emergency Do department admission 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.
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1 2 3 4							36/bmJopen-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	Selective reporting	Conflict of interest	Other
8			Probably High	Low	Probably Low	Low	Low X	Probably Low	Low	Low
9 10	48	Krall et al.	PM _{2.5} 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 22			There was no information	Diseases, 9th Revision		area, the	However, any	evidence that		
23			about missing data.	(ICD-9), the study		7-county	potential errors			
24				considered subcategories		Birmingham	or missing data	was free of		
25 26				of respiratory diseases		metropolitan	did not depend			
27				including pneumonia		area, the 8	on air pollution	report.		
28				(ICD-9 codes 480–486),		Missouri and 8	levels.			
29 30				chronic obstructive		Illinois counties	19, 2024 by			
31				pulmonary disease		in the St. Louis	24 b	-		
32				(491,492,496), upper		metropolitan	y gu			
33 24				respiratory infection		area, and the	guest.			
34 35				(URI) (460–465, 466.0,		12-county Dallas		ו		
36				477), and asthma and/or		metropolitan	Protected			
37				wheeze (493, 786.07).		area.				
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1 2 3 4							36/bmjopen-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete og outcome data⇔	Selective	Conflict of interest	Other
8			Probably Low	Low	Probably Low	Low	Low X	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	49	O'Lenick et al. 2017	The 24-hour average concentration of EC was evaluated. Pollutant concentration estimates were obtained by fusing observational data from available network monitors with pollutant concentration simulations from the Community Multi-Scale Air Quality emissions-based chemical transport model at 12×12km grids over Atlanta. 24-hour average EC were evaluated. Daily data was available and no missing data was reported.	Patient-level emergency department visit data from 1 January 2002 to 31 December 2008 were acquired from hospitals located within the 20-county metropolitan area of Atlanta; Relevant data elements included admission date, International Classification of Diseases Ninth Revision (ICD-9) diagnosis codes, age and ZIP code of patient residence.	Adjusted for season, periods of hospital participation and holidays, temperature and mean dew point, interaction terms between season and maximum temperature and day of year.	Study included all emergency department visit data acquired directly from hospitals (2002–2004 period) and the Georgia Hospital Association (2005–2008 period) located within the 20-county metropolitan area of Atlanta.	Daily counts for emergency Development department visit 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.	Competing interests: None declared.	No other potential sources of bias identified.
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1 2 3 4							an-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete of the second seco	Selective	Conflict of interest	Other
8 9			Probably Low	Low	Probably Low	Low	Low X	Probably Low	Low	Low
9 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 13			monitoring location in	pediatric asthma related	of the week,	department visits	asthma related	information	they have	sources of
14			Atlanta. Daily data was	emergency department	hospital, holidays,	for pediatric	emergency	about	no	bias
15			available and no missing	visits for children ages 5	temperature and	asthma of	department	selective	competing	identified.
16 17			data was reported.	to 18 years from 41	dew point.	children ages 5 to	visits were	outcome to	interests.	
18				hospitals within		18 years from 41	obtained, so	judge for low		
19 20				metropolitan Atlanta; and		hospitals within	likely have all			
20 21				defined emergency		metropolitan	outcome data.			
22				department visits for pediatric asthma as all		Atlanta for study period.	However, any	evidence that suggests study		
23 24				visits with a code for		period.	or missing data			
25				asthma (493.0–493.9) or			did not depend			
26				wheeze (786.07) using			on air pollution			
27 28				the International				:		
29				Classification of			9, 20			
30				Diseases, 9th Revision.			024			
31 32							levels. 19, 2024 by gues			
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34 35							Pro			
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1 2 3 4							Incomplete			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias		Selective reporting	Conflict of interest	Other
8			Low	Low	Probably Low	Low	Low X	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	51	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, 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.
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Selective reporting	Conflict of interest	Other
reporting		Other
Prohably I ow		
1 IODdoly LOW	Low	Low
There was	No conflict	No other
insufficient	of interests.	potential
information		sources of
about		bias
		identified.
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suggests study		
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5. 2 7		
	Probably Low There was insufficient information	Probably Low Low There was No conflict insufficient of interests. information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of selective report.

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1 2 3 4							36/bmjopen-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete og outcome data∝	Selective	Conflict of interest	Other
8			Probably High	Low	Probably Low	Low	Low X	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	53	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 _{2.5} 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.
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Page 111 of 136 BMJ Open							36/bmjop			
1 2 3 4							36/bmjopen-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete of the second seco	Selective reporting	Conflict of interest	Other
8			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	information	have no	sources of
13 14			constituents in particle	Classification of	of smoking,	\geq 30 years old.	follow up.	about	actual or	bias
15			diameters ranging from	Diseases, 10th Revision	secondhand smoke		ed fro	selective	potential	identified.
16 17			0.01 to 10µm through	(ICD-10) for the	exposure, body		m	outcome to	competing	
17			calculations that describe	following outcomes:	mass index,		, dit (judge for low	financial	
19			emissions, transport,	all-cause deaths	lifetime physical			risk, but	interests.	
20			diffusion, deposition,	excluding those with an	activity, alcohol		Jope	indirect		
21 22			coagulation, gas- and	external cause	consumption,		en.b	evidence that		
23			particle-phase chemistry,	(A00–R99),	average daily		, <u>"</u> ,	suggests study		
24			and gas-to-particle	cardiovascular deaths	dietary intake of	en.	Ŭ M	was free of		
25 26			conversion. The	(I00–I99), Ischemic heart	fat, calories,		Р Я	selective		
27			University of California	disease deaths (I20–I25),	menopausal status,		Apri	report.		
28			Davis/California Institute	and pulmonary deaths	family history of					
29 30			of Technology model was	(C34, J00–J98).	myocardial		April 19, 2024 by gues			
31			used to estimate		infarction, stroke,		24 b			
32			ground-level		use of blood		y gu			
33			concentrations of 50 PM		pressure		lest.			
34 35			constituents over the		medication,			J		
36			major population regions		aspirin; living		Protected			
37			in California.		conditions					
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55 Gan et al. 2013 regree	Exposure assessment	Outcome assessment	Confounding bias (income, income inequality, education, population size, racial composition, unemployment).	Selection bias	36/bmjopen-2021-049516 on 3 May 2022. Downloaded from http outcome data outcome data	reporting	Conflict of interest	Other
55 Gan et al. 2013 regree	Exposure assessment	Outcome assessment	(income, income inequality, education, population size, racial composition,	Selection bias	⊂ outcome data⇔ ≤	reporting		Other
2013 resol regre		Forp	inequality, education, population size, racial composition,		ay 2022. Download			
2013 resol regre					ed from http			
2013 resol regre	Probably Low	Low	Probably High	Low	Probably Low		Low	Low
expo air p black 5-yea indiv ambi were perso posta	sing high spatial solution land use gression models to timate residential posure to traffic-related r pollutants including ack carbon. During the year exposure period, dividual exposures to nbient air pollutants ere estimated at each erson's residential ostal code centroid ing land use regression	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.	Individual-level covariates: age, sex, preexisting comorbid conditions; and neighborhood socioeconomic status (SES).	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 follow-up period.	During the 4-year follow-up period, 38,377 (8%) subjects (8%) subjects were lost to follow-up because of moving out of the province or dying from other diseases.	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.

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1 2	e 113 d	of 136		36/bmjopen-2021-0495						
3 4 5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	49 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	Selective	Conflict of interest	Other
8 9 10 11 12 13 14 15 16			models.	For			ay 2022. Downloaded fro			
17 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	Probably Low The PM, NO ₂ , BC, and O ₃ 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 ₂ , BC, and O ₃ .	Low 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 100–199) and respiratory (ICD10 codes J00–J99 and C34) subgroups of mortality.	Probably Low Age, sex, educational attainment, occupational status, marital status, marital status, smoking (status, intensity, and duration), environmental tobacco smoke (ETS), alcohol consumption, body mass index, waist circumference, fruit consumption, vegetable	Low Data obtained for a cohort of men and women aged 50–64 years residing in the areas of Copenhagen and Aarhus.	Probably Low There was no information on April 19, 2024 by guest. Protected by copyright.	There was insufficient information about selective outcome to judge for low	Low The authors declare they have no competing financial interests.	Low No other potential sources of bias identified.
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Page	1	14	of	136

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1 2 3 4							Incomplete outcome data			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	<	Selective reporting	Conflict of interest	Other
8 9 10 11 12 13 14				For.	consumption, physical activity; neighborhood level socioeconomic status (SES).		lay 2022. Downloaded			
15 16 17			Probably Low	Probably Low	Probably High	Low	Probably High		Low	Low
19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43							24 by guest. Protected by copyright.			
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete of 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 _{2.5} mass and trace constituents were obtained from U.S. Environmental Protection Agency Air Quality System. These PM _{2.5} constituent data were analyzed to derive estimates of source apportioned PM _{2.5} mass exposure concentrations using the absolute principal component analysis (APCA) PM _{2.5} 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 ² , 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.	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.
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1 2 3 4							יבטעביו טפּּייטיין בטעביו			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data	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	58	Yang et al. 2018	Land use regression models were derived from street level measurements collected during two sampling campaigns conducted in 2014 and 2015.	Deaths were coded according to the International classification of Diseases, 10th Revision (ICD-10; WHO 2010) including natural cause mortality (A00–R99), overall cardiovascular disease (I00–I99) and overall respiratory disease (J00–J47 and J80–J99). Subcategories included Ischemic heart disease (IHD) (I20–I25), cerebrovascular disease (I60–I69), Pneumonia (J12–J18) and chronic obstructive pulmonary disease (COPD) (J40–I44 and I47).	Age at entry, gender, individual smoking status, body mass index (BMI), physical activity, education level and monthly expenses; percentage of participants who were equal to or older than 65 years old, percentage of participants whose educational level was higher than secondary school, average income per month and percentage of smokers.	Data obtained for a cohort of people who were older than or equal to 65 years old.	There was no information on the rate of lost 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 they have no actual or potential competing financial interests.	No other potential sources of bias identified.
35 36 37			Probably Low	Low	Probably High	Low	Probably Low	Probably Low	Low	Low
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete 0 outcome data∝	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 26	59	Gan et al. 2011	Land use regression to estimate air pollution concentrations and exposure assigned to residential centroid.	A coronary heart disease hospitalization case is a record of hospitalization with the following International Statistical Classification of Diseases, 9th Revision codes, ICD-9, 410–414 and 429.2or 10th Revision (ICD-10), I20–I25, as the principal diagnosis (the most responsible diagnosis) for a hospital admission in the hospitalization database. A coronary heart disease death is a death record with coronary heart disease as the cause of death in the provincial death registration database.	Model adjusted for age, sex, preexisting comorbidity, and neighborhood socioeconomic status. No individual data on behavioral risk factors.	Study provided total number of subjects along with those lost during the follow-up period.	During the 4-year follow-up period, 17,542 (3.9%) moved out of the province and 16,367 (3.6%) died from other diseases, leaving 418,826 (92.5%) subjects at the end of 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 they have no actual or potential competing financial interests.	No other potential sources of bias identified.
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1 2 3 4							36/bmJopen-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete og 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	60	De Kluizenaa r et al. 2013	Used black smoke (BS) as an indicator of EC concentrations. Derived background EC concentrations from BS measured at two regional monitoring sites. Local traffic-related EC emission contributions were estimated based on fuel-specific EC content of exhaust PM_{10} emission. Used the traffic-related EC emissions as input to calculate local EC concentrations, assuming absence of other local EC sources. Also assumed that dispersion dynamics of EC are identical to	The study obtained information on the incidence of hospital-based Ischemic heart disease (International Classification of Diseases [ICD9] 410-414) and cerebrovascular disease (ICD9 430-438) in the study population.	Individual-level covariates: age, gender, marital status, education, smoking, alcohol use, physical activity, body mass index, living conditions (employment status, financial problems).	Data obtained for a cohort of 27,070 non-institutionali zed subjects.	There was no information on April 19, 2024 by guest. Protect	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.
36 37			those of PM ₁₀ . Probably Low	Probably Low	Probably Low	Low	Probably Low		Low	Low
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1 2 3 4							36/bmjopen-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	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	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.	2024 by guest. Protecte	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.
37 38			High	Low	Probably Low	Low	Low g	Probably Low	Low	Low
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o. Study I			BMJ Open BMJ Open Study Exposure assessment Outcome assessment Confounding bias Selection bias						
	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete og outcome data	Selective reporting	Conflict of interest	Other	
a et al. tw 2021 Se at mo fro Au ga Se an 2-s un	C were collected from vo monitors (Sharif and etad) with data recorded 5 min intervals. BC leasurements began om March 2017 to ugust 2017. But the aseous pollutant at the etad site were unreliable nd models utilizing the site data were insatisfactory. So, only the Sharif data were used.	Daily non-accidental 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).	Models adjusted for time, temperature, relative humidity, atmospheric pressure, PM2.5 data, Day of week (DOW) and public holidays.	Study included all daily non-accidental deaths from Ministry of Health and Medical Education database from March 2017 to August 2017.	Daily counts for death were 22. Downloaded obtained, so likely have all outcome data. diversion of the potential errors 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 report.	The authors of this article declare that they have no conflict of interests.	No other potential sources of bias identified.	
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Page 121	of 136 BMJ Open								
1 2 3 4 5 5 No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on 3 outcome data	Selective	Conflict of interest	Other
7 63 9 63 10 11 12 13 14 15 16 17 18 19 20 21 23 24 25 26 27 28 29 30 31 32 33 34 35 36	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 \leq 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.	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 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.
37 38		Probably Low	Low	Probably Low	Low			Low	Low
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No.StudyExposure assessmentOutcome assessmentConfounding biasSelection biasIncomplete of outcome datasetNo.StudyExposure assessmentOutcome assessmentConfounding biasSelection biasIncomplete of outcome dataset	interest	Other
acombination with a chemical transport model,maternal atopy, gestational age andin the Province of Ontario,ifrisk, b	icient declared pot nation that there is sou no conflict bia ve of interest. ide ne to for low ut ct ice that sts was f ve	o other tential arces of as entified.

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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	Probably Low	Probably Low	Low	Low
9 10	65	Rodins et	The study used the	Cardiovascular outcomes	Model adjusted for	The study used	There was no N	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 13			time-dependent,	determined by an	individual and	(2000–2003) and	the rate of lost $\frac{5}{2}$	information	they have	sources of
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	d fro	selective	competing	identified.
16 17			Dispersion chemistry	self-reports, physician	nighttime traffic	from the German	m	outcome to	financial	
17			transport model	and next-of-kin	noise exposure and	HNR Study, an	nttp:/	judge for low	interests or	
19			(EURAD) to estimate the	interviews, and medical	lifestyle factors:	ongoing	/bm	risk, but	personal	
20			exposure to EC.	records.	smoking, alcohol	population-based	mjope	indirect	relationship	
21 22					consumption,	prospective	n.b	evidence that	s that could	
23					physical activity	cohort study.	nj. o	suggests	have	
24 25					and nutritional		om/	study was	appeared to	
25 26					pattern.		on /	free of	influence	
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1 2 3 4							36/bmjopen-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete og outcome data⇔	Selective	Conflict of interest	Other
8			Probably Low	Low	Probably High	Low	Low 2	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	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 Download department (ED) visits were obtained, from http://bm so likely have all outcome data. However, bm open bm	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.
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete 0 outcome data⇔ ≤	Selective reporting	Conflict of interest	Other
8			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 N	There was	The authors	No other
11		al. 2020	using EnviMan (Opsis	plaque presence and	age, sex, air	cardiovascular	were missing	insufficient	declare that	potential
12 13			AB, Sweden) by the	CIMT of the right carotid	pollutant,	subcohort of the	data on plaque $\frac{3}{2}$	information	they have	sources of
13			Environmental	artery, which were	education level,	MDCS cohort,	and 20 on $\frac{\omega}{\omega}$	about	no known	bias
15			Department of Malm [°] o.	assessed by ultrasound	smoke score,	6031 participants	CIMT,	selective	competing	identified.
16 17			The program uses a	examination B-mode	apoB/apoA1 ratio,	who had a	respectively.	outcome to	financial	
17			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 22			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 analyse	suggests	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	free of	influence	
27					activity, alcohol	and 20 on CIMT,	analyses 6011. A	selective	the work	
28					consumption,	respectively. The	19,	report.	reported in	
29 30					median income	number of	2024 by		this paper.	
31					level in residential	participants	<u>14</u> b			
32					area, systolic blood	included in the	y guest			
33 24					pressure and being	plaque analyses	est.			
34 35					born outside of	were 5807 and in	Pro			
36					Sweden.	the CIMT	tect			
37						analyses 6011.	Protected by			
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete og outcome data⇔	Selective	Conflict of interest	Other
8			Probably High	Probably Low	Probably High	Low	Low ay 2	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	68	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 Downloaded for all patients Downloaded 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	The authors declare that they have no competing interests.	No other potential sources of bias identified.
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Page 127 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 og outcome data∞		Conflict of interest	Other
8			Probably Low	Low	Probably Low	Low	Probably Low	Probably Low	Low	Low
9 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 <u>so</u> comprehensive	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 17			study calculated source	were used to define IHD	consumption in	pooled cohorts	and death	outcome to	competing	
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 loss to follow-up for	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				
23			other sources in		socioeconomic	individuals were	our outcomes	suggests		
24			Gothenburg, Stockholm,		index by	included from all				
25 26			and Umeå.		occupation,	study areas.	Missing 9	free of		
27					education level,		information for			
28					occupation status,		variables < إ	report.		
29 30					and mean		5% not			
31					neighborhood		specified.			
32					individual income		5% not specified. 2024 by guest			
33 34					in persons of		•			
35					working age by		Prof			
36					Small Areas for		ecte			
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete og outcome data⇔	Selective	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 g	insufficient	declare that	potential
12 13			2010 were estimated at	diagnosis of International	status, smoking	cohorts within	106,727 Departicipants with complete	information	they have	sources of
13			the study participants'	Classification of	duration, smoking	the ELAPSE	with complete	about	no known	bias
15			baseline residential	Diseases, 9th Revision	intensity,	project with	air pollution	selective	competing	identified.
16 17			addresses, using	(ICD-9) codes 490–492,	body-mass index,	available	exposure data,	outcome to	financial	
17			standardized	and 494–496, or ICD-10	marital status,	information on	the study		interests or	
19			Europe-wide hybrid land	codes J40–44.	employment	COPD hospital	excluded 633 participants with COPD at	risk, but	personal	
20			use regression (LUR)		status, educational	discharge	participants	indirect	relationship	
21 22			models. The LUR model		level and	diagnoses. Mean		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 26			European Environment				participants 9		influence	
27			Agency (EEA) AirBase				with missing $\frac{1}{6}$ information on $\frac{1}{6}$	selective	the work	
28			for PM2.5, NO2, and O3,					report.	reported in	
29 30			and ESCAPE monitoring				confounders. No.		this paper.	
31			data for BC as the							
32			dependent variable. BC				u ĝ v			
33 34			was measured by the				by guest.			
35			reflectance of PM2.5				Protected			
36			filters and expressed in				tect			
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7Table S5 Assessment of certainty of evidence for outcome

Page 129 of 136						BMJ Open					36/bmjopen							
1 2 3 4 5 6 7Table S5 Ass	sessn	nent of certainty	y of c	evidence for outc	come	,							36/bmjopen-2021-049516 on 3 N					
8 9					Reaso	ons for downgrading							ay _{Rea}	sons for upgrading				Final
9 Evidence 10 11	A1	Rationale	A2	Rationale	A3	Rationale	A4	Rationale	A5	Rationale	B1	Rationale	022 D	Rationale	B3	Rationale	Overall	certainty assessment
12 P ³ Sute effects of BC k4EC on CVD in 15 P ^{M2,5-} unadjusted 16 P ³⁰ del	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	ownloadee from	Confounders would shift the RR in both directions	+1	Evidence of increase in risk with increasing exposure	0	Moderate
18 1.Secute effects of BC 20 BC or EC on CVD 21 202PM _{2.5} -adjusted 2320del 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	http://bmjopen.bmj.com	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 25 c or EC on RES 28 10 PM ₂₅ -unadjusted 29 30 del	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	∕ on April⇔19, 2024	Confounders would shift the RR in both directions	0	No evidence of a clear increasing risk with exposure	0	Moderate
31 32 33 34 34 35 34 35 34 35 34 35 34 35 36 36 37	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	upgrading	by guest. Protected t	Confounders would shift the RR in both directions	0	No evidence of a clear increasing risk with exposure	0	Moderate
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	sessin	ent of certaint	y or e	vidence for out	come													
6 7					Reaso	ns for downgrading							on ຜື	asons for upgrading				Final
7 Evidence													May				Overall	certainty
9	A1	Rationale	A2	Rationale	A3	Rationale	A4	Rationale	A5	Rationale	B1	Rationale	¥220	Rationale	B3	Rationale		assessment
10								Risk estimates					22.					
Chronic effects of				All included studies		80% PI 1.068 (95%CI:		reported by the					Dov	Confounders would		No evidence of a		
1BC or EC on CVD	0	Little influence on	0	were consistent with	0	0.965, 1.181) include	0	studies are	0	No evidence of	0	Insufficient basis for	Vnte	shift the RR in both	+1	clear increasing risk	+1	High
13 in PM _{2.5} -unadjusted 14	ted the overall effect		the overall effect our prespect	our prespecified		unity but no larger than		sufficiently		publication bias		upgrading	wntoade	directions		with exposure		
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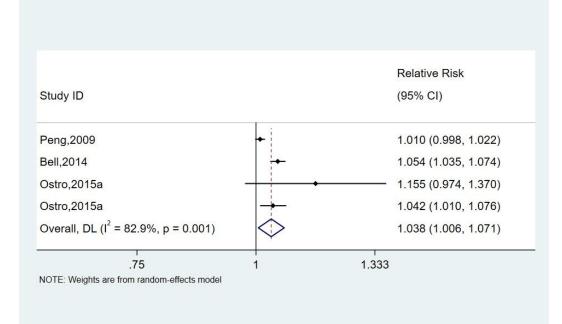


Figure S1 Impact of short-term exposure to BC or EC on respiratory diseases in 65+ years age

group in the PM_{2.5}-unadjusted model.

group and Study ID	Relative Risk (95% Cl)
Asia	
Geng.2013	1.012 (1.002, 1.021)
Wang,2019a	1.011 (0.999, 1.023)
Gong.2019	1.002 (1.001, 1.003)
Huang.2012	1.005 (0.998, 1.010)
Lin,2016a	1.002 (0.999, 1.005)
Son,2012	1.001 (0.981, 1.021)
Heo,2014	1.006 (0.994, 1.017)
Subgroup, DL (l ² = 21.5%, p = 0.266)	1.003 (1.001, 1.005)
Europe	
Basagana,2015	0.979 (0.944, 1.016)
Ostro,2015a	0.994 (0.953, 1.038)
Ostro,2015a	1.005 (0.979, 1.031)
Atkinson,2016	0.987 (0.973, 1.001)
Subgroup, DL (1 ² = 0.0%, p = 0.602)	0.990 (0.979, 1.001)
America	
Ito,2011	1.003 (0.982, 1.024)
Maynard,2007	1.076 (0.980, 1.179)
Ostro,2007	1.026 (1.004, 1.049)
Kim,2015	1.031 (0.935, 1.133)
Subgroup, DL (l ² = 20.8%, p = 0.285)	1.017 (0.998, 1.037)
Heterogeneity between groups: p = 0.030	
.8 1	1.25

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

geographical locations.

group and Study ID	Relative Risk (95% CI)
Europe	
Basagana,2015 +	1.026 (1.006, 1.047)
Subgroup, DL ($I^2 = 0.0\%$, p = .)	1.026 (1.006, 1.047)
America	
Bell,2014	1.036 (1.023, 1.050)
Sarnat,2015	1.038 (1.005, 1.073)
Ito,2011	1.019 (1.007, 1.034)
Winquist,2015	1.048 (1.012, 1.085)
Tolbert,2007	1.013 (1.004, 1.022)
Lall,2011	1.022 (0.999, 1.046)
Metzger,2004	1.017 (1.007, 1.027)
Peng,2009	1.018 (1.011, 1.025)
Liu,2016a	0.960 (0.857, 1.076)
Liu,2016b	1.020 (0.858, 1.214)
Kim,2012 +	1.056 (1.018, 1.094)
Subgroup, DL (l^2 = 39.7%, p = 0.084)	1.022 (1.016, 1.029)
Heterogeneity between groups: p = 0.720	
.8 1	1.25

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

geographical locations.

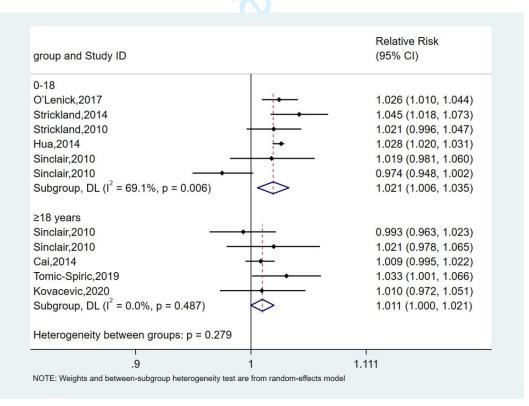


Figure S4 Impact of short-term exposure to BC or EC on asthma morbidity in different age

groups.

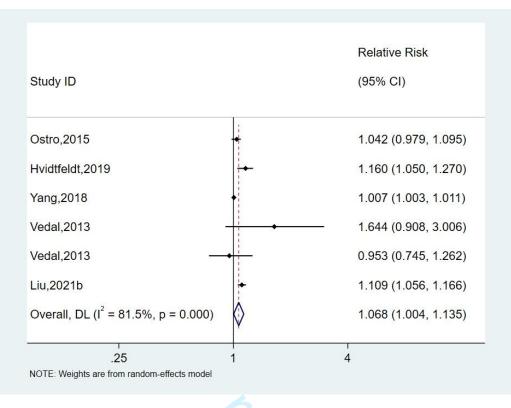


Figure S5 Impact of long-term exposure to BC or EC on cardiovascular diseases.

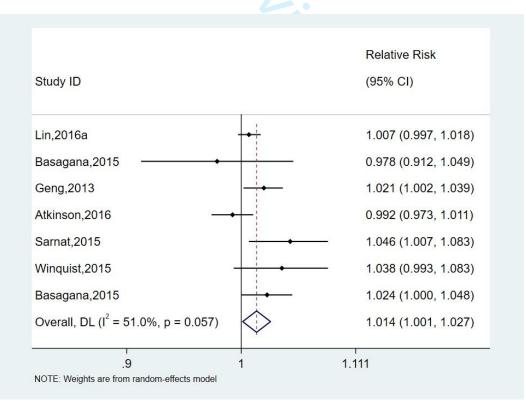


Figure S6 Impact of short-term exposure to BC or EC on cardiovascular diseases in the

PM_{2.5}-adjusted model.

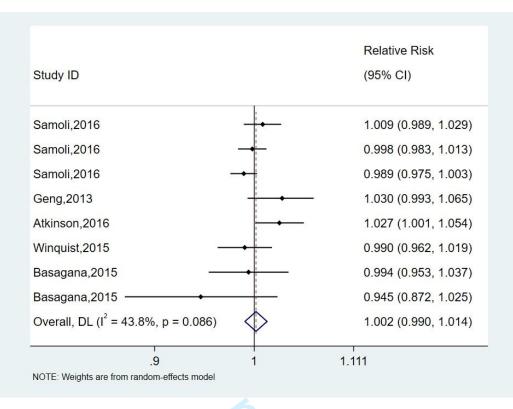


Figure S7 Impact of short-term exposure to BC or EC on respiratory diseases in the

PM_{2.5}-adjusted model.



PRISMA 2020 Checklist

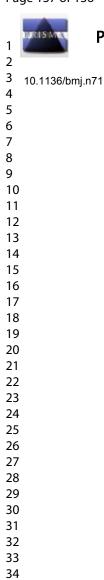
Page 135 of 136		BMJ Open		
	5MA 2	020 Checklist		
Section and Topic	ltem #	Checklist item		Location where item is reported
TITLE	<u> </u>	0 6		
Title	1	Identify the report as a systematic review.		#1
ABSTRACT		۵۵ ۲		
Abstract	2	See the PRISMA 2020 for Abstracts checklist.		#3-4
INTRODUCTION				
2 Rationale	3	Describe the rationale for the review in the context of existing knowledge.	, 	#6-7
3 Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.		#7
4 METHODS				
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.		#8
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to the date when each source was last searched or consulted.	entify studies. Specify the	#8
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.		#8
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many review and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the second		#9
2 Data collection 3 process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of approcess.		#9-10
5 Data items 6	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each a study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results		#9-10
7 8	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding assumptions made about any missing or unclear information.	sources). Describe any	#9-10
 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 study and whether they worked independently, and if applicable, details of automation tools used in the process.	y reviewers assessed each	#10-11
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
2 3 Synthesis 7 methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study interget comparing against the planned groups for each synthesis (item #5)).		#9
4 5	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summa conversions.	ry statistics, or data	#10
6 7	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.		#9
1 8 9	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed and extent of statistical heterogeneity, and software package(s) used.	rmed, describe the	#11-12
Į	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis,		#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)		#13
4	15	Describe any methods use to assess certainty (draconfildence) in the body of evidence for ab batcone of		#11
44 discussion and 44 discussion and 44 discussion and 45 discussion and 46 discussio	15	Describe any methods used topassess/certainty (or confidence) in the body of evidence/igniah butcontern		



PRISMA 2020 Checklist

		BMJ Open 1136	Page 136 of
	MA 2	020 Checklist	
Section and Topic	ltem #	Checklist item	Location where iten is reported
assessment			
RESULTS		S S	
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 execuded.	#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 effed 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 optice 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> </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. $\frac{14}{\sigma}$	#25-26
OTHER INFORMA	TION	<u>6</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.	#7
protocor	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 readiew.	#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

Page 137 of 136



 PRISMA 2020 Checklist

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

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Secondary Subject Heading:	Cardiovascular medicine, Respiratory medicine
Keywords:	PUBLIC HEALTH, RESPIRATORY MEDICINE (see Thoracic Medicine), CARDIOLOGY

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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

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Abstract

Background Adverse health effects of fine particles ($PM_{2.5}$) 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 μ g/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

 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.

 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.
 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.¹ 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_{2.5}, are well documented. In 2017, a total of 2.94 million deaths resulted from ambient PM worldwide.³⁻⁵ PM_{2.5} 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.^{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.^{8, 9} 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.⁴ 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.¹³ 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.¹⁴ 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.^{17, 18} Compared with Yang et al. 2019¹⁹, this study included recently

Page 9 of 136

BMJ Open

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 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 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) 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)

Page 11 of 136

BMJ Open

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.²⁰ In addition, the estimate was converted to a standardized increment (1 μ g/m³) of RR. The following formula was used to calculate the standardized risk estimates:

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

Two studies did not show the overall risk, while stratified risk estimates by age and location were reported.^{21, 22} 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.²³ 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.²⁴⁻²⁶

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

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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.²⁹ 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 $PM_{2.5}$ is a potential confounder in assessing the health effects of $PM_{2.5}$ constituents.⁷ For overall and outcome analysis, PM_{2.5}-adjusted estimates and PM_{2.5}-unadjusted estimates in the models were combined, respectively where more than three estimates were available. Regarding the subgroup analysis, PM_{2.5}-unadjusted estimates were analyzed, while PM_{2.5}-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

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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 2^{covariate}. Space3 is Space1 times Space2. Space3 is the total analysis search space. Search spaces were computed by the method introduced in Young et al, 2019.³⁰

The p-value plot was used to inspect the distribution condition of the p-values.³¹ 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.³¹ 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 = (lnCl high - lnCl 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.^{32, 33} Of these, 70 fulfilled the inclusion criteria (Figure 1).^{7, 21-26, 34-96} 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 μ 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 μ 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 μ g/m³, 95% CI: 1.006–1.016), and then diminished on lag 1 (RR=1.005 per 1 μ g/m³, 95% CI: 1.002–1.008) and lag 2 (RR=1.002 per 1 μ 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 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.²³ In addition, just one study in Asia was performed assessing the short-term effects of BC or EC on stroke morbidity (Figure S2).⁶⁶

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).

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		PM _{2.5} -unadjusted model					ω PM _{2.5} -adjusted model			
Subgroup Analysis	No. of No. of Studies Estimates		Relative Risk (95%CI)		Egger regression test (p value)		Estimates	Relative Risk (95%CI)	I ²	
Cardiovascular Diseases						22. C				
Age						Downloaded				
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)	_	_	 	_	_	_	
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%	_	—	—	_	—	
Outcome						http://bmjop				
Morbidity	12	12	1.022 (1.016, 1.029)	37.20%	0.163	4 .b	5	1.018 (1.006, 1.031)	39.50%	
Mortality	14	15	1.003 (1.001, 1.006)	29.70%	0.266	4 mj.com/	4	1.006 (0.993, 1.019)	42.90%	
Respiratory Diseases), mo				
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	Ģ,		—		
≥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	3 ^s t. P	5	0.996 (0.987, 1.004)	0	
Mortality	10	11	1.013 (0.997, 1.030)	66.40%	0.328	3 rote	3	1.017 (0.985, 1.050)	48.30%	
			18			cted by copyright.				

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*10⁻⁴⁵ 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.^{25, 60, 68, 75} However, one study analyzed COPD. It indicated that long-term exposure to BC or $\frac{20}{1000}$

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).²⁴

3.4 Results from the PM_{2.5}-adjusted model

In the PM_{2.5}-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 μ 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_{2.5}-unadjusted model. In addition, the impact of BC or EC on cardiovascular morbidity in the PM_{2.5}-adjusted model (RR=1.018 per 1 μ g/m³, 95% CI: 1.006-1.031) was consistent with the results in the PM_{2.5}-unadjusted model (RR=1.022 per 1 μ 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 μ g/m³, 95% CI: 1.001-1.006), while no association was observed in the PM_{2.5}-adjusted model (RR=1.006 per 1 μ 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 μ g/m³, 95% CI: 1.002-1.010) by eliminating studies with partial overlap from the same geographical location.^{21, 23, 38, 80} In addition, no statistical significance was observed (RR=1.008 per 1 μ 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.^{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 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).

No. Study	Key criteria				Other criteria				
	Study	Exposure	Outcome	Confounding	Selection	Incomplete	Selective	Conflict of	Othe
		assessment	assessment	bias	bias	outcome data	reporting	interest	011
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								

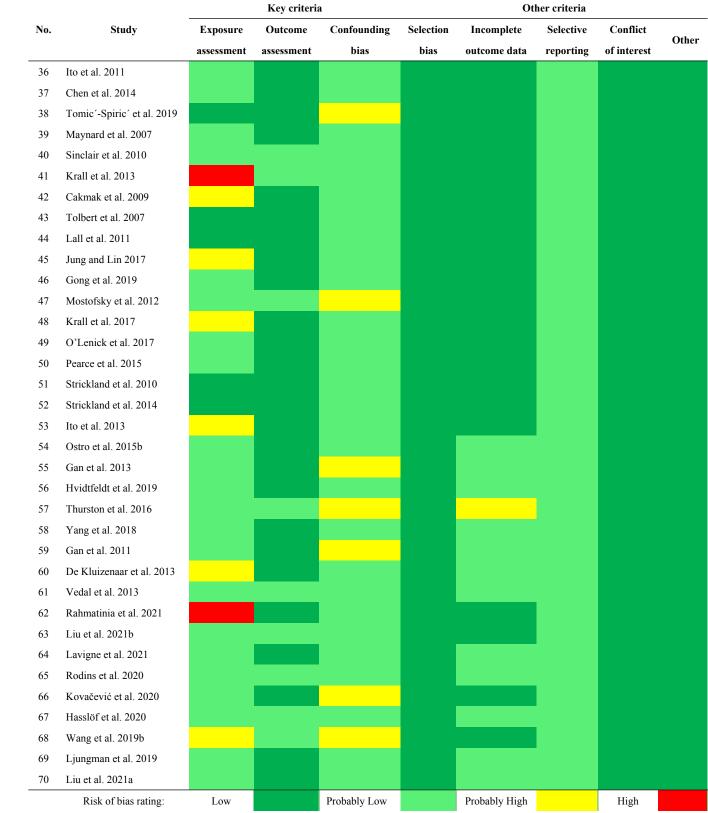
Table 4 Results of risk of bias assessment

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Table 4 Results of risk of bias assessment (continued)



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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_{2.5}-adjusted model and the PM_{2.5}-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.

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However, the association between BC or EC and cardiovascular mortality should be further explored by further studies, which should pay more attention to the PM₂₅-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 PM2.5-unadjusted model and PM2.5-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.^{22, 63, 93} However, in the PM_{2.5}-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_{2.5}-adjusted model and PM_{2.5}-unadjusted model.^{22, 85} 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 $PM_{2.5}$ -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 $PM_{2.5}$ -unadjusted/adjusted model and chronic effects of BC or EC on cardiovascular diseases in $PM_{2.5}$ -unadjusted model) upgrade one level on concentration-response gradient for an increase in risk with increasing BC or EC.²⁹ 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.¹⁰⁰ In addition, lung function and mucociliary clearance decline with long-term exposure to pollutants and increasing age.^{5, 101} 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 $PM_{2.5}$.

4.3 Underlying pathological mechanism

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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.¹⁰³ 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.¹⁰⁴ 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.¹⁰⁴ 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 PM₁₀ and PM_{2.5}, which performed by Mustafic et al, 2012.¹⁰⁵ A critique is given in Young et al, 2019, who

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 $PM_{2.5}$ when assessing the health effect of $PM_{2.5}$ constituents. Mostofsky et al. proved that $PM_{2.5}$ may be associated with both health and its constituents. Constituent having closer association with $PM_{2.5}$

may illustrate a stronger association with diseases. Therefore, the results of PM_{2.5}-unadjusted model could introduce bias.⁷ 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.

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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 all authors.

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Competing interests

We declare that all authors have no competing interests.

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Data sharing statement

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

information.

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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.

BMJ Open

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_{2.5} 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.

BMJ Open

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.

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.
 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

Page 43 of 136

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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 $PM_{2.5}$ -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 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_{2.5}-adjusted model.



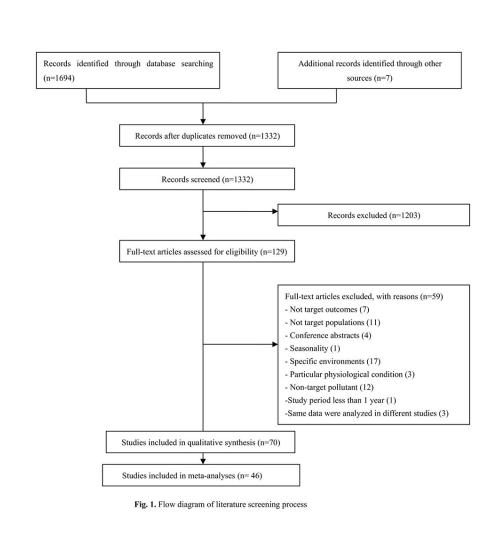


Figure 1 Flow diagram of literature screening process.

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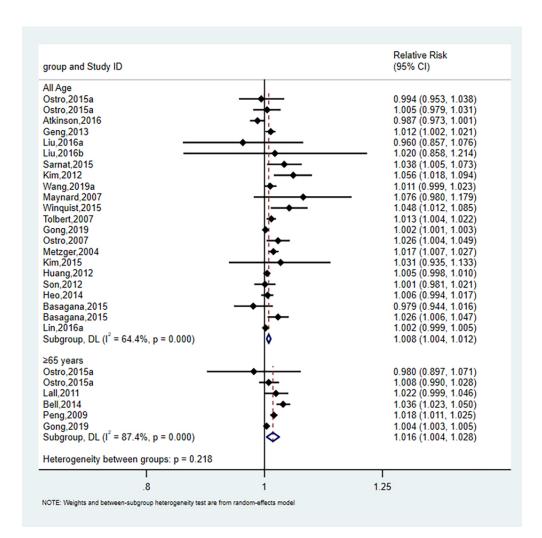
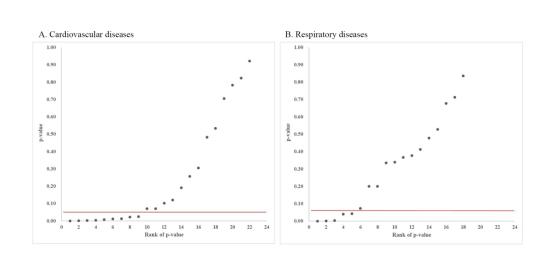
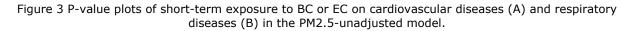


Figure 2 Impact of short-term exposure to BC or EC on cardiovascular diseases in the PM2.5-unadjusted model.

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SUPPLEMENTARY APPENDIX

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

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Supplementary data

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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_{2.5}-adjusted model.

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Study	Study Design	Country	Study Period	Outcome	Age	Pollutant	ICD code	C S S S S S S S S S S S S S S S S S S S
Atkinson et al. 2016	TS	UK	2011-2012	Mortality	All	BC,EC	ICD-10	CVD(ICD-10:100-I99),RES(ICD-10:J00-J99)
								RES[COPD(ICD-9-CM:490-492,RTI(ICD-9-CM:464466, 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	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) To
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	BC	ICD-10	429),PVD(ICD-9-CM:440-448)] None Asthma(ICD-10:J45) Image: CVD(ICD-10:100-I99),RES(ICD-10:J00-J98) Asthma(ICD-10:J45) Image: CVD(ICD-10:I00-I99),RES(ICD-10:J00-J99) CVD(ICD-10:100-I99),RES(ICD-10:J00-J99) Image: CVD(ICD-10:I00-I99),RES(ICD-10:J00-J99) CVD(ICD-10:I00-I99),RES(ICD-10:J00-J99) Image: 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	BC	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(10D-9:460-519),COPD(ICD-9:490-492,494,496),Pneumonia(I CD-9:480-486),Asthma(ICD-9:493),SSID(ICD-9:78
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)

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	Table S2 Charac	Study Design	Of Included s	Studies in the Study Period	Systematic re Outcome	Age	Pollutant	IS. ICD code	S S S S S S S S S S S S S S S S S S S
	Ostro et al. 2009	TS	USA	2000-2003	Morbidity	<19	EC	ICD9	RES(ICD-9:460-519),Asthma(ICD-9:493),Acute brochitis(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-I98),CVD(ICD-10:100-I99)
									CVD[Cardiac Dysrhythmias(ICD-9:428),Heart Rhytken 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	ط 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:I00-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, ICD-10	CVD(ICD-9:390-459,ICD-10:100-I99),RES(ICD-9:440-519,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(ICO 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	CVD(ICD-10:100-199),RES(ICD-10:100-198)
	Klemm et al. 2011	TS	USA	1998-2007	Mortality	≥65	EC	ICD-10	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-9:410-414,427,
	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)
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Table S2 Charac	cteristics (Study Design	of included Country	studies in the Study Period	systematic Outcome	review and ma	eta-analys Pollutant	IS. ICD code	-049 516 on Sajseases
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)
								CVD[IHD(ICD-9:410-414),AMI(ICD-9:410),cardiaco
fetzger et al. 2004	TS	USA	1993-2000	Morbidity	All	EC	ICD-9	dysrhythmias(ICD-9:427),CA(ICD-9:427.5),CHF(ICE9:428),PVD and cerebrovascular
								events(ICD-9:433-437,440,443-444,451-453),CHD(IGD-9:440),Stroke(ICD-9:436)]
1ar et al. 2000	TS	USA	1995-1997	Mortality	All	EC	ICD-9	CVD(ICD-9:390-448.9)
Vang et al. 2019a	TS	China	2013-2015	Mortality	All	EC	ICD-10	CVD(ICD-9:390-448.9) 3 CVD(ICD-10:100-199),RES(ICD-10:J00-J99) 3 Stroke(ICD-10:160-166) 9
Lin et al. 2016b	TS	China	2007-2011	Mortality	All	EC	ICD-10	Stroke(ICD-10:160-166)
Ostro et al. 2008	TS	USA	2000-2003	Mortality	All	EC	ICD-10	CVD(ICD-10:I00-I99)
lto et al. 2011	TS	USA	2000-2006	Morbidity, Mortality	≥40	EC	ICD-9, ICD-10	CVD[Hypertensive Diseases(ICD-9:402,ICD-10:111) MI(ICD-9:410;ICD-10:121-I22),IHD (ICD-9:414,ICD-10:125),Dysrhythmias(ICD-9:427,ICD-10:148),HF(ICD-9:428,ICD-10:I50),Stroke(ICD-9:430-43 9,ICD-10:160-I69)]
Chen et al. 2014	TS	China	2004-2008	Morbidity	All	EC	ICD-9	Stroke[Ischemic Stroke(ICD-9:433-434),HemorrhagiesStroke(ICD-9:430-432)]
Fomic'-Spiric' et al. 2019	CS	Serbia	2012-2014	Morbidity	≥18	BC	ICD-10	Allergic RES[AR(ICD-10:J.30.4),AA(ICD-10:J.45.0)
Maynard et al. 2007	CS	USA	1995-1997,	Mortality	All	BC	ICD-9,	CVD(ICD-9:390-429,ICD-10:101-152),Stroke(ICD-9930-438,ICD-10:160-169),RES(ICD-9:460-519,ICD-10:J00-J
			1999-2002				ICD-10	99) Gues
Sinclair et al. 2010	TS	USA	1998-2002	Morbidity	All	EC	NR	A otherso LIDTLI DTL
Krall et al. 2013	TS	USA	2000-2005	Mortality	All	EC	NR	Asuma, OKTI, EKTI D CVD and RES(NR) O RES(ICD-9:460-519) O
Cakmak et al. 2009	TS	Canada	2001-2006	Morbidity	All	EC	ICD-9	RES(ICD-9:460-519)

age 5	5 of 136						В	MJ Oper	36/bm оре
	Table S2 Charac	teristics of	of included	studies in the s	ystematic re	eview and r	neta-analysi	is.	36/bmjopen-2021-049516 (
	Study	Study Design	Country	Study Period	Outcome	Age	Pollutant	ICD code	S S S S S S S S S S S S S S S S S S S
	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 :491,492,496),URTI(ICD-9:460-465,460.0,477),Pneumonia (ICD-9:480-486),Bronchiolitis(ICD-9:466.1,466.11,466.19)]
	Lall et al. 2011	TS	USA	2001-2002	Morbidity	≥65	EC	ICD-9	RES[Pneumonia(ICD-9:480-486),COPD(ICD-9:490, 2,496),Acute Bronchitis and Bronchiolitis(ICD-9:466),Asthma(ICD-9:493)],CVD bysrhythmia(ICD-9:427),IHD(ICD-9:410-414),HF(ICD-9:4 28) Strelar(ICD, 9:421, 427)]
	Jung and Lin 2017	CS	China	2000-2010	Morbidity	0-20	BC	ICD-9	Asthma(ICD-9-CM:493)
	Gong et al. 2019 Mostofsky et al. 2012	TS CS	China USA	2006-2011 2003-2008	Mortality Morbidity	All ≥21	BC BC	ICD-10 NO	CVD(ICD-10:100-199) Openation Acute Ischemic Stroke Openation
	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	26),3t08e(ICD-9.431437)] 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)] Q00 Acthma(ICD-9:402,0,402,0),Whaaaad(CD, 0,766,075)
	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 Strickland et al. 2010	TS CS	USA USA	1999-2008 1993-2004	Morbidity Morbidity	5–17 5-17	EC EC	ICD-9 ICD-9	Asthma(ICD-9:493.0-493.9),Wheeze(ICD-9:786.07)
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Table S2 Charac	teristics	of included s	studies in the	systematic	review and mo	eta-analys	is.	36/bmjopen-2021-049516 c	
Study	Study Design	Country	Study Period	Outcome	Age	Pollutant	ICD code	S Usease D	s
Strickland et al. 2014	TS	USA	2000-2010	Morbidity	2-16	EC	ICD-9	Asthma(codes beginning with 493),Wheeze (ICD-9:786.07)	
Ito et al. 2013	TS	USA	2001-2006	Morbidity, Mortality	all (mortality), ≥65(morbidity)	EC	ICD-9, ICD-10	CVD(ICD-10:101-179),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(ICL	D-10:C34,J00-J98)
Gan et al. 2013	Со	Canada	1999-2002	Morbidity, Mortality	45-85	BC	ICD-9, ICD-10	COPD(ICD-9:490-492,496,ICD10:J40-J44)	
Hvidtfeldt et al. 2019	Со	Denmark	1993-2015	Mortality	50-64	BC	ICD-10	CVD(ICD-10:I00-I99),RES(ICD-10:J00-J99,C34)	
Thurston et al. 2016	Со	USA	1988-2004	Mortality	≥30	EC	ICD-9, ICD-10	IHD(ICD-9:410-414,ICD-10:120-125)	
Yang et al. 2018	Со	China	1998-2011	Mortality	≥65	BC	ICD-10	CVD(ICD-10:I00-I99),RES(ICD-10:J00-J47,J80-J999	
Gan et al. 2011	Со	Canada	1999-2002	Morbidity, Mortality	45-85	BC	ICD-9, ICD-10	CHD(ICD-9:410-414,429.2),(ICD-10:120-125)	
De Kluizenaar et al. 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	Со	USA	1994-2005	Morbidity, 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	0-125)
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	CHD T	
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	Atherosclerosis in the carotid arteries	

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Starday.	Study	Garratura	Study	0	A ==-	De llectere t	ICD	S Wiseases
Study	Design	Country	Period	Outcome	Age	Pollutant	code	a a a a a a a a a a a a a a a a a a a
Wang et al. 2019b	CS	USA	2005-2016	Morbidity	All	BC	NR	STEMI 8
Ljungman et al. 2019	Со	Sweden	1990-2011	Morbidity,	All	BC	ICD-9,	IHD(ICD-9:410–414 and ICD-10:I20-25);stroke(ICD=2:431–436 and ICD-10:I61–I65)
Ljungman et al. 2019	0	Sweden	1990-2011	Mortality	All	БС	ICD-10	ND(1CD-9.410-414 and 1CD-10.120-23),Subke(1CD-4.10-430 and 1CD-10.101-103)
Liu et al. 2021a	Co	Sweden,	1992-2004	Morbidity	All	BC	ICD-9,	COPD(ICD-9:490–492, and 494–496, or ICD-10:J40244)
Liu et al. 2021a	0	Denmark	1792-2004	woroldity	All	BC	ICD-10	

 ...retin; CHD: Coro.

 ...r. allergic asthma; AR: allergic r.

 ...rotor; ARTI: Acute respiratory infections.

 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; and the contract 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 medication; 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. http://bmjopen.bmj.com/ on April 19, 2024 by guest. Protected by copyright

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

Subgroup Analysis	No. of Studies	No. of Estimates	Relative Risk (95%CI)	I ²	Egger Regression Test (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	_

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Table S4 Details of risk of bias assessment.

No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete		Conflict of interest	Other
1	Atkinson	Probably Low	Low	Probably Low	Low	Low N	Probably Low	Low	Low
	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
		measured at the central	1 January 2011 to 31	(seasonality,	daily counts of	for death were	insufficient	declare no	potential
		London background	December 2012 were	long-term trend),	deaths in	obtained, so	information	conflict of	sources of
		monitoring site at North	obtained from the Office	temperature,	London, United	likely have all		interest.	bias
		Kensington. All	for National Statistics.	humidity, day of	Kingdom for the	outcome data.			identified.
		measurements were 24-h	Daily counts of deaths in	week and public	period 1 January	However, any	outcome to		
		averages except for CO.	London, United Kingdom	holidays.	2011 to 31	potential errors	judge for low		
		The number of all	were classified as all		December 2012.	or missing data			
		observations was	disease-related causes,			did not depend	indirect		
		621-693 (<25% missing	cardiovascular			on air pollution	evidence that		
		data).	(International		101.	levels.	suggests study		
			Classification of			on	was free of		
			Diseases,10th			Apr	selective		
			revision-ICD10: I00-I99)			April 19, 2024 by guest. Protected by copyright	report.		
			and respiratory (ICD10:			202			
			J00-J99) diseases.			i4 by	-		
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1 2 3 4							Incomplete			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	Selective reporting	Conflict of interest	Other
8 9	2	Bell et al.	Probably High	Low	Probably Low	Low	Low	Probably Low	Low	Low
9 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 13			optical reflectance.	denominator file from the	(seasonality,	individuals ≥65	admissions	information	conflict of	sources of
14			Monitors from 5 sites	Centers for Medicare and	long-term trend),	years of age	were obtained,		interest.	bias
15 16			across 4 counties were	Medicaid Services. Cause	day of week,	enrolled in the	so likely have	selective		identified.
17			used. Sampling occurred	of admission was	temperature, and	Medicare	all outcome	outcome to		
18			daily, with some missing	determined by principal	dew point.	fee-for-service	data. However,			
19 20			periods, for Hartford, New Haven, and	discharge diagnosis code according to International		plan during August 2000 to	any potential errors or	risk, but indirect		
21			Springfield, and every	Classification of		February 2004.	missing data	evidence that		
22			third day for Bridgeport	Diseases, Ninth Revision,		reordary 2001.	did not depend	-		
23 24			and Danbury. Days with	Clinical Modification			on air pollution			
25			missing data were	(ICD-9-CM; National			levels.			
26 27			omitted from analysis	Center for Health						
27			(the number of missing	Statistics 2006).				-		
29			data was not reported).				April 19, 2024 by gues			
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete		Conflict of interest	Other
8	3	Cai et al.	Probably Low	Low	Probably Low	Low	Low	Probably Low	Low	Low
9 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 13			fixed-site station. Daily	the Shanghai Health	long-term trend),	hospitalization	hospitalization		competing	sources of
14			data was available and no	Insurance Bureau	temperature,	for adult	were obtained,		financial	bias
15			missing data was	(SHIB). The causes of	relative humidity	residents living	so likely have		interests.	identified.
16 17			reported.	hospital admission were	and day of the	in the nine urban	all outcome	outcome to		
18				coded according to	week.	districts between	data. However,			
19 20				International		January 1, 2005	any potential	- ,		
20				Classification of Diseases, Revision 10		and December 31, 2011(2922	errors or missing data	indirect evidence that		
22				(ICD-10): Asthma (J45).		days) from the	did not depend	T		
23 24				(ICD-10). Astinia (343).		Shanghai Health	on air pollution			
25						Insurance	levels.	selective		
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete of the second seco		Conflict of interest	Other
8 9			Probably High	Low	Probably Low	Low	Low X	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		declare no	potential
12 13			PM _{2.5} were measured	Municipal Center of	long-term trend),	(excluding	obtained, so		conflict of	sources of
14			continuously and 24hr	Disease Control and	temperature,	accidents or	likely have all		interest.	bias
15 16			averaged was estimated if	Prevention database. The	humidity and day	injuries) deaths	outcome data.			identified.
17			>75% of the 1hr values was available for that	causes of death were	of week.	during over the	However, any			
18			day. Missing data was not	coded according to the International	0	study	or missing data			
19 20			replaced by other values.	Classification of		study.	did not depend			
21			replaced by other values.	Diseases, Revision 10			on air pollution			
22 23				(ICD 10).			levels.	suggests study		
24						101		was free of		
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	incomplete g outcome data		Conflict of interest	Other
8			Probably High	Low	Probably Low	Low	Low A	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	5	Hua et al. 2014	Daily 24h average PM _{2.5} and BC data was obtained from a fixed-site station. The study only used the actual collected data and did not fill in the missing data for PM _{2.5} and black carbon.	Daily asthma hospital admission data was obtained from Shanghai Children's Medical Center. Dates of admission and discharge, and diagnoses using the International Classification of Diseases, Revision 10.	Adjusted for long-term and seasonal trend, day of week, temperature and relative humidity.	Study included all asthma hospital admissions of children ≤ 14 years of age from Shanghai Children's Medical Center between1 January 2007 and 31 July 2012 in nine urban districts of Shanghai.	Daily counts for asthma hospital admissions of children 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.
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	5	Conflict of interest	Other
8 9			Probably Low	Low	Low	Low	Low 2	Probably Low	Low	Low
9 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 13			obtained from one station	mortality for all ages	(year, month, day	counts of	obtained, so	information	competing	sources of
14			in Barcelona and Athens.	were collected (excluding	of week) trends,	all-cause	likely have all		interests.	bias
15			Daily data was available	deaths from external	temperature,	mortality for all	outcome data.			identified.
16 17			and no missing data was	causes, International	holidays, summer	ages and daily	However, any	7		
18			reported.	Classification of	vacations and	counts of	potential errors			
19				Disease-ICD9: 001799,	influenza.	cardiovascular,	or missing data			
20 21				ICD10 A00R99), as well		respiratory and	did not depend			
21				as daily counts of		all-cause	on air pollution	7		
23				cardiovascular (ICD9:	l l	mortality for	levels.	suggests study		
24 25				390459, ICD10: I00I99),		those greater than		was free of		
26				respiratory		age 65.		selective		
27				(ICD9:460519,				report.		
28 29				ICD10:J00J99) and			, u			
30				all-cause mortality for						
31				those greater than age 65.			on April 19, 2024 by gues	`		
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete of the second secon	Selective	Conflict of interest	Other
8			Low	Low	Probably Low	Low	Low 2	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	7	Samoli et al. 2016	Daily concentrations of 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 (BC urban in PM _{2.5}) and 702 (BC in PM _{2.5}) between 2011 and 2012 (<25% missing data).	Based on the primary discharge diagnosis, daily numbers of admissions for cardiovascular disease (International Classification of Diseases, 10th revision-ICD-10: I00-I99) for those aged 15-64 (adult) and 65+ years (elderly), and respiratory diseases (ICD-10: J00-J99) for those aged 0-14 years (paediatric), adult and the elderly were calculated.	Adjusted for long term and seasonal trends, temperature, relative humidity, regulated pollutants (PM ₁₀ , PM _{2.5} , NO ₂ , SO ₂ and O ₃), day of the week and public	Study included all cardiovascular and respiratory hospital admissions in London, UK between 2011 and 2012.	Daily counts for all emergency hospital admissions 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 interests.	No other potential sources of bias identified.
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1 2 3 4							36/bm)open-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	Selective	Conflict of interest	Other
8 9			Probably High	Low	Probably Low	Low	Low X	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	8	Zanobetti and Schwartz 2006	Ambient BC from one monitor. The hourly measurements for BC and PM _{2.5} 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.	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 revision-ICD-9:410), and pneumonia (ICD-9: 480–487), from Medicare billing records for the years 1995–1999.	Adjusted for temperature, day of the week, seasonality, long-term trends, humidity, barometric pressure, and the extinction coefficient.	Data consisted of all U.S. Medicare hospital admissions in the Boston Metropolitan area for myocardial infarction during the study duration.	Daily counts for hospital admissions were obtained, add 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	Authors declared no competing interests.	No other potential sources of bias identified.
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1 2 3 4							36/bmjopen-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete g	Selective reporting	Conflict of interest	Other
8 9			Probably High	Low	Probably Low	Low	Low Y	Probably Low	Low	Low
9 10	9	Liu et al.	EC were collected from a	Emergency department	Adjusted for time	Study included	Daily counts	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 13			one-in-three or one-in-six	from the Blue Cross Blue	seasonal trend),	emergency	department <u>So</u>	information	potential	sources of
14			day schedule. EC were	Shield Texa. International	day of week,	department visits	visits were		competing	bias
15 16			measured for 566 days	Classification of Diseases	temperature, dew	for Greater	obtained, so	selective	financial	identified.
17			from April 02, 2009, to	9th Revision (ICD-9)	point and	Houston from	likely have all	•	interests.	
18			December 30, 2013, <25% missing for the	diagnosis codes were used to classify outcome	population growth.	claims data insured from	outcome data. However, any			
19 20			frequency of sampling.	groups.		January 1, 2008	potential errors			
21			frequency of sampling.	groups.		through	or missing data			
22 23						December 31,	did not depend			
23 24						2013.	on air pollution			
25							levels.			
26 27										
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1 2 3 4							36/bmjopen-2021-049516 o Incomplete			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete \int_{Ω}^{10} outcome data ω		Conflict of interest	Other
8			Probably 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	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.	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.
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete		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	11	Sarnat et al. 2015	24hr average concentration of PM _{2.5} 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 department visits were obtained, hence one hospital not providing data after 26 April 2002. 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 they have no actual or potential competing financial interests.	No other potential sources of bias identified.
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1 2 3 4							Incomplete			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	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	12	Kim et al. 2012	PM _{2.5} 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	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.
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1 2 3 4							30/bmJopen-2021-0493			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	Selective reporting	Conflict of interest	Other
8			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	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 hospitalization s of children were obtained, so likely have all outcome data. However, any potential errors or missing data did not depend on air pollution	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.
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1 2 3 4							Incomplete o			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete		Conflict of interest	Other
8 9			Probably Low	Low	Probably Low	Low	Low X	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 _{2.5} samples were	metropolitan Denver	for longer-term	all deaths over	for death were		authors has	potential
12 13			collected from single,	were computed from the	temporal trend, as	the course of the	obtained, so		any actual	sources of
14			central-site monitor. The	Colorado Health	time since the	study in a	likely have all		or potential	bias
15 16			observations of EC was	Information Dataset	study began, day	defined	outcome data.		competing	identified.
17			1809 days from 2003	compiled by the Colorado	of week, and daily	geographical	However, any		interests.	
18			through 2007 (missing	Department of Public Health and Environment.	temperature and humidity.	area.	potential errors			
19 20			data <25%).	Data included cause of	numany.		or missing data did not depend			
21				death by the International			on air pollution			
22 23				Classification of Diseases			levels.			
23 24				10th Revision (ICD-10)				was free of		
25				code.		ien		selective		
26 27							Apr	report.		
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1 2 3 4							36/bmjopen-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete of the second secon	Selective	Conflict of interest	Other
8			Probably Low	Low	Probably Low	Probably Low	Low Y	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	15	Huang et al. 2012	Daily average concentrations of PM _{2.5} were obtained from a single, central-site monitor. Daily average concentrations of EC in PM _{2.5} 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.	for death were Do obtained, so likely have all outcome data. However, any potential errors or missing data did not dependo	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.
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No. Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	and the second	Selective	Conflict of interest	Other
	Probably High	Low	Probably Low	Low	Low X	Probably Low	Low	Low
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 was not replaced by other values.	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 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 report.	The authors declare they have no competing financial interests.	No other potential sources of bias identified.

Pag	e 75 of	136			BMJ Oper	1	36/bmjopen-2021			
1 2 3 4							en-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	incomplete og outcome dataఆ	Selective reporting	Conflict of interest	Other
8			Probably High	Low	Probably Low	Low	Low X	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	17	Levy et al. 2012	The U.S. Environmental Protection Agency established the PM Speciation Trends Network (STN) to measure more than 50 PM _{2.5} 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 missing data.	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 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.
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1 2 3 4 _							S6/bmjopen-2021-049516 on Incomplete			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	Selective reporting	Conflict of interest	Other
8 9			Probably Low	Low	Probably Low	Low	Low X	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 13			central-site monitor. The	National Statistical	trends and	deaths over the	obtained, so	information	have no	sources of
14			monitoring system	Office. The study	seasonality), day	course of the	likely have all		actual or	bias
15 16			produces hourly	classified mortality data	of week,	study.	outcome data.		potential	identified.
17			estimates of $PM_{2.5}$ total	into all causes of death	temperature and		However, any		competing	
18			mass, and $PM_{2.5}$ levels of EC. Daily data was	[International Classification of	relative humidity.		potential errors		financial interests.	
19 20			available and no missing	Diseases, 10th Revision			or missing data		interests.	
21			data was reported.	(ICD-10; codes			on air pollution			
22			dutu was reported.	A00–R99),			levels.	suggests study		
23 24				cardiovascular causes				was free of		
25				(codes I00–I99), and						
26 27				respiratory causes (codes			Ap	report.		
28				J00–J99)] (World Health						
29				Organization 2007).			9, 20			
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	Selective	Conflict of interest	Other
8			Probably High	Low	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	19	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	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.
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1 2 3 4							36/bm)open-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete 0 outcome data∝	Selective	Conflict of interest	Other
8			Probably High	Low	Probably Low	Low	Low A	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	20	Basagaña et al. 2015	Single central-site monitor in each city. For each city, PM constituents with >20% of the values below the detection limit or missing were excluded. Otherwise, non-detectable were replaced by half the limit of detection. Air pollution data was collected daily in Bologna (n=472), twice a week in Barcelona (n=736) and Madrid (n=104), and once a week in Huelva (n=406). There was no information about missing data.	Daily mortality counts for all non-external causes [International Classification of Diseases, 9th Revision (ICD9) codes 001–799; 10th revision (ICD10) codes A00–R99], cardiovascular (ICD9 codes 390–459, ICD-10 codes 100–I99) and respiratory (ICD9 codes 460–519, ICD10 codes J00–J99) were collected. Cardiovascular and respiratory hospitalizations were defined on the basis of the primary discharge diagnosis using the same ICD codes defined above.	Models adjusted for holidays, summer population decrease, influenza epidemics, seasonality, long-term trends and temperature.	Data consisted of all deaths over the course of the study in a defined geographical area.	Daily counts for death and emergency hospital admissions 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 report.	The authors have no conflicts of interest to disclose.	No other potential sources of bias identified.
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete of outcome data		Conflict of interest	Other
8			Probably High	Low	Probably Low	Low	Low X	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	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 _{2.5} 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 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 report.	The authors declare they have no actual or potential competing financial interests.	No other potential sources of bias identified.
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete og outcome data⇔		Conflict of interest	Other
8			Probably Low	Low	Low	Low	Low A	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	22	Lin et al. 2016a	The concentrations of different particle size fractions and PM _{2.5} 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-10:100-199) 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.	There was insufficient information about selective outcome to judge for low risk, but indirect evidence that	The authors declare they have no actual or potential competing financial interests.	No other potential sources of bias identified.
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Pag	e 81 of	f 136			BMJ Oper	1	do[uua/ag			
1 2 3 4							so/pmjopen-zuzi-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	Selective reporting	Conflict of interest	Other
8			Probably Low	Low	Probably Low	Low	Low 2	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	23	Cao et al. 2012	Daily concentrations of EC was obtained from a single monitoring site. The observations of EC was 1749 in 1827 days (missing data <25%).	The study obtained numbers of deaths in Xi'an for each day from the Shanxi Provincial Center for Disease Control and Prevention (SPCDCP). SPCDCP staff then classify the cause of death according to the International Classification of Diseases, 10th Revision [ICD-10; World Health Organization (WHO) 1992] as due to total nonaccidental causes (ICD-10 codes A00–R99), cardiovascular diseases (I00–I99), respiratory diseases(J00–J98), or injury (S00–T98).	Model adjusted for long-term and seasonal trends, day of week, temperature, humidity, and SO ₂ and NO ₂ concentrations.	Data consisted of all nonaccidental causes deaths during 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.	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.
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				36/bmjopen-2021-0495			
No. Study Exposure asses	ssment Outcome assessment	Confounding bias	Selection bias	Incomplete og outcome data∞	Selective	Conflict of interest	Other
Probably Lo	ow Low	Probably Low	Low	Low 2	Probably Low	Low	Low
24 Klemm et al. 2011 Daily 24-hr avera measurements are available for Atla during the study p The observations was 3317 days fro August 1998 to December 31, 200 Missing data <25 There was no info for monitor statio	age ECRecords of individual deaths were provided by the Georgia Department of Human Resources.of ECCause of death is	Adjusted for time (seasonality, long-term trends), temperature, and day of the week.	Study included all nonaccidental deaths during over the course of the study.	Daily counts for death were obtained, so likely have all outcome data.	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.

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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete ວ outcome dataຜ	Selective	Conflict of interest	Other
8			Probably Low	Low	Probably Low	Low	Low X	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 _{2.5} 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.	, 2024 by guest. P	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.
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					Incomplete			
No. Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	Selective reporting	Conflict of interest	Other
	Probably Low	Low	Probably Low	Low	Low 2	Probably Low	Low	Low
26 Winquis et al. 201	Daily EC and BC were	Individual-level datawere obtained from theMissouri HospitalAssociation for allemergency departmentvisits to 36 of 43acute-care non-federalhospitals with emergencydepartment visits in the16-county St Louismetropolitan statisticalarea during 1 June 2001through 30 April 2003.Cardiorespiratoryoutcomes of interest weredefined based on theprimary ICD-9(InternationalClassification ofDiseases, version 9)diagnosis code for thevisit.	Adjusted for time trends, day of week, holidays, season, temperature and dew point.	Study included emergency department visits in St Louis metropolitan statistical area during 1 June 2001 through 30 April 2003.	Daily counts for emergency department visit 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.

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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	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	27	Ostro et al. 2007	Each of the six counties had two monitors measuring PM _{2.5} components and mass. Fresno, Kern, Riverside, and Sacramento Counties reported data every third day, whereas San Diego and Santa Clara Counties reported data every sixth day. For the speciation analyses, the number of observation days available ranged from 243 (San Diego County) to 395 (Sacramento County) from 2000 to 2003. There was no specific information about missing data.	Daily mortality data were obtained from the California Department of Health Services, Center for Health Statistics. The study determined daily total mortality counts for those > 65 years of age and for deaths from respiratory disease [International Classification of Diseases, 10th Revision (ICD10; World Health Organization 1993) codes J00–J98] and cardiovascular disease (codes I00–I99).	Adjusted for time trend, day of week, seasonality, long-term trends, 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 selective report.	The authors declare they have no competing financial interests.	No other potential sources of bias identified.
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2 3 4							021-04951 			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete S S outcome data	Selective reporting	Conflict of interest	Other
8 9			Probably Low	Low	Probably Low	Low	Low X	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 13			observation of EC was	obtained from the	long-term trends),	department visits	department visits were	information	competing	sources of
14			356 in 365 days, missing	emergency department	temperature, dew	of the			financial	bias
15 16			data <25%.	visits participating in the	point, and day of	participating	obtained, so	selective	interests.	identified.
17				study. Several case	week.	hospitals in the Atlanta	likely have all			
18				groups are being defined using the primary ICD-9	04	Metropolitan	However, any			
19 20				(International	- F	Statistical Area,	potential errors			
21				Classification of		including 33	or missing data			
22 23				Diseases, 9th Revision)		hospitals	did not depend			
23				diagnostic code.		between January	on air pollution			
25						1 1993-August	<pre></pre>	-		
26 27						31 2000, 4	Apr	report.		
28						hospitals		-		
29 30						between January	, 20			
30 31						1 1993-February	24 D	-		
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	Selective reporting	Conflict of interest	Other
8			Low	Low	Probably Low	Low	Low X	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	29	Wang and Lin 2016	The hourly data were simply averaged to calculate the daily average data for PM ₁₀ , PM _{2.5} 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.	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 Revision (ICD-9 CM).	Adjusted for temperature, relative humidity, wind speed, barometric pressure, holidays, day of the week, pneumonia and influenza.	Study included elderly (≧65 years) mortality from 2004 to 2008 and all population EVR from 2004 to 2010 in Taipei, Taiwan.	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 depend on air pollution levels.	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.
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No. Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	Selective	Conflict of interest	Other
	Low	Low	Low	Low	Probably Low	Probably Low	Low	Low
30 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 of department visit were obtained. In the earliest years of the study, not all hospitals were participating. 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 report.	Authors declared no competing financial interests.	No other potential sources of bias identified.

Pag	e 89 of	e 89 of 136 BMJ Open								
1 2 3 4							30/0mJopen-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	incomplete of 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	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 of 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.
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2 3 4 5 6	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	Selective	Conflict of	Other
7 8	1.00		-				outcome data	reporting	interest	
o 9			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	32	Mar et al. 2000	Hourly PM _{2.5} chemical composition data from a single, central-site monitor. Daily data was available and no missing data was reported.	Mortality data for all of Maricopa County from 1995 to 1997 were obtained from the Arizona Center for Health Statistics in Phoenix. Death certificate data included residence zip code and the primary cause of death as identified by the International Classification of Diseases, Ninth Revision (ICD-9, World Health Organization, Geneva).	Adjusted for time trend, seasonality, day of week, temperature and relative humidity.	Data consisted of all cardiovascular deaths during over the course of the study.	, zoz4 by guesi.	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.
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1 2 3 4							30/0mJopen-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	Selective	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	33	Wang et al. 2019a	Hourly data of PM _{2.5} were collected at 10 Chinese air quality monitoring sites in Shanghai. Hourly mass concentrations of PM _{2.5} 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.	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.	No competing financial interests.	No other potential sources of bias identified.
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4 5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete of outcome data	Selective	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	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:I60–I66), and sub-categories, including ischemic stroke (ICD-10:I63–I66), and hemorrhagic stroke (ICD-10: 160–I62) 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.	information about selective outcome to judge for low risk, but indirect evidence that	Authors declared no conflict of interest.	No other potential sources of bias identified.
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1 2 3 4							36/bmjopen-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete \int_{Ω}^{10} outcome data ω	Selective reporting	Conflict of interest	Other
8 9			Probably High	Low	Probably Low	Low	Low ay	Probably Low	Low	Low
9 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 13			measuring components of	obtained from the	humidity and day	cardiovascular	obtained, so	information	competing	sources of
14			PM _{2.5} . Fresno, Kern,	California Department of	of the week.	mortality for all	likely have all		interests.	bias
15			Riverside and	Health Services, Center		California	outcome data.	1		identified.
16 17			Sacramento counties	for Health Statistics.		residents from 1	However, any			
18			reported 24-hour average	Daily counts of deaths		January 2000 to	potential errors			
19 20			EC in $PM_{2.5}$ every third	from cardiovascular		31 December	or missing data			
20 21			day; San Diego and Santa Clara counties reported	disease (International Classification of		2003.	did not depend on air pollution			
22			data every sixth day. The	Diseases, Tenth Revision			levels.	suggests study		
23 24			study included only	(ICD10) = I00 - I99) were				was free of		
25			species for which at least	calculated.			n on	selective		
26			50% of the observations	curculutou.			_			
27 28			were above the level of							
29			detection.				April 19, 2024 by gues			
30 31							024 t			
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1 2 3 4							Incomplete			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	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	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.	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.
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	ີດ Incomplete ິຊ outcome dataຜ ຊ	Selective reporting	Conflict of interest	Other
8 9			Probably Low	Low	Probably Low	Low	Low ay 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 _{2.5}	emergency room visits	for time, day of	all emergency	for emergency	insufficient	competing	potential
12 13			and the four $PM_{2.5}$	were obtained from the	week, temperature,	department visits	room visit	information	financial	sources of
14			constituents obtained	National Taiwan	seasonality and	during the study	were obtained,		interests.	bias
15 16			from a Supersite (single,	University Hospital. The	relative humidity.	period for	so likely have and all outcome			identified.
17			central site monitoring location). The	emergency room visit data were coded		ischemic and		outcome to		
18			observations of EC was	regarding the discharge	04	hemorrhagic	any potential			
19 20			1599 in 1705 days	diagnosis using the	er rel	SHOKE.	errors or	indirect		
21			(missing data <25%).	International			missing data	evidence that		
22 23				Classification of Disease,			did not depend			
23 24				9th revision (ICD-9).		10	on air pollution			
25							levels. 9			
26 27							Apr			
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29							, 20			
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1 2 3 4							-2021-0496			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete og outcome data∝ ≊	Selective reporting	Conflict of interest	Other
8			Low	Low	Probably High	Low	Low X	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	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	0.	from 1 July 2012	outcome data.	judge for low		
19			information about	general hospital in Užice.		to 30 June 2014	However, any			
20			missing data.	The inclusion criteria		in the Zlatibor	potential errors	indirect		
21 22				were adults aged 18 years		District, Western	or missing data			
23				and older with the		Serbia.	did not depend	suggests study		
24				diagnosis of allergic		· ()	on air pollution	was free of		
25 26				rhinitis (International			levels. 9	selective		
27				Classification of			Apri	report.		
28				Diseases, 10th revision,						
29 30				code J.30.4), allergic			April 19, 2024 by guess			
31				asthma (International			24 D	-		
32				Classification of			y gu			
33				Diseases, 10th revision,			lest.			
34 35				code J.45.0), or asthma						
36				with coexisting allergic			Protected			
37				rhinitis.						
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1 2 3 4							36/bmjopen-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	Selective reporting	Conflict of interest	Other
8			Probably Low	Low	Probably Low	Low	Low X	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	39	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.	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 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.
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	Selective reporting	Conflict of interest	Other
8			Probably Low	Probably 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	40	Sinclair et al. 2010	Daily 24-hr averages EC was from a single monitor site. The total observed rate of EC was 95.2%.	Daily outpatient visits were obtained from the electronic patient data warehouse of a not-for-profit, group-model managed care organization (MCO) in the metropolitan Atlanta area between August 1, 1998 and December 31, 2002. Visits that met acute visit definition and that had a visit diagnosis code of asthma, upper respiratory infection (URI), or lower respiratory infection (LRI) were included in the study.	Adjusted for season, day of week, federal holidays, study month, time, temperature and dew point.	Study included daily outpatient visits for acute respiratory diseases from the electronic patient data warehouse of a not-for-profit, group-model managed care organization (MCO) in the metropolitan Atlanta area between August 1, 1998 and December 31, 2002.	Daily counts for outpatient 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.
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	outcome data ع	Selective reporting	Conflict of interest	Other
8			High	Probably Low	Probably Low	Low	Low X	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	41	Krall et al. 2013	Monitors typically measure PM _{2.5} constituent concentrations every third or sixth day. Some communities with a single monitor. The observation of EC was 58-921 days,some communities had >25% missing data.	All-cause mortality data (excluding accidental deaths) were aggregated from death certificate data obtained from the National Center for Health Statistics for 2000 to 2005.	Adjusted for temperature, day of week, long-term and seasonal trends.	Study included all death (excluding accidental deaths) for 108 urban communities from 2000 to 2005.	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.	The authors declare they have no actual or potential competing financial interests.	No other potential sources of bias identified.
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5 No. Study 7	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete og outcome data∝	Selective	Conflict of interest	Other
8	Probably High	Low	Probably Low	Low	Low A	Probably Low	Low	Low
9 42 Cakmak et 10 42 Cakmak et 11 al. 2009 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	Daily PM _{2.5} aerosol samples approximately 1 of every 4 days from a single monitor site. Sampling occurred daily during the cold season (April through September) and alternate days during the warm season (October through March). Missing data <25% for that frequency.	Diseases were coded using the WHO International Classification of Disease, 9th Revision (ICD-9). The daily number of emergency department visits for all nonaccidental (ICD-9 < 800) and respiratory (ICD-9 460–519) causes in Santiago Centro, Cerrillos, and Pudahuel were obtained from the Departamento de Estad' isticas e InformaciónenSalud (DEIS) of the Ministry of Health from April 2001 through August 2006.	Adjusted for temperature and humidity, day of week, long-term and seasonal trends.	Study included all emergency department visits obtained from the Departamento de Es-tad' isticas e InformaciónenSa lud (DEIS) of the Ministry of Health from April 2001 through August 2006.	Daily counts for emergency department visit 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.

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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	Selective	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	43	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 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 report.	No competing financial interests.	No other potential sources of bias identified.
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1 2 3 4							36/bmjopen-2021-049516 on Incomplete			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on the second seco	Selective reporting	Conflict of interest	Other
8 9			Low	Low	Probably Low	Low	Low Y	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 13			monitors. Daily data was	based on codes from the	influenza episode,	hospital	admission were	information	have no	sources of
14			available and no missing	International	weather, day of	admissions over	obtained, so	about	actual or	bias
15 16			data was reported.	Classification of	week, and other	the course of the	likely have all	selective	potential	identified.
17				Diseases, revision 9 (ICD-9).	possible confounders (e.g.,	study.	However, any		competing financial	
18				(ICD-9).	federal holidays).		potential errors		interests.	
19 20					rederar nondays).		or missing datag		interests.	
21							did not depend			
22 23							on air pollution			
23						101	levels.			
25						ien	on	selective		
26 27							Apr	report.		
28										
29 30							202			
31							levels. on April 19, 2024 by guest			
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	Selective	Conflict of interest	Other
8			Probably High	Low	Probably Low	Low	Low A	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	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 _{2.5} 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, 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.
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4 5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete of the second secon	Selective	Conflict of interest	Other
8			Probably Low	Low	Probably Low	Low	Low 2	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	46	Gong et al. 2019	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 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) were obtained.	Adjusted for calendar effects, long-term trends, temperature, humidity, day of week, NO ₂ and SO ₂ .	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.	Daily counts for all deaths were obtained, bill 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	Authors declared no conflict of interest.	No other potential sources of bias identified.
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1 2 3 4							36/bmjopen-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete of the second seco		Conflict of interest	Other
8			Probably Low	Probably Low	Probably High	Low	Low X	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	47	Mostofsky et al. 2012	Ambient EC obtained from one monitor. BC concentrations were measured continuously. Daily data was available and no missing data was reported.	Patients potentially eligible for this study were identified by reviewing daily emergency department admission logs, stroke service admission logs, stroke service consult logs, and hospital electronic discharge records.	Model adjusted for seasonality, time-trends, temperature, dew point temperature, barometric pressure and chronic and slowly-varying potential confounders.	Population consisted of patients ≥21 years of age admitted to the hospital with neurologist-confi rmed ischemic stroke and residing in the Boston metropolitan region. Also patients had to reside within 40 km of the air pollution monitor.	N N	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.
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No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	16 Incomplete 0 outcome dataయ		Conflict of interest	Other
		Probably High	Low	Probably Low	Low	Low N	Probably Low	Low	Low
48	Krall et al.	PM _{2.5} constituents from	The study obtained	Adjusted for	Study included	Daily counts	There was	The authors	No other
	2017	one urban, ambient	electronic billing data for	holidays,	all emergency	for emergency	insufficient	declare they	potential
		monitor located in each	respiratory disease	long-term trends,	department visits	department <u>S</u>	information	have no	sources of
		city. Daily pollution data	emergency department	day of the week,	for respiratory	visits of	about	actual or	bias
		were available in Atlanta;	visits for all ages at acute	season,	disease at acute	respiratory	selective	potential	identified.
		however, data were only	care hospitals. Using	hospitalsreporting	care hospitals in	disease were	outcome to	competing	
		available approximately	diagnosis codes from the	data, temperature	the 20-county	obtained, so	judge for low	financial	
		every third day in the	International	and dew point.	Atlanta	likely have all	risk, but	interests.	
		remaining three cities.	Classification of		metropolitan	outcome data.	indirect		
		There was no information	Diseases, 9th Revision	1 0	area, the	However, any	evidence that		
		about missing data.	(ICD-9), the study		7-county	potential errors.	suggests study		
			considered subcategories		Birmingham	or missing data	was free of		
			of respiratory diseases		metropolitan	did not depend g	selective		
			including pneumonia		area, the 8	on air pollution	report.		
			(ICD-9 codes 480–486),		Missouri and 8	levels.			
			chronic obstructive		Illinois counties	9, 20			
			pulmonary disease		in the St. Louis	124 t			
			(491,492,496), upper		metropolitan	2024 by guest.			
			respiratory infection		area, and the	uest			
			(URI) (460–465, 466.0,		12-county Dallas				
			477), and asthma and/or		metropolitan	Protected by copyright			
			wheeze (493, 786.07).		area.				

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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete of outcome data∝	Selective reporting	Conflict of interest	Other
8			Probably Low	Low	Probably Low	Low	Low X	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	49	O'Lenick et al. 2017	The 24-hour average concentration of EC was evaluated. Pollutant concentration estimates were obtained by fusing observational data from available network monitors with pollutant concentration simulations from the Community Multi-Scale Air Quality emissions-based chemical transport model at 12×12km grids over Atlanta. 24-hour average EC were evaluated. Daily data was available and no missing data was reported.	Patient-level emergency department visit data from 1 January 2002 to 31 December 2008 were acquired from hospitals located within the 20-county metropolitan area of Atlanta; Relevant data elements included admission date, International Classification of Diseases Ninth Revision (ICD-9) diagnosis codes, age and ZIP code of patient residence.	Adjusted for season, periods of hospital participation and holidays, temperature and mean dew point, interaction terms between season and maximum temperature and day of year.	Study included all emergency department visit data acquired directly from hospitals (2002–2004 period) and the Georgia Hospital Association (2005–2008 period) located within the 20-county metropolitan area of Atlanta.	Daily counts for emergency department visit 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.	Competing interests: None declared.	No other potential sources of bias identified.
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4 5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	Selective	Conflict of interest	Other
8			Probably Low	Low	Probably Low	Low	Low A	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	50	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.	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.
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	Selective reporting	Conflict of interest	Other
8			Low	Low	Probably Low	Low	Low 2	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	51	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, 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.
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1 2 3 4							36/bm)open-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete og outcome data∝	Selective	Conflict of interest	Other
8			Low	Low	Probably Low	Low	Low X	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	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 of asthma or wheeze disease were obtained, so likely have all outcome data. However, any potential errors or missing data did not depend of 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.
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete of the second secon	Selective reporting	Conflict of interest	Other
8			Probably High	Low	Probably Low	Low	Low X	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	53	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 _{2.5} 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.
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	Selective reporting	Conflict of interest	Other
8			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		The authors	No other
11 12		al. 2015b	track the mass and	codes based on the	status, smoking	a cohort of	information on	2	declare they	potential
13			concentrations of the PM constituents in particle	International Classification of	status, pack-years of smoking,	female teachers ≥30 years old.	the rate of lost	information about	have no actual or	sources of bias
14 15			diameters ranging from	Diseases, 10th Revision	secondhand smoke	≥50 years old.		selective	potential	identified.
16			0.01 to $10\mu m$ through	(ICD-10) for the	exposure, body			outcome to	competing	identified.
17			calculations that describe	following outcomes:	mass index,			judge for low	financial	
18 19			emissions, transport,	all-cause deaths	lifetime physical			risk, but	interests.	
20			diffusion, deposition,	excluding those with an	activity, alcohol			indirect		
21			coagulation, gas- and	external cause	consumption,			evidence that		
22 23			particle-phase chemistry,	(A00–R99),	average daily			suggests study		
24			and gas-to-particle	cardiovascular deaths	dietary intake of	en.		was free of		
25 26			conversion. The	(I00–I99), Ischemic heart	fat, calories,		g	selective		
20			University of California	disease deaths (I20–I25),	menopausal status,			report.		
28			Davis/California Institute	and pulmonary deaths	family history of		, i			
29 30			of Technology model was	(C34, J00–J98).	myocardial					
31			used to estimate		infarction, stroke,		Aprill 19, 2024 by gues	<u> </u>		
32			ground-level		use of blood		gue			
33 34			concentrations of 50 PM constituents over the		pressure medication,					
35			major population regions		aspirin; living					
36 37			in California.		conditions					
38					conditions					<u> </u>
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	Selective	Conflict of interest	Other
8 9 10 11 12 13 14 15 16 17				Forpe	(income, income inequality, education, population size, racial composition, unemployment).		ay 2022. Downloaded from http://www.loaded.			
18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37	55	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 use regression	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 follow-up period.	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.	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.
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No	. Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	Selective	Conflict of interest	Other
		models.	For						
56	Hvidtfeldt et al. 2019	Probably Low The PM, NO ₂ , BC, and O ₃ 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 ₂ , BC, and O ₃ .	Low 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.	Probably Low Age, sex, educational attainment, occupational status, marital status, marital status, smoking (status, intensity, and duration), environmental tobacco smoke (ETS), alcohol consumption, body mass index, waist circumference, fruit consumption,	Low Data obtained for a cohort of men and women aged 50–64 years residing in the areas of Copenhagen and Aarhus.	Probably Low There was no information on the rate of lost follow up.	There was insufficient information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of selective	Low The authors declare they have no competing financial interests.	Low No other potential sources of bias identified.
2 3 4 5 6 7 8 9 0 1 2 3 4		sources of precursors to	codes I00–I99) and respiratory (ICD10 codes J00–J99 and C34) subgroups of mortality.	consumption, body mass index, waist circumference,	.com/site/about/gui	. Protected by copyright.	was free of selective report.		

Page	1	15	of	136
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1 2 3 4	Image: ge 115 of 136 BMJ Open No. Study Exposure assessment Outcome assessment Confounding bias Selection bias Incomplete outcome data									
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	ت Incomplete 0 outcome dataد ≤	Selective reporting	Conflict of interest	Other
8 9 10 11 12 13 14 15				For	consumption, physical activity; neighborhood level socioeconomic status (SES).		outcome data Ma V ZUZZ: Down Doaged Too Probably Highm			
16 17			Probably Low	Probably Low	Probably High	Low	Probably High	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 39 40 41 42 43							24 by guest. Protected by copyright.			
43 44				For peer review only	y - http://bmjopen.bmj	.com/site/about/guid	delines.xhtml			

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No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	Selective	Conflict of interest	Other
57 57 57 57 57 57 57 57 57 57 57 57 57 5	Thurston et al. 2016	The mean concentrations of $PM_{2.5}$ mass and trace constituents were obtained from U.S. Environmental Protection Agency Air Quality System. These $PM_{2.5}$ constituent data were analyzed to derive estimates of source apportioned $PM_{2.5}$ mass exposure concentrations using the absolute principal component analysis (APCA) $PM_{2.5}$ 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 ² , 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.	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.
5 5 7 3		Probably Low	Low	covariates. Probably Low	Low	Probably Lows		Low	Low
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1 2 3 4							2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	outcome data ع مutcome data	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 36	58	Yang et al. 2018	Land use regression models were derived from street level measurements collected during two sampling campaigns conducted in 2014 and 2015.	Deaths were coded according to the International classification of Diseases, 10th Revision (ICD-10; WHO 2010) including natural cause mortality (A00–R99), overall cardiovascular disease (I00–I99) and overall respiratory disease (J00–J47 and J80–J99). Subcategories included Ischemic heart disease (IHD) (I20–I25), cerebrovascular disease (I60–I69), Pneumonia (J12–J18) and chronic obstructive pulmonary disease (COPD) (J40–I44 and I47).	Age at entry, gender, individual smoking status, body mass index (BMI), physical activity, education level and monthly expenses; percentage of participants who were equal to or older than 65 years old, percentage of participants whose educational level was higher than secondary school, average income per month and percentage of smokers.	Data obtained for a cohort of people who were older than or equal to 65 years old.	There was no information on April 19, 2024 by guest. From http://omjopen.bmj.com/ on April 19, 2024 by guest. From	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.
37			Probably Low	Low	Probably High	Low	Probably Low	Probably Low	Low	Low
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1 2 3 4							30/bmJopen-2021-0493			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete		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	59	Gan et al. 2011	Land use regression to estimate air pollution concentrations and exposure assigned to residential centroid.	A coronary heart disease hospitalization case is a record of hospitalization with the following International Statistical Classification of Diseases, 9th Revision codes, ICD-9, 410–414 and 429.2or 10th Revision (ICD-10), I20–I25, as the principal diagnosis (the most responsible diagnosis) for a hospital admission in the hospitalization database. A coronary heart disease death is a death record with coronary heart disease as the cause of death in the provincial death registration database.	Model adjusted for age, sex, preexisting comorbidity, and neighborhood socioeconomic status. No individual data on behavioral risk factors.	Study provided total number of subjects along with those lost during the follow-up period.	During the 4-year follow-up period, 17,542 (3.9%) moved out of the province and 16,367 (3.6%) died from other diseases, leaving 418,826 (9 _{2.5} %) subjects at the end of follow-up.	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.
36 37			Probably High	Low	Probably Low	Low	Probably Low	Probably Low	Low	Low
38 39 40 41 42							соругари.			

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1 2 3 4							317-2021-0498			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete ్ల outcome dataచ	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	60	De Kluizenaa r et al. 2013	Used black smoke (BS) as an indicator of EC concentrations. Derived background EC concentrations from BS measured at two regional monitoring sites. Local traffic-related EC emission contributions were estimated based on fuel-specific EC content of exhaust PM_{10} emission. Used the traffic-related EC emissions as input to calculate local EC concentrations, assuming absence of other local EC sources. Also assumed that dispersion dynamics of EC are identical to those of PM_{10} .	The study obtained information on the incidence of hospital-based Ischemic heart disease (International Classification of Diseases [ICD9] 410-414) and cerebrovascular disease (ICD9 430-438) in the study population.	Individual-level covariates: age, gender, marital status, education, smoking, alcohol use, physical activity, body mass index, living conditions (employment status, financial problems).	Data obtained for a cohort of 27,070 non-institutionali zed subjects.	There was no information on April 19, 2024 by guest. From http://omjopen.omj.com/ on April 19, 2024 by guest. From	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.
36 37			Probably Low	Probably Low	Probably Low	Low		Probably Low	Low	Low
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1 2 3 4										
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data	5	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	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.	There was no information on the rate of lost follow up.	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.
37 38			High	Low	Probably Low	Low	Low S	2	Low	Low
39 40 41 42			·	·		·				
43 44				For peer review only	/ - http://bmjopen.bmj	.com/site/about/guid	delines.xhtml			

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3 4 5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	049516 Incomplete on 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 26	62	Rahmatini a et al. 2021	BC were collected from 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 the Sharif data were used.	Daily non-accidental 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).	Models adjusted for time, temperature, relative humidity, atmospheric pressure, PM2.5 data, Day of week (DOW) and public holidays.	Study included all daily non-accidental deaths from Ministry of Health and Medical Education database from March 2017 to August 2017.	Daily counts for death were 2022. Downloaded 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 report.	The authors of this article declare that they have no conflict of interests.	No other potential sources of bias identified.
36 37			Probably Low	Probably Low	Probably Low	Low	Low ed	Probably Low	Low	Low
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Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	outcome data⇔ ≤		interest	Other
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 \leq 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.	who completed from http://bmjopen.bmj.com/ on April 19, 2024 by guest.	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.
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	Liu et al.	Liu et al. 2021bAnnual 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.	Liu et al. 2021bAnnual 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.Image: transition of the disease classification codebook for Chinese Family Panel Studies.	Liu et al. 2021bAnnual 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 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 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).Image: Descent content of the strate of the upper and lower quartiles, urbanicity (urban/rural, defined by CFPS participants' home addresses).Image: Descent content of the upper and lower quartiles, urbanicity (urban/rural, defined by CFPS participants' home addresses).Image: Descent content of the upper and lower quartiles, urbanicity (urban/rural, defined by CFPS participants' home addresses).	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Survey of social-demograp Image: Probably Low Low Probably Low Low Probably Low Low Probably Low Probably Low Probably Low	StudyExposure assessmentOutcome assessmentContounding basSelection basoutcome datareportingLiu et al. 2021bAnnual county-level exposures of PM2.5 and participant were assessed eardiovascular satellite-derived estimates at a monthy time-scale and 1 km-resolution.The three cardiovascular cardiovascular disease, including but not limited to hypertension and stroke; 2) hypertension; for Chinese Family PanelModel adjusted for age, gender, caucation level (illiteracy, primary to middle school, and high school or at a monthy time-scale and 1 km-resolution.All of apertension and stroke; 2) hypertension; above), household income (RMB, University strata of ≤ 15,000, 15, Social Science Survey (ISSS) in autionan onging autionan onging autionan autome advey of selectiveThere was insufficient above), household above), household according to the Disease carcording to the Disease study was necording to the Disease study was necording to the Disease succording to the disease, urbanicity (urban/rra1, defined by CPPS participants' home addresse),In the cohort succording to the succording to the succording to the participants' home addresse),The of succording to the <td>StudyExposure assessmentOutcome assessmentContouring baseSelection baseoutcome datareportinginterestLiu et al. 2021bAnnual county-level exposures of PM2.5 and its constituents for each by aggregating satellite-derived estimates at a monthly time-scale and 1 km-resolution.The three cardiovascular events as health outcomes: 1) total to hypertension; and according to the Disease Classification Codebook for Chinese Family Panel Studies.Model adjusted for age, gender, data file school, and high school or above), household to mydel school, and 1 km-resolution.All of age, gender, data monthly time-scale at a monthly time-scale all km-resolution.There was according to the Disease Classification Codebook for Chinese Family Panel Studies.Model adjusted for age, gender, data school or above), household to mydel school or albove), household to mydel school or (Lassification Codebook urbanicity urbanicityAll of drawn from the data monthly time-scale albove), household by PekingThe cohort information three waves of gender to mydel school or indirectThe authors declare that dolow-up.10strate of by 000 - 40,000, and according to the upper and lower quartiles, urbanicity (urban/rural, defined by CFPS participants' home adfresses).Not one social Science social-demograp hy in China.The authors three waves of suggests study was the work report.Not how on the authors three waves of social-demograp hy in China.The cohort three waves of social-demograp hy in China.The cohort three waves of social</br></br></br></br></br></br></br></br></br></br></br></br></br></br></br></br></td>	StudyExposure assessmentOutcome assessmentContouring baseSelection baseoutcome datareportinginterestLiu et al. 2021bAnnual county-level

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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete \int_{Ω}^{Ω} outcome data \Im	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 4 35 36 37	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.	May 2022. Downloaded from http://bmjopen.bmj.com/ on April 19, 2024 by guest. Protected	information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of selective report.	The authors declared that there is no conflict of interest.	No other potential sources of bias identified.
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1 2 3 4							-2021-0495			
4 5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	outcome data	Selective	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	65	Rodins et al. 2020	The study used the validated, time-dependent, three-dimensional European Air Pollution Dispersion chemistry transport model (EURAD) to estimate the exposure to EC.	Cardiovascular outcomes in the HNR Study were determined by an independent endpoint committee based on self-reports, physician and next-of-kin interviews, and medical records.	Model adjusted for age, sex, individual and neighborhood SES, BMI, nighttime traffic noise exposure and lifestyle factors: smoking, alcohol consumption, physical activity and nutritional pattern.	The study used baseline (2000–2003) and 14 years follow-up data from the German HNR Study, an ongoing population-based prospective cohort study.	There was no 22. Downloaded from http://bmjopen.bmj.com/ on April 19, 2024 by guest. Protected by copyright.	There was insufficient information about selective outcome to judge for low	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.
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete og outcome data∝	Selective reporting	Conflict of interest	Other
8			Probably Low	Low	Probably High	Low	Low X	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	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 Development (ED) visits were obtained, for all outcome data. However, by 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.
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1 2 3 4							-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	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 N	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 13			AB, Sweden) by the	CIMT of the right carotid	pollutant,	subcohort of the	data on plaque $\frac{5}{2}$	information	they have	sources of
14			Environmental	artery, which were	education level,	MDCS cohort,	data on plaque	about	no known	bias
15			Department of Malm [°] o.	assessed by ultrasound	smoke score,	6031 participants	CIMT,	selective	competing	identified.
16 17			The program uses a	examination B-mode	apoB/apoA1 ratio,	who had a	respectively.	outcome to	financial	
17			Gaussian dispersion	ultrasonography,	use of lipid	residential	Hence, the number of participants included in 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 22			emission database for the		cardiovascular	modelling area.		evidence that	s that could	
23			county of Scania in		heredity, diabetes	Of these, 224	plaque analyse	suggests	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 g	free of	influence	
27					activity, alcohol	and 20 on CIMT,	analyses 6011.₽	selective	the work	
28					consumption,	respectively. The			reported in	
29 30					median income	number of	20		this paper.	
31					level in residential	participants	24 b			
32					area, systolic blood	included in the	y gr			
33					pressure and being	plaque analyses	l			
34 35					born outside of	were 5807 and in	Pr			
36					Sweden.	the CIMT	otect			
37						analyses 6011.	ted t			
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1 2 3 4							36/bmJopen-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete og outcome data⇔	Selective	Conflict of interest	Other
8 9			Probably High	Probably Low	Probably High	Low	Low X	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 13			monitoring site operated	Laboratory (Cath Lab) at	long-term trends,	treated at the	were obtained,	information	they have	sources of
13			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 17			Environmental	within 15 miles of the		Laboratory (Cath	data. However,	outcome to	interests.	
17			Conservation	pollution monitoring		Lab) at URMC	any potential			
19			continuously throughout	station in Rochester were		in Rochester, NY	errors or			
20			the study period	included. American		for STEMI	missing data			
21 22			(2005–2016). There was	College of Cardiology		throughout the	did not depend			
23			no information about	(ACC)/American Heart		study period	on air pollution			
24			missing data.	Association (AHA)		(2005–2016).	levels.	study was		
25 26				guidelines were used at			on			
27				the time of Cath Lab		· · · · (April April	selective		
28				admission to diagnose			19,	report.		
29 30				STEMI.			202			
31							2024 by gues			
32							, gu			
33 34							est.			
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No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete 9 outcome data⇔	Selective	Conflict of interest	Other
		Probably Low	Low	Probably Low	Low	Probably Low	Probably Low	Low	Low
69	Ljungman	Based on detailed	The International	Model adjusted for	The study	The study used		The authors	No other
	et al. 2019	emission databases,	Classification of	sex, calendar year,	included	high-quality	insufficient	declare they	potential
		monitoring data, and	Diseases, Ninth Revision	subcohort,	individuals in	and n	information	have no	sources of
		high-resolution	(ICD-9) codes 410-414	smoking status,	two cohorts from		about	actual or	bias
		dispersion models, the	and ICD-10 I20-25 codes	alcohol	Gothenburg, four	national patient	selective	potential	identified.
		study calculated source	were used to define IHD	consumption in	pooled cohorts	and death \exists	outcome to	competing	
		contributions to black	and ICD-9 codes	Stockholm and	from Stockholm,	registries,	judge for low	financial	
		carbon (BC) from road	431–436 and ICD-10	Umeå, physical	and one cohort	minimizing	risk, but	interests.	
		wear, traffic exhaust,	codes I61–I65 were used	activity, marital	from Umeå. In	loss to	indirect		
		residential heating, and	to define stroke.	status,	total, 114,758	follow-up for	evidence that		
		other sources in		socioeconomic	individuals were	our outcomes of interest.	suggests		
		Gothenburg, Stockholm,		index by	included from all	of interest.	study was		
		and Umeå.		occupation,	study areas.	Missing 9	free of		
				education level,		information for	selective		
				occupation status,		variables \leq	report.		
				and mean		5% not			
				neighborhood		5% not specified. 2024 by guest			
				individual income		ן ע פר			
				in persons of		lest.			
				working age by		Pro			
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				Market Statistics.					

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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	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	about	no known	bias
15			baseline residential	Diseases, 9th Revision	intensity,	project with	air pollution	selective	competing	identified.
16 17			addresses, using	(ICD-9) codes 490–492,	body-mass index,	available	exposure data,	outcome to	financial	
17			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 21			use regression (LUR)		status, educational	discharge	participants	indirect	relationship	
21			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 \exists	suggests	have	
24 25			monitoring data from the		year income.	16.6 years.	7,586 <u>9</u>	study was	appeared to	
25 26			European Environment				participants 9	free of	influence	
27			Agency (EEA) AirBase				with missing $\frac{A}{P_{1}}$	selective	the work	
28			for PM2.5, NO2, and O3,				information on	report.	reported in	
29 30			and ESCAPE monitoring				confounders.		this paper.	
31			data for BC as the				confounders. 2024 by			
32			dependent variable. BC				y guest			
33 34			was measured by the				est.			
35			reflectance of PM2.5				Prot			
36			filters and expressed in				Protected			
37 38			absorbance units.							
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40							ругі			
41 42							ght.			

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1 2 3 4 5 6 7Table S5 Ass	sessi	nent of certaint	ty of	evidence for the o	outc	omes.							36/bmjopen-2021-049516 on 3 N					
8					Reaso	ons for downgrading						<u>6</u>	ע Rea	asons for upgrading				Final
9 _{Evidence} 10 11	A1	Rationale	A2	Rationale	A3	Rationale	A4	Rationale	A5	Rationale	B1	Rationale	2022#2	Rationale	B3	Rationale	Overall	certainty assessment
12 1 ⁴ Stute effects of BC 1 ⁴ AEC on CVD in 1 ⁵ M _{2.5} -unadjusted 16 1 ¹⁹ O ^{del}	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	wnloadee from	Confounders would shift the RR in both directions	0	Evidence of increase in risk with increasing exposure	-1	Low
18 1.2 20 BC or EC on CVD 21 20PM ₂₅ -adjusted 2.3 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	http://bmjopen.bmj.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 21 c or EC on CVD 28 10 PM _{2.5} -unadjusted 29 30 del	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	n/ on April≏19, 2024 ∣	Confounders would shift the RR in both directions	0	No evidence of a clear increasing risk with exposure	0	Moderate
						[•] diseases; RES: respirator = large RR; B2 = all conf							Al by guest. Protected by copyright.	= limitations in studies	s (risk	of bias); A2 =		

5					BMJ Ope	en			36/bmjopen-2021-049516		
Table S6 The p-value	e calculatio	on process for eac	h study usin	g RR, CI lov	v and CI high	h. InRR	InCI low	lnCI high	21-049516 on 3 M	Z	p-values
	1	Ostro,2015a	0.994000	0.953000	1.038000	0.006018	0.048140	0.037296	20.021795	0.276122	0.782454
	2	Ostro,2015a	1.005000	0.979000	1.031000	0.004988	0.021224	0.030529	N 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	wnlo 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	ā f 0.088539	0.223661	0.823021
	7	Sarnat,2015	1.038000	1.005000	1.073000	0.037296	0.004988	0.070458	0.016702	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
~	11	Winquist,2015	1.048000	1.012000	1.085000	0.046884	0.011929	0.081580	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	prii 0.005017	3.360055	0.000779
	16	Kim,2015	1.031000	0.935000	1.133000	0.030529	0.067209	0.124869	<u>,</u> 0 .048999	0.623052	0.533250
	17	Huang,2012	1.005000	0.998000	1.010000	0.004988	0.002002	0.009950	N0.003049	1.635761	0.101890
	18	Son,2012	1.001000	0.981000	1.021000	0.001000	0.019183	0.020783	4 0.010195	0.098036	0.921904
	19	Heo,2014	1.006000	0.994000	1.017000	0.005982	0.006018	0.016857	gue 0.005836	1.025116	0.305308
	20	Basagana,2015	0.979000	0.944000	1.016000	0.021224	0.057629	0.015873	est 0.018751	1.131889	0.257681
	21	Basagana,2015	1.026000	1.006000	1.047000	0.025668	0.005982	0.045929	Po 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
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		BMJ Open 6000000000000000000000000000000000000										Pag
	1	Atkinson,2016	1.013000	0.993000	1.033000	0.012916	0.007025	0.032467	-0495 16 0.010074	1.282079	0.199815	
	2	Geng,2013	1.002000	0.983000	1.021000	0.001998	0.017146	0.020783	ο ω ^{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	N 0.013585	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	No.017529	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	
Respiratory Diseases	9	Heo,2014	0.988000	0.962000	1.015000	0.012073	0.038741	0.014889	ਰੋ ^{0.013681}	0.882435	0.377541	
Respiratory Diseases	10	Basagana,2015	0.986000	0.949000	1.026000	0.014099	0.052346	0.025668	B 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	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	2 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>9</u> .0.003328	0.902791	0.366637	
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group and Study ID	Relative Risk (95% Cl)
Asia	
Geng,2013	1.012 (1.002, 1.021)
Wang 2019a	1.011 (0.999, 1.023)
Gong 2019	1.002 (1.001, 1.003)
Huang.2012	1.005 (0.998, 1.010)
Lin.2016a	1.002 (0.999, 1.005)
Son.2012	1.001 (0.981, 1.021)
Heo,2014	1.006 (0.994, 1.017)
Subgroup, DL (I ² = 21.5%, p = 0.266)	1.003 (1.001, 1.005)
Europe	
Basagana,2015	0.979 (0.944, 1.016)
Ostro,2015a	0.994 (0.953, 1.038)
Ostro,2015a	1.005 (0.979, 1.031)
Atkinson,2016	0.987 (0.973, 1.001)
Subgroup, DL (I ² = 0.0%, p = 0.602)	0.990 (0.979, 1.001)
America	
to,2011 +	1.003 (0.982, 1.024)
Maynard,2007	 1.076 (0.980, 1.179)
Ostro,2007	1.026 (1.004, 1.049)
Kim,2015	1.031 (0.935, 1.133)
Subgroup, DL ($I^2 = 20.8\%$, p = 0.285)	1.017 (0.998, 1.037)
Heterogeneity between groups: p = 0.030	
.8 1	1.25

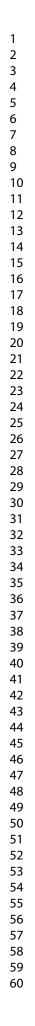
Figure S1 Impact of short-term exposure to BC or EC on cardiovascular mortality stratified by

geographical locations.

group and Study ID	Relative Risk (95% Cl)
Europe	
Basagana,2015 +	1.026 (1.006, 1.047)
Subgroup, DL ($I^2 = 0.0\%$, p = .)	1.026 (1.006, 1.047)
America	
Bell,2014	1.036 (1.023, 1.050)
Sarnat,2015	1.038 (1.005, 1.073)
Ito,2011	1.019 (1.007, 1.034)
Winquist,2015	1.048 (1.012, 1.085)
Tolbert,2007 +	1.013 (1.004, 1.022)
Lall,2011	1.022 (0.999, 1.046)
Metzger,2004	1.017 (1.007, 1.027)
Peng,2009	1.018 (1.011, 1.025)
Liu,2016a	0.960 (0.857, 1.076)
Liu,2016b	1.020 (0.858, 1.214)
Kim,2012	1.056 (1.018, 1.094)
Subgroup, DL ($I^2 = 39.7\%$, p = 0.084)	1.022 (1.016, 1.029)
Heterogeneity between groups: p = 0.720	
.8 1	1.25

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

geographical locations.



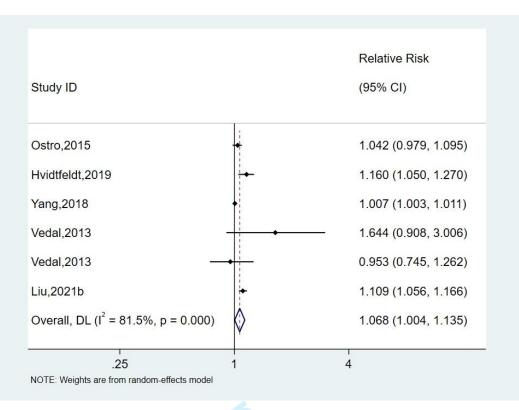


Figure S3 Impact of long-term exposure to BC or EC on cardiovascular diseases.

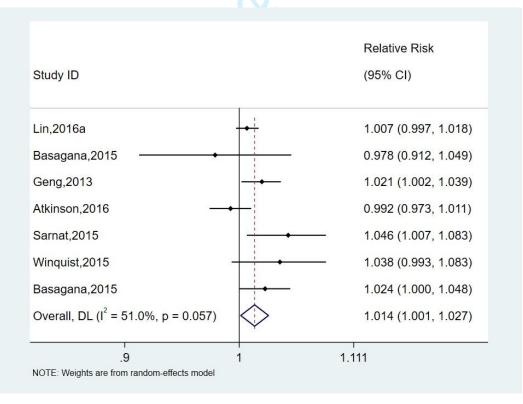


Figure S4 Impact of short-term exposure to BC or EC on cardiovascular diseases in the

 $PM_{2.5}\mbox{-}adjusted\ model.$



PRISMA 2020 Checklist

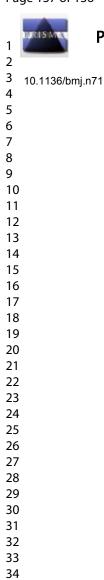
Page 135 of 136		BMJ Open	-1136/b	
PRIS	5MA 2	020 Checklist	bmiopen-2	
Section and Topic	ltem #	Checklist item	021-049	Location where item is reported
TITLE			0 0	
Title	1	Identify the report as a systematic review.	on	#1
ABSTRACT	1		\leq	
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	a <	#3-4
INTRODUCTION	1		2022	
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.	0 X	#8
	1			
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 date when each source was last searched or consulted.	Hentify studies. Specify the	#8-9
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	http	#8-9
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many rev and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in		#10
2 Data collection 3 process 4	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of a process.		#10-11
5 Data items 6	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which result		#10-11
7 8	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, fundir assumptions made about any missing or unclear information.	o g sources). Describe any	#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 ma study and whether they worked independently, and if applicable, details of automation tools used in the process.	ع. ny reviewers assessed each ن	#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	No of results.	#11
2 Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study inter comparing against the planned groups for each synthesis (item #5)).	₽ ⊈ention characteristics and ♀	#11
5	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summ conversions.	ary statistics, or data	#11, 14-15
5 7	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	rote	#11
1 8 9	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was perf model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	ormed, describe the	#11-12
1	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysi	č	#11-12
1	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	o, , , , , , , , , , , , , , , , , , ,	#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 used to assess certainty (or confidence) in the body of syldboce for all butsomern		#11
б		Conso and morriage generalized entrempt (antality entrempted of the entrempted interaction devices and an encoding and the en		



PRISMA 2020 Checklist

		BMJ Open	Page 136 of
PRIS	MA 2	020 Checklist	
Section and Topic	ltem #	Checklist item	Location where iten is reported
assessment		51 0	
RESULTS		S S	
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 execuded.	#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 effed 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 optice 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			
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	1		
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
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	#8
0	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 review.	#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

Page 137 of 136



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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

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Manuscript ID	bmjopen-2021-049516.R3
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Date Submitted by the Author:	18-Mar-2022
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Primary Subject Heading :	Public health
Secondary Subject Heading:	Cardiovascular medicine, Respiratory medicine
Keywords:	PUBLIC HEALTH, RESPIRATORY MEDICINE (see Thoracic Medicine), CARDIOLOGY





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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

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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 19th, 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 μ g/m³ in the elderly; (ii) Long-term exposure to BC/EC was associated with

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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

 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.¹ Elemental carbon (EC), another carbonaceous material with a graphitic structure, is commonly measured by thermal or thermo-optical method.^{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 PM_{2.5}, are well documented. In 2017, a total of 2.94 million deaths resulted from ambient PM worldwide.³⁻⁵ PM_{2.5} 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.^{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.^{8, 9} 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.⁴ 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.¹³

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.¹⁴ 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).^{15, 16} 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.^{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

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with Yang et al. 2019¹⁹, 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

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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.²⁰ In addition, the estimate was converted to a

standardized increment (1 μ 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.^{21, 22} 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.²³ In addition, if the same cohort data were analyzed in different studies and the latest study was included.²⁴⁻²⁶

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.²⁹ 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 $PM_{2.5}$ is a potential confounder in assessing the health effects of $PM_{2.5}$ constituents.⁷ For overall and outcome analysis, PM_{2.5}-adjusted estimates and PM_{2.5}-unadjusted estimates in the models were combined, respectively where more three estimates were available. Regarding than the subgroup analysis, PM_{2.5}-unadjusted estimates were analyzed, while PM_{2.5}-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,

Page 15 of 133

BMJ Open

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^{covariate}. Space3 is Space1 times Space2. Space3 is the total analysis search space. Search spaces were computed by the method introduced in Young et al, 2019.³⁰

The p-value plot was used to inspect the distribution condition of the p-values.³¹ 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.³¹ 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.^{32, 33} Of these, 70 fulfilled the inclusion criteria (Figure 1).^{7, 21-26, 34-96} 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 μ g/m³, 95% CI: 1.002–1.011) (adjusted by

Page 17 of 133

BMJ Open

trim and fill method) in overall analyses (Table 1 and Figure 2). Cardiovascular diseases (RR=1.016 per 1 μ 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 μ g/m³, 95% CI: 1.006–1.016), and then diminished on lag 1 (RR=1.005 per 1 μ g/m³, 95% CI: 1.002–1.008) and lag 2 (RR=1.002 per 1 μ 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/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.²³ In addition, just one study in Asia performed the short-term effects of BC/EC on stroke morbidity (Figure S2).⁶⁶

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).

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Fable 1 Short-term impacts of BC/EC on cardiovase	cular and re		eases in different mod	els		-049516 on 3		2.5-adjusted model		
Subgroup Analysis	No. of Studies	No. of Estimates	Relative Risk (95%CI)	I ²	Egger regression test (p value)	No. of A Studies	No. of	Relative Risk (95%CI)	I ²	
Cardiovascular Diseases						22. [
Age						Dowi				
All population	20	22	1.008 (1.004, 1.012)	64.40%	0.007	6 f	7	1.014 (1.001, 1.027)	51.00%	
Relative risk adjusted for publication bias with trim and ill method	24	26	1.007 (1.002, 1.011)	—	_	Downloaded from http://bmjopen.bmj.com/ on 6 4 4 4	_	_	_	
ensitive analysis on study of partial temporal overlap rom the same geographical location	16	16	1.006 (1.002, 1.010)	60.00%	0.020	— http	_	_	_	
:65 years	5	6	1.016 (1.004, 1.028)	87.40%	—	//bn	—	—	—	
Dutcome						njope				
Aorbidity	12	12	1.022 (1.016, 1.029)	37.20%	0.163	4 br	5	1.018 (1.006, 1.031)	39.50%	
Aortality	14	15	1.003 (1.001, 1.006)	29.70%	0.266	4 <u>j</u>	4	1.006 (0.993, 1.019)	42.90%	
Respiratory Diseases) mc				
Age										
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	19, 2024	_	_	_	
65	3	4	1.038 (1.006, 1.071)	82.90%	—	— by	—	—	_	
Dutcome						guest.				
Aorbidity	10	10	1.012 (0.993, 1.031)	91.80%	0.671	3	5	0.996 (0.987, 1.004)	0	
Aortality	10	11	1.013 (0.997, 1.030)	66.40%	0.328	Protected by copyright.	3	1.017 (0.985, 1.050)	48.30%	

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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*10⁻⁴⁵ 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.

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

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.^{25, 60, 68, 75} 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).²⁴

3.4 Results from the PM_{2.5}-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 μ 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_{2.5}-unadjusted model. In addition, the impact of BC/EC on cardiovascular morbidity in the PM_{2.5}-adjusted model (RR=1.018 per 1 μ g/m³, 95% CI: 1.006-1.031) was consistent with the results in the PM_{2.5}-unadjusted model (RR=1.022 per 1 μ g/m³, 95% CI: 1.016-1.029). However, an increased risk was found between BC/EC and cardiovascular mortality in the PM_{2.5}-unadjusted model (RR=1.003 per 1 μ g/m³, 95% CI: 1.001-1.006), while no association was observed in the PM_{2.5}-adjusted model (RR=1.006 per 1 μ 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 μ g/m³, 95% CI: 1.002-1.010) by eliminating studies with partial overlap from the same geographical location.^{21, 23, 38, 80} In addition, no statistical significance was observed (RR=1.008 per 1 μ g/m³, 95% CI: 0.992-1.023) between respiratory diseases and BC/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 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.

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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_{2.5}-adjusted model and the PM_{2.5}-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_{2.5}-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_{2.5}-unadjusted model and PM_{2.5}-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 PM2.5-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 PM25-adjusted model and PM25-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 $PM_{2.5}$ -unadjusted model was evaluated as "moderate". We downgraded one level for publication bias, hence the estimate was adjusted using the trim and fill method.²⁹ 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

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clearance decline with long-term exposure to pollutants and increasing age.^{5, 101} 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 $PM_{2.5}$.¹⁰²

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.¹⁰³ 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.¹⁰⁴ 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.¹⁰⁴ On 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 PM₁₀ and PM_{2.5}, which performed by Mustafic et al, 2012.¹⁰⁵ A critique was given in Young et al, 2019, who used p-value plots to call those claims into question.³⁰

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 PM2.5 when assessing the health effect of PM_{2.5} constituents. Mostofsky et al. proved that PM_{2.5} may be associated with both health and its constituents. Constituent having closer association with PM_{2.5} may illustrate a stronger association with diseases. Therefore, the results of PM_{2.5}-unadjusted model could introduce bias.⁷ 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.

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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 all authors.

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Competing interests

We declare that all authors have no competing interests.

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Data sharing statement

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

information.

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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.

BMJ Open

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_{2.5} 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.

BMJ Open

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.

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.
 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

Page 39 of 133

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BMJ Open

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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_{2.5}-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.

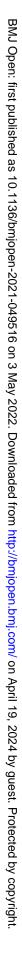
 Table S8 The p-value calculation process for each study using RR, CI low and CI high.

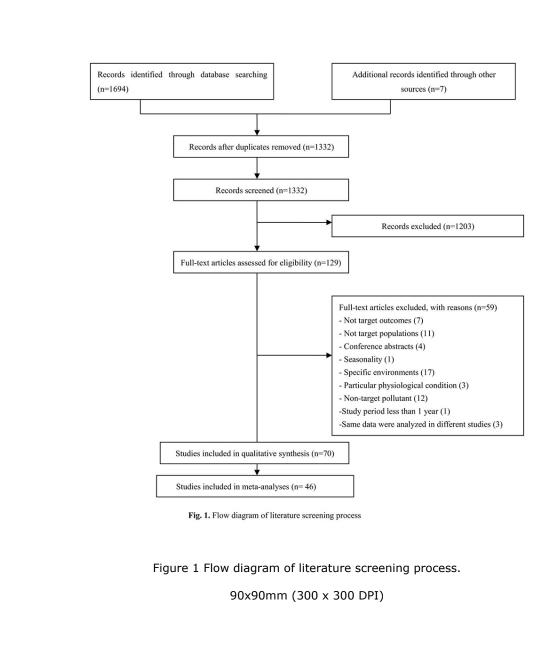
Figure S1 Impact of short-term exposure to BC/EC on cardiovascular mortality stratified by geographical locations.

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_{2.5}-adjusted model.





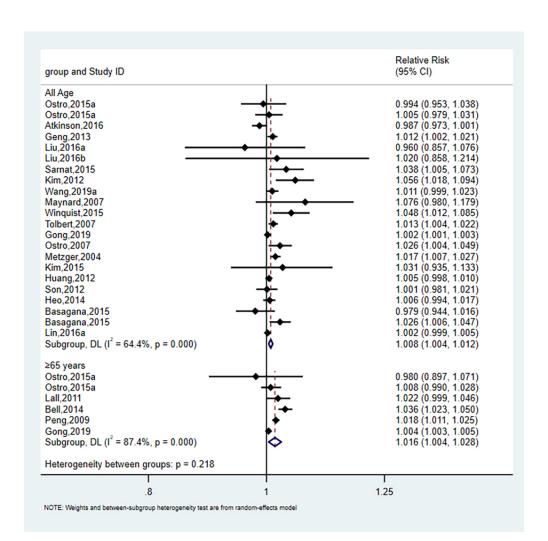
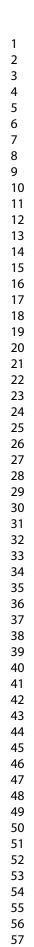


Figure 2 Impact of short-term exposure to BC/EC on cardiovascular diseases in the PM2.5-unadjusted model.

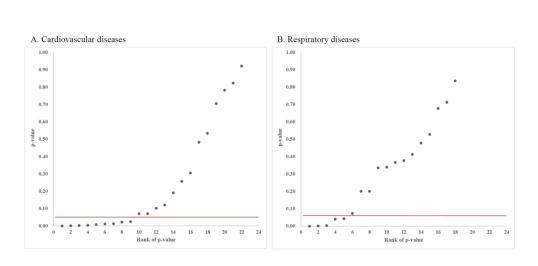
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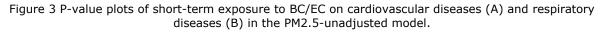
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SUPPLEMENTARY APPENDIX

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

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Supplementary data

Table S1 Search strategy in PubMed.

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

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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_{2.5}-adjusted model.

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No.	Search Strategy	<u> </u>
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udy	ristics Study Design	of included Country	studies in the s Study Period	Systematic Outcome	review and m	eta-analys Pollutant	is. ICD code	A G G G G G G G G G G G G G G G G G G G	
son et al. 2016	TS	UK	2011-2012	Mortality	All	BC,EC	ICD-10	CVD(ICD-10:100-199),RES(ICD-10:100-199) 8	_
t al. 2014	TS	USA	2000-2004	Morbidity	≥65	BC	ICD-9	RES[COPD(ICD-9-CM:490-492,RTI(ICD-9-CM:462)466, 480-487)];CVD[HF(ICD-9-CM:428),Heart Rhyt Disturbances(ICD-9-CM:426-427), Cerebrovascular gvents(ICD-9-CM:430-438),IHD(ICD-9-CM:410-414,	ım
al. 2014	TS	China	2005-2011	Morbidity	≥18	BC	ICD-10	429),PVD(ICD-9-CM:440-448)] Asthma(ICD-10:J45)	
et al. 2013	TS	China	2007-2008	Mortality	All	BC	ICD-10	CVD(ICD-10:I00-I99),RES(ICD-10:J00-J98)	
t al. 2014	TS	China	2007-2012	Morbidity	0-14	BC	ICD-10	Asthma(ICD-10:J45)	
et al. 2015a	CS	Spain, Greece	2008-2009 (Athens), 2009-2010(Barc elona)	Mortality	All	BC	ICD-10	CVD(ICD-10:100-I99),RES(ICD-10:J00-J98) Top Asthma(ICD-10:J45) Top CVD(ICD-10:100-I99),RES(ICD-10:J00-J99) Top CVD(ICD-10:100-I99),RES(ICD-10:J00-J99) Top CVD(ICD-10:100-I99),RES(ICD-10:J00-J99) Top G Top <	
i 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)	
etti and Schwartz	CS	USA	1995-1999	Morbidity	≥65	BC	ICD-9	MI(ICD-9:410),Pneumonia (ICD-9: 480–487)	
al. 2016a	TS	USA	2008-2013	Morbidity	All	EC	ICD-9	CVD(ICD-9:390-429),Stroke(ICD-9:430-438),RES(CD-9:460-519),COPD(ICD-9:490-492,494,496),Pneumo CD-9:480-486),Asthma(ICD-9:493),SSID(ICD-9:78	nia(I
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),Pneum (ICD-9:480-486),Asthma(ICD-9:493) CVD[IHD(ICD9:410-414),Cardiac Dysrhythmias(ICD) 9:427),CHF(ICD9:428),Other CVD	onia
t 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 (ICD9:433-437,440,443-445,451-453)],RES[Pneumcara(ICD9:480-486),COPD (ICD:491,492,496),Asthma/Wheeze (ICD9:493,786.	
t al. 2012	TS	USA	2003-2007	Morbidity	All	EC	ICD-9	CVD(ICD-9:390-459),RES(ICD-9:460-519)	
								(ICD:491,492,496),Asthma/Wheeze (ICD9:493,786.),Other RES(ICD9:460–466,477)]	

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	Table S2 Chara	cteristics (ofincluded	studies in the	systematic re	view and	meta-analys	ic	36/bmjopen-2021-049516
	Study	Study Design	Country	Study Period	Outcome	Age	Pollutant	ICD code	O D Diseases
	Ostro et al. 2009	TS	USA	2000-2003	Morbidity	<19	EC	ICD9	RES(ICD-9:460-519),Asthma(ICD-9:493),Acute brochitis(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-10:100-198),CVD(ICD-10:100-199)
	Peng et al. 2009	TS	USA	2000-2006	Morbidity	≥65	EC	ICD-9	CVD[Cardiac Dysrhythmias(ICD-9:428),Heart Rhyton Disturbances(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, 20, 20, 20, 20, 20, 20, 20, 20, 20, 2
	Levy et al. 2012	TS	USA	2000-2008	Morbidity	≥65	EC	ICD-9	CVD(ICD-9:390-459),RES(ICD-9:464-466 and 480-77).
	Son et al. 2012	TS	Korea	2008-2009	Mortality	All	EC	ICD-10	CVD(ICD-10:100-199),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, ICD-10	eg CVD(ICD-9:390-459,ICD-10:I00-I99),RES(ICD-9:469-519,ICD-10:J00-J99) ع.
	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 10:I21-I22),Stroke(ICD-10:I60-I69)
	Lin et al. 2016a	TS	China	2007-2011	Mortality	All	EC	ICD-10	CVD(ICD-10:100-199) 9
	Cao et al. 2012	TS	China	2004-2008	Mortality	All	EC	ICD-10	CVD(ICD-10:100-199),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-J99)
	Zhou et al. 2011	TS	USA	2002-2004	Mortality	All	EC	ICD-10	CVD(ICD-10:I01-I99),RES(ICD-10:J00-J99) 8
	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-9:410-414,427,
	Ostro et al. 2007	TS	USA	2000-2003	Mortality	All	EC	ICD-10	428,433-437,440,443-445,451-453) CVD(ICD-10:100-199),RES(ICD-10:100-198) St
	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)
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Table S2 Charac	cteristics of Study Design	of included : Country	studies in the Study Period	systematic Outcome	review and me	eta-analys Pollutant	is. ICD code	21 -04 95 16 0 0 0 3 3 3 seases ay	
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)	
								CVD[IHD(ICD-9:410,AMI(ICD-9:410),cardia@	
letzger et al. 2004	TS	USA	1993-2000	Morbidity	All	EC	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)]	
far et al. 2000	TS	USA	1995-1997	Mortality	All	EC	ICD-9	CVD(ICD-9:390-448.9)	
Vang et al. 2019a	TS	China	2013-2015	Mortality	All	EC	ICD-10	CVD(ICD-9:390-448.9) Description CVD(ICD-10:I00-I99),RES(ICD-10:J00-J99) Description Stroke(ICD-10:I60-I66) Description CVD(ICD-10:I00-I99) Description	
lin et al. 2016b	TS	China	2007-2011	Mortality	All	EC	ICD-10	Stroke(ICD-10:160-166)	
Ostro et al. 2008	TS	USA	2000-2003	Mortality	All	EC	ICD-10	CVD(ICD-10:100-199)	
to et al. 2011	TS	USA	2000-2006	Morbidity, Mortality	≥40	EC	ICD-9, ICD-10	CVD[Hypertensive Diseases(ICD-9:402,ICD-10:111]] (ICD-9:414,ICD-10:125),Dysrhythmias(ICD-9:427,ICD-10:148),HF(ICD-9:428,ICD-10:150),Stroke(ICD-9 9,ICD-10:160-169)]	9:430-43
Chen et al. 2014	TS	China	2004-2008	Morbidity	All	EC	ICD-9	Stroke[Ischemic Stroke(ICD-9:433-434),Hemorrhagi	
Fomic'-Spiric' et al. 2019	CS	Serbia	2012-2014	Morbidity	≥18	BC	ICD-10	4llergic 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:I01-I52),Stroke(ICD-9,430-438,ICD-10:I60-I69),RES(ICD-9:460-519,ICD- 99)	10:J00-J
Sinclair et al. 2010	TS	USA	1998-2002	Morbidity	All	EC	NR		
Krall et al. 2013	TS	USA	2000-2005	Mortality	All	EC	NR	Asinma, OKTI, LKTI D CVD and RES(NR) 000000000000000000000000000000000000	
Cakmak et al. 2009	TS	Canada	2001-2006	Morbidity	All	EC	ICD-9	RES(ICD-9:460-519)	

Page 51	of 133
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Table S2 Charact	eristics o	f included		ystematic re	eview and n	neta-analysi	is. ICD	9
Study	Design	Country	Study Period	Outcome	Age	Pollutant	code	မ်းseases ဆ
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),COPD(ICD),C491,492,496),URTI(ICD-9:460-465,460.0,477),Pneumonia (ICD-9:480-486),Bronchiolitis(ICD-9:466.1,466.11,466.11),466.19)]
Lall et al. 2011	TS	USA	2001-2002	Morbidity	≥65	EC	ICD-9	RES[Pneumonia(ICD-9:480-486),COPD(ICD-9:490, Acute Bronchitis and Bronchiolitis(ICD-9:466),Asthma(ICD-9:493)],CVDB ysrhythmia(ICD-9:427),IHD(ICD-9:410-414),HF(ICD-9:4 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	BC	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
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	PRES[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)] 19 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)

ncluded studies i Stud Perio USA 2000-2 USA 2001-2 USA 2001-2 Canada 1999-2 Denmark 1993-2 USA 1988-2	y Outcome od Outcome 010 Morbidity 006 Morbidity, 007 Mortality 002 Morbidity, Morbidity, 015 Mortality	e review and m Age 2-16 all (mortality), $\geq 65(morbidity)$ ≥ 30 45-85 50-64	eta-analys Pollutant EC EC EC BC	ICD code ICD-9 ICD-10 ICD-10 ICD-9,	in Softmjöpen-2021-049516 Asthma(codes beginning with 493), Wheeze (ICD-9: 20:07) CVD(ICD-10:101-179), RES(ICD-10:J00-J99) CVD(ICD-10:101-179), RES(ICD-10:J00-J99) CVD(ICD-10:100-199), IHD(ICD-10:120-125), Pulmor ary (ICD-10:C34, J00-J98) COPD(ICD-9:490, 492, 496, ICD10:140, 144)	
Period USA 2000-2 USA 2001-2 USA 2001-2 Canada 1999-2 Denmark 1993-2	od 010 Morbidity 006 Morbidity, 007 Mortality 002 Morbidity, 005 Mortality	2-16 all (mortality), ≥65(morbidity) ≥30 45-85	EC EC EC	ICD-9 ICD-9, ICD-10 ICD-10 ICD-9,	Asthma(codes beginning with 493),Wheeze (ICD-9: 20.07)	
USA 2001-2 USA 2001-2 Canada 1999-2 Denmark 1993-2	006 Morbidity, Mortality 007 Mortality 002 Morbidity, Morbidity, 015 Mortality	all (mortality), ≥65(morbidity) ≥30 45-85	EC EC	ICD-9, ICD-10 ICD-10 ICD-9,	CVD(ICD-10:I01-I79),RES(ICD-10:J00-J99)	
USA 2001-2 Canada 1999-2 Denmark 1993-2	006 Mortality 007 Mortality 002 Morbidity, Mortality 015 Mortality	≥65(morbidity) ≥30 45-85	EC	ICD-10 ICD-10 ICD-9,	CVD(ICD-10:I01-I79),RES(ICD-10:J00-J99)	1
Canada 1999-2 Denmark 1993-2	002 Morbidity, Mortality 015 Mortality	45-85		ICD-9,		
Denmark 1993-2	002 Mortality 015 Mortality		BC			
		50 -64		ICD-10	fo	
USA 1988-2	004 Martality		BC	ICD-10	CVD(ICD-10:I00-I99),RES(ICD-10:J00-J99,C34)	
	004 Mortality	≥30	EC	ICD-9, ICD-10	CVD(ICD-10:100-I99),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	-
China 1998-2	011 Mortality	≥65	BC	ICD-10	CVD(ICD-10:I00-I99),RES(ICD-10:J00-J47,J80-J9992	
Canada 1999-2	Morbidity, 002 Mortality	45-85	BC	ICD-9, ICD-10		-
etherlands 1991-2	003 Morbidity	15-74	EC	ICD-9	IHD(ICD-9:410-414),CHD(ICD-9:430-438) ♀ ►	
USA 1994-2	Morbidity, 005 Mortality	50-79	EC	ICD-9		
Iran 2014-2	017 Mortality	All	BC	ICD-10	RES(ICD10:J00- J99),CVD(ICD10:I00-I99),IHD(IC	
China 2010–2	2017 Morbidity	All	BC	NR	CVD(including but not limited to hypertension and stocke)	
Canada 2006-2	014 Morbidity	≤6	BC	ICD-10	Asthma(ICD-10:J45)	
Germany 2000-2	015 Morbidity	All	EC	NR		
Serbia 2012-2	014 Morbidity	≥18	BC	ICD-10	AA(ICD-10:J45.0) or asthma with coexisting AR	
Sweden 1991-1	994 Morbidity	All	BC	NR		_
et C Ge	herlands 1991-2 USA 1994-2 Iran 2014-2 China 2010-2 anada 2006-2 ermany 2000-2 Serbia 2012-2	Mortality herlands 1991-2003 Morbidity USA 1994-2005 Morbidity, Mortality Iran 2014-2017 Mortality China 2010-2017 Morbidity anada 2006-2014 Morbidity ermany 2000-2015 Morbidity	Mortalityherlands1991-2003Morbidity15-74USA1994-2005Morbidity, Mortality50-79Iran2014-2017MorbidityAllChina2010-2017MorbidityAllanada2006-2014Morbidity≤6ermany2000-2015MorbidityAllSerbia2012-2014Morbidity≥18	Mortalityherlands1991-2003Morbidity15-74ECUSA1994-2005Morbidity, Mortality50-79ECIran2014-2017MorbidityAllBCChina2010-2017MorbidityAllBCanada2006-2014Morbidity≤6BCermany2000-2015MorbidityAllEC	Mortality ICD-10 herlands 1991-2003 Morbidity 15-74 EC ICD-9 USA 1994-2005 Morbidity, Mortality 50-79 EC ICD-9 Iran 2014-2017 Morbidity All BC ICD-10 China 2010-2017 Morbidity All BC NR anada 2006-2014 Morbidity ≤6 BC ICD-10 ermany 2002-2015 Morbidity ≥18 BC ICD-10	Mortality ICD-10 Market is and the second seco

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

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Study	Study	Country	Study	Outcome	ICD Age Pollutant		ICD	⊐ W Diseases
Study	Design	Country	Period	Outcome	Age	code	D D	
Wang et al. 2019b	CS	USA	2005-2016	Morbidity	All	BC	NR	STEMI N
Livremon et al. 2010	Со	Sweden	1990-2011	Morbidity,	A 11	DC	ICD-9,	IHD(ICD-9:410–414 and ICD-10:120-25);stroke(ICD E9 :431–436 and ICD-10:161–165)
Ljungman et al. 2019	0	Sweden	1990-2011	Mortality	All	All BC	ICD-10	InD(ICD-9:410-414 and ICD-10:120-23);Stroke(ICD9:431-450 and ICD-10:101-103)
Liu et al. 2021a	Co	Sweden,	1002 2004	Morbidity	All	DC	ICD-9,	تح COPD(ICD-9:490–492, and 494–496, or ICD-10:J40244)
Liu et al. 2021a	0	1992-2004 Denmark	Morbialty	All	BC	ICD-10	COPD(ICD-9:490-492, and 494-490, or ICD-10:340(344)	

vbreviations: 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: chemic 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 m 🗟 cardial infarction; CA: cardiac arrest; STEMI: ST segment http://bmjopen.bmj.com/ on April 19, 2024 by guest. Protected by copyright vation myocardial infarction; RTI: respiratory tract infection; URTI: Upper Respiratory Infection; LRTI: Lower Respiratory Infection; ARTI: Acute respiratory infections.

review only

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

····	No. of	No. of	Relative Risk	I ²	Egger Regression Test	
Subgroup Analysis	Studies	Estimates	(95%CI)	Ľ	(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.

		1 2	1
Statistic	Space1	Space2	Space3
maximum	704	128	22528
quartile	273	64	15360
median	198	64	12000
quartile	42	32	2688
minimum	8	32	256

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Table S5 Results of risk of bias assessment.

			Key criteria			Oth	er criteria		
No.	Study	Exposure	Outcome	Confounding	Selection	Incomplete	Selective	Conflict of	0
		assessment	assessment	bias	bias	outcome data	reporting	interest	0
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								
0	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								

			Key criteria	l		Ot	her criteria		
No.	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	

Table S5 Results of risk of bias assessment. (continued)

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Table S6 Details of risk of bias assessment.

No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	Selective reporting	Conflict of interest	Other
1	Atkinson	Probably Low	Low	Probably Low	Low	Low N	Probably Low	Low	Low
	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
		measured at the central	1 January 2011 to 31	(seasonality,	daily counts of	for death were	insufficient	declare no	potential
		London background	December 2012 were	long-term trend),	deaths in	obtained, so	information	conflict of	sources of
		monitoring site at North	obtained from the Office	temperature,	London, United	likely have all	about	interest.	bias
		Kensington. All	for National Statistics.	humidity, day of	Kingdom for the	outcome data.	selective		identified.
		measurements were 24-h	Daily counts of deaths in	week and public	period 1 January	However, any	outcome to		
		averages except for CO.	London, United Kingdom	holidays.	2011 to 31	potential errors	judge for low		
		The number of all	were classified as all		December 2012.	or missing data	risk, but		
		observations was	disease-related causes,			did not depend	indirect		
		621-693 (<25% missing	cardiovascular			on air pollution	evidence that		
		data).	(International		101.	levels.	suggests study		
			Classification of			on	was free of		
			Diseases,10th			Apr	selective		
			revision-ICD10: I00-I99) and respiratory (ICD10:			" 19, 200	report.		
			J00-J99) diseases.			24 by g) - -		
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1 2 3 4							Incomplete			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete of outcome data	5	Conflict of interest	Other
8 9	2	Bell et al.	Probably High	Low	Probably Low	Low	Low	Probably Low	Low	Low
9 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 13			optical reflectance.	denominator file from the	(seasonality,	individuals ≥65	admissions	information	conflict of	sources of
14			Monitors from 5 sites	Centers for Medicare and	long-term trend),	years of age	were obtained,		interest.	bias
15			across 4 counties were	Medicaid Services. Cause	day of week,	enrolled in the	so likely have	5		identified.
16 17			used. Sampling occurred	of admission was	temperature, and	Medicare	all outcome			
18			daily, with some missing	determined by principal	dew point.	fee-for-service	data. However,			
19 20			periods, for Hartford,	discharge diagnosis code		plan during	any potential errors or	risk, but indirect		
20			New Haven, and Springfield, and every	according to International Classification of		August 2000 to February 2004.	errors or missing data	evidence that		
22			third day for Bridgeport	Diseases, Ninth Revision,		reordary 2004.	did not depend	5		
23 24			and Danbury. Days with	Clinical Modification			on air pollution			
25			missing data were	(ICD-9-CM; National			levels.	4		
26 27			omitted from analysis	Center for Health				, i i i i i i i i i i i i i i i i i i i		
27			(the number of missing	Statistics 2006).				<u>s.</u>		
29			data was not reported).				Aprill 19, 2024 by gues	2		
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	5	Conflict of interest	Other
8 9	3	Cai et al.	Probably Low	Low	Probably Low	Low	Low	Probably Low	Low	Low
9 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 13			fixed-site station. Daily	the Shanghai Health	long-term trend),	hospitalization	hospitalization		competing	sources of
14			data was available and no	Insurance Bureau	temperature,	for adult	were obtained,		financial	bias
15 16			missing data was	(SHIB). The causes of	relative humidity	residents living	so likely have		interests.	identified.
17			reported.	hospital admission were	and day of the	in the nine urban	all outcome	outcome to		
18				coded according to	week.	districts between January 1, 2005	data. However,			
19 20				Classification of		and December	any potential errors or			
21				Diseases, Revision 10		31, 2011(2922	missing data	evidence that		
22 23				(ICD-10): Asthma (J45).		days) from the	did not depend	F		
23 24						Shanghai Health	on air pollution			
25						Insurance	levels.	selective		
26 27						Bureau.	Apr	report.		
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1 2 3 4							Jord Jord Jones 16 of Strange 10 of Strange			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete of the second seco		Conflict of interest	Other
8			Probably High	Low	Probably Low	Low	Low X	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	4	Geng et al. 2013	Single, central-site monitor. Daily BC and PM _{2.5} were measured continuously and 24hr averaged was estimated if >75% of the 1hr values was available for that day. Missing data was not replaced by other values.	Health data were obtained from Shanghai Municipal Center of Disease Control and Prevention database. The	Models included time (seasonality, long-term trend), temperature, humidity and day of week.	Data consisted of all causes (excluding accidents or injuries) deaths	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.	The authors declare no conflict of interest.	No other potential sources of bias identified.
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	incomplete g outcome data		Conflict of interest	Other
8			Probably High	Low	Probably Low	Low	Low X	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	5	Hua et al. 2014	Daily 24h average PM _{2.5} and BC data was obtained from a fixed-site station. The study only used the actual collected data and did not fill in the missing data for PM _{2.5} and black carbon.	Daily asthma hospital admission data was obtained from Shanghai Children's Medical Center. Dates of admission and discharge, and diagnoses using the International Classification of Diseases, Revision 10.	Adjusted for long-term and seasonal trend, day of week, temperature and relative humidity.	Study included all asthma hospital admissions of children ≤ 14 years of age from Shanghai Children's Medical Center between1 January 2007 and 31 July 2012 in nine urban districts of Shanghai.	Daily counts for asthma hospital admissions of children 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 report.	Authors declared no competing financial interests.	No other potential sources of bias identified.
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias		Selective reporting	Conflict of interest	Other
8			Probably Low	Low	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	6	Ostro et al. 2015a	Daily 24hr average BC concentrations were obtained from one station in Barcelona and Athens. Daily data was available and no missing data was reported.	For both cities daily counts of all-cause mortality for all ages were collected (excluding deaths from external causes, International Classification of Disease-ICD9: 001799, ICD10 A00R99), as well as daily counts of cardiovascular (ICD9: 390459, ICD10: I00I99), respiratory (ICD9:460519, ICD10:J00J99) and all-cause mortality for those greater than age 65.	Adjusted for long term and seasonal (year, month, day of week) trends, temperature, holidays, summer vacations and influenza.	Study population consisted of daily counts of all-cause mortality for all ages and daily counts of cardiovascular, respiratory and all-cause mortality for those greater than age 65.	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	Authors declared no competing interests.	No other potential sources of bias identified.
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data	Selective	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	7	Samoli et al. 2016	Daily concentrations of 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 (BC urban in PM _{2.5}) and 702 (BC in PM _{2.5}) between 2011 and 2012 (<25% missing data).	Based on the primary discharge diagnosis, daily numbers of admissions for cardiovascular disease (International Classification of Diseases, 10th revision-ICD-10: I00-I99) for those aged 15-64 (adult) and 65+ years (elderly), and respiratory diseases (ICD-10: J00-J99) for those aged 0-14 years (paediatric), adult and the elderly were calculated.	Adjusted for long term and seasonal trends, temperature, relative humidity, regulated pollutants (PM ₁₀ , PM _{2.5} , NO ₂ , SO ₂ and O ₃), day of the week and public	Study included all cardiovascular and respiratory hospital admissions in London, UK between 2011 and 2012.	Daily counts for all emergency hospital admissions 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 interests.	No other potential sources of bias identified.
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4 5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete og outcome data⇔	Selective reporting	Conflict of interest	Other
8			Probably High	Low	Probably Low	Low	Low a	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 13		Schwartz	measurements for BC and	for residents of the	of the week,	hospital	admissions <u>A</u>	information	competing	sources of
14		2006	$PM_{2.5}$ were not complete.	Boston Metropolitan area	seasonality,	admissions in the	were obtained,		interests.	bias
15			Missing values were	who were admitted to the	long-term trends,	Boston	so likely have	selective		identified.
16 17			replaced with the	hospital (in the Boston	humidity,	Metropolitan	all outcome	outcome to		
18			predicted values.	area) with a primary	barometric	area for	data. However,			
19			Additionally BC data was	diagnosis of MI	pressure, and the	myocardial	any potential	risk, but		
20 21			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		
23			not included in the study.	Diseases, 9th	L L	duration.	did not depend			
24				revision-ICD-9:410), and			on air pollution			
25 26				pneumonia (ICD-9:			levels.	selective		
27 28 29 30 31				480–487), from Medicare billing records for the years 1995–1999.			April 19, 2024 by guest. Protected by copyright	report.		
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete g outcome data⇔	Selective reporting	Conflict of interest	Other
8 9			Probably High	Low	Probably Low	Low	Low Y	Probably Low	Low	Low
9 10	9	Liu et al.	EC were collected from a	Emergency department	Adjusted for time	Study included	Daily counts	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 13			one-in-three or one-in-six	from the Blue Cross Blue	seasonal trend),	emergency	department <u>So</u>	information	potential	sources of
14			day schedule. EC were	Shield Texa. International	day of week,	department visits	visits were		competing	bias
15 16			measured for 566 days	Classification of Diseases	temperature, dew	for Greater	obtained, so	selective	financial	identified.
17			from April 02, 2009, to	9th Revision (ICD-9)	point and	Houston from	likely have all		interests.	
18			December 30, 2013, <25% missing for the	diagnosis codes were used to classify outcome	population growth.	claims data insured from	outcome data.			
19 20			frequency of sampling.	groups.		January 1, 2008	potential errors			
21			inequency of sampling.	groups.		through	or missing data			
22 23						December 31,	did not depend			
25 24						2013.	on air pollution			
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	BMJ Open					Page 66 of				
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete \int_{Ω}^{Ω} outcome data ω		Conflict of interest	Other
8			Probably 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	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.	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.
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data	Selective	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	11	Sarnat et al. 2015	24hr average concentration of PM _{2.5} 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 one hospital not providing data after 26 April 2002. However, any potential errors or missing data did not depend 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 they have no actual or potential competing financial interests.	No other potential sources of bias identified.
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1 2 3 4							Incomplete			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	Selective reporting	Conflict of interest	Other
8			Probably Low	Low	Probably Low	Low	Low X	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	12	Kim et al. 2012	PM _{2.5} 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	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.
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	5	Conflict of interest	Other
8			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	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 hospitalization s of children 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.
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4 5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	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	14	Kim et al. 2015	Daily 24-hour composite PM _{2.5} samples were collected from single, central-site monitor. The observations of EC was 1809 days from 2003 through 2007 (missing data <25%).	Daily mortality counts for 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.	Models adjusted for longer-term temporal trend, as time since the study began, day of week, and daily temperature and humidity.	Data consisted of all deaths over the course of the study in a defined geographical area.	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	None of the authors has any actual or potential competing interests.	No other potential sources of bias identified.
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	Selective	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 38	15	Huang et al. 2012	Daily average concentrations of PM _{2.5} were obtained from a single, central-site monitor. Daily average concentrations of EC in PM _{2.5} 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	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.
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete 0 outcome data∝		Conflict of interest	Other
8			Probably High	Low	Probably Low	Low	Low X	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	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 was not replaced by other values.	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 data did not depend on air pollution levels.	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.
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	Selective	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	17	Levy et al. 2012	The U.S. Environmental Protection Agency established the PM Speciation Trends Network (STN) to measure more than 50 PM _{2.5} 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 missing data.	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 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.
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4 5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	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 39	18	Son et al. 2012	Hourly air samples were obtained from a single, central-site monitor. The monitoring system produces hourly estimates of PM _{2.5} total mass, and PM _{2.5} levels of EC. Daily data was available and no missing data was reported.	Daily death counts were obtained from the National Statistical Office. The study classified mortality data into all causes of death [International Classification of Diseases, 10th Revision (ICD-10; codes A00–R99), cardiovascular causes (codes I00–I99), and respiratory causes (codes J00–J99)] (World Health Organization 2007).	Models adjusted for time (long-term trends and seasonality), day of week, temperature and relative 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.	There was insufficient information about selective outcome to judge for low risk, but indirect evidence that	The authors declare they have no actual or potential competing financial interests.	No other potential sources of bias identified.
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete of the second seco	Selective	Conflict of interest	Other
8			Probably High	Low	Low	Low	Low 2	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	19	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	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.
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias			Conflict of interest	Other
8 9			Probably High	Low	Probably Low	Low	Low	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	20	Basagaña et al. 2015	Single central-site monitor in each city. For each city, PM constituents with >20% of the values below the detection limit or missing were excluded. Otherwise, non-detectable were replaced by half the limit of detection. Air pollution data was collected daily in Bologna (n=472), twice a week in Barcelona (n=736) and Madrid (n=104), and once a week in Huelva (n=406). There was no information about	Daily mortality counts for all non-external causes [International Classification of Diseases, 9th Revision (ICD9) codes 001–799; 10th revision (ICD10) codes A00–R99], cardiovascular (ICD9 codes 390–459, ICD-10 codes 390–459, ICD-10 codes 100–I99) and respiratory (ICD9 codes 460–519, ICD10 codes J00–J99) were collected. Cardiovascular and respiratory hospitalizations were defined on the basis of the primary discharge	Models adjusted for holidays, summer population decrease, influenza epidemics, seasonality, long-term trends and temperature.	Data consisted of all deaths over the course of the study in a defined geographical area.	Daily counts for death and emergency hospital admissions 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 report.	The authors have no conflicts of interest to disclose.	No other potential sources of bias identified.
34 35 36 37 38 39 40 41 42			missing data.	diagnosis using the same ICD codes defined above.			C Protected by copyright.			

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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete of outcome data		Conflict of interest	Other
8 0			Probably High	Low	Probably Low	Low	Low X	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	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 _{2.5} 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 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 report.	The authors declare they have no actual or potential competing financial interests.	No other potential sources of bias identified.
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4 5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete		Conflict of interest	Other
8			Probably Low	Low	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	22	Lin et al. 2016a	The concentrations of different particle size fractions and PM _{2.5} 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.	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.
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	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	23	Cao et al. 2012	Daily concentrations of EC was obtained from a single monitoring site. The observations of EC was 1749 in 1827 days (missing data <25%).	The study obtained numbers of deaths in Xi'an for each day from the Shanxi Provincial Center for Disease Control and Prevention (SPCDCP). SPCDCP staff then classify the cause of death according to the International Classification of Diseases, 10th Revision [ICD-10; World Health Organization (WHO) 1992] as due to total nonaccidental causes (ICD-10 codes A00–R99), cardiovascular diseases (I00–I99), respiratory diseases(J00–J98), or injury (S00–T98).	Model adjusted for long-term and seasonal trends, day of week, temperature, humidity, and SO ₂ and NO ₂ concentrations.	Data consisted of all nonaccidental causes deaths during 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.	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.
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6 7 8 9 10No.StudyExposure assessmentOutcome assessmentContounding biasSelection biasoutcome datareportinginterestOther8 9 1024Klemm et al. 2011Probably LowLowLowLowLowProbably LowLowNo other11 12 13 14 15al. 2011Aligu 24-hr average EC neasurements are available for Atlanta during the study period. 15Records of individual the Georgia Department of Human Resources. Cause of death is categorized using the August 1998 to 19Adjusted for time (categorized using the August 1998 to December 31, 2007.Records of individual the Georgia Log of Human Resources.Study included (categorized using the day of the week. of the study.Daily counts of temperature, and over the courseNo ther about temperature, and outcome data. of the study.Interest.Authors to death were of over the courseNo other insufficient outcome data. outcome data. outcome data. outcome data. outcome data. outcome to potential errors or missing data timicrect evidence that suggests studyInterest.Identified.11NoInternational (ICD-10), including circulatory conditions. (ICD-19), respiratoryDiseases, 10th edition circulatory conditions (ICD-19), respiratoryNoInterest temperature, and outcome data.Interest.Identified.12NoInternational circulatory conditions (ICD-19), respiratoryDiseases, 10th edition circulatory conditions (ICD-10), including circulatory cond	3							1-2021-049e			
924Klemm et al. 2011Daily 24-hr average EC measurements are available for Atlanta during the study period. The observations of EC Missing data <25%.	5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias				Other
1024Klemm et al. 2011Daily 24-hr average EC measurements are available for Atlanta during the study period.Records of individual deaths were provided by available for Atlanta 				Probably Low	Low	Probably Low	Low	Low X	Probably Low	Low	Low
33 respiratory, or cancer est. Protected 34 causes). 36 37 38 39 40 41	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	24		Daily 24-hr average EC measurements are available for Atlanta during the study period. The observations of EC was 3317 days from August 1998 to December 31, 2007. Missing data <25%. There was no information	Records of individual deaths were provided by the Georgia Department of Human Resources. Cause of death is categorized using the International Classification of Diseases, 10th edition (ICD-10), including circulatory conditions (I00–I99), respiratory conditions (J00–J99), malignant neoplasm (cancer; C00–D48), or other nonaccidental causes (A00-R99, excluding cardiovascular, respiratory, or cancer	Adjusted for time (seasonality, long-term trends), temperature, and day of the week.	Study included all nonaccidental deaths during 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.	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

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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete g outcome data	Selective reporting	Conflict of interest	Other
8			Probably Low	Low	Probably Low	Low	Low X	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 _{2.5} 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 (ICD10, 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.	, zuz4 by guest.	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.
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No. Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete g		Conflict of interest	Other
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0 26 Winquist 1 et al. 2015 3 i 4 i 5 i 6 i 7 i 8 i 9 i 0 i 1 i 2 i 3 i 4 i 5 i 6 i 7 i 8 i 9 i 1 i 2 i 3 i 4 i 5 i 6 i 7 i 8 i 9 i 0 i 1 i 2 i 3 i 4 i 5 i 6 i 7 i 8 i 9 i<	Daily EC and BC were from a single monitor site. All species of pollutant statistics are missing less than 5%.	Individual-level data were obtained from the Missouri Hospital Association for all emergency department visits to 36 of 43 acute-care non-federal hospitals with emergency department visits in the 16-county St Louis metropolitan statistical area during 1 June 2001 through 30 April 2003. Cardiorespiratory outcomes of interest were defined based on the primary ICD-9 (International Classification of Diseases, version 9) diagnosis code for the visit.	Adjusted for time trends, day of week, holidays, season, temperature and dew point.	Study included emergency department visits in St Louis metropolitan statistical area during 1 June 2001 through 30 April 2003.	Daily counts for emergency Development department visit were obtained, so likely have all outcome data. However, any potential errors	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.

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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	Selective reporting	Conflict of interest	Other
8			Probably High	Low	Probably Low	Low	Low X	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	27	Ostro et al. 2007	Each of the six counties had two monitors measuring PM _{2.5} components and mass. Fresno, Kern, Riverside, and Sacramento Counties reported data every third day, whereas San Diego and Santa Clara Counties reported data every sixth day. For the speciation analyses, the number of observation days available ranged from 243 (San Diego County) to 395 (Sacramento County) from 2000 to 2003. There was no specific information about missing data.	Daily mortality data were obtained from the California Department of Health Services, Center for Health Statistics. The study determined daily total mortality counts for those > 65 years of age and for deaths from respiratory disease [International Classification of Diseases, 10th Revision (ICD10; World Health Organization 1993) codes J00–J98] and cardiovascular disease (codes I00–I99).	Adjusted for time trend, day of week, seasonality, long-term trends, 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.	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.
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3 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			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	28	Tolbert et al. 2000	Daily 24h EC from a single monitor site. The observation of EC was 356 in 365 days, missing data <25%.	Computerized billing record data are being obtained from the emergency department visits participating in the study. Several case groups are being defined using the primary ICD-9 (International Classification of Diseases, 9th Revision) diagnostic code.	Adjusted for time (seasonality, long-term trends), temperature, dew point, and day of week.	Study included emergency department visits of the participating hospitals in the Atlanta Metropolitan Statistical Area, including 33 hospitals between January 1 1993-August 31 2000, 4 hospitals between January 1 1993-February 30 2000.	Daily count 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.	Authors declared no competing financial interests.	No other potential sources of bias identified.
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	Selective	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	29	Wang and Lin 2016	The hourly data were simply averaged to calculate the daily average data for PM ₁₀ , PM _{2.5} 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.	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 Revision (ICD-9 CM).	Adjusted for temperature, relative humidity, wind speed, barometric pressure, holidays, day of the week, pneumonia and influenza.	Study included elderly (≧65 years) mortality from 2004 to 2008 and all population EVR from 2004 to 2010 in Taipei, Taiwan.	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 depend on air pollution levels.	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.
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No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete of outcome data	Selective reporting	Conflict of interest	Other
		Low	Low	Low	Low	Probably Low	Probably Low	Low	Low
30	Darrow et	Daily 24-hour average	Health data were	Adjusted for dew	Study included	Daily counts	There was	Authors	No other
	al. 2014	EC was from ambient	obtained from 41	point, temperature,	daily emergency	for emergency	insufficient	declared no	potential
		monitoring networks.	metropolitan Atlanta	seasonality,	department visit	department	information	competing	sources of
		Missing data <1%.	hospitals and the Georgia	long-term trends,	data from 41	visit were	about	financial	bias
			Hospital Association. The	day of week,	metropolitan	obtained. In the		interests.	identified.
			diagnoses of respiratory	holiday and	Atlanta hospitals	earliest years	outcome to		
			infection were based on	influenza	for the period	of the study,	judge for low		
			International	epidemics.	January 1, 1993,	not all	risk, but		
			Classification of		to December 31,	hospitals were			
			Diseases, 9th Revision		2004 (not all	participating.	evidence that		
			(ICD-9), diagnosis codes:		hospitals	However, any			
			acute bronchitis or		contributed the	potential errors			
			bronchiolitis (code 466);		full period), and	or missing datag			
			pneumonia (codes		from the Georgia	did not depend			
			480–486); and upper		Hospital	on air pollution			
			respiratory infection		Association for	levels.			
			(codes 460–465).		the period	4 by			
					January 1, 2005,	gue			
					to June 30, 2010.				
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	Selective	Conflict of interest	Other
8			Probably High	Low	Probably Low	Low	Low X	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	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 of department visits were obtained, so likely have all outcome data. However, any potential errors or missing data	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.
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1 2 3 4							36/bmjopen-2021-049516 o Incomplete			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete of the second seco		Conflict of interest	Other
8 9			Probably Low	Low	Probably Low	Low	Low 2	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	32	Mar et al. 2000	Hourly PM _{2.5} chemical composition data from a single, central-site monitor. Daily data was available and no missing data was reported.	Mortality data for all of Maricopa County from 1995 to 1997 were obtained from the Arizona Center for Health Statistics in Phoenix. Death certificate data included residence zip code and the primary cause of death as identified by the International Classification of Diseases, Ninth Revision (ICD-9, World Health Organization, Geneva).	Adjusted for time trend, seasonality, day of week, temperature and relative humidity.	Data consisted of all cardiovascular deaths during 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	No competing financial interests.	No other potential sources of bias identified.
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1 2 3 4							36/bmJopen-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete of outcome data⇔	Selective	Conflict of interest	Other
8			Low	Low	Probably Low	Low	Low X	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	33	Wang et al. 2019a	Hourly data of PM _{2.5} were collected at 10 Chinese air quality monitoring sites in Shanghai. Hourly mass concentrations of PM _{2.5} 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.	19, 2024 by guest. Protected by	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.
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3 4 5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	4956 Incomplete م outcome data	Selective	Conflict of interest	Other
8			Probably High	Low	Probably Low	Low	Low a	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	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:I60–I66), and sub-categories, including ischemic stroke (ICD-10:I63–I66), and hemorrhagic stroke (ICD-10: 160–I62) 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.	There was insufficient information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of	Authors declared no conflict of interest.	No other potential sources of bias identified.
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1 2 3 4							36/bmJopen-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	ີດ Incomplete ິ outcome dataຜ ≤	Selective reporting	Conflict of interest	Other
8 9			Probably High	Low	Probably Low	Low	Low X	Probably Low	Low	Low
9 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 13			measuring components of	obtained from the	humidity and day	cardiovascular	obtained, so	information	competing	sources of
14			PM _{2.5} . Fresno, Kern,	California Department of	of the week.	mortality for all	likely have all		interests.	bias
15 16			Riverside and	Health Services, Center		California	outcome data.	1		identified.
17			Sacramento counties	for Health Statistics. Daily counts of deaths		residents from 1 January 2000 to	However, any			
18			reported 24-hour average EC in PM _{2.5} every third	from cardiovascular		31 December	or missing data			
19 20			day; San Diego and Santa	disease (International		2003.	did not depend			
21			Clara counties reported	Classification of		2003.	on air pollution			
22 23			data every sixth day. The	Diseases, Tenth Revision			levels.	suggests study		
23 24			study included only	(ICD10) =I00–I99) were		101		was free of		
25			species for which at least	calculated.			on v	selective		
26 27			50% of the observations				Apr	report.		
28			were above the level of							
29 30			detection.				202			
31							April 19, 2024 by gues			
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete og outcome data∝ ≤		Conflict of interest	Other
8			Probably Low	Low	Probably Low	Low	Low X	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.	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.
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data	Selective	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 39	37	Chen et al. 2014	Hourly mass concentrations of PM _{2.5} and the four PM _{2.5} constituents obtained from a Supersite (single, central site monitoring location). The observations of EC was 1599 in 1705 days (missing data <25%).	The counts of daily emergency room visits were obtained from the National Taiwan University Hospital. The emergency room visit data were coded regarding the discharge diagnosis using the International Classification of Disease, 9th revision (ICD-9).	Models adjusted for time, day of week, temperature, seasonality and relative humidity.	Data consisted of all emergency department visits during the study period for ischemic and hemorrhagic stroke.	Daily counts for emergency room visit 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.
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete og outcome data⇔		Conflict of interest	Other
8			Low	Low	Probably High	Low	Low X	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	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 17			air quality monitoring	visits in Užice, Sevojno,		allergic asthma	likely have all	-		
18			stations. There was no	and Kosjeri' c, or from a		from 1 July 2012	outcome data.			
19			information about	general hospital in Užice.		to 30 June 2014	However, any			
20 21			missing data.	The inclusion criteria		in the Zlatibor	potential errors			
21				were adults aged 18 years		District, Western	or missing data			
23				and older with the		Serbia.		suggests study		
24 25				diagnosis of allergic			on air pollution			
25 26				rhinitis (International			levels.	selective		
27				Classification of			April 19, 2024 by guest	report.		
28				Diseases, 10th revision,			Ŀ,			
29 30				code J.30.4), allergic			202			
31				asthma (International			4 by			
32				Classification of			gue			
33 34				Diseases, 10th revision,			•			
35				code J.45.0), or asthma			Protected			
36				with coexisting allergic			ecte			
37 38				rhinitis.						
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	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 39	39	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 report.	Authors declared no competing financial interests.	No other potential sources of bias identified.
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	Selective reporting	Conflict of interest	Other
8			Probably Low	Probably 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	40	Sinclair et al. 2010	Daily 24-hr averages EC was from a single monitor site. The total observed rate of EC was 95.2%.	Daily outpatient visits were obtained from the electronic patient data warehouse of a not-for-profit, group-model managed care organization (MCO) in the metropolitan Atlanta area between August 1, 1998 and December 31, 2002. Visits that met acute visit definition and that had a visit diagnosis code of asthma, upper respiratory infection (URI), or lower respiratory infection (LRI) were included in the study.	Adjusted for season, day of week, federal holidays, study month, time, temperature and dew point.	Study included daily outpatient visits for acute respiratory diseases from the electronic patient data warehouse of a not-for-profit, group-model managed care organization (MCO) in the metropolitan Atlanta area between August 1, 1998 and December 31, 2002.	Daily counts for outpatient 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.
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1 2 3 4							30/bm)open-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	i la	Conflict of interest	Other
8			High	Probably Low	Probably Low	Low	Low X	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	41	Krall et al. 2013	Monitors typically measure PM _{2.5} constituent concentrations every third or sixth day. Some communities with a single monitor. The observation of EC was 58-921 days,some communities had >25% missing data.	All-cause mortality data (excluding accidental deaths) were aggregated from death certificate data obtained from the National Center for Health Statistics for 2000 to 2005.	Adjusted for temperature, day of week, long-term and seasonal trends.	Study included all death (excluding accidental deaths) for 108 urban communities from 2000 to 2005.	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.	The authors declare they have no actual or potential competing financial interests.	No other potential sources of bias identified.
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4 5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete of outcome data	Selective	Conflict of interest	Other
8			Probably High	Low	Probably Low	Low	Low X	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	42	Cakmak et al. 2009	Daily PM _{2.5} aerosol samples approximately 1 of every 4 days from a single monitor site. Sampling occurred daily during the cold season (April through September) and alternate days during the warm season (October through March). Missing data <25% for that frequency.	Diseases were coded using the WHO International Classification of Disease, 9th Revision (ICD-9). The daily number of emergency department visits for all nonaccidental (ICD-9 < 800) and respiratory (ICD-9 460–519) causes in Santiago Centro, Cerrillos, and Pudahuel were obtained from the Departamento de Estad' isticas e InformaciónenSalud (DEIS) of the Ministry of Health from April 2001 through August 2006.	Adjusted for temperature and humidity, day of week, long-term and seasonal trends.	Study included all emergency department visits obtained from the Departamento de Es-tad' 1sticas e InformaciónenSa lud (DEIS) of the Ministry of Health from April 2001 through August 2006.	Daily counts for emergency Downloaded for emergency department visit were obtained, so likely have all outcome data. However, any potential errors or missing data did not depend. 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	No competing financial interests.	No other potential sources of bias identified.
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1 2 3 4										
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	Selective	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	43	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 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.
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4 5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	Selective	Conflict of interest	Other
8			Low	Low	Probably Low	Low	Low X	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 26	44	Lall et al. 2011	Daily EC data were obtained from two monitors. Daily data was available and no missing data was reported.	The categorization of the admissions data was based on codes from the International Classification of Diseases, revision 9 (ICD-9).	Model adjusted for season, wintertime influenza episode, weather, day of week, and other possible confounders (e.g., federal holidays).	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.	 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.
35 36 37 38 39 40 41 42 43					/ - http://bmjopen.bmj					

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1 2 3 4							36/bm)open-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	Selective	Conflict of interest	Other
8 9			Probably High	Low	Probably Low	Low	Low X	Probably Low	Low	Low
10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28	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 _{2.5} 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.	for asthma outpatient visits (0-20 years old) data 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 study was free of selective report.	No competing financial interests.	No other potential sources of bias identified.
29 30 31 32 33 34 35 36 37 38 39 40 41 42							levels. 19, 2024 by guest. Protected by copyright.			

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1 2 3 4							Incomplete			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	Selective reporting	Conflict of interest	Other
8			Probably Low	Low	Probably Low	Low	Low X	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	46	Gong et al. 2019	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 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) were obtained.	Adjusted for calendar effects, long-term trends, temperature, humidity, day of week, NO ₂ and SO ₂ .	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.	Daily counts for all deaths 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 conflict of interest.	No other potential sources of bias identified.
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1 2 3 4							36/bm)open-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	i	Conflict of interest	Other
8			Probably Low	Probably Low	Probably High	Low	Low X	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	47	Mostofsky et al. 2012	Ambient EC obtained from one monitor. BC concentrations were measured continuously. Daily data was available and no missing data was reported.	Patients potentially eligible for this study were identified by reviewing daily emergency department admission logs, stroke service admission logs, stroke service consult logs, and hospital electronic discharge records.	Model adjusted for seasonality, time-trends, temperature, dew point temperature, barometric pressure and chronic and slowly-varying potential confounders.	Population consisted of patients ≥21 years of age admitted to the hospital with neurologist-confi rmed ischemic stroke and residing in the Boston metropolitan region. Also patients had to reside within 40 km of the air pollution monitor.	Daily counts for emergency of department admission 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.
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1 2 3 4 _							36/bmjopen-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete og outcome data∝	Selective	Conflict of interest	Other
8			Probably High	Low	Probably Low	Low	Low X	Probably Low	Low	Low
9 10	48	Krall et al.	PM _{2.5} 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 22			There was no information	Diseases, 9th Revision		area, the	However, any	evidence that		
23			about missing data.	(ICD-9), the study		7-county	potential errors			
24				considered subcategories		Birmingham	or missing data			
25 26				of respiratory diseases		metropolitan	did not depend			
27				including pneumonia		area, the 8	on air pollution ≩	report.		
28				(ICD-9 codes 480–486),		Missouri and 8	levels.			
29 30				chronic obstructive		Illinois counties	levels. 19, 2024 by guess			
31				pulmonary disease		in the St. Louis				
32				(491,492,496), upper		metropolitan	y gu			
33				respiratory infection		area, and the	est.			
34 35				(URI) (460–465, 466.0,		12-county Dallas	Рго Г	J		
36				477), and asthma and/or		metropolitan	Protected			
37				wheeze (493, 786.07).		area.				
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	Selective	Conflict of interest	Other
8			Probably Low	Low	Probably Low	Low	Low X	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	49	O'Lenick et al. 2017	The 24-hour average concentration of EC was evaluated. Pollutant concentration estimates were obtained by fusing observational data from available network monitors with pollutant concentration simulations from the Community Multi-Scale Air Quality emissions-based chemical transport model at 12×12km grids over Atlanta. 24-hour average EC were evaluated. Daily data was available and no missing data was reported.	Patient-level emergency department visit data from 1 January 2002 to 31 December 2008 were acquired from hospitals located within the 20-county metropolitan area of Atlanta; Relevant data elements included admission date, International Classification of Diseases Ninth Revision (ICD-9) diagnosis codes, age and ZIP code of patient residence.	Adjusted for season, periods of hospital participation and holidays, temperature and mean dew point, interaction terms between season and maximum temperature and day of year.	Study included all emergency department visit data acquired directly from hospitals (2002–2004 period) and the Georgia Hospital Association (2005–2008 period) located within the 20-county metropolitan area of Atlanta.	Daily counts for emergency department visit 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.	Competing interests: None declared.	No other potential sources of bias identified.
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1 2 3 4							Incomplete on			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	Selective reporting	Conflict of interest	Other
8 9			Probably Low	Low	Probably Low	Low	Low X	Probably Low	Low	Low
9 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		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 department	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	0.	18 years from 41	obtained, so	judge for low		
19				metropolitan Atlanta; and		hospitals within	likely have all			
20				defined emergency		metropolitan	outcome data.			
21 22				department visits for		Atlanta for study	However, any	-		
23				pediatric asthma as all	ŀ	period.	potential errors			
24				visits with a code for		· ()	or missing data	was free of		
25 26				asthma (493.0–493.9) or			did not depend			
20				wheeze (786.07) using			on air pollution	report.		
28				the International			levels.			
29 30				Classification of			∑∆			
30 31				Diseases, 9th Revision.			24 D	-		
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete		Conflict of interest	Other
8			Low	Low	Probably Low	Low	Low X	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	51	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, 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.
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4 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 2	Probably Low	Low	Low
9 10	52	Strickland	24-hour average EC were	Daily counts of	Adjusted for	Study included	Daily counts	There was	No conflict	No other
11		et al. 2014	obtained from 6	emergency department	season, dew point,	all emergency	for emergency		of interests.	potential
12 13			monitors. Missing data	visits for asthma or	temperature, day	department visits	room visits of			sources of
14			was 1%.	wheeze among children	of week, and	for asthma or	asthma or			bias
15				aged 2 to 16 years were	holiday.	wheeze among	wheeze disease			identified.
16 17				collected from the		children 2 to 16	were obtained,			
18				Georgia Hospital		years of age from	so likely have			
19				Association from 1		the Georgia	all outcome	risk, but		
20 21				January 2002 through 30		Hospital	data. However,	indirect		
22				June 2010. The study		Association.	any potential =	evidence that		
23				identified all emergency			errors or missing data	suggests study		
24 25				department visits with an						
26				International			did not depend			
27				Classification of			on air pollution	report.		
28 29				Diseases, 9th revision			levels.			
30				(ICD-9) code for asthma						
31				(codes beginning with			+ by	-		
32 33				493) or wheeze (code 786.07) present in any			gue			
33 34				diagnosis field.						
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete of the second seco	Selective	Conflict of interest	Other
8			Probably High	Low	Probably Low	Low	Low X	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	53	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 _{2.5} 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.
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data	Selective	Conflict of interest	Other
8 9			Probably Low	Low	Probably Low	Low	Probably Low	Probably Low	Low	Low
10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 30 31 32 33 34 35	54	Ostro et al. 2015b	The model calculations track the mass and concentrations of the PM constituents in particle diameters ranging from 0.01 to 10µm through calculations that describe emissions, transport, diffusion, deposition, coagulation, gas- and particle-phase chemistry, and gas-to-particle conversion. The University of California Davis/California Institute of Technology model was used to estimate ground-level concentrations of 50 PM constituents over the	Deaths were assigned codes based on the International Classification of Diseases, 10th Revision (ICD-10) for the following outcomes: all-cause deaths excluding those with an external cause (A00–R99), cardiovascular deaths (I00–I99), Ischemic heart disease deaths (I20–I25), and pulmonary deaths (C34, J00–J98).	ge, race, marital status, smoking status, pack-years of smoking, secondhand smoke exposure, body mass index, lifetime physical activity, alcohol consumption, average daily dietary intake of fat, calories, menopausal status, family history of myocardial infarction, stroke, use of blood pressure medication,	Data obtained for a cohort of female teachers ≥30 years old.	There was no the rate of lost 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 they have no actual or potential competing financial interests.	No other potential sources of bias identified.
36 37			major population regions in California.		aspirin; living conditions					
38 39 40 41 42				1		1			1	1

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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete og outcome data∝	Selective	Conflict of interest	Other
8 9 10 11 12 13 14 15 16 17 18				Forpe	(income, income inequality, education, population size, racial composition, unemployment).		ay 2022. Downloaded from http			
19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37	55	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 use regression models.	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 follow-up period.	Probably Low During the 4-year follow-up period, 38,377 (8%) subjects were lost to follow-up because of moving out of 4 the province or dying from other diseases.	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.
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1 2 3 4							Incomplete o			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete of outcome data		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	56	Hvidtfeldt et al. 2019	The PM, NO ₂ , BC, and O ₃ 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 ₂ , BC, and O ₃ .	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 100–199) 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 consumption, physical activity; neighborhood level socioeconomic status (SES).	Data obtained for a cohort of men and women aged 50–64 years residing in the areas of Copenhagen and Aarhus.	There was no V. information on Low the rate of lost follow up. follow up. UZ4 by guest. Protected	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.
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13 14 15obtained from U.S. Environmental Protection Agency Air Quality System. These PM2.5 analyzed to derive approtioned PM2.5 mass estimates of source approtioned PM2.5 mass estimates of source approtioned PM2.5 mass estimates of source approtioned PM2.5 mass exposure, analysis (APCA) PM2.5 source apportionment method.International marital status, exposure, and BMI? consumption, quintile of consumption, quintile of corvariates.about including source at least including source at least source apportionment method.interests.bias identified.13obtained from U.S. possible workplace consumption of principal component method.International principal component method.International consumption, quintile of consumption, fat consumption, Six ecologie covariates.30 years of age, including source at least source apportionment method.about interests.interests.bias identified.13and resided in all exposure concentrations using the absolute principal component method.10-414; ICD-10 codes and BMI?and resided in all bistrict of consumption of beer, wine, and occurring outring outring the analysis (APCA) PM2.5indirect method.indirect respondent analysis (APCA) PM2.5indirect method.indirect method.indirect method.14obtained from U.S. consumption, gitted of consumption, gitted of consumption, gitted of covariates.indirect consumption, gitted of covariates.indirect coursumption, gitted of coursumption, gitted of covariates.indirect <th>Pag</th> <th>je 113 o</th> <th>of 133</th> <th></th> <th></th> <th>BMJ Oper</th> <th>1</th> <th>do[ma/op</th> <th></th> <th></th> <th></th>	Pag	je 113 o	of 133			BMJ Oper	1	do[ma/op			
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1057ThurstonThe mean concentrationsMore than 99% of knownActive smokingData obtained forThe mean concentrationsThe mean concentrationsNoNo othering11et al. 2016of PM23 mass and tracedeaths were assigned a constituents wereand formera cohort ofcohort includeed principals.informationfinancial informationsources of information1314obtained from U.S.Internationalsmoke exposure, smoke exposure,30 years of age, includingparticipants, staboutadoutinterests.bias15Environmental Protection Agency Air QualityDiseases, 9th and 10th System. These PM25Revision (ICD-9 codes total 14(1CD-10 codescompationalsomecne at leastdisease deaths at giaces of ageof for all of giaces, 1pik, but indicetindicet16analyzed to derive estimates of source apportioned PM25 mass exposure concentrations120–125).and BM17 consumption of totar alcohol, quintile of dietary (consumption, quintile of comsumption, quintile of icet alcohol, quintile of dietaryfollow-up.follow-up.follow-up.follow-up.13and solut principal component method.Financial source apportionment method.Financial econsumption, quintile of covariates.follow-up.follow-up.follow-up.14Financial source apportionment method.Financial econsumption, six ecologic covariates.follow-up.follow-up.follow-up.15fiber consumption, 				Probably Low	Probably Low	Probably High	Low	Probably High	Probably Low	Low	Low
11 12 13et al. 2016of PM25 mass and trace constituents were obtained from U.S.deaths were assigned a cause using the and using the smoking, passive smoke exposure, 30 years of age, participants, add includinginformation aboutinformation informationfinancial sources of information14 14 15obtained from U.S.International (Lassification of Diseases, 9th and 10th System. These PM2_5possible workplace passible workplacein householdswith 34,408 aboutselective outcome to index of tableselective outcome to index of tableidentified.17 17 17 17 17 17 17 17 17 17 17 17System. These PM2_5 constituent data were analyzed to derive apportioned PM23 mass using the absolute principal component mathed.10414; ICD-10 codes tablediminess index, table table45 years of age table table table(of a total of table table table tableindex of table table tableindex of table table tableindex of table tableindex of table table12 12 13apportioned PM23 mass using the absolute principal component method.Index of table table table table table tableIndex of table table table table tableIndex of table table table table table table table tableIndex of table table table table tableindex of table table table table table tableindex of table table table table tableindex of table table table table tableindex of table table<		57	Thurston	The mean concentrations	More than 99% of known	Active smoking	Data obtained for	The analytic	There was	No	No other
13Constrained from U.S.InternationalSmoke exposure, possible workplace1000000000000000000000000000000000000	11		et al. 2016	of PM _{2.5} mass and trace	deaths were assigned a	and former	a cohort of	cohort included	insufficient	competing	potential
14 15Obtained from U.S.Internationalsmoke exposure, subscience30 years of age, in householdsparticipants, aboutaboutinterests.bas15Environmental ProtectionClassification of Diseases, 9th and 10th occupationalcossible workplace occupationalin householdswith 34,408selectiveidentified.16Agency Air Quality constituent data were analyzed to derive estimates of source apportioned PM2.5 mass using the absolute410-414; ICD-10 codes 120-125).dirtiness index, education, BMI and BMI?45 years of age source from all beer, wine, and poter of Rico.(of a total of principal component analysis (APCA) PM2.5 source apportionment method.102-125).marital status, education, BMI and BMI?indirect causes)indirect evidence that suggests studywas free of selective24exposure concentrations using the absolute principal component analysis (APCA) PM2.5 source apportionment method.juintle of dietary commition, quintile of dietary vegetable, fruit, fiber consumption, Six ecologic covariates.For of selectiveselective report.For of selective33analysis (APCA) PM2.5 source apportionment method.indirect commitment, quintile of commitment, fiber consumption, Six ecologic covariates.indirect covariates.indirect covariates.indirect source apportionment six ecologic covariates.indirect covariates.indirect source apportionment six ecologic covariates.indirect source apportionment six ecologic<				constituents were	cause using the	smoking, passive	persons at least	445,860	information	financial	sources of
15Environmental ProtectionClassification of Diseases, 9th and 10th System. These PM2.5possible workplace exposure to PM, occupationalincluding includingischemic heart 3 idease deaths 4 judge for lowincluding outcome to judge for lowincluding outcome to outcome to judge for lowincluding outcome to judge for lowincluding outcome to judge for lowincluding outcome to judge for lowincluding outcome to outcome to judge for lowincluding outcome to outcome to isses deaths 4 judge for lowincluding outcome to judge for lowincluding outcome to judge for lowincluding outcome to someone at least outcome to isses deaths 4 judge for lowincluding outcome to sole at least outcome to isses deaths 4 judge for lowincluding outcome to sole at least outcome to isses deaths 4 judge for low outcome to outcome to outcome to outcome to outcome to outcome				obtained from U.S.	International	smoke exposure,	30 years of age,	participants,	about	interests.	bias
17 18 19System. These PM2.5 constituent data were analyzed to derive estimates of source apportioned PM2.5 mass exposure concentrations using the absolute principal component analysis (APCA) PM2.5 source apportionment method.Revision (ICD-9 codes 410-414; ICD-10 codes 120-125).sourcond occupational dirtiness index, marital status, education, BMI and BMI2, consumption of beer, wine, and puerto Rico.someone at least 45 years of age and resided in all bistrict of causes)disease deaths 5 risk, but indirect evidence that suggests study was free of selective26 27 28 29 30using the absolute principal component analysis (APCA) PM2.5 source apportionment method.Revision (ICD-9 codes 410-414; ICD-10 codes to derive education, BMI and BMI2, consumption of quintile of dictary vegetable, fruit, fiber consumption; Six ecologic covariates.someone at least 45 years of age and resided in all District of columbia, and occurring during to derive follow-up.disease deaths 5 to all of of a total of of to all of of a total of of total of of a total of of total of of all of of all of of total of of all of of of all of of total of of of all of of of	15			Environmental Protection	Classification of	possible workplace	in households		1		identified.
18 19System. Inese PM2.5 constituent data were analyzed to derive estimates of source apportioned PM2.5 mass exposure concentrations using the absolute principal component analysis (APCA) PM2.5 source apportionment method.410-414; ICD-10 codes diriness index, and BMI2, consumption of beer, wine, and other alcohol, quintile of dietary fat consumption, quintile of combined dietary vegetable, fruit, fiber consumption; Six ecologic covariates.disease deatins of constant and reside in all to fat consumption follow-up.judge for low risk, but indirect evidant of suggests study was free of selective10exposure concentrations using the absolute principal component analysis (APCA) PM2.5 source apportionment method.100Columbia, and puerto Rico.00euring to follow-up.0eerive evidant and selective20and selective exposure concentrations using the absolute principal component analysis (APCA) PM2.5 source apportionment method.and selective to follow-up.follow-up.0follow-up.021combined dietary vegetable, fruit, fiber consumption; Six ecologic covariates.consumption; six ecologic covariates.10000023additional dietary source apportionment method.additional dietary six ecologic covariates.000024consumption; six ecologic covariates.1000000025analysis (APCA) PM2.5 six ecologic covariates.100000<				Agency Air Quality		exposure to PM,	including	_			
19constituent data were analyzed to derive estimates of source apportioned PM2_5 mass exposure concentrations using the absolute principal component analysis (APCA) PM2_5 source apportionment method.410-414; ICD-10 codes marital status, education, BM1 and BM12, consumption of beer, wine, and other alcohol, quintile of dietary fat consumption, quintile of combined dietary vegetable, fruit, fiber consumption; Six ecologic covariates.45 years of age and resided in all to 157,572 deaths to 157,572 deaths widence that suggests study vegets study vegetable, fruit, fiber consumption; Six ecologic covariates.(of a total of of to 157,572 deaths to 0 states, the to 0 states, the from all to 20 states, the from all to 20 states, the to 20 state, the to 20 state				System. These PM _{2.5}	Revision (ICD-9 codes	occupational	someone at least	disease deaths	judge for low		
21 22 23estimates of source apportioned PM2.5 mass exposure concentrations using the absolute principal component analysis (APCA) PM2.5 source apportionment method.education, BMI and BMI ² , consumption of other alcohol, quintile of dietary fat consumption, quintile of combined dietary vegetable, fruit, fiber consumption; Six ecologic covariates.50 states, the consumption of principal component fat consumption, guintile of combined dietary source apportionment method.follow-up.evidence that sugests study was free of selective report.29 30 31 32 33 34 34 35 38source apportionment method.follow-up.follow-up.follow-up.10 30 31 33 33 34source apportionment method.follow-up.follow-up.follow-up.29 30 31 32 33 33 34source apportionment method.guintile of follow-up.source apportionment fiber consumption; Six ecologic covariates.source apportioned planet follow-up.follow-up.31 32 33 33 34source apportioned planet fiber consumption; Six ecologic covariates.source apportioned planet follow-up.source apportioned planet follow-up.follow-up.34 35 36 37source apportioned planet fiber consumption; six ecologic covariates.source apportioned planet follow-up.source apportioned planet follow-up.source apportioned planet follow-up.34 35 36 37source apportioned planet follow-up.source apportioned planet follow-up.source apportioned plan	19			constituent data were	410–414; ICD-10 codes	dirtiness index,					
22 23 24 25 26apportioned PM2.5 mass exposure concentrations using the absolute principal component analysis (APCA) PM2.5 source apportionment method.and BMI ² , consumption of beer, wine, and other alcohol, quintile of dietary fat consumption, quintile of combined dietary vegetable, fruit, fiber consumption; Six ecologic covariates.District of causes)causes) using the absolute was free of selective report.26 27 29 30analysis (APCA) PM2.5 source apportionment method.quintile of dietary fat consumption, quintile of combined dietary Six ecologic covariates.follow-up.The port.31 32 33 34method.guintile of covariates.follow-up.The port.					I20–I25).	marital status,	and resided in all	157,572 deaths			
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25 26 27 28 29 30 31 31 31 32 33 33 33 36 38using the absolute principal component analysis (APCA) PM2.5 source apportionment method.beer, wine, and other alcohol, quintile of dietary fat consumption, quintile of combined dietary vegetable, fruit, fiber consumption; Six ecologic covariates.Puerto Rico.during to T follow-up. beer, wine, and follow-up.selective report.				apportioned PM _{2.5} mass		and BMI ² ,		causes)			
26 27 28principal component analysis (APCA) PM2.5 source apportionment method.other alcohol, quintile of dietary fat consumption, quintile of combined dietary vegetable, fruit, fiber consumption;full of heat				-				~ <			
27principal componentother alcohol,follow-up.follow-up.follow-up.report.28analysis (APCA) PM2.5quintile of dietaryyyyy30source apportionmentfat consumption,yyyy31method.combined dietaryyyyyy33fiber consumption;fiber consumption;fiber consumption;pyyy36source apportsource apportsource apportsource apportsource apportsource apport33source apportsource apportsource apportsource apportsource apportsource apport31method.source apportsource apportsource apportsource apportsource apport33source apportsource apportsource apportsource apportsource apportsource apport33source apportsource apportsource apportsource apportsource apportsource apport34source apportsource apportsource apportsource apportsource apportsource apport36source apportsource apportsource apportsource apportsource apportsource apport38source apportsource apportsource apportsource apportsource apportsource apport38source apportsource apportsource apportsource apportsource apportsource apport38source apportsource				-			Puerto Rico.				
34 fiber consumption; 35 Six ecologic 36 covariates. 38 Subscription;						,		follow-up.	report.		
34 fiber consumption; 35 Six ecologic 36 covariates. 38 Subscription;								, U			
34 fiber consumption; 35 Six ecologic 36 covariates. 38 Subscription;						-					
34 fiber consumption; 35 Six ecologic 36 covariates. 38 Subscription;				method.		-			-		
34 fiber consumption; 35 Six ecologic 36 covariates. 38 Subscription;						-) gu			
35 36 36 Six ecologic 37 covariates. 38 Y											
						1 ,					
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						covariates.			-		
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41 42								ynt.			

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1 2							2021-(
3 4 5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data	Selective	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	58	Yang et al. 2018	Land use regression models were derived from street level measurements collected during two sampling campaigns conducted in 2014 and 2015.	Deaths were coded according to the International classification of Diseases, 10th Revision (ICD-10; WHO 2010) including natural cause mortality (A00–R99), overall cardiovascular disease (I00–I99) and overall respiratory disease (J00–J47 and J80–J99). Subcategories included Ischemic heart disease (IHD) (I20–I25), cerebrovascular disease (I60–I69), Pneumonia (J12–J18) and chronic obstructive pulmonary disease (COPD) (J40–I44	Age at entry, gender, individual smoking status, body mass index (BMI), physical activity, education level and monthly expenses; percentage of participants who were equal to or older than 65 years old, percentage of participants whose educational level was higher than secondary school, average income per month and	Data obtained for a cohort of people who were older than or equal to 65 years old.	There was no	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 interests.	No other potential sources of bias identified.
35 36 37				and I47).	percentage of smokers.		Protected b			
38 39 40 41 42							y copyright.			

Page 115 of 133

 36/bmjopen

No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete ි outcome dataය	Selective reporting	Conflict of interest	Other
		Probably Low	Low	Probably High	Low	Probably Low	Probably Low	Low	Low
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
	2011	estimate air pollution	hospitalization case is a	age, sex,	total number of	4-year	insufficient	declare they	potential
		concentrations and	record of hospitalization	preexisting	subjects along	follow-up	information	have no	sources of
		exposure assigned to	with the following	comorbidity, and	with those lost	period, 17,542	about	actual or	bias
		residential centroid.	International Statistical	neighborhood	during the	(3.9%) moved $\frac{d}{d}$	selective	potential	identified
			Classification of	socioeconomic	follow-up period.	out of the \exists	outcome to	competing	
			Diseases, 9th Revision	status. No		province and	judge for low	financial	
			codes, ICD-9, 410–414	individual data on		16,367 (3.6%)	risk, but	interests.	
			and 429.2or 10th	behavioral risk		died from other	indirect		
			Revision (ICD-10),	factors.		diseases,	evidence that		
			I20–I25, as the principal			leaving 🚊	suggests study		
			diagnosis (the most		101	418,826	was free of		
			responsible diagnosis) for			(92.5%)	selective		
			a hospital admission in			subjects at the 궐	report.		
			the hospitalization						
			database. A coronary			follow-up.			
			heart disease death is a			024			
			death record with			by g			
			coronary heart disease as			lues			
			the cause of death in the						
			provincial death			follow-up. 2024 by guest. Protected by			
			registration database.			cted			

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1 2 3 4										
4 5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	Selective	Conflict of interest	Other
8			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 13		r et al.	concentrations. Derived	incidence of	gender, marital	27,070	the rate of lost $\frac{1}{2}$		financial	sources of
13		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.		selective		identified.
16 17			measured at two regional	(International	use, physical		m	outcome to		
17			monitoring sites. Local	Classification of Diseases	activity, body mass		l ight	judge for low		
19			traffic-related EC	[ICD9] 410-414) and	index, living			risk, but		
20			emission contributions	cerebrovascular disease	conditions		Jope	indirect		
21 22			were estimated based on	(ICD9 430-438) in the	(employment) 	evidence that		
23			fuel-specific EC content	study population.	status, financial		<u></u> .	suggests study		
24			of exhaust PM ₁₀		problems).			was free of		
25 26			emission. Used the				on	selective		
27			traffic-related EC			· · · (April April	report.		
28			emissions as input to				19,			
29 30			calculate local EC				202			
31			concentrations, assuming					:		
32			absence of other local EC				on April 19, 2024 by guest. Protected by			
33 34			sources. Also assumed				est.			
35			that dispersion dynamics				Prot	1		
36			of EC are identical to				ecte			
37 38			those of PM ₁₀ .				j ĝ			
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2 3 4										
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete ရှိ outcome dataယ	5	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 38	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,	Data obtained for a cohort of postmenopausal women.	There was no information on to the rate of lost 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 financial interests.	No other potential sources of bias identified.
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			BMJ Oper	n	36/bmjopen-2			Page 118
No. Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	36/bmjopen-2021-049516 on 3 Incomplete outcome data	Selective reporting	Conflict of interest	Other
	High	Low	Probably Low	Low	Low	Probably Low	Low	Low
62 Rahmatini a et al. 2021		Daily non-accidental 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).	Models adjusted for time, temperature, relative humidity, atmospheric pressure, PM2.5 data, Day of week (DOW) and public holidays.	Study included 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 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 of this article declare that they have no conflict of interests.	No other potential sources of bias identified.

1235No.StudyExposure assessmentOutcome assessmentConfounding biasSelection bias6863Liu et al. 2021bProbably LowProbably LowProbably LowOutcome assessmentConfounding biasSelection bias963Liu et al. 2021bProbably LowProbably LowProbably LowProbably LowLow11122021bAnnual county-level exposures of PM2.5 and its constituents for each participant were assessedThe three cardiovascular events as health outcomes: 1) total cardiovascular disease, (illiteracy, primaryAll of participants were drawn from the China Family	36/bmjopen-2021-0495 Incomplete On Selective Col	
5No.StudyExposure assessmentOutcome assessmentConfounding biasSelection bias8963Liu et al. 2021bProbably LowProbably LowProbably LowLow11121314Annual county-level exposures of PM2.5 and its constituents for eachThe three cardiovascular 	49	
9 1063Liu et al. 2021bAnnual county-level exposures of PM2.5 and its constituents for eachThe three cardiovascular events as health outcomes: 1) totalModel adjusted for age, gender, education levelAll of participants were drawn from the	Incomplete $\overset{\circ}{\overset{\circ}{\overset{\circ}{\overset{\circ}{\overset{\circ}{\overset{\circ}{\overset{\circ}{\overset{\circ}$	nflict of terest Other
1063Liu et al. 2021bAnnual county-level exposures of PM2.5 and its constituents for eachThe three cardiovascular 	Low Y Probably Low	Low Low
14 15 16 17participant were assessed by aggregating satellite-derived estimates at a monthly time-scale 20 21 22 21 22 23 23 24cardiovascular disease, including but not limited to hypertension and 3) stroke were defined according to the Disease Classification Codebook for Chinese Family PanelChina Family Panel Studies dowe, household by Peking Institute of Social Science23 24 25 261Social Science strata of ≤ 15,000, 15,000 - 40,000, and 40,000Survey (ISSS) in +, grouped according to the upper and lower quartiles), urbanicity 44 defined by CFPS participants' home addresses).Survey of social-demograp hy in China.28 29 30 31111139311130311131 33 34111133 34 34111134 35 36111135 36 37111139111139111131 34 35111132 34 34111134 35 36111135 36 37111136 37111137 38111138 3911113911 <td< td=""><td>cluded 4,331 adults ho completed ree waves of for information they about no k selective com outcome to finan- judge for low inter- risk, but pers indirect relate evidence that s that suggests have study was appe- free of influ- selective the v on April 10 report. report. report</td><td>tionship at could</td></td<>	cluded 4,331 adults ho completed ree waves of for information they about no k selective com outcome to finan- judge for low inter- risk, but pers indirect relate evidence that s that suggests have study was appe- free of influ- selective the v on April 10 report. report. report	tionship at could

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1 2 3 4							Incomplete o			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete		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		declared	potential
12			approximately 1-km2	identified according to	breastfeeding	live births that	the rate of lost $\frac{1}{2}$	information	that there is	sources of
13 14			was derived using	International	status at the time	occurred	the rate of lost	about	no conflict	bias
15			multiple satellite-based	Classification of Diseases	of discharge,	between April 1st	d fro	selective	of interest.	identified.
16 17			retrievals of aerosol	[ICD]-10: J45.	maternal smoking	2006 and March	m	outcome to		
17			optical depth in		during pregnancy,	31st 2014 in the	nttp://bmjopen.bmj.com/	judge for low		
19			combination with a		maternal atopy,	Province of		risk, but		
20			chemical transport model,		gestational age and	Ontario, Canada.	Jope	indirect		
21 22			and enhanced through		birth weight.	Mother-infant)	evidence that		
23			statistical incorporation		L L	pair data were	<u></u> .	suggests		
24			of ground- based			obtained from		study was		
25 26			observations (including			the Better	on			
27			BC).			Outcomes	April April	selective		
28						Registry &	, PL	report.		
29 30						Network	April 19, 2024 by guest			
31						(BORN) Ontario,				
32						a province wide) gu			
33 34						birth registry that				
35						captures	Prot			
36						perinatal health	Protected by copyright.			
37 38						information.	j j			
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40							pyriq			
41 42							ynt.			
42							nt.			

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1 2 3 4							36/bm)open-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete of outcome data	Selective	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	65	Rodins et al. 2020	The study used the validated, time-dependent, three-dimensional European Air Pollution Dispersion chemistry transport model (EURAD) to estimate the exposure to EC.	Cardiovascular outcomes in the HNR Study were determined by an independent endpoint committee based on self-reports, physician and next-of-kin interviews, and medical records.	Model adjusted for age, sex, individual and neighborhood SES, BMI, nighttime traffic noise exposure and lifestyle factors: smoking, alcohol consumption, physical activity and nutritional pattern.	The study used baseline (2000–2003) and 14 years follow-up data from the German HNR Study, an ongoing population-based prospective cohort study.	There was no 22. Information on Down the rate of lost no 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 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.
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			BMJ Oper	1	36/bmjopen-2021-0495			Page 122
					-2021-0495			
No. Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete 0 on outcome data 3 ≤	Selective reporting	Conflict of interest	Other
	Probably Low	Low	Probably High	Low	Low X	Probably Low	Low	Low
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 Downloaded from http://bmjopen.bmj.com/ (ED) visits were obtained, from http://bmjopen.bmj.com/ all outcome data. However, bmj.com/ 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 no conflict of interest.	No other potential sources of bias identified.

Pag	e 123 o	of 133			BMJ Oper	1	36/bmjop			
1 2 3 4							36/bmjopen-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete og outcome data∝	Selective	Conflict of interest	Other
8			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	insufficient	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 22			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	suggests	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 g	100 01	influence	
27					activity, alcohol	and 20 on CIMT,	analyses 6011.줮	selective	the work	
28					consumption,	respectively. The	119,	report.	reported in	
29 30					median income	number of			this paper.	
30 31					level in residential	participants	2024 by			
32					area, systolic blood	included in the	ע פר			
33					pressure and being	plaque analyses	r guest.			
34 35					born outside of	were 5807 and in	Prc			
36					Sweden.	the CIMT				
37						analyses 6011.	Protected by			
38 39										
40							copyright			
41 42							ght.			

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1 2 3 4							36/bmjopen-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete og outcome data∞	Selective	Conflict of interest	Other
8			Probably High	Probably Low	Probably High	Low	Low X	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 R	There was	The authors	No other
11		al. 2019b	routine air quality	Cardiac Catheterization	seasonality,	all patients	for all patients \bigtriangledown		declare that	potential
12 13			monitoring site operated	Laboratory (Cath Lab) at	long-term trends,	treated at the	were obtained, $\frac{5}{2}$	information	they have	sources of
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 17			Environmental	within 15 miles of the		Laboratory (Cath	data. However,	outcome to	interests.	
18			Conservation	pollution monitoring		Lab) at URMC	any potential	judge for low		
19			continuously throughout	station in Rochester were		in Rochester, NY	errors or missing data	risk, but		
20 21			the study period	included. American		for STEMI				
22			(2005–2016). There was	College of Cardiology		throughout the	did not depend			
23 24			no information about	(ACC)/American Heart Association (AHA)		study period (2005–2016).	on air pollution	suggests study was		
24 25			missing data.	guidelines were used at		(2003–2016).	く	free of		
26				the time of Cath Lab			on A			
27 28				admission to diagnose				report.		
20				STEMI.			9, 2	Teport.		
30							April 19, 2024 by guest			
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41 42							ight.			

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1 2 3 4							36/bmjopen-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete og outcome data∞ ≤	Selective	Conflict of interest	Other
8 9			Probably Low	Low	Probably Low	Low	Probably Low	Probably Low	Low	Low
9 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 13			monitoring data, and	Diseases, Ninth Revision	subcohort,	individuals in	and <u>S</u>	information	have no	sources of
14			high-resolution	(ICD-9) codes 410–414	smoking status,	two cohorts from	comprehensive		actual or	bias
15			dispersion models, the	and ICD-10 I20-25 codes	alcohol	Gothenburg, four	national patien	selective	potential	identified.
16 17			study calculated source	were used to define IHD	consumption in	pooled cohorts	and death \exists	outcome to	competing	
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	,	interests.	
20 21			wear, traffic exhaust,	codes I61–I65 were used	activity, marital	from Umeå. In	loss to	indirect		
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 25			Gothenburg, Stockholm,		index by	included from all	of interest.	study was		
26			and Umeå.		occupation,	study areas.	Missing 9	free of		
27					education level,		information forg			
28 29					occupation status, and mean		variables $\leq \frac{1}{9}$ 5% not \geq			
30					neighborhood		5% not specified.			
31					individual income		specified.			
32 33					in persons of		' guest			
34					working age by		• *			
35					Small Areas for		rote			
36 37					Market Statistics.		Protected by			
38					inter Statistics.					
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3 4							-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete of outcome data	Selective	Conflict of interest	Other
8			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 g	insufficient	declare that	potential
12 13			2010 were estimated at	diagnosis of International	status, smoking	cohorts within	106,727 Departicipants with complete	information	they have	sources of
13			the study participants'	Classification of	duration, smoking	the ELAPSE	with complete	about	no known	bias
15			baseline residential	Diseases, 9th Revision	intensity,	project with	air pollution	selective	competing	identified.
16 17			addresses, using	(ICD-9) codes 490–492,	body-mass index,	available	exposure data,	outcome to	financial	
17			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	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 26			European Environment				participants 9	free of	influence	
27			Agency (EEA) AirBase				with missing		the work	
28			for PM2.5, NO2, and O3,				information on	report.	reported in	
29 30			and ESCAPE monitoring				confounders. NO		this paper.	
31			data for BC as the							
32			dependent variable. BC				by guest.			
33 34			was measured by the							
35			reflectance of PM2.5				Pro			
36			filters and expressed in				Protected			
37 38			absorbance units.							
38 39							by copyright			
40							pyri			
41 42							ght.			

Page 127 of 13	33	33 BMJ Open								86/bmjop								
1 2 3 4 5 6 7Table S7 Ass	ssessr	nent of certaint	ty of	evidence for the o	outc	omes.							36/bmjopen-2021-049516 on 3 N					
8					Reas	sons for downgrading							a VRea	asons for upgrading				Final
9 _{Evidence} 10 11	A1	Rationale	A2	Rationale	A3		A4	Rationale	A5	Rationale	B1	Rationale	2022 D	Rationale	B3	Rationale	Overall	certainty assessment
12 1 ⁴ 3 ^{ute} effects of 114 ² /EC on CVD in 15 15 16 1 ¹⁰ / ¹⁰ / ¹⁰	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	wnloadee from	Confounders would shift the RR in both directions	0	Evidence of increase in risk with increasing exposure	-1	Low
18 1,Quite effects of BC 20 _BC/EC on CVD in 21 22 ^{12,5-adjusted} 232del 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	http://bmjopen.bmj.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 25 C/EC on CVD in 28 M _{2.5} -unadjusted 29 30 del	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	m/ on April⊄19, 2024	Confounders would shift the RR in both directions	0	No evidence of a clear increasing risk with exposure	0	Moderate
						r diseases; RES: respirator <u>;</u> = large RR; B2 = all confo						val; CI: confidence interva e gradient.	-	= limitations in studies	(risk	of bias); A2 =		

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					BMJ Ope	en			36/bmjopen-2021-049516		
ble S8 The p-value	calculatio	n process for each	n study using RR	g RR, CI low CI low	and CI high	ı. InRR	InCI low	InCI high	-049516 on 3 Ma	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	N 0.013202	0.377780	0.705594
	3	Atkinson,2016	0.987000	0.973000	1.001000	0.013085	0.027371	0.001000	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	5 ^{0.088539}	0.223661	0.823021
	7	Sarnat,2015	1.038000	1.005000	1.073000	0.037296	0.004988	0.070458	B 0.016702	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
1. I. D.	11	Winquist,2015	1.048000	1.012000	1.085000	0.046884	0.011929	0.081580	0.017768	2.638621	0.008324
diovascular 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	0.005017	3.360055	0.000779
	16	Kim,2015	1.031000	0.935000	1.133000	0.030529	0.067209	0.124869	<u>0</u> .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	4 by 0.010195	0.098036	0.921904
	19	Heo,2014	1.006000	0.994000	1.017000	0.005982	0.006018	0.016857	Que 0.005836	1.025116	0.305308
	20	Basagana,2015	0.979000	0.944000	1.016000	0.021224	0.057629	0.015873	St 0.018751	1.131889	0.257681
	21	Basagana,2015	1.026000	1.006000	1.047000	0.025668	0.005982	0.045929	Po 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

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									36/bmjopen-2021-049516		
Table S8 The p-value	ue calculatio	n process for eac	h study using	g RR, CI low	v and CI high CI high	n. (continued	l) InCI low	lnCI high	6 on 3 Ma	Z	p-values
	1	Atkinson,2016	1.013000	0.993000	1.033000	0.012916	0.007025	0.032467	8 ^{0.010074}	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	no 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	ਰ ਰਿ ^{0.006092}	0.818666	0.412977
	7	Son,2012	0.989000	0.956000	1.024000	0.011061	0.044997	0.023717	B 0.017529	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
Decoinctony Discosso	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	00 0.090672	0.415806	0.677552
	15	Kim,2012	1.100000	0.949000	1.270000	0.095310	0.052346	0.239017	₽ <u>0.074327</u>	1.282302	0.199737
	16	Cakmak,2009	1.036000	1.031000	1.041000	0.035367	0.030529	0.040182	<u>0</u> 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	b 0.003328	0.902791	0.366637

group and Study ID		Relative Risk (95% Cl)
Asia		
Geng,2013	+	1.012 (1.002, 1.021)
Wang,2019a	+	1.011 (0.999, 1.023)
Gong,2019	+	1.002 (1.001, 1.003)
Huang,2012	+	1.005 (0.998, 1.010)
Lin,2016a	+	1.002 (0.999, 1.005)
Son,2012		1.001 (0.981, 1.021)
Heo,2014	+	1.006 (0.994, 1.017)
Subgroup, DL (I ² = 21.5%, p = 0.266)	•	1.003 (1.001, 1.005)
Europe		
Basagana,2015	+ <u>i</u>	0.979 (0.944, 1.016)
Ostro,2015a	+	0.994 (0.953, 1.038)
Ostro,2015a		1.005 (0.979, 1.031)
Atkinson,2016	-	0.987 (0.973, 1.001)
Subgroup, DL (I ² = 0.0%, p = 0.602)	\diamond	0.990 (0.979, 1.001)
America		
Ito,2011	_ + +	1.003 (0.982, 1.024)
Maynard,2007	++ +	1.076 (0.980, 1.179)
Ostro,2007	- -	1.026 (1.004, 1.049)
Kim,2015 -		- 1.031 (0.935, 1.133)
Subgroup, DL (I ² = 20.8%, p = 0.285)	\diamond	1.017 (0.998, 1.037)
Heterogeneity between groups: p = 0.030	5	
1	1	1.25

Figure S1 Impact of short-term exposure to BC/EC on cardiovascular mortality stratified by

geographical locations.

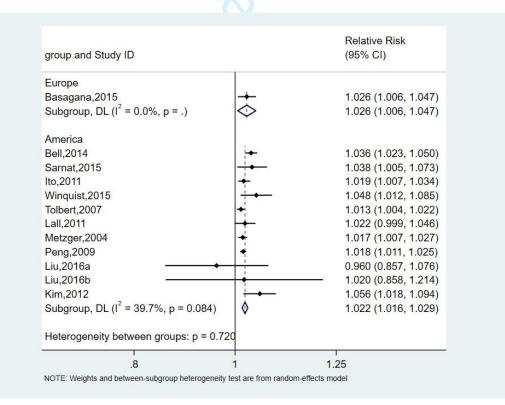


Figure S2 Impact of short-term exposure to BC/EC on cardiovascular morbidity stratified by

geographical locations.

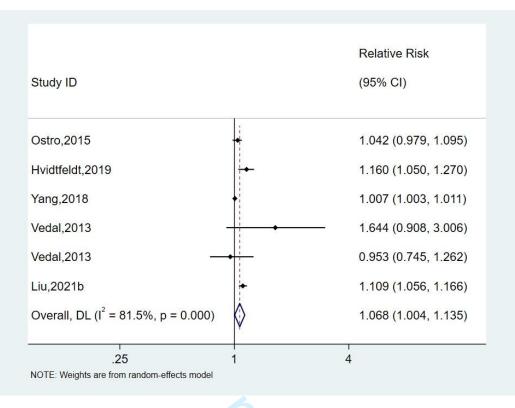


Figure S3 Impact of long-term exposure to BC/EC on cardiovascular diseases.

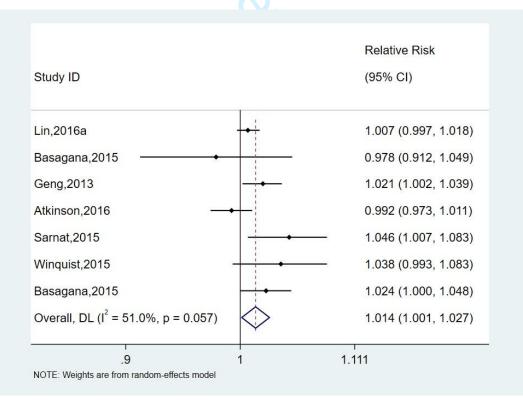


Figure S4 Impact of short-term exposure to BC/EC on cardiovascular diseases in the

 $PM_{2.5}\mbox{-}adjusted\ model.$



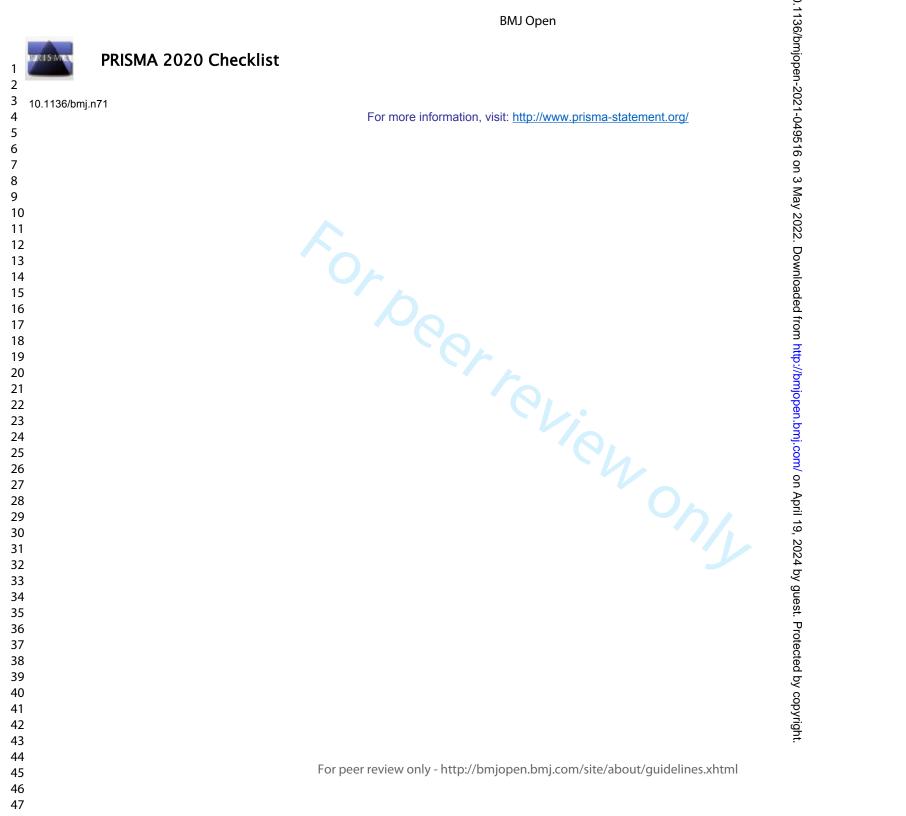
PRISMA 2020 Checklist

		BMJ Open	1136	Page 132 of 1
	MAA 0	020 Checklist	36/bmiopen	
PRIS		UZU Checklist	open	
			-20	
Section and Topic	ltem #	Checklist item	21-049	Location where item is reported
TITLE			0 2 0	
Title	1	Identify the report as a systematic review.	on	#1
ABSTRACT			≅	
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	a <	#3-4
INTRODUCTION				
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				
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 date when each source was last searched or consulted.	Identify studies. Specify the	#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 rev and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in		#10
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of a 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 study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results		#10-11
7	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, fundir assumptions made about any missing or unclear information.	o g sources). Describe any ⊖	#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 ma study and whether they worked independently, and if applicable, details of automation tools used in the process.	<u>ع.</u> ny reviewers assessed each ص	#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 inter comparing against the planned groups for each synthesis (item #5)).	ention characteristics and Ω	#11
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summ conversions.	ary statistics, or data	#11, 14-15
5	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	rote	#11
1 3 9	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was perf model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	ormed, describe the	#11-12
•	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysi	< ◙, meta-regression).	#11-12
	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 used to assess certainty (or confidence) in the body of syldboce for all butsomern		#11



PRISMA 2020 Checklist

ge 133 of 133		BMJ Open 13	
PRIS	MA 2	020 Checklist	
Section and Topic	ltem #	Checklist item	Location where iten is reported
assessment			
RESULTS			
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 effed 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 optime 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 assess	#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
	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	с	
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 red iew.	#34
Competing interests	26	Declare any competing interests of review authors. <t< td=""><td>#35</td></t<>	#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

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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

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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 19th, 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 μ g/m³ in the elderly; (ii) Long-term exposure to BC/EC was associated with

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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

 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.¹ Elemental carbon (EC), another carbonaceous material with a graphitic structure, is commonly measured by thermal or thermo-optical method.^{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 PM_{2.5}, are well documented. In 2017, a total of 2.94 million deaths resulted from ambient PM worldwide.³⁻⁵ PM_{2.5} 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.^{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.^{8, 9} 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.⁴ 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.¹³

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.¹⁴ 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).^{15, 16} 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

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with Yang et al. 2019¹⁹, 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

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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.²⁰ In addition, the estimate was converted to a

standardized increment (1 μ 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.^{21, 22} 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.²³ In addition, if the same cohort data were analyzed in different studies and the latest study was included.²⁴⁻²⁶

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.²⁹ 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 $PM_{2.5}$ is a potential confounder in assessing the health effects of $PM_{2.5}$ constituents.⁷ For overall and outcome analysis, PM_{2.5}-adjusted estimates and PM_{2.5}-unadjusted estimates in the models were combined, respectively where more three estimates were available. Regarding than the subgroup analysis, PM_{2.5}-unadjusted estimates were analyzed, while PM_{2.5}-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,

Page 15 of 133

BMJ Open

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^{covariate}. Space3 is Space1 times Space2. Space3 is the total analysis search space. Search spaces were computed by the method introduced in Young et al, 2019.³⁰

The p-value plot was used to inspect the distribution condition of the p-values.³¹ 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.³¹ 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.^{32, 33} Of these, 70 fulfilled the inclusion criteria (Figure 1).^{7, 21-26, 34-96} 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

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Overall, short-term exposure to BC/EC was associated with an increased risk of cardiovascular diseases (RR=1.007 per 1 μ 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 μ 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 μ g/m³, 95% CI: 1.006–1.016), and then diminished on lag 1 (RR=1.005 per 1 μ g/m³, 95% CI: 1.002–1.008) and lag 2 (RR=1.002 per 1 μ 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/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 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.²³ In addition, just one study in Asia performed the short-term effects of BC/EC on stroke morbidity (Figure S2).⁶⁶

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).

	BMJ Open				36/bmjopen-2021-049516			Page		
Fable 1 Short-term impacts of BC/EC on cardiovasc	cular and re		eases in different mod	els		-049516 on 3		2.5-adjusted model		
Subgroup Analysis	No. of Studies	No. of Estimates	Relative Risk (95%CI)	I ²	Egger regression test (p value)	No. of a Studies	No. of	Relative Risk (95%CI)	I ²	
Cardiovascular Diseases						22. [
\ge						Dowi				
Il population	20	22	1.008 (1.004, 1.012)	64.40%	0.007	6 f	7	1.014 (1.001, 1.027)	51.00%	
telative risk adjusted for publication bias with trim and ill method	24	26	1.007 (1.002, 1.011)	—	_	Downloaded from http://bmjopen.bmj.com/ on 6 4 4 4	_	_	_	
ensitive analysis on study of partial temporal overlap rom 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, 1.028)	87.40%	—	//bn	—	—	—	
Dutcome						njope				
Iorbidity	12	12	1.022 (1.016, 1.029)	37.20%	0.163	4 b	5	1.018 (1.006, 1.031)	39.50%	
Iortality	14	15	1.003 (1.001, 1.006)	29.70%	0.266	4 10	4	1.006 (0.993, 1.019)	42.90%	
Respiratory Diseases) mc				
\ge										
All population	16	18	1.010 (0.996, 1.025)	87.20%	0.627	April 19,	8	1.002 (0.990, 1.014)	43.80%	
ensitive analysis on study of partial temporal overlap rom the same geographical location	12	12	1.008 (0.992, 1.023)	90.30%	0.449	19, 2024	_	_	_	
.65	3	4	1.038 (1.006, 1.071)	82.90%	—	— by	—	—	_	
Jutcome						guest.				
Aorbidity	10	10	1.012 (0.993, 1.031)	91.80%	0.671	3 . 3 . 7	5	0.996 (0.987, 1.004)	0	
Aortality	10	11	1.013 (0.997, 1.030)	66.40%	0.328	Protected by copyright.	3	1.017 (0.985, 1.050)	48.30%	

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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*10⁻⁴⁵ 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.

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

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.^{25, 60, 68, 75} 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).²⁴

3.4 Results from the PM_{2.5}-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 μ 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_{2.5}-unadjusted model. In addition, the impact of BC/EC on cardiovascular morbidity in the PM_{2.5}-adjusted model (RR=1.018 per 1 μ g/m³, 95% CI: 1.006-1.031) was consistent with the results in the PM_{2.5}-unadjusted model (RR=1.022 per 1 μ g/m³, 95% CI: 1.016-1.029). However, an increased risk was found between BC/EC and cardiovascular mortality in the PM_{2.5}-unadjusted model (RR=1.003 per 1 μ g/m³, 95% CI: 1.001-1.006), while no association was observed in the PM_{2.5}-adjusted model (RR=1.006 per 1 μ 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 μ g/m³, 95% CI: 1.002-1.010) by eliminating studies with partial overlap from the same geographical location.^{21, 23, 38, 80} In addition, no statistical significance was observed (RR=1.008 per 1 μ g/m³, 95% CI: 0.992-1.023) between respiratory diseases and BC/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 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.

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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_{2.5}-adjusted model and the PM_{2.5}-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_{2.5}-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_{2.5}-unadjusted model and PM_{2.5}-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 PM2.5-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 PM25-adjusted model and PM25-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 $PM_{2.5}$ -unadjusted model was evaluated as "moderate". We downgraded one level for publication bias, hence the estimate was adjusted using the trim and fill method.²⁹ 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

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clearance decline with long-term exposure to pollutants and increasing age.^{5, 101} 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 $PM_{2.5}$.¹⁰²

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.¹⁰³ 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.¹⁰⁴ 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.¹⁰⁴ On 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 PM₁₀ and PM_{2.5}, which performed by Mustafic et al, 2012.¹⁰⁵ A critique was given in Young et al, 2019, who used p-value plots to call those claims into question.³⁰

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 PM2.5 when assessing the health effect of PM_{2.5} constituents. Mostofsky et al. showed that PM_{2.5} may be associated with both health and its constituents. Constituents having closer association with PM_{2.5} may illustrate a stronger association with diseases. Therefore, the results of PM_{2.5}-unadjusted model could introduce bias.⁷ 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.

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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 all authors.

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Competing interests

We declare that all authors have no competing interests.

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Data sharing statement

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

information.

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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.

BMJ Open

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_{2.5} 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.

BMJ Open

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.

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.
 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

Page 39 of 133

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BMJ Open

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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_{2.5}-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.

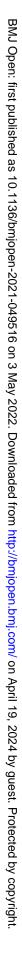
 Table S8 Assessment of certainty of evidence for the outcomes.

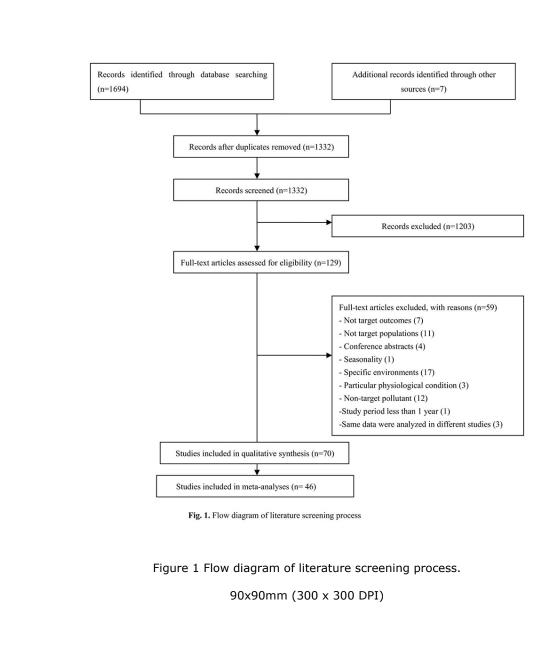
Figure S1 Impact of short-term exposure to BC/EC on cardiovascular mortality stratified by geographical locations.

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_{2.5}-adjusted model.





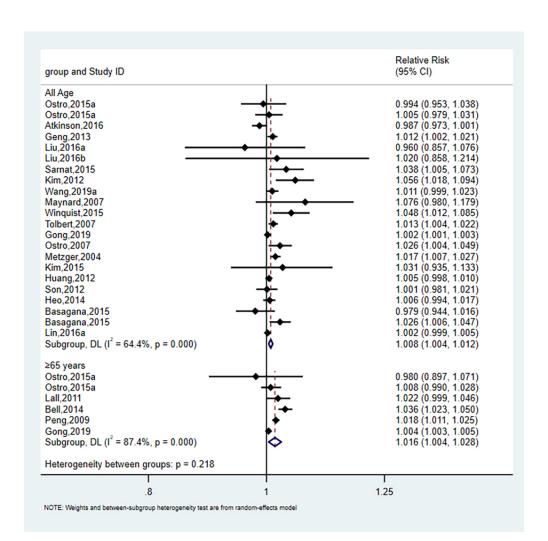
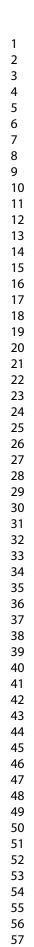


Figure 2 Impact of short-term exposure to BC/EC on cardiovascular diseases in the PM2.5-unadjusted model.

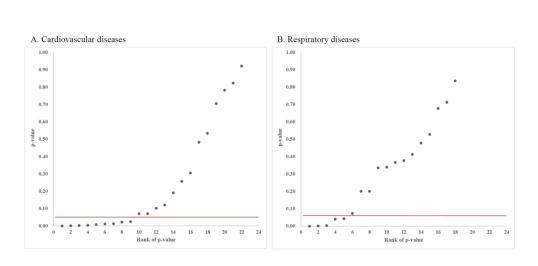
90x90mm (300 x 300 DPI)

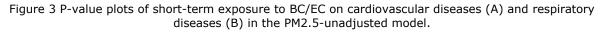
BMJ Open: first published as 10.1136/bmjopen-2021-049516 on 3 May 2022. Downloaded from http://bmjopen.bmj.com/ on April 19, 2024 by guest. Protected by copyright.



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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^a, Yue Hu^a, Yan Ma^a, Liangzhen Jiang^a, Xinyi Wang^c, Anchen Shi^d, Junxian Zhao^a, Yunxu Liu^a, Yafei Liu^a, Jing Tang^a, Xiayang Li^a, Xiaoling Zhang^{*b}, Yong Guo^e, Shigong Wang^{*b}

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R. R. ONI

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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_{2.5}-adjusted model.

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No.	Search Strategy	<u> </u>
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#3	"PM".tw.	2022
#4	or/1,2,3	
#5	"EC" /or "BC".tw.	Downloaded
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#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.	d
#12	cardio*/or cardiop*/or cardior*/or heart/or coronary/or vascular/or blood/or cardiac.ti,ab.	- <u>m</u> jop e
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udy	ristics Study Design	of included Country	studies in the s Study Period	Systematic Outcome	review and m	eta-analys Pollutant	is. ICD code	A G G G G G G G G G G G G G G G G G G G	
son et al. 2016	TS	UK	2011-2012	Mortality	All	BC,EC	ICD-10	CVD(ICD-10:100-199),RES(ICD-10:100-199) 8	_
t al. 2014	TS	USA	2000-2004	Morbidity	≥65	BC	ICD-9	RES[COPD(ICD-9-CM:490-492,RTI(ICD-9-CM:462)466, 480-487)];CVD[HF(ICD-9-CM:428),Heart Rhyt Disturbances(ICD-9-CM:426-427), Cerebrovascular gvents(ICD-9-CM:430-438),IHD(ICD-9-CM:410-414,	ım
al. 2014	TS	China	2005-2011	Morbidity	≥18	BC	ICD-10	429),PVD(ICD-9-CM:440-448)] Asthma(ICD-10:J45)	
et al. 2013	TS	China	2007-2008	Mortality	All	BC	ICD-10	CVD(ICD-10:I00-I99),RES(ICD-10:J00-J98)	
t al. 2014	TS	China	2007-2012	Morbidity	0-14	BC	ICD-10	Asthma(ICD-10:J45)	
et al. 2015a	CS	Spain, Greece	2008-2009 (Athens), 2009-2010(Barc elona)	Mortality	All	BC	ICD-10	CVD(ICD-10:100-I99),RES(ICD-10:J00-J98) Top Asthma(ICD-10:J45) Top CVD(ICD-10:100-I99),RES(ICD-10:J00-J99) Top CVD(ICD-10:100-I99),RES(ICD-10:J00-J99) Top CVD(ICD-10:100-I99),RES(ICD-10:J00-J99) Top G Top <	
i 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)	
etti and Schwartz	CS	USA	1995-1999	Morbidity	≥65	BC	ICD-9	MI(ICD-9:410),Pneumonia (ICD-9: 480–487)	
al. 2016a	TS	USA	2008-2013	Morbidity	All	EC	ICD-9	CVD(ICD-9:390-429),Stroke(ICD-9:430-438),RES(CD-9:460-519),COPD(ICD-9:490-492,494,496),Pneumo CD-9:480-486),Asthma(ICD-9:493),SSID(ICD-9:78	nia(I
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),Pneum (ICD-9:480-486),Asthma(ICD-9:493) CVD[IHD(ICD9:410-414),Cardiac Dysrhythmias(ICD) 9:427),CHF(ICD9:428),Other CVD	onia
t 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 (ICD9:433-437,440,443-445,451-453)],RES[Pneumcara(ICD9:480-486),COPD (ICD:491,492,496),Asthma/Wheeze (ICD9:493,786.	
t al. 2012	TS	USA	2003-2007	Morbidity	All	EC	ICD-9	CVD(ICD-9:390-459),RES(ICD-9:460-519)	
								(ICD:491,492,496),Asthma/Wheeze (ICD9:493,786.),Other RES(ICD9:460–466,477)]	

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	Table S2 Chara	cteristics (ofincluded	studies in the	systematic re	view and	meta-analys	ic	36/bmjopen-2021-049516
	Study	Study Design	Country	Study Period	Outcome	Age	Pollutant	ICD code	O D Diseases
	Ostro et al. 2009	TS	USA	2000-2003	Morbidity	<19	EC	ICD9	RES(ICD-9:460-519),Asthma(ICD-9:493),Acute brochitis(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-10:100-198),CVD(ICD-10:100-199)
	Peng et al. 2009	TS	USA	2000-2006	Morbidity	≥65	EC	ICD-9	CVD[Cardiac Dysrhythmias(ICD-9:428),Heart Rhyton Disturbances(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, 20, 20, 20, 20, 20, 20, 20, 20, 20, 2
	Levy et al. 2012	TS	USA	2000-2008	Morbidity	≥65	EC	ICD-9	CVD(ICD-9:390-459),RES(ICD-9:464-466 and 480-77).
	Son et al. 2012	TS	Korea	2008-2009	Mortality	All	EC	ICD-10	CVD(ICD-10:100-199),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, ICD-10	eg CVD(ICD-9:390-459,ICD-10:I00-I99),RES(ICD-9:469-519,ICD-10:J00-J99) ع.
	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 10:I21-I22),Stroke(ICD-10:I60-I69)
	Lin et al. 2016a	TS	China	2007-2011	Mortality	All	EC	ICD-10	CVD(ICD-10:100-199) 9
	Cao et al. 2012	TS	China	2004-2008	Mortality	All	EC	ICD-10	CVD(ICD-10:100-199),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-J99)
	Zhou et al. 2011	TS	USA	2002-2004	Mortality	All	EC	ICD-10	CVD(ICD-10:I01-I99),RES(ICD-10:J00-J99) 8
	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-9:410-414,427,
	Ostro et al. 2007	TS	USA	2000-2003	Mortality	All	EC	ICD-10	428,433-437,440,443-445,451-453) CVD(ICD-10:100-199),RES(ICD-10:100-198) St
	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)
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Table S2 Charac	cteristics of Study Design	of included : Country	studies in the Study Period	systematic Outcome	review and me	eta-analys Pollutant	is. ICD code	21 -04 95 16 0 0 0 3 3 3 seases ay	
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)	
								CVD[IHD(ICD-9:410-414),AMI(ICD-9:410),cardiaco	
letzger et al. 2004	TS	USA	1993-2000	Morbidity	All	EC	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)]	
far et al. 2000	TS	USA	1995-1997	Mortality	All	EC	ICD-9	CVD(ICD-9:390-448.9)	
Vang et al. 2019a	TS	China	2013-2015	Mortality	All	EC	ICD-10	CVD(ICD-9:390-448.9) Description CVD(ICD-10:I00-I99),RES(ICD-10:J00-J99) Description Stroke(ICD-10:I60-I66) Description CVD(ICD-10:I00-I99) Description	
lin et al. 2016b	TS	China	2007-2011	Mortality	All	EC	ICD-10	Stroke(ICD-10:160-166)	
Ostro et al. 2008	TS	USA	2000-2003	Mortality	All	EC	ICD-10	CVD(ICD-10:100-199)	
to et al. 2011	TS	USA	2000-2006	Morbidity, Mortality	≥40	EC	ICD-9, ICD-10	CVD[Hypertensive Diseases(ICD-9:402,ICD-10:111]] (ICD-9:414,ICD-10:125),Dysrhythmias(ICD-9:427,ICD-10:148),HF(ICD-9:428,ICD-10:150),Stroke(ICD-9 9,ICD-10:160-169)]	9:430-43
Chen et al. 2014	TS	China	2004-2008	Morbidity	All	EC	ICD-9	Stroke[Ischemic Stroke(ICD-9:433-434),Hemorrhagi	
Fomic'-Spiric' et al. 2019	CS	Serbia	2012-2014	Morbidity	≥18	BC	ICD-10	4llergic 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:I01-I52),Stroke(ICD-9,430-438,ICD-10:I60-I69),RES(ICD-9:460-519,ICD- 99)	10:J00-J
Sinclair et al. 2010	TS	USA	1998-2002	Morbidity	All	EC	NR		
Krall et al. 2013	TS	USA	2000-2005	Mortality	All	EC	NR	Asinma, OKTI, LKTI D CVD and RES(NR) 000000000000000000000000000000000000	
Cakmak et al. 2009	TS	Canada	2001-2006	Morbidity	All	EC	ICD-9	RES(ICD-9:460-519)	

Page 51	of 133
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Table S2 Charact	eristics o	f included		ystematic re	eview and n	neta-analysi	is. ICD	9
Study	Design	Country	Study Period	Outcome	Age	Pollutant	code	မ်းseases ဆ
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),COPD(ICD),C491,492,496),URTI(ICD-9:460-465,460.0,477),Pneumonia (ICD-9:480-486),Bronchiolitis(ICD-9:466.1,466.11,466.11),466.19)]
Lall et al. 2011	TS	USA	2001-2002	Morbidity	≥65	EC	ICD-9	RES[Pneumonia(ICD-9:480-486),COPD(ICD-9:490, Acute Bronchitis and Bronchiolitis(ICD-9:466),Asthma(ICD-9:493)],CVDB ysrhythmia(ICD-9:427),IHD(ICD-9:410-414),HF(ICD-9:4 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	BC	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
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	PRES[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)] 19 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)

ncluded studies i Stud Perio USA 2000-2 USA 2001-2 USA 2001-2 Canada 1999-2 Denmark 1993-2 USA 1988-2	y Outcome od Outcome 010 Morbidity 006 Morbidity, 007 Mortality 002 Morbidity, Morbidity, 015 Mortality	e review and m Age 2-16 all (mortality), $\geq 65(morbidity)$ ≥ 30 45-85 50-64	eta-analys Pollutant EC EC EC BC	ICD code ICD-9 ICD-10 ICD-10 ICD-9,	in Softmjöpen-2021-049516 Asthma(codes beginning with 493), Wheeze (ICD-9: 20:07) CVD(ICD-10:101-179), RES(ICD-10:J00-J99) CVD(ICD-10:101-179), RES(ICD-10:J00-J99) CVD(ICD-10:100-199), IHD(ICD-10:120-125), Pulmor ary (ICD-10:C34, J00-J98) COPD(ICD-9:490, 492, 496, ICD10:140, 144)	
Period USA 2000-2 USA 2001-2 USA 2001-2 Canada 1999-2 Denmark 1993-2	od 010 Morbidity 006 Morbidity, 007 Mortality 002 Morbidity, 005 Mortality	2-16 all (mortality), ≥65(morbidity) ≥30 45-85	EC EC EC	ICD-9 ICD-9, ICD-10 ICD-10 ICD-9,	Asthma(codes beginning with 493),Wheeze (ICD-9: 20.07)	
USA 2001-2 USA 2001-2 Canada 1999-2 Denmark 1993-2	006 Morbidity, Mortality 007 Mortality 002 Morbidity, Morbidity, 015 Mortality	all (mortality), ≥65(morbidity) ≥30 45-85	EC EC	ICD-9, ICD-10 ICD-10 ICD-9,	CVD(ICD-10:I01-I79),RES(ICD-10:J00-J99)	
USA 2001-2 Canada 1999-2 Denmark 1993-2	006 Mortality 007 Mortality 002 Morbidity, Mortality 015 Mortality	≥65(morbidity) ≥30 45-85	EC	ICD-10 ICD-10 ICD-9,	CVD(ICD-10:I01-I79),RES(ICD-10:J00-J99)	1
Canada 1999-2 Denmark 1993-2	002 Morbidity, Mortality 015 Mortality	45-85		ICD-9,		
Denmark 1993-2	002 Mortality 015 Mortality		BC			
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USA 1988-2	004 Martality		BC	ICD-10	CVD(ICD-10:I00-I99),RES(ICD-10:J00-J99,C34)	
	004 Mortality	≥30	EC	ICD-9, ICD-10	CVD(ICD-10:100-I99),RES(ICD-10:J00-J99,C34) IHD(ICD-9:410-414,ICD-10:120-125) CVD(ICD-10:100-I99),RES(ICD-10:J00-J47,J80-J999	-
China 1998-2	011 Mortality	≥65	BC	ICD-10	CVD(ICD-10:I00-I99),RES(ICD-10:J00-J47,J80-J9992	
Canada 1999-2	Morbidity, 002 Mortality	45-85	BC	ICD-9, ICD-10		-
etherlands 1991-2	003 Morbidity	15-74	EC	ICD-9	IHD(ICD-9:410-414),CHD(ICD-9:430-438) ♀ ►	
USA 1994-2	Morbidity, 005 Mortality	50-79	EC	ICD-9		
Iran 2014-2	017 Mortality	All	BC	ICD-10	RES(ICD10:J00- J99),CVD(ICD10:I00-I99),IHD(IC	
China 2010–2	2017 Morbidity	All	BC	NR	CVD(including but not limited to hypertension and stocke)	
Canada 2006-2	014 Morbidity	≤6	BC	ICD-10	Asthma(ICD-10:J45)	
Germany 2000-2	015 Morbidity	All	EC	NR		
Serbia 2012-2	014 Morbidity	≥18	BC	ICD-10	AA(ICD-10:J45.0) or asthma with coexisting AR	
Sweden 1991-1	994 Morbidity	All	BC	NR		_
et C Ge	herlands 1991-2 USA 1994-2 Iran 2014-2 China 2010-2 anada 2006-2 ermany 2000-2 Serbia 2012-2	Mortality herlands 1991-2003 Morbidity USA 1994-2005 Morbidity, Mortality Iran 2014-2017 Mortality China 2010-2017 Morbidity anada 2006-2014 Morbidity ermany 2000-2015 Morbidity	Mortalityherlands1991-2003Morbidity15-74USA1994-2005Morbidity, Mortality50-79Iran2014-2017MorbidityAllChina2010-2017MorbidityAllanada2006-2014Morbidity≤6ermany2000-2015MorbidityAllSerbia2012-2014Morbidity≥18	Mortalityherlands1991-2003Morbidity15-74ECUSA1994-2005Morbidity, Mortality50-79ECIran2014-2017MorbidityAllBCChina2010-2017MorbidityAllBCanada2006-2014Morbidity≤6BCermany2000-2015MorbidityAllEC	Mortality ICD-10 herlands 1991-2003 Morbidity 15-74 EC ICD-9 USA 1994-2005 Morbidity, Mortality 50-79 EC ICD-9 Iran 2014-2017 Morbidity All BC ICD-10 China 2010-2017 Morbidity All BC NR anada 2006-2014 Morbidity ≤6 BC ICD-10 ermany 2002-2015 Morbidity ≥18 BC ICD-10	Mortality ICD-10 Market is and the second seco

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

		Ji merudeu i	studies in the	systematic re		neta analysi		0
Study	Study	Country	Study	Outcome	Ago	Pollutant	ICD	⊐ W Diseases
Study	Design	Country	Period	Outcome	Age	1 onutant	code	D D
Wang et al. 2019b	CS	USA	2005-2016	Morbidity	All	BC	NR	STEMI N
Livremon et al. 2010	Со	Sweden	1990-2011	Morbidity,	All	DC	ICD-9,	IHD(ICD-9:410–414 and ICD-10:120-25);stroke(ICD E9 :431–436 and ICD-10:161–165)
Ljungman et al. 2019	0	Sweden	1990-2011	Mortality	All	BC	ICD-10	InD(ICD-9:410-414 and ICD-10:120-23);Stroke(ICD9:431-450 and ICD-10:101-103)
Livet al. 2021a	Co	Sweden,	1002 2004	Morbidity	All	DC	ICD-9,	تح COPD(ICD-9:490–492, and 494–496, or ICD-10:J40244)
Liu et al. 2021a	0	1992-2004 Denmark	Morbialty	All	All BC	ICD-10	COPD(ICD-9:490-492, and 494-490, or ICD-10:340(344)	

vbreviations: 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: chemic 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 m 🗟 cardial infarction; CA: cardiac arrest; STEMI: ST segment http://bmjopen.bmj.com/ on April 19, 2024 by guest. Protected by copyright vation myocardial infarction; RTI: respiratory tract infection; URTI: Upper Respiratory Infection; LRTI: Lower Respiratory Infection; ARTI: Acute respiratory infections.

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

····	No. of	No. of	Relative Risk	I ²	Egger Regression Test
Subgroup Analysis	Studies	Estimates	(95%CI)	ľ	(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.

		1 2	1
Statistic	Space1	Space2	Space3
maximum	704	128	22528
quartile	273	64	15360
median	198	64	12000
quartile	42	32	2688
minimum	8	32	256

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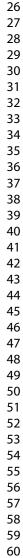
Гаble S5 The p-value		n process for eac	h etudy usin	g PR CLlow	BMJ Ope				36/bmjopen-2021-049516		
	Number	Study ID	RR	CI low	CI high	InRR	InCI low	lnCI high	on ω ≤SE	Z	p-values
	1	Ostro,2015a	0.994000	0.953000	1.038000	0.006018	0.048140	0.037296	<u>a</u> 20.021795	0.276122	0.782454
	2	Ostro,2015a	1.005000	0.979000	1.031000	0.004988	0.021224	0.030529	N 0.013202	0.377780	0.705594
	3	Atkinson,2016	0.987000	0.973000	1.001000	0.013085	0.027371	0.001000	D 0.007237	1.807997	0.070607
	4	Geng,2013	1.012000	1.002000	1.021000	0.011929	0.001998	0.020783	nlo.004792	2.489281	0.012800
	5	Liu,2016a	0.960000	0.857000	1.076000	0.040822	0.154317	0.073250	ade 0.058053	0.703185	0.481941
	6	Liu,2016b	1.020000	0.858000	1.214000	0.019803	0.153151	0.193921	5 ^{0.088539}	0.223661	0.823021
	7	Sarnat,2015	1.038000	1.005000	1.073000	0.037296	0.004988	0.070458	B 0.016702	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
Carulovascular Discases	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	Ž 0.000509	3.923916	0.000087
	14	Ostro,2007	1.026000	1.004000	1.049000	0.025668	0.003992	0.047837	$\stackrel{G}{\rightarrow}_{0.011185}$	2.294831	0.021743
	15	Metzger,2004	1.017000	1.007000	1.027000	0.016857	0.006976	0.026642	<u>9</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	20.003049	1.635761	0.101890
	18	Son,2012	1.001000	0.981000	1.021000	0.001000	0.019183	0.020783	by 0.010195	0.098036	0.921904
	19	Heo,2014	1.006000	0.994000	1.017000	0.005982	0.006018	0.016857	Que 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	Prote 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
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Table S5 The p-val	ue calculatio	n process for eacl	n study using	RR, CI low	BMJ Ope))		36/bmjopen-2021-049516 c		
	Number	Study ID	RR	CI low	CI high	InRR	InCI low	InCI high	Ω SE a	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 0041852	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	5 ^{0.006092}	0.818666	0.412977
	7	Son,2012	0.989000	0.956000	1.024000	0.011061	0.044997	0.023717	B 0.017529	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
Respiratory Diseases	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	D 0.090672	0.415806	0.677552
	15	Kim,2012	1.100000	0.949000	1.270000	0.095310	0.052346	0.239017	₽ <u>0.074327</u>	1.282302	0.199737
	16	Cakmak,2009	1.036000	1.031000	1.041000	0.035367	0.030529	0.040182	<u>0</u> 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



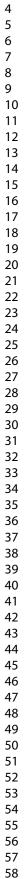
		Key criteria Other criteria							
No.	Study	Exposure	Outcome	Confounding	Selection	Incomplete	Selective	Conflict of	Oth
		assessment	assessment	bias	bias	outcome data	reporting	interest	Oth
1	Atkinson et al. 2016								
2	Bell et al. 2014								
3	Cai et al. 2014								
4	Geng et al. 2013								
5	Hua et al. 2014								
6	Ostro et al. 2015a								
7	Samoli et al. 2016								
	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								
12	Ostro et al. 2009								
14	Kim et al. 2015								
15	Huang et al. 2012								
16	Peng et al. 2009					l			
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



			Key criteria	Ot	Other criteria				
No.	Study	Exposure	Outcome	Confounding	Selection	Incomplete	Selective	Conflict	Oth
		assessment	assessment	bias	bias	outcome data	reporting	of interest	Oth
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	

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Table S7 Details of risk of bias assessment.
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here was The au	authors No other
sufficient declare	are no potential
formation conflic	lict of sources of
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	5 · · · · · · · · · · · · · · · · · ·	Conflict of interest	Other
8 9	2	Bell et al.	Probably High	Low	Probably Low	Low	Low	Probably Low	Low	Low
9 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 13			optical reflectance.	denominator file from the	(seasonality,	individuals ≥65	admissions	information	conflict of	sources of
14			Monitors from 5 sites	Centers for Medicare and	long-term trend),	years of age	were obtained,		interest.	bias
15			across 4 counties were	Medicaid Services. Cause	day of week,	enrolled in the	so likely have			identified.
16 17			used. Sampling occurred	of admission was	temperature, and	Medicare	all outcome			
18			daily, with some missing	determined by principal	dew point.	fee-for-service	data. However,			
19 20			periods, for Hartford, New Haven, and	discharge diagnosis code according to International		plan during August 2000 to	any potential errors or	risk, but indirect		
20			Springfield, and every	Classification of		February 2004.	errors or missing data	evidence that		
22			third day for Bridgeport	Diseases, Ninth Revision,		reordary 2004.	did not depend	F		
23 24			and Danbury. Days with	Clinical Modification			on air pollution			
25			missing data were	(ICD-9-CM; National			levels.	4		
26 27			omitted from analysis	Center for Health						
27			(the number of missing	Statistics 2006).						
29			data was not reported).				April 19, 2024 by gues			
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete		Conflict of interest	Other
8 9	3	Cai et al.	Probably Low	Low	Probably Low	Low	Low	Probably Low	Low	Low
9 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 13			fixed-site station. Daily	the Shanghai Health	long-term trend),	hospitalization	hospitalization		competing	sources of
14			data was available and no	Insurance Bureau	temperature,	for adult	were obtained,		financial	bias
15 16			missing data was	(SHIB). The causes of	relative humidity	residents living	so likely have		interests.	identified.
17			reported.	hospital admission were	and day of the	in the nine urban	all outcome	outcome to		
18				coded according to	week.	districts between January 1, 2005	data. However,			
19 20				Classification of		and December	any potential errors or			
21				Diseases, Revision 10		31, 2011(2922	missing data	evidence that		
22 23				(ICD-10): Asthma (J45).		days) from the	did not depend	7		
23 24						Shanghai Health	on air pollution			
25						Insurance	levels.	selective		
26 27						Bureau.	Apr	report.		
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete of the second seco		Conflict of interest	Other
8			Probably High	Low	Probably Low	Low	Low X	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	4	Geng et al. 2013	Single, central-site monitor. Daily BC and PM _{2.5} were measured continuously and 24hr averaged was estimated if >75% of the 1hr values was available for that day. Missing data was not replaced by other values.	Health data were obtained from Shanghai Municipal Center of Disease Control and Prevention database. The	Models included time (seasonality, long-term trend), temperature, humidity and day of week.	Data consisted of all causes (excluding accidents or injuries) deaths	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.	The authors declare no conflict of interest.	No other potential sources of bias identified.
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data	Selective	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	5	Hua et al. 2014	Daily 24h average PM _{2.5} and BC data was obtained from a fixed-site station. The study only used the actual collected data and did not fill in the missing data for PM _{2.5} and black carbon.	Daily asthma hospital admission data was obtained from Shanghai Children's Medical Center. Dates of admission and discharge, and diagnoses using the International Classification of Diseases, Revision 10.	Adjusted for long-term and seasonal trend, day of week, temperature and relative humidity.	Study included all asthma hospital admissions of children ≤ 14 years of age from Shanghai Children's Medical Center between1 January 2007 and 31 July 2012 in nine urban districts of Shanghai.	Daily counts	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.
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	Selective reporting	Conflict of interest	Other
8 9			Probably Low	Low	Low	Low	Low	Probably Low	Low	Low
9 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 13			obtained from one station	mortality for all ages	(year, month, day	counts of	obtained, so	information	competing	sources of
14			in Barcelona and Athens.	were collected (excluding	of week) trends,	all-cause	likely have all		interests.	bias
15			Daily data was available	deaths from external	temperature,	mortality for all	outcome data.	1		identified.
16 17			and no missing data was	causes, International	holidays, summer	ages and daily	However, any	-		
18			reported.	Classification of	vacations and	counts of	potential errors			
19				Disease-ICD9: 001799,	influenza.	cardiovascular,	or missing data			
20				ICD10 A00R99), as well		respiratory and	did not depend			
21 22				as daily counts of		all-cause	on air pollution			
23				cardiovascular (ICD9:		mortality for	levels.	. suggests study		
24				390459, ICD10: I00I99),		those greater than				
25 26				respiratory		age 65.	on v	selective		
27				(ICD9:460519,				report.		
28				ICD10:J00J99) and			, ,			
29 30				all-cause mortality for						
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	Selective	Conflict of interest	Other
8			Low	Low	Probably Low	Low	Low X	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 20	7	Samoli et al. 2016	Daily concentrations of 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 (BC urban in PM _{2.5}) and 702 (BC in PM _{2.5}) between 2011 and 2012 (<25% missing data).	Based on the primary discharge diagnosis, daily numbers of admissions for cardiovascular disease (International Classification of Diseases, 10th revision-ICD-10: I00-I99) for those aged 15-64 (adult) and 65+ years (elderly), and respiratory diseases (ICD-10: J00-J99) for those aged 0-14 years (paediatric), adult and the elderly were calculated.	Adjusted for long term and seasonal trends, temperature, relative humidity, regulated pollutants (PM ₁₀ , PM _{2.5} , NO ₂ , SO ₂ and O ₃), day of the week and public	Study included all cardiovascular and respiratory hospital admissions in London, UK between 2011 and 2012.	N N	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.
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4 5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete og outcome data⇔	Selective reporting	Conflict of interest	Other
8			Probably High	Low	Probably Low	Low	Low a	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 13		Schwartz	measurements for BC and	for residents of the	of the week,	hospital	admissions <u>A</u>	information	competing	sources of
14		2006	$PM_{2.5}$ were not complete.	Boston Metropolitan area	seasonality,	admissions in the	were obtained,		interests.	bias
15			Missing values were	who were admitted to the	long-term trends,	Boston	so likely have	selective		identified.
16 17			replaced with the	hospital (in the Boston	humidity,	Metropolitan	all outcome	outcome to		
18			predicted values.	area) with a primary	barometric	area for	data. However,			
19			Additionally BC data was	diagnosis of MI	pressure, and the	myocardial	any potential	risk, but		
20 21			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		
23			not included in the study.	Diseases, 9th	L L	duration.	did not depend			
24				revision-ICD-9:410), and			on air pollution			
25 26				pneumonia (ICD-9:			levels.	selective		
27 28 29 30 31				480–487), from Medicare billing records for the years 1995–1999.			April 19, 2024 by guest. Protected by copyright	report.		
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1 2 3 4							-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete g outcome data⇔	Selective reporting	Conflict of interest	Other
8 9			Probably High	Low	Probably Low	Low	Low 2	Probably Low	Low	Low
9 10	9	Liu et al.	EC were collected from a	Emergency department	Adjusted for time	Study included	Daily counts	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 13			one-in-three or one-in-six	from the Blue Cross Blue	seasonal trend),	emergency	department A	information	potential	sources of
14			day schedule. EC were	Shield Texa. International	day of week,	department visits	visits were		competing	bias
15			measured for 566 days	Classification of Diseases	temperature, dew	for Greater	obtained, so	selective	financial	identified.
16 17			from April 02, 2009, to	9th Revision (ICD-9)	point and	Houston from	likely have all		interests.	
18			December 30, 2013,	diagnosis codes were	population growth.	claims data	outcome data.			
19 20			<25% missing for the frequency of sampling.	used to classify outcome		insured from	However, any potential errors			
20			inequency of sampling.	groups.		January 1, 2008 through	or missing data			
22						December 31,	did not depend			
23 24						2013.	on air pollution			
25							levels.			
26 27										
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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 outcome data⇔		Conflict of interest	Other
8			Probably High	Low	Probably Low	Low	Low a	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	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.	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.
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1 2 3 4							e1-2021-0490			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data	Selective	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	11	Sarnat et al. 2015	24hr average concentration of PM _{2.5} 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 department visits were obtained, hence one hospital not providing data after 26 April 2002. However, any potential errors or missing data did not depend 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 they have no actual or potential competing financial interests.	No other potential sources of bias identified.
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1 2 3 4							Incomplete			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	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	12	Kim et al. 2012	PM _{2.5} 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	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.
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete 0 outcome data∝	Selective	Conflict of interest	Other
8			High	Low	Probably Low	Low	Low X	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 hospitalization s of children 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.
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4 5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete of outcome data	Selective reporting	Conflict of interest	Other
8			Probably Low	Low	Probably Low	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	14	Kim et al. 2015	Probably Low Daily 24-hour composite PM _{2.5} samples were collected from single, central-site monitor. The observations of EC was 1809 days from 2003 through 2007 (missing data <25%).	Low Daily mortality counts for 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.	Probably Low Models adjusted for longer-term temporal trend, as time since the study began, day of week, and daily temperature and humidity.	Low Data consisted of all deaths over the course of the study in a defined geographical area.	Low Daily counts 22. 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	Low None of the authors has any actual or potential competing interests.	Low No other potential sources of bias identified.
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete of the second secon	Selective	Conflict of interest	Other
8			Probably Low	Low	Probably Low	Probably Low	Low 2	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	15	Huang et al. 2012	Daily average concentrations of PM _{2.5} were obtained from a single, central-site monitor. Daily average concentrations of EC in PM _{2.5} 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 dependo	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.
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete 0 outcome data∝		Conflict of interest	Other
8			Probably High	Low	Probably Low	Low	Low X	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	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 was not replaced by other values.	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 data did not depend on air pollution levels.	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.
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1 2 3 4							en-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	Selective	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	17	Levy et al. 2012	The U.S. Environmental Protection Agency established the PM Speciation Trends Network (STN) to measure more than 50 PM _{2.5} 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 missing data.	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 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.
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4 5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	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 39	18	Son et al. 2012	Hourly air samples were obtained from a single, central-site monitor. The monitoring system produces hourly estimates of PM _{2.5} total mass, and PM _{2.5} levels of EC. Daily data was available and no missing data was reported.	Daily death counts were obtained from the National Statistical Office. The study classified mortality data into all causes of death [International Classification of Diseases, 10th Revision (ICD-10; codes A00–R99), cardiovascular causes (codes I00–I99), and respiratory causes (codes J00–J99)] (World Health Organization 2007).	Models adjusted for time (long-term trends and seasonality), day of week, temperature and relative 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.	There was insufficient information about selective outcome to judge for low risk, but indirect evidence that	The authors declare they have no actual or potential competing financial interests.	No other potential sources of bias identified.
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1 2 3 4							36/bmJopen-2021-04951			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on the second seco	Selective	Conflict of interest	Other
8			Probably High	Low	Low	Low	Low X	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	19	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.
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias			Conflict of interest	Other
8 9			Probably High	Low	Probably Low	Low	Low	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	20	Basagaña et al. 2015	Single central-site monitor in each city. For each city, PM constituents with >20% of the values below the detection limit or missing were excluded. Otherwise, non-detectable were replaced by half the limit of detection. Air pollution data was collected daily in Bologna (n=472), twice a week in Barcelona (n=736) and Madrid (n=104), and once a week in Huelva (n=406). There was no information about	Daily mortality counts for all non-external causes [International Classification of Diseases, 9th Revision (ICD9) codes 001–799; 10th revision (ICD10) codes A00–R99], cardiovascular (ICD9 codes 390–459, ICD-10 codes 390–459, ICD-10 codes 100–I99) and respiratory (ICD9 codes 460–519, ICD10 codes J00–J99) were collected. Cardiovascular and respiratory hospitalizations were defined on the basis of the primary discharge	Models adjusted for holidays, summer population decrease, influenza epidemics, seasonality, long-term trends and temperature.	Data consisted of all deaths over the course of the study in a defined geographical area.	Daily counts for death and emergency hospital admissions 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 report.	The authors have no conflicts of interest to disclose.	No other potential sources of bias identified.
34 35 36 37 38 39 40 41 42			missing data.	diagnosis using the same ICD codes defined above.			C Protected by copyright.			

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1 2 3 4							36/bmJopen-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete of outcome data		Conflict of interest	Other
8			Probably High	Low	Probably Low	Low	Low X	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	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 _{2.5} 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 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 report.	The authors declare they have no actual or potential competing financial interests.	No other potential sources of bias identified.
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article size 1 Jan	mortality data from		Low	Low ay 2	Probably Low	Low	Low
ured at two airGuang stations. ECCenterured for fourContreach year fromThe cagh 2010.codedperiodInterr, theClassof missingDiseaery low(ICD-com 1% to 2%).cardidemicalextract	ember 2011 were ned from ngdong Provincial er for Disease rol and Prevention. cause of death was d using the national sification of ases, Tenth Revision -10). Mortality from ovascular diseases -10:I00-I99) were cted to construct the	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.	• ·	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.
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	Selective	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	23	Cao et al. 2012	Daily concentrations of EC was obtained from a single monitoring site. The observations of EC was 1749 in 1827 days (missing data <25%).	The study obtained numbers of deaths in Xi'an for each day from the Shanxi Provincial Center for Disease Control and Prevention (SPCDCP). SPCDCP staff then classify the cause of death according to the International Classification of Diseases, 10th Revision [ICD-10; World Health Organization (WHO) 1992] as due to total nonaccidental causes (ICD-10 codes A00–R99), cardiovascular diseases (I00–I99), respiratory diseases(J00–J98), or injury (S00–T98).	Model adjusted for long-term and seasonal trends, day of week, temperature, humidity, and SO ₂ and NO ₂ concentrations.	Data consisted of all nonaccidental causes deaths during 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.	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.
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	Selective reporting	Conflict of interest	Other
8			Probably Low	Low	Probably Low	Low	Low X	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	24	Klemm et al. 2011	Daily 24-hr average EC measurements are available for Atlanta during the study period. The observations of EC was 3317 days from August 1998 to December 31, 2007. Missing data <25%. There was no information for monitor stations.	Records of individual deaths were provided by the Georgia Department of Human Resources. Cause of death is	Adjusted for time (seasonality, long-term trends), temperature, and day of the week.	Study included all nonaccidental deaths during over the course of the study.	Daily counts for death were obtained, so likely have all outcome data.	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.
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	Selective	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 _{2.5} 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 (ICD10, 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.	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.
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No. Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete		Conflict of interest	Other
	Probably Low	Low	Probably Low	Low	Low X	Probably Low	Low	Low
26 Winquist et al. 2015	Daily EC and BC were from a single monitor site. All species of pollutant statistics are missing less than 5%.	Individual-level data were obtained from the Missouri Hospital Association for all emergency department visits to 36 of 43 acute-care non-federal hospitals with emergency department visits in the 16-county St Louis metropolitan statistical area during 1 June 2001 through 30 April 2003. Cardiorespiratory outcomes of interest were defined based on the primary ICD-9 (International Classification of Diseases, version 9) diagnosis code for the visit.	Adjusted for time trends, day of week, holidays, season, temperature and dew point.	Study included emergency department visits in St Louis metropolitan statistical area during 1 June 2001 through 30 April 2003.	Daily counts for emergency Development visit 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.

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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete og outcome data		Conflict of interest	Other
8			Probably High	Low	Probably Low	Low	Low A	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	27	Ostro et al. 2007	Each of the six counties had two monitors measuring PM _{2.5} components and mass. Fresno, Kern, Riverside, and Sacramento Counties reported data every third day, whereas San Diego and Santa Clara Counties reported data every sixth day. For the speciation analyses, the number of observation days available ranged from 243 (San Diego County) to 395 (Sacramento County) from 2000 to 2003. There was no specific information about missing data.	Daily mortality data were obtained from the California Department of Health Services, Center for Health Statistics. The study determined daily total mortality counts for those > 65 years of age and for deaths from respiratory disease [International Classification of Diseases, 10th Revision (ICD10; World Health Organization 1993) codes J00–J98] and cardiovascular disease (codes I00–I99).	Adjusted for time trend, day of week, seasonality, long-term trends, temperature and humidity.	Data consisted of all cardiovascular deaths over the course of the study.	19, 2024 by guest.	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.
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3 4 5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete of 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	28	Tolbert et al. 2000	Daily 24h EC from a single monitor site. The observation of EC was 356 in 365 days, missing data <25%.	Computerized billing record data are being obtained from the emergency department visits participating in the study. Several case groups are being defined using the primary ICD-9 (International Classification of Diseases, 9th Revision) diagnostic code.	Adjusted for time (seasonality, long-term trends), temperature, dew point, and day of week.	Study included emergency department visits of the participating hospitals in the Atlanta Metropolitan Statistical Area, including 33 hospitals between January 1 1993-August 31 2000, 4 hospitals between January 1 1993-February 30 2000.	Daily count for emergency department visits were obtained, so likely have all outcome data. However, any potential errors or missing data did not depend levels.	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.
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	Selective	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	29	Wang and Lin 2016	The hourly data were simply averaged to calculate the daily average data for PM ₁₀ , PM _{2.5} 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.	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 Revision (ICD-9 CM).	Adjusted for temperature, relative humidity, wind speed, barometric pressure, holidays, day of the week, pneumonia and influenza.	Study included elderly (≧65 years) mortality from 2004 to 2008 and all population EVR from 2004 to 2010 in Taipei, Taiwan.	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 depend on air pollution levels.	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.
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4 5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete of outcome data	Selective	Conflict of interest	Other
8			Low	Low	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	30	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 Downloaded department visit were obtained. In the earliest years of the study, not all hospitals were participating. However, any potential errors or missing dataon did not depend pillion 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.
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	Selective	Conflict of interest	Other
8			Probably High	Low	Probably Low	Low	Low X	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	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 of department visits were obtained, so likely have all outcome data. However, any potential errors or missing data	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.
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete \int_{Ω}^{Ω} outcome data ω		Conflict of interest	Other
8 9			Probably Low	Low	Probably Low	Low	Low ay	Probably Low	Low	Low
9 10	32	Mar et al.	Hourly PM _{2.5} 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		competing	potential
12 13			single, central-site	1995 to 1997 were	day of week,	deaths during	obtained, so $\frac{M}{O}$		financial	sources of
14			monitor. Daily data was	obtained from the	temperature and	over the course	likely have all		interests.	bias
15 16			available and no missing	Arizona Center for Health Statistics in	relative humidity.	of the study.	outcome data.	1		identified.
17			data was reported.	Phoenix. Death certificate	er rei		potential errors			
18 19				data included residence	24		or missing data			
20				zip code and the primary	the second secon		did not depend			
21				cause of death as	(0)		on air pollution			
22 23				identified by the			levels.	suggests study		
24				International		101		was free of		
25 26				Classification of			on	selective		
20				Diseases, Ninth Revision			April	report.		
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29 30				Organization, Geneva).			202			
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete og outcome data⇔	Selective	Conflict of interest	Other
8			Low	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 38 20	33	Wang et al. 2019a	Hourly data of PM _{2.5} were collected at 10 Chinese air quality monitoring sites in Shanghai. Hourly mass concentrations of PM _{2.5} 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.	for death were Do obtained, so likely have all outcome data. However, any potential errors or missing data	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.
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4 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 High	Low	Probably Low	Low	Low X	Probably Low	Low	Low
10 11 12 13 14 15 16 17 18		2016b	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	obtained from the death registry system. The cause of death was coded using the International Classification of Diseases, Tenth Revision	long-term trends, seasonality, temperature, humidity, day of week and public holidays.	the residents who died of ischemic or hemorrhagic strokes in urban districts of Guangzhou	for death were Do obtained, so likely have all outcome data. However, any potential errors	information about selective outcome to	declared no conflict of interest.	potential sources of bias identified.
19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38			2%).	(ICD-10). Mortality from stroke (ICD-10:I60–I66), and sub-categories, including ischemic stroke (ICD-10:I63–I66), and hemorrhagic stroke (ICD-10: I60–I62) were extracted to construct the time series.	rel e	between 2007 and 2011.	or missing data did not dependend on air pollution levels. Protected by copyright	indirect evidence that suggests study		
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	Selective reporting	Conflict of interest	Other
8			Probably High	Low	Probably Low	Low	Low X	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	35	Lin et al. 2016b	Each of the six counties had two monitors measuring components of PM _{2.5} . Fresno, Kern, Riverside and Sacramento counties reported 24-hour average EC in PM _{2.5} 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.	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 calculated.	Adjusted for time, temperature, humidity and day of the week.	Study included daily cardiovascular mortality for all California residents from 1 January 2000 to 31 December 2003.	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 report.	Authors declared no competing interests.	No other potential sources of bias identified.
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete		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	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.	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.
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	Selective	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 39	37	Chen et al. 2014	Hourly mass concentrations of PM _{2.5} and the four PM _{2.5} constituents obtained from a Supersite (single, central site monitoring location). The observations of EC was 1599 in 1705 days (missing data <25%).	The counts of daily emergency room visits were obtained from the National Taiwan University Hospital. The emergency room visit	Models adjusted for time, day of week, temperature, seasonality and relative humidity.	Data consisted of all emergency department visits during the study period for ischemic and	Daily counts for emergency room visit were obtained, so likely have all outcome	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.
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete og outcome data⇔		Conflict of interest	Other
8			Low	Low	Probably High	Low	Low X	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	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	0.	from 1 July 2012	outcome data.	judge for low		
19			information about	general hospital in Užice.		to 30 June 2014	However, any			
20			missing data.	The inclusion criteria		in the Zlatibor	potential errors	indirect		
21 22				were adults aged 18 years		District, Western	or missing data	evidence that		
23				and older with the		Serbia.	did not depend	. suggests study		
24				diagnosis of allergic		101	on air pollution	was free of		
25 26				rhinitis (International			levels.	selective		
20				Classification of			Apr	report.		
28				Diseases, 10th revision,			Pr P			
29				code J.30.4), allergic			ZQ			
30 31				asthma (International			April 19, 2024 by guest	-		
32				Classification of			y gr			
33				Diseases, 10th revision,			lest.			
34 35				code J.45.0), or asthma			ייש דע. דע דע דע	J		
36				with coexisting allergic			Protected			
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Page 97 of 133

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4 5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias		Selective	Conflict of interest	Other
8			Probably Low	Low	Probably Low	Low	Low a	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	39	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 levels.	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.
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias		Selective reporting	Conflict of interest	Other
8			Probably Low	Probably Low	Probably Low	Low	Low X	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 4 35 36	40	Sinclair et al. 2010	Daily 24-hr averages EC was from a single monitor site. The total observed rate of EC was 95.2%.	Daily outpatient visits were obtained from the electronic patient data warehouse of a not-for-profit, group-model managed care organization (MCO) in the metropolitan Atlanta area between August 1, 1998 and December 31, 2002. Visits that met acute visit definition and that had a visit diagnosis code of asthma, upper respiratory infection (URI), or lower respiratory infection (LRI) were included in the study.	Adjusted for season, day of week, federal holidays, study month, time, temperature and dew point.	Study included daily outpatient visits for acute respiratory diseases from the electronic patient data warehouse of a not-for-profit, group-model managed care organization (MCO) in the metropolitan Atlanta area between August 1, 1998 and December 31, 2002.	Daily counts for outpatient 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.
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete og outcome data	i la	Conflict of interest	Other
8			High	Probably Low	Probably Low	Low	Low X	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	41	Krall et al. 2013	Monitors typically measure PM _{2.5} constituent concentrations every third or sixth day. Some communities with a single monitor. The observation of EC was 58-921 days,some communities had >25% missing data.	All-cause mortality data (excluding accidental deaths) were aggregated from death certificate data obtained from the National Center for Health Statistics for 2000 to 2005.	Adjusted for temperature, day of week, long-term and seasonal trends.	Study included all death (excluding accidental deaths) for 108 urban communities from 2000 to 2005.	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.	The authors declare they have no actual or potential competing financial interests.	No other potential sources of bias identified.
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1 2 3 4							30/bm)open-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	incomplete of outcome data	Selective reporting	Conflict of interest	Other
8			Probably High	Low	Probably Low	Low	Low 2	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	42	Cakmak et al. 2009	Daily PM _{2.5} aerosol samples approximately 1 of every 4 days from a single monitor site. Sampling occurred daily during the cold season (April through September) and alternate days during the warm season (October through March). Missing data <25% for that frequency.	Diseases were coded using the WHO International Classification of Disease, 9th Revision (ICD-9). The daily number of emergency department visits for all nonaccidental (ICD-9 < 800) and respiratory (ICD-9 460–519) causes in Santiago Centro, Cerrillos, and Pudahuel were obtained from the Departamento de Estad' isticas e InformaciónenSalud (DEIS) of the Ministry of Health from April 2001 through August 2006.	Adjusted for temperature and humidity, day of week, long-term and seasonal trends.	Study included all emergency department visits obtained from the Departamento de Es-tad' isticas e InformaciónenSa lud (DEIS) of the Ministry of Health from April 2001 through August 2006.	Daily counts for emergency department visit 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 report.	No competing financial interests.	No other potential sources of bias identified.
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data	Selective	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	43	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 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.
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4 5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	Selective	Conflict of interest	Other
8			Low	Low	Probably Low	Low	Low X	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 26	44	Lall et al. 2011	Daily EC data were obtained from two monitors. Daily data was available and no missing data was reported.	The categorization of the admissions data was based on codes from the International Classification of Diseases, revision 9 (ICD-9).	Model adjusted for season, wintertime influenza episode, weather, day of week, and other possible confounders (e.g., federal holidays).	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.	 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.
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	Selective	Conflict of interest	Other
8 9			Probably High	Low	Probably Low	Low	Low X	Probably Low	Low	Low
9 10	45	Jung and	A total of 153 daily	The health data used in	Adjusted for	Study included		There was	No	No other
11		Lin 2017	samples (approximately 4	the study were sourced	seasonal trend, day	all asthma	for asthma		competing	potential
12 13			weeks per season) from a	from Longitudinal Health	of week,	outpatient visits	outpatient visits (0-20	information	financial	sources of
14			single monitor site were	Insurance Database 2000.	temperature,	(0-20 years old)	visits (0-20 years old) data		interests.	bias
15 16			collected. Multiple linear regression models were	Daily outpatient visits for asthma (International	precipitation and wind vectors.	in Shalu district from	were obtained,			identified.
17			used to back extrapolate	Classification of	wind vectors.	Longitudinal	so likely have			
18			the historic concentration	Diseases, Ninth Revision,	Cr.	Health Insurance	all outcome	risk, but		
19 20			of individual components	Clinical Modification,		Database 2000	data. However,	, , , , , , , , , , , , , , , , , , ,		
21			of PM _{2.5} from 2000	ICD-9-CM code 493)		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				Insurance Database 2000.		2010.	did not depend	selective		
26 27							on air pollution	report.		
28							levels.	-		
29 30							levels. 19, 2024 by guess			
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1 2 3 4							Incomplete			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	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	46	Gong et al. 2019	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 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) were obtained.	Adjusted for calendar effects, long-term trends, temperature, humidity, day of week, NO ₂ and SO ₂ .	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.	Daily counts for all deaths 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 conflict of interest.	No other potential sources of bias identified.
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1 2 3 4							36/bmjopen-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete of the second seco		Conflict of interest	Other
8			Probably Low	Probably Low	Probably High	Low	Low X	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	47	Mostofsky et al. 2012	Ambient EC obtained from one monitor. BC concentrations were measured continuously. Daily data was available and no missing data was reported.	Patients potentially eligible for this study were identified by reviewing daily emergency department admission logs, stroke service admission logs, stroke service consult logs, and hospital electronic discharge records.	Model adjusted for seasonality, time-trends, temperature, dew point temperature, barometric pressure and chronic and slowly-varying potential confounders.	Population consisted of patients ≥21 years of age admitted to the hospital with neurologist-confi rmed ischemic stroke and residing in the Boston metropolitan region. Also patients had to reside within 40 km of the air pollution monitor.	Daily counts for emergency Do department admission 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.
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1 2 3 4 _							36/bmJopen-2021-0495			
5	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias		Selective	Conflict of interest	Other
3)			Probably High	Low	Probably Low	Low	Low X	Probably Low	Low	Low
0	48	Krall et al.	PM _{2.5} 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
} 			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.
5			however, data were only	care hospitals. Using	hospitalsreporting	care hospitals in	disease were	outcome to	competing	
			available approximately	diagnosis codes from the	data, temperature	the 20-county	obtained, so	judge for low	financial	
•			every third day in the	International	and dew point.	Atlanta	likely have all	risk, but	interests.	
			remaining three cities.	Classification of		metropolitan	outcome data.	indirect		
2			There was no information	Diseases, 9th Revision		area, the	However, any	evidence that		
3			about missing data.	(ICD-9), the study	ŀ	7-county	potential errors			
1 5				considered subcategories		Birmingham	or missing data	was free of		
				of respiratory diseases		metropolitan	did not depend			
				including pneumonia		area, the 8	on air pollution	report.		
				(ICD-9 codes 480–486),		Missouri and 8	levels.			
)				chronic obstructive		Illinois counties				
				pulmonary disease		in the St. Louis	levels. 19, 2024 by guess			
2				(491,492,496), upper		metropolitan	y gu			
3				respiratory infection		area, and the	est.			
1 5				(URI) (460–465, 466.0,		12-county Dallas		J		
5				477), and asthma and/or		metropolitan	Protected			
7				wheeze (493, 786.07).		area.				
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Pag	e 107 d	of 133			BMJ Oper)	do[un a/op			
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	Selective	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 39	49	O'Lenick et al. 2017	The 24-hour average concentration of EC was evaluated. Pollutant concentration estimates were obtained by fusing observational data from available network monitors with pollutant concentration simulations from the Community Multi-Scale Air Quality emissions-based chemical transport model at 12×12km grids over Atlanta. 24-hour average EC were evaluated. Daily data was available and no missing data was reported.	Patient-level emergency department visit data from 1 January 2002 to 31 December 2008 were acquired from hospitals located within the 20-county metropolitan area of Atlanta; Relevant data elements included admission date, International Classification of Diseases Ninth Revision (ICD-9) diagnosis codes, age and ZIP code of patient residence.	Adjusted for season, periods of hospital participation and holidays, temperature and mean dew point, interaction terms between season and maximum temperature and day of year.	Study included all emergency department visit data acquired directly from hospitals (2002–2004 period) and the Georgia Hospital Association (2005–2008 period) located within the 20-county metropolitan area of Atlanta.	Daily counts for emergency department visit 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.	Competing interests: None declared.	No other potential sources of bias identified.
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1 2 3 4							Incomplete on			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	Selective reporting	Conflict of interest	Other
8 9			Probably Low	Low	Probably Low	Low	Low X	Probably Low	Low	Low
9 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		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 department	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	0.	18 years from 41	obtained, so	judge for low		
19				metropolitan Atlanta; and		hospitals within	likely have all	-		
20				defined emergency		metropolitan	outcome data.			
21 22				department visits for		Atlanta for study	However, any	-		
23				pediatric asthma as all	ŀ	period.	potential errors			
24				visits with a code for		· ()	or missing data	was free of		
25 26				asthma (493.0–493.9) or			did not depend			
20				wheeze (786.07) using			on air pollution	report.		
28				the International			levels.			
29 30				Classification of			∑∆			
30 31				Diseases, 9th Revision.			24 D	-		
32							y gu			
33 24							lest.			
34 35								ז		
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	Selective reporting	Conflict of interest	Other
8			Low	Low	Probably Low	Low	Low X	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	51	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, so likely have all outcome data. However, any potential errors or missing data did not depend of 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.
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1 2 3 4							Incomplete o			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete		Conflict of interest	Other
8			Low	Low	Probably Low	Low	Low X	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	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 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.
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Pag	e 111 d	of 133			BMJ Oper	1	36/bmJope			
1 2 3 4							36/bmJopen-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	Selective reporting	Conflict of interest	Other
8 9			Probably High	Low	Probably Low	Low	Low X	Probably Low	Low	Low
9 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 13			areas where the data from	Diseases, 10th Revision	confounding	all-cause,	emergency	information		sources of
13			at least one Chemical	(ICD-10) codes, the study	temporal trends	cardiovascular	hospitalization			bias
15			Species Network monitor	aggregated daily death	(annual cycles and	disease and	were obtained,			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 _{2.5}	cardiovascular disease	day-of-week	emergency	data. However,	, , , , , , , , , , , , , , , , , , ,		
20			components were	and respiratory deaths.	patterns and	hospitalizations	any potential			
21 22			available either every	Using International	temperature.	for the elderly	errors or	evidence that		
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			
25 26			information about	(ICD-9) codes,		cardiovascular	on air pollution	selective		
27			missing data.	emergency		disease and	levels.	report.		
28				hospitalizations for the		respiratory	19,			
29 30				elderly (those 65 and		diseases.	levels. April 19, 2024 by guest			
31				older) data were divided				-		
32				into cardiovascular			u gu			
33 34				disease and respiratory			est.			
35				categories.			Pro	D		
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No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data	Selective reporting	Conflict of interest	Other
		Probably Low	Low	Probably Low	Low	Probably Low	Probably Low	Low	Low
0 54 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 5 6 7 8 9 0 1 2 3 4 5 5 7 8 9 0 1 1 2 3 4 5 5 6 7 8 9 0 1 1 2 3 4 5 5 6 7 8 9 9 0 1 2 5 5 6 7 7 8 9 0 1 2 5 5 6 7 7 8 9 0 0 1 1 2 5 5 7 8 9 0 0 1 1 2 5 5 7 8 9 0 1 2 5 5 7 8 9 0 0 1 1 2 5 5 7 8 7 8 7 8 7 8 7 8 7 8 7 8 7 8	Ostro et al. 2015b	The model calculations track the mass and concentrations of the PM constituents in particle diameters ranging from 0.01 to 10µm through calculations that describe emissions, transport, diffusion, deposition, coagulation, gas- and particle-phase chemistry, and gas-to-particle conversion. The University of California Davis/California Institute of Technology model was used to estimate ground-level concentrations of 50 PM constituents over the	Deaths were assigned codes based on the International Classification of Diseases, 10th Revision (ICD-10) for the following outcomes: all-cause deaths excluding those with an external cause (A00–R99), cardiovascular deaths (I00–I99), Ischemic heart disease deaths (I20–I25), and pulmonary deaths (C34, J00–J98).	ge, race, marital status, smoking status, pack-years of smoking, secondhand smoke exposure, body mass index, lifetime physical activity, alcohol consumption, average daily dietary intake of fat, calories, menopausal status, family history of myocardial infarction, stroke, use of blood pressure medication,	Data obtained for a cohort of female teachers ≥30 years old.	There was no the rate of lost 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 they have no actual or potential competing financial interests.	No other potential sources of bias identified.
6 7		major population regions in California.		aspirin; living conditions					

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Pag	je 113 d	113 of 133 BMJ Open								
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete og outcome data∝	Selective	Conflict of interest	Other
8 9 10 11 12 13 14 15 16 17 18				Forpe	(income, income inequality, education, population size, racial composition, unemployment).		ay 2022. Downloaded from http			
19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37	55	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 use regression models.	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 follow-up period.	Probably Low During the 4-year follow-up period, 38,377 (8%) subjects were lost to follow-up because of moving out of 4 the province or dying from other diseases.	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.
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1 2 3 4							Incomplete o			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete og outcome data∝ ≤		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	56	Hvidtfeldt et al. 2019	The PM, NO ₂ , BC, and O ₃ 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 ₂ , BC, and O ₃ .	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 consumption, physical activity; neighborhood level socioeconomic status (SES).	Data obtained for a cohort of men and women aged 50–64 years residing in the areas of Copenhagen and Aarhus.	There was no ¹ / ₂ . Information on Jow no add the rate of lost no follow up. follow up. ¹ / ₂ , 2024 by guest. Protected	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.
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Pag	e 115 d	15 of 133 BMJ Open 30 op								
1 2 3 4							36/bm)open-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete ວ outcome dataຜ ຊ	Selective reporting	Conflict of interest	Other
8			Probably Low	Probably Low	Probably High	Low	Probably High	Probably Low	Low	Low
9 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 _{2.5} 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			
17			System. These PM _{2.5}	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	-		
20			analyzed to derive	I20–I25).	marital status,	and resided in all	157,572 deaths			
21 22			estimates of source		education, BMI	50 states, the	from all	evidence that		
23			apportioned PM _{2.5} mass		and BMI ² ,	District of	causes)	. suggests study		
24			exposure concentrations		consumption of	Columbia, and	occurring	was free of		
25 26			using the absolute		beer, wine, and	Puerto Rico.	during 9			
27			principal component		other alcohol,		follow-up.	report.		
28			analysis (APCA) PM _{2.5}		quintile of dietary		Ŀ,			
29 30			source apportionment		fat consumption,		202			
31			method.		quintile of		4 by	-		
32					combined dietary		follow-up. April 19, 2024 by gues			
33 34					vegetable, fruit,					
35					fiber consumption;		Prot			
36					Six ecologic		ecte			
37 38					covariates.		Protected by	=		
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41 42							nt.			

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3 4 5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete on outcome data	Selective	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	58	Yang et al. 2018	Land use regression models were derived from street level measurements collected during two sampling campaigns conducted in 2014 and 2015.	Deaths were coded according to the International classification of Diseases, 10th Revision (ICD-10; WHO 2010) including natural cause mortality (A00–R99), overall cardiovascular disease (I00–I99) and overall respiratory disease (J00–J47 and J80–J99). Subcategories included Ischemic heart disease (IHD) (I20–I25), cerebrovascular disease (I60–I69), Pneumonia (J12–J18) and chronic obstructive pulmonary disease (COPD) (J40–I44	Age at entry, gender, individual smoking status, body mass index (BMI), physical activity, education level and monthly expenses; percentage of participants who were equal to or older than 65 years old, percentage of participants whose educational level was higher than secondary school, average income per month and	Data obtained for a cohort of people who were older than or equal to 65 years old.	There was no	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 interests.	No other potential sources of bias identified.
35 36 37				and I47).	percentage of smokers.		Protected b			
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1 2 3 4		Conflict of	
	a → reporting		
5 6 7No.StudyExposure assessmentOutcome assessmentConfounding biasSelection biasIncomplete outcome data	2	interest	Other
8 Probably Low Low Probably High Low Probably Low	Probably Low	Low	Low
9 1059Gan et al.Land use regression toA coronary heart diseaseModel adjusted forStudy providedDuring 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
13 14exposure assigned towith the followingresponse of the followingresponse of the following13 14exposure assigned towith the followingcomorbidity, andwith those lostperiod, 17,542	about	actual or	bias
15residential centroid.International Statisticalneighborhoodduring the(3.9%) moved	selective	potential	identified.
16 Classification of socioeconomic follow-up period. out of the	outcome to	competing	
17 18Diseases, 9th Revisionstatus. Noprovince and	judge for low	financial	
10 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 22Revision (ICD-10),factors.diseases,	evidence that		
22 120–125, as the principal leaving	suggests study		
24 diagnosis (the most 418,826	was free of		
25 responsible diagnosis) for (92.5%)	g selective		
20 a hospital admission in subjects at the	report.		
	19		
29 database. A coronary follow-up.	19 2024 by quest		
30 1 31 heart disease death is a	24 b		
32 death record with			
	lest		
34 the cause of death in the	Pro		
36 provincial death	Protected		
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5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete of the second secon	Selective	Conflict of interest	Other
8			Probably High	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	60	De Kluizenaa r et al. 2013	Used black smoke (BS) as an indicator of EC concentrations. Derived background EC concentrations from BS measured at two regional monitoring sites. Local traffic-related EC emission contributions were estimated based on fuel-specific EC content of exhaust PM ₁₀ emission. Used the traffic-related EC emissions as input to calculate local EC concentrations, assuming absence of other local EC	The study obtained information on the incidence of hospital-based Ischemic heart disease (International Classification of Diseases [ICD9] 410-414) and cerebrovascular disease (ICD9 430-438) in the study population.	Individual-level covariates: age, gender, marital status, education, smoking, alcohol use, physical activity, body mass index, living conditions (employment status, financial problems).	Data obtained for a cohort of 27,070 non-institutionali zed subjects.	There was no ¹ / ₂ . Information on Downloaded from http://bmjopen.bmj.com/ on April 19, 2024 by guest. Protected by	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.
33 34 35 36 37 38			sources. Also assumed that dispersion dynamics of EC are identical to those of PM_{10} .				Juest. Protected by			
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43

1 2	e 119 c	of 133		BMJ Open 2027-2027 - 0495						
3 4 5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Hybrid Incomplete م outcome data	Selective	Conflict of interest	Other
8 0			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 22 33 34 35 36 37 38 23	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. Protected by	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.
39 40 41 42							copyright.			

		36/bmjopen-20			Page 12			
No. Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	36/bmjopen-2021-049516 on 3 Incomplete outcome data	Selective reporting	Conflict of interest	Other
	High	Low	Probably Low	Low	Low X	Probably Low	Low	Low
62 Rahmatini a et al. 2021		Daily non-accidental 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).	Models adjusted for time, temperature, relative humidity, atmospheric pressure, PM2.5 data, Day of week (DOW) and public holidays.	Study included 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 death outcome data. However, any potential errors or missing data did not depended 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 of this article declare that they have no conflict of interests.	No other potential sources of bias identified.

Pag	e 121 c	21 of 133 BMJ Open								
1 2 3 4							Incomplete			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete	Selective reporting	Conflict of interest	Other
9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27	63	Liu et al. 2021b	Probably Low 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.	Probably Low 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.	Probably Low 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	Low 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	Low View No. 2007 The cohort Included 14,331 adults who completed adults who completed from http://bmjopen.bmj.com/ on April 19, 2024 by guess	There was insufficient information about selective	Low The authors declare that they have no known competing financial interests or personal relationship s that could have appeared to influence the work	Low No other potential sources of bias identified.
28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45				For peer review only	quartiles), urbanicity (urban/rural, defined by CFPS participants' home addresses).	survey of social-demograp hy in China.	. Protected by copyright.		reported in this paper.	

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1 2 3							-2021-0495			
4 5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete of outcome data	Selective	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		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	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 tr	selective	of interest.	identified.
16			retrievals of aerosol	[ICD]-10: J45.	maternal smoking	2006 and March		outcome to		
17 18			optical depth in		during pregnancy,	31st 2014 in the	http	judge for low		
19			combination with a		maternal atopy,	Province of	.//bn	risk, but		
20			chemical transport model,		gestational age and	Ontario, Canada.	l op	indirect		
21 22			and enhanced through		birth weight.	Mother-infant	en.t	evidence that		
22			statistical incorporation			pair data were	, mj.	suggests		
24			of ground- based			obtained from	Com	study was		
25			observations (including			the Better	on	free of		
26 27			BC).			Outcomes	Apr	selective		
28						Registry &		report.		
29						Network	9, 20			
30 31						(BORN) Ontario,	24 t			
32						a province wide	b Ác			
33						birth registry that	on April 19, 2024 by guest.			
34 35						captures				
35 36						perinatal health	otec			
37						information.	l ted			
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1 2 3 4							36/bm)open-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete of outcome data	Selective	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	65	Rodins et al. 2020	The study used the validated, time-dependent, three-dimensional European Air Pollution Dispersion chemistry transport model (EURAD) to estimate the exposure to EC.	Cardiovascular outcomes in the HNR Study were determined by an independent endpoint committee based on self-reports, physician and next-of-kin interviews, and medical records.	Model adjusted for age, sex, individual and neighborhood SES, BMI, nighttime traffic noise exposure and lifestyle factors: smoking, alcohol consumption, physical activity and nutritional pattern.	The study used baseline (2000–2003) and 14 years follow-up data from the German HNR Study, an ongoing population-based prospective cohort study.	There was no 22. Information on Down the rate of lost no 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 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.
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					BMJ Oper	1	36/bmjop			Page 124 o
1 2 3 4							36/bmjopen-2021-0498			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete og outcome data∝	Selective reporting	Conflict of interest	Other
8			Probably Low	Low	Probably High	Low	Low X	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	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 Do 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.
37 38 39 40 41 42							by copyright.			

Pag	e 125 d	of 133			BMJ Oper	1	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			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 R	There was	The authors	No other
11		al. 2020	using EnviMan (Opsis	plaque presence and	age, sex, air	cardiovascular	were missing	insufficient	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 $\frac{30}{6}$	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 22			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	suggests	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 g	free of	influence	
27					activity, alcohol	and 20 on CIMT,	analyses 6011.궑	selective	the work	
28					consumption,	respectively. The	1 19,	report.	reported in	
29 30					median income	number of	200		this paper.	
30 31					level in residential	participants	2024 by			
32					area, systolic blood	included in the	y gu			
33 24					pressure and being	plaque analyses	r guest.			
34 35					born outside of	were 5807 and in	Prc			
36					Sweden.	the CIMT				
37						analyses 6011.	Protected by			
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1 2 3 4							36/bmjopen-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete og outcome data⇔	Selective	Conflict of interest	Other
8			Probably High	Probably Low	Probably High	Low	Low 2	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		declare that	potential
12 13			monitoring site operated	Laboratory (Cath Lab) at	long-term trends,	treated at the	were obtained, $\frac{5}{2}$	information	they have	sources of
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 17			Environmental	within 15 miles of the		Laboratory (Cath	data. However,	outcome to	interests.	
18			Conservation	pollution monitoring		Lab) at URMC	any potential	Judge for low		
19			continuously throughout	station in Rochester were		in Rochester, NY	errors or missing data	risk, but		
20 21			the study period	included. American		for STEMI				
22			(2005–2016). There was no information about	College of Cardiology		throughout the	did not depend			
23 24			missing data.	(ACC)/American Heart Association (AHA)		study period (2005–2016).	levels.	suggests study was		
24				guidelines were used at		(2003–2010).	। <i>२</i>	free of		
26				the time of Cath Lab			on Ar			
27 28				admission to diagnose				report.		
29				STEMI.			9, 2	1 port		
30							April 19, 2024 by guest	9 9		
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1 2 3 4							36/bmjopen-2021-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete \int_{Ω}^{10} outcome data ω	Selective reporting	Conflict of interest	Other
8			Probably Low	Low	Probably Low	Low	Probably Low	Probably Low	Low	Low
9 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 13			monitoring data, and	Diseases, Ninth Revision	subcohort,	individuals in	and <u>N</u>	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 \exists	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	11011, 0 00	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		
20					education level,		information for	selective		
28					occupation status,		variables $\leq \frac{1}{20}$	report.		
29 30					and mean		5% not			
31					neighborhood		5% not specified.			
32					individual income		y gues			
33 24					in persons of		lest.			
34 35					working age by		Pro			
36					Small Areas for		Protected			
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3 4							-0495			
5 6 7	No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete of outcome data	Selective	Conflict of interest	Other
8			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 g	insufficient	declare that	potential
12 13			2010 were estimated at	diagnosis of International	status, smoking	cohorts within	106,727 Departicipants with complete	information	they have	sources of
13			the study participants'	Classification of	duration, smoking	the ELAPSE	with complete	about	no known	bias
15			baseline residential	Diseases, 9th Revision	intensity,	project with	air pollution	selective	competing	identified.
16 17			addresses, using	(ICD-9) codes 490–492,	body-mass index,	available	exposure data,		financial	
17			standardized	and 494–496, or ICD-10	marital status,	information on	the study		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	participants	indirect	relationship	
21 22			models. The LUR model		level and	diagnoses. Mean	with COPD at		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 26			European Environment				participants 9		influence	
27			Agency (EEA) AirBase				with missing		the work	
28			for PM2.5, NO2, and O3,				information on	report.	reported in	
29 30			and ESCAPE monitoring				confounders. NO		this paper.	
31			data for BC as the							
32			dependent variable. BC				by guest.			
33 34			was measured by the							
35			reflectance of PM2.5				Pro			
36			filters and expressed in				Protected			
37 38			absorbance units.							
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40							pyri			
41 42							ght.			

Page 129 of 13	33	BMJ Open											86/bmjop					
1 2 3 4 5 6 7Table S8 Ass	sessr	nent of certaint	y of t	evidence for the o	outc	omes.							36/bmjopen-2021-049516 on 3 N					
8													D Rea	asons for upgrading				Final
3 4 5 6 7Table S8 Asset 8 9 Evidence 10 11 12 13^{2} Evidence 10 11 12 13^{2} Evidence 14 12^{2} C on CVD in 15 14^{2} /EC on CVD in 16 17^{2} del 18 12^{2} C on CVD in 21 23^{2} del 24 25 26^{2} ronic effects of 24 25 26^{2} ronic effects of 24 29 30^{2} del 31 32 Abbreviations: B 33 indirectness; A3 34 35 36 37 38 39 40 41	A1	Rationale	A2	Rationale	A3	Rationale	A4	Rationale	A5	Rationale	B1	Rationale	2022 D	Rationale	B3 Rationale		Overall	certainty assessment
12 1 ⁴ 3 ^{sute} effects of 1 ¹ 4 [*] /EC on CVD in 15 1 ⁵ / _{12.5} -unadjusted 16 1 ¹⁰ / ₁ ⁴⁰ del	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	wnloadee from	Confounders would shift the RR in both directions	0	Evidence of increase in risk with increasing exposure	-1	Low
1. Reute effects of BC 20 BC/EC on CVD in 21 22 12.5-adjusted 2. Sodel	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	http://bmjopen.bmj.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 28 C/EC on CVD in 28 M _{2.5} -unadjusted 29 30 del	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	m/ on April≏19, 2024	Confounders would shift the RR in both directions	0	No evidence of a clear increasing risk with exposure	0	Moderate
32 Abbreviations: F 33 indirectness; A3 34 35 36 37 38 39 40						r diseases; RES: respirator						val; CI: confidence interva	~	= limitations in studies	(risk	of bias); A2 =		

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group and Study ID		Relative Risk (95% Cl)
Asia		
Geng,2013	+	1.012 (1.002, 1.021)
Wang,2019a	! ←	1.011 (0.999, 1.023)
Gong,2019	+	1.002 (1.001, 1.003)
Huang,2012	+	1.005 (0.998, 1.010)
Lin,2016a	+	1.002 (0.999, 1.005)
Son,2012	-	1.001 (0.981, 1.021)
Heo,2014	+	1.006 (0.994, 1.017)
Subgroup, DL (I ² = 21.5%, p = 0.266)	•	1.003 (1.001, 1.005)
Europe		
Basagana,2015	-+ <u>+</u> -	0.979 (0.944, 1.016)
Ostro,2015a		0.994 (0.953, 1.038)
Ostro,2015a	<u>.</u>	1.005 (0.979, 1.031)
Atkinson,2016	-	0.987 (0.973, 1.001)
Subgroup, DL (I ² = 0.0%, p = 0.602)	\diamond	0.990 (0.979, 1.001)
America		
lto,2011	→ +	1.003 (0.982, 1.024)
Maynard,2007	-+ <u>+</u> ++	1.076 (0.980, 1.179)
Ostro,2007	- 1 •	1.026 (1.004, 1.049)
Kim,2015 ·	i•	- 1.031 (0.935, 1.133)
Subgroup, DL (I ² = 20.8%, p = 0.285)	\diamond	1.017 (0.998, 1.037)
Heterogeneity between groups: p = 0.030	D	
I 8		1.25

Figure S1 Impact of short-term exposure to BC/EC on cardiovascular mortality stratified by

geographical locations.

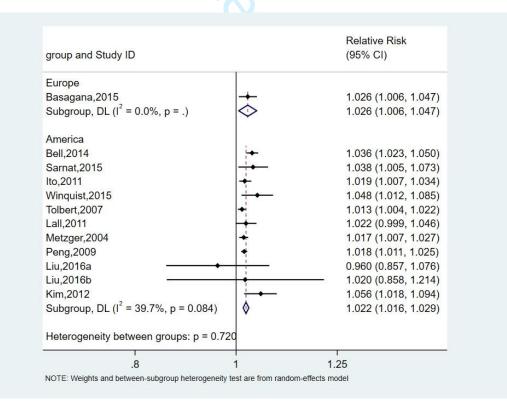


Figure S2 Impact of short-term exposure to BC/EC on cardiovascular morbidity stratified by

geographical locations.

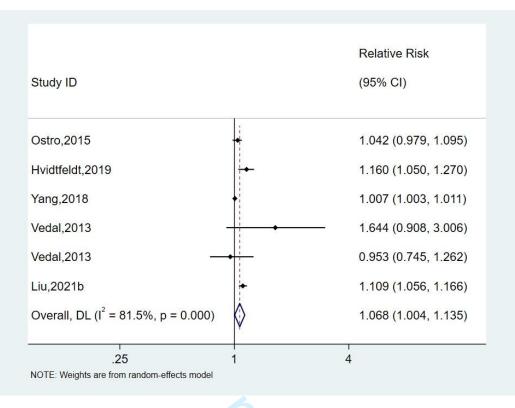


Figure S3 Impact of long-term exposure to BC/EC on cardiovascular diseases.

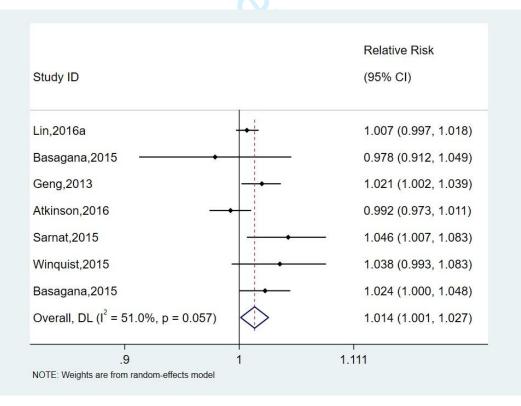


Figure S4 Impact of short-term exposure to BC/EC on cardiovascular diseases in the

 $PM_{2.5}\mbox{-}adjusted\ model.$



47

PRISMA 2020 Checklist

		BMJ Open		Page 132 of 1
			36/bmiopen	
PRIS PRIS	6MA 2	020 Checklist	oper	
			-1-20	
Section and	Item		21-1	Location
Торіс	#	Checklist item	049	where item is reported
TITLE			0 1 0	
Title	1	Identify the report as a systematic review.	on	#1
ABSTRACT			∞ ≤	
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	a <	#3-4
INTRODUCTION	1		022	
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.	Ő Š	#8
METHODS	1			
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 date when each source was last searched or consulted.	dentify studies. Specify the	#8-9
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	http	#8-9
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many rev and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in		#10
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of a 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 study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which result		#10-11
7	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, fundir assumptions made about any missing or unclear information.	o g sources). Describe any	#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 ma study and whether they worked independently, and if applicable, details of automation tools used in the process.	<u>≞.</u> ny reviewers assessed each ∽	#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	No of results.	#11
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study inter comparing against the planned groups for each synthesis (item #5)).	4	#11
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summ conversions.	ary statistics, or data	#11, 14-15
7	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	rote	#11
8	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was per model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	grmed, describe the	#11-12
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analys	≷ g, meta-regression).	#11-12
	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 biase	<u></u>	#12
Certainty	15	Describe any methods used to assess centainty (or confidence) in the body of by dence for a butcomem		#11



PRISMA 2020 Checklist

ge 133 of 133		BMJ Open 13	
PRIS	MA 2	020 Checklist	
Section and Topic	ltem #	Checklist item	Location where iten is reported
assessment			
RESULTS			
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 effed 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 optime 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 assess	#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
	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>ح</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 red iew.	#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

